UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

T2DM LADA T1DM

GADA titre

Number of islet-cell autoantibodies

HLA susceptibility

C-peptide

Age

Metabolic syndrome

Inflammation

RESEARCH YEARBOOK

2018

Summary

Foreword

Foreword

Dear Stakeholder,

this 2018 edition of the Research Yearbook provides you an overview of Research activities and organization at the Campus Bio-Medico University of Rome (UCBM). It presents our research policies and strategies, and it reports specifically about the main facts, projects, scientific and innovation outputs produced by our institution in the 2018 calendar year. In line with past editions, the contents of this 2018 Research Yearbook have been selected and developed having in mind three main goals, namely:

- **Dissemination and Promotion.** The Yearbook aims at providing to all those interested in UCBM research a comprehensive digest of the main ongoing research projects, and a simplified directory of the expertise, scientific equipment, technological facilities and services, research units and other organisational structures available in our university. We expect that all our stakeholders (e.g. students, researchers, experts and decision-makers from companies and from public and private institutions), will be able to easily retrieve from this document the basic answers to their knowledge and innovation needs, and identify the specific group(s) in our community and networks that will best fit for the purpose of effectively satisfying such needs. Extended information on our research activities can be retrieved on the research section of our official website http://www.unicampus.it/eng/research/;

- **Accountability.** This Yearbook is also intended to provide our main sponsors and external supporters a direct, basic source of information on how resources have been used, on which main outputs such resources contributed to generate and on the innovation potential of those outputs. From our perspective, it is a very important, crucial action of transparency and acknowledgement toward that part of the society which expressed trustiness in our research and innovation capabilities;

- **Self-assessment.** The facts and data briefly presented in this Yearbook are fully instrumental in providing a clearset of internal and external benchmarks to our research community, to stimulate continuous improvement of our performance and of the quality of our research work. The Yearbook also includes a brief description of the internal quality assurance policies

Overall, the 2018 research facts and figures clearly confirm that UCBM Research stands at the same level, both in qualitative and quantitative terms, of the top Italian universities: about 60% of our publications appeared on journals belonging to the first quartile (Q1) of the Scopus/Scimago international periodicals ranking; about 20% of the faculty members are now included in the so-called Top Italian Scientists community; and an overall success rate of about 16% has been reached on competitive calls.

Finally, we want to acknowledge all researchers, clinical personnel and administrative and technical staff for their continued effort to keep the high-quality standards of our activities and outputs. Special thanks to the many contributors to this Yearbook, and especially to Maria Dora Morgante, Head of the Library Services, Riccardo Adriani, Head of the Graphics and Editing Services, and to the team of the Research Administrative Area, for the hard work in the preparation of this document.

We do hope that you will enjoy this 2018 Yearbook and use it as the main reference to get in touch with those actors in our university who could best fit your expectations. We will be very happy to receive any remarks and suggestions aimed at improving its structure and contents; please address your feedback message to the mailbox of our Center for Integrated Research (CIR), that is cir@unicampus.it

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Eugenio Guglielmelli
Pro-Rector for Research

Campus Bio-Medico
University of Rome

Raffaele Calabrò
Rector (Chancellor)

Campus Bio-Medico
University of Rome

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On the Cover

On the cover

Latent Autoimmune Diabetes in Adults: A Review on Clinical Implications and Management

Latent autoimmune diabetes in adults (LADA) is a heterogeneous disease characterized by a less intensive autoimmune process and a broad clinical phenotype compared to classical type 1 diabetes mellitus (T1DM), sharing features with both type 2 diabetes mellitus (T2DM) and T1DM. Since patients affected by LADA are initially insulin independent and recognizable only by testing for islet-cell autoantibodies, it could be difficult to identify LADA in clinical setting and a high misdiagnosis rate still remains among patients with T2DM. Ideally, islet-cell autoantibodies screening should be performed in subjects with newly diagnosed T2DM, ensuring a closer monitoring of those resulted positive and avoiding treatment of hyperglycaemia which might increase the rate of ß-cells loss. Thus, since the autoimmune process in LADA seems to be slower than in classical T1DM, there is a wider window for new therapeutic interventions that may slow down ß-cell failure. This review summarizes the current understanding of LADA, by evaluating data from most recent studies, the actual gaps in diagnosis and management. Finally, we critically highlight and discuss novel findings and future perspectives on the therapeutic approach in LADA.
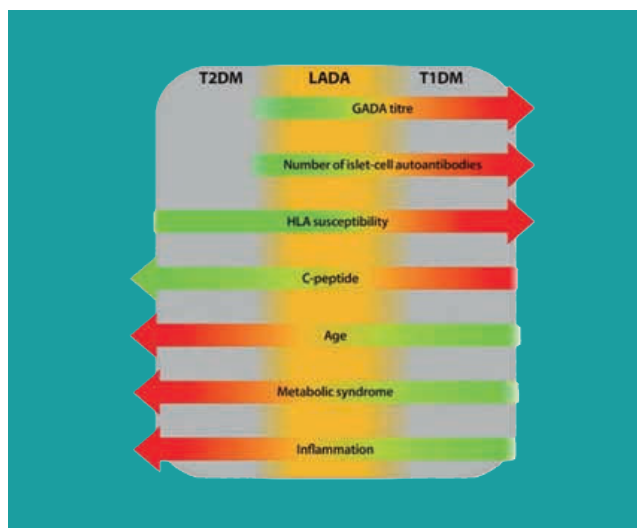
On the cover

2018 Research
Facts and Figures

2018 Research Facts and Figures

The research activities carried out in 2018 at the Campus Bio-Medico University of Rome have produced important outputs in terms of scientific publications, research projects, clinical trials and patents. More than 500 papers, 2000+ cumulative Impact Factor (I.F.), and 2200+ normalized I.F. have been published, about 60% of such publications appeared on journals belonging to the first quartile (Q1) of the Scopus/SCImago international periodicals ranking.
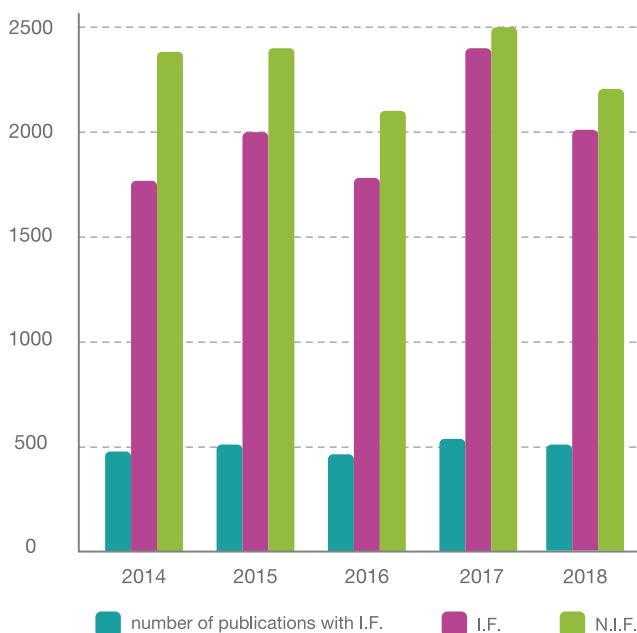
Figure 1 - *Number of publications with I.F., total I.F. and total N.I.F. in the last five years*

As shown in Figure 2 the number of publications per faculty member is about 4 and remained stable with respect to 2017; the number of faculty members increased of 42% in the last five years as shown in Figure 3.
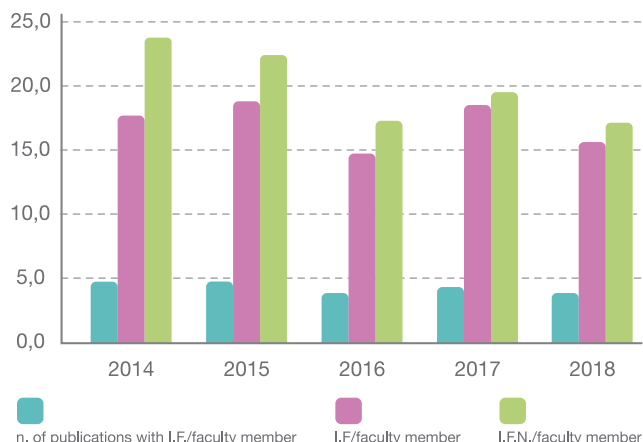
Figure 2 - *Number of publications with I.F., total I.F. and total N.I.F. per faculty member in the last five years*
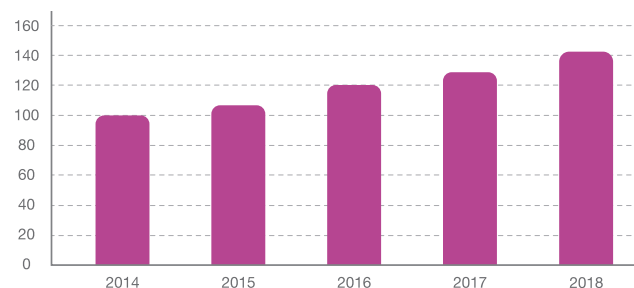
Figure 3 - *Number of faculty members in the last five years*

Figure 4 shows the overall scientific production in 2018 in terms of number of publications, Impact Factor (IF) and Normalized Impact Factor (NIF) for each of the 48 Research Units of the University.

There are several indicators, which provide objective evidence of the quality of the research carried out at the University such as, for example:
- Average of 4+ publications with Impact Factor per faculty member in 2018;
- 18% of faculty members (25 faculty members) with total Hirsch-index (h papers each of which has been cited in other papers at least h times) higher than 30 and included in the Top Italian Scientists list (www.topitalianscientists.org);
- 60% publications in the first quartile (Q1) according to SCImago ranking, which includes the top 25% journals in each subject category.

The numbered research units shown in the figure are:

1. Advanced Robotics and Human Centred Technologies
2. Allergology, Immunology, Rheumatology
3. Anesthesia, Intensive Care and Pain Management
4. Automation and Control Theory
5. Biochemistry and Molecular Biology
6. Breast Care
7. Cardiovascular Science
8. Chemical-Physics Fundamentals in Chemical Engineering
9. Clinical Laboratory Sciences
10. Computer Systems and Bioinformatics
11. Developmental Neuroscience
12. Diagnostic Imaging
13. Drug Sciences
14. Electronics for Sensor Systems
15. Endocrinology and Diabetes
16. Food Science and Nutrition
17. Gastroenterology
18. General Surgery
19. Geriatrics
20. Gynaecology and Obstetrics
21. Heart Surgery
22. Hematology, Stem Cell Transplantation, Transfusion Medicine and Cellular Therapy
23. Hygiene, Public Health and Statistics
24. Institute of Philosophy of Scientific and Technological Practice (FAST)
25. Internal Medicine and Hepatology
26. Measurements and Biomedical Instrumentation
27. Medical Statistic and Molecular Epidemiology
28. Microscopic and Ultrastructural Anatomy
29. Molecular Medicine and Biotechnology
30. Molecular Neurosciences
31. Molecular Psychiatry and Neurogenetics
32. Neurology, Neurophysiology, Neurobiology
33. Neurophysiology and Neuroengineering of Human-Technology Interaction
34. Nonlinear Physics and Mathematical Modeling
35. Nursing Science
36. Oncology
37. Ophthalmology
38. Orthopaedics and Trauma Surgery
39. Otorinolaringology
40. Pathology
41. Physical and Rehabilitation Medicine
42. Plastic Surgery and Dermatology
43. Process Engineering
44. Radiation Oncology
45. Tissue Engineering & Chemistry for Engineering
46. Urology
47. Vascular Surgery
48. Virology

N.I.F.
I.F.
number of publications with I.F.

*Figure 4* - *Number of publications, Impact Factor (I.F.) and Normalized Impact Factor (N.I.F.) per Research Unit*

In 2018, about 60 research projects, including clinical trials, were funded. The following figure illustrates the success rate on competitive calls during the period 2014-2018.


Figure 5 - Success rate on calls 2014-2018

The main funding bodies of 2018 ongoing projects were: European Commission, the National Institute for Insurance against Accidents at Work (INAIL), Italian Ministry of Education, University and Research, Italian Ministry of Health, Italian Ministry of Economic Development, Italian Space Agency, Lazio Regional Authority, Fondazione ANIA, European Foundation for the Study of Diabetes, as well as several business companies which have been supporting commissioned research and clinical trials; 65 internal clinical trials were also started.

As regards the activities related to exploitation of research results, in 2018, four applications for Italian patents, of which two co-owned with Italian organisations, were filed. A patented product, assigned by UCBM to an Italian SME in 2017, entered into the production and market phase.

As of 31st December 2018, the patent portfolio owned or co-owned by the University includes 20 families of patents (with a total of 39 patents, 26 already granted) in the field of rehabilitation engineering, microengineering, regenerative medicine, biomedical instrumentation, cancer diagnostics, food analysis, etc.

In 2018 two new startups have been accredited as spin-off of the University, joining three spin-offs born in the previous years.

More detailed information on ongoing projects is available in the section "Research projects" of this Yearbook, whereas in the section "The University Third Mission" the activities related to commissioned research, clini cal trials, University patents and University accredited spin-off companies are presented along with information about Public Engagement and other dissemination activities promoted by the University to enhance the impact on society of our research activities.

Research Quality Assurance Policies

Research Quality Assurance Policies

In accordance to relevant legislation and in conformity with the guidelines issued by the Italian National Agency for the Evaluation of the University and Research Systems (ANVUR), the Campus Bio-Medico University of Rome recognizes that quality is a fundamental value. Furthermore, it considers it its inspiring feature in the incessant effort to implement the University general mission as defined in its "Charter of the Aims". The main UCBM source of reference for the quality assurance policy has been the "2014-2016 Strategic Guidelines" document. Its motto, "More Quality, More Person", specifically identifies the strategic vision of combining the continuous improvement of all university activities with a systematic attention to the person, in teaching, research and healthcare.

The general principles guiding the quality assurance policy are:

- centrality of the person;
- special attention to the social impact and to the ethical implications of research;
- inseparable nature of teaching and research (or healthcare activities);
- efficient and effective use of resources;
- development of international cooperation activities and of research mobility programs;
- commitment to grant equal opportunities, to protect from discrimination and to remove barriers for the disabled;
- support to translational research to allow fast transfer of research results into medical practice and meaningful health outcomes;
- support to technological innovation and encouragement of socio-economic development, by promoting cooperation with local enterprises and institutions;
- support of University spin-off for the exploitation of research products.

Moreover, the University pursues systematic application of its "Charter of the Aims" and of its "Code of Ethics" to all research activities.

The Departments of Engineering and of Medicine and Surgery, supported by the Centre for Integrated Research, pursue continuous improvement of research activities paying special attention to the possible social impact of research outcomes by following these general guidelines:

- improvement of key performance indicators in terms of quality and impact of scientific production. Faculty and research staff are assessed annually using criteria and parameters recognized by the scientific community of reference, specifically by indicators defined by ANVUR for assessing quality of research (Evaluation of Research Quality - VQR);
- multidisciplinary and transdisciplinary dimension of research: implementation of measures aimed at fostering collaboration among the various Research Units (RU), especially those within different Departments. Collaborative activities within the Institute of Philosophy of Scientific and Technological Practice are specifically promoted;
- international dimension of research: implementation of activities aimed at encouraging international programs of incoming and outgoing mobility. The University also aims at increasing its ability to attract external resources through participation in competitive calls, especially at a European level and at promoting cooperation with foreign centres of excellence including "visiting professors" programs which encourage the assignment of foreign scientists at our University for extended periods of research and teaching;
- policies for young researchers: the goal is to enhance the collaboration among researchers in an integration and skill enhancement logic. Furthermore, the University wishes to help to achieve outcomes and scientific growth of young researchers through promotion of participation in internally or externally funded competitive calls.
- policies for Ph.D courses: programs to be activated are selected according to scientific areas of excellence and scientific sectors active in the Departments; the University is implementing strategies to ensure an adequate number of Ph.D scholarships provided both by University funding, and by external sources of funding, i.e. research competitive grants. Furthermore, it prefers to focus resources on its strategic research lines and anyhow on sectors that demonstrate high quality standards and scientific self-sustainability and productivity; it also promotes consolidation of Ph.D programs on topics of interest

in industrial activities by seeking external funding; it encourages the international dimension of Ph.D programs through participation in schools, conferences and visits to other universities or research centres featuring excellence in research;

- policies for the Third Mission: the University promotes initiatives to pursue its Third Mission through research, such as:
  - ▸ initiative to involve companies and other parties potentially interested in patents exploitation; measures to promote the incubation and acceleration of spin-off companies;
  - ▸ initiatives to improve diffusion and dissemination of scientific results;
  - ▸ fostering collaboration with public and private institutions, and companies, by publishing an annual report of its research activities, and by organizing a public engagement initiative, the Research Day with the aim of communicating the main research results.

The system for Quality Assurance in Research (QAR) intends to set research goals and objectives, to identify and plan what is required to achieve them, to monitor the regular course of each activity, as well as to verify the level of achievement of these objectives and propose corrective actions as appropriate.

Therefore, through the Quality Assurance in Research, the University implements its Quality Policy.

The boards and structures involved in the Quality Assurance in Research are:

- Quality Assurance Committee (Presidio di Qualità);

- Evaluation Committee (Nucleo di Valutazione);

- Academic Senate;

- Academic Research Board;

- Faculty Councils;

- Faculty Boards.

The Academic Research Board plays a key role as the QAR main body, in tight cooperation with the university Quality Assurance Committee.

Evaluation of Research Quality

(VQR 2011-2014)

Evaluation of Research Quality (VQR 2011-2014)

The VQR (Valutazione della Qualità della Ricerca, Evaluation of Research Quality) is the Italian research assessment exercise that ANVUR (the National Agency for the Evaluation of the University and Research system) regularly carries out on behalf of the Italian Ministry of Education, University and Research (MIUR). On February 21, 2017, ANVUR presented the new VQR Report, which is referred to the period January 2011-December 2014 (www.anvur.org/rapporto-2016).

With more than 130 participant organizations, almost 65,000 contributors, and 118,000 research products having been evaluated, the VQR is by far the most important and comprehensive research evaluation exercise ever attempted in Italy. For the period 2011-2014, the VQR has ranked UCBM second in the area of Biological Sciences among all Italian universities. UCBM was ranked fourth in other two areas, namely Chemical Sciences and Industrial and Information Engineering Areas, and UCBM was ranked tenth in the area of Medical Sciences.

The VQR Report also shows that, as regards the single scientific disciplinary sectors, UCBM gained the first place (out of twenty-three universities) in Orthopaedics sector and the second place (out of thirty-two universities) in Neurology sector. Moreover, UCBM has been ranked third in Computer Systems, Diagnostic Imaging and Pathology sectors, out of fity-three, thirty-seven and thirty-four universities respectively. These results are based on the very good UCBM performance as measured by the specific indicators used for this ANVUR assessment: UCBM stands well above the average performance of all other universities in terms of scientific products classified of "excellent" or "good" quality.

VQR results are presented in the table below, where also information about the separate ranking regarding only small universities is reported (i.e. dimensional range ranking) along with the percentage of UCBM scientific products classified in excellent and good classes.

Area	Overall ranking	Dimensional range ranking	% of publications in excellent and good levels
Area 03 Chemical Sciences	4° out of 56	4° out of 35	100%
Area 05 Biological Sciences	2° out of 62	2° out of 31	95,24%
Area 06 Medical Sciences	10° out of 52	8° out of 21	75,40%
Area 09 Industrial and Information Engineering	4° out of 63	4° out of 43	81,25%

Research Organization and Services

Research Organization and Services

Centre for Integrated Research

The Centre for Integrated Research (CIR) provides support to the Department of Medicine and Surgery and to the Department of Engineering for promotion, exploitation and administrative management of the research activities. It guarantees the proper management of funds for research activities, publications and scientific collaborations; it also ensures a correct execution of clinical trials according to relevant regulations, Good Clinical Practice and the Joint Commission International's standards. Amongst CIR's roles is the possibility of setting up and financing research units, groups and research programs open to the participation of scholars and researchers from national and international universities or research and cultural centres.

Academic Research Board

The Pro-Rector for Research chairs the Board, which is also composed of the Research Coordinators of the two UCBM Departments and of the Manager of Research Administrative Area. The Board ensures the necessary link between the two boards of the Departments, addressing and monitoring scientific research, and fostering their collaboration. The Board is primarily in charge of elaborating the University strategic plan for research development and of guiding the research quality assurance system (QAR).

Research Administrative Area

The Research Administrative Area promotes and fosters access to research funding sources, guarantees administrative management of research projects and of clinical trials, as well as exploitation of research results. The Research Administrative Area includes the following offices: Grant Office, Technology Transfer Office, Project Financial Management and Reporting Office. Activities of the offices are described below.

Grant Office

The Grant Office main objective is to assist researchers in finding the most appropriate funding sources, also carrying out internal scouting activities in order to promote and consolidate collaborations among different UCBM Research Units. With this aim, the Office provides researchers with the support during the whole process of presenting research projects, from identification and notification of the most suitable financing opportunities to assistance in preparation and submission under national, European Commission and international competitive calls. It also offers support and follow up of project management in close synergy with the Project Financial Management and Reporting Office.

At the same time, the Office organizes seminars, workshops and informative events on competitive calls announcements.

The Office also provides technical-scientific support to activities of the Academic Research Board.

Knowledge Transfer Office

The Knowledge Transfer Office assists UCBM researchers in finding and assessing the best strategy to protect intellectual property and exploit research results, it manages the University patent portfolio in strict synergy with inventors, and promotes research results to SME and large companies with the aim to exploit research activities through licensing of patents and implementation of joint research projects.

Furthermore, the Office supports the promotion of joint laboratories with industries and spin-off research processes as well as incubation of spin-off companies. Finally, it organizes seminars and workshops on technology transfer issues.

Project Financial Management and Reporting Office

The Project Financial Management and Reporting Office assists the Research Units in the daily administrative management of the research projects.

It guarantees the proper post-award management of all grants, research contracts and clinical trials, analytical accounting management of research projects, expense analysis and monitoring. It also takes care of the projects periodic financial reports according to national and international regulations.

Furthermore, it assists Research Units in the accounting administrative auditing of projects carried out by external auditing companies.

The office manages also the Unique Code Project a distinctive code for the identification of the project

(Law 3/2003 art.11; Law 136/2010).

Finally, it also interacts with other administrative areas, such as Purchasing, Economics-Finance, Personnel Areas and Management Secretary's Offices for an optimized administrative management of the research activities.

Clinical Innovation Office

The Clinical Innovation Office (CIO) promotes the quality system of the University's clinical research. This is an essential condition to make our University more and more competitive in the field of clinical research and, therefore, able to attract the main industrial players of pharmaceutical and biomedical sectors.

Objectives of the CIO are the improvement of the clinical trials' management conducted at Campus Bio-Medico of Rome according to Good Clinical Practices and the promotion of clinical research.

The CIO supports the investigators and sponsors providing a centralized point of contact for study budgets, contracts, regulatory affairs. The office is in charge of the preliminary feasibility analysis of the clinical studies, which is carried out in collaboration with the departments involved in the process of clinical trial authorization (University Hospital Board, Pharmacy, Clinical and Nursing Management, Research Administrative Area).

The CIO follows all the administrative and management steps of the study including the finalization of the formal contracts and agreements with the sponsoring partners. It also provides scientific and technical advice and offers support to the investigator during the start-up phase of the study, if required. During the execution of the clinical trials, the office carries out a regular reporting activity.

The office is also in charge of ensuring the full compliance with the quality standards established by the Joint Commission International (JCI) accreditation, including Principal Investigators training and updating on the best clinical research practices.

Core Facilities

In order to support the research programs of the various Faculties, the Campus Bio-Medico University offers facilities including work areas and the latest generation tools. The facilities can be used by staff for their own research as well as research to be conducted in collaboration with other Institutions. Collaborators, in fact, are often invited to visit the University to work together on innovative projects with high scientific impact.

Work area provided:
- Cytometry
- Cell Imaging
- Cell culture room
- Molecular Biology
- Radioisotope Facility
- Clean Room
- Engineering Department Facilities
- Department of Medicine and Surgery Facilities

Cytometry

The newly organized cytometry facility was created to support existing research lines at our University, to create new collaborations with other Institutes, and to promote flow cytometric methods in new areas of biomedical research and Engineering.

The Facility is equipped with cutting-edge tools and personnel available to collaborate with researchers in the design of the experimental panels, in the selection of the most suitable reagents and in the use of the instrumentation.

The area is equipped with:
- CytoFlex (BeckmanCoulter)

The Flow Cytomer Cytoflex is based on photodiode

technology, it includes five channels of the 488 nm (Blue) laser, three of the 638 nm (Red) laser and two channels of the 405 nm (Violet) laser.

Optical Configuration:

Laser Blue 488nm	Laser Red 638nm	Laser Violet 405 nm
488\8SSC	660\20	450\45
525\40	712\25	525\40
585\42	780\60	
610\20		
690\50		
780\40		

MoFlo Astrios EQ (Beckman Coulter)

Our MoFloAstriosEQ is a cell sorter equipped with 2 lasers: 488 nm (Blue) and 640 nm (Red)

Technical features:
- jet-in-air system:;
- temperature regulation for sampling and collection tubes;
- high-speed cell sorting (up to 70.000 cells/sec);
- nozzles available : 70μm, 100μm
- X-Y-Z stage for microplates, tubes (up to 6 populations can be separated at the same time) and slides.
- Sorting mode:
- purity;
- single cell (CLONING);
- enrichment.

CELL IMAGING

Fluorescent Microscope NIKON ECLIPSE Ti
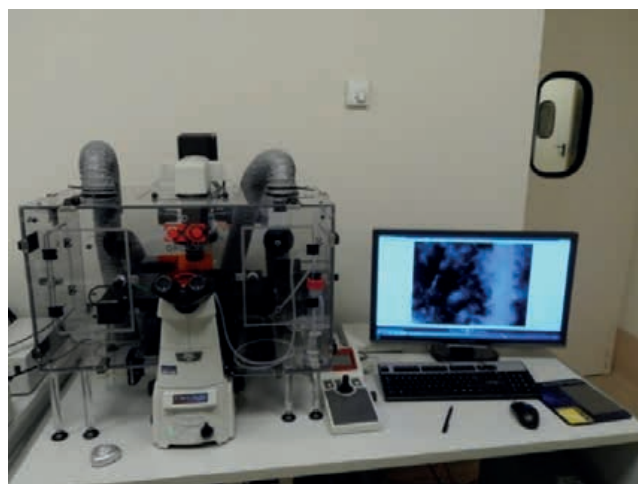
The **Nikon Eclipse Ti** is a fluorescence microscope with a Nikon camera. It is equipped with a motorized system with high stability and solidity particularly suitable for micromanipulation and imaging applications. It can be used for different types of observation methods: light and dark field and phase contrast. It is also equipped with the **Okolab System**, that consist in a cage incubator for the inverted microscope complete of humidification system with external scrubber, CO_2 control unit and temperature sensor (from 3 °C to 50 °C) for the study of cell culture. Thus allowing time-lapse acquisition on biologic samples.

Confocal Microscope NIKON ECLIPSE Ti2

The **Nikon A1+R Confocal Microscope** is equipped with a **4-channel detector** unit with high-sensitivity Gasp PMTs, allowing the acquisition of bright signals with minimal background noise, and a **spectral detector** for the simultaneous acquisition of 32-channel spectral images. Beside conventional galvano scanning mode, the microscope also features a **resonant scanner** for high speed scanning with minimal phototoxicity and photobleaching, ideal for live sample acquisition. The system is equipped with a **cage incubator** for prolonged observations of living cells.

TEM (Transmission Electron Microscope) Tecnai G2 Spirit –FEI Company

The FEI Tecnai Spirit 12G model can reach over 600,000 magnifications with high-contrast and high-resolution imaging, allowing it to work not only on cells but also on nano materials.

Critical point drying (CPD, Emitech K850)
This system allows preparing cell sample for SEM observation replacing intracellular water with alcohol, alcohol phase with liquid CO_2 first and then gaseous CO_2.

CELL CULTURE ROOM

This Facility is available to all researchers who need to prepare their animal or human cell culture on site. This roomis equipped with:
- laminar flow hoods,
- CO_2 incubators for cell culture,
- thermostatic bath,
- inverted microscope.

MOLECULAR BIOLOGY

7900HT Fast Real –Time PCR System Applied Biosystem

The Fast Real-Time PCR System makes it possible to carry out Real-Time Quantitative polymerase chain

reaction. It can analyze 96 and 384 well plates and is compatible with the TaqMan system array also gives the possibility to work in Fast Real -Time PCR mode. The tool allows performing gene expression analysis (relative and absolute quantification) genotyping (mutation analysis) and methylation analysis.

Plate reader Tecan Infinite M200 PRO

Tecan Infinite 200Pro is a multimode plate reader equipped with monochromator optics, which allows the operator to select any wavelength, from UV to NIR, for absorbance, chemiluminescence and fluorescence readings on plates from 6 to 384 wells and on cuvettes. It is provided of two channels Te-Inject module that allows adding volumes of reagents starting from 1 µl to 100 µl.

This tool allows you to do:
- quantification of proteins and nucleic acids in a sample volumes as little as 2 µl;
- enzymatic and immunochemical assays;
- ELISA tests;
- assays of gene expression

RADIOISOTOPE FACILITY

The Radioisotope facility is equipped with a fume hood and a biosafety cabinet to operate with beta-emitting radionuclides (3H, 14C). The laboratory is also equipped with basic equipment for cell biology and with an automated scintillation counter (Tricarb, Perkin Elmer).

CLEAN ROOM

Our Clean Room is Class 1000 facility and it is de-

signed to emit minimal levels of air contaminates and airborne particulates. It is used for controlled manufacturing process in a clean production environment. Our Clean Room is equipped with pure water, vacuum, clean compressed air, pure gas such as oxygen, nitrogen and argon.

Furthermore it is provided of:

- Chemical Hood;
- Plasma Cleaner (FEMTO, Diener Electronic);
- Spin coating system (Model P6700);
- Mask aligner (SUSS MicroTec);
- Sputter coater (Bal-Tec SCD500);
- Heating plates.

ENGINEERING DEPARTMENT FACILITIES

Our Engineering Department has tools that can be used for a wide range of research carried out by various laboratories:

- Freeze dryer Lio-5P (-55°C) (image);
- Oscilloscope;
- Voltage generator;
- Uniaxial testing machine (Instron 3365) (image);
- Computer Software license agreement (COM-SOL and Maple).

DEPARTMENT OF MEDICINE AND SURGERY FACILITIES

Set Up for electrophysiological recordings

The electrophysiology setup fully equipped with upright microscope, camera, micromanipulators, recording amplifier, computer and acquisition software, is dedicated to performing field- and patch-clamp recordings from living neurons in brain slices or from cells in culture. The laboratory is also equipped with an electrode puller and a Vibratome for brain-slicing.

The Library

The Library mission is to provide comprehensive resources and services in support of the research, teaching, and learning needs. To fulfil this mission, the Library is committed to acquire, deliver and integrate information to support excellence in research, in education, and in patient care. The focus is to build broad print and e-resources collections, including access to specific databases and striving to make electronic content easily accessible to all users.

The concrete support given to research activities, with reference to the scientific productivity, deals with the use of research evaluation metrics and its application to the analysis of research systems.

Specifically it assists single users, departments or research units in the recovery of bibliometric indicators, such as the Impact Factor and the normalized Impact Factor, as well as the citation index data from Web of Science and Scopus.

Document supply service

The Library operates an advanced system for handling users' requests of documentation. The service allows registered users to request items, which are not available in the University Library.

The service is accessible on campus, upon registration through the online form available on the Library website.

Doctoral dissertations theses repository

The Library offers a storage and consultation service of doctoral dissertations repository. Full text doctoral dissertations theses are stored in the open access repository ILITHIA. The repository is indexed in Open-DOAR, an authoritative worldwide directory of academic open access repositories.

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Ethics Committee

Ethics Committee

The Ethics Committee is an independent body whose tasks involve assessment, approval and monitoring of clinical trials, researcher training and consultancy services. The Ethics committee is composed of experts from the various fields of biomedical research, health care and safeguarding patients' rights. It protects and promotes respect for human life, from the moment of conception to natural death by taking inspiration from the Charters of Human Rights, recommendation from international bodies, medical deontology and, in particular, the Helsinki Declaration and Good Clinical Practice guidelines. The Ethics Committee meets once a month for the evaluation of the studies.

Technical–scientific secretariat of the Ethics Committee

The Technical-scientific secretariat of the Ethics Committee prepares all the needed documentation for Ethics Committee's assessment and assists the subsequent authorization steps, in accordance with the current regulation on the execution of clinical trials (Legislative Decree 211 / 2003 and ss) and the UCBM Ethics Committee Regulation. The office, within the scope of its responsibilities, also takes care of relationships with the Regulatory Authorities (Ministry of Health, Istituto Superiore Sanità, AIFA, EMA, FDA).

Technical–scientific secretariat of the Ethics Committee

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Raffaele Antonelli Incalzi, *Deputy Chair*
Daniele Santini, *Clinician*
Angelo Insola, *Clinician*
Giuseppe Perrone, *Clinician*
Stefano De Lillo, *Territorial General Practitioner*
Bruno Nobili, *Pediatrician*
Maurizio Genuardi, *Genetist*
Anita Paoletto, *Representative of Voluntary Associations*
Massimo Ciccozzi, *Biostatistician*
Pierantonio Menna, *Pharmacologist*
Gianna Carrillo, *Pharmacist*
Domenica Ioele, *Pharmacist*
Alessandra Mecozzi, *Pharmacist*

Andrea Di Mattia, *Expert in Medical Devices*
Lorenzo Sommella, *Health Director*
Patrizio Rossi, *Expert in Legal and Insurance Matters*
Vittoradolfo Tambone, *Bioethicist*
Raffaella Gualandi, *Representative of Health Professions*
Sara Emerenziani, *Nutrition Expert*
Velio Macellari, *Clinical Engineer*
Bruno Beomonte Zobel, *Clinical Expert on New Diagnostic and Therapeutic Procedures*
Francesco Grigioni, *Clinician*
Dario Tuccinardi, *Clinician*
Giuseppe Umile Longo, *Clinician*
Pietro Ferrara, *Clinician*

Research Units
overview and main 2018 scientific outputs

Advanced Robotics and Human Centred Technologies

Head L. Zollo (E. Guglielmelli until 30th September)

Faculty F. Cordella, F. Taffoni

Other Personnel G. Carpino, A. L. Ciancio, A. Dellacasa Bellingegni, A. Demofonti, C. Gentile, E. Gruppioni, C. Lauretti, F. Leone, F. Mereu, E. Noce, I. Portaccio, R. A. Romeo, M. Rossini, F. Salvadori, F. Scotto Di Luzio, D. Simonetti, M. Stefano, C. Tamantini, S. Valentini

Description

Advanced Robotics and Human Centred Technologies investigates the application of mechatronic and robotic technologies to medicine and biology, by proposing innovative solutions for diagnosis, healthcare and improvement of patient quality of life. The Advanced Robotics and Human Centred Technologies Lab strongly benefits from the tight link with the Department of Medicine and Surgery and the University Hospital for developing and experimentally validating innovative robotic and mechatronic technologies based on a human-centered design approach. Main research areas are:

- **Rehabilitation and assistive technologies:** upper-limb and lower-limb therapy robots, motor and functional assessment, behavioral analysis, technical aids for independent living and work reintegration, assistive robots, upper limb prostheses, man-machine interfaces;
- **Surgical Robotics:** mechatronic tools for urological applications, haptic interfaces and biofeedback, master-slave robotic systems, teleoperated control;
- **Biomicrosystems:** miniaturized sensors, invasive neural micro-interfaces, microfluidic platforms;
- **Neuroengineering and Neurodevelopmental Engineering:** design and development of mechatronic components and systems to study and modelling motor behavior in adults (healthy and suffering from neurological disorders) and motor development in childhood.

Main research activities

Main research projects:
- AIDE – Adaptive Multimodal Interfaces to Assist Disabled People in Daily Activities – H2020, Call ICT–22-2014: Multimodal and Natural computer interaction, 2016-2018.
- PPRAS 1/3 – Control of hand prosthesis by invasive neural interfaces – funded by the National Institute for Insurance against Accidents at Work-2017-2020
- BRiC/RehabRobo@Work – Bio-cooperative robotic system for upper-limb rehabilitation in working contests – funded by the National Institute for Insurance against Accidents at Work- 2017-2019
- PCR 1/2 – New procedures to treat limb amputation for bionic prostheses – funded by National Institute for Insurance against Accidents at Work, 2017-2020
- SIRASI – Robotic system for upper- and lower-limb rehabilitation – funded by Regione Lazio - Bando INTESE, 2018-2019
- "Upper-limb bionic prostheses with personalized closed-loop interfaces for patients with macrolesions due to car accidents", funded by National Association of Insurance Agencies (ANIA), 2018-2020
- PON/ARONA – Surgery Navigation assisted by Advanced Robotics – funded by Italian Ministry of Education, Universities and Research, 2018-2021
- Experimental Assessment of feeding skills in newborns: effect of different feeding teats, research project supported by Artsana S.p.A

Main collaborations

- INAIL Prosthetic Centre, Italy
- INAIL, Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Italy
- Institute of Cognitive Sciences and Technologies, National Research Council (CNR), Italy
- Fraunhofer IBMT, St. Ingbert, Germany
- Fetal Neonatal Neuroimaging and Developmental Science Center. Boston Children Hospital, USA
- University College London, UK
- Applied Neurotechnology Laboratory, Department of Psychiatry and Psychotherapy, University Hospital of Tübingen, Tübingen, Germany
- Perelman School of Medicine, University of Pennsylvania, USA
- Universidad Miguel Hernandez de Elche, Spain
- Sant'Anna School of Advanced Studies, Italy
- Cagliari University, Italy
- Politecnico di Milano, Italy
- MASMEC SpA, Italy
- Pal Robotics, Spain

Most important publications

Tamilia E., Park E.H., Percivati S., Bolton J., Taffoni F., Peters J.M., Grant P.E., Pearl P.L., Madsen J.R., Papadelis C.

Surgical resection of ripple onset predicts outcome in pediatric epilepsy.

Ann Neurol. 2018 Sep; 84(3):331-346. PubMed PMID: 30022519. IF 10,25

In patients with medically refractory epilepsy (MRE), interictal ripples (80–250Hz) are observed in large brain areas whose resection may be unnecessary for seizure freedom. This limits their utility as epilepsy biomarkers for surgery. We assessed the spatiotemporal propagation of interictal ripples on intracranial electroencephalography (iEEG) in children with MRE, compared it with the propagation of spikes, identified ripples that initiated propagation (onset-ripples), and evaluated their clinical value as epilepsy biomarkers.

Crea S., Nann M., Trigili E., Cordella F., Baldoni A., Badesa F.J., Catalán J.M., Zollo L., Vitiello N., Aracil N.G., Soekadar S.R.

Feasibility and safety of shared EEG/EOG and vision-guided autonomous whole-arm exoskeleton control to perform activities of daily living.

Sci Rep. 2018 Jul 17; 8(1):10823. PubMed PMID: 30018334. IF 4,122

Arm and finger paralysis, e.g. due to brain stem stroke, often results in the inability to perform activities of daily living (ADLs) such as eating and drinking. Recently, it was shown that a hybrid electroencephalography/electrooculography (EEG/EOG) brain/neural hand exoskeleton can restore hand function to quadriplegics, but it was unknown whether such control paradigm can be also used for fluent, reliable and safe operation of a semi-autonomous whole-arm exoskeleton restoring ADLs.

To test this, seven abled-bodied participants (seven right-handed males, mean age 30 ± 8 years) were instructed to use an EEG/EOG-controlled whole-arm exoskeleton attached to their right arm to perform a drinking task comprising multiple sub-tasks (reaching, grasping, drinking, moving back and releasing a cup). Fluent and reliable control was defined as average 'time to initialize' (TTI) execution of each sub-task below 3 s with successful initializations of at least 75% of sub-tasks within 5 s. During use of the system, no undesired side effects were reported. All participants were able to fluently and reliably control the vision-guided autonomous whole-arm exoskeleton (average TTI 2.12 ± 0.78 s across modalities with 75% successful initializations reached at 1.9 s for EOG and 4.1 s for EEG control) paving the way for restoring ADLs in severe arm and hand paralysis.

Scotto di Luzio F., Simonetti D., Cordella F., Miccinilli S., Sterzi S., Draicchio F., Zollo L.

Bio-cooperative approach for the human-in-the-loop control of an end-effector rehabilitation robot.

Front Neurorobot. 2018 Oct 11;12:67. PubMed PMID: 30364325. IF 3,508

The design of patient-tailored rehabilitative protocols represents one of the crucial factors that influence motor recovery mechanisms, such as neuroplasticity. This approach, including the patient in the control loop and characterized by a control strategy adaptable to the user's requirements, is expected to significantly improve functional recovery in robot-aided rehabilitation. In this paper, a novel 3D bio-cooperative robotic platform is developed. A new arm-weight support system is included into an operational robotic platform for 3D upper limb robot-aided rehabilitation. The robotic platform is capable of adapting therapy characteristics to specific patient needs, thanks to biomechanical and physiological measurements, and thus closing the subject in the control loop. The level of arm-weight support and the level of the assistance provided by the end-effector robot are varied on the basis of muscular fatigue and biomechanical indicators. An assistance-as-needed approach is applied to provide the appropriate amount of assistance. The proposed platform has been experimentally validated on 10 healthy subjects; they performed 3D point-to-point tasks in two different conditions, i.e., with and without assistance-as-needed. The results have demonstrated the capability of the proposed system to properly adapt to real needs of the patients. Moreover, the provided assistance was shown to reduce the muscular fatigue without negatively influencing motion execution.

Allergology, Immunology, Rheumatology

Head A. Afeltra

Faculty D.P.E. Margiotta

Other Personnel L. Arcarese, M. Lo Vullo, L. Navarini, A. Rigon, M. Vadacca

Description

The unit's research interests concern epidemiology, pathogenesis, diagnosis and therapy of the systemic autoimmune diseases. The most important research topics are Systemic Lupus Erythematosus, Rheumatoid Arthritis and Spondyloarthritis (Psoriatic Arthritis and Axial Spondyloarthritis). The unit's research methodology is based on the integration of clinical tools, diagnostic imaging (muscoloskeletal ultrasonography and capillaroscopy) and laboratory methods (immunofluorescence, enzyme immunoassay, immunoblot).

Main research activities

- Quality of life in systemic lupus erythematosus (SLE) and systemic sclerosis (SS) (collaboration: Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples): extensive evaluation of fatigue, work disability and physical activity
- Cardiovascular disease in rheumatic diseases (collaboration: Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples; Rheumatology Unit, University Federico II of Naples): relationship between remission and cardiovascular disease in SLE; performance of cardiovascular risk algorithms in psoriatic arthritis
- Angiogenic and angiostatic factors in SS (collaboration: Scleroderma Unit, Sapienza University of Rome): relationship between VEGF/endostatin and parasympathetic activity, erectile dysfunction, microvascular damage and digital ulcers
- Lipid mediators in systemic autoimmune diseases (in collaboration with Biochemistry and Molecular Biology Unit, Università Campus Bio-Medico di Roma): endocannabinoid system and resolving D1 in SLE.

Main collaborations

- Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples
- Scleroderma Unit, La Sapienza University of Rome

Most important publications

Navarini L., Margiotta D.P.E, Vadacca M., Afeltra A.

Leptin in autoimmune mechanisms of systemic rheumatic diseases.
Cancer Lett. 2018 Jun 1;423: 139-146. PubMed PMID: 29548819. IF 6,491

In the last two decades, white adipose tissue (WAT) has been recognized as a key actor of many physiological and pathological conditions. WAT is able to produce mediators, named "adipokines", which may affect systemic homeostasis. In particular, leptin is not only involved in appetite and energy metabolism, but also in immune system. Increasing evidence established that leptin can regulate both innate and adaptive immunity mainly with pro-inflammatory effects but also, to a lesser extent, with anti-inflammatory features. In autoimmune diseases, a failure or breakdown of the mechanisms of self-tolerance is observed. Leptin, which plays an important role in the control of immune balance, has been involved in autoimmunity generation and maintenance. In this review, it has been provided

an up-to-date report about the role of leptin in systemic autoimmune diseases, with particular reference to connective tissue diseases, inflammatory arthritis, and vasculitis.

Margiotta D.P.E., Basta F., Dolcini G., Batani V., Lo Vullo M., Vernuccio A., Navarini L., Afeltra A.

Physical activity and sedentary behavior in patients with Systemic Lupus Erythematosus.
PLoS One. 2018 Mar 5;13(3):e0193728. PubMed PMID: 29505598. IF 2,766

Introduction: The aim of this study was to evaluate the proportion of patients with Systemic Lupus Erythematosus (SLE) who did not met the WHO recommendations for physical activity and to evaluate the amount of time spent in sedentary behavior.

Methods: SLE patients were consecutively enrolled in a cross sectional study. The type and the time spent in physical activity and sedentary behavior were evaluated using the IPAQ short form questionnaire. The adequate physical activity was defined according to the 2010 WHO recommendations for health and the sedentary behavior according to the 2017 SBRN consensus. We also assessed quality of life using SF-36, mood disorders using BDI and HAM-H, fatigue using Facit-Fatigue and sleep disorders using PSQI scores. RESULTS: Physical activity was not sufficient to meet WHO recommendations in 56 of 93 SLE patients (60%). SLE patients spent a median (95% range) of 180 (0-600) minutes everyday in sedentary activities. The length of daily sedentary time was more than 6 hours in 25% of SLE patients. In multivariable analysis, the factors associated to the probability of not meeting WHO criteria was only the time of exposure to antimalarials (OR 0.88, p 0.03) and the factors related to the probability of being in the upper tertile of sedentary time (more than 270 minutes) were age (OR 1.04, p 0.02), disease activity expressed by SELENA-SLEDAI score (OR 1.2, p 0.01) and Facit-fatigue score (OR 0.94, p 0.04).

Conclusion: A relevant proportion of SLE patients were inadequately physically active. It is essential to improve the awareness of the importance of increase physical activity and reduce sedentary time. A better control of disease activity and fatigue and a prolonged use of antimalarials could help to reach this notable goal.

Navarini L., Bisogno T., Mozetic P., Piscitelli F., Margiotta D.P.E., Basta F., Afeltra A, Maccarrone M.

Endocannabinoid system in systemic lupus erythematosus: first evidence for a deranged 2-arachidonoylglycerol metabolism.
Int J Biochem Cell Biol. 2018 Jun; 99:161-168. PubMed PMID: 29655919. IF 3,247

The endocannabinoid (eCB) system plays a key role in many physiological and pathological conditions and its dysregulation has been described in several rheumatological and autoimmune diseases. Yet, its possible alteration in systemic lupus erythematosus (SLE) has never been investigated. Here, we aimed filling this gap in plasma and peripheral blood mononuclear cells (PBMCs) of patients with SLE and age- and sex- matched healthy subjects (HS). Liquid chromatography-mass spectrometry quantitation of eCB levels highlighted that plasma levels of 2-arachidonoylglycerol (2-AG) were significantly increased in SLE patients compared to HS (p = 0.0059), and among SLE patients, highest 2-AG levels were associated with a lower disease activity. No differences were found in N-arachidonoylethanolamine (AEA) and its congeners N-palmitoylethanolamine (PEA) and N-oleoylethanolamine (OEA) concentrations between the two groups. Moreover, gene expression analysis of metabolic enzymes and receptor targets of eCBs and investigation of functional activity and protein expression of selected components of eCB system disclosed a deranged 2-AG metabolism in patients with SLE. Indeed, expression and functional activity of 2-AG biosynthetic enzyme DAGL were selectively enhanced in PBMCs of SLE patients compared to HS. In conclusion, our results demonstrate, for the first time, an alteration of eCB system in SLE patients. They represents the first step toward the understanding of the role of eCB system in SLE that likely suggest DAGL and 2-AG as potential biomarkers of SLE in easily accessible blood samples. Our data provides proof-of-concept to the development of cannabis-based medicine as immune-modulating agents.

Anesthesia, Intensive Care and Pain Management

Head F.E. Agrò

Faculty M. Carassiti, R. Cataldo

Description

The AIC&PM Research Unit works in different areas of research and applications concerning:

- Airway management:
  - ▸ Difficult airway management in Anesthesia and Intensive Care;
  - ▸ Tracheal intubation: advanced techniques;
  - ▸ Research on extraglottic devices and oxygenation rescue techniques;
  - ▸ Forces and pressures during direct and video laryngoscopy.
- Mechanical ventilation in Operating Theatre and ICU;
- Pain therapy;
- Loco-Regional Anesthesia and Ultra Sounds;
- Good Clinical Pathways for Obese Patients;
- Obstructive Sleep Apnea and Anesthesia.

Main research activities

The AIC&PM Research Unit focuses its activities on:

- Anesthesia
  - ▸ Ultra Sounds and Loco-Regional anesthesia: techniques and risks;
  - ▸ Airway management in Emergency and Elective scenarios;
  - ▸ Guidelines for Difficult Airway management;
  - ▸ Airway management devices and innovations;
  - ▸ Cardiac anesthesia and drugs;
  - ▸ Obesity and perioperative safety;
  - ▸ Obstructive Sleep Apnea and Anesthesia;
  - ▸ Good Clinical Practice in Anesthesia;
  - ▸ Pain management in perioperative medicine and serratus blocks;
  - ▸ Multimodal care in pancreatic Surgery;
  - ▸ "in vitro" airway management strategies simulation to improve patients safety;
  - ▸ Cardiac surgery and controlled trial of volatile anesthetics.
- Intensive therapy
  - ▸ Cardiac output: monitoring innovations in mechanically ventilated patients;
  - ▸ Advanced pain control strategies in ICU;
  - ▸ Ecocardiography in post cardio-surgical patients in ICU.
- Pain Therapy
  - ▸ Pain Management and epidural space detection in vitro and in vivo- FBSS (Patents development);
  - ▸ Post Herpetic pain and neurobiological modifications;
  - ▸ Head of Clinical Integrated Life Project 2020 Heremos prot A0112-2016-13311 Financial Research 2018-2019.

Most important publications

Del Buono R., Costa F., Pascarella G., Basso V., Doyle J.D., Agrò F.E.

The trapezius plane block: a technique for regional anaesthesia of the superficial posterior thorax.
Eur J Anaesthesiol. 2018 May; 35(5):401-402. PubMed PMID: 29601420. IF 3,979

Surgery of the trunk can sometimes be challenging for the anaesthesiologist. In recent years, ultrasound blocks have been developed for trunk structures We would like to report our experience in performing an ultrasound guided fascial plane block targeting the dorsal rami of the spinal nerves, as they pass through the posterior muscles of the thorax and innervate the skin and subcutaneous tissue The case series shows a field block that provides a selective analgesia on the area innervated by the dorsal rami of spinal nerves. The TPB provides a wider area of analgesia if compared with local anaesthesia alone and can be used for small surgeries performed on the posterior haemithorax.

Menna P., Salvatorelli E., Mattei A., Cappiello D., Minotti G., Carassiti M.

Modified colistin regimen for critically ill patients with acute renal impairmentand continuous renal replacement therapy.
Chemotherapy. 2018; 63(1):35-38.PubMed PMID: 29334366. IF 2

Colistin is a last resort antibiotic to treat multidrug-resistant Gram-negative bacteria infections. Colistin is administered intravenously in the form of its inactive prodrug colistin methanesulfonate (CMS). For patients with acute kidney impairment and continuous renal replacement therapy high extracorporeal clearance may cause a substantial removal of active colistin from the bloodstream, eventually decreasing its antibacterial efficacy. Currently recommended doses of CMS may therefore be inadequate for these patients. We report on the potential value of a modified regimen that adopts a loading dose of CMS (bolus of 9 MU vs. conventional 3 MU every 8 h), followed by maintenance (3 MU every 8 h). Preliminary pharmacokinetic evidence for the feasibility and efficacy of this regimen is described for 2 patients.

Sorbello M., Falcetta S., Di Giacinto I., Cataldo R.
Neuromuscular blocking agents and intubation.
Anaesthesia. 2018 Nov;73(11):1440. PubMed PMID: 30298584. IF 5,431

We describe some concerns regarding intubating conditions during, and postoperative morbidity after, McGrath videolaryngoscopy with or without non-depolarising neuromuscular blockade.

Automation and Control Theory

Head R. Setola

Faculty G. Oliva, M. Papi, F. Smarrazzo

Other Personnel G. Assenza, L. Faramondi, M. Menci, S. Ott

Description

The Unit of Automation is marked by an innovative approach that combines theoretical research activities with practical technology solutions in a wide range of domains, such as automation technologies, industrial automation, control and robotics, biomedical engineering, computer science and, primarily, Critical Infrastructures.

The activities of the Unit are focused on the development of innovative and strongly multi-disciplinary methodologies, tools and technologies. Among others, the Unit provides both theoretical and applicative contributions in the fields of cyber-physical systems, optimization, sparse and distributed algorithms, data fusion, localization, and modelling and simulation of complex systems.

The group is involved in 1 European research project and 6 national projects. Professor Setola is the Coordinator of 3 European projects. The Unit jointly with University Campus Bio-Medico of Rome created in 2009 a Post Graduate Program (PGP) in Homeland Security that aims at training security experts able to cope with the actual socio-technological threats of modern infrastructures.

Main research activities

The unit has contributed to several projects and collaborations:

- SMARTBENCH: development of an innovative platform integrating mobile technology, web and IOT solutions, improving the safety and security of workers in dangerous zones.
- HANSEL: providing an integrated test, training and validation environment for industrial automation, Hospital 4.0 applications, eHealth systems and for applications such as food supply chain and water management.
- RAFAEL: System for Risk Analysis and Forecast for Critical Infrastructure in the ApenninEs dorsaL Regions: optimizing and integrating methodologies and technologies in the field of Critical Infrastructure Protection into a Decision System (DSS) labeled CIPCast.
- BLOCKCHAIN: identifying the motivations, advantages and interests of introducing the blockchain system within a food supply chain.
- SPS: Smart Patient's Security: improving the safety of the patients contributing to reduce the clinical risk with an electronic wristband that creates a patient's BAN (Body Area Network) that can interface with enabled devices.

Most important publications

Faramondi L., Setola R., Oliva G.

Performance and robustness of discrete and finite time average consensus algorithms.
Int J Syst Sci. 2018; 49(12): 2704-2724. DOI 10.1080/00207721.2018.1510059 IF 2,185

In this paper, we review some of the main discrete and finite time average consensus implementations in the literature, discussing their strengths and shortcomings from a theoretical and empirical point of view. In particular, we compare the computational characteristics of the different algorithms, their behaviour considering different underlying network topologies, their ability to withstand packet losses and their robustness to attacks where a malicious node aims to steer the result of the algorithm towards a desired value, without letting the other nodes detect the attack.

Oliva G., Setola R., Glielmo L., Hadjicostis C. N.

Distributed cycle detection and removal.
IEEE Transactions on Control of Network Systems. 2018; 5(1):194-204. DOI: 10.1109/TCNS.2016.2593264

In this paper, we provide distributed algorithms to detect and remove cycles in a directed relational graph by exploiting the underlying undirected communication graph; the relational graph models a relation among the agents, e.g., a pairwise ordering, while the communication graph captures how information can be shared among them. The proposed algorithm considerably improves transmission efficiency (the number of messages and bandwidth required) compared to the state of the art. The methodology provided in this paper finds application in several distributed control problems where the agents must be interconnected via a directed acyclic graph, such as cluster consensus, formation control or multiple leader election.

Moll S., Smarrazzo, F.

Strong solutions to a parabolic equation with linear growth with respect to the gradient variable.
J Differ Equ. 2018; 264(11): 6710-6751. DOI: 10.1016/j.jde.2018.01.050 IF 1,782

The paper deals with existence and uniqueness of strong solutions to the homogenous Neumann problem associated to a nonlinear flux-saturated parabolic equation, which can be seen as a generalization of the time-dependent minimal surface equation with Lagrangian corresponding to the non-parametric area integrand. These problems arise in several models of physical systems which describe, for instance, the motion of capillary surfaces or the motion of grain boundaries.
From the Mathematical point of view, existence and regularity in time of the solution is proved by means of a suitable pseudoparabolic relaxed approximation of the equation and a passage to the limit, an approach which seems to be new in this framework, as completely different from the use of semigroup theory.

Biochemistry and Molecular Biology

Head M. Maccarrone

Faculty V. Chiurchiù

Other Personnel M. Fava, A. Leuti, A. Piccoli, A.M. Sardanelli

Description

The Research Unit has a long and widely recognized experience in chemistry, biochemistry, molecular biology, pharmacology, immunology and epigenetics of lipid signaling, that is interrogated under different disease conditions (most notably, neurodegenerative disorders [Alzheimer's disease (AD) and Multiple Sclerosis (MS)], and defective reproductive events). In this context, up-to-date techniques are used to design new drugs and to determine the drivers of signal transduction mediated by bioactive lipids like endocannabinoids (N-arachidonoylethanolamine and 2-arachidonoylglycerol) and specialized pro-resolving mediators (i.e. resolvins and maresins), through their specific receptor targets in several primary human and animal cells (immune and brain cells), as well as in vivo. In addition, metabolism of these ω-3 and ω-6 polyunsaturated fatty acid derivatives through multiple biosynthetic and degradative routes is studied by means of radiometric assays, in order to disclose the impact of metabolic regulation on the biological activity of these compounds. The effect of bioactive food components on signaling is an additional focus of the Research Unit.

Main research activities

In collaboration with Prof. Mechoulam (Hebrew University of Jerusalem, Israel) we demonstrated for the first time that several bioactive acyl ethanolamides (palmitoyl ethanolamide, oleoyl ethanolamide and stearoyl ethanolamide) are able to reduce the activation and inflammatory responses of pathogenic CD8 and CD4 T helper cells, suggesting a role for their involvement in T-cell mediated chronic inflammatory diseases. We also demonstrated that type-1 cannabinoid receptor shows alterations in membrane localization and signalling activity in the transgenic mouse model of Alzheimer's disease at a stage of disease that precedes the typical symptoms. In addition, we unravelled the epigenetic regulation of several mood disorders, including bipolar disorder and deficit hyperactivity disorder, where we found novel mechanisms and biomarkers for such conditions.

Main collaborations

- Hebrew University of Jerusalem, Israel.

Most important publications

Chiurchiù V., Leuti A., Smoum R., Mechoulam R., Maccarrone M.

Bioactive lipids ALIAmides differentially modulate inflammatory responses of distinct subsets of primary human T lymphocytes.
FASEB J. 2018 Oct;32(10):5716-5723. PubMed PMID: 29879374. IF 5,595

Autacoid local injury antagonist amides (ALIAmides) are a family of endogenous bioactive acyl ethanolamides that include the renowned palmitoyl ethanolamide (PEA), oleoyl ethanolamide (OEA), and stearoyl ethanolamide (SEA), and that are involved in several biologic processes such as nociception, lipid metabolism, and inflammation. The role of ALIAmides in the control of inflammatory processes has recently gained much attention and prompted the use of these molecules or their analogues, and the pharmacologic manipulation of

their endogenous levels, as plausible therapeutic strategies in the treatment of several chronic inflammatory conditions. Since chronic inflammation is mainly driven by cells of adaptive immunity, particularly T lymphocytes, we aimed at investigating whether such bio-active lipids could directly modulate T-cell responses. We found that OEA, PEA, and eicosatrienoyl ethanolamide (ETEA) could directly inhibit both T-cell responses by reducing their production of TNF-α and IFN-γ from CD8 T cells and TNF-α, IFN-γ and IL-17 from CD4 T cells. Furthermore, neither SEA nor docosatrienoyl ethanolamide (DTEA) could affect cytokine production from both T cell subsets. Interestingly, unlike OEA and ETEA, PEA was also able to enhance de novo generation of forkhead box P3 (FoxP3)-expressing regulatory T cells from CD4-naive T cells. Our findings show for the first time that specific ALIAmides can directly affect different T-cell subsets, and provide proof of their anti-inflammatory role in chronic inflammation, ultimately suggesting that these bioactive lipids could offer novel tools for the management of T-cell dependent chronic inflammatory diseases.

Maccarrone M., Totaro A., Leuti A., Giacovazzo G., Scipioni L., Mango D., Coccurello R., Nisticò R., Oddi S.

Early alteration of distribution and activity of hippocampal type-1 cannabinoid receptor in Alzheimer's disease-like mice overexpressing the human mutant amyloid precursor protein.

Besides its involvement in Alzheimer's disease (AD) as precursor of the neurotoxic amyloid peptides, the pathophysiological impact of brain accumulation of amyloid precursor protein (APP) is not yet well understood. Recent studies reported that APP interacts with other membrane proteins, including G protein coupled receptors, affecting their biological functions. Here, we focused on the study of the potential impact of human mutant APP on expression, distribution and activity of type-1 cannabinoid (CB1) receptor in the hippocampus of Tg2576 mice, an AD-like mice model. By using biochemical and electrophysiological measures, we found that in a presymptomatic phase, when amyloid plaques have not yet formed and there is no sign of cognitive deficits, the over-expression of full-length APP in the hippocampus of Tg2576 mice altered membrane localization and inhibitory signalling activity of CB1 receptor, possibly by binding to the receptor and reducing its specific interaction with caveolin-1 and G proteins.

D'Addario C., Palazzo M.C, Benatti B., Grancini B., Pucci M., Di Francesco A., Camuri G., Galimberti D., Fenoglio C., Scarpini E., Altamura A.C., Maccarrone M., Dell'Osso B.

Regulation of gene transcription in bipolar disorders: role of DNA methylation in the relationship between prodynorphin and brain derived neurotrophic factor.

Bipolar Disorder (BD) is a prevalent and disabling condition, determined by gene-environment interactions, possibly mediated by epigenetic mechanisms. The present study aimed at investigating the transcriptional regulation of BD selected target genes by DNA methylation in peripheral blood mononuclear cells of patients with a DSM-5 diagnosis of type I (BD-I) and type II (BD-II) Bipolar Disorders (n=99), as well as of healthy controls (CT, n=42). Gene expression analysis revealed prodynorphin (PDYN) mRNA levels significantly reduced in subjects with BD-II but not in those with BD-I, when compared to CT. Other target genes (i.e. catechol-O-methyltransferase (COMT), glutamate decarboxylase (GAD67), serotonin transporter (SERT) mRNA levels remained unaltered. Consistently, an increase in DNA methylation at PDYN gene promoter was observed in BD-II patients vs CT. After stratifying data on the basis of pharmacotherapy, patients on mood-stabilizers (i.e., lithium and anticonvulsants) were found to have lower DNA methylation at PDYN gene promoter. A significantly positive correlation in promoter DNA methylation was observed in all subjects between PDYN and brain derived neurotrophic factor (BDNF), whose methylation status had been previously found altered in BD. Moreover, among key genes relevant for DNA methylation establishment here analysed, an up-regulation of DNA Methyl Transferases 3b (DNMT3b) and of the methyl binding protein MeCP2 (methyl CpG binding protein 2) mRNA levels was also observed again just in BD-II subjects. A clear selective role of DNA methylation involvement in BD-II is shown here, further supporting a role for BDNF and its possible interaction with PDYN. These data might be relevant in the pathophysiology of BD, both in relation to BDNF and for the improvement of available treatments and development of novel ones that modulate epigenetic signatures.

Breast Care

Head V. Altomare

Other Personnel A. Grasso, P. Orsaria

Description

Over the past years, the research activity related to breast cancer has significantly expanded. The research unit is actively enrolled in the field of tailored therapies, in order to individualize the treatment with and integrated approach, in the era of precision medicine. The mission of the Breast Care Unit is to provide the highest quality clinical service, research and education to guarantee the reduction of breast cancer mortality together with the quality of life improvement, in the context of a multidisciplinary setting with complex intellectual architecture. Specifically, Breast Cancer Surgeons are committed to:

- Providing the highest quality in all aspects of diagnosis, resection, reconstruction and clinical management.
- Achieving competence in a broad range of comprehensive oncological, radioguided and reconstructive procedures with structured educational supervision, assessment and feedback.
- Continuously increasing the use of oncoplastic conserving procedures to offer solutions for challenging scenarios, while preserving the natural shape and appearance of the breast.

Main research activities

- New techniques of loco-regional anaesthesia performed by breast surgeon to improve surgical outcomes (pain control, opioid-free analgesia, prevention of chronic pain).
- Multicentric study "Prevention of the third millennium: liquid biopsy", to detect fragments of circulating DNA in peripheral blood. This approach considers breast cancer as a "moving target", a heterogeneous disease continuously evolving and changing.
- Management of B3 lesions (lesions of unknown biological potential) to investigate the role of possible new biomarkers for high risk patients
- International collaboration with Ministry of Health of Palestine to study the epidemiology of breast cancer in West Bank Area and the role of mini-invasive diagnostic techniques to improve surgical outcome and quality of life.
- Oncoplastic breast surgery as an innovative approach that aims at the safe and effective treatment of the cancerous lesion while achieving the best possible aesthetic outcome, consisting of large lumpectomy and remodelling techniques such as breast-reshaping by therapeutic reduction mammoplasty or volume replacement by local glandular flaps or regional/distant flaps.

Main collaborations

- Isabel Teresa Rubio, Head of Breast Surgical Oncology at Clinica Universidad de Navarra, Spain
- Jakob De Vries, Surgical Oncologist University at Groningen Medical Center, The Netherlands

Most important publications

Barone M., Cogliandro A., Grasso A., Altomare V., Persichetti P.

Direct-to-implant versus two-stage tissue expander/implant reconstruction: 2-year risks and patient-reported outcomes from a prospective, multicenter study
Plast Reconstr Surg. 2018 Jul;142(1):89e-91e. PubMed PMID: 29952915. IF 3,62

We read with great interest the article published in the Journal in November of 2017 by Srinivasa et al., and we would like to add our experience in the analysis of patient satisfaction following breast reconstruction.

We use the BREAST-Q in our clinical practice for each breast operation.2–5 In this case, we designed a retrospective cohort study of patients. The subjects of our study population were further divided into two groups: patients exposed to mastectomy alone (group 1) and patients exposed to mastectomy with tissue expander and definitive breast reconstruction (group 2). All patients were treated at our hospital between 2005 and 2016 and were asked to complete the postoperative BREAST-Q reconstruction questionnaire, independently from the group to which they had been assigned. Furthermore, in group 2, each patient was asked to complete the BREAST-Q questionnaire twice, after the first breast reconstruction with a tissue expander and after the second breast reconstruction with definite implants. <..>

To the best of our knowledge, our study is novel, compared with previous research, for two reasons: (1) our study evaluates the satisfaction of patients not only by comparing patients following mastectomy alone versus breast reconstruction but by further dividing patients exposed to reconstruction between first (tissue expander) and second (definite implants) breast reconstructions; and (2) our study represents the largest number of patients who completed the BREAST-Q questionnaire following mastectomy with a control group.

Cardiovascular Science

Head G. Di Sciascio

Faculty F. Grigioni, F. Mangiacapra, R. Melfi, A. Nusca, G.P. Ussia

Other Personnel M.C. Bono, V. Calabrese, P. Gallo, C. Goffredo, S. Mega, M. Miglionico, D. Ricciardi, E. Ricottini, G. Salvati

Description

The Cardiovascular Science Research Unit comprises clinical cardiologists, interventional cardiologists, expert cardiologists in echocardiography and electrophysiology. Our Unit is involved in several national and international multicentre clinical trials, mainly focusing on new devices for percutaneous coronary and structural intervention and new drugs for management of patients with ardiovascular diseases. Moreover, we performed and are performing several prospective experimental studies on a wide range of clinical settings such as interventional pharmacology, glycaemic variability assessment, biological markers and cardiac electrophysiology.

Main research activities

The randomized RIVENDEL study, investigating the effects of Ivabradine on vascular endothelial function, has been finalized and published; Substudies of the multicentre MATRIX study, comparing radial versus femoral approach in patients with acute coronary syndromes treated with PCI, have been published.
Ongoing research projects:
- Predictive role of a combined evaluation of carotid atherosclerosis and peripheral endothelial function on the presence and extent of coronary artery disease;
- Comparison of prasugrel and ticagrelor in protecting coronary microcirculation in patients with stable coronary artery disease undergoing PCI (PRO-MICRO 3 study);
- Impact of glycaemic variability assessed by a glucose continuous monitoring on platelet reactivity;
- Effects of ranolazine on glycemic control in diabetic patients;
- Impact of micro-RNA evaluation on cardiac resynchronization therapy outcome.

Main collaborations

Our Unit collaborates with several other Italian and international universities and research institutions:
- Cardiovascular Research Center Aalst, Belgium;
- Harvard Clinical Research Institute, Boston, USA;
- Technical University of Eindhoven, The Netherlands;
- Virginia Commonwealth University, USA.

Most important publications

Mangiacapra F., Pellicano M., Di Serafino L., Bressi E., Peace A.J., Di Gioia G., Morisco C., Bartunek J., Wijns W., Bruyne B., Barbato E.

Platelet reactivity and coronary microvascular impairment after percutaneous revascularization in stable patients receiving clopidogrel or prasugrel.
Atherosclerosis. 2018 Nov; 278: 23-28. PubMed PMID: 30236867. IF 4,467

Backgroud and Aims: Increased platelet reactivity (PR) associated with variable degree of coronary microvascular impairment has been reported in patients on clopidogrel after elective percutaneous coronary intervention (PCI). Prasugrel provides more potent platelet inhibition than clopidogrel, though it is unknown whether it might also prevent PCI-related platelet activation. In stable patients undergoing elective PCI, we compared: (1) the effects of prasugrel vs. clopidogrel on peri-procedural variations of PR and (2) the correlation of platelet inhibition potency with PCI-induced coronary microvascular impairment.

Methods: Forty thienopyridine-naive patients were randomly assigned to a loading dose of either prasugrel 60 mg (n = 20) or clopidogrel 600 mg (n = 20) at least 12 h before PCI. At the time of PCI, we assessed adenosine diphosphate (ADP)-induced PR with the Multiplate Analyzer, and the pressure-derived index of microvascular resistance (IMR) in the treated coronary, both at baseline and post-procedure. Results: ADP-induced PR was significantly lower in the prasugrel compared with clopidogrel group both at baseline (16.0 ± 8.7 vs. 33.9 ± 18.0 aggregation units [AU], $p < 0.001$) and post-procedure (16.2 ± 9.0 vs. 39.0 ± 18.6 AU, $p < 0.001$). A significant peri-procedural increase in PR was observed in the clopidogrel group ($p = 0.008$), but not in the prasugrel group ($p = 0.822$). A significant correlation was found between IMR and PR both at baseline ($r = 0.458$, $p = 0.003$) and post-PCI ($r = 0.487$, $p = 0.001$).
Conclusions: A loading dose of prasugrel compared with clopidogrel is able to attenuate PCI-related increase in PR in patients with stable CAD undergoing PCI, which might contribute to the beneficial effect of this drug on peri-procedural coronary microvascular function.

Ricottini E., Mangiacapra F., Nusca A., Melfi R., Cavallari I., Miglionico M., Gallo P., Pozzilli P., Di Sciascio G.

Relation of platelet indexes to platelet reactivity and periprocedural myocardial infarction in patients who underwent percutaneous coronary angioplasty.
Am J Cardiol. 2018 May 1;121(9):1027-1031. PubMed PMID: 29571721. IF 3,171

No comprehensive data are available on the role of platelet indexes (PI) in the periprocedural risk stratification of patients who underwent percutaneous coronary intervention (PCI). The aim of this study was to investigate the relation of PI to platelet reactivity (PR) and periprocedural myocardial infarction (PMI) in patients receiving PCI. A total of 502 PCI patients had preprocedural measurement of PI and PR, the latter assessed by VerifyNow P2Y12 assay. Study end points were incidence of PMI and high platelet reactivity (HPR) according to tertiles of PI and evaluation of PI in HPR patients. Incidence of PMI in the overall population was 6.6%. Rates of PMI were not different in PI tertiles: platelet count (I: 6.0%, II: 7.1%, III: 6.5%; $p = 0.74$), mean platelet volume (MPV, I: 6.6%, II: 7.3%, III: 5.8%; $p = 0.86$), platelet distribution width (I: 7.2%, II: 7.2%, III: 5.8%; $p = 0.74$), and MPV/P ratio (I: 6.6%, II: 6.0%, III: 7.1%; $p = 0.91$). The occurrence of PMI was significantly different in PR tertiles (I: 3%, II: 5.4%, III: 11.4%; $p = 0.006$). Platelet count and MPV/P ratio were significantly different in patients with and without HPR (221.8 ± 58.6 × 103/μL vs 207 ± 59.4 × 103/μL, $p = 0.008$; 51.73 ± 15.17 vs 56.7 ± 18.3, $p = 0.002$). In conclusion, this study showed no relation between PI and PMI in PCI patients but confirms the association of HPR with increased incidence of PMI; thus, PI seem to be not able to identify patients at higher periprocedural risk, but monitoring PR by a bedside assay remains a useful tool for risk stratification.

Montone R.A., Niccoli G., Vergni F., Vetrugno V., Russo M., Mangiacapra F., Fracassi F., Porto I., Leone A.M., Burzotta F., D'Amario D., Aurigemma C., Trani C., Lanza G.A., Crea F.

Endothelial dysfunction as predictor of angina recurrence after successful percutaneous coronary intervention using second generation drug eluting stents.
Eur J Prev Cardiol. 2018 Sep; 25(13):1360-1370. PubMed PMID: 29785885. IF 4,542

Background: The role of endothelial dysfunction in predicting angina recurrence after percutaneous coronary intervention is unknown. Design: We assessed the role of peripheral endothelial dysfunction measured by reactive-hyperaemia peripheral-artery tonometry (RH-PAT) in predicting recurrence of angina after percutaneous coronary intervention. Methods: We enrolled consecutive patients undergoing percutaneous coronary intervention with second-generation drug-eluting stents. RH-PAT was measured at discharge. The endpoint was repeated coronary angiography for angina recurrence and/or evidence of myocardial ischaemia at follow-up. Patients with in-stent restenosis and/or significant de novo stenosis were defined as having angina with obstructed coronary arteries (AOCA); all other patients as having angina with non-obstructed coronary arteries (ANOCA). Results: Among 100 patients (mean age 66.7 ± 10.4 years, 80 (80.0%) male, median follow-up 16 (3-20) months), AOCA occurred in 14 patients (14%), ANOCA in nine patients (9%). Repeated coronary angiography occurred more frequently among patients in the lower RH-PAT index tertile compared with middle and upper tertiles (14 (41.2%) vs. 6 (18.2%) vs. 3 (9.1%), $p = 0.006$, respectively). ANOCA was more frequent in the lower RH-PAT index tertile compared with middle and upper tertiles. In the multivariate regression analysis, the RH-PAT index only predicted angina recurrence. The receiver operating characteristic curve of the RH-PAT index to predict the angina recurrence demonstrated an area under the curve of 0.79 (95% confidence interval: 0.69-0.89; $p < 0.001$), with a cut-off value of 1.705, having sensitivity 74% and specificity 70%. Conclusions: Non-invasive assessment of peripheral endothelial dysfunction using RH-PAT might help in the prediction of recurrent angina after percutaneous coronary intervention, thus identifying patients who may need more intense pharmacological treatment and risk factor control.

Chemical–Physics Fundamentals in Chemical Engineering

Head V. Piemonte

Faculty L. Di Paola

Other Personnel L. Marrelli

Description

The Research Unit follows a methodology at the very basis of Process Engineering operative methods. To develop a new technology in the field, two steps are required:

▶ first, the theoretical elements characterizing the technology must be assessed, supported by purposed experimental campaigns;

▶ second, mathematical modeling, process simulation and economical assessment provide the essential framework to fully develop the technology.

Main research activities

- Predictive models development for artificial pancreas (In collaboration with the Unit of Endocrinology and Diabetes, Campus Bio-Medico University of Rome, Italy)
- Functionalized nanoparticles development for artificial Liver optimization (in collaboration with the Unit of Tissue Engineering & Chemistry for Engineering, Campus Bio-Medico University of Rome).
- Gastro-intestinal system modelling for in silico trials of drug bio-availability (in collaboration with Unit of Gastroenterology and Unit of Biochemistry and Molecular Biology, Campus Bio-Medico University of Rome).
- Computational biochemistry proteins as networks (in collaboration with National Institute of Health, Italy, National Research Council (CNR), Italy, University of Rome "Tor Vergata", University of Catania, Italy).
- Computational approach for developmental biology (in collaboration with Sapienza University, Italy and John Innes Centre, UK);
- Bioartificial liver optimization (in collaboration with Piaggio Research Centre, University of Pisa, Italy).
- Energy storage tanks for CSP plants with molten salts. Modelling and optimization (In collaboration with the Italian National Agency for New Technologies, Energy and Sustainable Development
- ENEA, Casaccia Research Centre, Rome, Italy).
- Biogas production by anaerobic co-digestion of sludge and food waste (in collaboration with IRSA, Italy).

Main collaborations

- IRSA, Italy;
- Italian National Agency for New Technologies, Energy and Sustainable Development - ENEA, Casaccia Research Centre, Rome, Italy;
- John Innes Centre, UK;
- National Institute of Health, Italy;
- National Research Council (CNR), Italy;
- Piaggio Research Centre, University of Pisa, Italy;
- University of Catania, Italy;
- Sapienza University, Italy;
- University of Rome "Tor Vergata", Italy.

Most important publications

Tortora F., Innocenzi V., di Celso G. M., Vegliò F., Capocelli M., Piemonte V., Prisciandaro M.

Application of micellar-enhanced ultrafiltration in the pre-treatment of seawater for boron removal.
Desalination 2018; 428: 21-28. DOI 10.1016/j.desal.2017.11.016 IF 6,603

In this research, micellar enhanced ultrafiltration (MEUF) is tested as a seawater pre-treatment before entering RO. The experimental tests were performed by means of monotubular ceramic membranes of 210 kDa and 1 kDa. Boron is removed from the water flow using sodium dodecyl sulphate as a surfactant. The synthetic solutions contain 5 mg/L of boron and SDS concentrations are equal to 1.15 g/L and 2.88 g/L, under and above the critical micellar concentration, respectively.
Experimental data showed that MUEF is efficient in removing boron, with best performances obtained at low pressure, with a low or null surfactant concentration for 1 kDa membrane and a high surfactant concentration for 210 kDa membrane. Moreover, experimental results have been used to perform a preliminary process analysis for a hypothetic sea-water desalination plant, with MEUF as a pretreatment for the RO section. The results showed that the MEUF guarantees a boron concentration after RO below the allowed threshold, by using a single step osmosis; moreover, in this way it was possible to reduce the energy consumption thus resulting in an appreciable reduction of carbon footprint as well as of the unit cost of water.

Piemonte V., Cerbelli S., Capocelli M., Di Paola L., Prisciandaro M., Basile A.

Design of microfluidic bioreactors: transport regimes.
Asia-Pacific J Chem Eng. 2018; 3(5): e2238. DOI 10.1002/apj.2238 IF 1,238

An advection–diffusion–reaction transport model for a continuous reactor characterized by a simple geometry is simulated to provide a design guidance for the realization of an optimized experimental prototype consisting of a rectangular channel hosting a scaffold slab that provides an immobilizing support for the cells. A counter-current carrier flow crossing the channel feeds the oxygen and growth factors and ensures the removal of metabolic products. A more complex sinusoidal configuration, which has been recently used as for hepatocyte culture, is proposed and evaluated. Silico tests shows how the designed device is able to replicate the endothelial–parenchymal interface of a liver sinusoid.

Maurizi A.R., Piemonte V., Pozzilli P.

Diabetes on demand and novel technologies.
Diabetes Metab Res Rev. 2018 Feb; 34:e2985. PubMed PMID: 29377511. IF 3,904

To date, the use of technology for the management of diabetes represents a promising area of innovation that can dramatically change diabetics' lives. In the past decade, the use of diabetes devices has widely grown and looks to have partially improved diabetes management. The combination of cloud technology with real-expert intervention saves time and improves efficiency, as well as empowering the patient. The application of mathematical models applied to diabetes therapy could lead to significant improvement in life quality and challenge the burden of hypoglycaemia. Events where an individual needs support are instantly achieved, triggering outreach alerts via cloud and wireless connectivity, thereby improving patient compliance and reducing disease costs.

Clinical Laboratory Sciences

Head S. Angeletti

Faculty G. Gherardi

Other Personnel M. De Cesaris, L. De Florio, E. Ferraro, M. Fogolari, A. Lai

Description

The research unit is actively interested in research studies aimed to investigate bioumoral markers involved in the diagnosis and prognosis of important disease such as chronic disease or sepsis. Further fields of research included the molecular evolution of microorganisms causing important epidemic in Italy as well as worldwide and the antimicrobial resistant microorganisms circulating in different settings, especially in nosocomial. Furthermore, the activity of the research unit was extended also to the evaluation of interesting clinical case diagnosed at the Internal medicine Department of the University Campus Bio-Medico in terms of prompt diagnosis and treatment.

Main research activities

In the year 2018, the most important activities developed by the research unit have been in the areas of infectious disease, antibiotic resistance and their pathogenesis. Different collaboration were established with several department of internal medicine, surgery and geriatrics of the university hospital campus bio-medico. Furthermore, the research unit by a scientific agreement with the extraordinary reception center for migrants and refugees "mondo migliore" at Rocca di Papa in Rome continued the collaboration began in the year 2017. By this agreement, a protocol for migrant's surveillance was developed and results of the surveillance reported in some publication on international peer-reviewed scientific journals. Other important agreement have been continued since 2016 with the public health institute of Montenegro (Podgorica), the public institute of Bulgaria (Sofia) and with the department of pathology and laboratory medicine of the University of Florida, Gainesville, USA. By these agreements, several scientific publications on international and peer-reviewed journals have been published and new scientific collaborations are ongoing. The research unit actively collaborate with other research units of the university campus bio-medico such as " virology" directed by prof Elisabetta Riva, "biochemistry and molecular biology" directed prof M. Maccarrone, "endocrinology and diabetology" directed by prof P. Pozzilli, "general surgery" directed by prof r. Coppola, "geriatric" directed by prof r. Antonelli Incalzi, "gastroenterology" directed by prof m. Cicala; rheumatology unit directed by prof a. Afeltra; and with the department of "anatomic pathology" directed by Dr Anna Crescenzi and the department of "internal medicine" directed by prof Sebastiano Costantino.

Most important publications

Spoto S., Valeriani E., Caputo D., Cella E., Fogolari M., Pesce E., Mulè M.T., Cartillone M., Costantino S., Dicuonzo G., Coppola R., Ciccozzi M., Angeletti S.

The role of procalcitonin in the diagnosis of bacterial infection after major abdominal surgery: Advantage from daily measurement.
Medicine (Baltimore). 2018 Jan; 97(3): e9496. PubMed PMID: 29504973. IF 2,028

Postsurgical infections represent an important cause of morbidity after abdominal surgery. The microbiological diagnosis is not achieved in at least 30% of culture with consequent worsening of patient outcome. In this study, procalcitonin measurement, during the first 3 days after abdominal surgery, has been evaluated for the early diagnosis of postsurgical infection.ninety consecutive patients subjected

to major abdominal surgery at the university campus bio-medico of rome, have been included. Pct concentrations were measured by time-resolved amplified cryptate emission (trace) assay at admission and at the first, second, and third day after surgery. Pct levels were compared using the mann-whitney test and by anova test for variance analysis. Receiver operating characteristic (roc) analysis was performed to define the diagnostic ability of pct in case of postsurgical infections.pct values resulted significantly different between patients developing or not developing postsurgical infections. Pct >1.0ng/ml at first or second day after surgery and >0.5ng/ml at third day resulted diagnostic for infectious complication, whereas a value <0.5ng/ml at the fifth day after surgery was useful for early and safety discharge of patients.in conclusion, pct daily measurement could represent a useful diagnostic tool improving health care in the postsurgical period following major abdominal surgery and should be recommended.

Spoto S., Cella E., de Cesaris M., Locorriere L., Mazzaroppi S., Nobile E., Lanotte A.M., Pedicino L., Fogolari M., Costantino S., Dicuonzo G., Ciccozzi M., Angeletti S.

Procalcitonin and MR-Proadrenomedullin combination with SOFA and qSOFA Scores for Sepsis diagnosis and prognosis: a diagnostic algorithm.
Shock. 2018 Jul; 50(1):44-52. PubMed PMID: 29023361. IF 3,005

Purpose: The third Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) defined sepsis as an organ dysfunction consequent to infection. A Sequential Organ Failure Assessment (SOFA) score at least 2 identifies sepsis. In this study, procalcitonin (PCT) and midregional pro-adrenomedullin (MR-proADM) were evaluated along with SOFA and quick SOFA (qSOFA) scores in patients with sepsis or septic shock. **Methods:** A total of 109 septic patients and 50 patients with noninfectious disease admitted at the Department of Internal Medicine and General Surgery of the University Hospital Campus Bio-Medico of Rome were enrolled. PCT and MR-proADM were measured with immunoluminometric assays (Brahms, Hennigsdorf, Germany). Data were analyzed with receiver-operating characteristic (ROC) curve analysis, likelihood ratios, and Mann-Whitney U test using MedCalc 11.6.1.0 package. **Results:** At ROC curve analysis, PCT showed the highest area under the curve and positive likelihood ratio values of 27.42 in sepsis and 43.62 in septic shock. MR-proADM and SOFA score showed a comparable performance. In septic shock, lactate showed the most accurate diagnostic ability. In sepsis, the best combination was PCT with MR-proADM with a posttest probability of 0.988. Based upon these results, an algorithm for sepsis and septic shock diagnosis has been developed. MR-proADM, SOFA, and qSOFA scores significantly discriminated survivors from nonsurvivors. **Conclusions:** PCT and MR-proADM test combination represent a good tool in sepsis diagnosis and prognosis suggesting their inclusion in the diagnostic algorithm besides SOFA and qSOFA scores. Furthermore, MR-proADM as marker of organ dysfunction, with a turn around time of about 30 min, has the advantage to be more objective and rapid than SOFA score

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Cella E., Golkocheva-Markova E.N., Trandeva-Bankova D., Gregori G., Bruni R., Taffon S., Equestre M., Costantino A., Spoto S., Curtis M., Ciccaglione A.R., Ciccozzi M., Angeletti S.

The genetic diversity of hepatitis A genotype I in Bulgaria.
Medicine (Baltimore). 2018 Jan; 97(3):e9632. PubMed PMID: 29504993. IF 2,028

The purpose of this study was to analyze sequences of hepatitis A virus (HAV) Ia and Ib genotypes from Bulgarian patients to investigate the molecular epidemiology of HAV genotype I during the years 2012 to 2014. Around 105 serum samples were collected by the Department of Virology of the National Center of Infectious and Parasitic Diseases in Bulgaria. The sequenced region encompassed the VP1/2A region of HAV genome. The sequences obtained from the samples were 103. For the phylogenetic analyses, 5 datasets were built to investigate the viral gene in/out flow among distinct HAV subpopulations in different geographic areas and to build a Bayesian dated tree, Bayesian phylogenetic and migration pattern analyses were performed. HAV Ib Bulgarian sequences mostly grouped into a single clade. This indicates that the Bulgarian epidemic is partially compartmentalized. It originated from a limited number of viruses and then spread through fecal-oral local transmission. HAV Ia Bulgarian sequences were intermixed with European sequences, suggesting that an Ia epidemic is not restricted to Bulgaria but can affect other European countries. The time-scaled phylogeny reconstruction showed the root of the tree dating in 2008 for genotype Ib and in 1999 for genotype Ia with a second epidemic entrance in 2003. The Bayesian skyline plot for genotype Ib showed a slow but continuous growth, sustained by fecal-oral route transmission. For genotype Ia, there was an exponential growth followed by a plateau, which suggests better infection control. Bidirectional viral flow for Ib genotype, involving different Bulgarian areas, was observed, whereas a unidirectional flow from Sofia to Ihtiman for genotype Ia was highlighted, suggesting the fecal-oral transmission route for Ia.

Computer Systems and Bioinformatics

Head G. Iannello

Faculty F. Cacace, P. Soda, L. Vollero

Other Personnel P. Afferni, L. Ardito, E. Cordelli, M. Merone, R. Sicilia, R. Valenti

Description

The research activities of the Computer Science and Bioinformaics (CoSBI) Research Unit are focused on the analysis of data, signals, and images with a special attention to biomedical applications. The Unit has also experience on high performance computing, machine learning and data analytics, computer networks with special focus on wireless networks, modeling dynamic stochastic system, and innovation management.

Main research activities

More specifically, the Unit is working on:
- CAD systems for automatic analysis of Indirect Immunofluorescence (IIF) images.
- Decision Support Systems for clinical applications.
- Radiomics, which is decoding tumour phenotypes by non-invasive quantitative imaging.
- Social media analysis
- Algorithms for the analysis of EEG and EEG-TMS signals, and of fRMI images.
- Computer Networks and Wireless Systems.
- Control and estimation theory for stochastic, distributed and time-delayed systems, and control and systems technology for health-care applications: artificial pancreas, control of tumor growth
- Patent analysis and evaluation of innovation value, digital innovation.

Main collaborations

- BPCOMedia srl to develop AI-based tools forecast worrisome events of patients suffering from BPCO.
- Catholic University of the Sacred Heart, to develop AI strategies for diabetes data analysis; Unit of Oncologic Radiotherapy
- Centre for Enterprise, Innovation and Growth (Birmingham City University) to analyze SMEs innovation performance.
- Centro Diagnostico Italiano SpA for radiomics research.
- Departments of Information and Electrical Engineering (L'Aquila)
- Eindhoven University of Technology to detect rumour in social microblogs.
- Gerontology Unit to develop AI methods for BPCO data analysis.
- Haematology and the Vascular Surgery Units to develop mobile apps to monitor patients' conditions.
- IASI-CNR to develop estimation methods for mathematical models of biological systems.
- Informatics and Automation (Roma "La Sapienza")
- Measurements and Biomedical Instrumentation Unit to implement a framework to manage wearable sensors.
- Neurology Unit to identify age-related excitability and connectivity cortical changes.

Most important publications

Sicilia R., Giudice S. L., Pei Y., Pechenizkiy M., Soda P.

Twitter rumour detection in the health domain.
Expert Syst Appl. 2018; 110: 33-40. DOI: 10.1016/j.eswa.2018.05.019 IF 3,768

In the last years social networks have emerged as a critical mean for information spreading bringing along several advantages. At the same time, unverified and instrumentally relevant information statements in circulation, named as rumours, are becoming a potential threat to the society. For this reason, although the identification in social microblogs of which topic is a rumour has been studied in several works, there is the need to detect if a post is either a rumor or not. In this paper we cope with this last challenge presenting a novel rumour detection system that leverages on newly designed features, including influence potential and network characteristics measures. We tested our approach on a real dataset composed of health-related posts collected from Twitter microblog. We observe promising results, as the system is able to correctly detect about 90% of rumours, with acceptable levels of precision.

Erturk M. A., Vollero L., Aydin M. A.

Optimal joint load balancing and EDCA configuration of IEEE 802.11 wireless hotspots.
Int J Commun Syst. 2018; 31(2): e3455. DOI: 10.1002/dac.3455 IF 1,717

Wireless hotspots are today the most common solution in providing Internet access. Load balancing (LB) solutions aim at mitigating the problem of uneven distribution of users to access points (APs). In this study, we propose a QoS-LB solution based on the cell breathing technique with the goal of balancing the load in IEEE 802.11e Enhanced Distributed Channel Access (EDCA) Hotspots. The algorithm has been analytically defined and its performance evaluated through simulations and tests in a real test bed. The results prove that the proposed solution is effective in solving the optimal QoS-LB configuration problem in WiFi hotspots of average size.

Battilotti S., Cacace F., d'Angelo M., Germani A.

The polynomial approach to the LQ non-Gaussian regulator problem through output injection.
IEEE Trans Autom Control. 2018; 64(2): 538-552. DOI: 10.1109/TAC.2018.2814685 IF 5,007

In this paper, an improved approach for the solution of the regulator problem for linear discrete-time dynamical systems with non-Gaussian disturbances and quadratic cost functional is proposed. We show that when the system is not asymptotically stable the polynomial control does not improve over the classical LQG solution. In order to enlarge the class of systems that can be controlled, we propose a new method based on a suitable rewriting of the system by means of an output injection term. We show that this allows us to design a polynomial optimal controller also for non asymptotically stable systems. Numerical results show the effectiveness of the method.

Developmental Neuroscience

Head F. Keller

Other Personnel V. Focaroli, R. Marino

Description

The Developmental Neuroscience unit investigates developmental mechanisms at the molecular, cellular and systemic levels, both in animal models and in human infants. One major focus of the lab has been the interaction between reelin, a protein of the extracellular matrix and environmental factors, in particular gonadal hormones, during rain development. The reelin gene is a candidate gene for autism, a pervasive developmental disorders that is more frequent in males. The other major focus of the lab is the role of motor development and other embodied functions for development of cognitive functions and mental processes. Specifically, we are investigating early motor signs of autism risk in high-risk babies, who have an older sibling affected by this disorder. A new research focus of the lab is the investigation of embodied music erception in children.

Main collaborations

- Dr. Alessandra Micera, G. B. Bietti Foundation for Study and Research in Ophthalmology, Italy;
- Dr. Nicola Di Stefano, Istituto FAST; Dr. Fabrizio Taffoni, Lab of Biomedical Robotics;
- Prof. Jana M. Iverson, University of Pittsburgh.

Most important publications

Nobili A., Krashia P., Cordella A., La Barbera L., Dell'Acqua M.C., Caruso A., Pignataro A., Marino R., Sciarra F., Biamonte F., Scattoni M.L., Ammassari-Teule M., Cecconi F., Berretta N., Keller F., Mercuri N.B., D'Amelio M.

Ambra1 shapes hippocampal inhibition/excitation balance: role in neurodevelopmental disorders.
Mol Neurobiol. 2018 Oct; 55(10):7921-7940. PubMed PMID: 29488136. IF 5,076

Imbalances between excitatory and inhibitory synaptic transmission cause brain network dysfunction and are central to the pathogenesis of neurodevelopmental disorders. Parvalbumin interneurons are highly implicated in this imbalance. Here, we probed the social behavior and hippocampal function of mice carrying a haploinsufficiency for Ambra1, a pro-autophagic gene crucial for brain deve-

lopment. We show that heterozygous Ambra1 mice (Ambra+/-) are characterized by loss of hippocampal parvalbumin interneurons, decreases in the inhibition/excitation ratio, and altered social behaviors that are solely restricted to the female gender. Loss of parvalbumin interneurons in Ambra1+/- females is further linked to reductions of the inhibitory drive onto principal neurons and alterations in network oscillatory activity, CA1 synaptic plasticity, and pyramidal neuron spine density. Parvalbumin interneuron loss is underlined by increased apoptosis during the embryonic development of progenitor neurons in the medial ganglionic eminence. Together, these findings identify an Ambra1-dependent mechanism that drives inhibition/excitation imbalance in the hippocampus, contributing to abnormal brain activity reminiscent of neurodevelopmental disorders.

Cordella A., Krashia P., Nobili A., Pignataro A., La Barbera L., Viscomi M.T., Valzania A., Keller F., Ammassari-Teule M., Mercuri N.B., Berretta N., D'Amelio M.

Dopamine loss alters the hippocampus-nucleus accumbens synaptic transmission in the Tg2576 mouse model of Alzheimer's disease.

The functional loop involving the ventral tegmental area (VTA), dorsal hippocampus and nucleus accumbens (NAc) plays a pivotal role in the formation of spatial memory and persistent memory traces. In particular, the dopaminergic innervation from the VTA to the hippocampus is critical for hippocampal-related memory function and alterations in the midbrain dopaminergic system are frequently reported in Alzheimer's disease (AD), contributing to age-related decline in memory and non-cognitive functions. However, much less is known about the hippocampus-NAc connectivity in AD. Here, we evaluated the functioning of the hippocampus-to-NAc core connectivity in the Tg2576 mouse model of AD that shows a selective and progressive degeneration of VTA dopaminergic neurons. We show that reduced dopaminergic innervation in the Tg2576 hippocampus results in reduced synaptic plasticity and excitability of dorsal subiculum pyramidal neurons. Importantly, the glutamatergic transmission from the hippocampus to the NAc core is also impaired. Chemogenetic depolarisation of Tg2576 subicular pyramidal neurons with an excitatory Designer Receptor Exclusively Activated by Designer Drugs, or systemic administration of the DA precursor levodopa, can both rescue the deficits in Tg2576 mice. Our data suggest that the dopaminergic signalling in the hippocampus is essential for the proper functioning of the hippocampus-NAc excitatory synaptic transmission.

Keller F., Di Stefano N.

The robustness of musical language: a perspective from complex systems theory.

Within the field of systems theory, the term robustness has typically been applied to different contexts such as automatic control, genetic networks, metabolic pathways, morphogenesis, and ecosystems. All these systems involve either man-made machines, or living organisms. In this chapter, we will consider music as a peculiar complex system, involving both the realm of machines (the musical instrument) and the realm of biology (the player and the listeners). We will discuss some of the properties of music experience in terms of different attributes of robustness, focusing in particular on stability, the property enabling a complex system to maintain its function against a wide range of external and internal changes. We will provide examples of the human ability of isolating and maintaining stable information within the perceptual flow and despite changes in the external world that reach our perceptions, leading towards a characterization of robustness in music perception as referred both to the search for regularities and to the range of tolerance that perception admits to regularities. Finally, we will list four multiple interaction cycles that typically characterize music experience and that involve both internal properties of the organism and the environment.

Diagnostic Imaging

Head B. Beomonte Zobel

Faculty E. Faiella, R.F. Grasso

Other Personnel V. Cirimele, G. Frauenfelder, S. Gaudio, C. A. Mallio, C.C. Quattrocchi, D. Santucci

Description

Research is carried out following different lines, in co-operation with other research units, both inside and outside our University:

- Neuroimaging, that is the correlation of MRI with diagnosis, treatment or rehabilitation of different acute and chronic diseases;
- Interventional Radiology, how radiologists use small invasive approaches and specific technologies for diagnosis and treatment of several diseases;
- Image based navigations systems, that use mechatronics and images acquired directly from the patients to guide diagnostic and therapeutic procedures in Medicine;
- Elderly Imaging, how senescence processes can modify the functionality and the morphology of different organs and tissues;
- Oncologic Imaging, how radiologists can improve the diagnosis, the treatment and the follow-up of oncologic patients;
- Radiomics, that is the correlation between some imaging biomarkers and genetic characteristics of different diseases;
- Artificial Intelligence and Machine Learning in Imaging, how neural networks can be trained and used to increase the value, efficiency and accuracy of radiologists.

Main research activities

The main publications, during 2018, dealt with:

- Contrast media, evaluating in vivo Gadolinium pharma kinetics and dynamics of linear MRI contrast agents.
- Interventional Radiology, suggesting the percutaneous management of bone metastases and evaluating the clinical efficacy of augmented reality navigation systems.
- Neuroimaging, evaluating specific aspects of functional connectivity and of brain circuitry in patients affected by eating disorders.
- Oncologic imaging, assessing clinical and radiological features driving diagnosis and performing of percutaneous biopsies in patients with prostatic carcinoma.

Most important publications

Faiella E., Frauenfelder G., Santucci D., Luppi G., Schena E., Beomonte Zobel B., Grasso R.F.

Percutaneous low-dose CT-guided lung biopsy with an augmented reality navigation system: validation of the technique on 496 suspected lesions.
Clin Imaging. 2018 May – Jun; 49:101-105. PubMed PMID: 29207301. IF 1,014

Purpose: To validate a CT-navigation system during percutaneous lung biopsy (PLB).
Methods: Four hundred-ninety-six patients underwent low-dose CT-guided PLB. Lesion diameter (LD), procedural time (PT), histologic validity, lesion distance from pleural surface (DPS), needle distance travelled during procedure (DTP), complications and radiation exposure were recorded.
Results: Hysto-patological diagnosis was obtained in 96.2% cases. Mean PT, DPS, DTP, LD were respectively
29.5 min, 12.4 mm, 17.9 mm, 20.7 mm. In cases of major complications (4.6%), higher values of DTP were measured.
Conclusions: CT-navigation system allowed a good success in terms of diagnosis in small lesions and when a long DTP is required.

Quattrocchi C.C., Errante Y., Mallio C.A., Marinelli L., LoVullo G., Giannotti G., Della Sala S.W., van der Molen A.J., Beomonte Zobel B.

Effect of age on high T1 signal intensity of the dentate nucleus and globus pallidus in a large population exposed to gadodiamide.
Invest Radiol. 2018 Apr; 53(4):214-222. PubMed PMID: 29166300. IF 6,224

T1w signal intensity ratios were obtained from a large population of 2500 consecutive enhanced MRI scans. Of these, 1906 of patients not previously exposed to any gadolinium (Gd)-based contrast agent were used as control group and were compared with 892 of patients with documented prior exposure to intravenous gadodiamide.
In the Gd-exposed patients, multivariate regression analysis showed age ($\beta = -0.285$; $P < 0.0001$) and the number of previous injections of gadodiamide ($\beta = 0.224$; $P < 0.0001$) to be powerful predictors of Dn/Po ratio and Gp/Th ratio (age: $\beta = 0.269$; $P < 0.0001$) (gadodiamide: $\beta = 0.127$; $P < 0.0001$).
So the number of previous gadodiamide injections is a powerful predictor of the signal intensity increase of the Dn/Po and Gp/Th ratios and demonstrate that aging influences the T1 signal intensity of DN and GP in Gd-naïve and in Gd-exposed subjects.

Gaudio S., Olivo G., Beomonte Zobel B., Schiöth H.B.

Altered cerebellar-insular-parietal-cingular subnetwork in adolescents in the earliest stages of anorexia nervosa: a network-based statistic analysis.
Transl Psychiatry. 2018 Jul 6; 8(1):127. PubMed PMID: 29980676. IF 4,691

Few functional magnetic resonance imaging (fMRI) studies have explored resting-state functional connectivity (RSFC) in anorexia nervosa (AN) patients. The aim of the present study is to investigate RSFC in a sample of adolescents at the earliest stages of AN Resting-state fMRI data was obtained from 15 treatment-naive female adolescents with AN restrictive type (AN-r) in its earliest stages and 15 age-matched healthy female controls. Group comparison showed a decreased connectivity in a sub-network of connections encompassing the left and right rostral anterior cingulate cortex, left paracentral lobule, left cerebellum (10th sub-division), left posterior insula, left medial fronto-orbital gyrus, and right superior occipital gyrus in AN patients. Results were not associated to alterations in intranodal or global connectivity. Our findings suggest that RSFC may be specifically affected at the earliest stages of AN.

Drug Sciences

Head G. Minotti

Faculty E. Salvatorelli

Other Personnel P. Menna

Description

This Research Unit is committed to elucidating pharmacological foundations and clinical correlates of cardiovascular liability of antitumor drugs. It designs and performs clinical studies and preclinical experiments (molecular modelling, cell biology, ex vivo human tissue biopsies, optical and mass spectrometry techniques).

Main research activities

- Recalculation of cumulative anthracycline doses associated with 5% risk of heart failure.
- Clinical trajectories of cardio-oncology
- Clinical phenotypes of cardiovascular toxicity from tyrosine kinase inhibitors
- Clinical characterization of early diastolic dysfunction induced by anthracyclines and nonanthracycline chemotherapeutics
- Clinical pharmacology of hemodynamic effects of natriuretic peptides in patients treated by cancer drugs

Most important publications

Minotti G.

The International Cardioncology Society-ONE trial: not all that glitters is for cardioncologists only.
Eur J Cancer. 2018 Jul; 97:27-29. PubMed PMID: 29731230. IF 7,191

This paper describes the role of pharmacologists in clinical cardio-oncology trials.

Salvatorelli E., Menna P., Chello M., Covino E., Minotti G.

Low-dose anthracycline and risk of heart failure in a pharmacokinetic model of human myocardium exposure: analog specificity and role of secondary alcohol metabolites.
J Pharmacol Exp Ther. 2018 Feb; 364(2):323-331. PubMed PMID: 29222131. IF 3,706

Cumulative doses of doxorubicin and other antitumor anthracyclines may cause heart failure (HF). Concerns exist that HF might be caused by cumulative anthracycline doses that were thought to be safe. We developed a pharmacokinetic model that simulated clinical exposure of human myocardium to anthracyclines and incorporated simulations of polymorphisms that increase formation of toxic anthracycline secondary alcohol metabolites. The results support concerns about HF risk from low-dose anthracycline, characterize the anthracycline analog specificity of HF risk, and illuminate the role of secondary alcohol metabolites.

Menna P., Calabrese V., Armento G., Annibali O., Greco C., Salvatorelli E., Marchesi F., Reggiardo G., Minotti G.

Pharmacology of cardio-oncology: chronotropic and lusitropic effects of B-type natriuretic peptide in cancer patients with early diastolic dysfunction induced by anthracycline or nonanthracycline chemotherapy.
J Pharmacol Exp Ther. 2018 Jul; 366(1):158-168. PubMed PMID: 29720563. IF 3,706

B-type natriuretic peptide (BNP) is widely used as a diagnostic marker of systolic dysfunction. Here we describes pharmacologic analyses of cancer patients showing that: 1) impaired relaxation and persistent elevations of BNP were mutually exclusive manifestations of diastolic dysfunction by chemotherapy; 2) in some patients, BNP elevations were induced by an early compromise of myocardial relaxation; 3) BNP elevations then halted further deterioration of relaxation; and 4) high BNP increased heart rate (HR). These findings describe a pharmacologic scenario in which cancer drugs cause an early diastolic dysfunction that in some patients is both heralded and modulated by BNP elevations.

Electronics for Sensor Systems

Head G. Pennazza

Faculty: M. Santonico

Other Personnel S. Grasso, A. Sabatini, A. Zompanti

Description

The Unit of Electronics for Sensor Systems (ESS) has a long experience in the study, design, development and test of sensors and electronic interfaces for sensor systems, especially for medical applications and food monitoring. Its main characteristic is the multidisciplinary approach: designing sensors and electronic interfaces is the core activity, and it is addressed to specific issues in the bio-medical context or coming from food-industry. ESS staff includes Electronic Engineers, Biomedical Engineers and a Biotechnologist. This unit is able to cover many steps of the development process of innovative technologies, starting from the basic research on electronic circuits and on new sensing materials. ESS transforms this research in a new technology concept and it is also able to integrate a prototype system in an engineered version, and to test them in the lab and in a relevant environment. This unit also applies multivariate data analysis techniques for the elaboration of the data.

Main research activities

In the frame of a FLAG-ERA project, Convergence (Frictionless Energy Efficient Convergent Wearables for Healthcare and Lifestyle Applications), this unit developed, during 2018, a low-power and wireless CO_2 and RH sensor, tested by ENEA.

The collaboration with CNR Institute of Biomedicine and Molecular Immunology of Palermo for the monitoring of paediatric asthma achieved, during 2018, novel and promising results, described in a paper accepted in 2018.

In 2018 the project AUDIO (Acoustic Upgraded Diagnostics In-Orbit) started; it is funded by the Italian Space Agency, in the context of the human space flights for research and technological demonstration on the International Space Station. It aims at developing a device for measuring Oto Acoustic Emissions in orbit, in order to monitor the auditory function of the astronauts.

In 2018 project COMETA (Quality testing of organoleptic properties of COffee blends via genetic and METAbolic fingerprinting) started. The project is coordinated by Danesi caffè SpA. It is devoted to the characterization of coffee blend during the roasting processing for which this unit has to develop a non-destructive sensor system.

Main collaborations

- CNR Institute of Biomedicine and Molecular Immunology of Palermo
- Italian Space Agency
- Danesi caffè SpA

Most important publications

Pennazza G., Santonico M., Vollero L., Zompanti A., Sabatini A., Kumar N., Pini I., Quiros Solano W.F., Sarro L., D'Amico A.

Advances in the electronics for cyclic voltammetry: the case of gas detection by using microfabricated electrodes.
Front Chem. 2018 Aug 10; 6:327. PubMed PMID: 30148129. IF 4,155

This paper presents an advanced voltammetric system to be used as electronic tongue for liquid and gas analysis. It has been designed to be more flexible and accurate with respect to other existing and similar systems. It features improved electronics and additional operative conditions. Among others these include the possibility to optically excite the solution and to treat the output signal by a differentiation process in order to better evidence the existence of small details in the response curve. Finally by the same type of tongue preliminary results are shown dealing with O_2 and CO_2 concentration measurements in appropriate solutions.

DRocco G., Pennazza G., Santonico M., Longo F., Rocco R., Crucitti P., Antonelli Incalzi R.

Breathprinting and early diagnosis of lung cancer.
J Thorac Oncol. 2018 Jul; 13(7):883-894. PubMed PMID: 29526822. IF 10,34

The electronic nose (e-nose) is a promising technology as a useful addition to the currently available modalities to achieve lung cancer diagnosis. The e-nose can assess the volatile organic compounds detected in the breath and derived from the cellular metabolism. Volatile organic compounds can be analyzed to identify the individual chemical elements as well as their pattern of expression to reproduce a sensorial combination similar to a fingerprint (breathprint). The e-nose can be used alone, mimicking the combinatorial selectivity of the human olfactory system, or as part of a multisensorial platform. This review analyzes the progress made by investigators interested in this technology as well as the perspectives for its future utilization.

D'Amico A., Santonico, M., Pennazza G., Zompanti A., Scipioni E., Ferri G., Stornelli V., Salmeri M., Lojacono R.

Resonant directly coupled inductors-capacitors ladder network shows a new, interesting property useful for application in the sensor field, down to micrometric dimensions
Micromachines. 2018; 9(7): 343. DOI: 10.3390/mi9070343. IF 2,222

The study of ladder networks made by sequences of directly coupled inductor–capacitor single cells has led us to discover a new property, which may be of certain interest in the sensor field. In the case of n cells, the n-frequencies vector characterizing each node may allow for the identification of that capacitor (sensor), which has experienced a variation of its nominal value. This localization is possible independently from the observable node of the ladder network as proven by the application of the following multivariate data analysis techniques: principal component analysis and partial least square discriminant analysis. This property can be applied on a large scale down to micrometric dimensions in agreement with the technologic ability to shrink the capacitive sensor dimensions.

Endocrinology and Diabetes

Head P. Pozzilli

Faculty S. Manfrini, N. Napoli

Other Personnel S.I. Briganti, F. Cannata, I. Cavallari, G. Defeudis, R. Del Toro, A. Di Mauro, S. Fallucca, E. Fioriti, C. Guglielmi, G. Leanza, E. Maddaloni, D. Maggi, A.R. Maurizi, L. Monte, A. Naciu, A. Palermo, A. Piccoli, S. Pieralice, A. Soare, R. Strollo, G. Tabacco, F. Tramontana, D. Tuccinardi, C. Vinci
Lab Technician L. Valente **Scientific Secretary** S. Miglietta **Secretary** A. Suppa

Description

Over the years, the research activity related to endocrine and metabolic diseases has expanded significantly placing the Area of Endocrinology, Campus Bio-Medico University of Rome as a reference point for a range of national and international projects. Our area has been and still is the Coordinator Center of scientific projects of the Ministry of Education and Ministry of Health and of clinical trials of novel therapies, especially in the field of diabetes. Our group collaborates with centers of excellence in Europe, Asia and North America. In these areas, our group works closely with scientific communities and governmental and non-governmental organizations on joint research programs.

Main research activities

- Pathogenesis and immunotherapy of type 1 diabetes (T1D);
- Type 2 diabetes (T2D), obesity and nutrition;
- Pathophysiological mechanisms of bone loss in diabetes, obesity and in post-menopause;
- Early diagnosis of thyroid cancer (microbiopsy and RAMAN technology);
- Extraskeletal effects of vitamin D;
- Risk of fracture in T1D and T2D.

Main collaborations

- D. Black, Univesity of California, San Francisco, USA;
- R. Civitelli, Washington Univesity, Saint Louis, USA;
- D. Leslie, Queen Mary, University of London, UK;
- Nissim, Queen Mary, University of London, UK;
- Raz Hadassah, Center for the Prevention of Diabetes, Jerusalem, Israel;
- J. Weng Sun Yat-Sen, University, Guangdong, China.

Most important publications

Writing Group for the TRIGR Study Group, Knip M., Åkerblom H.K., Al Taji E., Becker D., Bruining J., Castano L., Danne T., de Beaufort C., Dosch H.M., Dupre J., Fraser W.D., Howard N., Ilonen J., Konrad D., Kordonouri O., Krischer J.P., Lawson M.L., Ludvigsson J., Madacsy L., Mahon J.L., Ormisson A., Palmer J.P., Pozzilli P., Savilahti E., Serrano-Rios M., Songini M., Taback S., Vaarala O., White NH, Virtanen SM, Wasikowa R.

Effect of hydrolyzed infant formula vs conventional formula on risk of type 1 diabetes: the TRIGR randomized clinical trial.
JAMA. 2018 Jan 2;319(1):38-48. PubMed PMID: 29297078. IF 47,661

Early exposure to complex dietary proteins may increase the risk of type 1 diabetes (T1D) in children with genetic disease susceptibility. In this double-blind randomized clinical trial 2159 infants with human leukocyte antigen–conferred disease susceptibility and a

first-degree relative with T1D were recruited. They received either a casein hydrolysate or a conventional adapted cow's milk formula. Primary outcome was T1D diagnosis. Secondary outcomes included age at diabetes diagnosis and safety. Among infants at risk for T1D, weaning to a hydrolyzed formula compared with a conventional formula did not reduce the cumulative incidence of T1D after median follow-up for 11.5 years.

Palermo A., Fosca M., Tabacco G., Marini F., Graziani V., Santarsia M.C., Longo F., Lauria A., Cesareo R., Giovannoni I., Taffon C., Rocchia M., Manfrini S., Crucitti P., Pozzilli P., Crescenzi A., Rau JV.

Raman spectroscopy applied to parathyroid tissues: a new diagnostic tool to discriminate normal tissue from adenoma.
Anal Chem. 2018 Jan 2;90(1):847-854. PubMed PMID: 29227640. IF 6,042

Primary hyperparathyroidism is an endocrine disorder characterized by autonomous production of parathyroid hormone. Patients with the symptomatic disease should be referred for parathyroidectomy. However, the distinction between the pathological condition and the benign one is very challenging in the surgical setting; therefore, accurate recognition is important to ensure success during minimally invasive surgery. At present, all intraoperative techniques significantly increase surgical time and, consequently, cost. In this proof-of-concept study, Raman microscopy was used to differentiate between healthy parathyroid tissue and parathyroid adenoma from 18 patients. The data showed different spectroscopic features for the two main tissue types of healthy and adenoma. Moreover, the parathyroid adenoma subtypes (chief cells and oxyphil cells) were characterized by their own Raman spectra. The partial least-squares discriminant analysis (PLS-DA) model built to discriminate healthy from adenomatous parathyroid tissue was able to correctly classify all samples in the calibration and validation data sets, providing 100% prediction accuracy. The PLS-DA model built to discriminate chief cell adenoma from oxyphil cell adenoma allowed us to correctly classify >99% of the spectra during calibration and cross-validation and to correctly predict 100% of oxyphil and 99.8% of chief cells in the external validation data set. The results clearly demonstrate the great potential of Raman spectroscopy. The final goal would be development of a Raman portable fiber probe device for intraoperative optical biopsy, both to improve the surgical success rate and reduce surgical cost.

Napoli N., Schwartz AV., Schafer AL., Vittinghoff E., Cawthon PM., Parimi N., Orwoll E., Strotmeyer ES., Hoffman AR., Barrett-Connor E., Black D.M.; Osteoporotic Fractures in Men (MrOS) Study Research Group.

Vertebral fracture risk in diabetic elderly men: The MrOS study.
J Bone Miner Res. 2018 Jan;33(1):63-69. PubMed PMID: 28861910. IF 6,314

Type 2 diabetes (T2DM) is associated with a significant increase in risk of nonvertebral fractures, but information on risk of vertebral fractures (VFs) in subjects with T2DM, particularly among men, is lacking. Furthermore, it is not known whether spine bone mineral density (BMD) can predict the risk of VF in T2DM. We sought to examine the effect of diabetes status on prevalent and incident vertebral fracture, and to estimate the effect of lumbar spine BMD (areal and volumetric) as a risk factor for prevalent and incident morphometric vertebral fracture in T2DM (n = 875) and nondiabetic men (n = 4679). We used data from the Osteoporotic Fractures in Men (MrOS) Study, which enrolled men aged ≥65 years. Lumbar spine areal BMD (aBMD) was measured with dual-energy X-ray absorptiometry (DXA), and volumetric BMD (vBMD) by quantitative computed tomography (QCT). Prevalence (7.0% versus 7.7%) and incidence (4.4% versus 4.5%) of VFs were not higher in T2DM versus nondiabetic men. The risk of prevalent (OR, 1.05; 95% CI, 0.78 to 1.40) or incident vertebral-fracture (OR, 1.28; 95% CI, 0.81 to 2.00) was not higher in T2DM versus nondiabetic men in models adjusted for age, clinic site, race, BMI, and aBMD. Higher spine aBMD was associated with lower risk of prevalent VF in T2DM (OR, 0.55; 95% CI, 0.48 to 0.63) and nondiabetic men (OR, 0.66; 95% CI, 0.5 to 0.88) (p for interaction = 0.24) and of incident VF in T2DM (OR, 0.50; 95% CI, 0.41 to 0.60) and nondiabetic men (OR, 0.54; 95% CI, 0.33 to 0.88) (p for interaction = 0.77). Results were similar for vBMD. In conclusion, T2DM was not associated with higher prevalent or incident VF in older men, even after adjustment for BMI and BMD. Higher spine aBMD and vBMD are associated with lower prevalence and incidence of VF in T2DM as well as nondiabetic men.

Food Science and Nutrition

Head L. De Gara

Faculty L. Dugo, C. Fanali, V. Locato, M. Russo

External Members P. Dugo, E. Marconi, L. Mondello

Description

Research unit interests:
- metabolism in plants and characterization of bio-active phytochemicals with particular attention to antioxidants, oligo- and saccharides;
- Chemical characterization of bioactive compounds in foods employing liquid and gas chromatography techniques.
- Set up of green chemistry techniques for the extraction characterization and purification of bioactive molecule from food and food waste
- validation of multisensorial platform based on electronic sensors for its use on shelf life
- monitoring and food quality assessment;
- in vitro and ex vivo tests evaluating nutritional / health value of food matrixes and nutraceutical compounds;
- Climate change effects on plant growth and productivity - plant signalling in the responses to environmental stresses.
- Food education and scientific divulgation related to food and nutrition

Research unit expertise:
- plant molecular biology and biochemistry, plant and animal cell cultures, analytical chemistry of metabolites with traditional and omics approaches, food chemistry, plant and food biotechnology.

Main research activities

- Prof. Fanali, PI – project granted by AGER2 "VIOLIN – Valorization of Italian Olive products through Innovative analytical tools";
- Prof. De Gara, PI – Project granted by MIUR – PRIN "Adattamento e tolleranza delle piante agli stress abiotici in condizioni ambientali mutevoli".
- Prof De Gara, PI – Project granted by Nestlè Italy "Nutripiatto" a toof of nutritional education for children between 4 to 12 years old

Most important publications

Locato V., Cimini S., De Gara L.

ROS and redox balance as multifaceted players of cross-tolerance: epigenetic and retrograde control of gene expression.
J Exp Bot. 2018 Jun 19; 69(14):3373-3391. PubMed PMID: 29722828. IF 5,354

Retrograde pathways occurring between chloroplasts, mitochondria, and the nucleus involve oxidative and antioxidative signals that, working in a synergistic or antagonistic mode, control the expression of specific patterns of genes following stress perception. Increasing evidence also underlines the relevance of mitochondrion–chloroplast–nucleus crosstalk in modulating the whole cellular redox metabolism by a controlled and integrated flux of information. Plants can maintain the acquired tolerance by a stress memory, also operating at the transgenerational level, via epigenetic and miRNA-based mechanisms controlling gene expression. Data discussed in this review strengthen the idea that ROS, redox signals, and shifts in cellular redox balance permeate the signalling network leading to cross-tolerance. The identification of specific ROS/antioxidative signatures leading a plant to different fates under stress is pivotal for identifying strategies to monitor and increase plant fitness in a changing environment. This review provides an update of the plant redox signalling network implicated in stress responses, in particular in cross-tolerance acquisition. The interplay between reactive oxygen species (ROS), ROS-derived sig.

Dugo L., Tripodo G., Santi L., Fanali C.

Cocoa polyphenols: chemistry, bioavailability and effects on cardiovascular performance.
Curr Med Chem. 2018; 25(37):4903-4917. PubMed PMID: 27655076. IF 3,469

This review gives an overview of the phenolic compounds composition of cocoa beans and their modification during manufacturing processes to the final products. Recently published papers dealing with the qualitative and quantitative analysis of the different classes of cocoa phenolic compounds will be discussed. Modifications of the qualitative profile and amount of phenolic compounds in cocoa after the main processes of production chain, fermentation, drying, roasting, and alkalization, will be described. The second part will focus on some of the biological effects described for cocoa phenolic compounds in vitro and in vivo. In particular, the effects of cocoa flavanols on cardiovascular health and endothelial function have been extensively investigated over the last decades, with interesting results from nutritional intervention trials and molecular studies. A few recent updates on the role of cocoa and chocolate consumption on sport performances will be reported.

Rigano F., Oteri M., Russo M., Dugo P., Mondello L.

Proposal of a linear retention index system for improving identification reliability of triacylglycerol profiles in lipid samples by liquid chromatography methods.
Anal Chem. 2018 Mar 6; 90(5):3313-3320. PubMed PMID: 29380598. IF 6,042

The retention index system was proposed in 1958 by Kováts. It is based on the correlation between the retention time of the analytes and the ones of a series of reference standards, making retention data dependent on the chromatographic phenomenon only, viz., on the three-term interaction analyte-stationary phase-mobile phase. Particularly in GC, because the mobile phase has a negligible influence, the retention of the analytes depends almost entirely on the stationary phase and it is as independent as possible from operating conditions. This makes retention index databases usable in samples identification at both the intra- and interlaboratory levels. The scope of this research was to create a similar identification system in LC, where the identification of unknowns is still a challenge because of the unavailability of spectral databases related to the low reproducibility of mass spectra generated by means of the atmospheric pressure ionization technique normally interfaced to LC. Lipid compounds, specifically triacylglycerols, were selected as target analytes mainly due to their regular chromatographic LC profile under reversed phase conditions. The odd carbon chain number triacylglycerol series from trinonain to trinonadecanoin was chosen as the basis of the retention index scale and a database of 209 triacylglycerols was built. For this purpose an ultra high-performance LC method, able to maximize the baseline separation of triacylglycerols in different real-world samples (vegetable oils, fish, and milk samples) was developed.

Gastroenterology

Head M. Cicala

Faculty S. Emerenziani, M.P.L. Guarino

Other Personnel A. Altomare, P. Balestrieri, M. Ribolsi, L.Trillo, A. Tullio

Description

The Research Unit carries out basic and translational research projects through molecular biology analysis and electrophysiological study of mucosal integrity and of muscle contraction with dedicated devices (Ussing Chamber System for measuring epithelial membrane properties and Radnoti organ bath system, Fig 1-2).

The Gastro-intestinal Laboratory collaborates with several Research Units of the University, such as Food Sciences and Human Nutrition Unit, Nonlinear Physics and Mathematical Modeling Laboratory and Biochemical Laboratory. Through the employment of high-quality instruments (high-resolution manometry and pH-impendance measuring), the GI Unit also conducts clinical research protocols, both spontaneous and sponsored, for the study of pathophysiology and diagnosis of gastro-esophageal reflux disease and esophageal motility disorders.

Main research activities

The GI laboratory focuses on the following research topics: immunomodulation of intestinal motility, modulation of microbiota and effect of prebiotics and probiotics in Health and Gastrointestinal diseases, physio-pathological mechanisms of Inflammatory and functional gastrointestinal disorders (Inflammatory Bowel Disease, Irritable Bowel Syndrome, Paralytic ileus and chronic constipation).

The Clinical Nutrition Unit carries out the following projects: Impact of pre-operative nutritional status on surgical outcome in cancer patients and on nutritional therapy in Inflammatory Bowel Disease patients.

Moreover, the Research Unit carries on several phase II and III clinical trials to test new biological and small molecule agents for the treatment of Crohn disease and Ulcerative Colitis (IBD), and esophageal and ano-rectal motility study with High Resolution manometry in patients affected by Achalasia, Eosinophilic Esophagitis and ano-rectal motor disorders.

Most important publications

Ribolsi M., Cicala M., Zentilin P., Neri M., Mauro A., Efthymakis K., Petitti T., Savarino V., Penagini R.

Prevalence and clinical characteristics of refractoriness to optimal proton pump inhibitor therapy in non-erosive reflux disease.
Aliment Pharmacol Ther. 2018 Nov; 48(10):1074-1081. PubMed PMID: 30294924 IF 7,357

Resistance of gastro-esophageal reflux disease (GERD) symptoms to proton pump inhibitors (PPI) is a challenging problem in practice. To evaluate the prevalence of refractoriness and the contribution of different GERD phenotypes to PPI refractoriness, in this multicenter Italian study frequency and severity of GERD symptoms were evaluated in patients previously classified as non-responders. Non-responders patients also underwent 24-hour multichannel intraluminal impedance-pH monitoring to better define diagnosis. True refractoriness in patients with GERD symptoms attending a secondary care setting is lower than previously reported. Following a careful history and optimal PPI dosing, the rate of refractoriness was 20%. Non-erosive reflux disease constitutes a third of the PPI-refractory group.

Carotti S., Guarino M.P.L., Valentini F., Porzio S., Vespasiani-Gentilucci U., Perrone G., Zingariello M., Gallo P., Cicala M., Picardi A., Morini S.

Impairment of GH/IGF-1 axis in the liver of patients with HCV-related chronic hepatitis.
Horm Metab Res. 2018 Feb; 50(2):145-151. PubMed PMID: 28922679. IF 2,560

In the liver of patients with HCV-related chronic hepatitis, insulin-like growth factor-1 (IGF-1) and signal transducer and activator of transcription (nuclear STAT5-p) positivity scores showed negative correlations with fibrosis stage, while suppressor of cytokine signaling (SOCS-3) score a positive one. The reduction of IGF-1 expression was associated with the serological parameters of liver damage and with the increase of the IGF-1 expression by hepatic stellate cells. IGF-1 expression reduced with fibrosis progression. The inverse correlation between IGF-1 expressed by hepatocytes and by hepatic stellate cells suggests that IGF-1 may exert specific functions in different hepatic cells.

Cremon C., Guglielmetti S., Gargari G., Taverniti V., Castellazzi A.M., Valsecchi C., Tagliacarne C., Fiore W., Bellini M., Bertani L., Gambaccini D., Cicala M., Germanà B., Vecchi M., Pagano I., Barbaro M.R., Bellacosa L., Stanghellini V., Barbara G.

Effect of Lactobacillus paracasei CNCM I-1572 on symptoms, gut microbiota, short chain fatty acids, and immune activation in patients with irritable bowel syndrome: a pilot randomized clinical trial.
United European Gastroenterol J. 2018 May; 6(4):604-613. PubMed PMID: 29881616. IF 3,477

Background: Evidence suggests a role of intestinal microbiota-host interactions in the pathophysiology and symptoms of irritable bowel syndrome (IBS).
Objective: The objective of this article is to assess the effects of Lactobacillus paracasei CNCM I-1572 on clinical and gut microbiota-related factors in IBS.
Methods: We conducted a multicenter, randomized, double-blind, cross-over, 18-week, placebo-controlled, pilot trial assessing the effect of Lactobacillus paracasei CNCM I-1572 on symptoms, gut microbiota composition, fecal short chain fatty acid (SCFA), immunoglobulin A, and cytokines in IBS. The intestinal microbial ecosystem was characterized by 16S rRNA gene profiling.
Results: Forty IBS patients were enrolled from five Italian centers. Lactobacillus paracasei CNCM I-1572 did not significantly improve IBS symptoms, including primary efficacy variables worst abdominal pain/discomfort and IBS degree of relief. Interestingly, Lactobacillus paracasei CNCM I-1572 induced a significant reduction in genus Ruminococcus, dominated by taxa related to Ruminococcus bromii and Ruminococcus callidus, a significant increase in the SCFAs acetate and butyrate, and a significant reduction in the pro-inflammatory cytokine interleukin-15.
Conclusions: This pilot study shows that Lactobacillus paracasei CNCM I-1572 is able to modulate gut microbiota structure/function and reduce immune activation in IBS. As no statistically significant effect on IBS-symptoms was found, further studies are necessary to determine the role of this probiotic in IBS. The study was registered at ClinicalTrials.gov registry under identifier NCT02371499.

General Surgery

Head R. Coppola

Faculty R. Alloni, D. Borzomati, D. Caputo, M. Caricato, P. Crucitti, V. Ripetti

Other Personnel V. Bruni, G. Capolupo, V. La Vaccara, S. Valeri

Description

Surgical Oncology represents the main topic of research of the Unit. Pancreatic, colorectal and lung cancer are the most important investigated diseases. The Unit carries out its activity in the field of both basic and clinical research of the above-mentioned neoplastic conditions. Thyroid endocrine dysfunction of surgical interest are also studied.

Main research activities

- Exploitation of nanoparticle blood interaction for early diagnosis of pancreatic and colorectal cancer.
- AIRC project "Nanoparticle-enabled blood test for pancreatic cancer detection".
- Diagnosis, treatment and control of infections in pancreatic and colorectal cancer.
- Indications, technique and outcome of TaTME,
- Raman spectroscopy for the diagnosis of cancer.
- Anastomotic leak in colorectal surgery: economic analysis of the in-hospital impact.
- Breathprinting and early diagnosis of lung cancer.

Main collaborations

- Department of Molecular Medicine, Sapienza University of Rome;
- Harvard Medical School, Boston MA, USA;
- University of Roma Tre, Rome;
- National Research Council (CNR), Rome;
- Amsterdam Universitair Medische Center, The Netherands;
- University of Hamburg, Germany;
- Pelican Cancer Foundation, UK

Most important publications

Caputo D., Cartillone M., Cascone C., Pozzi D., Digiacomo L., Palchetti S., Caracciolo G., Coppola R.

Improving the accuracy of pancreatic cancer clinical staging by exploitation of nanoparticle-blood interactions: a pilot study.

Pancreatology. 2018 Sep; 18(6):661-665. PubMed PMID: 29914752. IF 2,763

Pancreatic ductal adenocarcinoma (PDAC) early diagnosis is crucial and new, cheap and user-friendly techniques for biomarker identification are needed. "Protein corona" (PC) is emerging a new bio-interface potentially useful in tumor early diagnosis. In a previous investigation, we showed that relevant differences between the protein patterns of PCs formed on lipid NPs after exposure to PDAC and non-cancer plasma samples exist. To extend that research. We performed this pilot study to investigate the effect of PDAC tumor size and distant meta-

stases on PC composition. Twenty PDACs were clinically staged according to the UICC TNM staging system 8 t h Edition. Collected plasma samples were let to interact with lipid NPs; resulting PCs were characterized by SDSPAGE. To properly evaluate changes in the PC, the protein intensity profiles were reduced to four regions of molecular weight: < 25 kDa, 25e50 kDa, 50e120 kDa, > 120 kDa. Results: Data analysis allowed to distinguish T1-T2 cases from T3 and above all from metastatic ones (p < 0.05). Discrimination power was particularly due to a subset of plasma proteins with molecular weight comprised between 25-50 kDa and 50e120 kDa. PC composition is critically influenced by tumor size and presence of distant metastases in PDAC. If our findings will be further confirmed, we envision that future developments of cheap and userfriendly PC-based tools will allow to improve the accuracy of PDAC clinical staging, identifying among resectable PDACs with potentially better prognosis (i.e. T1 and T2) those at higher risk of occult distant metastases.

Pezzuto A., Stellato M., Catania G., Mazzara C., Tonini S., Caricato M., Crucitti P., Tonini G.

Short-term benefit of smoking cessation along with glycopirronium on lung function and respiratory symptoms in mild COPD patients: a retrospective study.

To determine whether quitting smoking, obtained by smoking cessation treatment combined with the use of a new long-acting muscarinic antagonist bronchodilator (LAMA), can improve lung function tests and respiratory symptoms more than the use of LAMA alone we retrospectively evaluated the functional and clinical data of 120 patients who were current smokers affected by mild COPD and who quit smoking using smoking cessation treatment combined with glycopirronium. We compared them with a group of 80 patients with mild COPD undergoing the same treatment but who did not quit smoking. All patients underwent functional and clinical tests at baseline and at a third-month check. The two groups were homogeneous in terms of demographic data without significant differences. All patients used varenicline for smoking cessation. They all performed the following tests: a spirometry with detection of resistances, the 6 min walking test, haemogasanalysis, the exhaled CO test, the COPD assessment test (CAT) and finally the modified Medical Research Council test (mMRC). A significant improvement in the functional tests at the third-month check was found in both groups-quitters and non-quitters. However, a notable increase in the examined parameters was registered in the group of patients who quit smoking, in particular, we observed a significant increase at the third-month check of the parameter forced expiratory volume in 1 s (FEV1) of more than 200 ml with p < 0.001. A comparison between quitters and non-quitters revealed a major benefit derived from smoking cessation in terms of functional changes and symptom relief. In particular, not only FEV1 but also forced expiratory flow at 25%-75% of vital capacity (FEF 25-75) (p < 0.01) and CAT (p < 0.001) were found to be significantly improved in patients who quit than in patients who did not at the check time point.CONCLUSIONS: Smoking cessation treatment obtained by varenicline was confirmed as a crucial therapeutic option, especially when combined with bronchodilator in mild COPD. Patients who quit smoking could already benefit from both treatments in the short term, improving lung function and respiratory symptoms and therefore improving their quality of life.

Rocco G., Pennazza G., Santonico M., Longo F., Rocco R., Crucitti P., Antonelli Incalzi R.

Breathprinting and early diagnosis of lung cancer.

The electronic nose (e-nose) is a promising technology as a useful addition to the currently available modalities to achieve lung cancer diagnosis. The e-nose can assess the volatile organic compounds detected in the breath and derived from the cellular metabolism. Volatile organic compounds can be analyzed to identify the individual chemical elements as well as their pattern of expression to reproduce a sensorial combination similar to a fingerprint (breathprint). The e-nose can be used alone, mimicking the combinatorial selectivity of the human olfactory system, or as part of a multisensorial platform. This review analyzes the progress made by investigators interested in this technology as well as the perspectives for its future utilization.

Geriatrics

Head R. Antonelli Incalzi

Faculty C. Pedone, S. Scarlata

Other Personnel A. Bertini, A. Cavalli, C. Celesti, I. Chiarella, L. Cortese, L. Costanzo, E. Falanga, A. Ferrini, P. Finamore, D. Fontana, F. Galdi, A. Laudisio, D. Lelli, E. Lo Greco, M. Ludovisi, C. Rivera, C. Peccenini, G. Perri, D. Spitaleri, A. Zito

Description

This Unit is made up by researcher and clinicians that bring together their skills to produce cutting-edge scientific evidences and provide the best available care for older people. About 60% of the research is based on the clinical activities carried on by the Unit, while the remaining includes analysis of data from epidemiological studies (such as the InCHIANTI and the SARA study) and systematic reviews and meta-analysis. The lines of research currently ongoing are:

- Evaluation of health status and frailty;
- Evaluation of respiratory function with special focus on the interpretation of spirometric results;
- Evaluation of the diagnostic/prognostic properties of volatile organic compounds (VOCs) in different chronic and acute diseases;
- Development and implementation of system for remote telemonitoring of chronic diseases;
- Evaluation of nutritional intake as a determinant of the health status;
- Assessing the biological bases of and risk factors for antibiotic resistance and its spreading.

Most important publications

Scarlata S., Finamore P., Santangelo S., Giannunzio G., Pennazza G., Grasso S., Santonico M., Incalzi R.A.

Cluster analysis on breath print of newly diagnosed COPD patients: effects of therapy.
J Breath Res. 2018 Jun 8; 12(3):036022. PubMed PMID: 29724960. IF 3,489

Objective: verify to which extent exhaled volatile organic compounds (VOCs) can characterize newly diagnosed COPD patients and change in response to inhaled therapy.
Methods: Fifty newly diagnosed COPD patients were consecutively recruited and VOCs were collected using the Pneumopipe® and analysed by the BIONOTE electronic nose both at baseline and after 12 weeks of inhaled therapy.
Results: BIONOTE identified three clusters of subjects with specific clinical features. Inhaled bronchodilators caused a quantitative reduction in of VOCs profile, while inhaled steroids provided a qualitative modification of the breath print.
Conclusions: VOCs patterns categorize newly diagnosed COPD subjects. VOCs production declines after bronchodilators administration and changes in quality after topic steroid treatment.

Lelli D., Pedone C., Alemanno P., Bertini A., Di Gioia C., Fazzina S., Pennazza G., Santonico M., Grasso S., Zompanti A., Angeletti S., Antonelli Incalzi R.

Voltammetric analysis for fast and inexpensive diagnosis of urinary tract infection: a diagnostic study.
J Transl Med. 2018 Jan 25; 16(1):17. PubMed PMID: 29370807. IF 4,197

Objectives: compare accuracy of voltammetric analysis (VA) and dipstick test (DT) to detect urinary tract infections (UTI), and its usefulness as a second-stage test (SST) in positive DT.
Methods: we enrolled 142 patients. VA was performed using the BIONOTE device.
Results: VA had a better overall performance respect to DT in detecting UTI with accuracy 81.7% vs 75.9%, specificity 90.8% vs 82.5%, similar sensibility. VA had an 82.4% accuracy in discriminating bacterial/fungal infections. Used as a SST, VA had a net specificity of 91.7% and sensitivity 54%.
Conclusion: VA may be used as a second stage after DT to reduce the number of urine culture and of inappropriate antibiotic prescriptions.

Lelli D., Antonelli-Incalzi R., Bandinelli S., Ferrucci L., Pedone C.

Association between sodium excretion and cardiovascular disease and mortality in the elderly: a cohort study.
J Am Med Dir Assoc. 2018 Mar; 19(3):229-234. PubMed PMID: 29042264. IF 5,325

Objective: evaluate the correlation between sodium intake and cardiovascular events (CE) and mortality in community-dwelling older adults.
Methods: we enrolled 920 participants aged ≥65 years, followed-up for 9 years.
Results: There was an increased risk of mortality only below sodium excretion of 6.25 g/d (HR 1.12, 95%CI 1.04-1.22). Stratifying for frailty phenotype, the association was stronger in frail participants (adj HR 1.23, 95%CI 1.02-1.50 vs HR 1.11, 95%CI 1.01-1.22). There was no association with CE.
Conclusion: Reduced sodium excretion is associated with increased mortality, especially among frail participants; high levels are not associated with adverse outcomes.

Gynaecology and Obstetrics

Head R. Angioli

Faculty C. De Cicco Nardone, F. Plotti, C. Terranova

Other Personnel C. Battista, R. Montera, G.B. Serra

Description

The Unit's work is mainly focused on gynecologic oncology, gynecological surgery for both benign and malignant diseases, endoscopy (laparoscopy and hysteroscopy), endometriosis and uro-gynecology.

Main research activities

Our research activity is focused on the identification of biomarkers for the early diagnosis and prognosis of endometrial cancer, on the evaluation of the quality of life of patients affected by gynecological cancers and on the different chemotherapy schemes for cervical cancer. In collaboration with Yale University, we synthesized and characterized polylactic-co-glycolic-acid (PLGA) nanoparticles (NPs) modified with the carboxy-terminal-binding domain of CPE (c-CPE-NP) for the delivery of suicide gene therapy to chemotherapy-resistant ovarian cancer cells. Besides, with the George Mason University and the University of Arizona Cancer Center we explored the kinase-driven metabolic signalling in early and advanced epithelial ovarian cancers, and its role in tumor progression and response to carboplatin-paclitaxel treatment.

Most important publications

Maldonado L., Brait M., Izumchenko E., Begum S., Chatterjee A., Sen T., Loyo M., Barbosa A., Poeta M.L., Makarev E., Zhavoronkov A., Fazio V.M., Angioli R., Rabitti C., Ongenaert M., Van Criekinge W., Noordhuis M.G., de Graeff P., Wisman G.B.A, van der Zee A.G.J., Hoque M.O.

Integrated transcriptomic and epigenomic analysis of ovarian cancer reveals epigenetically silenced GULP1.
Cancer Lett. 2018 Oct 1;433:242-251. PubMed PMID: 29964205. IF 6,491

Many epigenetically inactivated genes involved in ovarian cancer (OC) development and progression remain to be identified. In this study, we undertook an integrated approach that consisted of identification of genome-wide expression patterns of primary OC samples and normal ovarian surface epithelium along with a pharmacologic unmasking strategy using 3 OC and 3 immortalized normal ovarian epithelial cell lines. Our filtering scheme identified 43 OC specific methylated genes and among the 5 top candidates (GULP1, CLIP4, BAMBI, NT5E, TGFβ2), we performed extended studies of GULP1. In a training set, we identified GULP1 methylation in 21/61 (34%) of cases with 100% specificity. In an independent cohort, the observed methylation was 40% (146/365) in OC, 12.5% (2/16) in borderline tumors, 11% (2/18) in cystadenoma and 0% (0/13) in normal ovarian epithelium samples. GULP1 methylation was associated with

clinicopathological parameters such as stage III/IV (p = 0.001), poorly differentiated grade (p = 0.033), residual disease (p < 0.0003), worse overall (p = 0.02) and disease specific survival (p = 0.01). Depletion of GULP1 in OC cells led to increased pro-survival signaling, inducing survival and colony formation, whereas reconstitution of GULP1 negated these effects, suggesting that GULP1 is required for maintaining cellular growth control.

Angioli R., Luvero D., Armento G., Capriglione S., Plotti F., Scaletta G., Lopez S., Montera R., Gatti A., Serra G.B., Benedetti Panici P., Terranova C.

Hormone replacement therapy in cancer survivors: utopia?

As growing of old women population, menopausal women will also increase: an accurate estimation of postmenopausal population is an essential information for health care providers considering that with aging, the incidence of all cancers is expected to increase. Hormone replacement therapy (HRT) has proven to be highly effective in alleviating menopausal symptoms such as hot flashes, night sweats, dyspareunia, sexual disorders, and insomnia and in preventing osteoporosis. According to preclinical data, estrogen and progesterone are supposed to be involved in the induction and progression of breast and endometrial cancers. Similarly, in epithelial ovarian cancer (EOC), the pathogenesis seems to be at least partly hormonally influenced. Is HRT in gynecological cancer survivors possible? The literature data are controversial. Many clinicians remain reluctant to prescribe HRT for these patients due to the fear of relapse and the risk to develop coronary heart disease or breast cancer. Before the decision to use HRT an accurate counselling should be mandatory in order to individualizing on the basis of potential risks and benefits, including a close follow-up. Nevertheless, we do believe that with strong informed consent doctors may individually consider to prescribe some course of HRT in order to minimize menopausal symptoms and disease related to hormonal reduction.

Montera R., Miranda A., Plotti F. Terranova C., Luvero D., Capriglione S., Scaletta G., Zullo M.A., Buscarini M., Lopez S., Gatti A., Schirò T., De Cicco Nardone C., Angioli R.

Anterior colporrhaphy plus inside-out tension-free vaginal tape for associated stress urinary incontinence and cystocele: 10-year follow up results.

AIMS: We report the success rate and complications rate of combined ultralateral anterior Colporrhaphy plus Tension-free Vaginal Tape (TVT-O) in a long-term (10 year) follow-up prospective survey.
METHODS: Patients previously treated for associated stress urinary incontinence (SUI) and cystocele were subjected to annual follow-up for 10 year with a complete urogynecologic evaluation. Furthermore, an urodynamic assessment and a quality of life questionnaire (ICIQ-UI SF) were recorded at the 5th and 10th year of follow up.
RESULTS: Fifty patients treated between June 2004 and May 2006 were included in the analysis. Five patients did not return to 5-yr follow-up: two patients developed a median tape erosion and three patients withdraw. At 10-yr follow-up two more patients withdraw for a total of seven patients lost to follow-up. After 10 years patients objectively cured from cystocele were 41 (95%) while patients objectively cured from SUI were 39 (91%). At 10th year follow-up 38 patients (89%) result cured from both SUI and cystocele, 3 (7%) patients result cured only from prolapse, 1 (2%) patient only from SUI, and 1 (2%) patient result objectively failed for both SUI and cystocele. The ICIQ-UI SF scores at 10th year follow-up was 6.2 ± 3.7. The late complication rate at 10th year follow-up was 32% (OAB symptoms 20%; Mixed incontinence 2%; Bladder outlet obstruction 0%; Dyspareunia 6%; Chronic pelvic pain 0%; Vaginal tape erosion 4%; Detrusor hyperactivity 0%).
CONCLUSIONS: The combined procedures shown proved to be an effective and safe procedure to treat concomitant SUI and cystocele.

Heart Surgery

Head M. Chello

Faculty M. Lusini

External Members F. Nappi, C. Spadaccio

Description

This research unit focuses both on clinical research and on basic, translational and surgical research in the field of cardiac surgery. Current and future research focuses on the clinical evaluation of patients undergoing adult cardiac surgery procedures, with regards to preoperative strategies to reduce complications. Also, intraoperative research on myocardial protection and early postoperative care play a pivotal role in the surgical outcomes and are under continuous development. The preclinical field of research, experienced in aging and in the development of bioresorbable scaffolds and biomaterials, offers parallelism with the clinical research by means of an introduction of materials and methods of research in the surgical scenario. A new area of research has been achieved in the field of safety during cardiac surgery. It is geared to develop a model for analysing and preventing the risk of electric microshock.

Main research activities

Research results focused on the effect of statin in postoperative atrial fibrillation and bleeding (unpublished results), development of an experimental model of the Ross operation and the effect of aging in conduction system. Collaborations with other departments within the institution, such as the Biomaterials and Bioengineering Dept., or other departments in other nstitutions (Centre Cardiologique du Nord, Golden Jubilee National Hospital) set the basis for ongoing researches. Current project include the evaluation of the heart rate variability in ostoperative cardiac surgery patients to prevent atrial fibrillation and complications (submitted for PRIN), effect of statins in postoperative bleeding, degeneration of native and prosthetic aortic valve and their connections with pharmacologic approaches, the role of advanced glycation end products in aging and potential therapeutic approaches in cardiac surgery. In addition, myocardial protection with a detailed cardioplegia protocol comparison and intraoperative bleeding depending on preoperative treatment with newer antiplatelet agents are currently under investigation. In the field of safety uring cardiac surgery a study has been carried out that produced an interesting increase of knowledge, in partnership with Dept. of Astronautics, Electrical and Energetics Engineering of Sapienza University of Rome, and with the Dept. of Technological Innovations and Safety of Power Plants, Apparatus and Human Settlements of INAIL, Italy. The study provides a scientific method, based on quantitative data obtained by models, measurements and literature reviews, to assess the microshock risk during a real surgical intervention.

Most important publications

Nappi F., Nenna A., Petitti T., Spadaccio C., Gambardella I., Lusini M., Chello M., Acar C.
Long-term outcome of cryopreserved allograft for aortic valve replacement.
J Thorac Cardiovasc Surg. 2018 Oct; 156(4):1357-1365.e6. PubMed PMID: 29759737. IF 4,88

Objective: The most efficient surgical approach to severe aortic valve disease in the young adult is still debated: cryopreserved aortic allograft offers excellent hemodynamic and avoid anticoagulation, but long-term durability is influenced by structural valve deterioration (SVD). This study aimed to describe long-term results of aortic allografts and to identify factors influencing long-term durability. **Methods:** From January 1993 to August 2010, 210 patients underwent aortic allograft replacement via the free-hand subcoronary implantation technique (N = 55) or root replacement with coronary reimplantation (N = 155). Clinic and echocardiographic follow-up was updated to April 2016. **Results:** Overall mortality and cardiac mortality occurred in 80 (38.1%) and 64 (30.5%) patients, respectively. Reoperation was required in 69 cases (32.8%), whereas SVD required reoperation in 57 cases (27.1%). No early endocarditis occurred, whereas late endocarditis occurred in 4 patients. The free-hand technique seems to be associated with improved left ventricular remodeling compared with the root-replacement technique, and

smaller allograft size represents a predictor of reoperation independently on the surgical technique used. In the overall population, there were 44 women of childbearing age, and 37 patients remained pregnant during the follow-up of the study. No differences were found in the clinical outcomes among women who had children and who did not. **Conclusions:** Cryopreserved allograft is a valid option, especially in complex infective endocarditis and in women of childbearing age. A careful choice of allograft size and implantation technique can reduce the risk of SVD.

Nappi F., Nenna A., Larobina D., Carotenuto A.R., Jarraya M., Spadaccio C., Fraldi M., Chello M., Acar C., Carrel T.

Simulating the ideal geometrical and biomechanical parameters of the pulmonary autograft to prevent failure in the Ross operation.

Interact Cardiovasc Thorac Surg. 2018 Aug 1; 27(2):269-276. PubMed PMID: 29538653. IF 1,756

Objective: Reinforcements for the pulmonary autograft (PA) in the Ross operation have been introduced to avoid the drawback of conduit expansion and failure. With the aid of an in silico simulation, the biomechanical boundaries applied to a healthy PA during the operation were studied to tailor the best implant technique to prevent reoperation. **Methods:** Follow-up echocardiograms of 66 Ross procedures were reviewed. Changes in the dimensions and geometry of reinforced and non-reinforced PAs were evaluated. Miniroot and subcoronary implantation techniques were used in this series. Mechanical stress tests were performed on 36 human pulmonary and aortic roots explanted from donor hearts. Finite element analysis was applied to obtain high-fidelity simulation under static and dynamic conditions of the biomechanical properties and applied stresses on the PA root and leaflet and the similar components of the native aorta. **Results:** The non-reinforced group showed increases in the percentages of the mean diameter that were significantly higher than those in the reinforced group at the level of the Valsalva sinuses (3.9%) and the annulus (12.1%). The mechanical simulation confirmed geometrical and dimensional changes detected by clinical imaging and demonstrated the non-linear biomechanical behaviour of the PA anastomosed to the aorta, a stiffer behaviour of the aortic root in relation to the PA and similar qualitative and quantitative behaviours of leaflets of the 2 tissues. The annulus was the most significant constraint to dilation and affected the distribution of stress and strain within the entire complex, with particular strain on the sutured regions. The PA was able to evenly absorb mechanical stresses but was less adaptable to circumferential stresses, potentially explaining its known dilatation tendency over time. **Conclusions:** The absence of reinforcement leads to a more marked increase in the diameter of the PA. Preservation of the native geometry of the PA root is crucial; the miniroot technique with external reinforcement is the most suitable strategy in this context.

Spadaccio C., Nenna A., Nappi F., Barbato R., Greco S.M., Nusca A., Sommariva L., Chello M.

Single-territory incomplete surgical revascularization improves regional wall motion of remote ventricular areas: results from a propensity-matched study.

J Geriatr Cardiol. 2018 Jul; 15(7):479-485. PubMed PMID: 30364760. IF 1,581

Objective: Basic science studies demonstrated a general intramyocardial angiogenetic response potentially responsible for the creation of a microvascular neocapillaries network assisting myocardial function. We hypothesized that the benefit provided by the reperfusion of left anterior descending (LAD) territories and the biological angiogenetic drive triggered by the revascularization could translate in a global improvement in ventricular contractility, not restricted to the grafted area. **Methods:** High-risk patients with multivessel coronary artery disease and preoperative wall motion abnormalities were retrospectively analyzed to compare outcomes and regional ventricular function of those who received optimal medical therapy (OMT) versus those who underwent off-pump coronary artery bypass grafting (OPCABG) and received an incomplete myocardial revascularization using left internal mammary artery (LIMA) on LAD (OPCABG group). From January 2007 to December 2014, 206 patients (OMT, n = 136, OPCABG, n = 70) were propensity-score matched to have 70 matched pairs. Variables included in propensity score analyses were ejection fraction (EF), left ventricular end diastolic volume (LVEDVi), EuroSCORE II. Primary endpoint was the variation in the global wall motion score index (ΔWMSI) as evaluated by transthoracic echocardiography. Follow up was completed at 3 years from surgery or hospital discharge. **Results:** Regional analysis of ventricular function revealed a regional WMSI improvement in the OPCABG group not only for LAD territories but also for non-LAD regions, associated with a reduction in the negative left ventricular ischemic remodeling, compared to patients discharged in optimal medical therapy. Global ΔWMSI was negative in OPCABG group (-3.4 ± 2.8%) and positive in the OMT group (5.9 ± 3.1%), indicating a better wall motion score for OPCAB patients. Surprisingly, regional WMSI improved also in non-grafted territories in the off-pump CABG group with a delta value of -3.7 ± 5.3% for left circumflex artery (LCX) area and -3.5 ± 5.4% for right coronary artery (RCA) area. **Conclusions:** In patients with multivessel coronary artery disease, LIMA-to-LAD grafting is associated with an improvement in the WMSI involving also the surrounding non-LAD ungrafted segments and with the attenuation of negative global and regional ischemic ventricular remodeling.

Hematology, Stem Cell Transplantation, Transfusion Medicine and Cellular Therapy

Head G. Avvisati

Faculty M.C. Tirindelli, O. Annibali

Other Personnel D. Armiento, M. Becilli, E. Cerchiara, E.Circhetta, M. De Muro, M. Di Cerbo, S. Ferraro, B. Giannetti, C. Gregorj, F. Landi, A.M. Morgia, C. Nobile, A. Pagano, S. Paolasini, C. Sarlo, A. Scardocci, S. Spurio, M.A. Tafuri, V. Tomarchio

Description

The research unit is involved in several trials on the treatments of adult lymphoproliferative and myeloproliferative disorders and their main complications. Laboratory's Instrumentations to perform research activities are located by the Policlinic Blood Bank.

Main collaborations

- International Extranodal Lymphoma Study Group (IELSG), Switzerland;
- Italian Group of Hematologic Diseases in the Adult (GIMENA), Italy;
- Italian Lymphoma Foundation, Italy;
- Rome Transplant Network (RTN), Italy.

Main research activities

The Unit, as member of the Rome transplant network (RTN), performs autologous hematopoietic stem cells (HSC) transplantation and, in collaboration with the Urology Unit, has a leading national position in the treatment of severe resistant hemorrhagic cystitis, which may appear in these patients. In addition, the unit participate in several clinical Trials, proposed by the following cooperative Group: FIL (Fondazione Italiana Linfomi), IELSG (International Extranodal Lymphoma Study Group), GIMEMA (Gruppo Italiano Malattie Ematologiche dell'Adulto). Moreover, in cooperation with the Orthopaedic and Trauma Surgery Unit, performs research studies on the use of platelet rich plasma in degenerative articular pathologies. Furthermore, the unit is deeply involved in a multicentre cytofluorimetric standardization project for the detection of circulating endothelial cells (CEC) and their progenitors (endothelial progenitor cells: EPC). Finally, in cooperation with the Virology Unit, is conducting a study dealing with CMV reactivation in HSC transplanted patients. The Unit collaborates with the Computer Systems and Bioinformatics of this University to develop a mobile App for monitoring of side effects during treatment with kinase inhibitors in chronic lymphoproliferative diseases. In addition, the unit collaborate with the Pathology Unit for the study of PD-1/PD-L1 axis in lymphoproliferative diseases. The head of the Unit has a leading international role in the treatment of acute promyelocytic leukemia and from January 2008 to December 2013 has served as a member of the editorial board of Blood (official journal of the American Society of Hematology).

Most important publications

Annibali O., Crescenzi A., Tomarchio V., Pagano A., Bianchi A., Grifoni A., Avvisati G.

PD-1 /PD-L1 checkpoint in hematological malignancies.
Leuk Res. 2018 Apr;67: 45-55. PubMed PMID: 29428449. IF 2,319

Programmed cell death protein 1 (PD-1), is a cell surface receptor with an important role in down-regulating the immune system and promoting self-tolerance by suppressing T cell inflammatory activity. PD-1/PDL1 axis represents a checkpoint to control immune responses and it is often used as a mechanism of immune escaping by cancers and infectious diseases. Many data demonstrate its important role in solid tumors and report emerging evidences in lymphoproliferative disorders. In this review, we summarized the available data on the role of PD-1/PD-L1 checkpoint in lymphoproliferative diseases and the therapeutics use of monoclonal blocking antibodies.

Annibali O., Piccioni L., Tomarchio V., Circhetta E., Sarlo C., Franceschini L., Cantonetti M., Rizzo E., Angeletti S., Tirindelli M.C., Scagnolari C., Statzu M., Avvisati G., Riva E.

Impact of IFN lambda 3/4 single nucleotide polymorphisms on the cytomegalovirus reactivation in autologous stem cell transplant patients.
PLoS One. 2018 Jul 23; 13(7):e0200221. PubMed PMID: 30036376. IF 2,766

Cytomegalovirus (CMV) infection represents one of the main cause mortality after Stem Cell Transplantation. Recently, a protective effect of the T allele of rs12979860 IL28B Single Nucleotide Polymorphisms (SNPs) against CMV infection in the allogenic stem cell transplantation was suggested. We investigate whether the rs12979860 IL28B SNP and the relative rs368234815 (IFNλ4) genotype may affect the incidence of active CMV infection in Autologous stem cell transplantation (Auto-SCT) setting. The study included 99 patients who underwent to Auto-SCT. IL28 and IFNΔ4 SNPs were correlated with CMV reactivation along with other clinical and treatment parameters. CMV reactivation by CMV DNAemia was evaluated once a week until day 100 from Auto-SCT. CMV reactivation was documented in 50% (TT-ΔG/ΔG), 35% (CC-TT/TT) and 29.2% (CT-TT/ΔG) of the patients respectively. No differences in CMV copies number were recorded at reactivation between different IL28/IFNλ4 genotypes. The analysis of patients older than 60 years showed a significantly higher incidence of active CMV infection in the TT-ΔG/ΔG (83%) population with respect to CC-TT/TT (21%) and CT-TT/ΔG (40%) patients. Our data suggest a negative role of TT-ΔG/ΔG genotype in the CMV reactivation in Auto-SCT. The exposure to rituximab and the pre-infusion presence of anti CMV IgG also significantly influenced CMV reactivation.

Majore S., Bonaccorsi di Patti M.C., Valiante M., Policelli F., Cortese A., Di Bartolomeo S., De Bernardo C., De Muro M., Faienza F., Radio F.C., Grammatico P., Musci G.

Characterization of three novel pathogenic SLC40A1 mutations and genotype/phenotype correlations in 7 Italian families with type 4 hereditary hemochromatosis.
Biochim Biophys Acta Mol Basis Dis. 2018 Feb; 1864(2):464-470. PubMed PMID: 29154924. IF 5,108

Mutations of SLC40A1 encoding ferroportin (Fpn), the unique cellular iron exporter, severely affect iron homeostasis causing type 4 hereditary hemochromatosis, an autosomal dominant iron overload condition with variable phenotypic manifestations. This disease can be classified as type 4A, better known as "ferroportin disease", which is due to "loss of function" mutations that lead to decreased iron export from cells, or as type 4B hemochromatosis, which is caused by "gain of function" mutations, conferring partial or complete resistance to hepcidin-mediated Fpn degradation. In this work, we discuss clinical and molecular findings on a group of patients in whom a SLC40A1 single copy missense variant was identified. Three novel variants, p.D181N, p.G204R and p.R296Q were functionally characterized. Fpn D181N and R296Q mutants can be classified as full or partial loss of function, respectively. Replacement of G204 with arginine appears to cause a more complex defect with impact both on iron export function and hepcidin sensitivity. This finding confirms the difficulty of predicting the effect of a mutation on the molecular properties of Fpn in order to provide an exhaustive explanation to the wide variability of the phenotype in type 4 hereditary hemochromatosis.

Hygiene, Public Health and Statistics

Head T. Petitti

Faculty A. Ianni

Other Personnel A. Picchia (Fondazione don Carlo Gnocchi ONLUS)

Description

Main research interests include:

- Methodological and operational support to the research unit of the Faculty of Medicine and other national research institutions for the definition of the research protocol activities, collection and organization of data, analysis and presentation of results;
- Models data scouting and data analysis of hospital current database (management and clinical) with the objective of identifying useful indicators to management and clinicians.
- Evaluation of Outcomes of innovative rehabilitative pathways (both in technological and organizational terms) in the field of subacute and chronic disability.

Main research activities

In 2018 collaborations with internal research groups at the Campus Bio-Medico University of Rome (General Surgery, Digestive Endoscopy, Respiratory Pathophysiology, Medical Imaging, Nursing, Cardiac Surgery, Pediatrics) as well as National and European research institutions (National Cancer Institute - IRCCS "Fondazione G. Pascale" - Naples; Department of Public Health, Section of Hygiene, Catholic University of the Sacred Heart – Rome; Hopital de Hautepierre, Strasbourg; Hôpital Européen Georges Pompidou, Paris; Humanitas Research Hospital, Milan, IRCCS Fondazione don Carlo Gnocchi ONLUS) were initiated. As part of these collaborations there are ongoing scientific studies that have produced results published in national and international journals in 2018 and are currently being published.

Main collaborations

- Department of Public Health, Section of Hygiene, Catholic University of the Sacred Heart – Rome;
- Hôpital Européen Georges Pompidou, Paris, France;
- Hospital de Hautepierre, Strasbourg, France;
- Humanitas Research Hospital, Milan,
- IRCCS "Fondazione G. Pascale", Naples.
- IRCCS Fondazione don Carlo Gnocchi ONLUS, Rome.
- National Cancer Institute.

Most important publications

Nappi F., Nenna A., Petitti T., Spadaccio C., Gambardella I., Lusini M., Chello M., Acar C.

Long-term outcome of cryopreserved allograft for aortic valve replacement.
J Thorac Cardiovasc Surg. 2018 Oct;156(4):1357-1365.e6. PubMed PMID: 29759737. IF 4,88

Objective: The most efficient surgical approach to severe aortic valve disease in the young adult is still debated: cryopreserved aortic allograft offers excellent hemodynamic and avoid anticoagulation, but long-term durability is influenced by structural valve deterioration (SVD). This study aimed to describe long-term results of aortic allografts and to identify factors influencing long-term durability. **Methods:** From January 1993 to August 2010, 210 patients underwent aortic allograft replacement via the free-hand subcoronary implantation technique (N = 55) or root replacement with coronary reimplantation (N = 155). Clinic and echocardiographic follow-up was

updated to April 2016. **Results:** Overall mortality and cardiac mortality occurred in 80 (38.1%) and 64 (30.5%) patients, respectively. Reoperation was required in 69 cases (32.8%), whereas SVD required reoperation in 57 cases (27.1%). No early endocarditis occurred, whereas late endocarditis occurred in 4 patients. The free-hand technique seems to be associated with improved left ventricular remodeling compared with the root-replacement technique, and smaller allograft size represents a predictor of reoperation independently on the surgical technique used. In the overall population, there were 44 women of childbearing age, and 37 patients remained pregnant during the follow-up of the study. No differences were found in the clinical outcomes among women who had children and who did not. **Conclusions:** Cryopreserved allograft is a valid option, especially in complex infective endocarditis and in women of childbearing age. A careful choice of allograft size and implantation technique can reduce the risk of SVD.

Artico M., Dante A., D'Angelo D., Lamarca L., Mastroianni C., Petitti T., Piredda M., De Marinis M.G.

Prevalence, incidence and associated factors of pressure ulcers in home palliative care patients: a retrospective chart review.
Palliat Med. 2018 Jan;32(1):299-307. PubMed PMID: 29130416. IF 3,780

Background: Terminally ill patients are at high risk of pressure ulcers, which have a negative impact on quality of life. Data about pressure ulcers' prevalence, incidence and associated factors are largely insufficient. **Aim:** To document the point prevalence at admission and the cumulative incidence of pressure ulcers in terminally ill patients admitted to an Italian home palliative care unit, and to analyse the patients' and caregivers' characteristics associated with their occurrence. **Design:** Retrospective chart review. Setting/participants: Patients (n = 574) with a life expectancy ≤6 months admitted to a palliative home care service were included in this study. **Results:** The prevalence and incidence rates were 13.1% and 13.0%, respectively. The logistic regression models showed body mass index (p < 0.001), Braden score at risk (p < 0.001), Karnofsky Performance Scale index <30 (p < 0.001), patients' female gender, patients' age >70 and >1 caregiver at home as the dichotomous variables predictors of presenting with a pressure ulcer at time of admission and during home palliative care. **Conclusion:** The notable pressure ulcers' incidence and prevalence rates suggest the need to include this issue among the main outcomes to pursue during home palliative care. The accuracy of body mass index, Braden Scale and Karnofsky Performance Scale in predicting the pressure ulcers risk is confirmed. Therefore, they appear as essential tools, in combination with nurses' clinical judgment, for a structured approach to pressure ulcers prevention. Further research is needed to explore the home caregivers' characteristics and attitudes associated with the occurrence of pressure ulcers and the relations between their strategies for pressure ulcer prevention and gender-related patient's needs.

Artico M., D'Angelo D., Piredda M., Petitti T., Lamarca L., De Marinis M.G., Dante A., Lusignani M., Matarese M.

Pressure injury progression and factors associated with different end-points in a home palliative care setting: a retrospective chart review study.
J Pain Symptom Manage. 2018 Jul;56(1):23-32. PubMed PMID: 29548891. IF 3,249

Context: Patients with advanced illnesses show the highest prevalence for pressure injuries. In the palliative care setting, the ultimate goal is injury healing, but equally important is wound maintenance, wound palliation (wound-related pain and symptom management), and primary and secondary wound prevention. **Objectives:** To describe the course of healing for pressure injuries in a home palliative care setting according to different end-points, and to explore patient and caregiver characteristics and specific care activities associated with their achievement. **Methods:** Four-year retrospective chart review of 669 patients cared for in a home palliative care service, of those 124 patients (18.5%) had at least one pressure injury with a survival rate less than or equal to six months. Results: The proportion of healed pressure injuries was 24.4%. Of the injuries not healed, 34.0% were in a maintenance phase, whereas 63.6% were in a process of deterioration. Body mass index (P = 0.0014), artificial nutrition (P = 0.002), and age <70 years (P = 0.022) emerged as predictive factors of pressure injury complete healing. Artificial nutrition, age, male caregiver (P = 0.034), and spouse (P = 0.036) were factors significantly associated with a more rapid pressure injury healing. Continuous deep sedation was a predictive factor for pressure injury deterioration and significantly associated with a more rapid worsening. **Conclusion:** Pressure injury healing is a realistic aim in home palliative care, particularly for injuries not exceeding Stage II occurring at least two weeks before death. When assessing pressure injuries, our results highlight the need to also pay attention to artificial nutrition, continuous deep sedation, and the caregiver's role and gender.

Institute of Philosophy of Scientific and Technological Practice (FAST)

Head L. Borghi

Faculty M. Bertolaso, G. Ghilardi, G. La Monaca, V. Tambone

Other Personnel G. Andronico, S. Anzilotti, M. Barone, C. Beneduce, L. Campanozzi, N. Di Stefano, R. Esposito, A. Marchetti, G. Mottini, P. Pellegrino, M. Pennacchini, A. Pensotti, M.T. Russo, A. Sisto

Board M. T. Bettetini, F. Keller, G. Tanzella-Nitti

Description

The Institute coordinates the University's Educational and research activities in the Humanities: Anthropology, Ethics, Aesthetics, Professional Ethics, General Bioethics, Clinical Bioethics, Moral Philosophy, Logic and Philosophy of Science, Forensic Medicine, History of Medicine, History of Science and Technology, Social Psychology and Social Medicine.

FAST's education and research are conducted via interdisciplinary work, carried out both within the borders of the Campus Bio-Medico University and in collaboration with other Institutions, with the scope of creating a dialogue between philosophers, researchers and teachers of the various scientific and technological disciplines.

Main research activities

Mauro Barone
- Appearance Pain: definition, disease classification, literature review, creation, development and validation of a self-assessment questionnaire.

Chiara Beneduce
- Personalized Medicine. A Multidisciplinary Approach to Complexity.

Marta Bertolaso
- Research project "Hospital_4.0: towards a new model of care integrating territorial needs with emerging technologies in the service of people".

Luca Borghi
- Setting up of the UCBM historical archive and publication of a monograph on the origins and first developments of this University with Dr. Giulia Andronico.

Laura Campanozzi
- Collaboration with McGill University (Montreal) on the teaching of clinical reasoning in medical schools.

Nicola Di Stefano
- Collaboration with NextLab on topics related to neurosciences, robotics and music.

Giampaolo Ghilardi
- Ethics of scientific and technological practice, applying the research to the fields of zygote ontology and free will.

Most important publications

Plutynski A., Bertolaso M.

What and how do cancer systems biologists explain?
Philosophy of Science 2018; 85(5):942-954. DOI: 10.1086/699716 IF 0,973

In this article, it is argued that there are very different research projects falling under the heading of "systems biology of cancer." While sharing some general features, they differ in their aims and theoretical commitments. It is also argued that some explanations in systems biology of cancer are concerned with properties of signaling networks (i.e. robustness; fragility) and how they may play an important causal role in patterns of vulnerability to cancer. Further, some systems biological explanations are compelling illustrations of how "top-down" and "bottom-up" approaches to the same phenomena may be integrated.

Borghi L., Marchetti A.

Introducing the trained and educated gentlewoman into the wards of a children's hospital. The role of Charles West M.D. (1816-1898) in the rise of pediatric nursing.
Medicina Historica 2018; 2(2): 63-74.

Charles West (1816-1898), the well-known pioneer of pediatrics, had a fundamental role in the birth and first development of pediatric nursing. His initiatives (most notably the establishment of the first pediatric hospital in London, the Great Ormond Street Hospital for Sick Children) and his ideas on nursing were often misunderstood and opposed by his contemporaries. Nowadays they appear to us very relevant and forward-looking, centered as they are on the rigorous selection and the full human and professional training of the new nurses for "sick children". He also played a fundamental role in the professional education and advancement of one of the leading figures of early pediatric nursing: Catherine Jane Wood.

Keller, F., Di Stefano, N.

The robustness of musical language: a perspective from complex systems theory.
In: Bertolaso M., Caianiello S., Serrelli E., (Eds). Biological robustness. Emerging perspectives from within the life sciences. Springer, Cham, 2018, pp. 207-217. DOI: 10.1007/978-3-030-01198-7_11

In this chapter, we consider music as a peculiar complex system, involving both the realm of machines (the musical instrument) and the realm of biology (the player and the listeners). We provide examples of the human ability of isolating and maintaining stable information within the perceptual flow and despite changes in the external world. Finally, a list of four multiple interaction cycles that typically characterize music experience is presented and discussed.

Internal Medicine and Hepatology

Head A. Picardi

Faculty U. Vespasiani Gentilucci

Other Personnel A. De Vincentis, G. Galati, P. Gallo

Description

Our Unit is involved in both spontaneous and collaborative clinical studies on internal medicine (poly-pathology & therapies; drug interactions), and on liver disease (non-alcoholic steatohepatitis, HCC, cirrhosis). Collaborative studies are coordinated by scientific societies such as the Italian Society of Internal Medicine (SIMI) and the Italian Association for the Study of the Liver (AISF). We are also involved in sponsored clinical RCTs on new drugs for the treatment of NASH and of primary biliary cholangitis (PBC). Of particular interest is a scientific collaboration with the Club of the Hospital Hepatologist (CLEO), a scientific association with a wide almost national diffusion. Main scientific collaborations involve other Units from our University; the Department of Molecular and Clinical Medicine of the University of Gothenburg, Sweden; the University of Navarra, Spain; IRCCS Bambino Gesù Paediatric Hospital, Italy, and the University "Tor Vergata" in Rome.

Main research activities

We obtained essential advances in understanding the pathogenic role of predisposing factors by combining genetic and acquired factors in a risk score for NAFLD evolution toward NASH, and the pathogenic role of gut microbiota in NAFLD. In the field of cirrhosis, more relevant achievements considered platelet count in the definition of the risk of major bleedings; the pathogenic role of GH –IGF-1 axis and the effects of HCV eradication by means of the new direct antiviral agents (DAA) on HCC recurrence/occurrence. Internist investigations regarded atrial fibrillation and COPD as determinants of major cardiovascular event risk; the prognostic role of renal function evaluation at hospital admission for defining in-hospital and after discharge mortalities in elder patients; and the correlation of ALT levels with frailty in the Elderly. In-House collaborations are set with the areas of Geriatrics and the Unit of Electronics for Sensor Systems, Department of Engineering.

Main collaborations

- Italian Society of Internal Medicine (SIMI);
- Italian Association for the Study of the Liver (AISF);
- Club of the Hospital Hepatologist (CLEO);
- Dep. of Molecular and Clinical Medicine of the University of Gothenburg, Sweden;
- University of Navarra, Spain;
- IRCCS Bambino Gesù Paediatric Hospital, Italy
- University "Tor Vergata", Rome.

Most important publications

Basili S., Raparelli V., Napoleone L., Talerico G., Corazza G.R., Perticone F., Sacerdoti D., Andriulli A., Licata A., Pietrangelo A., Picardi A., Raimondo G., Violi F.

Platelet count does not predict bleeding in cirrhotic patients: results from the PRO-LIVER study.
Am J Gastroenterol. 2018 Mar;113(3):368-375. PubMed PMID: 29257146. IF 10,231

Thrombocytopenia is a hallmark for patients with cirrhosis, perceived as a risk factor for bleeding events. However, the relationship between platelet count and bleeding is still unclear. 280 cirrhotic patients followed up for a median of 1,129 days yielded 953.12 patient-year of observation. The annual rate of any significant bleeding was 5.45%/year; 52 (18.6%) patients experienced major or minor bleeding events from gastrointestinal origin. Platelets were similar in patients with major or minor bleedings. Conversely, INR was slightly higher in patients with overall or major bleeding. In conclusion, platelet count does not predict unprovoked major or minor bleeding in cirrhotic patients.

Vespasiani-Gentilucci U., De Vincentis A., Ferrucci L., Bandinelli S., Antonelli Incalzi R., Picardi A.

Low alanine aminotransferase levels in the elderly population: frailty, disability, sarcopenia, and reduced survival.
J Gerontol A Biol Sci Med Sci. 2018 Jun 14;73(7):925-930. PubMed PMID: 28633440. IF 4,902

Low ALT were associated with poor outcomes in elders. Data refer to 765 pts (75.3 YO, † 61.8%). Frailty defined by Fried criteria, sarcopenia by peripheral Quantitative-CT, disability as self-reported need for help. ALT associated inversely with frailty, sarcopenia, disability, and pyridoxine. Higher ALT was confirmed to be protective respect to overall and cardiovascular mortality (overall HR 0.98 [0.96-1], p = .02; cardiovascular: 0.94 [0.9-0.98], p < .01). The association of ALT activity and mortality was J-shaped. Our results suggest that reduced ALT levels in elders can be considered as a marker of frailty, disability, and sarcopenia, and as an independent predictor of adverse outcomes.

Gallo P., De Vincentis A., Pedone C., Nobili A., Tettamanti M., Gentilucci U.V., Picardi A., Mannucci P.M., Incalzi R.A., REPOSI Investigators.

Prognostic relevance of glomerular filtration rate estimation obtained through different equations in hospitalized elderly patients.
Eur J Intern Med. 2018 Aug; 54:60-64. PubMed PMID: 29650358. IF 3,282

eGFR reductions associate with in-hospital and after discharge mortalities. The best method for estimating GFR is vague. We compared prognostic values of different formulas in predicting the risk of in-hospital morbid-mortality. 4621 pts were included; 4.2% died in-hospital, 14.2% within 90 days from discharge. On admission eGFR > 60 ml/min/1.73m2 associates with very low risk of overall mortality. eGFR < 60 ml/min/1.73 m2 was associated with unfavourable outcomes, although with a poor level of accuracy (AUC 0.60-0.66). We found no difference in predictive power among 4 common equations. Physicians should be aware of eGFR prognostic role in a comprehensive assessment of elderly in-patients.

Measurements and Biomedical Instrumentation

Head S. Silvestri

Faculty E. Schena

Other Personnel A. Carnevale, J. Di Toccom, D. Lo Presti, C. Massaroni

Description

The Research Unit scientific activity is mainly focused on measurements and measurement systems for clinical diagnostics and applied to human wellbeing. The research activity is particularly focused on the development of novel sensors and measurement systems for measuring forces, gas flow-rate, cardiac output, temperature, human motion, optical absorption and respiratory parameters. The research unit realized instruments for the respiratory simulation and performance testing of artificial ventilators and optoelectronic systems dedicated to respiratory mechanics along with uncertainty evaluation. Researches are carried out on novel modalities and procedures to obtain measurements and/or information from physio-pathological processes, opto-mechanical variables, wearable system for vital signs monitoring, performance assessment and quality evaluation of medical instruments and their clinical efficacy with a particular emphasis on non-invasive processes.

Main research activities

The research activity has been focused on innovative methods to obtain a temperature map of organs by means of invasive and contactless methods, innovative MR-compatible optical fibre sensors for medical applications, wearable systems for vital signs monitoring and experimental estimation of tissue optical properties for modelling laser-tissue interaction. During the last two years, five research projects have been funded by national and international agencies.

Most important publications

Di Matteo F.M., Saccomandi P., Martino M., Pandolfi M., Pizzicannella M., Balassone V., Schena E., Pacella C.M., Silvestri S., Costamagna G.

Feasibility of EUS-guided Nd:YAG laser ablation of unresectable pancreatic adenocarcinoma.
Gastrointest Endosc. 2018 Jul;88(1):168-174.e1. PubMed PMID: 29452076. IF 7,204

Background and Aims: EUS has become an interventional technique in which a needle may be used as a vehicle to deliver therapeutic agents. Laser ablation (LA) has been used to treat many primary and secondary neoplasms. This study aimed to assess the feasibility of EUS-guided LA for unresectable (UR) pancreatic cancer. Methods: Patients with stage IIb-III pancreatic cancer underwent EUS-guided LA. All patients were unresponsive to previous chemoradiotherapy. LA was performed by using a 300-μm flexible fiber preloaded onto

a 22-gauge fine needle. A 1064-nm wavelength neodymium-yttrium aluminum garnet (Nd:YAG) laser light with different power settings of 2 W for 800 J, 1000 J, and 1200 J; 3 W for 800 J, 1000 J, and 1200 J; and 4 W for 800 J, 1000 J, and 1200 J was used. Each patient was treated with a single application of 1 of these settings. The application time of the power settings ranged from 200 to 600 seconds. Results: Nine patients (median age, 74.7; range 55-85) underwent Nd:Yag LA. The mean size of the focal lesion was 35.4 mm (range, 21-45). The ablation area, demonstrated by 24-hour CT, ranged from 0.4 cm3 (for the lower power setting of 2 W/800 J) to a maximum of 6.4 cm3 (for 4 W/1000 J). The procedure was completed in all 9 patients without adverse events. Conclusion: In our human experience, EUS-guided LA was feasible and well tolerated in patients with UR pancreatic cancer.

Massaroni C., Venanzi C., Silvatti A.P., Lo Presti D., Saccomandi P., Formica D., Giurazza F., Caponero M.A., Schena E.

Smart textile for respiratory monitoring and thoraco-abdominal motion pattern evaluation.
J Biophotonics. 2018 May;11(5):e201700263. PubMed PMID: 29297202. IF 3,768

The use of wearable systems for monitoring vital parameters has gained wide popularity in several medical fields. The focus of the present study is the experimental assessment of a smart textile based on 12 fiber Bragg grating sensors for breathing monitoring and thoraco-abdominal motion pattern analysis. The feasibility of the smart textile for monitoring several temporal respiratory parameters (ie, breath-by-breath respiratory period, breathing frequency, duration of inspiratory and expiratory phases), volume variations of the whole chest wall and of its compartments is performed on 8 healthy male volunteers. Values gathered by the textile are compared to the data obtained by a motion analysis system, used as the reference instrument. Good agreement between the 2 systems on both respiratory period (bias of 0.01 seconds), breathing frequency (bias of −0.02 breaths/min) and tidal volume (bias of 0.09 L) values is demonstrated. Smart textile shows good performance in the monitoring of thoraco-abdominal pattern and its variation, as well.

Massaroni C., Lopes D.S., Lo Presti D., Schena E., Silvestri S.

Contactless monitoring of breathing patterns and respiratory rate at the pit of the neck: a single camera approach.
J Sens. 2018; ID 4567213. DOI: 10.1155/2018/4567213 IF 2,057

Vital signs monitoring is pivotal not only in clinical settings but also in home environments. Remote monitoring devices, systems, and services are emerging as tracking vital signs must be performed on a daily basis. Different types of sensors can be used to monitor breathing patterns and respiratory rate. However, the latter remains the least measured vital sign in several scenarios due to the intrusiveness of most adopted sensors. In this paper, we propose an inexpensive, off-the-shelf, and contactless measuring system for respiration signals taking as region of interest the pit of the neck. The system analyses video recorded by a single RGB camera and extracts the respiratory pattern from intensity variations of reflected light at the level of the collar bones and above the sternum. Breath-by-breath respiratory rate is then estimated from the processed breathing pattern. In addition, the effect of image resolution on monitoring breathing patterns and respiratory rate has been investigated. The proposed system was tested on twelve healthy volunteers (males and females) during quiet breathing at different sensor resolution (i.e., HD 720, PAL, WVGA, VGA, SVGA, and NTSC). Signals collected with the proposed system have been compared against a reference signal in both the frequency domain and time domain. By using the HD 720 resolution, frequency domain analysis showed perfect agreement between average breathing frequency values gathered by the proposed measuring system and reference instrument. An average mean absolute error (MAE) of 0.55 breaths/min was assessed in breath-by-breath monitoring in the time domain, while Bland-Altman showed a bias of −0.03 ± 1.78 breaths/min. Even in the case of lower camera resolution setting (i.e., NTSC), the system demonstrated good performances (MAE of 1.53 breaths/min, bias of −0.06 ± 2.08 breaths/min) for contactless monitoring of both breathing pattern and breath-by-breath respiratory rate over time.

Medical Statistics and Molecular Epidemiology

Head M. Ciccozzi

Other Personnel D. Benvenuto, C. Deflora, C. Leuter, L. Navarini

External Members I. Alexiev, R. Bazzardi, A. Borsetti, G. Ceccarelli, B. Demir, A. Lai, B. Mugosa, C. Sagnelli, M. Salemi, G. el Sawaf, G. Zehender

Description

The research unit is actively interested in research studies aimed to investigate epidemics and nosocomial infection biomarkers involved in the diagnosis and prognosis of communicable and non-communicable disease. Further fields of research included the molecular evolution of microorganisms causing important epidemic in Italy as well as worldwide and the antimicrobial resistant microorganisms circulating in nosocomial setting. Furthermore, the activity of the research unit was extended also to the evaluation of public health in Migrants subjects. The statistical analysis is also extended to different research groups in Italy in different studies.

Main research activities

In the year 2018, the most important activities developed by the research unit have been in the areas of evolution of infectious disease and antibiotic resistance. Statistical collaboration and epidemiology has been established with several Unit of Internal medicine, Surgery and Geriatrics of the University Hospital Campus Bio-Medico. Migrants has been an important chapter for epidemiological research, developing epidemiological surveillance system in different center for Migrants were agreement has been signed (CARA Centre of Castelnuovo di Porto and Rocca di Papa). The results of the surveillance reported in some publication on international peer-reviewed scientific journals. The unit have been also participate in resolving epidemics I Italy (Chikungunya) so as worldwide as reported in some publications. Other important agreement have been continued since 2015 with the Public Health Institute of Montenegro, the Public Institute of Bulgaria (Sofia) and with the Department of Pathology and Laboratory medicine of the University of Florida, Gainesville, USA. By these agreements, several scientific publications on international and peer-reviewed journals have been published and new scientific collaborations are ongoing. Moreover we are also consultant for WHO for nosocomial surveillance system I Montenegro. We are also finalizing scientific agreement with the University of Izmir (Turkey) and of Alessandria of Egypt for study epidemics and nosocomial infection. The unit published in 2018 29 articles in international journals.

Main collaborations

- Public Health Institute of Montenegro;
- Public Institute of Bulgaria, Sofia, Bulgaria;
- University of Alessandria, Egypt;
- University of Florida, Gainesville, USA;
- University of Izmir, Turkey.

Most important publications

Cella E., Foley B.T., Riva E., Scolamacchia V., Ceccarelli G., Vita S., Iannetta M., Ciardi MR., D'Ettorre G., Angeletti S., Ciccozzi M.

HIV-2 infection in a migrant from Gambia: the history of the disease combined with phylogenetic analysis revealed the real source of infection.
AIDS Res Hum Retroviruses. 2018 Aug 15; 34(12):1090-1094. PubMed PMID: 29954191. IF 1,935

Human immunodeficiency virus type 2 (HIV-2) infection prevalence is increasing in some European countries. The increasing migratory

flow from countries where HIV-2 is endemic has facilitated the spread of the virus into Europe and other regions. We describe a case of HIV-2 infection in a migrant individual in the Asylum Seekers Centre (ASC) in Italy. The patient's virus was sequenced and found to be a typical HIV-2 genotype A virus. Bayesian evolutionary analysis revealed that the HIV-2 sequence from migrant dated back to 1986 in a subcluster, including sequences from Guinea Bissau. This was coherent with the history of the migrant who lived in Guinea Bissau from his birth until 1998 when he was 13 years old. Monitoring for HIV-2 infection in migrants from western Africa is necessary using adequate molecular tools to improve the diagnosis and understand the real origin of infection.

Angeletti S., Cella E., Prosperi M., Spoto S., Fogolari M., De Florio L., Antonelli F., Dedej E., De Flora C., Ferraro E., Incalzi R.A., Coppola R., Dicuonzo G., Francescato F., Pascarella S., Ciccozzi M.

Multi-drug resistant Pseudomonas aeruginosa nosocomial strains: molecular epidemiology and evolution.

Pseudomonas aeruginosa causes a wide variety of nosocomial infections. In the study, phylogenetic, selective pressure analysis and homology modelling were applied to oprD efflux pump gene with the aim to characterize multi-drug resistant strains circulating in the nosocomial setting, their transmission dynamics and ongoing evolution. One hundred ninety-three consecutive inpatients with Pseudomonas aeruginosa infection were enrolled at the University Campus Bio-Medico of Rome, between January 2015 and December 2016. oprD gene was sequenced in 20 nosocomial multi-drug resistant P. aeruginosa strains. Phylogeographic, selective pressure, residue conservation analysis and homology modelling were performed. Clinical epidemiological data were extracted from patient medical records. Multi-drug resistant strains accounted for the 36% of total strains and were responsible of 20 cases of nosocomial infections. P. aeruginosa infections occurred prevalently in the West area, especially at the location IIIW and in the Geriatric ward. The time of the most recent common ancestor indicated that strains could have been introduced in the hospital since the end of the year 2009 with the most probable location in general surgery ward. By selective pressure analysis, 29 positions under diversifying selection have been identified and mapped onto the OprD model. Most of the observed residue substitutions are predicted to be destabilizing and some of them occurred in the Loops 2 and 3 that are involved in solute selection and carbapenem susceptibility. The molecular and evolutionary analysis of Multi-drug resistant strains circulating in the nosocomial setting may provide useful insights into the epidemiology and the mechanisms leading to resistance, contributing to infection control improvement.

Cella E., Riva E., Angeletti S., Fogolari M., Blasi A., Scolamacchia V., Spoto S., Bazzardi R. Lai A., Sagnelli C., Sagnelli E., Ciccozzi M.

Genotype I hepatitis A virus introduction in Italy: bayesian phylogenetic analysis to date different epidemics.

Despite a significant decrease in acute hepatitis A in the last 2 decades in Italy, outbreaks were observed occurring mostly in southern Italy. In this study, Bayesian phylogenetic analysis was used to analyze the origin of these epidemics. With this aim, 5 different data sets of hepatitis A virus sequences were built to perform genotyping by the neighbor-joining method to estimate the evolutionary rates by using a Bayesian Markov chain Monte Carlo approach and to investigate the demographic history by independent Markov chain Monte Carlo runs enforcing both a strict and relaxed clock. The estimated mean value of the evolutionary rate, representing Ia and Ib strains, was $1.21 \times 10-3$ and $2.0 \times 10-3$ substitutions/site/year, respectively. The Bayesian maximum clade credibility tree of hepatitis A virus (HAV) Ia and Ib strains showed that Italian sequences mostly formed separate clusters. The root of the time for the most recent common ancestor (tMRCA) for HAV Ia and Ib strains dated back to 1981 and to 1988, respectively, showing in both cases different epidemic entrances. Phylodynamic analysis showed that genotype Ia increased in 1997, when the Apulia epidemic started, then suffered a bottleneck, probably consequent to vaccination and to the herd immunity, followed by a new increase in virus population in the years 2013-2014 consequent to the epidemic caused by the ingestion of mixed frozen berries. A similar trend without an evident bottleneck was observed also in the case of genotype Ib. In conclusion, the Bayesian phylogenetic analysis represents a good tool to measure the effectiveness of the public health plans used for HAV control.

Microscopic and Ultrastructural Anatomy

Head S. Morini

Faculty S. Carotti, F. Zalfa

External Members F. Cimini, M. Francesconi, V. Panasiti, L. Sancillo, M. Zingariello

Description

The Microscopic and Ultrastructural Anatomy Unit applies techniques for morphological and molecular analysis of cells and tissues with particular reference to the digestive system and skin. The main research fields are the study of the liver diseases, focusing on the morphological features and molecular mechanisms of hepatic fibrogenesis and carcinogenesis. Structural, ultrastructural analysis by light, fluorescence, confocal and transmission electron microscopy are performed using histochemical, immunohistochemistry, immunofluorescence and immunogold techniques; morphometry by systems and softwares for image analysis is used. Molecular analysis and cell biology, are applied to the study of liver, pancreas and skin diseases. In particular, gene expression analysis and post-transcriptional regulation mechanisms are investigated using advanced technologies.

Main research activities

Histo-morphology of liver tissue, biochemical serological parameters, cellular and molecular biology techniques and the genetic signatures were investigated in order to identify factors connecting liver inflammation and fibrosis during non-tumoral liver diseases. We could evaluate the hepatic expression of the GH/IGF-1 axis components in the liver of patients with HCV-related chronic hepatitis at different fibrosis stages and the effects of disease-associated variants at different loci to multiply the risk of NAFLD and NASH-cirrhosis.

By applying immunohistochemistry and immunofluorescence on specimens from patients treated with breast implant capsules, we could investigate the role of neo-angiogenesis, inflammation and estrogen receptors in peri-prosthetic tissue development and remodeling.

Most important publications

Vespasiani-Gentilucci U., Dell'Unto C., De Vincentis A., Baiocchini A., Delle Monache M., Cecere R., Pellicelli A.M., Giannelli V., Carotti S., Galati G., Gallo P., Valentini F., Del Nonno F., Rosati D., Morini S., Antonelli-Incalzi R., Picardi A.

Combining genetic variants to improve risk prediction for NAFLD and its progression to cirrhosis: a proof of concept study.
Can J Gastroenterol Hepatol. 2018 Mar 14; 2018:7564835. PubMed PMID: 29732362. IF 1,622

Background&Aims. Identifying NAFLD patients at risk of progression is crucial to orient medical care and resources. We aimed to verify if the effects determined by different single nucleotide polymorphisms (SNPs) could add up tomultiply the risk ofNAFLDand NASH-cirrhosis.
Methods. Three study populations, that is, patients diagnosed with NASH-cirrhosis or with noncirrhotic NAFLD and healthy controls, were enrolled. PNPLA3 rs738409, TM6SF2 rs58542926, KLF6 rs3750861, SOD2 rs4880, and LPIN1 rs13412852 were genotyped.
Results. One hundred and seven NASH-cirrhotics, 93 noncirrhotic NAFLD, and 90 controls were enrolled. At least one difference in

allele frequency between groups was significant, or nearly significant, for the PNPLA3, TM6SF2, and KLF6 variants ($p < 0.001$, $p < 0.05$, and $p = 0.06$, resp.), and a risk score based on these SNPs was generated. No differences were observed for SOD2 and LPIN1 SNPs. When compared to a score of 0, a score of 1-2 quadrupled, and a score of 3-4 increased 20-fold the risk of noncirrhotic NAFLD; a score of 3-4 quadrupled the risk of NASH-cirrhosis.

Conclusions. The effects determined by disease-associated variants at different loci can add up to multiply the risk of NAFLD and NASH-cirrhosis. Combining different disease-associated variants may represent the way for genetics to keep strength in NAFLD diagnostics.

Carotti S., Guarino M.P.L., Valentini F., Porzio S., Vespasiani-Gentilucci U., Perrone G., Zingariello M., Gallo P., Cicala M., Picardi A., Morini S.

Impairment of GH/IGF-1 axis in the liver of patients with HCV-related chronic hepatitis.

Resistance to the action of growth hormone (GH) frequently complicates liver cirrhosis, while, physiologically, the activation of GH receptor (GHR) determines phosphorylation of signal transducer and activator of transcription (STAT)-5 and the consequent induction of insulin-like growth factor-1 (IGF-1) expression. The suppressor of cytokine signaling (SOCS)-3 negatively regulates this intracellular cascade. We aimed to evaluate the hepatic expression of the GH/IGF-1 axis components in the liver of patients with HCV-related chronic hepatitis at different fibrosis stages. The expression of GH/IGF-1 axis components, such as GHR, IGF-1, STAT5-p, and SOCS-3, was assessed by immunohistochemistry at the lobular level in 61 patients with HCV-related hepatitis. At the hepatocyte level, IGF-1 and nuclear STAT5-p positivity scores showed negative correlations with fibrosis stage, while SOCS-3 score a positive one ($p < 0.05$ for all). Furthermore, the reduction of hepatocyte score of IGF-1 expression was associated with the serological parameters of liver damage ($p < 0.05$) and with the increase of the score of IGF-1 expression by hepatic stellate cells ($p < 0.05$). IGF-1 expression by hepatocytes was reduced with fibrosis progression, probably due to the impairment of GHR intracellular cascade by the SOCS-3 activation already in pre-cirrhotic stages. The inverse correlation between IGF-1 expressed by hepatocytes and by hepatic stellate cells suggests that IGF-1 may exert specific functions in different hepatic cells.

Segreto F., Carotti S., Marangi G.F., Tosi D., Zingariello M., Pendolino A.L., Sancillo L., Morini S., Persichetti P.

The role of angiogenesis, inflammation and estrogen receptors in breast implant capsules development and remodeling.

Background: Capsular contracture is the most common complication following breast implant placement. The multiple factors unbalancing the physiological response to the foreign body have not been fully elucidated. The aim of this study was to investigate the role of neo-angiogenesis, inflammation and estrogen receptors in peri-prosthetic tissue development and remodeling.

Methods: The study enrolled 31 women who underwent expander substitution with definitive implant. Specimens were stained with hematoxylin/eosin, Masson trichrome, immunohistochemistry and immunofluorescence for alpha-smooth muscle actin, estrogen receptor-α (ER-α), estrogen receptor-β (ER-β), Collagen type I and III, CD31 (as a marker of neo-angiogenesis) and vascular endothelial growth factor (VEGF). Inflammatory infiltration was quantified and analyzed. Transmission electron microscopy was performed for ultrastructural evaluation.

Results: Myofibroblasts, mainly localized in the middle layer of capsular tissue, expressed VEGF, ER-α and ER-β. ER-β expression positively correlated with Collagen type I deposition ($p = 0.025$). Neo-angiogenesis was predominant in the middle layer. CD31 expression positively correlated with Collagen type I expression ($p = 0.009$) and inflammatory infiltration grade ($p = 0.004$). The degree of inflammatory infiltration negatively correlated with the time from implantation ($p = 0.022$).

Discussion: The middle layer is key in the development and remodeling of capsular tissue. Myofibroblasts produce VEGF that induces neo-angiogenesis. New vessels formation is also correlated to the inflammatory response. Collagen deposition is associated with ER-β expression and neo-angiogenesis. These findings may prelude to targeted pharmacologic therapies able to control such interactions, thus hampering the self-sustaining loop promoting the progression of physiologic fibrosis toward pathologic contracture.

Molecular Medicine and Biotechnology

Head V.M. Fazio

Other Personnel M. Costantini, F. Picardo, S. Virga

External Members M. De Robertis, M.L. Poeta, E. Signori

Description

The permanent staff is composed only by VM Fazio and S Virga. Researchers from other University (MLP) and CNR (ES, MD) actively cooperate both on research projects and the didactic activities.

Residents (Scuola di Specializzazione in Patologia Clinica e Biochimica Clinica): Angela Pantalone, Marta Fogolari, Marco Vicari, Maria Francesconi, Annamaria Puglielli, Francesco Romano, Maria Carmina Manzorra.

Main research activities

The specific competences of the RU are focused on molecular genetics and epigenetics; development of in vitro and in vivo cancer models; in vitro and in vivo gene transfer; histopathology technologies; cytofluorimetric analysis and cell sorting; bioinformatics and biostatistics studies in collaboration with leading groups.

Three main projects are in development:

- Study of the leading epigenetic and genetic mechanisms that control the reprogramming of stem cells during the first phases of carcinogenesis and the cancer progression, in the two-way connection with the microenvironment, including exosomes and circulating nucleic acids;
- Intra- and inter- tumor heterogeneity, tumor cell subpopulations, philogenetics evolution of tumor in the course of cancer progression;
- Study of genetic and epigenetic biomarkers for the development of multilevel genomics-based cancer taxonomy, prediction of cancer progression, response to therapy and metastasization (renal, colorectal, lung, breast tumors).

Most important publications

De Robertis M., Poeta M.L., Signori E., Fazio V.M.

Current understanding and clinical utility of miRNAs regulation of colon cancer stem cells.
Semin Cancer Biol. 2018 Dec; 53:232-247. PubMed PMID: 30130662. IF 10,198

Cancer stem cells (CSCs) in colorectal tumorigenesis are suggested to be responsible for initiation, development and propagation of colorectal cancer (CRC) and have been extensively characterized by the expression of phenotypic determinants, such as surface or intracellular proteins. The generation of CSCs is likely due to a dysregulation of the signaling pathways that principally control self-renewal and pluripotency in normal intestinal stem cells (ISCs) through different (epi)genetic changes that define cell fate, identity, and phenotype of CSCs. These aspects are currently under intense investigation. In the framework of the oncogenic signaling pathways controlled by microRNAs (miRNAs) during CRC development, a plethora of data suggests that miRNAs can play a key role in several regulatory pathways involving CSCs biology, epithelial-mesenchymal transition (EMT), angiogenesis, metastatization, and pharmacore-

sistance. This review examines the most relevant evidences about the role of miRNAs in the etiology of CRC, through the regulation of colon CSCs and the principal differences between colorectal CSCs and benign stem cells. In this perspective, the utility of the principal CSCs-related miRNAs changes is explored, emphasizing their use as potential biomarkers to aid in diagnosis, prognosis and predicting response to therapy in CRC patients, but also as promising targets for more effective and personalized anti-CRC treatments.

De Robertis M., Mazza T., Fusilli C., Loiacono L., Poeta M.L., Sanchez M., Massi E., Lamorte G., Diodoro M.G., Pescarmona E., Signori E., Pesole G., Vescovi A.L., Garcia-Foncillas J., Fazio V.M.

EphB2 stem-related and EphA2 progression-related miRNA-based networks in progressive stages of CRC evolution: clinical significance and potential miRNA drivers.

Mol Cancer. 2018 Nov 30;17(1):169. PubMed PMID: 30501625. IF 7,776

EphB2 and EphA2 control stemness and differentiation in the intestinal mucosa, but the way they cooperate with the complex mechanisms underlying tumor heterogeneity and how they affect the therapeutic outcome in colorectal cancer (CRC) patients, remain unclear. MicroRNA (miRNA) expression profiling along with pathway analysis provide comprehensive information on the dysregulation of multiple crucial pathways in CRC. Through a network-based approach founded on the characterization of progressive miRNAomes centered on EphA2/EphB2 signaling during tumor development in the AOM/DSS murine model, we found a miRNA-dependent orchestration of EphB2-specific stem-like properties in earlier phases of colorectal tumorigenesis and the EphA2-specific control of tumor progression in the latest CRC phases. Furthermore, two transcriptional signatures that are specifically dependent on the EphA2/EphB2 signaling pathways were identified, namely EphA2, miR-423-5p, CREB1, ADAMTS14, and EphB2, miR-31-5p, mir-31-3p, CRK, CXCL12, ARPC5, SRC.EphA2- and EphB2-related signatures were validated for their expression and clinical value in 1663 CRC patients. In multivariate analysis, both signatures were predictive of survival and tumor progression. The early dysregulation of miRs-31, as observed in the murine samples, was also confirmed on 49 human tissue samples including preneoplastic lesions and tumors. In light of these findings, miRs-31 emerged as novel potential drivers of CRC initiation. Our study evidenced a miRNA-dependent orchestration of EphB2 stem-related networks at the onset and EphA2-related cancer-progression networks in advanced stages of CRC evolution, suggesting new predictive biomarkers and potential therapeutic targets.

Maldonado L., Brait M., Izumchenko E., Begum S., Chatterjee A., Sen T., Loyo M., Barbosa A., Poeta M.L., Makarev E., Zhavoronkov A., Fazio V.M., Angioli R., Rabitti C., Ongenaert M., Van Criekinge W., Noordhuis M.G., de Graeff P., Wisman G.B.A., van der Zee A.G.J., Hoque M.O.

Integrated transcriptomic and epigenomic analysis of ovarian cancer reveals epigenetically silenced GULP1.

Cancer Lett. 2018 Oct 1; 433:242-251. PubMed PMID: 29964205. IF 6,491

Many epigenetically inactivated genes involved in ovarian cancer (OC) development and progression remain to be identified. In this study we undertook an integrated approach that consisted of identification of genome-wide expression patterns of primary OC samples and normal ovarian surface epithelium along with a pharmacologic unmasking strategy using 3 OC and 3 immortalized normal ovarian epithelial cell lines. Our filtering scheme identified 43 OC specific methylated genes and among the 5 top candidates (GULP1, CLIP4, BAMBI, NT5E, TGFβ2), we performed extended studies of GULP1. In a training set, we identified GULP1 methylation in 21/61 (34%) of cases with 100% specificity. In an independent cohort, the observed methylation was 40% (146/365) in OC, 12.5% (2/16) in borderline tumors, 11% (2/18) in cystadenoma and 0% (0/13) in normal ovarian epithelium samples. GULP1 methylation was associated with clinicopathological parameters such as stage III/IV (p = 0.001), poorly differentiated grade (p = 0.033), residual disease (p < 0.0003), worse overall (p = 0.02) and disease specific survival (p = 0.01). Depletion of GULP1 in OC cells led to increased pro-survival signaling, inducing survival and colony formation, whereas reconstitution of GULP1 negated these effects, suggesting that GULP1 is required for maintaining cellular growth control.

Molecular Neurosciences

Head M. D'Amelio

Other Personnel A. Cordella, A. Nobili

External Members P. Krashia, L. La Barbera

Description

The Molecular Neurosciences Unit focuses on neurodegenerative diseases and other neuropsychiatric conditions by means of the application of biologic techniques. We have a particular interest in the pathogenesis of β-amyloid neurodegenerative disorders such as Alzheimer's disease (AD). We use cell and transgenic mouse models to gain an understanding of the pathogenesis of the disorder, and also to assist in the development of novel therapeutic techniques.

We have applied similar techniques for the study of Parkinson's disease (PD) and spinal muscular atrophy (SMA). We have identified several novel proteins involved in the pathogenesis of AD, and we have cell and mouse models of the disease. We are also applying similar techniques to psychiatric conditions such as autism and schizophrenia. The laboratory offers research opportunities to undergraduates, graduate students, postdoctoral fellows and other interested scientists.

Main research activities

During last year, the Molecular Neurosciences Unit consolidated scientific collaborations with national and international partners. In particular, the Laboratory collaborated with the National Research Council (CNR) of Rome, "Roma Tre" University, Sapienza University of Rome, Université Libre de Bruxelles, Center of Excellence for Biomedical Research, University of Genova and University of Perugia. The aforementioned collaborations involve the study of neuronal function alterations in several models of human neurological disease.

During last year, the Molecular Neurosciences Unit published several papers in the field of neurodegenerative disorders. Among these, a Nature Communication paper disclosing the crucial role of dopaminergic brain stem in early phase of Alzheimer's disease by using a validated model of the disease.

Main collaborations

- National Research Council (CNR) of Rome;
- Roma Tre University, Rome;
- Sapienza University of Rome;
- Université Libre de Bruxelles, Belgium;
- Center of Excellence for Biomedical Research
- University of Genova;
- University of Perugia.

Most important publications

Cordella A., Krashia P., Nobili A., Pignataro A., La Barbera L., Viscomi M.T., Valzania A., Keller F., Ammassari-Teule M., Mercuri N.B., Berretta N., D'Amelio M.

Dopamine loss alters the hippocampus-nucleus accumbens synaptic transmission in the Tg2576 mouse model of Alzheimer's disease.
Neurobiol Dis. 2018 Aug; 116:142-154. PubMed PMID: 29778899. IF 5,227

The functional loop involving the ventral tegmental area (VTA), dorsal hippocampus and nucleus accumbens (NAc) plays a pivotal role in the formation of spatial memory and persistent memory traces. In particular, the dopaminergic innervation from the VTA to the hippocampus is critical for hippocampal-related memory function and alterations in the midbrain dopaminergic system are frequently reported in Alzheimer's disease (AD), contributing to age-related decline in memory and non-cognitive functions. However, much less is known about the hippocampus-NAc connectivity in AD. Here, we evaluated the functioning of the hippocampus-to-NAc core connectivity in the Tg2576 mouse model of AD that shows a selective and progressive degeneration of VTA dopaminergic neurons. We show that reduced dopaminergic innervation in the Tg2576 hippocampus results in reduced synaptic plasticity and excitability of dorsal subiculum pyramidal neurons. Importantly, the glutamatergic transmission from the hippocampus to the NAc core is also impaired. Chemogenetic depolarisation of Tg2576 subicular pyramidal neurons with an excitatory Designer Receptor Exclusively Activated by Designer Drugs, or systemic administration of the DA precursor levodopa, can both rescue the deficits in Tg2576 mice. Our data suggest that the dopaminergic signalling in the hippocampus is essential for the proper functioning of the hippocampus-NAc excitatory synaptic transmission.

Serra L., D'Amelio M., Di Domenico C., Dipasquale O., Marra C., Mercuri N.B., Caltagirone C., Cercignani M., Bozzali M.

In vivo mapping of brainstem nuclei functional connectivity disruption in Alzheimer's disease.
Neurobiol Aging. 2018 Dec;72:72-82. PubMed PMID: 30237073. IF 4,454

We assessed here functional connectivity changes in the locus coeruleus (LC) and ventral tegmental area (VTA) of patients with Alzheimer's disease (AD). We recruited 169 patients with either AD or amnestic mild cognitive impairment due to AD and 37 elderly controls who underwent cognitive and neuropsychiatric assessments and resting-state functional magnetic resonance imaging at 3T. Connectivity was assessed between LC and VTA and the rest of the brain. In amnestic mild cognitive impairment patients, VTA disconnection was predominant with parietal regions, while in AD patients, it involved the posterior nodes of the default-mode network. We also looked at the association between neuropsychiatric symptoms (assessed by the neuropsychiatric inventory) and VTA connectivity. Symptoms such as agitation, irritability, and disinhibition were associated with VTA connectivity with the parahippocampal gyrus and cerebellar vermis, while sleep and eating disorders were associated with VTA connectivity to the striatum and the insular cortex. This suggests a contribution of VTA degeneration to AD pathophysiology and to the occurrence of neuropsychiatric symptoms. We did not find evidence of LC disconnection, but this could be explained by the size of this nucleus, which makes it difficult to isolate. These results are consistent with animal findings and have potential implications for AD prognosis and therapies.

D'Amelio M., Serra L., Bozzali M.

Ventral tegmental area in prodromal Alzheimer's disease: bridging the gap between mice and humans.
J Alzheimers Dis. 2018;63(1):181-183. PubMed PMID: 29630556. IF 3,476

Alzheimer's disease (AD) is a progressive neurological disorder characterized by several cognitive and non-cognitive symptoms, with episodic memory being the earliest and most prominently impaired cognitive function. Dopaminergic signals are required for encoding hippocampal memory for new events and the ventral tegmental area (VTA), together with the locus coeruleus, are the primary sources of dopamine acting on dopaminergic receptors in the hippocampus. With this in mind, a recent study on a validated mouse model of AD highlighted on the hippocampal dysfunction and its correlation with an early degeneration of dopaminergic neurons in the VTA. In this issue, De Marco and Venneri test the hypothesis that the volume of the VTA nucleus in humans might be associated with cognitive features of AD.

Molecular Psychiatry and Neurogenetics

Head A.M. Persico

Other Personnel G. Barbieri, C. Cannizzaro, A. Costa, G. Ferrarelli, SC. Lintas, R. Sacco

Genomics Lab. Mafalda Luce Centre, Milan M. Baccarin, P. Castronovo, C. Picinelli, P. Tomaiuolo

Description

The Unit is responsible for investigating the pathogenic aspects, especially of a genetic nature, the biochemical and the neuroimmunological aspects applicable to childhood psychiatric disorders, such as autism and ADHD. The aim of these studies is to place them in connection with specific clinical signs and/or symptoms, psychopathological traits and behavioral response patterns. The study of biomarkers is intended not only to obtain a better understanding of the pathophysiology, related to the organic components of these disorders, but is also aimed at early detection of the disorder for the benefit of the child's development. Privileged methods of study are array-CGH, genomic sequencing and qPCR (Neurogenetics and transcriptomics); analysis by western blotting and ELISA both associated with anti-brain antibodies tissues as well as with specific cytokines (Neuroimmunology); the HPLC for assay of plasma serotonin and specific urinary metabolites (biochemical). Finally, in clinical research settings EEG and eye tracking (Tobii TX300) are also used.

Main collaborations

- Biological Science Department and Interdepartmental Centre for Stem Cell Research Milano University, Italy.
- Brain Centre Rudolf Magnu, The Netherlands;
- Department of Translational Neuroscience, University Medical Centre Utrecht, The Netherlands;
- Institute of Psychiatry, King's College London, UK.
- Neurotoxicology & Neuroendocrine Department, Italian National Institute of Health (ISS), Italy;
- Proteomics Laboratory, Tuscia University, Viterbo, Italy
- Psychology Department Sapienza University, Italy

Most important publications

Lintas C., Persico A.M.

Unraveling molecular pathways shared by Kabuki and Kabuki-like syndromes.
Clin Genet. 2018 Oct; 94(3-4):283-295. PubMed PMID: 28139835. IF 3,512

Kabuki syndrome (KS) is a rare genetic syndrome characterized by a typical facial gestalt, variable degrees of intellectual disability, organ malformations, postnatal growth retardation and skeletal abnormalities. So far, KMT2D or KDM6A mutation has been identified as the main cause of KS, accounting for 56%-75% and 3%-8% of cases, respectively. Patients without mutations in 1 of the 2 causative KS genes are often referred to as affected by Kabuki-like syndrome. Overall, they represent approximately 30% of KS cases, pointing toward substantial genetic heterogeneity for this condition. Here, we review all currently available literature describing KS-like phenotypes (or phenocopies) associated with genetic variants located in loci different from KMT2D and KDM6A. We also report on a new KS phenocopy harboring a 5 Mb de novo deletion in chr10p11.22-11.21. An enrichment analysis aimed at identifying functional Gene Ontology classes shared by the 2 known KS causative genes and by new candidate genes currently associated with KS-like phenotypes primarily converges upon abnormal chromatin remodeling and transcriptional dysregulation as pivotal to the pathophysiology of KS phenotypic hallmarks. The identification of mutations in genes belonging to the same functional pathways of KMT2D and KDM6A can help design molecular screenings targeted to KS-like phenotypes.

Tillmann J., Ashwood K., Absoud M., Bölte S., Bonnet-Brilhault F., Buitelaar J.K., Calderoni S., Calvo R., Canal-Bedia R., Canitano R., De Bildt A., Gomot M., Hoekstra P.J., Kaale A., McConachie H., Murphy D.G., Narzisi A., Oosterling I., Pejovic-Milovancevic M., Persico A.M., Puig O., Roeyers H., Rommelse N., Sacco R., Scandurra V., Stanfield A.C., Zander E., Charman T.

Evaluating sex and age differences in ADI-R and ADOS scores in a large European multi-site sample of individuals with autism spectrum disorder.
J Autism Dev Disord. 2018 Jul; 48(7):2490-2505. PubMed PMID: 29468576. IF 3,476

Research on sex-related differences in Autism Spectrum Disorder (ASD) has been impeded by small samples. We pooled 28 datasets from 18 sites across nine European countries to examine sex differences in the ASD phenotype on the ADI-R (376 females, 1763 males) and ADOS (233 females, 1187 males). On the ADI-R, early childhood restricted and repetitive behaviours were lower in females than males, alongside comparable levels of social interaction and communication difficulties in females and males. Current ADI-R and ADOS scores showed no sex differences for ASD severity. There were lower socio-communicative symptoms in older compared to younger individuals. This large European ASD sample adds to the literature on sex and age variations of ASD symptomatology.

Isaksson J., Tammimies K., Neufeld J., Cauvet É., Lundin K., Buitelaar J.K., Loth E., Murphy D.G.M., Spooren W., Bölte S., EU-AIMS LEAP group [Persico A.M., Sacco R.].

EU-AIMS longitudinal European autism project (LEAP): the autism twin cohort.
Mol Autism. 2018 Apr 13; 9:26. PubMed PMID: 29682271. IF 5,872

EU-AIMS is the largest European research program aiming to identify stratification biomarkers and novel interventions for autism spectrum disorder (ASD). Within the program, the Longitudinal European Autism Project (LEAP) has recruited and comprehensively phenotyped a rare sample of 76 monozygotic and dizygotic twins, discordant, or concordant for ASD plus 30 typically developing twins. The aim of this letter is to complete previous descriptions of the LEAP case-control sample, clinically characterize, and investigate the suitability of the sample for ASD twin-control analyses purposes and share some 'lessons learnt.' Among the twins, a diagnosis of ASD is associated with increased symptom levels of ADHD, higher rates of intellectual disability, and lower family income. For the future, we conclude that the LEAP twin cohort offers multiple options for analyses of genetic and shared and non-shared environmental factors to generate new hypotheses for the larger cohort of LEAP singletons, but particularly cross-validate and refine evidence from it.

Neurology, Neurophysiology, Neurobiology

Head V. Di Lazzaro

Faculty G. Assenza, M. Tombini, F. Vernieri

Other Personnel C. Altamura, M. Boscarino, N. Brunelli, ML. Caminiti, F. Capone, A. Cascio Rizzo, G. Cecchi, G. Corrao, C. Costa, L. Di Biase, A. Di Santo, A. De Liso, E. Falato, A. Fallacara, M. Ferrante, J. Lanzone, M. Marano, F. Motolese, F. Ranieri, L. Ricci, MG. Rossi, M. Ulivi, F. Ursini, C. Vico

Description

The main area of research of the Research Unit is the study of the pathophysiology of a variety of neurological disorders, including stroke, degenerative diseases (dementias, Parkinson's disease, tremor, amyotrophic lateral sclerosis), inflammatory diseases of the central nervous system (multiple sclerosis), spinal cord diseases, epilepsy, and headache. Another relevant area of interest is the use of electrophysiological techniques (EEG, EMG, evoked potentials), noninvasive brain stimulation (TMS, tDCS, tACS, vagal stimulation) and neurosonology (cerebral hemodynamics evaluation, functional TCD, TCD with bubble test), for the diagnosis of neurological disorders, and for the evaluation of the effects of drugs on the intact human brain and the study of human brain plasticity.

Main research activities

The research Unit has provided a relevant contribution in understanding of the physiological bases of non-invasive human brain stimulation and in the development of innovative methods of neuromodulation aimed at enhancing human brain plasticity. Significant results were obtained in the study of brain connectivity in epileptic patients and in the field of deep brain stimulation in movement disorders. Other relevant scientific contributions were provided in the field of rare neurodegenerative disorders such as Huntington Disease. Research activity involving patients with migraine led to the publication of relevant studies on the diagnosis (cerebral hemodynamic evaluation) and on the innovative treatment (monoclonal antibodies), of this neurological disorder.

Most important publications

Di Lazzaro V., Rothwell J., Capogna M.

Noninvasive stimulation of the human brain: activation of multiple cortical circuits.
Neuroscientist. 2018 Jun; 24(3):246-260. PubMed PMID: 28659070. IF 7,461

Noninvasive brain stimulation methods, such as transcranial electric stimulation and transcranial magnetic stimulation are widely used tools for both basic research and clinical applications. However, the cortical circuits underlying their effects are poorly defined. Here we review the current knowledge based on data mostly coming from experiments performed on human subjects, and also to a lesser extent on rodent or primate models. The data suggest that multiple mechanisms are likely to be involved, such as the direct activation of layer V pyramidal neurons, but also of different types of GABAergic interneurons. In this regard, we propose a key role for a specific type of interneuron known as neurogliaform cell.

Migliore S., Curcio G., Couyoumdjian A., Ghazaryan A., Landi D., Moffa F., Quintiliani L., Squitieri F., Palmieri M.G., Filippi M.M., Vernieri F.

Executive functioning in relapsing-remitting multiple sclerosis patients without cognitive impairment: a task-switching protocol.
Mult Scler. 2018 Sep; 24(10):1328-1336. PubMed PMID: 28675956. IF 5,280

Cognitive dysfunction affects 40%-65% of multiple sclerosis (MS) patients, most often affecting information processing speed and working memory, mediated by the pre-frontal cortex (PFC). Our study aimed to investigate PFC functioning through a task-switching protocol in relapsing-remitting multiple sclerosis (RRMS) patients without cognitive impairment. A total of 24 RRMS patients and 25 controls were enrolled. Two different tasks were performed in rapid and random succession, so that the task was either changed from one trial to the next one (switch trials) or repeated (repetition trials). Switch trials are usually slower than repetitions, causing a so-called switch cost (SC). Patients had worse performance than controls only in the switch trials, as indicated by increased SC and reaction times. Moreover, patients showed a reduced ability to reconfigure the task-set for the execution of a new task and to disengage from the previous one. Our results showed a primary deficit in executive control processes involved in the task-switching performance in RRMS patients without cognitive impairment. This deficit may depend on the functional impairment of the PFC, which is essential to adjust behaviour rapidly and flexibly in response to environmental changes, representing one of the most sophisticated human abilities.

De Stefano V., Carobbio A., Di Lazzaro V., Guglielmelli P., Iurlo A., Finazzi M.C., Rumi E., Cervantes F., Elli E.M., Randi M.L., Griesshammer M., Palandri F., Bonifacio M., Hernandez-Boluda J.C., Cacciola R., Miroslava P., Carli G., Beggiato E., Ellis M.H., Musolino C., Gaidano G., Rapezzi D., Tieghi A., Lunghi F., Loscocco G.G., Cattaneo D., Cortelezzi A., Betti S., Rossi E., Finazzi G., Censori B., Cazzola M., Bellini M., Arellano-Rodrigo E., Bertozzi I., Sadjadian P., Vianelli N., Scaffidi L., Gomez M., Cacciola E., Vannucchi A.M., Barbui T.

Benefit-risk profile of cytoreductive drugs along with antiplatelet and antithrombotic therapy after transient ischemic attack or ischemic stroke in myeloproliferative neoplasms.
Blood Cancer J. 2018 Feb 28;8(3):25. PubMed PMID: 29535299. IF 8,125

We analyzed 597 patients with myeloproliferative neoplasms (MPN) who presented transient ischemic attacks (TIA, n = 270) or ischemic stroke (IS, n = 327). Treatment included aspirin, oral anticoagulants, and cytoreductive drugs. The composite incidence of recurrent TIA and IS, acute myocardial infarction (AMI), and cardiovascular (CV) death was 4.21 and 19.2%, respectively at one and five years after the index event, an estimate unexpectedly lower than reported in the general population. Patients tended to replicate the first clinical manifestation (hazard ratio, HR: 2.41 and 4.41 for recurrent TIA and IS, respectively); additional factors for recurrent TIA were previous TIA (HR: 3.40) and microvascular disturbances (HR: 2.30); for recurrent IS arterial hypertension (HR: 4.24) and IS occurrence after MPN diagnosis (HR: 4.47). CV mortality was predicted by age over 60 years (HR: 3.98), an index IS (HR: 3.61), and the occurrence of index events after MPN diagnosis (HR: 2.62). Cytoreductive therapy was a strong protective factor (HR: 0.24). The rate of major bleeding was similar to the general population (0.90 per 100 patient-years). In conclusion, the long-term clinical outcome after TIA and IS in MPN appears even more favorable than in the general population, suggesting an advantageous benefit-risk profile of antithrombotic and cytoreductive treatment.

Neurophysiology and Neuroengineering of Human–Technology Interaction

Head G. Di Pino

Faculty D. Formica

Other Personnel M. D'Alonzo, E. Falato, F. Le Jeune, A. Mioli, G. Musumeci, A. Noccaro, M. Pinardi, L. Raiano

Description

The Research Unit investigates the neurophysiological processes underlying complex interaction between the human nervous system and technological artifacts.

Today, more and more often, the man is part of artificial/organic mixed complex, interacting with devices, robots, or with tool for functional replacement (e.g. prostheses). From a neuroscience perspective, this may strongly impact on well-known concepts, such sensory feedback, motor control, biomechanics, learning, functional recovery.

The Unit object of study is no longer humans as such, but modern humans in the era of the confluence with the technology, both in their physiological and pathological manifestations.

Furthermore, the Research Unit aim to investigate classical themes of neurophysiology of systems (motor control, body representation) using typical neuroengineering tools (e.g. modeling, objectification, automation).

Its multidisciplinary flavor favors direct applications on the healthy subjects and patients.

Main research activities

- Development of enabling technology of ERC RESHAPE project.
- Design and development of Hardware and Software Systems of virtual and augmented reality, and of cognitive studies that integrate VR-AR stimuli, external stimulations (e.g. tDCS, TMS) and the recording and processing of biological signals (EEG, fMRI, EMG)
- Development of a robot aided transcranial magnetic stimulation guided by artificial vision
- Investigation protocols to neuromodulated ownership during the rubber hand illusion paradigm.
- Effect of tDCS neuromodulation on redundant task with the wrist.
- Design and validation of the PDMeter, a wearable device to monitor Parkinson Disease motor state at home.
- Clinical trial of implanted intraneural electrodes.

Most important publications

Mioli A., D'Alonzo M., Pellegrino G., Formica D., Di Pino G.

Intermittent theta burst stimulation over ventral premotor cortex or inferior parietal lobule does not enhance the rubber hand illusion.
Front Neurosci. 2018 Nov 23;12:870. PubMed PMID: 30532689. IF 3,877

An enhanced sense of prosthesis ownership could improve amputees' quality of life. In this study in 28 healthy subjects, neuronavigated intermittent Theta Burst Stimulation (iTBS) delivered over the right ventral premotor cortex or inferior parietal lobule was tested, compared to sham stimulation, to enhance embodiment in the rubber hand illusion paradigm. Neuromodulation of both areas did not result in an enhancement of embodiment. In all cases, the illusion was induced. The low consistency of iTBS over brain regions other than primary motor cortex may account for the absence of effect, suggesting to test other neuromodulating techniques to enhance artificial hand embodiment.

Pellegrino G., Maran M., Turco C., Weis L., Di Pino G., Piccione F., Arcara G.

Bilateral transcranial direct current stimulation reshapes resting-state brain networks: a magnetoencephalography assessment.
Neural Plast. 2018 Jan 11; 2018:2782804. PubMed PMID: 29593782 IF 3,161

Transcranial direct current stimulation (tDCS) is potentially useful to treat patients affected by neurological conditions. However, little is known about tDCS effects on resting-state brain networks, which are largely involved in brain physiological functions and in diseases. In this study on healthy subjects, we assessed the effect of bilateral tDCS applied over the sensorimotor cortices on brain and network activity using a whole-head magnetoencephalography system. Compared to control condition, the employed tDCS technique increases global connectivity in consistent way across bands and widespread. These results may be of help in personalizing treatments in neurological disorders.

Massaroni C., Venanzi C., Silvatti A.P., Lo Presti D., Saccomandi P., Formica D., Giurazza F., Caponero M.A., Schena E.

Smart textile for respiratory monitoring and thoraco-abdominal motion pattern evaluation.
J Biophotonics. 2018 May; 11(5):e201700263. PubMed PMID: 29297202. IF 3,768

The use of wearable systems for monitoring vital parameters has gained wide popularity in several medical fields. The focus of the present study is the experimental assessment of a smart textile based on 12 fiber Bragg grating sensors for breathing monitoring and thoraco-abdominal motion pattern analysis. The feasibility of the smart textile for monitoring several temporal respiratory parameters (ie, breath-by-breath respiratory period, breathing frequency, duration of inspiratory and expiratory phases), volume variations of the whole chest wall and of its compartments is performed on 8 healthy male volunteers. Values gathered by the textile are compared to the data obtained by a motion analysis system, used as the reference instrument. Good agreement between the 2 systems on both respiratory period (bias of 0.01 seconds), breathing frequency (bias of -0.02 breaths/min) and tidal volume (bias of 0.09 L) values is demonstrated. Smart textile shows good performance in the monitoring of thoraco-abdominal pattern and its variation, as well.

Nonlinear Physics and Mathematical Modeling

Head S. Filippi

Faculty C. Cherubini, L. Chiodo, A. Gizzi, A. Loppini

Other Personnel F. H. Fenton, M. Nicoletti, R. Ruiz-Baier

Description

The Nonlinear Physics and Mathematical Modelling research unit investigates different interdisciplinary problems. Theoretical, analytical and numerical tools are applied to study complex dynamics underlying biological systems as well as astrophysics and classical and quantum field theories, with particular attention to fluid dynamics, nonlinear solid mechanics, condensed matter physics and stellar and black hole dynamics. Regarding biophysics, research activities focus on animal and human physiopathology of cardiac, intestine, neural, endocrine systems through the derivation and solution of mathematical models calibrated on experiments. To this aim, advanced tools of numerical calculus, atomistic simulations, as well as data analysis, are implemented to obtain predictive information regarding complex systems. The unit moreover extends its skills through national and international networks of collaborations.

Main research activities

In 2018 the research Unit has continued its long-lasting collaboration with the International Center for Relativistic Astrophysics Network (ICRANet) being awarded of the ICRANet Grant UCB-181017 for the research lines "Interdisciplinary Complex Systems: Theoretical Physics Methods in Systems Biology" and "Self Gravitating Systems, Galactic Structures and Galactic Dynamics" which lead the Unit to several publications on international journals. In the frame-work of a scientific agreement between UCBM and the Italian Institute for Technology (IIT), the group is working at a neuroscience project focused on the computational and experimental investigation of physiological neural networks. The Unit also contributed into the scientific organization of special sessions at the ICCM9 "Multiscale material modeling in biomechanics and mechanobiology" and 13th WCCM "Advances in theoretical and computational mechanics and mechanobiology of soft tissues".

Main collaborations

- International Center for Relativistic Astrophysics Network (ICRANet)
- Italian Institute for Technology (IIT)

Most important publications

Loppini A., Gizzi A., Ruiz-Baier R., Cherubini C., Fenton F.H., Filippi S.

Competing mechanisms of stress-assisted diffusivity and stretch-activated currents in cardiac electromechanics.
Front Physiol. 2018 Dec 3; 9:1714. PubMed PMID: 30559677. IF 3,394

The role of mechanical stress in modifying the conductivity properties of cardiac tissue are investigated assessing their impact on computational models for cardiac electromechanics. Following Cherubini et al. (2017), the adapted models are compared against experimental data of pig ventricle fluorescence optical mapping. The novel approach incorporates stretch-activated currents (SAC) and stress-assisted diffusion (SAD) founding that only specific combinations of the two effects allow proper conduction velocity; expected heterogeneities and anisotropies are obtained; spiral wave meandering and drifting is highly mediated by the applied mechanical loading.

Simone P., Carusi C., Segreto F., Iannuzzi R., Buscaglione S., Gizzi A., Giannitelli S., Rainer A., Filippi S., Persichetti P.

Postbariatric brachioplasty with posteromedial scar: physical model, technical refinements, and clinical outcomes.
Plast Reconstr Surg. 2018 Feb; 141(2):344-353. PubMed PMID: 29369986. IF 3,621

Background: Brachioplasty is an increasingly performed procedure following massive weight loss. A visible scar is the main hindrance to this surgery. The aims of the study were to develop a physical model to investigate the ideal location of the surgical incision and to present the authors' technical refinements with the posteromedial scar approach. **Methods:** Twenty-four postbariatric patients underwent brachioplasty with posteromedial scar placement, concomitant liposuction, fascial plication, and axillary Z-plasty. Skin specimens were tested and a physical model of the arm was set up to investigate the difference in mechanical stress on the posteromedial and medial scars. The validated Patient and Observer Scar Assessment Scale, the Vancouver Scar Scale, and a questionnaire assessing subjective improvements were administered to patients. Preoperative and postoperative photographs were assessed by three independent plastic surgeons. **Results:** The physical model showed that stress intensity and distribution along the scar were reduced in the posteromedial location, with smaller scar displacement in the loading simulations. Twenty-three patients healed uneventfully. One (4.1 percent) had a 2-cm dehiscence. Mean Patient and Observer Scar Assessment Scale scores were, respectively, 2 ± 0.76 and 2.13 ± 0.64 in the patients' and observers' questionnaires. The mean Vancouver Scar Scale value was 3.5 ± 1.7. Questionnaires assessing the subjective outcomes showed a mean value of 3.45 ± 0.63 of 4. The surgeons' assessment resulted in a score of 4.5 ± 0.4 of 5. **Conclusions:** The physical model demonstrated that the posteromedial scar was subjected to lower mechanical stress and displacement. The reported technical refinements allowed pleasant arm recontouring to be achieved with acceptable scarring and a low incidence of complications.
Clinical question/level of evidence: Therapeutic, IV.

Chiodo L., Malliavin T.E., Giuffrida S., Maragliano L., Cottone G.

Closed-locked and apo-resting state structures of the human α7 nicotinic receptor: a computational study.
J Chem Inf Model. 2018 Nov 26; 58(11):2278-2293. PubMed PMID: 30359518. IF 3,804

Nicotinic acetylcholine receptors are membrane proteins present in neurons and at neuromuscular junctions. The knowledge of their conformational transition is fundamental for drug design applications. We provide all-atom structural models of the human $\alpha7$ nicotinic receptor in two different nonconductive states, "closed-locked" (bound to the antagonist α-conotoxin lml), apo-resting state, and compare them with our models for the open and the desensitized states. Our models contribute to the structural characterization of the conformational landscape of the human $\alpha7$ receptor and suggest benchmarks to discriminate among conformations found in experiments or in simulations of LGICs.

Nursing Science

Head M.G. De Marinis

Faculty M. Matarese, M. Piredda, D. Tartaglini

Other Personnel A. Marchetti

Description

The Unit investigates topics within clinical, pedagogical and organizational areas using quantitative and qualitative methods. Clinical areas include nursing in palliative care and multiple chronic diseases, and geriatrics and cancer nursing. Palliative care topics include pressure ulcers in hospice and home care, patient's transition, adolescents losing a parent. Multi-chronic disease topics relate to self-care of COPD and multiple morbidity patients and caregiver's contribution. Geriatric topics include self-care, discharge process, continuity of care, ageism. Cancer topics include adherence to oral therapy, protective isolation in hematology, decisional conflict in patients receiving CVCs and nursing care dependence. Pedagogical top-ics focus on hidden curriculum in nursing education. Organizational topics include missed nursing care, use of mobile technology in healthcare and prevention of errors during administration of intravenous therapy in critical care.

Main research activities

Ongoing multicenter projects include:
- Self-care experiences from the perspective of the people with COPD
- Mindfulness based stress reduction Intervention in patieNts with COPD and their caregivers (MIND)
- The contribution of the patient/caregiver dyad on self-care in CODP (RESPYRO)
- Self-care and quality of life in older adults with chronic dis-eases
- Self-care Of patient and caregiver DyAd in chronic conditions: a LongITudinal studY (SODALITY)
- Development and psychometric testing of a measure of cancer patients' perception of care dependency
- Prevalence, incidence and associated factors to pressure ulcers in hospice inpatients (PRELUdiHO)
- Alliance between generations: ageism
- Care complexity in nurses' views
- Nutritional self-efficacy in elderly people (NUSESE)
- Nursing decision-making in artificial nutrition and hydration of patient with cancer at the end-of-life
- Development and psychometric testing of a measure of care needs of adolescents losing a parent.

Most important publications

Artico M., D'Angelo D., Piredda M., Petitti T., Lamarca L., De Marinis M.G., Dante A., Lusignani M., Matarese M.

Pressure injury progression and factors associated with different end-points in a home palliative care setting: a retrospective chart review study.
J Pain Symptom Manage. 2018 Jul; 56(1):23-32. PubMed PMID: 29548891. IF 3,249

Context: Patients with advanced illnesses show the highest prevalence for pressure injuries. In the palliative care setting, the ultimate goal is injury healing, but equally important is wound maintenance, wound palliation (wound-related pain and symptom management), and primary and secondary wound prevention.
Objectives: To describe the course of healing for pressure injuries in a home palliative care setting according to different end-points, and to explore patient and caregiver characteristics and specific care activities associated with their achievement.
Methods: Four-year retrospective chart review of 669 patients cared for in a home palliative care service, of those 124 patients (18.5%) had at least one pressure injury with a survival rate less than or equal to six months.
Results: The proportion of healed pressure injuries was 24.4%. Of the injuries not healed, 34.0% were in a maintenance phase, whereas 63.6% were in a process of deterioration. Body mass index (P = 0.0014), artificial nutrition (P = 0.002), and age <70 years (P = 0.022) emerged as predictive factors of pressure injury complete healing. Artificial nutrition, age, male caregiver (P = 0.034), and spouse (P = 0.036) were factors significantly associated with a more rapid pressure injury healing. Continuous deep sedation was a predictive factor for pressure injury deterioration and significantly associated with a more rapid worsening.
Conclusion: Pressure injury healing is a realistic aim in home palliative care, particularly for injuries not exceeding Stage II occurring at least two weeks before death. When assessing pressure injuries, our results highlight the need to also pay attention to artificial nutrition, continuous deep sedation, and the caregiver's role and gender.

Matarese M., Lommi M., De Marinis M.G., Riegel B.

A systematic review and integration of concept analyses of self-care and related concepts.
J Nurs Scholarsh. 2018 May; 50(3):296-305. PubMed PMID: 29645402. IF 2,662

This review followed the guidelines of the Joanna Briggs Institute. CINAHL, PubMed, PsycINFO and EMBASE were searched for concept analyses published in the past 20 years. A total of 26 concept analyses were identified on self-care, self-care agency, self-monitoring, self-management, self-management support, symptom management, and self-efficacy. A model was delineated, explaining the relations among these concepts from the nursing perspective. Self-care is a broad concept including others, which describe more specific individual levels of activities and processes. Nurses are actively involved in disease management, self-management support and in promoting self-care.

Artico M., Dante A., D'Angelo D., Lamarca L., Mastroianni C., Petitti T., Piredda M., De Marinis M.G.

Prevalence, incidence and associated factors of pressure ulcers in home palliative care patients: a retrospective chart review.
Palliat Med. 2018 Jan; 32(1):299-307. PubMed PMID: 29130416. IF 3,780

This study described point prevalence at admission (13.1%) and cumulative incidence (13.0%) of pressure ulcers (PU) in 574 terminally ill patients admitted to an Italian home palliative care unit. Logistic regression models showed BMI (p<0.001), Braden score at risk (p<0.001), Karnofsky Performance Scale index (KPS) <30 (p<0.001), patients' female gender, patients' age >70 and >1 caregiver at home as predictors of a PU. PUs' rates suggest the need to include this issue among the main outcomes to pursue during home palliative care. The accuracy of BMI, Braden Scale and KPS in predicting the PU risk was confirmed. They appear as essential tools for a structured approach to prevention of PUs.

Oncology

Head G. Tonini

Faculty F. Pantano, D. Santini, B. Vincenzi

Other Personnel C. Anesi, G. Armento, F. Citarella, M.C. Cursano, G. Catania, L. D'Onofrio, D. De Lisi, E. Dell'Aquila, I. Fioroni, A. Galletti, C. Grilli, M. Iuliani, A. La Cesa, E. Marrucci, A. Mazzocca, A. Napolitano, A. Onorato, R. Ratta, G. Ribelli, M. Russano, M. Silletta, M. Spalato Ceruso, S. Simonetti, M. Stellato, L. Stumbo, A. Terenzio, V. Virzì, T. Zeppola; Data manager: T. Grassani, T. Pignatelli, C. Potestà

Description

The Oncology Research Unit is a multidisciplinary group of clinicians and scientists with expertise across the fields of clinical medicine, cancer care, epidemiology, bioinformatics and statistics, cell and molecular biology and immunology.

A key aim of the Department of Oncology is the optimal translation of fundamental research into patient benefit. Our Translational Laboratory is physically closely located with the hospital and our strategy is to promote a tight interaction between basic scientists and clinicians. Research activities are mainly focused on diagnosis, treatment and prevention of cancers and can be divided into two broad disciplines: Translational and Clinical Research. Teaching is one of our principal mission promoted by training and education activities including PhD and Resident-Specialty programs in Medical Oncology.

Main research activities

Translational research is focused on:
- Identification of cellular and molecular profiles to predict immunotherapy response in advanced solid tumors
- Evaluation of the effects of new molecular target therapies for renal carcinoma on the bone tumor microenvironment
- Analyses of the effects of cyclin-dependent kinase inhibitors (CDK4/6) on pre-clinical models of bone metastases from breast cancer
- Identification of new therapeutic targets in castration-resistant prostate cancer
- Study of new biomarkers involved in tumor progression and resistance to anticancer treatments in patients affected by soft tissue sarcomas
- Use of novel non-invasive approaches to identify biomarkers of response to immunotherapy in non-small cell lung cancer

Clinical Trial Unit focuses on:
- breast, prostate, renal, colorectal and lung cancers, but it also run trials in other rarer cancer types, including sarcoma. The unit is specialized in phase II exploratory and phase III randomized trials of new treatments

Most important publications

Dell'Aquila E., Cremolini C., Zeppola T., Lonardi S., Bergamo F., Masi G., Stellato M., Marmorino F., Schirripa M., Urbano F., Ronzoni M., Tomasello G., Zaniboni A., Racca P., Buonadonna A., Allegrini G., Fea E., Di Donato S., Chiara S., Tonini G., Tomcikova D., Boni L., Falcone A., Santini D.

Prognostic and predictive role of neutrophil/ lymphocytes ratio in metastatic colorectal cancer: a retrospective analysis of the TRIBE study by GONO.
Ann Oncol. 2018 Apr 1;29(4):924-930. PubMed PMID: 29324972. IF 13,93

The aim of our study was to evaluate the prognostic role of Neutrophil/lymphocyte ratio (NLR) in the TRIBE trial in which metastatic colorectal cancer patients (mCRC pts) received FOLFOXIRI or FOLFIRI plus bevacizumab. A cut-off value of 3 was adopted to discriminate pts with low versus high NLR. Univariate analysis showed that patients with high NLR had significantly shorter progression-free survival (PFS) and overall survival (OS) than patients with low NLR. In the multivariable model, NLR retained a significant association with OS, but not with PFS. Pts with low and high NLR achieved similar PFS and OS benefit from the triplet. This study confirmed the negative prognostic role of high NLR in mCRC pts treated with bevacizumab plus chemotherapy.

Croset M., Pantano F., Kan C.W.S., Bonnelye E., Descotes F., Alix-Panabieres C., Lecellier C.H., Bachelier R., Allioli N., Hong S.S., Bartkowiak K., Pantel K., Clezardin P.

miRNA-30 family members inhibit breast cancer Invasion, osteomimicry, and bone destruction by directly targeting multiple bone metastasis-associated genes.
Cancer Res. 2018 Sep 15;78(18):5259-5273. PubMed PMID: 30042152. IF 9,13

Here, we establish miR-30 family members as suppressors of breast cancer (BC) bone metastasis. In particular, lower miR-30 expression was found in estrogen receptor negative/progesterone receptor negative BC cells and was associated with poor relapse-free survival. Overexpression of miR-30 in triple negative BC cells resulted in the reduction of bone metastasis burden in vivo. Moreover, we found that miR-30 repressed genes associated with osteoclastogenesis stimulation, osteoblastogenesis inhibition, tumor cell osteomimicry, and invasiveness. Overall, our findings provide evidence that miR-30 family members employ multiple mechanisms to impede BC bone metastasis and may represent attractive therapeutic targets.

Fioramonti M., Fausti V., Pantano F., Iuliani M., Ribelli G., Lotti F., Pignochino Y., Grignani G., Santini D., Tonini G., Vincenzi B.

Cabozantinib affects osteosarcoma growth through a direct effect on tumor cells and modifications in bone microenvironment.
Sci Rep. 2018 Mar 8;8(1):4177. PubMed PMID: 29520051. IF 4,122

The study aimed to evaluate the effect of c-MET inhibitor cabozantinib (CBZ) on Osteosarcoma (OS) both directly and through its action on bone microenvironment. We found that CBZ is able to decrease proliferation and migration of OS cells, inhibiting ERK and AKT signaling pathways. Furthermore, CBZ leads to the inhibition of the proliferation of OS cells expressing receptor activator of nuclear factor κB (RANK), due to its effect on bone microenvironment, where it causes an overproduction of osteoprotegerin and a decrease of production of RANK ligand by osteoblasts. Overall, our data demonstrate that CBZ might represent a new potential treatment against OS, affecting both OS cells and their microenvironment.

Ophthalmology

Head S. Bonini

Faculty M. Coassin, A. Di Zazzo

Other Personnel G. Cupo, C. Giusti, A. Micera, R. Sgrulletta

Description

The Ophthalmology area with its diagnostic and research laboratory of Ocular surface performs diagnostic activities focused on the eye surface, corneal, conjunctival dealing with an extremely peculiar eye section.

Moreover, several research studies are investigating clinical and molecular aspects of retinal diseases; such age-related macular degeneration, diabetic retinopathy and vitro- retinal interface abnormalities.

Main research activities

The research activities of the Ophthalmology Unit has been significant since many years, being among the top teams in the national landscape. An advanced research lab is part of this area, allowing to mix the most innovative techniques and discoveries of basic research in daily clinical activity. The research areas are developed in various fields:

- Pathogenesis of allergic eye diseases;
- Pathogenesis and therapy of dry-eye disease;
- Corneal transplants, indications and treatment;
- Immunological Management of Graft-Versus Host Disease (GVHD) and related complications;
- Neuromediators and Nerve Growth Factor (NGF) at ocular surface;
- Endocrine System effect at ocular surface.

The clinical and chirurgic team has a very pronounced international background that still offers educational, clinical and research exchanges with the major national and international institutions such as the one below

The clinical and chirurgic team has a very pronounced international background that still offers educational, clinical and research exchanges with the major national and international institutions such as the one below.

Most important publications

Bonini S., Lambiase A., Rama P., Filatori I., Allegretti M., Chao W., Mantelli F., REPARO Study Group.

Phase I trial of recombinant human nerve growth factor for neurotrophic keratitis.
Ophthalmology. 2018 Sep;125(9):1468-1471. PubMed PMID: 29653861. IF 7,479

Neurotrophic keratitis/keratopathy (NK), a rare degenerative corneal disease, lacks effective pharmacologic therapies.1 Because NK pathology involves trigeminal nerve damage and loss of corneal innervation, nerve growth factor (NGF) is surmised to promote healing of NK.2 Preliminary studies with murine NGF demonstrated efficacy for treating corneal neurotrophic ulcers;3 however, the complex

tertiary structure of NGF has complicated the production of recombinant human NGF (rhNGF) suitable for clinical development. To this end, we developed an Escherichia coli–derived rhNGF formulation that demonstrated to be well tolerated and safe for topical ophthalmic use in a phase I study in healthy volunteers.4 We report phase I results of topical rhNGF for patients with moderate-to-severe NK.

Bonini S., Lambiase A., Rama P., Sinigaglia F., Allegretti M., Chao W., Mantelli F., REPARO Study Group.

Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis.
Ophthalmology. 2018 Sep; 125(9):1332-1343. PubMed PMID: 29653858. IF 7,479

Purpose: To evaluate the safety and efficacy of topical recombinant human nerve growth factor (rhNGF) for treating moderate-to-severe neurotrophic keratitis (NK), a rare degenerative corneal disease resulting from impaired corneal innervation.
Design: Phase II multicenter, randomized, double-masked, vehicle-controlled trial.
Participants: Patients with stage 2 (moderate) or stage 3 (severe) NK in 1 eye.
Methods: The REPARO phase II study assessed safety and efficacy in 156 patients randomized 1:1:1 to rhNGF 10 μg/ml, 20 μg/ml, or vehicle. Treatment was administered 6 drops per day for 8 weeks. Patients then entered a 48- or 56-week follow-up period. Safety was assessed in all patients who received study treatment, whereas efficacy was by intention to treat.
Main outcome measures: Corneal healing (defined as <0.5-mm maximum diameter of fluorescein staining in the lesion area) was assessed by masked central readers at week 4 (primary efficacy end point) and week 8 (key secondary end point) of controlled treatment. Corneal healing was reassessed post hoc by masked central readers using a more conservative measure (0-mm staining in the lesion area and no other persistent staining).
Results: At week 4 (primary end point), 19.6% of vehicle-treated patients achieved corneal healing (<0.5-mm lesion staining) versus 54.9% receiving rhNGF 10 μg/ml (+35.3%; 97.06% confidence interval [CI], 15.88-54.71; P < 0.001) and 58.0% receiving rhNGF 20 μg/ml (+38.4%; 97.06% CI, 18.96-57.83; P < 0.001). At week 8 (key secondary end point), 43.1% of vehicle-treated patients achieved less than 0.5-mm lesion staining versus 74.5% receiving rhNGF 10 μg/ml (+31.4%; 97.06% CI, 11.25-51.49; P = 0.001) and 74.0% receiving rhNGF 20 μg/ml (+30.9%; 97.06% CI, 10.60-51.13; P = 0.002). Post hoc analysis of corneal healing by the more conservative measure (0-mm lesion staining and no other persistent staining) maintained statistically significant differences between rhNGF and vehicle at weeks 4 and 8. More than 96% of patients who healed after controlled rhNGF treatment remained recurrence free during follow-up. Treatment with rhNGF was well tolerated; adverse effects were mostly local, mild, and transient.
Conclusions: Topical rhNGF is safe and more effective than vehicle in promoting healing of moderate-to-severe NK.

Coassin M., Mastrofilippo V., Stewart J.M., Fanti A., Belpoliti M., Cimino L., Iovieno A., Fontana L.

Lamellar macular holes: surgical outcome of 106 patients with long-term follow-up.
Graefes Arch Clin Exp Ophthalmol. 2018 Jul;256(7):1265-1273. PubMed PMID: 29785511. IF 2,249

Purpose: To determine long-term results of vitrectomy for lamellar macular holes (LMH). To evaluate how the type of lamellar macular hole (tractional vs. degenerative) and the crystalline lens status might influence visual outcomes.
Methods: We collected data from 106 patients with symptomatic lamellar macular hole that underwent pars plana vitrectomy with membranectomy and internal limiting membrane peeling. Best-corrected visual acuity (BCVA) and optical coherence tomography appearance were determined preoperatively and postoperatively.
Results: Most of the lamellar holes were of tractional type (65%). Mean follow-up after surgery was 36 months. Mean BCVA increased from 20/50 to 20/43 at 6 months and 20/33 at last follow-up visit (p < 0.001). Vision improved in 74 (70%), remained stable in 11 (10%), and decreased in 21 (20%) eyes. Subgroup analysis showed that visual acuity significantly increased in the tractional but not in the degenerative forms of LMH. Thirteen eyes lost two or more ETDRS lines after surgery. Preoperative phakic/pseudophakic status influenced the functional outcomes.
Conclusions: Surgery may be effective in some subsets of patients with lamellar macular hole, but postoperative visual loss is not uncommon and prospective controlled studies are warranted.

Orthopaedic and Trauma Surgery

Head R. Papalia

Faculty F. Franceschi, U.G. Longo, A. Marinozzi, G. Vadalà

Other Personnel C. Amato, S. Campi, F. Cancilleri, V. Denaro, G. Di Giacomo, F. Franceschetti, G. Marineo, A. Palumbo, N. Papapietro, G. Rizzello

PhD Students A. Berton, M. Ciuffreda, L. Diaz, A. Guarnieri, F. Russo, G. Salvatore, S. Vasta, B. Zampogna

Residents E. Albo, A. Alifano, A. Baldari, L. Binci, G. Cortina, F. Buschini, V. Candela, C. De Andreis, G. De Angelis, S. De Salvatore, C. Di Naro, A. Gambineri, M. Paciotti, A. Perrino, F. Pollara, S. Santini, G. Stelitano, G. Torre, F. Vorini

Description

The UCBM Research Unit of Orthopaedic Surgery and Trauma Surgery is devoted to the study of new surgical and biological strategies for the treatment of degenerative and traumatic diseases of the musculoskeletal system, in particular upper and lower limbs and spine. The research topics are related to the use of Adult Stem Cells and Platelet Rich Plasma for the treatment cartilage, disc, bone and tendon regeneration. Moreover, research on bone tumors and sport related trauma with the use of finite elements models are also being investigated. As part of the Centre of Integrated Research, research is approached with a multidisciplinary view in order to get new cutting age hypothesis and objectives to achieve the best results for the patients. The Research Unit is also equipped with a Laboratory of Regenerative Orthopeadic where basic and preclinical researches are performed. Two full time biologist with cell and molecular biology expertise as well as histology work in the laboratory. Preclinical studies have been carried out for several years at the Animal Facility of Tor Vergata University of Rome and in collaboration with the Veterinary Hospital at University of Padua.

Main research activities

- Development of a multidisciplinary and integrated approach, for the management of work affected by degenerative pathologies of the spine:

study of occupational aspects and innovative regenerative treatment of the intervertebral disc to favour the return to work (ACTIVE);
- Intra-articular injection of Irisin combined with Hyaluronic Acid can promote Cartilage Regeneration in a Murine Model of Osteoarthritis;
- Efficacy of intradiscal injection of allogeneic mesenchymal stem cells from bone marrow in subjects with low back pain caused by degenerative intervertebral disc disease not responsive to conventional therapy (RESPINE);
- Advanced injectable nanocomposite biomaterials with therapeutic-regenerative activity for the treatment of bone metastases (ACTION);
- Intervertebral disc regeneration mediated by intradiscal injection of autologous mesenchymal stem cells: phase IIB randomized clinical trial;
- Impending fracture of the metastatic lumbar spine: identification of prognostic factors and optimization of preventive vertebroplasty;
- Development of a computer model to study shoulder instability;
- Induced Pluripotent Stem Cells for Vertebral Regeneration (iPSpine);
- Isolated reconstruction of the medial patello-femoral ligament in patients with patellofemoral instability
- Reverse shoulder arthroplasty: the role of the teres minor and the humeral version in the performance of daily activities;
- Clinical controlled study on the use of computer-assisted navigation for the total knee arthroplasty: clinical and radiological evaluation;

- Improving accuracy in reverse shoulder prosthesis: new frontiers of computer navigation
- Enhancing the osteo-chondrogenic regenerative properties of a three-dimensional matrix: a multiphase study;
- Periprosthetic infections: get the diagnosis quickly and with low-cost techniques;
- Evaluation of the outcomes of the trapezoid-metacarpal prosthesis for the treatment of rhizoarthrosis compared to trapeziectomy and suspension tenoplasty. Randomized prospective clinical trial;
- Effect of lateralization in the reverse shoulder prosthesis: where lateralize improves outcomes. Correlation between the variations of the pre and postoperative morphological angles with rom improvement and pre and postoperative functional scores;
- Role of patellar prosthesis in knee arthroplasty. Randomized prospective clinical trial on the influence of patellar replacement in anterior post-operative pain and functional scores in knee arthroplasty;
- Volumetric analysis of the bony edema of the knee in case of anterior cruciate ligament injury and correlation with ligamentous stability parameters before and after intervention of reconstruction;
- Medial pivot vs postero-stabilized type knee replacement: clinical and radiological evaluation and analysis of patient satisfaction;
- Clinical and radiological study for the evaluation of the clinical outcomes of Cotton Osteotomy.

Most important publications

Vasta S., Andrade R., Pereira R., Bastos R., Battaglia A.G., Papalia R., Espregueira-Mendes J.

Bone morphology and morphometry of the lateral femoral condyle is a risk factor for ACL injury.

Purpose: The purpose of this study was to investigate the influence of the knee lateral compartment bony morphology and morphometry on risk of sustaining an anterior cruciate ligament (ACL) injury.

Methods: A total of 400 age and sex-matched patients (200 ACL-ruptured and 200 ACL-intact) were included. The lateral femoral and tibial bone morphology and morphometric parameters were measured on knee lateral radiographs, taken at 30° of knee flexion with overlapping of the femoral condyles. Radiographic measurements included: anteroposterior-flattened surface of the femur's lateral condyle (XY); femur's diaphysis anteroposterior distance (A); anteroposterior distance of the femur's lateral condyle (B); height of the femur's lateral condyle (C); anteroposterior distance of the tibial plateaus (AB); tibial slope. In addition, three morphological ratios were calculated: B/AB; B/XY; XY/AB (Porto ratio).

Results: Most of bone morphological parameters were different between genders (P < 0.05). ACL-ruptured female subjects showed statistical significant smaller condyle heights (C), smaller distances of the flattened surface of the distal femoral condyle (XY), smaller tibial plateau anteroposterior distances (AB), and higher XY/AB ratio (P < 0.05). ACL-ruptured male subjects had statistical significant smaller condyle height (C), anteroposterior distance of the femur's lateral condyle (B), tibial plateau anteroposterior distances (AB), and tibial slope (P < 0.05). Multivariate logistic regression model showed that five morphological parameters (A, XW, XY, XZ, and AB) were significantly associated with ACL rupture (AUC = 0.967, P < 0.001). Calculated ratios (XY/AB; B/AB; B/XY) showed a significant accuracy in identifying individuals with ACL injury (P < 0.001).

Conclusions: The most important finding of this study was that the calculated ratios (XY/AB; B/AB; B/XY) showed a significant accuracy in identifying the individuals with and without an ACL injury. Within this line, a longer flat surface of the lateral femoral condyle or higher Porto ratio (XY/AB) is associated with a lower the risk of ACL injury. Moreover, when considering the combination of five primary bone morphology and morphometric parameters (A, XW, XY, XZ, and AB), the accuracy in identifying these individuals was excellent (AUC = 0.967). These findings may contribute to injury risk assessment, sports participation, and injury prevention counseling and surgical planning refining by identifying high-risk patients who would benefit from the addition of associated procedures to the anatomic ACL reconstruction aiming the improvement of knee stability and decrease the risk of further injuries.

Vadalà G., Russo F., De Strobel F., Bernardini M., De Benedictis G.M., Cattani C., Denaro L., D'Este M., Eglin D., Alini M., Denaro V.

Novel stepwise model of intervertebral disc degeneration with intact annulus fibrosus to test regeneration strategies.

Novel preclinical models that do not damage the annulus fibrosus (AF) of the intervertebral disc are required to study the efficacy of new regenerative strategies for the nucleus pulposus (NP). The aim of the study was to characterize a preclinical ovine model of intervertebral disc degeneration (IDD) induced by endplate (EP) damage and repair via the transpedicular approach, with or without partial nucleotomy, while keeping the AF intact. Twelve adult sheep were used. By the transpedicular approach, a 2 mm tunnel was drilled to the NP through the EP. A partial-nucleotomy was performed. The tunnel was sealed using a polyurethane scaffold. Lumbar discs were assigned to different groups: L1-2: nucleotomy; L2-3: EP tunnel; L3-4: nucleotomy + EP repair; L4-5: EP tunnel + repair; L5-6: control. X-Ray and MRI were performed at 0, 1, 3, and 6 months after surgery. Disc height and MRI indexes were calculated. Macro- and micro-morphology were analyzed. Pfirrmann and Thompson grades were assigned. The treated discs exhibited a progressive decrease in NP signal intensity and MRI index, displaying specific grades of degeneration based on the surgical treatment. According to Pfirrmann and Thompson grades different procedures were staged as: EP tunnel + repair: grade-II; EP tunnel: grade-III, nucleotomy + EP repair: grade-IV; nucleotomy: grade-V. A new stepwise model of IDD to study and test safety and efficacy of novel strategies for NP regeneration has been characterized. The different degrees of IDD have been observed similar to Pfirrmann and Thompson grading system. The intact AF allows for loading studies and eliminating the need for AF closure. © 2018 Orthopaedic Research Society.

Longo U.G., Margiotti K., Petrillo S., Rizzello G., Fusilli C., Maffulli N., De Luca A., Denaro V.

Genetics of rotator cuff tears: no association of col5a1 gene in a case-control study.

Background: The incidence of RC tears increases with aging, affecting approximately 30 to 50% of individuals older than 50 years, and more than 50% of individuals older than 80 years. Intrinsic factors (age or gender), extrinsic factors (sports activity or occupation), and biological factors were identified in the onset and progression of RC tears. The attention in the study of aetiology of RC tendinopathy has shifted to the identification of gene variants. Genes encoding for proteins regulating the concentration of pyrophosphate in the extracellular matrix and genes encoding for fibroblastic growth factors, defensin beta 1 and estrogen-related receptor-beta were analyzed. However, only in one study the role of variants of collagen type V alpha 1 (col5a1) gene in RC tears was assessed. The objective of this study was to determine whether a col5a1 DNA sequence variant, rs12722 (C/T) was associated with rotator cuff (RC) tears in a case-control study.

Methods: The study included 93 Caucasian patients undergoing surgery for RC tears and 206 patients with no history and sign of RC disease as evaluated by MRI. Patients were divided into two groups. Group 1 included patients with RC tear diagnosed on clinical and imaging grounds and confirmed at the time of surgery. Group 2 (control group) included patients without history or clinical symptoms of RC disorders and with a MRI negative for RC disease. DNA was obtained from approximately 1.2 ml of venous blood using the MagCore extractor system H16 with a MagCore Genomic DNA Large Volume Whole Blood Kit (RBC Bioscience Corp., Taiwan). All study participants were genotyped for SNPs rs12722.

Results: We first estimated that our study had 92% power at $p < 0.05$ to detect a genetic effect size of 2.05 in the RT tears (93 individuals) and healthy population (206 individuals) cohorts, assuming a minor allele frequency for col5a1 variant rs12722 of 0.5707 in the Italian population (gnomAD frequency). No significant difference in allele and genotype frequencies was observed between RT tears patients and healthy controls. Similarly, no significant association was seen between the RT tears and healthy controls participants in the combined genotype distributions.

Conclusion: In conclusion, no correlations between the SNP rs12722 of col5a1 gene and RC tears susceptibility was found.

Otolaryngology

Head F. Salvinelli

Faculty M. Casale

Description

The research unit has been working for years in the design of new devices for topical therapy of upper airway, we are studying the endothelial dysfunction and the potential role of Nerve growth factor (NGF) and the inner ear disorders. We are working on new hearing aids and new methods of nasal breathing evaluation and innovative techniques for vertigo and sinus-nasal diseases.

Main research activities

- New devices for topical therapy for upper airway;
- Development of hearing aids "transparent" to maintain the spectral characteristics of the sound;
- New surgical techniques for the treatment of Meniere disease. Prospective study;
- Otologic disorders, temporo-mandibular dysfunction and serotomninergic pattern;
- Topical hyaluronic acid use in the upper airway inflammation;
- Endothelial dysfunction and inner ear disorders;
- New device to evaluate nasal breathing;
- The level of NGF and the expression of NGF receptors in nasal cavity and in the olfactory bulb.

Most important publications

Rinaldi V., Moffa A., Costantino A., Cassano M., Casale M.

The (templar) knight cap: a new and simple way to prevent hair interference during ear surgery.
Eur Arch Otorhinolaryngol. 2018 Nov;275(11):2889-2891. PubMed PMID: 30229452. IF 1,546

Introduction: Hair interference is a critical problem in ear surgery. The hair around the surgical area can get stuck unwantedly, making the surgeon habitually struggling with this hair rather than the surgery itself. Hair shaving can cause psychological discomfort, especially for women and data about shaving efficacy are conflicting. With the aim of solving this problem, we developed a new way to clear hair from the operating field named "The (Templar) Knight cap". **Technical description:** This is a medical elastic stocking open at the ear to be treated and at the face that recalls the typical cap worn by Templar knight. This cap allows good hair retention and marks the surgical site. It is easy to wear does not require additional time for clinical staff. **Conclusions:** The described cap could be a valid instrument during ear surgery with a low cost pricing, making it applicable in very poor settings, such as developing countries.

Salvinelli F., Frari V., Capuano F., Salvinelli B., Rocco M.L., Aloe L.

Endogenous nerve growth factor stimulation: effects on auditory pathway neural cells in a mouse model.
Eur Rev Med Pharmacol Sci. 2018 Oct; 22(20):7013-7019. PubMed PMID: 30402868. IF 2,387

Objective: In the present study, we investigated whether high-pressure hypotonic saline solution (Hphss) affects the basal level of Nerve Growth Factor (NGF) and expression of receptors in the cochlea, bark earing, retina, and visual cortex. **Materials and methods:** For this study, we used three weeks old female Sprague Dawley (SD) rats (n = 12). Rats were housed in polypropylene cages and were kept under standard conditions (12 h light:12 h dark cycle) with free access to water and food (Purina chow food). A specific dispenser was employed to deliver sterile hypotonic saline at high pressure (pressing emission level (PEL): 7 g/s; emission time (ET): 0.5 s). Rats were divided into two groups: untreated (n = 6) and treated with Hphss (n = 6), three times per day, for 10 consecutive days. Treatment was performed in both nostrils with 50 μl of Hphss using a microsyringe equipped with a plastic tip. **Results:** We observed a significant enhancement in the level of NGF in the cochlea and bark earing, but not in the retina and visual cortex. This is likely because the nasolacrimal duct pathway does not appear to have an effect on the retina, and the visual cortex appears to be too far from the cribriform plate to be reached by nasal NGF. **Conclusions:** This treatment can significantly protect and/or delay degeneration of cochlear auditory NGF-target cells. It is free from side effects and can be used in chronic diseases for as long as needed. It remains to be investigated whether the effects of short-term therapy are long-lasting, or if the treatment must be repeated.

Casale M., Moffa A., Cassano M., Carinci F., Lopez M.A., Trecca E.M.C., Torretta S., Rinaldi V., Pignataro L.

Saline nasal irrigations for chronic rhinosinusitis: from everyday practice to evidence-based medicine. An update.
Int J Immunopathol Pharmacol. 2018 Jan-Dec;32: 2058738418802676. PubMed PMID: 30350744. IF 2,117

Saline nasal irrigations (SNIs) are often recommended as an additional non-pharmacological treatment for adults with chronic rhinosinusitis (CRS), for which it could even be considered a first-line treatment. However, there is a wide range of different SNI protocols. The aim of this article is to review the published literature regarding all of the potential therapeutic effects of SNIs in adult CRS patients who had not undergone sinus surgery and clarify the role of the various saline nasal solutions and protocols (particularly the volume, frequency and duration of treatment), and describe the nasal devices used. A search was made of the PubMed, Google Scholar and Ovid databases using the key words 'saline nasal irrigation' and 'chronic rhinosinusitis', or medical subject headings. The search identified 11 studies involving 663 patients. There was no consensus about but substantial agreement concerning the frequency and duration of treatment, the type of device, and the amount of solution to be used when managing CRS. A hypertonic solution with the addition of the natural minerals and oligo-elements found in seawater and some thermal waters may be associated with greater clinical benefit in terms of endoscopic scores and mucociliary clearance than isotonic solutions. Further studies are required to compare the different forms of SNI and define SNI protocols and nasal devices, while considering patient compliance.

Pathology

Head G. Perrone

Faculty A. Onetti Muda, C. Rabitti

Other Personnel N. Orlando

Description

The Anatomic Pathology Lab is dedicated to medical diagnosis and scientific research activities. The latter is in turn divided into two main operative fields: development of research lines that are specific to the area, and collaboration within research lines in other areas.

Over the years, the laboratory has been furnished with a wide range of technologically advanced equipment, which allows it to better implement activities. Currently, procedures include:
- Histopathology and cytopathology;
- Histochemistry;
- Immunohistochemistry;
- APERIO Digital Pathology Slide Scanner;
- Fluorescence microscope with FISH equipment;
- Pyrosequencing station;
- Real-time PCR equipment;
- Idylla station, for fully-automated real-time PCR;
- N-Counter Nanostring for gene expression profiling.

Main research activities

Research topics:
- Morphological and molecular technologies for cancer characterization and correlation with disease progression/treatment outcome;
- Breast cancer - morphological and molecular characterization of breast cancer supporting innovative medical and surgical procedures;
- Gastrointestinal neoplasms - histological and immunohistochemical subtyping; validation of pre-operative molecular analysis as an additional mutodiagnostic tool for cancer;
- Neoplastic, metabolic and inflammatory liver diseases: morphological characterization and correlation with disease progression.

Funded projects:
- Extension of the RealQuant® Lung Fusion Genes kit validation to cytological specimens (OSLO) – Principal Investigator: G. Perrone;
- Utility of molecular sub-typing (PAM50) of breast cancer in clinical practice Principal Investigator: G. Perrone; Francesca Zalfa;
- Identification of new cancer biomarker in ovarian serous carcinoma (PAO65). Principal Investigator: G. Perrone; Francesca Zalfa;
- Colorectal cancer KRAS mutation status in liquid biopsies and tumor tissue (LIQUID36). Principal Investigator: G. Perrone.

Main collaborations

- Medical Oncology Department, Hospital Clínic. Universitat de Barcelona, Barcelona, Spain.
- Dept. of Pathology. Harvard University School of Medicine, Boston, USA.
- Dept. of Fundamental Neuroscience, Faculty of Biology and Medicine. University of Lausanne, Switzerland.
- Dept. of Clinical and Experimental Medicine. University of Florence.
- Dept. of Pharmacy - Pharmaceutical Sciences. University of Bari Aldo Moro.

Most important publications

Carotti S., Guarino M.P.L., Valentini F., Porzio S., Vespasiani-Gentilucci U., Perrone G., Zingariello M., Gallo P., Cicala M., Picardi A., Morini S.

Impairment of GH/IGF-1 axis in the liver of patients with HCV-related chronic hepatitis.
Horm Metab Res. 2018 Feb; 50(2):145-151. PubMed PMID: 28922679. IF 2,560

Resistance to the action of growth hormone (GH) frequently complicates liver cirrhosis, while, physiologically, the activation of GH

receptor (GHR) determines phosphorylation of signal transducer and activator of transcription (STAT)-5 and the consequent induction of insulin-like growth factor-1 (IGF-1) expression. The suppressor of cytokine signaling (SOCS)-3 negatively regulates this intracellular cascade. We aimed to evaluate the hepatic expression of the GH/IGF-1 axis components in the liver of patients with HCV-related chronic hepatitis at different fibrosis stages. The expression of GH/IGF-1 axis components, such as GHR, IGF-1, STAT5-p, and SOCS-3, was assessed by immunohistochemistry at the lobular level in 61 patients with HCV-related hepatitis. At the hepatocyte level, IGF-1 and nuclear STAT5-p positivity scores showed negative correlations with fibrosis stage, while SOCS-3 score a positive one (p<0.05 for all). Furthermore, the reduction of hepatocyte score of IGF-1 expression was associated with the serological parameters of liver damage (p<0.05) and with the increase of the score of IGF-1 expression by hepatic stellate cells (p<0.05). IGF-1 expression by hepatocytes was reduced with fibrosis progression, probably due to the impairment of GHR intracellular cascade by the SOCS-3 activation already in pre-cirrhotic stages. The inverse correlation between IGF-1 expressed by hepatocytes and by hepatic stellate cells suggests that IGF-1 may exert specific functions in different hepatic cells.

Maldonado L., Brait M., Izumchenko E., Begum S., Chatterjee A., Sen T., Loyo M., Barbosa A., Poeta M.L., Makarev E., Zhavoronkov A., Fazio V.M., Angioli R., Rabitti C., Ongenaert M., Van Criekinge W., Noordhuis M.G., de Graeff P., Wisman GBA., van der Zee A.G.J., Hoque MO.

Integrated transcriptomic and epigenomic analysis of ovarian cancer reveals epigenetically silenced GULP1.

Many epigenetically inactivated genes involved in ovarian cancer (OC) development and progression remain to be identified. In this study we undertook an integrated approach that consisted of identification of genome-wide expression patterns of primary OC samples and normal ovarian surface epithelium along with a pharmacologic unmasking strategy using 3 OC and 3 immortalized normal ovarian epithelial cell lines. Our filtering scheme identified 43 OC specific methylated genes and among the 5 top candidates (GULP1, CLIP4, BAMBI, NT5E, TGFβ2), we performed extended studies of GULP1. In a training set, we identified GULP1 methylation in 21/61 (34%) of cases with 100% specificity. In an independent cohort, the observed methylation was 40% (146/365) in OC, 12.5% (2/16) in borderline tumors, 11% (2/18) in cystadenoma and 0% (0/13) in normal ovarian epithelium samples. GULP1 methylation was associated with clinicopathological parameters such as stage III/IV (p = 0.001), poorly differentiated grade (p = 0.033), residual disease (p < 0.0003), worse overall (p = 0.02) and disease specific survival (p = 0.01). Depletion of GULP1 in OC cells led to increased pro-survival signaling, inducing survival and colony formation, whereas reconstitution of GULP1 negated these effects, suggesting that GULP1 is required for maintaining cellular growth control.

Marangi G.F., Pallara T., Lamberti D., Perrella E., Serra R., Stilo F., De Caridi G., Onetti Muda A., Persichetti P.

An electrical plasma dissection tool for surgical treatment of chronic ulcers: Results of a prospective randomised trial.

Cutaneous ulceration is a difficult medical problem and a major source of morbidity for patients. In the surgical treatment of ulcers, debridement is the first step, and it can be carried out using several surgical tools. Recently, new surgical devices have emerged using plasma-mediated electrical discharges with a lower peak temperature. A prospective single-blind trial was conducted on chronic ulcers not responsive to common non-surgical management. Patients were randomly separated into 2 groups: Group A received surgical debridement with conventional electrocautery, and Group B received surgical debridement using the plasma-mediated device. Histological samples were collected intraoperatively to evaluate the thermal damage during the surgical procedure and 2 weeks after surgery to evaluate the inflammatory response and collagen deposition. The width of coagulation necrosis at the incision margins in Group B was significantly shorter compared with Group A (P = .001). The inflammatory cell infiltration showed a cellular distribution percentage that was quite equal between the 2 groups. The granulation tissue showed an abundant deposition of dense and mature collagen in Group B, compared with Group A, where the mature collagen appeared in small quantities (P < .001). Microbial culture showed a lower incidence of postoperative infections in Group B compared with the control group (P < .05). The study demonstrated, based on the results, that the new technology with the use of a lower temperature electrosurgical device represents an effective therapeutic weapon for the surgical treatment of skin ulcers, both vascular and extravascular types.

Physical and Rehabilitation Medicine

Head S. Sterzi

Faculty F. Bressi

Other Personnel M. Bravi, M. Maselli, S. Miccinilli, M. Morrone, F. Santacaterina

Description

The research unit is equipped with a movement analysis laboratory, consisting in a stereophotogrammetric system of 8 cameras, two force platforms, a surface electromyography system and a dedicated software for the analysis of collected data. The main activities conducted in the laboratory are: optoelectronic plethysmography, gait analysis and analysis of the upper limb kinematics. Our unit is also equipped with the hand rehabilitation glove Gloreha, that provides computer-controlled, repetitive, passive and active assisted mobilization of the fingers, with multisensory feedback used for clinical trials involving the hand functional recovery after stroke. Recently we have available a new tool for gait and balance disorder, the Walker View, a high-tech treadmill capable of assessing gait in real time, as it is equipped with a 3D camera and a sensorized tape with load cells. This technology returns real-time feedbacks for the correction of the gait alterations.

Main research activities

- Gait analysis in hemiparethic/hemiplegic patients for optimization of orthotic prototypes.
- Gait analysis in patients after total hip arthroplasty or total knee arthroplasty.
- Validation of an Inertial Measurement Unit and a sensorized treadmill in performing gait analysis.
- Rehabilitation with robotic platforms of upper and the lower limbs in patients with hemiplegia/hemiparesis after stroke.
- Realization a bio-cooperative robotic system that integrates a virtual reality environment to deliver motor rehabilitation and visuomotor coordination, in personalized working scenarios, of people affected by work-related musculoskeletal pathologies of the upper extremities.
- Implantation of neural invasive interfaces for the bidirectional control of an upper limb cybernetic prosthesis and pain control in upper limb amputees.

Main collaborations

- IRCCS Bambino Gesù Paediatric Hospital, Italy
- Don Carlo Gnocchi Foundation.

Most important publications

Lauretti C., Cordella F., Ciancio A.L., Trigili E., Catalan J.M., Badesa F.J., Crea S., Pagliara S.M., Sterzi S., Vitiello N., Garcia Aracil N., Zollo L.

Learning by demonstration for motion planning of upper-limb exoskeletons.
Front Neurorobot. 2018 Feb 23; 12:5. PubMed PMID: 29527161. IF 3,508

This paper proposes a motion planning system, based on Learning by Demonstration, for upper-limb exoskeletons that allow successfully assisting patients during Activities of Daily Living in unstructured environment, while ensuring that anthropomorphic criteria are satisfied in the whole human-robot workspace. The motion planning system combines Learning by Demonstration with the computation of Dynamic Motion Primitives and machine learning techniques to construct task- and patient-specific joint trajectories based on the learnt trajectories. The achieved results showed a 100% success rate in the task fulfilment, with a high level of generalization with respect to the environment variability.

Scotto di Luzio F., Simonetti D., Cordella F., Miccinilli S., Sterzi S., Draicchio F., Zollo L.

Bio-cooperative approach for the human-in-the-loop control of an end-effector rehabilitation robot.
Front Neurorobot. 2018 Oct 11; 12:67. PubMed PMID: 30364325. IF 2,606

In this paper, a novel 3D bio-cooperative robotic platform is developed. A new arm-weight support system is included into an operational robotic platform for 3D upper limb robot-aided rehabilitation. The robotic platform is capable of adapting therapy characteristics to specific patient needs, thanks to biomechanical and physiological measurements, and thus closing the subject in the control loop. An assistance-as-needed approach is applied to provide the appropriate amount of assistance. The results have demonstrated the capability of the system to adapt to real needs of the patients. The provided assistance was shown to reduce the muscular fatigue without negatively influencing motion execution.

Miccinilli S., Bravi M., Morrone M., Santacaterina F., Stellato L., Bressi F., Sterzi S.

A triple application of kinesio taping supports rehabilitation program for rotator cuff tendinopathy: a randomized controlled trial.
Ortop Traumatol Rehabil. 2018 Dec 31;20(6):499-505. PubMed PMID: 30676323.

The aim of the study is to investigate the efficacy of Kinesio Taping (KT) combined with a standardized protocol of rehabilitative exercises in reducing pain and in functional recovery in patients affected by rotator cuff tendinopathy (RoCT). 21 patients were enrolled in a real group (RG) and 19 in a sham group (SG). RG received a real KT application and SG received a sham KT application. Both groups received the same rehabilitative protocol.
Our results showed that KT application combined with conventional rehabilitative treatment can facilitate immediate pain reduction during rehabilitative treatment, can increase function recovery and strength recovery. Our findings however are not strong enough to recommend the application of KT during rehabilitative treatment for RoCT.

Plastic Surgery and Dermatology

Head P. Persichetti

Faculty C. Dianzani, G.F. Marangi, S. Tenna

Other Personnel B. Brunetti, A. Cagli, B. Cogliandro, V. Panasiti, P. Simone

Description

Fields of interests and research:
- Reconstructive surgery following neoplasms, malformations or trauma of:
  - head and neck
  - upper and lower limb
  - thorax
  - abdomen
  - perineum
- Screening, diagnosis and treatment of skin cancer
- Breast reconstruction (Implants, Flap, Lipofilling)
- Treatment of ulcers:
  - vascular
  - diabetes
  - pressure sore
- Application of regenerative medicine with autologous fat plus Platelet Rich Plasma (PRP)
- Burns
- Body contouring procedures after bariatric surgery
- Cosmetic surgery and aesthetic medicine:
  - Head and neck (rhinoplasty, blepharoplasty, face lift, otoplasty)
  - Breast (augmentation, mastopexy, reduction mammaplasty)
  - Abdomen (abdominoplasty, liposuction)
  - Upper and lower limb (thigh lift, brachioplasty, liposuction)
  - Filler
  - Botulinum toxin
- Application of regenerative medicine in skin renjuvenation
- Application of regenerative medicine in the treatment of acne scars
- Lasers treatment of:
  - Hemangiomas
  - Scars
  - Cutaneous lesions
  - Photoaging
  - Hypertrichosis

Main research activities

- Application of regenerative medicine in treatment of atrophic acne scars: nanofat plus PRP infiltration and fractional CO_2 laser resurfacing;
- The use of PRP in breast implant capsule contracture;
- Treatment of venous ulcers with different combinations of fat graft and platelet rich plasma: a prospective comparative evaluation;
- Quality of life in patients affected by breast cancer treated with reconstructive procedures: application of the BREAST-Q questionnaire;
- Evaluation of the postero-medial scar brachioplasty technique associated to lipo-aspiration in the post-bariatric arm remodeling;
- Platelet-rich plasma in breast implant capsule contracture;
- IPL in the treatment of posterior blepharitis;
- The use of regenerative devices in chronic wounds: a prospective randomized control trial;
- Bioelectrochemical sensor to detect antibiotic-resistant Pseudomonas Aeruginosa;
- Evaluation of the periprosthetic breast capsule in patients subjected to breast reconstruction with tissue expanders with different surfaces;
- Association of human papilloma virus infection and keratoacanthoma clinal evolution;
- Correlation with dysfunction of the thyroid gland and skin pathology;
- Association of human papilloma virus infection and aktinic cheratosis;
- CDKN2A involvment in melanoma and mesothelioma susceptibility in rare familial cancer syndromes;
- Clinical evaluation of topical treatment in papulo cystic acne.
- Presence of a Multidisciplinary Research Group: "To be and to appear: objective indication to plastic surgery" of Campus Bio-Medico University of Rome, Rome, Italy.

Main collaborations

- Department of Plastic and Reconstructive Surgery, Kansai Medical Unive Department of Plastic and Reconstructive Surgery, Kansai Medical University, Japan;
- Singapore Centre for Environmental Life Sciences Engineering, Nanyang Technological University, Singapore, Japan;

Most important publications

Simone P., Carusi C., Segreto F., Iannuzzi R., Buscaglione S., Gizzi A., Giannitelli S., Rainer A. Filippi S., Persichetti P.

Postbariatric brachioplasty with posteromedial scar: physical model, technical refinements, and clinical outcomes.
Plast Reconstr Surg. 2018 Feb; 41(2):344-353. PubMed PMID: 29369986. IF 3,621

Brachioplasty is an increasingly performed procedure following massive weight loss. The aims of the study were to develop a physical model to investigate the ideal location of the surgical incision. 24 postbariatric patients underwent brachioplasty with posteromedial scar placement, concomitant liposuction, fascial plication, and axillary z-plasty. Skin specimens were tested and a physical model of the arm was set up to investigate the difference in mechanical stress on the posteromedial and medial scars. The physical model showed that stress intensity and distribution along the scar were reduced in the posteromedial location, with smaller scar displacement in the loading simulations.

Marangi G.F., Pallara T., Lamberti D., Perrella E., Serra R., Stilo F., De Caridi G., Onetti Muda A., Persichetti P.

An electrical plasma dissection tool for surgical treatment of chronic ulcers: results of a prospective randomised trial.
Int Wound J. 2018 Oct; 15(5):717-721. PubMed PMID: 29600828. IF 2,380

In the surgical treatment of ulcers, debridement is the first step that can be carried out using several surgical tools. A new surgical devices using plasma-mediated electrical discharges with a lower peak temperature is proposed. A prospective single-blind trial was conducted on chronic ulcers with patients randomly separated into: group a received surgical debridement with conventional electrocautery and group b with the plasma-mediated device. Histological samples were collected intraoperatively and 2 weeks after surgery. The study demonstrated that the new technology represents an effective therapeutic weapon for the surgical treatment of skin ulcers.

Cogliandro A., Brunetti B., Barone M., Favia G., Persichetti P.

Management of contralateral breast following mastectomy and breast reconstruction using a mirror adjustment with crescent mastopexy technique.
Breast Cancer. 2018 Jan; 25(1):94-99. PubMed PMID: 28819836. IF 1,772

TThe aim of this study is to present the use of crescent mastopexy technique with implants in contralateral adjustment following monolateral breast reconstruction. We used breast-q to evaluate breast perception and patient's satisfaction and surgeon-rated aesthetic outcomes were measured using the kroll evaluation. 55 patients who had undergone breast reconstruction with implants and contralateral breast symmetrizationwere enrolled. Statistical analysis was performed using fisher's exact test. In patients with a pseudo-ptosis or mild ptosis of the contralateral breast, crescent mastopexy could be a valid procedure with minimal scars, better symmetry and global cosmetic results than other procedures.

Process Engineering

Head M. De Falco

Faculty M. Capocelli

Other Personnel D. Barba, A. Germanà, N. Greco

Description

In the Research Unit, academic figures and business leaders (lecturers of the Master of Chemical Engineering for the Sustainable Development) work in close synergy with the objective to develop new technologies of industrial interest, aimed at increasing the compatibility of production systems with safeguarding the environment and human health. The scientific and technological approach derives from the belief that every production system should be equipped with advanced technologies able to improve the performance but, at the same time, reducing the pollutants emissions into the environment at the minimum values allowed by the state of technological knowledge.

Main research activities

- Analysis of CO_2 utilization processes, such as methanation and ethers production, in collaboration with NextChem (Maire Tecnimont group).
- Process analysis of a humidification-dehumidification-adsorption (HDHA) desalination method for the production of clean water from renewable energies, in collaboration with the University of Naples "Federico II".
- Microfluidic bioreactors, in collaboration with the Sapienza University, Rome.
- Thermal energy storage, in collaboration with ENEA.

Main collaborations

- Maire Tecnimont, Rome ;
- Sapienza University, Rome;
- University of Naples "Federico II".

Most important publications

Iaquaniello G., Setini S., Salladini A., De Falco M.

CO2 valorization through direct methanation of flue gas and renewable hydrogen: A technical and economic assessment.
Int J Hydrogen Energy 2018; 43(36):17069-17081. DOI: 10.1016/j.ijhydene.2018.07.099 IF 4,

Under the scenario of an increasing sharing of renewable energy, Power to Gas technology may offer an effective and valuable solution for surplus energy management, accounting for a large and long-term chemical storage. In the present study an innovative Power to Synthetic Natural Gas (SNG) process has been described and investigated from a techno-economic and environmental point of view. The configuration is based on a methanation process, directly applied on flue gas stream thus acting both as a CO2 capture and sequestration technology and as renewable energy storage mechanism. Reacting hydrogen is produced via water electrolysis powered by surplus of renewable energy, normally low-priced otherwise wasted.

Capocelli M., Balsamo M., Lancia A., Barba D.

Process analysis of a novel humidification-dehumidification-adsorption (HDHA) desalination method.
Desalination. 2018; 429(1):155-166. DOI 10.1016/j.desal.2017.12.020 IF 6,603 IF 6,603

The desalination through humidification-dehumidification (HDH) presents still a high energy-footprint but shows many unique attributes that pushed a recent revival of R&D for decentralized production of water. In this paper, a novel process scheme consisting of a multiple extraction humidification-dehumidification with vapour adsorption (HDHA) and brine recirculation is analysed. It works with bottom brine temperatures below the coldest heat source and direct recirculation. With respect to the common classification, the process can be considered a closed-air closed-water (CACW) HDH. The study of the degrees of freedom and the mathematical model for the sensitivity analysis are presented.

Tortora F., Innocenzi V., di Celso G. M., Vegliò F., Capocelli M., Piemonte V., Prisciandaro M.

Application of micellar-enhanced ultrafiltration in the pre-treatment of seawater for boron removal.
Desalination 2018; 428: 21-28. DOI 10.1016/j.desal.2017.11.016 IF 6,603

In this research, micellar enhanced ultrafiltration (MEUF) is tested as a seawater pre-treatment before entering RO. The experimental tests were performed by means of monotubular ceramic membranes of 210 kDa and 1 kDa. Boron is removed from the water flow using sodium dodecyl sulphate as a surfactant. The synthetic solutions contain 5 mg/L of boron and SDS concentrations are equal to 1.15 g/L and 2.88 g/L, under and above the critical micellar concentration, respectively.
Experimental data showed that MUEF is efficient in removing boron, with best performances obtained at low pressure, with a low or null surfactant concentration for 1 kDa membrane and a high surfactant concentration for 210 kDa membrane. Moreover, experimental results have been used to perform a preliminary process analysis for a hypothetic sea-water desalination plant, with MEUF as a pretreatment for the RO section. The results showed that the MEUF guarantees a boron concentration after RO below the allowed threshold, by using a single step osmosis; moreover, in this way it was possible to reduce the energy consumption thus resulting in an appreciable reduction of carbon footprint as well as of the unit cost of water.

Radiation Oncology

Head S. Ramella

Faculty R.M. D'Angelillo, M. Fiore, E. Ippolito

Other Personnel A. Carnevale, A. Di Donato, B. Floreno, C. Greco, A. Iurato, P. Matteucci, E. Molfese, C. G. Rinaldi, S. Silipigni, L.E. Trodella, L. Trodella

Description

The Radiation Oncology Research Unit's strategy focuses on the association between radiotherapy and systemic agents and on radiobiological and technical issues. In particular, combination of radiation and target agents, chemotherapy and immunotherapy in clinical and multidisciplinary setting is investigated. Special efforts are about combined treatment of lung cancer, prostate cancer, pancreatic cancer and rectal cancer. In addition, modern breast irradiation technique are explored in order to optimize dose distribution to the target and to the organs at risk. Special techniques such as stereotactic treatment, volumetric arc therapy and respiratory gating are implemented in radiation research protocols and in clinical practice. A novel interest of the research group involves radiomics which revealed itself as the needed bridge between medical imaging and personalized medicine. Moreover new tools to monitor patients' quality of life are being developed.

Main research activities

In the era of personalized medicine, the main topic developed has been exploiting radiopathomics data in NSCLC, in order to develop a RadioPathomics-based Decision Support Systems (RPDSSs) to predict the progression free survival (PFS), best response and pulmonary toxicity during chemoradiation. In castration resistant prostate cancer a national project about the role of radiation therapy with new hormonal drugs is ongoing. In addition the research unit is involved in three multicentric randomized interventional studies regarding second line treatment of refractory SCLC, adjuvant immunotherapy in locally advanced NSCLC treated with chemoradiation and the combination between immunotherapy and stereotactic radiotherapy in stage I NSCLC. Multidisciplinary treatment protocols in gastrointestinal cancer are also ongoing.

Most important publications

Nestle U., De Ruysscher D., Ricardi U., Geets X., Belderbos J., Pöttgen C., Dziadiuszko R., Peeters S., Lievens Y., Hurkmans C., Slotman B., Ramella S., Faivre-Finn C., McDonald F., Manapov F., Putora P.M., LePéchoux C., Van Houtte P.

ESTRO ACROP guidelines for target volume definition in the treatment of locally advanced non-small cell lung cancer.
Radiother Oncol. 2018 Apr; 127(1):1-5. PubMed PMID: 29605476. IF 4,942

Radiotherapy (RT) plays a major role in the curative treatment of locally advanced non-small cell lung cancer (NSCLC). Therefore, the ACROP committee was asked by the ESTRO to provide recommendations on target volume delineation for standard clinical scenarios in definitive (chemo)radiotherapy (RT) and adjuvant RT for locally advanced NSCLC. Recommendations are given for GTV delineation of primary tumour and lymph nodes followed by issues related to the delineation of CTVs for definitive and adjuvant radiotherapy. In the context of PTV delineation, recommendations about the management of geometric uncertainties and target motion are given.

Ramella S., Fiore M., Greco C., Cordelli E., Sicilia R., Merone M., Molfese E., Miele M., Cornacchione P., Ippolito E., Iannello G., D'Angelillo R.M., Soda P.

A radiomic approach for adaptive radiotherapy in non-small cell lung cancer patients.
PLoS One. 2018 Nov 21; 13(11):e0207455. PubMed PMID: 30462705. IF 2,766

This paper discusses the rationale supporting the concept of radiomics and the feasibility of its application to NSCLC in the field of radiation oncology. We studied 91 stage III patients treated with concurrent chemoradiation and adaptive approach in case of tumor reduction during treatment. We considered 12 statistics features and 230 textural features extracted from the CT images. In our study, we used an ensemble learning method to classify patients' data into either the adaptive or non-adaptive group during chemoradiation on the basis of the starting CT simulation. Our data supports the hypothesis that a specific signature can be identified (AUC 0.82).

Imbimbo M., Ottaviano M., Vitali M., Fabbri A., Leuzzi G., Fiore M., Franceschini D., Pasello G., Perrino M., Schiavon M., Pruneri G., Dei Tos A.P., Sangalli C., Garassino M.C., Berardi R., Alessi A., Calareso G., Petrini I., Scorsetti M., Scotti V., Rosso L., Rea F., Pastorino U., Casali P.G., Ramella S., Ricardi U., Abate-Daga L., Torri V., Trama A., Palmieri G., Marino M., Zucali P.A., TYME network collaborators.

Best practices for the management of thymic epithelial tumors: a position paper by the Italian collaborative group for ThYmic MalignanciEs (TYME).
Cancer Treat Rev. 2018 Dec; 71:76-87. PubMed PMID: 30366202. IF 8,122

Thymic epithelial tumors (TETs) are a heterogenous group of rare tumors. The recent introduction of the first TNM staging system, that is scheduled to replace the Masaoka-Koga system, may create further difficulties in TET management. As for other rare cancers it is crucial to create networks to coordinate the work among centres. In 2014 a network named TYME (ThYmic MalignanciEs), was founded in Italy. In September 2017 a panel of multidisciplinary experts convened a first Italian Expert meeting to explore the management of these tumors. In this paper we summarize the issues discussed during that meeting and we propose recommandations based on Masaoka Koga and the new TNM staging system.

Tissue Engineering & Chemistry for Engineering

Head M. Trombetta

Faculty F. Basoli, A. Rainer, S.M. Giannitelli, E. Mauri

Other Personnel F. Abbruzzese, M. Gori

Description

The Tissue Engineering and Chemistry for Engineering Research Unit works mainly on the following fields:
Tissue engineering: the Unit works on the synthesis and functionalization of biomaterials and manufacturing of scaffolds for regenerative medicine application. The Unit also develops advanced in vitro tissue and organ models for drug discovery and morphogenesis/pathogenesis studies. In particular, one of the most promising research lines is focused on the integration of micro-manufacturing technologies with tissue engineering ones, designed to miniaturize organ models to be combined with advanced imaging and spectroscopy techniques (organ-on-chip approach). At present, the Research Unit is involved in a Joint Laboratory for Nanotechnologies for the Life Sciences (nano4life), together with the Institute of Photonics and Nanotechnologies, National Research Council of Rome.
Nanomaterials for energy: ulphur, carbon and re-oxidation tolerant Solid Oxide Fuel Cells (SOFC) anodes.
Food crime: development of e-learning platforms to train Europol officers on food crime.
Critical Infrastructure Protection: creating added-value, decision-support capabilities with consequence analysis for national and multi-nation emergency management and CI owners.

Main research activities

Dr. Alberto Rainer has been awarded a research grant in the framework of the Internal Grant Program for the project "GUT2.0 - A multi-cellular 'gut-on-chip' technology for predictive human safety testing: an integrated experimental and modeling approach". GUT 2.0 foresees the application of an organ-on-chip model in the field of predictive safety. The approach proposed by the present method represents a significant advance in the field of in vitro models, as we foresee to recapitulate, within the 'chip' footprint, a multicellular gut environment. This approach re- presents an increased level of complexity if compared with the in vitro toxicological models for the intestine. Hence, its development should provide the necessary degree of interplay among different cell populations for a robust safety testing model.

Prof. Marcella Trombetta is National Coordinator of a PRIN2012 project entitled "aCTIoN - Cells-on-chip technologies for the study of the endocannabinoid system in an in vitro model of tumor/immune system interaction". The project aims to develop advanced models for the in vitro study of cellular interactions, taking advantage from 3D co-culture technologies within microfluidic devices.

In particular, the on-chip technologies will be applied to a model of tumor stem compartment to study its interaction with immune system cells) to investigate the role of the endocannabinoid system in the crosstalk between the two populations.

Prof. Marcella Trombetta is Scientific Coordinator and Leader of the Operational Activity 4.10 "BACCUS Class: an e-learning platform for training law enforcement officers to combat food crime" of the Europol project coordinated by Carabinieri NAS "ASKLEPIOS-Actions on food Supplements, faKe genuine (not) food exhibition, e-LEarning platform, action on Pesticides, operation "In Our Sites" and JAD" funded by EU Commission- Europol for the EMPACT activities under the OAP Counterfeit Goods. Prof. Marcella Trombetta is partner of the project CIPR-Net, Critical Infrastructure Research and Resilience Network Co-funded by EU FP7. CIPRNet establishes a Network of Excellence in Critical Infrastructure Protection (CIP). CIPRNet performs research and development that addresses a wide range of stakeholders including (multi)national emergency management, critical infrastructure operators, policy makers, and the society.

Most important publications

Costantini M., Guzowski J., Zuk P.J., Mozetic P., De Panfilis S., Jaroszewicz J., Heljak M., Massimi. M., Pierron M., Trombetta M., Dentini M., Swieszkowski W., Rainer A., Garstecki P., Barbetta A.

Electric field assisted microfluidic platform for generation of Tailorable porous microbeads as cell carriers for tissue engineering.
Adv Funct Mater. 2018 May 16; 28(20): 1800874. DOI 10.1002/adfm.201800874 IF 13,325

Injection of cell-laden scaffolds in the form of mesoscopic particles directly to the site of treatment is one of the most promising approaches to tissue regeneration. Here, a novel and highly efficient method is presented for preparation of porous microbeads of tailorable dimensions (in the range ≈300–1500 mm) and with a uniform and fully interconnected internal porous texture. The method starts with generation of a monodisperse oil-in-water emulsion inside a flow-focusing microfluidic device. This emulsion is later broken-up, with the use of electric field, into mesoscopic double droplets, that in turn serve as a template for the porous microbeads. By tuning the amplitude and frequency of the electric pulses, the template droplets and the resulting porous bead scaffolds are precisely produced. Furthermore, a model of pulsed electrodripping is proposed that predicts the size of the template droplets as a function of the applied voltage. To prove the potential of the porous microbeads as cell carries, they are tested with human mesenchymal stem cells and hepatic cells, with their viability and degree of microbead colonization being monitored. Finally, the presented porous microbeads are benchmarked against conventional microparticles with nonhomogenous internal texture, revealing their superior performance.

Maiullari F., Costantini M., Milan M., Pace V., Chirivì M., Maiullari S., Rainer A., Baci D., Marei H.E., Seliktar D., Gargioli C., Bearzi C., Rizzi R.

A multi-cellular 3D bioprinting approach for vascularized heart tissue engineering based on HUVECs and iPSC-derived cardiomyocytes.
Sci Rep. 2018 Sep 10;8(1):13532. PubMed PMID: 30201959. IF 4,122

The myocardium behaves like a sophisticated orchestra that expresses its true potential only if each member performs the correct task harmonically. Recapitulating its complexity within engineered 3D functional constructs with tailored biological and mechanical properties, is one of the current scientific priorities in the field of regenerative medicine and tissue engineering. In this study, driven by the necessity of fabricating advanced model of cardiac tissue, we present an innovative approach consisting of heterogeneous, multi-cellular constructs composed of Human Umbilical Vein Endothelial Cells (HUVECs) and induced pluripotent cell-derived cardiomyocytes (iPSC-CMs). Cells were encapsulated within hydrogel strands containing alginate and PEG-Fibrinogen (PF) and extruded through a custom microfluidic printing head (MPH) that allows to precisely tailor their 3D spatial deposition, guaranteeing a high printing fidelity and resolution. We obtained a 3D cardiac tissue compose of iPSC-derived CMs with a high orientation index imposed by the different defined geometries and blood vessel-like shapes generated by HUVECs which, as demonstrated by in vivo grafting, better support the integration of the engineered cardiac tissue with host's vasculature.

Ditaranto N., Basoli F., Trombetta M., Cioffi N., Rainer A.

Electrospun nanomaterials implementing antibacterial inorganic nanophases.
Appl. Sci. -Basel. 2018 Sep; 8(9): 1643. DOI 10.3390/app8091643 IF 1,689

Electrospinning is a versatile, simple, and low cost process for the controlled production of fibers. In recent years, its application to the development of multifunctional materials has encountered increasing success. In this paper, we briefly overview the general aspects of electrospinning and then we focus on the implementation of inorganic nanoantimicrobials, e.g., nanosized antimicrobial agents in electrospun fibers. The most relevant characteristics sought in nanoantimicrobials supported on (or dispersed into) polymeric materials are concisely discussed as well. The interesting literature issued in the last decade in the field of antimicrobial electrospun nanomaterials is critically described. A classification of the most relevant studies as a function of the different approaches chosen for incorporating nanoantimicrobials in the final material is also provided.

Urology

Head R. Papalia

Faculty M. Buscarini

Description

The research unit of Urology is focused on clinical and surgical research. The main fields of research are: modern diagnostic approaches to prostate cancer and advancements in robotic surgical techniques in bladder cancer and renal cancer.

Main research activities

Our cooperation with the National Cancer Institute of Rome allowed to publish our results on novel robotic surgical tequinique in bladder cancer in the most impacted Journal of Urolology. Our group was invited to write an Editorial Comment on Robot-assisted laparoscopic partial nephrectomy versus laparoscopic partial nephrectomy in the International Journal of Urology. We actively participated on a multicentric project on accuracy of elastic fusion biopsy in daily practice and published results in the the International Journal of Urology. The cooperation with ginecologist of our institution resulted in a pubblication on outcomes of anterior colporrhaphy plus inside-out tension-free vaginal tape for associated stress urinary incontinence and cystocele.

Most important publications

Simone G., Papalia R., Misuraca L., Tuderti G., Minisola F., Ferriero M., Vallati G., Guaglianone S., Gallucci M.
Robotic intracorporeal Padua ileal bladder: surgical technique, perioperative, oncologic and functional outcomes.
Eur Urol. 2018 Jun;73(6):934-940. PubMed PMID: 27780643. IF 17,581

Background: Robot-assisted radical cystectomy (RARC) with intracorporeal neobladder reconstruction is a challenging procedure. The need for surgical skills and the long operative times have led to concern about its reproducibility. **Objective:** To illustrate our technique for RARC and totally intracorporeal orthotopic Padua ileal bladder. **Design, setting, and participants:** From August 2012 to February 2014, 45 patients underwent this technique at a single tertiary referral centre. **Surgical procedure:** RARC, extended pelvic lymph node dissection, and intracorporeal partly stapled neobladder. Surgical steps are demonstrated in the accompanying video. **Measurements:** Demographics, clinical, and pathological data were collected. Perioperative, 2-yr oncologic and 2-yr functional outcomes were reported. **Results and limitations:** Intraoperative transfusion or conversion to open surgery was not necessary in any case and intracorporeal neobladder was successfully performed in all 45 patients. Median operative time was 305min (interquartile range [IQR]: 282-345). Median estimated blood loss was 210ml (IQR: 50-250). Median hospital stay was 9 d (IQR: 7-12). The overall incidence of perioperative, 30-d and 180-d complications were 44.4%, 57.8%, and 77.8%, respectively, while severe complications occurred in17.8%, 17.8%, and 35.5%, respectively. Two-yr daytime and night-time continence rates were 73.3% and 55.5%, respectively. Two-yr disease free survival, cancer specific survival, and overall survival rates were 72.5%, 82.3%, and 82.4%, respectively. The small sample size and high caseload of the centre might affect the reproducibility of these results. **Conclusions:** Our experience supports the feasibility of totally intracorporeal neobladder following RARC. Operative times and perioperative complication rates are likely to be reduced with increasing experience. **Patient summary:** We report the outcomes of our first 45 consecutive patients who underwent robot-assisted radical cystectomy with intracorporeal neobladders. Perioperative, oncologic, and functional outcomes support this technique as a feasible and safe surgical option in tertiary referral centres.

Papalia R., Mastroianni R.

Editorial comment to robot-assisted laparoscopic partial nephrectomy versus laparoscopic partial nephrectomy: a propensity score-matched comparative analysis of surgical outcomes and preserved renal parenchymal volume.
Int J Urol. 2018 Apr; 25(4):364-365. PubMed PMID: 29648703. IF 1,941

Purpose: To evaluate accuracy of MRI in detecting renal tumor pseudocapsule (PC) invasion and to propose a classification based on imaging of PC status in patients with renal cell carcinoma. **Methods:** From January 2017 to June 2018, 58 consecutive patients with localized renal cell carcinoma were prospectively enrolled. MRI was performed preoperatively and PC was classified, according to its features, as follows: MRI-Cap 0 (absence of PC), MRI-Cap 1 (presence of a clearly identifiable PC), MRI-Cap 2 (focally interrupted PC), and MRI-Cap 3 (clearly interrupted and infiltrated PC). A 3D image reconstruction showing MRI-Cap score was provided to both surgeon and pathologist to obtain complete preoperative evaluation and to compare imaging and pathology reports. All patients underwent laparoscopic partial nephrectomy. In surgical specimens, PC was classified according to the renal tumor capsule invasion scoring system (i-Cap). **Results:** A concordance between MRI-Cap and i-Cap was found in 50/58 (86%) cases. ρ coefficient for each MRI-cap and iCap categories was: MRI-Cap 0: 0.89 ($p < 0.0001$), MRI-Cap1: 0.75 ($p < 0.0001$), MRI-Cap 2: 0.76 ($p < 0.0001$), and MRI-Cap3: 0.87 ($p < 0.0001$). Sensitivity, specificity, positive predictive value, negative predictive value, and AUC were: MRI-Cap 0: Se 97.87% Spec 83.3%, PPV 95.8%, NPV 90.9%, and AUC 90.9; MRI-Cap 1: Se 77% Spec 95.5%, PPV 83.3%, NPV 93.5%, and AUC 0.86; MRI-Cap 2- iCap 2: Se 88% Spec 90%, PPV 79%, NPV 95%, and AUC 0.89; MRI-Cap 3: Se 94% Spec 95%, PPV 88%, NPV 97%, and AUC 0.94. **Conclusions:** MRI-Cap classification is accurate in evaluating renal tumor PC features. PC features can provide an imaging-guided landmark to figure out where a minimal margin could be preferable during nephron-sparing surgery.

Oderda M., Marra G., Albisinni S., Altobelli E., Baco E., Beatrici V., Cantiani A., Carbone A., Ciccariello M., Descotes J.L., Dubreuil-Chambardel M., Eldred-Evans D., Fasolis G., Ferriero M., Fiard G., Forte V., Giacobbe A., Kumar P., Lacetera V., Mozer P., Muto G., Papalia R., Pastore A., Peltier A., Piechaud T., Simone G., Roche J.B., Roupret M., Rouviere O., Van Velthoven R., Gontero P.

Accuracy of elastic fusion biopsy in daily practice: results of a multicenter study of 2115 patients.
Int J Urol. 2018 Dec; 25(12):990-997. PubMed PMID: 30187529. IF 1,941

Objectives: To assess the accuracy of Koelis fusion biopsy for the detection of prostate cancer and clinically significant prostate cancer in the everyday practice. **Methods:** We retrospectively enrolled 2115 patients from 15 institutions in four European countries undergoing transrectal Koelis fusionbiopsy from 2010 to 2017. A variable number of target (usually 2-4) and random cores (usually 10-14) were carried out, depending on the clinical case and institution habits. The overall and clinically significant prostate cancer detection rates were assessed, evaluating the diagnostic role of additional random biopsies. The cancer detection rate was correlated to multiparametric magnetic resonance imaging features and clinical variables. **Results:** The mean number of targeted and random cores taken were 3.9 (standard deviation 2.1) and 10.5 (standard deviation 5.0), respectively. The cancer detection rate of Koelis biopsies was 58% for all cancers and 43% for clinically significant prostate cancer. The performance of additional, random cores improved the cancer detection rate of 13% for all cancers (P < 0.001) and 9% for clinically significant prostate cancer (P < 0.001). Prostate cancer was detected in 31%, 66% and 89% of patients with lesions scored as Prostate Imaging Reporting and Data System 3, 4 and 5, respectively. Clinical stage and Prostate Imaging Reporting and Data System score were predictors of prostate cancer detection in multivariate analyses. Prostate-specific antigen was associated with prostate cancer detection only for clinically significant prostate cancer. **Conclusions:** Koelis fusion biopsy offers a good cancer detection rate, which is increased in patients with a high Prostate Imaging Reporting and Data System score and clinical stage. The performance of additional, random cores seems unavoidable for correct sampling. In our experience, the Prostate Imaging Reporting and Data System score and clinical stage are predictors of prostate cancer and clinically significant prostate cancer detection; prostate-specific antigen is associated only with clinically significant prostate cancer detection, and a higher number of biopsy cores are not associated with a higher cancer detection rate.

Vascular Surgery

Head F. Spinelli

Faculty F. Stilo

Other Personnel N. Montelione

Description

Our interests focus on all the aspects of arterial surgery, from the carotid artery endarterectomy/bypass for prevention of cerebral ischemia, down to the plantar revascularization for limb salvage, through all the diseases of the aorta. When endovascular treatment is the best choice for the patient, it strictly follows the Instructions for Use from the manufacturer. Large vessels reconstruction after tumor resection is one of our specific interest.

Main research activities

Decision making impacts on survival in Critical Limb Ischemia.
We already showed that the Endovascular technique and open bypass are complementary in treatment of CLI, as these apply to different patterns of disease. While the majority of patients with rest pain can be successfully treated by endovascular techniques despite the TASC II class, those with advanced necrosis and tissue loss are best treated by an open bypass whenever possible. In the last year, we could update our series and refine our ultrasound-based decision algorytm. The significant improvement of late survival of our patients, compared to most of the current series, confirmed the value of this approach

EVAR: How to make open conversion after supra renal grafts a safe operation.
EV treatment of endoleaks is not al-ways possible, and an open conversion is occasionally needed. In the case of suprarenal grafts, this can be a hazardous procedure. Following the principle of minimally invasive laparotomic aneurysm repair, we propose a technique to make open conversion safer, avoiding the removal of the whole suprarenal graft. This is based on the following principles:

- Clamp the aorta horizontally, flush to the renal arteries, without mobilizing the endograft.
- Open the sac and clamp the iliac branches by soft jaw external clamps close to the aortic bifurcation.
- Divide the graft 5 to 10 millimeters below the proximal clamp, and divide the iliac branches inside the sac as distal as possible. The metallic struts can be sectioned by a steel wire cutter. Remove the central part of the graft, leaving the aortic and iliac stumps in place.
- Clear the thrombus and oversaw the lumbar arteries.
- Pass a teflon felt band around the aorta near the proximal clamp and implant a new bifurcation graft by sawing the residual inner endograft, the native aortic wall and the external teflon band altoghether in order to obtain a firm and safe proximal anastomosis, double reinforced by the internal endograft and the external felt, without removing the suprarenal stent.
- Anastomose the iliacs to the residual iliac endografts and close the sac.

By avoiding the need to gain distal control, a mini laparotomy is fully adequate, and the patient can benefit of this less invasive technique.
In the last two years, we treated eleven patients without complications, a mean blood loss of 380 ml, and a mean post-operative hospital stay of 5 days.

Restenosis after CEA: carotid graft versus CAS.
Restenosis after CEA is currently treated by CAS. Late reports have shown suboptimal late results.
We already reported our series of carotid restenosis treated by a carotid vein graft in patients with a long life expectancy. We have updated our series with the late controls favoring this option versus CAS.

Endovascular and Open treatment of aortic embolism causing distal disease.
Critical limb ischemia due to aortic athero embolism is not as rare as it is currently believed. This is an insidious disease and If unrecognized can be at the origin of failures of treatment and bad outcomes. An endovascular aortic coverage, coupled with a femoral to popliteal or tibial graft seems to be a durable solution. We reviewed our series of such hybrid procedures, and described the diagnostic workout, technique and results.

Main collaborations

- Hospital Vall d'Hebron Barcelona, Spain;
- St. Thomas Hospital. University of London, UK;
- University of Messina;
- University of Sassari.

Most important publications

Marangi G.F., Pallara T., Lamberti D., Perrella E., Serra R., Stilo F., De Caridi G., Onetti Muda A., Persichetti P.

An electrical plasma dissection tool for surgical treatment of chronic ulcers: Results of a prospective randomised trial.

Int Wound J. 2018 Oct; 15(5):717-721. PubMed PMID: 29600828 IF 2,38

Cutaneous ulceration is a difficult medical problem and a major source of morbidity for patients. In the surgical treatment of ulcers, debridement is the first step, and it can be carried out using several surgical tools. Recently, new surgical devices have emerged using plasma-mediated electrical discharges with a lower peak temperature. A prospective single-blind trial was conducted on chronic ulcers not responsive to common non-surgical management. Patients were randomly separated into 2 groups: Group A received surgical debridement with conventional electrocautery, and Group B received surgical debridement using the plasma-mediated device. Histological samples were collected intraoperatively to evaluate the thermal damage during the surgical procedure and 2 weeks after surgery to evaluate the inflammatory response and collagen deposition. The width of coagulation necrosis at the incision margins in Group B was significantly shorter compared with Group A (P = .001). The inflammatory cell infiltration showed a cellular distribution percentage that was quite equal between the 2 groups. The granulation tissue showed an abundant deposition of dense and mature collagen in Group B, compared with Group A, where the mature collagen appeared in small quantities (P < .001). Microbial culture showed a lower incidence of postoperative infections in Group B compared with the control group (P < .05). The study demonstrated, based on the results, that the new technology with the use of a lower temperature electrosurgical device represents an effective therapeutic weapon for the surgical treatment of skin ulcers, both vascular and extravascular types.

Virology

Head E. Riva

Other Personnel F. Antonelli, C. Concato, L. Piccioni

Description

The Virology Research Unit is involved in both basic and clinical virology.

The main topics concern host's and viral factors able to predict the outcome and the treatment response of persistent viral infections such as HCV infection (in terms of Progression and treatment response) , CMV infection (in terms of reactivation and clinical progression in transplanted recipients) and HPV infections (in terms of HPV-related dysplasia progression).

Based on the past and the more recent experience, the Virology research staff is mainly involved in the field of molecular virology and in assays useful in identifying and monitoring viral infections other than specific Single nucleotide polymorphisms (SNPs) such as Real Time PCR, Melting and Pyrosequencing analysis and Syndromic molecular panels.

Main research activities

The specific SNPs that have been under study are mainly rs12979860, rs8099917, ss46945590 TT/delta G SNPs in Interferon lamda III-IV region. These SNP are mainly involved in host's innate immunity and in treatment response in chronic infectious diseases.

The Unit has been also involved in the comparison and validation of molecular methods applied for persistent virus (CMV, HCV, EBV and parvovirus) and emergent/acute infections (Chikungunya, respiratory viruses).

All these topics are addressed in ongoing studies which involve different areas of Campus Bio-Medico University Hospital.

The team Acts also in the contest of the project "Migrant and Health" aimed to prevent and monitoring infectious diseases in Migrants and in the implementation and validation of molecular syndromic panels (respiratory, CNS, sexual transmitted and enteric diseases).

Recent interest involve the relevance of respiratory infections in pediatric/adult immunodepressed. The Virology Unit is also in close collaboration with the Department of Molecular Medicine -Virology section-"Sapienza" University of Rome, AIFA/EMA and with the Virology Lab of Ospedale Pediatrico "Bambino Gesù" of Rome.

Main collaborations

- Department of Molecular Medicine -Virology section-"Sapienza" University of Rome;
- Virology Lab, IRCCS Bambino Gesù Paediatric Hospital, Italy.

Most important publications

Spoto S., Riva E., Fogolari M., Cella E., Costantino S., Angeletti S., Ciccozzi M.

Diffuse maculopapular rash: a family cluster during the last Chikungunya virus epidemic in Italy.
Clin Case Rep. 2018 Oct 22; 6(12):2322-2325. PubMed PMID: 30564322.

A family cluster of father, mother, and daughter with Chikungunya virus (CHIKV) infection was diagnosed during last epidemic in Italy. In temperate area, during the summer season, clinicians should consider CHIKV infection in the differential diagnosis of patients with fever, maculopapular rash, polyarthralgia, and conjunctival erythema.

Cella E., Foley B.T., Riva E., Scolamacchia V., Ceccarelli G., Vita S., Iannetta M., Ciardi MR., D'Ettorre G., Angeletti S., Ciccozzi M.

HIV-2 infection in a migrant from Gambia: the history of the disease combined with phylogenetic analysis revealed the real source of infection.
AIDS Res Hum Retroviruses. 2018 Aug 15; 34(12):1090-1094. PubMed PMID: 29954191. IF 1,935

Human immunodeficiency virus type 2 (HIV-2) infection prevalence is increasing in some European countries. The increasing migratory flow from countries where HIV-2 is endemic has facilitated the spread of the virus into Europe and other regions. We describe a case of HIV-2 infection in a migrant individual in the Asylum Seekers Centre (ASC) in Italy. The patient's virus was sequenced and found to be a typical HIV-2 genotype A virus. Bayesian evolutionary analysis revealed that the HIV-2 sequence from migrant dated back to 1986 in a subcluster, including sequences from Guinea Bissau. This was coherent with the history of the migrant who lived in Guinea Bissau from his birth until 1998 when he was 13 years old. Monitoring for HIV-2 infection in migrants from western Africa is necessary using adequate molecular tools to improve the diagnosis and understand the real origin of infection.

Ciccozzi M., Riva E., Vita S., Cella E., Fogolari M., Spoto S., Lopalco M., Ceccarelli G., Angeletti S.

An acute febrile outbreak in a refugee community of an Italian asylum seeker center: lessons learned.
Public Health. 2018 Oct; 163:16-19. PubMed PMID: 30031836. IF 1,441

The management of infectious outbreaks in closed settings represents an important public health issue. An outbreak of acute febrile syndrome affecting 22 refugees resident at the Asylum Seekers Centre of Castelnuovo di Porto in Rome has been reported, and the preventive and control measures adopted have been described as an example of public health safety.Pharyngeal swab and whole-blood samples were collected from 22 cases observed and analyzed for standard bacterial cultures and respiratory and herpesviruses by qualitative CLART PneumoVir2 and Entherpex microarray.A possible respiratory-transmitted etiology and a concomitant reactivation of multiple herpesviruses have been evidenced.The epidemiological investigation showed that the spread of the epidemic was promoted because patients were hosted in neighboring rooms or in the same room, facilitating the rapid spread of infectious disease.The potential way of transmission was supposed, and preventive measures for infection control were adopted. The measures adopted are an example of best practice for outbreak management, and the microbiological surveillance is recommended for public health improvement.

Research Projects

Grants from Competitive Calls

EUROPEAN COMMISSION

AIDE
Adaptive Multimodal Interfaces to Assist Disabled People in Daily Activities

Url: http://www.aideproject.eu/
Coordinator: Universidad Miguel Hernández
Partners: Sant'Anna School of Advanced Studies, Campus Bio-Medico University of Rome (Research Unit of Advanced Robotics and Human Centred Technologies), Universidad Politécnica de Valencia, University of Tübingen, Cedar Foundation, Zed World-wide S.A., Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V., B&J Adaptaciones
Funded under: H2020-ICT
End: 31/05/2018
Contacts: Loredana Zollo (l.zollo@unicampus.it), Research Unit of Advanced Robotics and Human Centred Technologies

The AIDE project has the ambition to strongly contribute to the improvement of the user technology interface by developing and testing a revolutionary modular and adaptive multimodal interface customizable to the individual needs of people with disabilities. Furthermore, the project will focus on the development of a totally new shared-control paradigm for assistive devices that merges together information on the user's residual abilities, behavior, emotional state and intentions with information about the environment and context factors. UCBM is responsible for the design of a modular architecture supporting the development of the multi-modal interface and for the design and development of a shared control for the assistive device based on reinforcement learning. Moreover, UCBM will be involved in: (i) definition of the experimental scenario, (ii) identification of user needs, (iii) characterization of the AIDE system and (iv) experimental validation of the AIDE system on end-users, in collaboration with "Centro Protesi INAIL" of Budrio.

EU-AIMS
European Autism Interventions – A Multicentre Study for Developing New Medications

Url: http://www.eu-aims.eu/
Coordinator: Roche
Partners: King's College London, Central Institute of Mental Health Mannheim, Radboud University, Cambridge University, deCODE Genetics, University Medical Centre, Universität Basel, Institut Pasteur, GABO:mi, Max-Planck Institute of Experimental Medicine, European Molecular, Biology Laboratory, NeuroSearch, Karolinska Institutet, Eli Lilly and Company Ltd., Janssen, Pharmaceutica, Institut de Recherches Servier, Vifor Pharma, Birkbeck College, Institute of Education, Campus Bio-Medico University of Rome (Research Unit of Molecular Psychiatry and Neurogenetics), Autism Speaks, Pfizer, CEA, Universität Ulm
Funded under: Innovative Medicine Initiatives
End: 31/03/2018
Contacts: Antonio Persico (a.persico@unicampus.it)

The main project objectives are development and validation of translational approaches for the advancement of novel therapies to treat ASD, setting new standards in research and clinical development to aid the drug discovery process, Identification and development of expert clinical sites across Europe to run clinical studies and trials, and the creation of an interactive platform for ASD professionals and patients. UCBM contributes to establish biomarkers of the autism phenotype.

RESHAPE
Restoring the Self with Embodiable Hand Prostheses

Principal Investigator: Dr. Giovanni Di Pino, Campus Bio-Medico University of Rome
Funding under: ERC-StG-2015 - ERC Starting Grant
End: 31/08/2021
Contacts: Giovanni Di Pino (g.dipino@unicampus.it), Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction
RESHAPE aims to study prosthesis embodiment, identify what makes a hand prosthesis easily embodiable, and test non-invasive brain stimulation to facilitate the embodiment.
The first of three phases develops the enabling technology and defines the embodiment protocol.
The following phase evaluates thirty myoelectric-prosthesis users and the first of two amputees implanted with peripheral neural electrodes, for functional ability, prosthesis embodiment and acceptability and for phantom limb pain (PLP), before and after neuromodulation.
In the last phase, a neuro-controlled prosthesis is optimized in line with the specifications defined in the previous phase and tested in the second implanted amputee.
Patients are stimulated with a homeostatic plasticity-based rTMS either on premotor cortex or on intraparietal sulcus. A robot-aided TMS compensates head-coil relative displacement, allowing the subject to operate the prosthesis during the stimulation.

RESPINE
Regenerative therapy of intervertebral disc: a double blind phase 2b trial of intradiscal injection of mesenchymal stromal cells in degenerative disc disease of the lomber spine unresponsive to conventional therapy

Coordinator: Centre Hospitalier Universitaire Montpellier
Partners: Campus Bio-Medico University of Rome, Universidad De Navarra, Universidad De Valladolid, Univercell-Biosolutions, National University Of Ireland, Galway, Citospin S.L., Institut De Terapia Regenerativa Tisular Sl, Assistance Publique - Hôpitaux De Paris, Centre Hospitalier Universitaire De Nantes, Centre National De La Recherche Scientifique (CNRS), Ecrin European Clinical Research Infrastructure Network, Bg Klinikum Bergmannstrost Halle Ggmbh, Universite De Montpellier
Funding under: H2020-SC1-2016-RTD
End: 31/12/2020
Contacts: Gianluca Vadalà (g.vadala@unicampus.it), Research Unit of Orthopaedic and Trauma Surgery

The World Health Organisation (WHO) has included low back pain in its list of twelve priority diseases. Notably, Degenerative disc disease (DDD) presents a large, unmet medical need that results in a disabling loss of mechanical function. To develop the world's first rigorously proven, effective treatment of DDD, RESPINE aims to assess, via a multicentre, randomized, controlled, phase 2b clinical trial including 112 patients with DDD, the efficacy of an allogenic intervertebral mesenchymal stem cell (MSC)-based therapy. This innovative therapy aims to rapidly (within 3 months) and sustainably (at least 24 months) reduce pain and disability. In addition, the consortium aims to provide new knowledge on immune response & safety associated with allogeneic BM-MSC intradiscal injection. This simple procedure would be cost-effective, minimally invasive, and standardised.

CONVERGENCE
Frictionless Energy Efficient Convergent Wearables for Healthcare and Lifestyle Applications

Url: https://www.convergence-era.org/
Coordinator: Ecole Polytechnique Fédérale de Lausanne (EPFL)
Partners: Campus Bio-Medico University of Rome, CEA LETI – Laboratoire d'Electronique et de Technologie de l'Information, Elektronikas un datorzinatnu instituts/Signal Processing Lab, Italian National Agency for New Technologies, Energy and Sustainable Economic (ENEA), ETHZ Eidgenössische Technische Hochschule Zürich / Department of Mechanical and Process Engineering, Institut Polytechnique de Grenoble, Hirslanden Clinic Cecil/Cardiovascular Center, Consorzio Nazionale Interuniversitario Per La Nano-elettronica (IUNET), Middle East Technical University, National Institute for R&D in Microtechnologies/Laboratory of Microsystems for Biomedical & Environmental Applications, ST Microelectronics, TAGLIAFERRI

Società Responsabilità Limitata, Tallinn University of Technology / Thomas Johann Seebeck Department of Electronics, Unit of Electronics for Sensor Systems, Department of Engineering, Università degli Studi di Cagliari/Department of Electrical and Electronic Engineering, Universitatea Transilvania din Brasov/Department of Automation and Information Technology, Université catholique de Louvain.
Funding under: JTC2016-PILOTS
End: 28/02/2020
Contacts: Marco Santonico (m.santonico@unicampus.it), Research Unit of Electronics for Sensor Systems

The project adopts a focused strategy centred on proofs-of-concepts related to energy efficient sensor networks for future wearables exploiting the convergence of multi-parameter biosensors and environmental sensors on an autonomous system technology platform, serving data fusion for preventive life-style and healthcare. We connect solidly a critical mass of research institutions in-between and to some end user, to set the foundation of future emerging research project in this field, at European level by connecting national competences and resources.

DETOP
Dexterous Transradial Osseointegrated Prosthesis with neural control and sensory feedback

Coordinator: Scuola Superiore Sant'Anna di Pisa
Partners: Campus Bio-Medico University of Rome, Goeteborgs Universitet, Prensilia Srl, Integrum ab, Lunds Universitet, CSEM Centre Suisse d'Electronique ed de Microelectronique, University of Essex, Istituto Nazionale Assicurazione Infortuni sul Lavoro, Istituto Ortopedico Rizzoli
Funding under: H2020-ICT-2015
End: 28/02/2020
Contacts: Vincenzo Denaro (denaro@unicampus.it), Research Unit of Orthopaedic and Trauma Surgery

This project addresses the problem of recovery of hand function after amputation. Amputees continue to use technology for powered prostheses developed over 40 years ago. These devices do not purposely provide sensory feedback and are known for their poor functionality, controllability and sensory feedback.

The consortium has pioneered the use of osseointegration as a long-term stable solution for the direct skeletal attachment of limb prostheses. This technology aside from providing an efficient mechanical coupling can also be used as a bidirectional communication interface between implanted electrodes and the prosthetic arm. The goal of the DeTOP project is to push the boundaries of this technology to the next TRL and to make it clinically available to the largest population of upper limb amputees, namely transradial amputees.

IPSPINE
Induced pluripotent stem cell–based therapy for spinal regeneration

Coordinator: Universiteit Utrecht
Partners: Campus Bio-Medico University of Rome, Universite de Nantes, Ecole Nationale Veterinaire Agroalimentaire et de l'Alimentation Nantes Atlantique, Universitair Medisch Centrum Utrecht, National University of Ireland Galway, Universitaet Ulm, Universitaet Bern, Institut National De la Sante ed de la Recherche Medicale, Naturwissenschaftliches und Medizinisches Institut an der Universitaet Tuebingen, Ao-Forschungsinstitut Davos, Scheffield Hallam University, Ntrans Technologies bv, Universite de Montpellier, University of Miami, Spineserv GMBH & Co.Kg, The University of Hong Kong, Pharmalex GMBH, Catalyze B.V., Stiching Nationaal Reumafonds
Funding under: H2020-SC1-BHC-2018-2020
End: 31/12/2023
Contacts: Gianluca Vadalà (g.vadala@unicampus.it), Research Unit of Orthopaedic and Trauma Surgery

Low back pain (LBP) is a leading cause of disability and morbidity worldwide. It is widely accepted that a major contributor to LBP is intervertebral disc degeneration (IDD). These patients receive conservative treatment (e.g. pain relief medication and physiotherapy). To date, no treatments halt or reverse IDD. The aim of the iPSpine team is to investigate and develop a new advanced therapy medicinal product (ATMP) of the future, based on a novel developmental biology-based therapeutic strategy employing pluripotent stem cells (iPSC) and smart biomaterials. The iPSpine consortium will develop and demonstrate Proof-of-concept with the aid of novel and extended knowledge, tools and technology platforms.

ITALIAN MINISTRY OF EDUCATION, UNIVERSITY AND RESEARCH

PRIN (Research Projects of National Interest) 2015

Adaptation and tolerance of plants to climate change-dependent abiotic stresses

Coordinator: Università di Milano
Partners: Research Unit of Food Science and Nutrition (UCBM), Università degli studi di Padova, Scuola Superiore di Studi Universitari e Perfezionamento Sant'Anna

Endocannabinoid Signaling in Alzheimer's Disease: A Novel Target for Mechanistic Understanding and Potential Therapeutics

Coordinator: Mauro Maccarrone - Research Unit of biochemistry and molecular biology (UCBM)
Partners: Consiglio Nazionale delle Ricerche, Università degli Studi di Roma "La Sapienza", Università degli Studi di Roma "Tor Vergata" Università degli Studi di Teramo

Pancreatic β-cell identity, glucose sensing and the control of insulin secretion

Coordinator: Paolo Pozzilli - Research Unit of endocrinology and diabetes
Partners: Università degli Studi di Verona, Università degli Studi di Catania, Università degli Studi di Parma, Università degli Studi di Roma "La Sapienza, Università Cattolica del Sacro Cuore, Università degli Studi di Siena, Università di PISA, Università degli Studi di Roma "Tor Vergata", Libera Università "Vita Salute S. Raffaele" Milano

FARE ERC
ENABLE - Empowering Novel Augmentation of Limb Embodiment

Principal Investigator: Dr. Giovanni Di Pino, Campus Bio-Medico University of Rome

PON (National Operational Program)

ARONA (Advanced Robotic-Assisted Surgical Navigation)

Coordinator: Masmec S.p.A.
Partners: Research Unit of Advanced Robotics and Human Centred Technologies (UCBM), Research Unit of Diagnostic Imaging (UCBM), Research Unit of Automation and Control Theory (UCBM), Research Unit of Computer Systems and Bioinformatics (UCBM), Scuola Superiore Sant'Anna di Pisa, Istituto Tumori Giovanni Paolo II di Bari, USL Toscana Nord Ovest

RAFAEL
System for Risk Analysis and Forecast for Critical Infrastructure in the Apennines dorsal Regions

Coordinator: Energy and Sustainable Economic (ENEA)
Partners: Research Unit of Automation and Control Theory (UCBM), INGV, ANAS SpA, TIM SpA, e-Distribuzione SpA, Centro Ricerche Elettro-Ottiche, GORI SpA, Università di Ferrara, Università dell'Aquila, Consorzio CUEIM, Consorzio MEDIS, Nuvap Srl, Tointech Srl, G&A Engineering Srl, Ylichron Srl, GEO-K Srl, Himet Srl

ITALIAN MINISTRY OF HEALTH
FINALISED RESEARCH

GR Ordinary 2011-2012

Daily at-home follow-up of Parkinson's disease patients motor performance through robotic and portable devices

Coordinator: IRCCS San Raffaele Pisana
Partners: Research Unit of Neurology, Neurophysiology, Neurobiology (UCBM), Research Unit of Advanced Robotics and Human Centred Technologies (UCBM), IRCCS San Raffaele Pisana

Cross Sectional study to evaluate the interactions between gut microflora and immune system at the cross-road of the pathogenesis of Inflammatory Bowel Diseases and Irritable Bowel Syndrome

Coordinator: Istituto Superiore di Sanità
Partners: Research Unit of Gastroenterology (UCBM), Research Unit of Clinical Pathology and Microbiology (UCBM), Istituto Superiore di Sanità, University of Roma "Tor Vergata"

Exploiting the Protein Corona effect for biomarker discovery and targeting of nanomedicines in pancreatic cancer

Coordinator: IRCCS Regina Elena (IFO-IRE)
Partners: Research Unit of General Surgery (UCBM), IRCCS Regina Elena, (IFO-IRE), Catholic University of the Sacred Heart

PE-Italian Researchers Abroad 2011-2012

Clinical and Genetic characterization of early complications in Juvenile Obesity

Coordinator: Bambino Gesù Paediatric Hospital
Partners: Research Unit of Endocrinology and Diabetes (UCBM), Washington University School of Medicine - Jewish Hospital of St. Louis

RF Ordinary 2011-2012

Cell-on-Chip technology as a novel tool to investigate the crosstalk between cancer and immune cell: role of the transcription factors Interferon Regulatory Factor 1 and 8 (IRF1, IRF8) in melanoma as a model system

Coordinator: Istituto Superiore di Sanità
Partner: Research Unit of Clinical Pathology and Microbiology (UCBM), Research Unit of Tissue Engineering and Chemistry for Engineering (UCBM), Istituto Superiore di Sanità, National Research Council

RF – Network Project 2013

Italian autism spectrum disorders network: filling the gaps in the National Health Care System

Coordinator: Istituto Superiore di Sanità
Partners: Research Unit of Molecular Psychiatry and Neurogenetics (UCBM), IRCCS Eugenio Medea – Associazione La Nostra Famiglia, Fondazione Stella Maris, Bambino Gesù

RF Industrial Co-Financing 2013

Extremely low frequency magnetic field (ELF-MF) stimulation as a neuroprotective treatment in acute ischemic stroke

Coordinator: UCBM
Partners: Research Unit of Neurology, Neurophysiology, Neurobiology (UCBM), IGEA S.p.A.

GR Ordinary 2013

Cerebellar-cortical circuits in Autism Spectrum Disorders: new perspectives for treatment implementation.

Coordinator: Santa Lucia Foundation
Partners: Research Unit of Neurology, Neurophysiology, Neurobiology (UCBM), Sapienza University, Rome

ITALIAN MINISTRY OF ECONOMIC DEVELOPMENT

B³– Bioscience, Patents and Business – Exploitation of research in the bioscience sector through knowledge transfer, human resources development and industrial properties transfer.

Coordinator: UCBM

INAIL BRIC

Bio–cooperative robotic system for upper–limb rehabilitation in working contexts

Funding Body: INAIL
PI: Research Unit of Advanced Robotics and Human Centred Technologies (UCBM)

SmartBench - Smart Industrial Safety Workbench

Funding Body: INAIL
PI: University of Rome "Tor Vergata"
Partner: Research Unit of Automatics (UCBM), University of Salento, University of Bologna, University of Messina

Active–Development of a multidisciplinary and integrated approach, for the management of the worker affected by degenerative pathologies of the spine: study of the occupational aspects and an innovative regenerative treatment of the intervertebral disc to favor the return to work

Coordinator: Research Unit of Orthopaedic and Trauma Surgery (UCBM)
Partners: University of Helsinki; IRCCS Foundation Ca 'Granda Maggiore Hospital Milan

SENSE-RISC - Development of wearable smart systems for improving worker safety

Coordinator: Sapienza University of Rome, Astronautical Engineering Department Electricity and Energy (DIAEE)

Partners: Research Unit of Measurements and Biomedical Instrumentation (UCBM); University of Pisa - Department of Chemistry and Industrial Chemistry (UP-DCCI); Sapienza University of Rome - Charles Darwin Biology and Biotechnology Department (UR-DBBCD); Sant'Anna Institute of Biorobotics (SSSA); Technological Pole, IRCCS Don Carlo Gnocchi Foundation (FDG); University of Pisa - Centro E. Piaggio (UP-CP).

LAZIO REGIONAL AUTHORITY

INTESE – Innovation and Technology transfer to support exploitation of research results

Coordinator: UCBM

HEREMOS – HEalth REmote MOnitoring System

Coordinator: RDSLAB srl
Partners: Research Unit of Measurements and Biomedical Instrumentation (UCBM)

COMETA - Quality testing of organoleptic properties of COffee blends via genetic and METAbolic fingerprinting

Coordinator: Danesi Caffè S.p.A.
Partners: Research Unit of Food Science and Nutrition (UCBM), Genechron s.r.l; Energy and Sustainable Economic (ENEA).

WINGED: WINe GrEen Distillery

Coordinator: Sire srl
Partners: Research Unit of Chemical-Physics Fundamentals in Chemical Engineering (UCBM), Sire Srl, Processi Innovativi srl, Sapienza University of Rome, Gotto D'Oro s.c.

OTHER GRANTS

A novel approach to identify COPD phenotypes, forecast clinical course and plan the therapeutic strategy

Funding Body: Fondazione Roma

Coordinator: Research Unit of Geriatrics (UCBM)
Partner: Research Unit of Diagnostic Imaging (UCBM), Research Unit of Electronics for Sensor Systems (UCBM), Research Unit of Computer System and Bioinformatics (UCBM).

Reaching, posture, object exploration, and language in high and low risk infants

Funding Body: National Institutes of Health
Coordinator: University of Pittsburgh, USA
Partners: Research Unit of Developmental Neuroscience (UCBM)

VIOLIN – Valorization of Italian products deriving from Oliva through innovative analytical techniques

Funding Body: Fondazione Cariplo
Coordinator: University of Messina
Partners: University of Rome La Sapienza, Alma Mater Studiorum University of Bologna, University of Turin, Edmund Mach Foundation, University of Sannio, university of Tuscia, University of Genoa, Campus Bio-Medico University of Rome, University of Bari, University of Verona.

SERISM: Role of the endocannabinoid system in reprogramming human pluripotent stem cells under microgravity

Funding Body: ASI – Italian Space Agency
Partners: Research Unit of Biochemistry and Molecular Biology (UCBM)

Interdisciplinary complex systems: theoretical physics methods in systems biology; Self-gravitating systems, galactic structures and galactic dynamics

Funding Body: ICRANet
Partners: Research Unit of Non Linear Physics and Mathematical Modeling (UCBM), ICRA

Hearth Remote monitoring – COR

Funding Body: ASI – Italian Space Agency
Coordinator: Altec S.p.A.
Partner: Research Unit of Electronics for Sensor Systems (UCBM)

Continuity of care for terminally ill patients: Data collection-Observation-Sperimentation (CA-IOS)

Funding Body: ENPAPI
Partners: Research Unit of Nursing Science (UCBM)

Hospital_4.0: towards a new model of care integrating territorial needs with emerging technologies in the service of people

Funding Body: Fondazione Cattolica Assicurazioni
Partners: Research Unit of Computer System and Bioinformatics (UCBM), Institute of Philosophy of Scientific and Technological Practice (FAST)

Antibodies to post-translationally modified insulin as biomarker of type 1 diabetes

Funding Body: EFSD (European Foundation for the Study of Diabetes), JDRF and Lilly
Partner: Research Unit of Endocrinology and Diabetes (UCBM)
PI: Rocky Strollo (Endocrinology and Diabetes, UCBM); **CoPI:** Ahuva Nissim (Queen Mary University of London);
CoPI: Paolo Pozzilli (Endocrinology and Diabetes, UCBM)

EFSD Mentorship Programme supported by AstraZeneca

Funding Body: EASD (European Association for the Study of Diabetes e V.)
Partner: Research Unit of Endocrinology and Diabetes (UCBM)

Evaluation of bone fragility in type 1 diabetes

Funding Body: SIOMMMS (Societá Italiana dell'Osteoporosi, del Metabolismo Minerale e delle Malattie dello Scheletro)
Partner: Research Unit of Endocrinology and Diabetes (UCBM)
PI (Young investigator): Rocky Strollo
Supervisor: Nicola Napoli (Endocrinology and Diabetes, UCBM)

Use of computer support for the evaluation and monitoring of kinase inhibitors in the course of

treatment for Chronic Lymphoid Leukemia and Lymphoma Follicular.

Funding Body: GILEAD Health Program
Partner: Research Unit of Hematology, Stem Cell Transplantation, Transfusion Medicine And Cellular Therapy (UCBM)
PI: Dr. Ombretta Annibali
Other Research Units involved: Research Unit of Computer Systems and Bioinformatics (UCBM)

Specialized pro-resolving lipid mediators as a novelstrategy to "resolve" the altered adaptive immuneresponses in multiple sclerosis

Funding Body: FISM
Partners: Research Unit of Biochemistry and Molecular Biology(UCBM)
P.I. Dr. Valerio Chiurchiù
Other Research Units involved: Santa Lucia Foundation of Rome, Policlinico Tor Vergata of Rome

Future leaders mentorship programme for clinical diabetologists

Funding Body: European Foundation for the Study of Diabetes
Partner: Research Unit of Endocrinology and Diabetes (UCBM); Cardiff University
PI: Dr. Rocky Strollo

Acoustic Upgraded Diagnostics In-Orbit)

Funding Body: Agenzia Spaziale Italiana (ASI)
Partners: Research Unit of Electronics for Sensor Systems (UCBM); University of Rome "Tor Vergata"

AARG-18-566270 - Targeting dopamine neuronal loss in a model of Alzheimer's Disease.

Funding Body: Alzheimer's Association
PI: Dr. D'Amelio Marcello, Research Unit of Molecular Neurosciences (UCBM)

Investigating AMyloid FIbrils mechanical properties via MUltiscale Simulations (AmFiMuS).

Funding Body: ISCRA-CINECA (National HPC Italian

Center)
PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling

STREET-OF-NY - Study of optoelecTRonic propErties of titanium dioxide nanosystEms in The frame OF the maNy body perturbation theorY

Funding Body: Computational grants awarded by PRACE (Partnership for Advanced Computing in Europe)
PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling

MDNICO–Molecular dynamics study of ion permeation in wild-type and mutants of the human α7 nicotinic receptor

Funding Body: Computational grants awarded by PRACE (Partnership for Advanced Computing in Europe).
PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling

Progetto di Supercalcolo, ISCRA-classe C - Italia, "SLEAN - Spatial Localization of Excitons in Anatase Nanostructures"

Funding Body: ISCRA-CINECA (National HPC Italian Center)
PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Progetto di Supercalcolo, ISCRA-classe C - Italia, "MaSCrIAM–Magneto Sensitive Cryptochrome Investigation via Atomistic Modeling"

Funding Body: ISCRA-CINECA (National HPC Italian Center)
Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Progetto di Supercalcolo, ISCRA-classe C - Italia, "PILSENER - Post processIng operations for the anaLysiS of ElectroNic propErties of titanium dioxide nanowiRes"

Funding Body: ISCRA-CINECA (National HPC Italian Center)
Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Progetto di Supercalcolo, ISCRA-classe C - Italia, " ExMoxC - EXcited state properties of Metal OXynitrides for photoCatalysis via Many Body Perturbation Theory - HP10CMVPR7"

Funding Body: ISCRA-CINECA (National HPC Italian Center)
Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

"Towards realistic NANOsized TiO2 particles: ELectronic and OPtical properties Many Body study (NanoElOp) - HP10B41C1L", 9.5M CPU hours, 2018-19

Funding Body: ISCRA- CINECA (National HPC Italian Center)
PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

"Thermodynamics and Kinetic of single ion permeation in human alpha 7 nicotinic recepot bound to partial agonit lobeline" (IONLOB) – HP10CKX0I9", 100k CPU hours, 2018-19, PI G. Cottone

Funding Body: ISCRA-CINECA (National HPC Italian Center)
PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Study of optoelecTRonic propErties of titanium dioxide nanosystEms in The frame OF the maNy body perturbation theorY–STREET-OF-NY, 2017-2018, PI I. Marri, 38 M standardised CPU hours, PRACE Project Access-14th

Funding Body: Computational grants awarded by PRACE (Partnership for Advanced Computing in Europe))
Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Research and the
"Third Mission" of the University

Impact of Research on Society

Impact of Research on Society

The key factor of UCBM policy for Third Mission activities is the centrality of human being to foster society innovation. According to its main mission for healthy living and improvement of quality of life, UCBM systematically pursues the activities related to third mission with the aim of transferring both knowledge and technology in order to enhance the socio-economic development at local and national level.

The activities are mainly devoted to strengthen competitiveness by promoting process and product innovation and by networking mainly with local SMEs but also with national and international companies with a twofold aim: placement of students and exploitation of the research activities of the Research Units of Engineering and Medicine and Surgery Departments. In this context the project "INTESE - Innovation and Technology transfer to support exploitation of research results" funded by Lazio Regional Authority is worth a mention. The main objectives of the project consist in developing collaborations with local companies of process and product innovation by exploiting competencies and technologies developed by UCBM Research Units and staff mobility, so fostering a mutual beneficial approach to create a critical mass of competencies and resources. During 2017, an internal call for projects within INTESE has co-funded five actions for the technology transfer of the results of UCBM research units (RU) that as of 2018 count the involvement of 15 companies, 2 new patent families, 1 of which exploited through a SME of the Lazio Region, the organization of workshops and events and 2 projects submitted to national and European calls.

Moreover, specific attention is devoted to ethical and anthropological issues thanks to the contribution of the Institute of Philosophy of Scientific and Technological Practice (FAST) and its research activities developed in close synergy with Research Units in order to enhance the social impact of research results.

In the last years, UCBM joined different National networks such as NETVAL (Italian Network of Technology Transfer Offices of Universities and Public Research Organizations), PNIcube (Italian Association of University Incubators and Local Business Plan Competitions) for technology transfer and ALMALAUREA for placement, and created a University-Enterprise Committee with the aim of collaborating with companies not only for technology transfer, but also for defining education and research strategies.

Third mission activities, in particular commissioned research, clinical trials, UCBM patent portfolio, UCBM spin-off companies, and public engagement activities, are briefly reported below.

COMMISSIONED RESEARCH

A software layer for OPC to ModBus conversion

Client: Algobrain srl
Contractor: Research Unit of Automation and Control Theory

Assessment of neonatal oro-motor performance during bottle feeding

Client: Artsana S.p.A.
Contractor: Research Unit of Advanced Robotics and Human Centred Technologies
Other partners involved: "Santa Maria Goretti" Hospital

Assessment of predictive molecular biomarkers, in response to antitumor therapy with "targeted" drugs used in normal clinical practice

Client: Diatech Pharmacogenetics srl
Contractor: Research Unit of Pathology

Autonomic Nervous System Study – Cardiac Autonomic Reflex tests. CARTs – Small Nerve Fiber (A–delta, B and C) health with in vivo corneal confocal microscopy

Client: Sapienza University of Rome
Contractor: Research Unit of Endocrinology and Diabetes

Biochemical markers of inflammatory bowel diseases

Client: University of Teramo
Contractor: Research Unit of Biochemistry and Molecular Biology

Biochemical profiling of new chemical entities with therapeutic potential

Client: F. Hoffmann-La Roche Ltd
Contractor: Research Unit of Biochemistry and Molecular Biology

Blockchain for food supply chain

Client: Poste Italiane SpA
Contractor: Research Unit of Automation and Control Theory

Design and development of an electronic differential sensor system for water characterization

Client: Puretech srl
Contractor: Research Unit of Electronics for Sensor Systems

Development and validation of a new quantitative analytical method of ponatinib in human plasma and CSF using LC–MS/MS

Client: Incyte Biosciences International s.a.r.l.
Contractor: Research Unit of Drug Sciences

Development of an algorithm to calculate the risk of stroke and to adopt strategies capable of substantially reducing it by intervening on modifiable factors

Client: Fondazione ANIA
Contractor: Research Unit of Neurology, Neurophysiology, Neurobiology

Development of upper limb bionic prostheses with personalized interface and sensory feedback for patients with amputation due to road accident

Client: Fondazione ANIA
Contractor: Research Unit of Advanced Robotics and Human Centred Technologies
Other Research Units involved: Research Unit of Physical and Rehabilitation Medicine, Research Unit of Neurology, Neurophysiology, Neurobiology, Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction

Efficacy of remote multiparametric monitoring based on selected sensors and a mini–invasive electronic device for the care of type 2 diabetes mellitus: a randomized controlled trial

Client: Laboratori di Informatica Applicata (L.I.A.)
Contractor: Research Unit of Geriatrics

GEPIKID

Client: National Institutes of Health
Contractor: Research Unit of Molecular Medicine and Biotechnology

IEEE Editorial Services Agreement

Client: The Institute of Electrical and Electronics Engineers, Incorporated ("IEEE")
Contractor: Research Unit of Advanced Robotics and Human Centred Technologies

Integration of the SofTaxic (EMS srl) neuronavigation system in a platform for robot–aided transcranial magnetic stimulation

Client: EMS srl
Contractor: Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction

Interleukin-8 and Programmed Cell Death Protein 1 Checkpoint in the Tumor Microenvironment

Client: Dompé Farmaceutici S.p.A.
Contractor: Research Unit of Biochemistry and Molecular Biology

In vitro profiling of MAGL inhibitors

Client: F. Hoffmann-La Roche Ltd
Contractor: Research Unit of Biochemistry and Molecular Biology

Liquid chromatography tandem mass spectrometry platforms to develop analytical protocols for drugs and metabolites in biologic fluids

Client: Eureka S.r.l.
Contractor: Research Unit of Drug Sciences

Markers of the endocannabinoid system in inflammation

Client: Vetagro SpA
Contractor: Research Unit of Biochemistry and Molecular Biology

Mindfulness-based stress reduction intervention in patients with chronic obstructive pulmonary disease and their caregivers

Client: OPI – CECRI (Ordine delle Professioni Infermieristiche – Centro di Eccellenza per la Cultura e la Ricerca Infermieristica
Contractor: Research Unit of Nursing Science

Nutrition education project "Nutripiatto"

Client: Nestlé Italiana SpA
Contractor: Research Unit of Food Science and Nutrition

PCR 1/2 Project
New methods in the treatment of limb amputation for the application of bionic prostheses

Client: INAIL-Centro per la Sperimentazione ed Applicazione di Protesi e Presidi Ortopedici di Vigorso di Budrio (BO)
Research Units involved: Research Unit of Orthopaedic and Trauma Surgery; Research Unit of Advanced Robotics and Human Centred Technologies; Research Unit of Physical and Rehabilitation Medicine; Research Unit of Neurology, Neurophysiology, Neurobiology; Research Unit of Neurophysiology and Neuroengineering of human-technology interaction.

PPR AS 1/3 Project
Implantable system for the control of upper-limb prosthesis with invasive neural interfaces and wireless communication

Client: INAIL-Centro per la Sperimentazione ed Applicazione di Protesi e Presidi Ortopedici di Vigorso di Budrio (BO)
Contractor: Research Unit of Advanced Robotics and Human Centred Technologies
Other Research Units involved: Research Unit of Physical Medicine and Rehabilitation, Research Unit of Orthopaedic and Trauma Surgery, Research Unit of Neurology, Neurophysiology, Neurobiology, Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction

Preliminary evaluation of the "Study on the potential application of the commercial products ApoGraftTM and ApoTrainerTM of the Cellect Biotechnology Ltd on oncological therapy"

Client: Avv. Gianluca De Micheli
Contractor: Research Unit of Tissue Engineering & Chemistry for Engineering
Research Units involved: Research Unit of Oncology

Remote multiparameter telemonitoring for the management of chronic pathologies in the elderly

Client: Fondazione ANIA
Contractor: Research Unit of Geriatrics
Other Research Units involved: Research Unit of Computer Systems and Bioinformatics

Smart Patient's Security

Client: Proge-Software srl
Contractor: Research Unit of Automation and Control Theory

Support for the technical contents of the web portal www.oil-gasportal.com

Client: Serintel S.r.l.
Contractor: Research Unit of Process Engineering

The contribution of caregiver and patient dyads to self-care in COPD: a mixed method study (1st phase)

Client: IPASVI
Contractor: Research Unit of Nursing Science

TraiNurse: innovative app for exploiting the skills of the nursing profession

Client: Artmediamix
Contractor: Research Unit of Nursing Science

CLINICAL TRIALS

During the year 2018, 160 studies have been approved by the independent Ethics Committee of the UCBM. 78 (48,75%) and 82 (51,25 %) of these projects were interventional or observational studies, respectively (Figure 1). The distribution of studies among the different Research Units is summarized in Figure 2. The very majority of the interventional trials is of Phase 2 or 3.

UCBM promoted 65 of the new studies approved in 2018 (40,62% of the total). On the other side, 56 projects were promoted by no profit institutions/research networks, and 39 projects were sponsored by Companies (pharmaceutical or developing medical devices) (Figure 3).
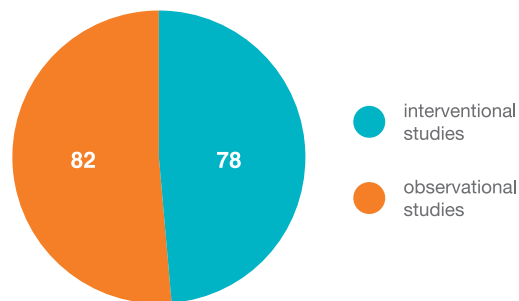
Figure 1 - Ethics Committee Evaluations 2018
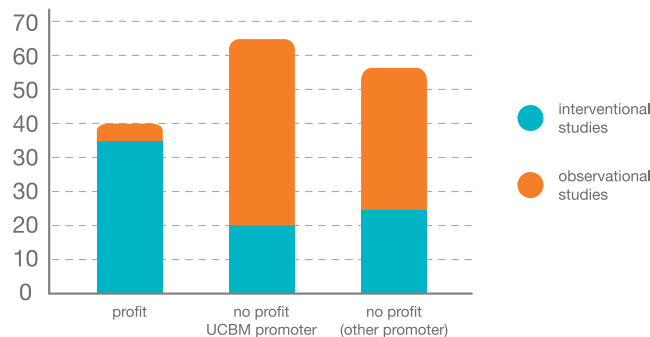
Figure 3 - Profit and no profit studies 2018

Figure 2 - Distribution of clinical trials among the different Research Units 2018
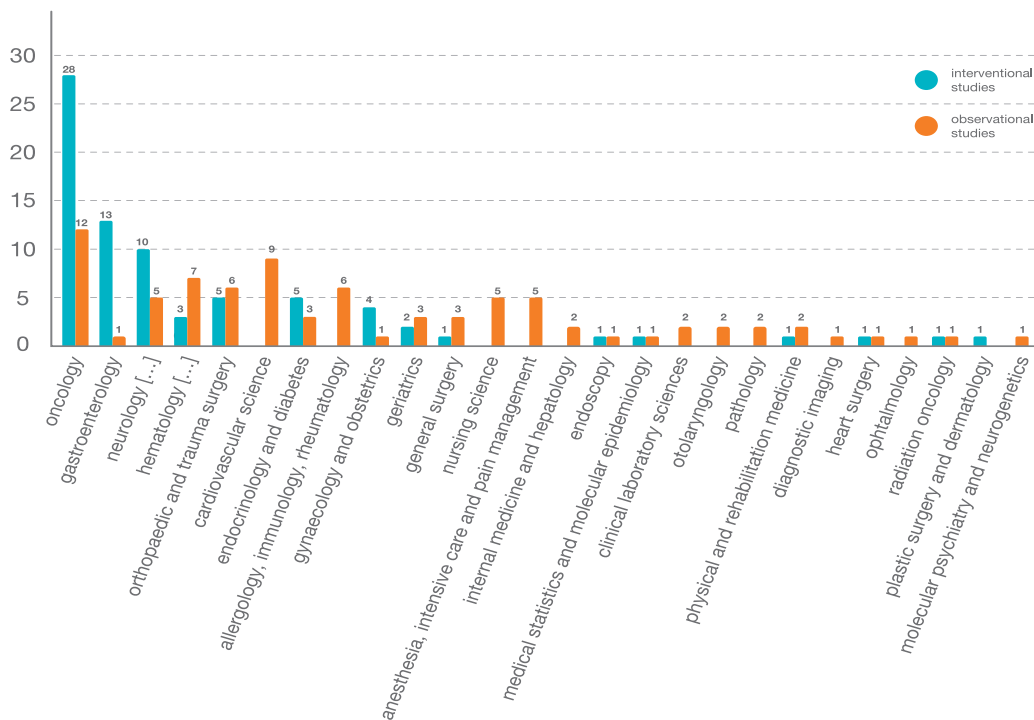
RESEARCH EXPLOITATION

Patent portfolio owned/co-owned by UCBM

- **A bioactive material for the regeneration of cartilage and process for the obtainement thereof (Italian patent);** Inventors: M. Centola, V. Denaro, A. Marsano, I. Martini, A. Rainer, M. Trombetta, G. Vadalà. Co-owner: Universitatsspital Basel.

- **Adipose tissue purification technique to obtain high concentration of adipose stem cells (Italian patent application);** Inventors: C. Gregorj, G. F. Marangi, F. Pantano, P. Persichetti, F. Segreto, M.C. Tirindelli.

- **Apparatus and method for videorhinohygrometric (vri) measures (USA patent);** Inventors: M. Casale, V. Cusimano, F. Salvinelli, R. Setola, P. Soda.

- **Device and method for controlled adhesion upon moist substrate (Italian, French, German and UK patents);** Inventors: D. Accoto, C. Esposito, M. T. Francomano.

- **Device for sampling food products (Italian patent);** Inventors: M. Dachà, A. D'Amico, G. Pennazza, M. Santonico, A. Zompanti.

- **Device for the sampling of the eye surface by imprinting (Italian patent, European and USA patent applications);** Inventors: B. Balzamino, I. Ghezzi, A. Micera, R. Sgrulletta, L. Zollo. Co-owner: Fondazione G. B. Bietti.

- **Diagnostic method of pancreas cancer based on the determination of mutations of K-RAS gene (Italian patent);** Inventors: A. Onetti Muda, G. Perrone.

- **Gradual compression medical device for supporting and optimizing the cutaneous scar (Italian patent);** Inventors: C. Falcinelli, S. Filippi, A. Gizzi, G.F. Marangi, P. Persichetti, F. Segreto.

- **Haptic interface module (Italian patent);** Inventors: D. Accoto, E. Cecchini, E. Guglielmelli.

- **Innovative functionalization on liquid phase sensors for the detection of bioactive lipids (Italian patent application);** Inventors: T. Bisogno, S. Grasso, M. Maccarrone, G. Pennazza, M. Santonico. Co-owner: CNR

- **Locomotion device for endoscopic applications and related methods (USA patent);** Inventors: D. Accoto, S. Passanisi.

- **Method for measuring the slipping between two surfaces (Italian patent application);** Inventors: E. Guglielmelli, R. Romeo, L. Zollo,. Co-owner: INAIL

- **Method for positioning receptors for sensory stimuli, a device obtained by said method and apparatuses comprising said device (Italian patent application);** Inventors: L. Beccai, M.C. Carrozza E. Guglielmelli, C. Oddo, R. Romeo, L. Zollo, . Co-owners: Scuola Superiore Sant'Anna, Istituto Italiano di Tecnologia.

- **Pneumopipe – Auxiliary device for collection and sampling of exhaled air (Italian, French, German, UK, Austrian and Dutch patents);** Inventors: R. Antonelli Incalzi, A. D'Amico, G. Pennazza, M. Petriaggi, M. Santonico .

- **Porous material for the inclusion of cytologic preparations, process for obtaining the same and its use. (Italian and international PCT patent applications);** Inventors: M. Costantini, A. Crescenzi, P. Mozetic, A. Rainer, A. Santoro, C. Taffon, M. Trombetta. Co-owner: UCS Diagnostic srl.

- **Predictive analysis of endometrial cancer risk (Italian patent application);** Inventors: R. Angioli, S. Capriglione, C. De Cicco, D. Luvero, R. Montera, F. Plotti, C. Terranova.

- **Robotic device for assistance and rehabilitation of lower limbs (Italian, French, German and UK patents);** Inventors: D. Accoto, G. Carpino, M. Di Palo, S. Galzerano, E. Guglielmelli, F. Sergi, N. L. Tagliamonte.

- **Robotic joint for prosthetic articulation (Italian patent application);** Inventors: L. Bramato, G. Carpino, D. Simonetti, L. Zollo. Co-owner: INAIL.

- **Sodium 2-Mercaptoethane Sulfonate for use in the treatment of lumbar pain (Italian, French, German and UK patents);** Inventors: F. E. Agrò, M. Carassiti, V. Denaro, A.C. Di Martino.

- **System for the estimation of cardiac output (Italian patent, European patent application);** Inventors: M. Carassiti, S. Cecchini, E. Schena, S. Silvestri.

UCBM spin-off companies

BHL – Bio Health Lab srl

BHL designs, develops and markets mobile app and software solutions related to healthcare sector. The solutions, with high innovative contents, are the result of research activities in several fields such as diagnostics, hospital organization and physician-patient communication.

Website: www.biohealthlab.it

Biomedical Research in Otolaryngology srl (B.R.I.O.)

BRIO produces and distributes innovative biomedical devices for the healthcare sector. In particular, the company is involved in the distribution of an innovative device for otolaryngology, manually operable, dispensing substances in the form of aerosol.

BPCO media srl

BPCO media deals with telemedicine and medical diagnostics research. Its innovative medical device allows patients to monitor their health state and detect the onset of flare-ups and critical clinical situations. It highlights prognostic symptoms that patients are not able to perceive and prompts them to contact their doctor in order to receive an early treatment and avoid potential dangerous situations before symptoms appear.

Website: www.bpcomedia.com

Epiclick srl

Epiclick aims at contributing to the prevention of melanoma by using modern technologies: by exploiting the immediacy of the information technology and through the joint use of epiluminescence and the best telematic tools, it allows early remote diagnosis of melanoma, avoiding long waiting lists of public service.

Website: www.epiclick.it

ICan Robotics srl

ICan Robotics is an innovative start-up company, founded in September 2014, active in the field of biomedical robotics, developing technologies for rehabilitation and physical assistance for patients with neurological, orthopedic or age-induced conditions. ICan robotics develops innovative and user-friendly products, which can be used not only in healthcare facilities, but also at patients' abodes, for the benefit of the quality of life of patients and their caregivers.

Website: www.icanrobotics.com

Public engagement activities

One of the priorities for the Campus Bio-Medico University of Rome is to design specific public engagement activities to meet special social needs. Projects for the protection of health are carried out regularly as for example, lung cancer prevention campaigns for smokers and former smokers, prevention days and screening of thyroid cancer, information days on osteoporosis and rheumatoid arthritis. Furthermore, a counselling service for relatives of chronic degenerative disease patient has been active since 2011.

Guidance programs and interaction with high school students take place regularly. Undergraduate Open Days, the "Salone dello studente" and the RomeCup annual event, are great opportunities to get information or get to visit the University. The University publishes the magazine "Lettere dal Campus" accessible on line as well, which typically includes a section focused on ongoing research activities, latest achievements and news from the UCBM research community. Finally, the University is also active on social media (Facebook, Twitter, YouTube, Google+, Flickr, Linkedin, Pinterest) having 30,000 users and a pool of 8 million annual contacts.

Below a list of the main public engagement activities carried out at UCBM in 2018 is reported.

Rome, 12 January 2018
Developmental biology of the mammary gland.
Discussant: Prof. Christine Watson of Cell and Cancer Biology at the University of Cambridge, member of the Nuffield Council on Bioethics and Deputy Editor of Breast Cancer Research and a Fellow of the Higher Education Academy.

Rome, 17 January 2018
Plastic surgery in the new millennium: from perforasomes and allotransplantation towards tissue engineering.
Discussant: Prof. Jan Jeroen Vranckx.

Rome, 25 January 2018
Interfaces for Neuroprostheses.
Discussant: Prof. Klaus-Peter Hoffmann, Division Director Biomedical Engineering, Head of Business Area Theranostics, Fraunhofer-Institut für Biomedizinische Technik (IBMT).
Seminar promoted by the Advanced Robotics and

Human Centred Technologies Research Unit, Campus Bio-Medico University of Rome.

Rome, 26 January 2018
Bionic Reconstruction of the Upper Extremity.
Discussant: Prof. Oskar C. Aszmann, Director of the Center for Restoration of Extremity Function, Division of Plastic and Reconstructive Surgery, Department of Surgery, University Clinics of Vienna.
Seminar promoted by the Orthopedics and Traumatology Unit, Campus Bio-Medico University of Rome.

Rome, 26 January 2018
Blockchain, big data and finance.
Discussant: Prof. Marta Bertolaso (UCBM).
Supervisors: Prof. Edwin Morley-Fletcher (Lynkeus srl), Prof. Paolo Soda (UCBM), Prof. Emiliano Ippoliti (Sapienza University of Rome).
Lunchtime meeting.

Rome, 9 February 2018
Late-Onset Pumps disease: pathogenetic, clinical and therapeutic aspects.
Discussant: Massimiliano Filosto (ERN-EURO NMD Center).
Seminar promoted by Neurology Unit, ASST "Spedali Civili" and University of Brescia.

Bethlehem, 12 February 2018 - 13 February 2018
Conference on Breast Cancer Unit.
Conference on Breast Cancer Unit represents the first worktable of Joint Technical Group Italian-Palestinian, a project of ONG ELIS, supported by Palestinian Ministry of Health and Italian Agency for Development Cooperation, with the participation of doctors of Breast Unit, Hospital Campus Bio-Medico University of Rome.

Rome, 15 February 2018
Master in Homeland Security "Systems, Methods and Tools for Security and Crisis Management".
Training course promoted by Nitel (National Inter-university Consortium for Transport and Logistics).

Rome, 16 February 2018
Diagnosis in ALS: current state and clues for the future.
Discussant: Prof. Mamede de Carvalho, Neurologist and Neurophysiologist (CHLN-HSM) Full Professor of Physiology (FMUL), Department of Medicine, Univer-

sity of Lisbon.
Seminar promoted by Neurology Unit.

Rome, 7 March 2018
"Clinical observation: to learn to see". Best Practice and Clinical Reasoning.
Discussant: Vittoradolfo Tambone, Giampaolo Ghilardi.

Rome, 8 March 2018
Broca's area.
Discussant: MD, Prof. Gabriele Miceli (Center for Mind/Brain Sciences), University of Trento.

Rome, 14 March 2018
"Masterplan International Design Competition International Symposium". Universities serving society and humanity.
Discussant: prof. Maria Chiara Carrozza (scientific director of Fondazione Don Carlo Gnocchi), Prof. Maria Cerezo (Logic and Philosophy of Science, University of Murcia), Prof. Fernando Fragueiro (member of the Broad of Austral University), Prof. Eugenio Guglielmelli (vice-rector for Research, UCBM) Prof. Maria Cristina Messa (director of Research Committee) and Prof. Christine Watson (Cell and Cancer Biology, University of Cambridge).

Rome, 19 March 2018
Cerebral Oxygenation: new insights, new challenges.
Discussant: Prof. Andre Denault, Department of Anesthesiology, Critical Care Program, Montreal Heart Institute, and Centre Hospitalier de l'Université de Montréal, Montreal, Canada.
Seminar promoted by the Anesthesia and Resuscitation Unit.

Rome, 21 March 2018
Best practise and Clinical Reasoning. "Insight in Medicine".
Discussant: Vittoradolfo Tambone, Giampaolo Ghilardi.

Rome, 21 March 2018
The role of Food Microbiology Laboratory.
Discussant: Dr. Francesco Dalla Torre Del Tempio di Sanguinetto.
Seminar promoted by the Food Science and Nutrition Unit.

Rome, 21 March 2018
Breast implant associated ALCL: overview and update.
Discussant: Mariangela Amoroso, Executive Medical Director Allergan and Maria Musumeci, Medical Affairs Manager Allergan.

Rome, 23 March 2018
Therapeutic strategy targeting B-cells in MS: ocrelizumab and the new era of DMTs.
Discussant: Dr. Stefano Sabatini, MSL Neuroscience & Immunology Roche.
Seminar promoted by Neurology Unit.

Rome, 23 March 2018
Novel surgical approaches in amputation surgery.
Discussant: Prof. Rickard Brånemark, University of California, San Francisco.
Seminar promoted by Orthopedics and Traumatology Unit, Neurology Unit, and Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab), Campus Bio-Medico University of Rome.

Rome, 23 March 2018
Neural control of osseointegrated prosthetic limbs and neurorehabilitation of pain.
Discussant: Dr. Max Jair Ortiz Catalan, Chalmers University of Technology.
Seminar promoted by Orthopedics and Traumatology Unit, Neurology Unit and Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab), Campus Bio-Medico University of Rome.

Rome, 04 April 2018
Best practice and Clinical Reasoning. "Control of Prosthesis".
Discussant: Vittoradolfo Tambone, Giampaolo Ghilardi.

Rome, 06 April 2018
Roche's commitment to neuroscience.
Discussant: Dr. Mario Pata, Roche Italy.
Seminar promoted by Neurology Unit, Campus Bio-Medico University of Rome.

Rome, 09 April 2018
Mechanisms of tendon generation, degeneration and regeneration.
Discussant: Prof. Denitsa Docheva, Director of Experimental Trauma Surgery, Department of Trauma Surgery, University Regensburg Medical Centre, Ger-

many.
Seminar promoted by Orthopedics and Traumatology Unit.

Rome, 09 April 2018
The 4 X 4 on sustainability with the top leaders in the world of production and services.
Discussant: Dr. Paolo Scaroni, vice president of Rothschild, former CEO of Enel and Eni between 2002 and 2014.
Seminar promoted by Chemical Engineering Unit for Sustainable Development and University-Enterprise Committee, Campus Bio-Medico University of Rome.

Rome, 16-18 April 2018
Rome Cup 2018 in collaboration with Mondo digitale Foundation
Multi-event day with competitions, conferences, laboratories and exhibition areas to spread innovation by connecting schools, research centers, universities, companies and institutions.

Rome, 16 April 2018
Robotics Seminars
Discussant: Prof. Oussama Khatib, Director of Robotics Centre, Stanford University, USA and Prof. Robert Riener, Diretctor of Sensory–Motor Systems Lab-ETH, Zurich.

Rome, 18 April 2018
Best practice and Clinical Reasoning. "Trasmission of diagnosis".
Discussant: Vittoradolfo Tambone, Giampaolo Ghilardi.

Rome, 19-20 April 2018
Neuroengineering and Biorobotics.
Discussant: Prof. Nitish Thakor, Director of the Singapore Institute for Neurotechnology (SiNAPSE), National University of Singapore and Johns Hopkins University, Baltimore (MD), USA.
Seminar promoted by the Biomedical Robotics Unit.

Rome, 19 April 2018
Blepharoptosis: diagnosis and treatment; Reconstruction of the eyelids.
Discussant: Dr. Carlos Alberto Affonso Ferreira, oculoplastic surgeon, Federal University of Sao Paulo (Brazil).

Rome, 24 April 2018
Determining the mechanical origin and propagation of tremor for future tremor suppression.
Discussant: Prof. Steven K. Charles, Mechanical Engineering and Neuroscience, Brigham Young University, Utah, USA.
Seminar promoted by Neurophysiology and Neuro-engineering of Human-Technology Interaction (NEXT-Lab), Campus Bio-Medico University of Rome.

Rome, 26 April 2018
Research topics in Applied Mathematics.
Discussant: Prof. Renato Spigler, Department of Mathematics and Physics of the University of Rome TRE.
Seminar promoted by Department of Engineering.

Rome, 3 May 2018
TaTME in Rome. International congress on the treatment of rectal cancer.
Discussant: Dr. Antonio Lacy, Chief of Gastrointestinal Surgery Department of the Clinic Hospital of Barcelona and the president of AIS Channel, Dr. Patricia Sylla of Mount Sinai Clinical Center of New York (NY) and Prof. Albert Wolthuis of the Catholic University of Leuven (Belgium).

Rome, 8 May 2018
Research activity at the INAIL Prosthesis Center: the network of collaborations and active projects.
Discussant: Ing. Emanuele Gruppioni, INAIL Prosthesis Center in Vigorso di Budrio, Technical and Health Research Area.
Seminar promoted by the Biomedical Engineering Unit, Campus Bio-Medico University of Rome.

Rome, 9 May 2018
Best practice and Clinical Reasoning. "Decisions".
Discussant: Vittoradolfo Tambone, Giampaolo Ghilardi.

Rome, 9 May 2018
Stroke path: basic knowledge.
Intervengono: Dr. Paolo Bovi, ISO Triveneto coordinator and Dr. Lorenza Spagnuolo, Angels Initiative, Consultant.
Seminar promoted by Neurology Unit, Campus Bio-Medico University of Rome.

Rome, 9 May 2018

Food safety and conformity certification: tools for companies to guarantee consumers.
Discussant: Dr. Rolando Manfredini, Head of Food and Production Safety Area, Coldiretti and Dr. Piero Bonato, Director General of CSQA.

Rome, 10 May 2018

Diagnostic aspects of Gaucher and Fabry diseases.
Discussant: Dr. Alberto Liuti, Shire Italia.
Seminar promoted by Neurology Unit, Campus Bio-Medico University of Rome.

Rome, 11 May 2018

Neuromorphic encoding of tactile information: "From bionic hand prostheses to haptic telepresence".
Discussant: Prof. Calogero Maria Oddo, Scuola Superiore Sant'Anna, The BioRobotics Institute.
Seminar promoted by the Biomedical Engineering Unit, Campus Bio-Medico University of Rome.

Rome, 16 May 2018

Building Bionics.
Discussant: Prof. Todd A. Kuiken, Center for Bionic Medicine (CBM), Northwestern University.
Seminar promoted by Orthopedics and Traumatology Unit, Neurology Unit, and Neurophysiology and Neuroengineering of Human-Technology Interaction Unit (NEXTLab).

Rome, 17 May 2018

Technology redevelopment and tech transfer at the Center for Bionic Medicine.
Discussant: Prof. Todd A. Kuiken, Center for Bionic Medicine (CBM), Northwestern University.
Seminar promoted by Department of Engineering, Campus Bio-Medico University of Rome.

Rome, 17 May 2018

Active contours in computer vision and visual tracking.
Discussant: Dr. Anthony Yezzi, Professor in the School School of Electrical and Computer Engineering at Georgia Tech.
Seminar promoted by Unit of Computer System and Bioinformatics.

Rome, 17 May 2018

The contemplative dimension of scientific re-
search.
Discussant: Prof. Eugenio Guglielmelli, Vice Rector for Research, Prof. Marcello D'Amelio, Molecular Neuroscience Lab., Prof. Christian Cherubini, Lab of Nonlinear Physics and Mathematical Models, Prof. Antoine Suarez, Centrum for Quantum Philosophy, Zurich and Geneva, Prof. Nicola Di Stefano, FAST Institute, Prof. Flavio Keller, Development Neuroscience Lab.

Rome, 18 May 2018

Bio-inspired robots for medical applications.
Discussant: Prof. Arianna Menciassi, Scuola Superiore Sant'Anna.
Seminar promoted by Department of Engineering, Campus Bio-Medico University of Rome.

Rome, 22 May 2018

Hands on ALR lower limb.
Workshop promoted by AOC di Anesthesia and Resuscitation, with the economic support of BBRaun and Molteni and the patronage of ESRA - European Society of Regional Anesthesia.

Rome, 23 May 2018

Best practice and Clinical Reasoning. "Follow up".
Discussant: Vittoradolfo Tambone, Giampaolo Ghilardi.

Rome, 23 May 2018

Alfie's Lesson: "Clinical, ethical and social aspects of medical decisions".
Discussant: Prof. Melazzini and MP. P. Binetti.
Seminar promoted by FAST, Campus Bio-Medico University of Rome.

Rome, 23 May 2018

Design considerations for implantable electronics.
Discussant: Dr. Dai Jiang, University College of London.
Seminar promoted by the Advanced Robotics and Human Centred Technologies Unit, Campus Bio-Medico University of Rome.

Rome, 25 May 2018

Digital spatial profiling: the digital pathology revolution.
Discussant: Dr. Nicholas Confuorto, Global Technical Sales Specialist DSP/3D, Nanostring technologies.
Seminar promoted by the Pathological Anatomy Unit, Campus Bio-Medico University of Rome.

Rome, 29 May 2018
Towards new therapeutic scenarios in Multiple Sclerosis: update on cladribine.
Discussant: Dr. Gorini Manuela, Medical Liason Merck.
Seminar promoted by Neurology Unit, Campus Bio-Medico University of Rome.

Rome, 29 May 2018
Targeting necroptosis in neurodegeneration.
Discussant: Prof. Ludovic Collin, NORD DTA, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Basel (Switzerland).
Seminar promoted by Biochemistry and Molecular Biology Unit.

Rome, 30 May 2018
From motor control to sensory perception, and back.
Discussant: prof. Silvia Ionta, Sensory-Motor Lab, Department of Ophthalmology, University of Lausanne, Jules Gonin Eye Hospital, Fondation Asile des Aveugles.
Seminar promoted by Neurophysiology and Neuro-engineering of Human-Technology Interaction Unit (NEXTLab), Campus Bio-Medico University of Rome.

Rome, 01 June 2018
Topology of bipedal locomotion.
Discussant: Prof. Carlo Tiseo, Rehabilitation Research Institute of Singapore/ School of Mechanical & Aerospace Engineering, Nanyang Technological University, Singapore.
Seminar promoted by the Advanced Robotics and Human Centred Technologies Unit, Campus Bio-Medico University of Rome.

Rome, 04 June 2018
Cerebral Oxygenation: new insights, new challenges.
Discussant: prof. Andre Denault, Department of Anesthesiology, Critical Care Program Montréal Heart Institute and University Hospital of Montreal, University of Montreal, Montreal, Quebec, Canada and Prof. Felice Eugenio Agrò, Director of Specialization School in Anesthesia, Resuscitation, Intensive Pain Therapy, Campus Bio-Medico University of Rome.

Rome, 11 June 2018
A.rtificial I.ntelligence & A.rtificial E.mpathy: "Truth and trust in dealing with robots".
Discussant: Prof. Luisa Damiano, Author of "Living with robots", University of Messina, DICAM Department of Ancient and Modern Civilizations and prof. Teresa Numerico, Author of "The digital humanist a critical inquiry", Roma Tre University, Department of philosophy, communication and performing arts.

Rome, 12 June 2018
Research activities @ B2efore - Biomaterials and Biofabrication Lab.
Discussant: Prof. Silvia Farè, and Prof. Lorenza Draghi, Department of Chemistry, Materials and Chemical Engineering "G. Natta", Polytechnic University of Milan.
Seminar promoted by the Tissue Engineering and Chemistry for Engineering Lab.

Rome, 12 June 2018
Image processing for medical decision support system.
Discussant: Dr. Albert Comelli, University of Palermo and Research Affiliate at the Laboratory of Computational Computer Vision (LCCV), Georgia Institute of Technology, Atlanta, USA; Ing. Alessandro Stefano, Institute of Molecular Bioimaging and Physiology, National Research Council (IBFM-CNR), Cefalù and Prof. Anthony Yezzi, School of Electrical and Comptuer Engineering, Georgia Institute of Technology.

Rome, 13 June 2018
Multidimensional and multilevel imaging of tissue disease: towards the 3D digital histology.
Discussant: Prof. Francesco S. Pavone, European Laboratory for NonLinear Spectroscopy, University of Florence.
Seminar promoted by Integrated Research Center.

Rome, 13 June 2018
EEG data analysis: theoretical and practical issues.
Discussant: prof. Giorgio Arcara, San Camillo Hospital IRCCS, Venezia.
Course promoted by Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab), Campus Bio-Medico University of Rome.

Rome, 21 June 2018
Human Robotics.
Discussant: Prof. Etienne Burdet, Human Robotics, Faculty of Engineering, Department of Bioengineering, Imperial College of Science, Technology and

Medicine, London, UK.
Seminar promoted by Neurophysiology and Neuro-engineering of Human-Technology Interaction (NEXT-Lab), Campus Bio-Medico University of Rome.

Rome, 21 June 2018
Prosopoplerosis: "Medical and surgical increase in face volumes".
Discussant: Dr. Daniele Spirito, University of Milan.
Seminar promoted by the Plastic, Reconstructive and Cosmetic Surgery Unit, Campus Bio-Medico University of Rome.

Rome, 22 June 2018
Making network and innovation through "Advanced School in Artificial Intelligence".
Discussant: prof. Daniele Caligiore, CNR, Institute of Cognitive Sciences and Technologies.
Seminar promoted by the Advanced Robotics and Human Centred Technologies Research Unit.

Rome, 2 July 2018
Mechanobiology of intervertebral disc and cartilage for regeneration.
Discussant: prof. Shuichi Mizuno, Orthopaedic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston (USA).
Seminar promoted by the Orthopedics Unit, Campus Bio-Medico University of Rome.

Rome, 9 July 2018
Breathing Biomechanics: optical measurement systems for thoracoabdominal analysis.
Discussant: Prof. Amanda Piaia Silvatti, Biomechanical Analysis Laboratory, Federal University of Viçosa, (Brazil).

Rome, 10 July 2018
Human and molecular genetics of non-alcoholic fatty liver disease (NAFLD).
Discussant: Prof. Stefano Romeo, Sahlgrenska University, Goteborg, Sweeden
Seminar promoted by Hepatology Unit, Campus Bio-Medico University of Rome.

Rome, 11 September 2018
Motor representation and motor awareness in the healthy and pathological human brain.
Discussant: Prof. Angela Sirigu, Institute of Cognitive Science, CNRS and University of Lyon.

Seminar promoted by Neurophysiology and Neuro-engineering of Human-Technology Interaction (NEXT-Lab), Campus Bio-Medico University of Rome.

Rome, 17 September 2018
Understanding vitamin D.
Discussant: Prof. Anastassios G. Pittas, Tufts University School of Medicine.

Rome, 18 September 2018
The two-way balance between embodiment and multisensory integration in immersive virtual reality.
Discussant: Prof. Antonella Maselli, Laboratory of Neuromotor Physiology, IRCCS Fondazione Santa Lucia, Rome.
Seminar promoted by Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab), Campus Bio-Medico University of Rome.

Rome, 19 September 2018
IBM Technologies for Biomedical Research.
Discussant: Gianfranco Cesareo (Watson Studio), Marco De Angelis (Watson IoT), Antonio Pelliccia (Watson for Drug Discovery), Bianca Romano (Watson Knowledge Studio), Massimo Chiriatti (Blockchain), Daniele Morgantini (IBM Cloud Private), Giorgio Richelli (Power AI).
Seminar promoted by Integrated Research Center – CIR.

Rome, 19 September 2018
Gluteal prosthesis.
Discussant: Dr. Ramón Calderón Nájera, Spanish Society of Reconstructive and Aesthetic Plastic Surgery (SECPRE).
Seminar promoted by the Plastic Surgery, Reconstructive and Aesthetic Unit.

Rome, 20 September 2018
OTSC system: Update in Operative Endoscopy.
Event promoted by the Operative Digestive Endoscopy Unit.

Rome, 25 September 2018
Clinical management and differential diagnosis of microbial keratitis.
Discussant: Dr. Merle Fernandes, Cornea and Anterior Segment Services, LV Prasad Eye Institute, GMRV Campus Visakhapatnam and Dr. Arundhati Borthakur,

Cornea and Anterior Segment, Lasik Laser Eyecare Center, Guwahati, India.
Seminar promoted by the Ophthalmology Area.

Rome, 25 September 2018
Treatment of the upper and lower limbs after great ponderal loss.
Discussant: prof. Francesco Mazzarone, Institute Ivo Pitanguy, Rio De Janeiro, (Brazil).
Seminar promoted by the UOC of Plastic Surgery, Reconstructive and Aesthetic Unit.

Rome, 26 September 2018
EEG Data Analysis: Low Resolution Elettromagnetic Tomography (LORETA).
Discussant: Prof. Claudio Imperatori, Department of Human Science, European University of Rome, Italy.
Seminar promoted by Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab), Campus Bio-Medico University of Rome.

Rome, 26 September 2018
Life & Robotics. Can we talk about analogy?
Discussant: Prof. Fabio Fossa, Philosophy, Institute of Biorobotics, Scuola Superiore Sant'Anna of Pisa, Anna Lisa Ciancio, Advanced Robotics and Human Centred Technologies (UCBM) , Chiara Beneduce, Philosophy of Science (UCBM) and Nicholas Windsor, Health Europe-Man and Technology web-site.
Lunchtime Meeting.

Rome, 28 September 2018
European Researchers' Night, in collaboration with Mondo Digitale Foundation
UCBM Open Night: becoming researchers.

Rome, 2 October 2018
Functional semi-blind source separation identifies primary motor area without active motor execution.
Discussant: Prof. Camillo Porcaro, Institute of Cognitive Sciences and Technologies (ISTC), National Research Council (CNR), Rome.

Rome, 10 October 2018
The natural death protocol.
UCBM protocol for the assistance of patients with deadly prognosis.
Discussant: Prof. Victoradolfo Tambone, Prof. Ros-

sana Alloni, Prof. Maria Grazia De Marinis and Prof. Giuseppe Tonini, Campus Bio-Medico University of Rome.

Rome, 10 October 2018
2600 years of Plastic Surgery - Anatomy of a rhinoplasty.
Discussant: Prof. Riccardo Mazzola, G. Sanvenero Foundation - Rosselli (Milan).
Seminar promoted by the Plastic, Reconstructive and Aesthetic Surgery Unit.

Rome, 24 October 2018
"Troppi diritti. L'Italia tradita dalla libertà", written by Alessandro Barbano.
Discussant: Prof. Massimo Adinolfi, Prof. Raffaele Calabrò, Francesco Giorgino, Fausto Bertinotti, Giovanni Lo Storto and Alessandro Barbano.
Event promoted by FAST, Campus Bio-Medico University of Rome.

Rome, 25 October 2018
Think Roma 2018: "The health of the future".
Discussant: Prof. Walter Ricciardi, Istituto Superiore di Sanità, Dr. Vincenzo Panella, Umberto I Policlinic of Rome, Prof. Vincenzo di Lazzaro, University of Campus Biomedico of Rome, Prof. Gianfranco Gensini, OSVA, ALTEMS and Dr. Fabrizio Ammirati, UOC Cardiology, Hospital G.B. Grassi.

Rome, 26 October 2018
Real-time brain functional connectivity: measures and interventions.
Discussant: prof. Paolo Belardinelli, Neurology Department, University Hospital, Eberhard Karls University Tuebingen.
Seminar promoted by the Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab) Research Unit, Campus Bio-Medico University of Rome.

Rome, 15 November 2018
Coding girls. V edition
In collaboration with Mondo Digitale Foundation

Rome, 15 November 2018
Wearable robotics: beyond science fiction.
Discussant: prof. Nicola Vitiello, Wearable Robotics Laboratory, The BioRobotics Institute, Scuola Superiore Sant'Anna.

Seminar promoted by the Department of Engineering.

Rome, 21 November 2018
You or me? The self-other body boundaries in normal and pathological brain.
Discussant: Prof. Francesca Garbarini, MANIBUS-Lab: Movement and body In Behavioral and Psychology Department, University of Turin.
Seminar promoted by the Neurophysiology and Neuroengineering of Human-Technology Interaction (NEXTLab) Research Unit, Campus Bio-Medico University of Rome.

Rome, 29 November 2018
In vitro disease models.
Workshop promoted by ITHACa – Integration of microfluidic devices within microscopy systems high-content screening for cell-on-a-chip application, financed by the University Campus Bio-Medico of Rome for the INTESE project.

Rome, 4 December 2018
Adipose tissue: between volume and regeneration.
Discussant: Prof. Angelo Trivisonno, Rome.
Seminar promoted by the Plastic Surgery, Reconstructive and Aesthetic Unit.

Rome, 5 December 2018
Tech-Care Hackathon: the challenge. Technology and solitude of the elderly.
Discussant: Prof. Vittoradolfo Tambone, Prof. Francesco Bruno, Prof. Alfonso Molina, Prof. Eugenio Guglielmelli and Prof. Giampaolo Ghilardi.
Seminar promoted by FAST, Campus Bio-Medico University of Rome.

Rome, 14 December 2018
Beauty Recovery Specialist.
Course promoted by the Plastic Surgery, Reconstructive and Aesthetic Unit in collaboration with Institute of Philosophy of Scientific and Technological Practice (FAST), with the technical support of Ripar Cosmetici and the contribution of Tricostarc.

Rome, 18 December 2018
The beer market: institutional and health profiles.
Discussant: Dott. Andrea Bagnolini, Assobirra-Confindustria, Prof. Laura De Gara and Prof. Francesco Bruno.

Seminar promoted by the Food Science and Nutrition Unit, Campus Bio-Medico University of Rome.

Rome, 19 December 2018
Bad news. How to communicate bad news in healthcare.
Discussant: Prof. Daniele Santini and Prof. Vittoradolfo Tambone.
Seminar promoted by FAST, Campus Bio-Medico University of Rome.

Research Agreements and Collaborations

Research Agreements and Collaborations

National agreements and collaborations

Ania Foundation, Rome, Italy

Biological Science Department and Interdepartmental Centre for Stem Cell Research Milano University, Italy

BPCOMedia srl

Casaccia Research Centre, Rome, Italy

Catholic University of the Sacred Heart, Department of Public Health, Section of Hygiene, Rome, Italy

Catholic University of the Sacred Heart, Italy

Center of Excellence for Biomedical Research, Genova, Italy

Centro Diagnostico Italiano SpA

Club of the Hospital Hepatologist (CLEO)

CNR Institute of Biomedicine and Molecular Immunology, Palermo, Italy

Danesi caffè SpA

Department of Molecular Medicine-Virology section. Sapienza University, Rome, Italy

Department of Molecular Medicine, Sapienza University, Rome, Italy

Departments of Information and Electrical Engineering, University of L'Aquila, Italy

Department of Clinical and Experimental Medicine. University of Florence, Italy

Department of Pharmacy - Pharmaceutical Sciences. University of Bari Aldo Moro, Italy

Don Carlo Gnocchi Foundation, Italy

Humanitas Research Hospital, Milan, Italy

INAIL Prosthetic Centre, Italy

INAIL, Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Italy

Informatics and Automation, Sapienza University, Rome, Italy

Institute of Cognitive Sciences and Technologies, National Research Council (CNR), Italy

International Center for Relativistic Astrophysics Network (ICRANet), Rome, Italy

IRCCS "Fondazione G. Pascale", Naples, Italy

IRCCS Bambino Gesù Paediatric Hospital, Italy

IRCCS Fondazione don Carlo Gnocchi ONLUS, Rome, Italy

IRSA, Water Research Institute, Italy

Italian Association for the Study of the Liver (AISF)

Italian Group of Hematologic Diseases in the Adult (GIMENA)

Italian Institute for Technology (IIT)

Italian Lymphoma Foundation

Italian National Agency for New Technologies, Energy and Sustainable Development, (ENEA)

Italian Society of Internal Medicine (SIMI)

Italian Space Agency

Maire Tecnimont, Rome, Italy

MASMEC SpA, Italy

Mondo Digitale Foundation, Rome, Italy

National Cancer Institute, Italy

National Institute of Health, Italy

National Research Council (CNR), Italy

Neurotoxicology & Neuroendocrine Department, Italian National Institute of Health (ISS), Italy

Piaggio Research Centre, University of Pisa, Italy

Politecnico di Milano, Italy

Proteomics Laboratory, Tuscia University, Viterbo, Italy

Psychology Department, Sapienza University, Italy

Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples, Italy

Roma Tre University, Rome, Italy

Rome Transplant Network (RTN), Italy

Sant'Anna School of Advanced Studies, Italy

Sapienza University, Rome, Italy

Scleroderma Unit, Sapienza University, Rome, Italy

University of Catania, Italy

University of Genova, Italy

University of Messina, Italy

University of Naples "Federico II", Italy

University of Perugia, Italy

University of Roma Tre, Rome, Italy

University of Rome "Tor Vergata", Italy

University of Sassari, Italy

Virology Lab, IRCCS Bambino Gesù Paediatric Hospital, Italy

International agreements and collaborations

Amsterdam Universitair Medische Center, The Netherands

Applied Neurotechnology Laboratory, Department of Psychiatry and Psychotherapy, University Hospital of Tübingen, Tübingen, Germany

Brain Centre Rudolf Magnu, The Netherlands

Cardiovascular Research Center Aalst, Belgium

Center for the Prevention of Diabetes, Jerusalem, Israel

Centre for Enterprise, Innovation and Growth, Birmingham City University, UK

Department of Molecular and Clinical Medicine, University of Gothenburg, Sweden

Department of Plastic and Reconstructive Surgery, Kansai Medical University, Osaka, Japan

Department of Translational Neuroscience, University Medical Centre Utrecht, The Netherlands

Department. of Fundamental Neuroscience, Faculty of Biology and Medicine. University of Lausanne, Switzerland.

Department of Pathology. Harvard University School of Medicine, Boston, USA

Fetal Neonatal Neuroimaging and Developmental Science Center. Boston Children Hospital, USA

Fraunhofer IBMT, St. Ingbert, Germany

Harvard Clinical Research Institute, Boston, USA

Harvard Medical School, Boston MA, USA

Hebrew University of Jerusalem, Israel

Hôpital Européen Georges Pompidou, Paris, France

Hospital de Hautepierre, Strasbourg, France

Hospital Vall d'Hebron Barcelona, Spain

IASI-CNR Eindhoven University of Technology, The Netherlands

Institute of Psychiatry, King's College London, UK

International Extranodal Lymphoma Study Group (IELSG), Switzerland

John Innes Centre, UK

Medical Oncology Department, Hospital Clínic. Universitat de Barcelona, Barcelona, Spain

Pal Robotics, Spain

Pelican Cancer Foundation, UK

Perelman School of Medicine, University of Pennsylvania, USA

Public Health Institute of Montenegro

Public Institute of Bulgaria, Sofia, Bulgaria

Queen Mary University of London, UK

Singapore Centre for Environmental Life Sciences Engineering, Nanyang Technological University, Singapore

St. Thomas Hospital. University of London, UK

Technical University of Eindhoven, The Netherlands

Universidad de Navarra, Spain

Universidad Miguel Hernandez de Elche, Spain

Université Libre de Bruxelles, Belgium

University at Groningen Medical Center, The Netherlands

University College London, UK

University of Alessandria, Egypt

University of California, San Francisco, USA

University of Florida, Gainesville, USA

University of Hamburg, Germany

University of Izmir, Turkey

University of Navarra, Spain

University of Guangdong, China

Virginia Commonwealth University, USA

Washington University, Saint Louis, USA

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Editorial board membership

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Soda P.	The Open Medical Devices Journal Associate Editor: Proceedings of the 40th Annual International Conference of the IEEE Engineering in Medicine & Biology Society.

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Vollero L.	Journal of Sensors
Zollo L.	IEEE Transactions on Medical Robotics and Bionics International Journal of Advanced Robotic Systems Springer Series on Biosystems and Biorobotics

PhD Courses and
XXX cycle theses (2015-2017)

Ph.D Courses

The Campus Bio-Medico University of Rome offers Ph.D courses to students motivated to gain autonomy and rigor in scientific research. Courses aim to provide doctoral students a scientific culture, methodological tools and advanced technical skills, thereby contributing to the growth of research and scholarship in Italy and internationally.

The primary purpose of Ph.D study is the preparation and presentation of a substantial piece of original research designed to be completed within three years of study.

Full text Ph.D dissertations are deposited in the open access repository ILITHIA. The repository is indexed in OpenDOAR, an authoritative worldwide directory of academic open access repositories. Link:<http://ilithia.unicampus.it/ilithia/Default.asp>.

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PH.D IN INTEGRATED BIOMEDICAL SCIENCES AND BIOETHICS

Duration 3 years
Coordinator Prof. Paolo Pozzilli

Students enrolled

XXXI Cycle (2015/2016): A. Aveta, E. Dell'Aquila, A. Di Mauro, P. Finamore, A. Grasso, E. Maddaloni, A. Pezzuto,V. Toto

XXXII Cycle (2016/2017): G. Armento, I. Cavallari, L. Costanzo, L. Di Biase, I. Giovannoni, A. Mioli, S. Santoro, F. Segreto, A. Sisto

XXXIII Cycle (2017/2018): M.M.C. Amato, M. Barone, A. Berton, A. Creta, R. Del Toro, L.A. Diaz Balzani, L. D'Onofrio, S. La Padula, D. Luvero, B. Marigliano, G. Manascià, A. M. Naciu, F. Picardo, M. Pinardi, F. Russo, G. Salvatore, S. Vasta, B. Zampogna, A. Zangrandi

XXXIV Cycle (2018/2019): F. Cannata, A. De Vincentis, M. Donati, Emma. Falato, M. Giuffreda, A. Guarnieri, M. Marano, G. Musumeci, M. Paolucci, M. Russano, F. Tramontana

Learning outcomes

The structure of the Ph.D in Integrated Biomedical Sciences and Bioethics is designed to produce graduates who have a thorough knowledge of the literature and comprehensive understanding of scientific methods and techniques applicable to their own research. This particular Ph.D focuses its attention in integration of the broader fields of biomedical research with a more philosophical approach, which include further study in anthropology, ethics, aesthetics, epistemology, and bioethics.

Research fields

The Ph.D in Integrated Biomedical Sciences and Bioethics is divided in various tracks:
- **Endocrinology:** MED/13, MED/09, MED/08, BIO/10, MED/16, MED/18
- **Bioethics:** MED/43, BIO/14, MED/26, BIO/16
- **Osteo-Oncology Pathology:** MED/06, MED/04, BIO/10, MED/15, MED/40, MED/16
- **Aging Sciences and of Tissue Regeneration:** MED/09, MED/19, MED/26, MED/15

PH.D IN BIOENGINEERING AND BIOSCIENCES

Duration 3 years
Coordinator Prof. Giulio Iannello

Students enrolled

XXXI Cycle (2015/2016): L. Acciai, E. Cordelli, M.C. De Maggio, E. Galassi, C. Lauretti, D. Lelli, I. Portaccio, P. Tomaiuolo, J. Tosi

XXXII Cycle (2016/2017): S. Cocca, C. Gentile, E. Gruppioni, M. Langone, M. Menci, A. Noccaro, F. Scotto Di Luzio, R. Sicilia, A. Vilmercati

Learning outcomes

The structure of the Ph.D in Bioengineering and Biosciences is designed to produce graduates with rigorous research and analytical skills, who are exceptionally well-equipped to carry out research in academic, industry, or government positions. The program is divided in two tracks: one oriented to biomedical engineering applications the other to Science and food technology and nutrition.

Ph.D program allows graduates to:

- develop new methods, instruments and systems, for biomedical engineering and for food sciences and nutrition;
- describe, plan, coordinate and carry out research programs developing technical and medical-biological skills;
- integrate traditional formation in the biomedicine, with knowledge such as maths and technology which can face the increasing complexity of "bioinspired" research fields.

Research fields

The main fields of study are:

- **Bioengineering:** study, design and development of new methods, systems and medical devices, medical and biological research, development of bioinspired medical technologies;
- **Material science and nanotechnology:** study, development and testing of materials for industrial applications with a particular consideration to medical and food applications;
- **Modelling:** study and use of complex systems models for applications in biology and medicine;
- **Food chemistry and plant physiology:** study and development of new knowledge and protocols for the characterization of bioactive molecules and their metabolism. Use of new technologies for the nutritional enhancement of traditional and innovative foods;
- **Nutrition:** use of advanced technological for the study of nutritional parameters and their impact in the prevention of diseases; Experimentation protocols and procedures applied to clinical nutrition.

PH.D IN SCIENCE AND ENGINEERING FOR HUMANS AND THE ENVIRONMENT

Duration 3 years
Coordinator Prof. Giulio Iannello

Students enrolled

XXXIII Cycle (2017/2018): M. Del Fabbro Arcopinto, S. Della Posta, G. Franchi, V. Giacinti, F. Leone, D. Lo Presti, M. Nicoletti, L. Raiano, A. Sabatini, M. Stefano

XXXIV Cycle (2018/2019): A. Carnevale, L. Corti, N.C. D'Amico, A. Demofonti, B. Di Sero, M. Gionfriddo, G. Lattanzi, F. Le Jeune, V. Madiai, F. Mereu, A. Pensotti, A. Salvati, M. Torre, A. Vaccaro

Learning outcomes

The Ph.D in Science and Engineering for Humans and the Environment aims at training experts capable of carrying out research activities for the care of the individual and the environment. The Ph.D is divided into courses that offer the development of complementary skills in engineering, as well as different scientific and technological fields, but likewise focused on improving the quality of life for individuals with reference to the environment they live in.

This goal is pursued thanks to the presence in the Academic Board of researchers from different macro-areas of study and having a long-standing commitment to the subject matter of the Ph.D course. The training courses also aim at stimulating doctoral students with a multi-disciplinary approach to problems regarding man and the environment.

Ph.D program allows graduates to:
- develop new methods, instruments and systems to promote health, well-being and personal safety, through the care of environment and also supported by the most up-to-date research results
- describe, plan, coordinate and carry out research programs in order to develop technical and multidisciplinary research combining different technical and scientific skills
- integrate the traditional type of education in biomedicine, with knowledge such as maths and technology which can help to face the increasing complexity of "bioinspired" research fields.

Research fields

The main fields of study are:
- study, design and development of new methods, systems and devices for biomedical applications, with particular reference to biorobotics, biomedical instrumentation, biomaterials, and tissue engineering;
- study and use complex systems models for applications in biology, medicine and environmental science;
- study and development of new knowledge and protocols for the characterization of bioactive molecules and their metabolism, their nutritional parameters and impact on diseases prevention, as well as experimentation of protocols and procedures applied to clinical nutrition;
- study, design and development of new methods, systems and devices based on information technology, with particular reference to the analysis of large amounts of data.

Graduate School – shared education platform

The Coordinating Board for Ph.D programs, formed by Doctoral program Coordinators and supported by the Centre for Integrated Research, in the academic year 2013/14 created a training event called 'Graduate School – a shared education platform'. Its goal was to offer a training course in Scientific Research, cutting across individual Degree Program, to investigate issues of common interest. The event is organized with a series of short lectures that address specific issues identified by Doctoral program Coordinators.

Monday 3 December 2018 Conference room PRABB	
09:30–10:30	Institutional greetings and introduction to 'Graduate School– a shared education platform' 2018.
10:30–11:45	Science, Democracy and Critical Thinking – Part One Marta Bertolaso, Department of Engineering, Campus Bio-Medico University of Rome.
	Coffee break
12.00–13.30	Science, Democracy and Critical Thinking – Part One Marta Bertolaso, Department of Engineering, Campus Bio-Medico University of Rome.
	Welcome lunch
14.30–15.30	The Italian way of open innovation Alberto Di Minin, Antonio Crupi, Sant'Anna School of Advanced Studies, Pisa
15.30–16.30	Identity, mission and cultural project of Campus Bio-Medico University of Rome Alessandra Torre, Human Resource, Campus Bio-Medico University of Rome
16.30–18.00	Your research is your brand Marco Magheri, Communication and Brand Management Area, Campus Bio-Medico University of Rome

Tuesday 4 December 2018 Conference room PRABB	
09.30–11.00	Ph.D Course in Bioengineering and Bioscience, Science and Engineering for Human and Environment Ph.D Course in Integrated Biomedical Sciences Submission of reports of Year-end for Ph.D students of XXXI, XXXII and XXXIII cycle
	Coffee break
11.30–13.30 Club House PRABB	Ph.D Course in Bioengineering and Bioscience, Science and Engineering for Human and Environment Submission of reports of Year-end for Ph.D students of XXXI, XXXII and XXXIII cycle
11.30–13.30 Conference room PRABB	Ph.D Course in Integrated Biomedical Science and Bioethics Submission of reports of Year-end for Ph.D students of XXXI, XXXII and XXXIII cycle
	Lunch break

14.30–17.00 Conference room PRABB	**Bias and mistaking in epidemiological studies** Massimo Ciccozzi, Department of Medicine and Surgery, Campus Bio-Medico University of Rome
17.30–18.30 Conference room PRABB	**TITOLO DA DEFINIRE** Robert Alexander or his delegate, IBM Italy

Wednesday 5 December 2018
Aula Magna Trapezio

09.00–10.30	**Scientific publications: From planning to publishing of a work and the scientific impact – Part One** Paolo Pozzilli, Prof. Nicola Napoli, Prof. Chiara Fanali, Department of Medicine and Surgery, Campus Bio-Medico University of Rome Alessio Gizzi, Department of Engineering, Campus Bio-Medico of Rome Comment of article "Surviving the Review Process" of IEEE Robotics & Automation Magazine
	Coffee break
11.00–13.30	**Scientific publications: From planning to publishing of a work and the scientific impact – Part Two** Maria Dora Morgante, chief librarian, Sara Fallucca, Rocky Strollo, Ernesto Maddaloni, Germano Di Sciascio, Department of Medicine and Surgery, Campus Bio-Medico University of Rome Martin Tilly, Wiley Publisher
	Lunch break
14.30–15.30	**Scientific publications: From planning to publishing of a work and the scientific impact – Part Three** Paolo Pozzilli, Andrea Palermo, Department of Medicine and Surgery, Campus Bio-Medico of Rome Round Table for the discussion between Publisher and young researchers (questions, prompts and debate) Moderator: Martin Tilly, Wiley Publisher
15.30–17.00	**Bench to biz: Challenge for Ph.D** Nicola Redi, VERTIS SGR

Thursday 6 December 2018
Club House

09.30–13.30	**Course of European design with home studies and working groups** Caterina Buonocore, APRE
	Lunch break
15.00–16.30	**Course of European design with home studies and working groups** Caterina Buonocore, APRE
17.30–18.30 Conference room PRABB	**Presentation of Research Yearbook 2017 and main results of Research Unit Presentation of projects: Course of European design with APRE**

Ph.D dissertations defended in 2018

*Link to full text dissertations: **http://ilithia.unicampus.it/ilithia/Default.asp**

ASSESSMENT OF VELOCITY RATE OF PROGRESSIVE DISEASE (VRPD) AS A BIOMARKER AND DEVELOPMENT OF A CLINICAL NOMOGRAM TO PREDICT THE OUTCOME OF THE SECOND LINE OF TREATMENT IN PATIENTS WITH METASTATIC COLORECTAL CANCER TREATED WITH BEVACIZUMAB BEYOND PROGRESSION OR AFLIBERCEPT

Ph.D student Emanuela Dell'Aquila
Tutor Giuseppe Tonini

Backgroud: In metastatic colorectal cancer (mCRC) there is the unmeet clinical need to predict outcome to 2nd line therapy. There aren't yet standardized prognostic or predictive parameters of outcome to the second line treatment that can predict at progression which are patients who can most benefit from systemic treatment next to the first line in mCRC patients treated with bevacizumab beyond progression or aflibercept. The aim of our study was to test if the velocity rate of progressive disease (VRPD) may be a new dynamic marker, can predict outcome in terms of 2nd line progression free survival (PFS) in mCRC patients (pts). Patients and Methods: We enrolled 167 pts treated with bevacizumab beyond progression or aflibercept in 2nd line. For each patient, VRPD was calculated as the ratio between the sum of the longest diameters (SLD) for target lesions evaluated by CT scan, according to RECIST criteria v 1.1, at the time of progression and the sum of the longest diameters (SLD) for target lesions evaluated by CT scan before progression multiplied for difference in months. For VRPD cut-off point estimation a mixture model of two Gaussian distributions was used. The optimal cutoff is determined as the value where the probability density functions of the mixing distribution coincide. Results: We enrolled 167 mCRC pts treated with bevacizumab beyond progression or aflibercept in second line. In second line 63% of pts were treated with bevacizumab plus doublet, 12% with bevacizumab in association with triplet and 25% of patients received aflibercept Folfiri. A cut-off value of 1.19 was unbiasedly generated using a mixture model of two Gaussian distributions. This cut-off discriminated pts with low (VRPD <1.19; 91% of pts) vs high (VRPD >1.19; 9% of pts) VRPD. At univariate analysis, high VRPD pts had a non-significant longer PFS than low VRPD pts (HR: 0,59 [95%CI: 0.34-1.03], p = 0.06). We collected data on 22 variables, which were chosen based on the previous literature. All the 22 available variables, including VRPD (considered either as a continuous or as a dichotomized variable) were included in the multivariate analysis to determine which factors could better predict PFS in second line. Six variables were selected and used to build a Nomogram. These six variables were: gender (0 = F; 1 = M); primary tumour location (0 = right; 1 = left), baseline Performance Status (PS), presence of liver metastases (0 = no; 1 = yes), first line PFS in weeks, sum of the longest diameters at time of progression (SLD0).
Conclusion: VRPD is a parameter never tested in metastatic colorectal cancer. Sex, primary tumor location, baseline PS, presence of liver metastases, first line PFS and sum of the longest diameters at time of progression, resulted as prognostic factors for determine second line PFS and were included in our nomogram. Validation of our nomogram using an external cohort is ongoing.

ANALYSIS OF VOLATILE ORGANIC COMPOUNDS (VOCS): AN INNOVATIVE APPROACH TO DISEASE CHARACTERIZATION IN ELDERLY PATIENTS

Ph.D student Panaiotis Finamore
Tutor Raffaele Antonelli Incalzi

Background and aim: Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are two of the leading causes of disability and death worldwide in the elderly. The differential diagnosis between the two is important for the correct therapeutic management, given the side-effects that cardiac medications may have in patients with lung disease and vice versa. The atypical clinical presentation, the lower reliability of laboratory tests and the difficulty to perform some instrumental tests, common in aged patients, limit the diagnostic accuracy, as well as the disease severity stratification and the prognostic assessment of these diseases. Therefore, the development of new, safe, non-invasive, repeatable and reproducible technologies are warranted. Human breath contains thousands of molecules of different size, chemical structure and concentration, known as volatile organic compounds (VOCs), which can potentially carry information on the physiologic and pathologic processes related to respiratory and non-respiratory diseases. This thesis aimed at investigating the role that VOC analysis using an electronic-nose (BIONOTE®) may have in the diagnosis, disease severity stratification and prognosis of COPD and CHF patients. Materials and methods. Firstly, a computerized literature search was performed to identify relevant articles reporting original data on the clinical use of breath analysis in respiratory diseases and heart failure. We recruited 89 subjects admitted to an acute care ward with acutely decompensated CHF, 117 healthy controls and 103 COPD patients and partial least square (PLS) analysis was used to evaluate discriminative capacity of VOCs. PLS analysis was also used to evaluate VOC ability to predict COPD patients' functional status and its variation over time in a sample of 63 COPD patients with a one-year follow-up. Furthermore, VOC ability to characterize newly diagnosed COPD patients and changes in response to inhaled therapy was assessed on 50 newly diagnosed COPD patients grouped using K-mean cluster analysis on BIONOTE responses. All patients were recruited among those attending the "Campus Bio-Medico" University Hospital. VOCs were collected using the Pneumopipe® and analyzed with the BIONOTE® electronic nose, an array of seven quartium-microbalances which provides a comprehensive and often peculiar VOC pattern named 'breath-fingerprint'. Results: Analysis of exhaled VOCs discriminates CHF from healthy controls and COPD patients with an accuracy of 81% and 69%, respectively. In CHF patients VOC pattern poorly predicts ejection fraction and systolic pulmonary arterial pressure. Three well distinguished groups of naïve COPD patients may be recognized basing on their breath-fingerprint: a) without remarkable comorbidities; b) with air trapping and higher BODE index score (mean 1.2); c) without air trapping and with a lower BODE index. Inhaled bronchodilators produce a quantitative reduction in VOCs amount, while inhaled steroids provides a qualitative modification of the breath profile. Furthermore, exhaled VOC analysis discriminates baseline functional status, assessed using the 6-minute walking distance normalized per squared height – n6MWD – (79% of accuracy) and BODE classes (86% of accuracy), and is able to predict 6MWD variation over one-year of follow-up with an accuracy of 86%, better than the GOLD classes (accuracy of 52%). Conclusion. Breath-fingerprint discriminates elderly people affected by CHF and COPD from healthy controls and, even with a lower accuracy, it discriminates CHF from COPD. It does not correlate with the severity of CHF, but is able to identify COPD patients with similar characteristics (phenotype), and predicts functional status and prognosis of COPD patients. Breath-fingerprints change in distinctive ways depending upon whether the COPD patients has been prescribed inhaled bronchodilators alone or any combinations of inhaled drugs including inhaled corticosteroids.

BIOCHEMICAL AND TECHNOLOGICAL CHARACTERIZATION OF C4 CYCLE GLUTEN FREE CEREALS: ERAGOSTIS TEF AND SORGHUM BICOLOR

Ph.D student Elena Galassi
Tutor Laura Gazza

The objective of this study was to evaluate five sorghum genotypes, one for zootechnical use and four food-grade hybrids, and two commercial teff genotypes (brown and white grain), for their technological, biochemical and nutritional traits, comparing them with a durum wheat cultivar as control, in order to identify the most suitable for the formulation of innovative wholegrain, gluten free products of high qualitative value to develop a sustainable agri-food chain. The data concerning kernel and flours properties of the sorghum food-grade, on average, reported lower values than durum wheat control for kernel weight (-56%), test weight (-14%), sedimentation test (-56%), falling number (-16%) and yellow index (-19%), whereas brown index was higher (+38%) and kernel hardness (+0.5%) comparable to control. Furthermore, teff genotypes showed lower values than durum wheat control for kernel weight (-99%), sedimentation test (-50%), falling number (-18%), yellow index (-11%), whereas brown index was higher (+90%) and test weight (+2%) was comparable to control. The results showed that, on average, sorghum food-grade hybrids had higher contents of resistant starch (RS) and RS/TS (Total Starch) ratio (about 6 times higher), yellow pigments, free polyphenol and anthocyanin contents (+600%, +400% and +100% than the control, respectively). Teff genotypes, on average, were comparable to durum wheat for resistant starch content, RS/TS ratio, yellow pigments and anthocyanin contents, whereas total starch and folate contents were higher (+6 % and +40%) than in wheat. Furthermore, the beverage transformations of these two gluten free cereals revealed malts with low amylase activity, typical of low-alcohol drinks, and useful for light and gluten-free beer market. Otherwise, the malts produced could be used in combination with other malts for the production of innovative fermented beverages, not yet available on the market. Finally, the teff-based "Tigelle", typical Italian unleavened focaccias from Emilia Romagna, presented good overall acceptance scores from the hedonic analysis carried out by not-expert people, with higher scores for crumb and crust color in white teff bread, whereas the sample with malt was preferred for its aroma and taste. In conclusion, the data of this study showed that the four food-grade sorghum hybrids and the two teff genotypes examined have technological and nutritional characteristics comparable with the durum wheat, used as control, for the most of the parameters examined. When the analyzed lines showed lower values than wheat, they are still acceptable for the transformation processes. The data obtained in this study, highlighted as sorghum and teff can constitute promising alternative ingredients in the gluten free market. Furthermore, given their resilience to both drought and heat stress, teff and sorghum could be one of the answer to global sustainability on food and nutrition security.

FEASIBILITY OF TEMPERATURE MONITORING BASED ON RADIOLOGICAL IMAGING DURING THERMAL ABLATION PROCEDURES ON BIOLOGICAL TISSUES

Ph.D student Francesco Giurazza
Tutor Emiliano Schena

Minimally invasive ablation techniques are nowadays part of the clinical practice in the field of oncological treatments. Thanks to the technological improvements, thermal energy delivered through a needle allows to destroy malignancies without requiring a traditional open surgical approach. However, to safely perform these procedures it is crucial to monitor the temperature distribution into the treated tissues, in order to reach the target temperature able to destroy malignant cells and to preserve healthy surrounding structures. Real time tissue

temperature monitoring can be obtained with invasive techniques (i.e. thermocouples and fiber optic sensors directly inserted close to the ablation area) and non-invasive techniques (i.e. imaging scans based on radiological techniques as Computed Tomography, Magnetic Resonance and Ultrasound). In this research project, first of all it has been investigated the role of Fiber Bragg grating sensors for temperature monitoring in ex vivo and in vivo biological tissues and then it has been assessed the feasibility of imaging based thermometry on ex vivo biological tissues (i.e. swine pancreas and livers) during ablation procedures performed with different forms of energy sources routinary applied in the clinical practice (i.e. Laser, Radiofrequency, Microwaves). The variations of Hounsfield Units on Computed Tomography, signal-to-noise ratios on Magnetic Resonance and shear wave velocities on Ultrasound have prooven to be reliable with tissue temperature changes occurring during thermal ablations ($>60°C$); mathematical equations to obtain tissue temperature values based on radiological imaging parameters have been so developed. According to the results provided, especially from experimental sessions on Computed Tomography and Magnetic Resonance, real time imaging based thermometry seems to be a safe and feasible biomedical methodology which could significantly improve the actual ablation settings and furthermore could lead the operators to treat a wider spectrum of malignant lesions sparing healthy tissues. Further studies on Ultrasound are necessary to make this technique applicable in clinical settings.

DIFFERENT BIOLOGIC BEHAVIORS AND RISK PROFILES AMONG B3 PROLIFERATIVE BREAST LESIONS

Ph.D student Antonella Grasso
Tutor Vittorio Altomare

Background /Aim: despite risk tailoring ongoing research on the different B3 entities most cases progress to surgical intervention, with ongoing fluctuations in trends of treatment or perceived associations with malignancy. The aim of this study was to access the outcome of lesions diagnosed in this category in a large series of screen-detected cases to evaluate the upgrade rates for the different histological subtypes. Patients and methods: a total of 2986 CNB's were performed for screen detected breast lesions over a fifteen-year period (2003-2018). B3 diagnosis comprised 10.1% (300/2986), and was correlated with final excision histology. Positive predictive values (PPVs) for detection of malignancy were calculated for all B3 core cases and different subtypes to provide a complementary risk characterization according to clinicopathological features and morphological variables. Moreover, cumulative incidence curves of new primary/relapses of BC after CNB were estimated with a Kaplan-Meier analysis. Results: the B3 lesions comprised the following histopathological diagnoses: 105 (35%) atypical ductal hyperplasia (ADH), 50 (16.7%) flat epithelial atypia (FEA), 68 (22.7%) lobular neoplasia (LN), 27 (9%) papillary lesion (PL), 26 (8.6%) phylloides tumor (PT), and 24 (8%) radial scar (RS). Screen-detected calcifications showed no higher upgrade rate (15.9%; 17/107) when compared to mass lesions (13.7%, 19/139) or architectural deformities (16.7%, 9/54) ($p = 0.828$). Malignant lesions included 25 (8.3%) DCIS and 20 (6.7%) invasive cancers, giving an overall PPV of 15% (45/300) based on excision histology. Lesion specific positive predictive values (PPV) for a subsequent diagnosis of carcinoma were as follows: ADH 20% (21/105), FEA 12% (6/50), LN 16.2% (11/68), PL 18.5% (5/27), PT 3.8% (1/26) and RS 4.1% (1/24), demonstrating a higher but not statistically significant tendency toward lesion upgrade for the 3 major atypical areas (ADH, FEA, LN) (OR: 2.05; 95% confidence interval [CI]: 0.87-4.81; $p = 0.092$). Interestingly, the Chi-Squared test also revealed a growing risk of subsequent new primary BC among patients with previous LN diagnosis (n = 8/19, 42.1%), (OR: 2.679; 95% [CI]: 1.031-6.957; $p = 0.037$) during the study period. Conclusion: lesions of uncertain malignant potential of the breast (B3) are heterogeneous in respect to risk of malignancy and careful radiological-pathological correlation is the prerequisite for an optimal disease-tailored approach. Therefore it is becoming clear that these different borderline categories should be subjected to further investigation for updating quality assurance targets and moving forward to a more conservative approach in selected cases, as a part of the screening assessment.

PATIENT-TAILORED BIDIRECTIONAL INTERFACES FOR REHABILITATION AND ASSISTIVE ROBOTS

Ph.D student Clemente Lauretti
Tutor Loredana Zollo

Bidirectional interfaces, which combine recording and stimulating systems in so-called closed-loop devices, are the new generation of interfaces. In order to guarantee attentive usage and fine control of the device, they are typically tailored on the users' particular needs and are designed by taking into account users' residual physical and cognitive abilities. Ambition of this thesis is to design and develop a patient-tailored bidirectional interface for rehabilitation and assistive robots that i) is adaptable to the user's residual functional and motor capabilities and ii) works well in unstructured environments and with different robot types (e.g. manipulators, exoskeletons or prostheses). The developed bidirectional interface is composed of two main modules, namely the humanmachine interface for the device control and the interface for sensory feedback. The human-machine interface for the device control was designed to be used by patients with different level of disabilities to drive their rehabilitation or assistive robot, e.g. an upper-limb prosthesis, a robotic manipulator or an upper-limb exoskeleton, both continuously and by means of a trigger-based approach. The interface proposed in this work is based on the coupled use of myoelectric and magnetoinertial sensors. It was first designed to be used by trans-humeral amputees to control their prosthetic device. In particular, with the proposed approach the user could operate the elbow flexion-extension, wrist prono-supination and hand opening-closing by exploiting the residual stump motions combined to the myoelectric activity of two target muscles, i.e. biceps and triceps. The proposed control interface was tested by eight healthy subjects who were asked to drive a trans-humeral prostesis in a virtual environment. A comparative analysis between the proposed control and the traditional myoelectric control used in literature to drive commercially available prostheses was carried out. Results demonstrated that the user, by using the proposed method, could manage simultaneous movements and more physiological reaching tasks compared to the traditional myoelectric control that enables only sequential movements. Subsequently, adaptability of the proposed control interface to patients with different levels of disability and different robot types were demonstrated. It was tested on people with severe motor disability to control their robotic rehabilitation/assistive device, such as a manipulator or an upper-limb exoskeleton, both continuously and by means of a trigger-based approach. Two experimental sessions were carried out. The first experimental session was aimed to compare the proposed interface, based on magneto inertial sensors and myoelectric electrodes, to a standard interface made of the voice recognizer. Sixteen healthy subjects were asked to continuously control the motion of a robotic manipulator, by using the two control interfaces, for assistive purposes. The obtained results pointed out that performance and level of acceptance were higher for the proposed interface with respect to the voice control. The second experimental session was aimed to evaluate user's preferences related to the amount of his/her intervention in the robot control. Two control modalities were implemented in order to modulate the frequency of the user's intervention in the robot control depending on the user's cognitive/physical state. They are the continuous control and the trigger control. They were compared in terms of effectiveness of the task fulfillment and user's personal feelings related to the interface usage. The obtained results demonstrated a high patient involvement in using the continuous control, but better performance, in terms of effectiveness of the task fulfillment, has been achieved with the trigger-based control. Differently from the continuous control, the trigger-based control requires only a few actions to the user in order to start the robot movement. Hence, a motion planning system was developed in order to allow the robot autonomously accomplish the task in a way that is completely safe and accepted by the user. In this work a motion planning system for rehabilitation and assistive robotics, grounded on a Learning by Demontration (LbD) approach, was proposed. The LbD algorithm presented in this work is grounded on Dynamic Movement Primitives (DMPs), but it is improved in terms of i) accuracy of the trajectory reconstruction, ii) adaptability of the DMPs to different subjects' anthropometry and robotic devices (e.g. manipulators or exoskeletons) ii) ability to reproduce human-like movements, iii) ability to solve orientation singularity in the DMP equations and iv) generalization capabilities with

respect to different target positions. This was confirmed by four experimental sessions that were carried out in order to assess the motion planner performance. The experiments involved healthy subjects and patients with Limb girdle muscular dystrophys who were asked to perform activities of daily living with the aid of different robot types, i.e. robotic manipulators and upper-limb exoskeletons. The interface for sensory feedback was designed and developed to improve user postural control during robot-aided daily living activities, both in standing and in sitting position. In particular, the proposed vibrotactile stimulation feedback was employed, during robotaided rehabilitation, to correct patients' spine posture. Three inertial sensors were used in order to measure trunk and neck flexion/extension (F/E) and information about user's incorrect posture were provided by two lightweight vibrating actuators located on the user's arms. The proposed stimulation feedback was compared to a typical approach used in literature to warn users about incorrect posture, i.e. visual feedback, in terms of i) effectiveness to improve the posture of the subject, ii) acceptability and iii) user's comfort. Ten healthy subjects were asked to perform 3D reaching movements with the aid of a robotic manipulator attached to their right wrist. During the rehabilitation session, they were provided with visual and vibrotactile feedback to retain their trunk and neck in a correct posture. Additionally they were asked to perform the tasks without any information about the correctness of their posture. The obtained results demonstrated that the users had a significant improvement in the spine posture when the task was performed with the aid of the visual and vibrotactile feedback compared to a no feedback condition.

CANCER ASSOCIATED FIBROBLASTS IN COLORECTAL CANCER: A HETEROGENEOUS POPULATION LEADING TO CANCER MIGRATION AND INVASIVENESS

Ph.D student Vincenzo La Vaccara
Tutor Giuseppe Tonini

Peri-tumoral activated fibroblasts are key players in tumorigenesis and cancer progression, and they are often referred as Cancer Associated Fibroblasts (CAFs). CAFs have a central role in the synthesis and remodeling of the desmoplastic stroma. Previous studies have shown that severe desmoplasia is correlated with poor prognosis in several tumors such as lung, pancreas, breast, and colorectal. In patients who underwent curative surgery for colon cancer, poor prognostic data (overall survival and disease free-survival) have been reported when the stromal component was prevalent than carcinoma cellularity. The definition of CAFs is still a debated issue because even if several markers have been suggested in the past to define CAFs, it is now being appreciated that these markers do not mark all CAFs and that their different expression could reveal a heterogeneous population of fibroblast. We develop a robust protocol for isolation of CAFs and their paired NFs by eco-guided FNAB sampling from a fresh specimen of colon and rectum resected for carcinoma. The present study revealed that Podoplanin was more differently expressed in CAF vs NFs, while similar levels of α-smooth muscle actin (α-SMA) were found in the two populations of fibroblasts. Moreover, HIC on paraffin sections was undertaken to assess if CAF markers (α-SMA and Podoplanin) expressed at the sample site previously marked with Indian Ink can be different. We found Podoplanin positive fibroblast in a linear disposition close to the tumoral cells that could be compared with the interstitial lining cells described as precursors of fibrogenic myofibroblast responders in peritumoral sclerosis revealed in the recent discovery of a new interstitium. Finally, we demonstrate that paracrine factors lead the invasion of colorectal tumor induced by CAF. When the wound healing assay was performed in order to evaluate the migration of colorectal tumoral cells (DLD1) earlier scratch closure was observed in cells supplemented by the CAF-conditioned medium (CAFc) compared to those treated with the NF-conditioned medium (NFc).

RISK FACTORS FOR FRAGILITY FRACTURES AND ROLE OF WNT SIGNALING IN TYPE-1 DIABETES RELATED BONE FRAGILITY: CLINICAL AND PRECLINICAL STUDIES

Ph.D student Giulia Leanza
Tutor Napoli Nicola

BACKGROUND Patients with Type 1 diabetes (T1D) have low bone mass and up to five times higher risk of hip fracture than normal peers, leading to an increased morbidity and mortality. However, risk factors for fractures in T1D have not been clearly identified and fractures are still a poorly screened diabetic complication. In a preliminary clinical study, we found high circulating levels of the Wnt inhibitor sclerostin in patients with T1D relative to normal controls. This result would be consistent with findings of decreased serum markers of bone formation in humans and preclinical models of T1D, suggesting reduced bone turnover in T1D. However, diabetes-related mechanisms underlying a lower bone quality and increased risk of fractures in diabetics are, similarly to clinical factors, still not well established. The overall objectives of the study were to evaluate risk factors for fractures in T1D and mechanisms underlying bone fragility in an experimental model of T1D. STUDY 1: CLINICAL STUDY OBJECTIVE: To determine clinical diabetes-related risk factors for fractures in type 1 diabetes. RESEARCH DESIGN AND METHODS: History of bone fragility fractures occurring after T1D diagnosis was assessed by questionnaire in this cross-sectional study in 600 T1D subjects. Glycated hemoglobin A1c (HbA1c) over the previous 5 years was used as an index of long-term glycemic control; complications were adjudicated by physician assessment. Multinomial logistic regression models were used to assess the associations between diabetes-related risk factors and fracture history. RESULTS: One-hundred-eleven patients (18,5%) reported at least one fracture; of these 73.8% had only one and 26.2% had more than one fracture. Average age was 41.9 ± 12.8 years, with even gender distribution; disease duration was 19.9 ± 12.0 years; and BMI was 24.4 ± 3.7 kg/m2. The 5-year average HbA1c was $7.6 \pm 1.0\%$ (60 mmol/mol). In adjusted models, reduced risk for 1 fracture was found in those with higher eGFR (RRR 0.22 [95%CI: 0.06-0.83] for 1 unit increase in lneGFR, $p = 0.03$) and increased risk in those with neuropathy (RRR 2.57 [1.21-5.46], $p = 0.01$). Increased risk for $>=2$ fractures was found in subjects in the highest tertile of HbA1c ($>=7.9\%$) compared with the lowest tertile ($<=7.17\%$) (RRR 3.50 [1.04-11.7], $p = 0.04$) and of disease duration ($>=26$ years versus <14 years) (RRR 7.59 [1.60-36.0], $p = 0.01$). Summary study 1: Poor glycemic control and long exposure to the disease are independent diabetes-related risk factors for multiple bone fractures in type 1 diabetes. STUDY 2: PRECLINICAL STUDY OBJECTIVE: To test the potential role of sclerostin and Wnt signaling in diabetes induced bone disease. RESEARCH DESIGN AND METHODS: We introduced the sclerostin-resistant Lrp5A214V mutation, associated with high bone mass (HBM), in mice carrying the Ins2Akita mutation (Akita), which causes hyperglycemia and hypoinsulinemia within 5 weeks after birth. Bone microarchitecture and body composition were longitudinally evaluated respectively by in vivo µ-CT and DXA. Glucose metabolism was evaluated by random blood capillary measurements and intraperitoneal glucose and insulin tolerance tests. RESULTS: Bone mass by DXA was significantly higher in Akita/HBM relative to Akita littermates at 12 weeks (88.2 ± 5.2 vs 67.9 ± 4 mg/cm2; $p <0.001$; n = 7-11), persisting higher for up to 26 weeks (90.2 ± 3.0 vs 70.4 ± 1.7mg/cm2; $p <0.001$ n = 5) despite overt diabetes. Further analysis by µCT at age 20 weeks revealed lower trabecular bone volume/total volume (BV/TV) in Akita compared to wild type (WT) mice (0.2 ± 0.02 vs 0.35 ± 0.05; $p <0.05$; n = 3-5). Conversely, both trabecular (Tb) and cortical (Ct) parameters were significantly higher in Akita/HBM mutants compared to Akita littermates, including total Ct area (1.6 ± 0.06 vs 1.2 ± 0.07mm2), bone area (0.9 ± 0.1 vs 0.6 ± 0.05mm2), and Ct thickness (0.2 ± 0.02 vs 0.1 ± 0.01 mm, $p <0.001$, n = 5-7). Tb BV/TV and Tb thickness were also higher in Akita/HBM mutants relative to Akita littermates (0.4 ± 0.05 vs 0.2 ± 0.02; and 0.1 ± 0.02 vs 0.09 ± 0.03mm, respectively, $p <0.001$, n = 3-5). We found no significant differences in total Ct area between Akita and WT mice, consistent with observations in humans with T1D. As expected, both Akita and Akita/HBM mutants developed diabetes (non-fasting blood glucose >300 mg/dl), albeit with different onset timing. At 8 weeks, only 40% of Akita/HBM mice had developed hyperglycemia, compared to 90% of Akita mice (n = 10). Only at 12 weeks were most Akita/HBM mice hyperglycemic. Intriguingly at age 6 and 8 weeks, glucose tolerance was significantly better in

Akita/HBM relative to Akita mice (p <0.05 for difference in areas under the curve, AUC; n = 3-6). Likewise, insulin sensitivity (by intraperitoneal insulin tolerance test) was higher in the Akita/HBM compared to the Akita group (p <0.01 for difference in AUC; n = 4-8) at age 7 weeks. Summary study 2: The metabolic changes caused by hypoinsulinemia (chronic hyperglycemia) do not alter the consequence of sclerostin resistance and Wnt hyperactivation on bone. Furthermore, Wnt activation retards the onset of metabolic abnormalities in T1D. CONCLUSIONS: Our data clearly show that T1D patients should be carefully screened for fragility fractures and we propose risk factors for any and multiple fragility fractures to use for a model of prediction for fractures. We have proved that HbA1c, disease duration, presence of neuropathy and eGFR values could be targeted for prevention of fractures in diabetes. With our preclinical study we explored for the first time in vivo the effect of T1D and sclerostin resistance on bone, demonstrating that targeting Wnt signaling protects bone mass in T1D. We also potentially target a role of sclerostin resistance to improve not only bone fragility but also glucose metabolism. This study provides novel scientific inputs in the relationship between glucose homeostasis and bone health and may offer new avenues for assessment and treatment of bone alterations in diabetes.

NUTRIENTS AND NUTRITION IN OLDER ADULTS: SEVERAL OPEN QUESTIONS AND SOME ANSWERS

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Tutor Claudio Pedone

Nutrition is the set of integrated processes by which cells, tissues, organs and the whole body acquire the energy and nutrients for physiological structure and function, which is achieved at body level through dietary supply, and transformation of substrates and cofactors necessary for metabolism. An appropriate nutrition starting early in the life course has a significant impact on health as it could determine the future resilience of the individual to stresses and susceptibility to disease. Not only the quantity, but also the quality of the diet is important to ensure healthy growth and the appropriate proportions of lean and fat mass. Furthermore, nutrition is not simply a matter of diet, but should also take into account physical activity level, stressors and underlying conditions (physical, behavioral, social), which modulate nutrient availability and handling. There is a clear evidence of the important role of nutrition in primary and secondary prevention for several diseases. With respect to primary prevention, this role is related both to specific dietary patterns, such as the Mediterranean diet, but also to single micronutrients, such as poli-unsaturated fatty acids (PUFAs). Besides Mediterranean diet, other nutritional patterns, such as some of spices used in in Asian cultures that have beneficial effects on human health and are commonly used in the Ayurveda, the Indian traditional medicine. One of these spices, curcumin, has also been studied in the occidental traditional medicine for its anti-inflammatory, anti-oxidant and anti-cancer properties, and new compounds derived from curcumin have been studied for the treatment of cancer and other diseases. On the other hand, also micronutrients usually introduced with the diet, such as vitamin D, or nutritional status per-se, have an important role in secondary prevention. Furthermore, nutrition can have a role in the context of other diseases, such as anemia in influencing biomarkers concentration in heart failure. While the role of nutrition seems to be well established, some questions remain open, especially in older adults that are a population usually less studied respect to younger adults. In fact, if we consider the "classical" associations, such as sodium intake and cardiovascular diseases, most of the studies did not include older adults, a population in which the coexistence of multiple diseases, polytherapy, frailty, high prevalence and risk of disability, might influence these associations. Therefore, an association evident in young adults might lack or being more evident in older adults, thus changing dietetic indications in this specific population. The aim of this thesis was to study the role of nutrition in influencing clinical outcomes in older adults, paying particular attention to: - The role of micronutrients in primary prevention; with respect to this, we studied the association between sodium and PUFA intake and mortality in older adults. - The role of micronutrients and nutritional

status in influencing outcomes; with respect to this, we studied the association between vitamin D and nutritional status in functional improvement in older adults admitted to rehabilitation settings and the association between nutritional status and functional status and outcomes in older adults affected by chronic heart failure. - The role of nutrition and nutrients in the context of other diseases; with respect to this, we studied the role of curcumin in lung diseases and melanoma and the role of anemia in influencing concentration of natriuretic peptides in older adults.

ADULTS WITH AUTOIMMUNE DIABETES: VASCULAR RISK, EMERGING COMPLICATIONS AND NOVEL DISEASE PATHWAYS

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Background. The population of adults with autoimmune diabetes has grown worldwide. This is largely the result of better care and increased longevity of people with young-onset type 1 diabetes (T1D), but also of the increased number of latent autoimmune diabetes of the adult (LADA) diagnoses. Adults with autoimmune diabetes differ from those with type 2 diabetes (T2D), with challenges and uncertainties about the impact of aging in people with autoimmune diabetes. In the immediate future, we will have to face complications of autoimmune diabetes in the context of aging and long exposure to the disease, but a paucity of data is available in this regard. Therefore, studies elucidating the pathophysiology, epidemiology and clinical features of autoimmune diabetes in adults and elderly people, both those with T1D and LADA, are needed. Hypothesis. We hypothesized that clinical features and risk of diabetic chronic complications may differ in adults with different forms of diabetes. Therefore, we also hypothesize that the study of vascular and bone disorders in adults with autoimmune diabetes may unveil novel risk factors and pathways of chronic complications. Aims and methods. The overall aim of this project was to investigate the pathophysiology and clinical features of autoimmune diabetes and its complications during the adulthood and the senescence. More specifically we aimed to: 1. Evaluate whether rates and risk factors for vascular complications differ between LADA and T2D. To this aim data from the UK Prospective Diabetes Study (UKPDS) have been retrieved and analyzed. Diabetes autoantibodies (AAb) were measured in 5,062 UKPDS participants. The incidence of major adverse CV events (MACE), defined as CV death, nonfatal myocardial infarction or nonfatal stroke, was compared in those with LADA (>/- 1 AAb test positive) with those without LADA (AAb negative). 2. Evaluate bone health and its relationship with vascular complications in adults and aging people with autoimmune diabetes. To this aim adults with T1D followed in the centers of the IMDIAB group and elderly people enrolled in the 50-Years Joslin Medalist Study were fully characterized in terms of history of metabolic control, chronic complications and bone fractures. Bone mineral density was measured by DEXA in a subgroup of these subjects. Risk factors for impaired bone health and the relationship between bone fragility and vascular complications were investigated in both young adults and elderly with long standing type 1 diabetes. 3. To investigate circulating osteoprogenitors as a new mechanism of vascular complication in type 1 diabetes Osteocalcin (OCN) + monocytes were studied in a unique population with ≥ 50 years of T1D, the 50-Year Joslin Medalists. CD45 bright/CD14+/OCN+ cells in the circulating mononuclear blood cell fraction were quantified by flow cytometry in and reported as percentage of CD45 bright cells. Mechanisms were studied by inducing OCN expression in human monocytes in vitro. Results: Specific aim 1. There were 567 participants with LADA (11.2%). Compared with T2D, they were younger, with higher mean HbA1c and HDL-cholesterol values but lower body mass index, total cholesterol and systolic blood pressure values (all p <0.01). After median (25th – 75th percentile) 17.3 (12.6-20.7) years follow-up, MACE occurred in 157 (17.4 per 1000 person-years) LADA and 1544 (23.5 per 1000 person-years) T2D participants respectively (HR 0.73, 95% Confidence Interval [CI] 0.62–0.86, p<0.001). However, after adjustment for confounders, this difference was no longer significant (HRadj 0.90, 95% CI 0.76–1.07, p = 0.22). Specific aim 2. Among 600 adult subjects with T1D (age: 41.9±12.8 years, disease duration: 19.9 ± 12.0 years; BMI: 24.4 ± 3.7 kg/m2; 5-year average HbA1c: 7.6 ± 1.0%), 18.5% experienced at

least one fragility fracture (73.8% had only one and 26.2% had more than one fracture). In this population, increased risk for >/-2 fractures was found in subjects in the highest tertile of HbA1c (>/-7.9%) compared with the lowest tertile (/-26 years versus <14 years) (RRR 7.59 [1.60-35.98], p = 0.01). The presence of neuropathy increased the risk of single fracture (RRR adj: 2.57 [95%CI: 1.21-5.46]), and multiple fractures (p-value for the difference of the effect on outcomes: 0.99). Differently, in a selected population of elderly T1D subjects (age: 66.0 ± 7.6 years) with an extreme disease duration (>50 years) we found a lower prevalence of fragility fractures (1.12%). Because of the low prevalence of chronic complications in this population (cardiovascular disease: 39.9%; retinopathy: 46.4%; nephropathy: 12.5%), we hypothesized an association between vascular complications and bone health. This was confirmed by a significant association found between history of cardiovascular disease and low bone mass at the femoral neck (RR: 4.6 [1.2–18.1], p = 0.03). Specific aim 3. Subjects without history of CVD (n = 16) showed lower levels of OCN+ monocytes than subjects with CVD (n = 14) (13.1 ± 8.4% vs 19.9 ±6.4%, p = 0.02). OCN+ monocytes level was inversely related to total high-density lipoprotein (HDL) cholesterol levels (r = -0.424, p = 0.02), large (r = -0.413, p = 0.02) and intermediate (r = -0.445, p = 0.01) HDL sub-fractions, but not to small HDL. In vitro, incubation with oxidized low-density lipoprotein (OxLDL) significantly increased the number of OCN+ monocytes (p <0.01). This action of OxLDL was significantly reduced by the addition of HDL in a concentration dependent manner (p <0.001). Inhibition of the scavenger receptor B1 (SR-B1) reduced the effects of both OxLDL and HDL (p <0.05). Conclusions: This project evaluated in depth the risk of cardiovascular disease, bone fragility and their intimate relationship in adult and elderly subjects with autoimmune diabetes. Our data show that the healthier cardiometabolic profile of subjects with LADA compared with T2D translates in a lower incidence of major cardiovascular events, which is mostly explained by traditional cardiovascular risk factors, including age, lipids and blood pressure. This highlights the importance of aggressively tackling these cardiovascular risk factors in autoimmune diabetes to keep the lower risk of CVD. On the other hand, we are showing an alarming increased risk of bone fractures in adults with T1D. As bone fragility fractures are among the most important causes of reduced life expectancy in elderly and because of the ageing of T1D population, our data claim for immediate action to tackle this emerging complication. Of note, we are showing a close relationship between bone fragility and chronic complications of diabetes, which has been confirmed also in a special population of elderly subjects with T1D protected from vascular complications. This might suggest that strategies to prevent vascular complications may also aid in preventing fragility fractures in T1D. Furthermore, this led to the hypothesis that common mechanisms of disease are shared between bone and vascular complications. This was explored by looking at the role of circulating osteoprogenitors in CVD, which were found lower in T1D subjects protected from CVD. Results regarding the regulation of OCN expression on monocytes by OxLDL and HDL through SR-B1 and its relationship with CVD provide new information on vascular pathophysiology specifically in T1D. Indeed, these findings may provide new insights on the mechanism of HDL-mediated cardiovascular protection in autoimmune diabetes and promote advances in therapeutic strategies in this population.

EXPRESSION OF HIF-1A IN ADVANCED NON SMALL CELL LUNG CANCER, COMPARISON BETWEEN PATIENTS WITH BONE METASTASIS AND WITHOUT BONE METASTASIS, THE INFLUENCE OF SMOKING HABIT: A RETROSPECTIVE ANALYSIS OVER TWO YEARS OF RECRUITMENT

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Background: HIF-1 is a transcription factor that allows cells to adapt to hypoxia. It consists of two forms HIF-1a and HIF-1ß. It is able upon activation, in hypoxia condition, to foster several oncogenes and proteins which in turn are involved in carcinogenesis, cell invasion and migration. Aim: to verify if HIF-1a tissue expression is associated

with lung cancer bone metastasis process and evaluate its influence on prognosis. Methods: a retrospective analysis was carried out on samples deriving from bronchial biopsy and CT-guided trans-thoracic needle biopsy. The data collected concerned advanced NSCLC patients and included age, staging, detailed histotype, pack-year, comorbidities. Detection of HIF-1 expression was performed by the use of a murine specific antibody. A comparison was carried out between group with visceral metastases and group having also bone metastases. Results: a total of 146 patients with mean age of about 70 were considered, the prevalent histotype was adenocarcinoma (67.1%). Former smokers accounted for 58.9%. The mean pack-year was 36.4. CT-guided trans-thoracic biopsy was the main source of the specimens. The population was subdivided in two groups based on the presence or absence of bone metastasis and the comparison showed non-significant differences about ECOG PS, age, and cardiovascular comorbidities. Significant differences were detected about pack-year($p = 0.02$), time to progression(TTP)($p = 0.001$) and COPD comorbidity($p = 0.04$). The Kaplan-Meier method with Log-rank test applied on survival analysis comparing the subgroups showed a longer TTP in patients with visceral metastases with HR of 1.3 and $p = 0.14$. The sample available for immunohistochemistry detection of HIF-1 a consisted of 61 patients. A higher intensity of expression along with higher positive cells percentage was recorded in the group with bone metastases. The main variable affecting HIF expression was the presence of bone metastasis($p = 0.01$), whereas histotype seems to influence the TTP($p = 0.04$).The product of intensity for percentage of positive cells was significantly higher in the group with bone metastases ($p = 0.02$). Conclusions: patients affected by NSCLC IV stage with both visceral and bone metastases have lower survival than those with only visceral metastases. The presence of bone metastasis is tightly linked with the expression of HIF-1a. The intensity combined with the percentage of positive expression is higher in patients with bone metastasis than in patients without it, suggesting a role of HIF-1a in cancer progression.

THE ROLE OF WNT PATHWAY AND ENDOCANNABINOID SYSTEM IN OBESITY AND THEIR INVOLVEMENT IN BONE FRAGILITY

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Obesity is a multifactorial condition, which leads to the excessive accumulation of fat both in adipose tissue and in ectopic depots; it is characterized by chronic low-grade inflammation, oxidative stress, an increased production of reactive oxygen species (ROS) and insulin resistance (IR). IR consists of an impaired response of insulin signaling in insulin-dependent peripheral tissues, such as adipose tissue, skeletal muscle, liver, pancreas, and it precedes type 2 diabetes (T2D) onset. ROS lead to oxidative modifications of proteins, including insulin (oxPTM-INS), which may determine cellular dysfunctions and increase immunogenicity and autoimmunity in both type 1 diabetes (T1D) and T2D. Bone is a target tissue of insulin and it is also involved in the glucose homeostasis. For this reason, the alterations related to obesity and IR may contribute to the promotion of bone fragility and fracture risk. The increase of abdominal fat is a risk factor for the decrease in the bone mineral density (BMD) and for osteoporosis, both in men and in women; however postmenopausal women seem to be more prone to fractures, due to lower bone formation and a poorer bone quality. WNT signaling pathway is highly involved in the control of different cellular lineages, including adipocytes, osteoblasts and myocytes, and it is a key modulator of metabolic pathways, such as insulin signaling. The Endocannabinoid System (ECS) is a well-preserved system formed by ligands, receptors and enzymes, which is involved in several physiological functions. Obesity is characterized by the chronic activation of ECS, favoring the increase and progression of factors related to IR and fat accumulation and altering the crosstalk between the tissues involved. AIM OF THE STUDY: to evaluate whether obesity is involved in bone fragility in elderly women and to investigate the potential mechanisms involved, through the evaluation of WNT pathway and ECS. METHODS: 68 elderly women (>65 years old), obese (32, BMI >30) and normal weight (36, BMI <25)

who underwent surgery for standard hip arthroplasty were enrolled in this project. During the procedure, biopsies of bone, subcutaneous fat and muscle have been collected and they have been analyzed for WNT pathway, tissue factors, ECS elements and bone turnover markers, by gene/protein expression analyses and ELISA tests. RESULTS: Adiponectin in the adipose tissue of obese resulted decreased than normal weight subjects while both WNT and ECS presented alterations in obese compared to the leans. Bone tissue showed important alterations in WNT signaling, which are reflected in the gene expression of Osteocalcin, which is significantly decreased in obesity ($p = 0.0423$). Finally, the skeletal muscle presented a light decrease of WNT signaling. CONCLUSIONS: obese subjects may present an impaired bone formation, which is demonstrated by WNT pathway alterations and by the significant decrease in the gene expression of Osteocalcin, not accompanied by the decrease in the serum levels of the same subjects. The evaluation of both WNT pathway and of tissue markers highlighted the presence of alterations in all three tissues considered, favoring the adipogenic differentiation to the detriment of other cell lineages. STUDY 2. AIM OF THE STUDY: to assess the possible effects of glycated vs. native insulin on adipocyte differentiation and on ECS regulation both in primary cell line and in primary cells. METHODS: human recombinant insulin was glycated in vitro and modifications were monitored by PAGE. Human preadipocytes (HPAd), a primary cell line from subcutaneous adipose tissue, and adipose-derived stem cells (ASCs), from tissues of lean and obese subjects (BMI <25 and BMI >30) were differentiated with standard adipogenic medium in the presence of native or glycated insulin. Cellular differentiation was assessed by gene and protein expression analyses of adipogenic markers (adiponectin, fatty acid binding protein –Fabp4-, peroxisome proliferator-activated receptor gamma -Ppargamma;-, glucose transporter 4 –Glut4-) and of receptors for adiponectin and insulin, through RT-PCR and immunoblot. Moreover, it was evaluated the gene expression of ECS in cells with native vs. glycated insulin. RESULTS: gene/protein expression analyses showed that preadipocytes (both HPAd and ASCs) treated with glycated insulin (Gly-Ins) had impaired differentiation capacities. In fact, there was an overall downregulation of adipogenic markers, with a significant decrease of adiponectin both in leans- and in obese-derived cells ($p = 0.007$ and $p = 0.017$, respectively), lower levels of Glut4 and a significant lower expression of Fabp4 ($p = 0.002$) in cells from leans with Gly-Ins. Moreover, it was observed a strong increase of Ppargamma; in leans ($p = 0.013$) and of AdipoR1 in obese-derived cells ($p = 0.005$) with Gly-Ins. Unlike gene expression, protein levels of INSR presented a significant downregulation in Gly-Ins cells, with a $p = 0.0266$ in leans and of 0.011 in obese subjects. Furthermore, the ECS evaluation showed a differential gene expression in cells differentiated with Gly-Ins vs. native form. CONCLUSIONS: Gly-Ins may affect human adipocytes differentiation and impair insulin receptor expression, maybe acting at translational and post-translational level or by increasing its degradation. The evaluation of ECS in these cells highlighted a possible over activation in cells exposed to modified insulin, suggesting a possible interaction between oxPTM insulin and ECS.

ROLE OF OSTEOBLASTS IN CASTRATION RESISTANT PROSTATE CANCER (CRPC) PROGRESSION

Ph.D student Ribelli Giulia
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Prostate cancer has the propensity to metastasize to the bone forming mainly osteoblastic lesions. Although androgen ablation remains the standard of care for advanced metastatic disease an eventual tumour progression occurs and androgen-independent disease develops. Prostate cancer can be considered a microenvironment-driven disease, indeed bone and tumour cells interaction is crucial for tumour progression and bone metastasis onset. Since this complex interplay is currently not completely elucidated, this research project was focused on osteoblast (OB) role in the progression of castration resistant prostate cancer (CRPC). We found that in direct co-cultures, OBs strongly inhibited AR receptor of CRPC cell line (C4-2B cells). Since AR activation is the driving

signal for prostate cancer cell growth, we analysed the impact of AR inhibition on tumour cell proliferation. Contrary to expectations, C4-2B cells proliferated significantly more when cultured with OBs, supporting the hypothesis that OBs stimulate an androgen-independent cancer growth. Moreover, we demonstrated that OB effects were mediated by the release of osteoblastic soluble factors, since AR inhibition persists when C4-2B cells were treated with osteoblastic conditional media (OCM). Our results showed also that OB-mediated AR inhibition is only partially restored adding an exogenous androgen, demonstrating that its repression could be in part androgen independent. In addition, the effect of Enzalutamide, an AR inhibitor was significantly lower in C4-2B treated with OCM. The lower effect of AR agonist (R1881) and inhibitor (Enzalutamide) could be a consequence of the reduced expression of AR mRNA and protein levels found in C4-2B cells after OCM treatment. Once again, together with the repression of the receptor, we observed that OBs promoted tumour cell growth also in indirect co-culture. In order to identify the molecules involved in this process, we focused on IL-6, IL-8, WNT16, DKK-1 and CXCL12 expression, finding that OBs presented higher mRNA levels of all these factors compared with C4-2B cells. According to literature data, IL-8 and IL-6 represent the best candidates to mediate OB effects, since their protein levels were highly express in OCM. However, further analyses are necessary to fully elucidate their role in the androgen-independent cancer cell growth. The identification of the targets responsible of OBs pro-tumour effects could represent a strong rationale for the development of new target therapies that could support the existing strategies of CRPC treatment.

MOTION SENSOR NETWORK BASED ON LOW POWER WIRELESS TECHNOLOGIES FOR THE ASSESSMENT OF NEUROLOGICAL DISEASES

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In the last years, the spread in the market of miniaturized magneto-inertial sensors, thet are so small, low cost and power efficient to be attachable to any system (human body included), has expanded their potential in a myriad of applications. Since their introduction on the market, bioengineers have exploited their potential for the motion analysis in healthy subjects, but also in patients for the assessment of pathologies characterized by motor disfunctions, such as neurological diseases. One of the main challenges related to the use of those sensors in biomedial applications is to develop an user friendly, low power, low cost and high throughput M-IMU systems which allow monitoring patients with motor impairments and acquiring reliable data to support clinical decisions. In fact, despite the large number of commerical devices based on magneto-inertial sensors available on the market, their use for clinical assessment in unstructured environments (e.g. at-home) is still limited. On one side most of the portable system coming from the consumer electronics market (smartbands or smartwatches) allow for pervasive, low-power communication with smart devices (thus usable at home), but do not permit a high throughput and multi-node information, but are quite expensive, usable only by trained staff and often have limited battery life capabilities (since are not based on low energy wireless communication) or use non-standard and widespread communication technology, making them suitable only for use in structured or semi-structured environments (i.e. research laboratories, research hospitals). To overcome these limitations, the overall aim of this Ph.D project is to design, test and validate a M-IMU based wireless sensor network, for motor assessment of neurological patients in unstructrured environments. To do this, our first goal is to select and test a suitable wireless technology, with reduced power consumption and wide compatibility with consumer electronics for out-of-the-lab and at-home applications. We found Bluetooth Low Energy (BLE) to be an excellent candidate for our requirements and we performed for the first time an extensive and systematic analysis of BLE, in order to demonstrate whether it is a suitable candidate for wireless communication in high throughput and low energy sensor network applications. Defining a standard methodology to test wireless seonsor networks, we tested BLE performance in a sensor network with a star topology, showing the possibility to use this communication technology in high datarate appli-

cations (~170 kbps), thus enabling the streaming of 5 nodes with 9-axes M-IMU data (16 bits of resolution per axis) at more than 200 Hz. The second goal of our work id to assess the reliability of M-IMU sonsors for motion analysis. In fact, despite their pervasive use in biomedical applications, the assessment of their accuracy and reliability for motion tracking has been only partially addressed. Our main contribution in this field is focused on the design of a standard methodology to tune and optimize filter parameters in M-IMU sensor fusion algorithms, able to measure the error with respect of a ground truth (represented by the optical motion tracking system), in order to evaluate the goodness of these filters. The results show how filters' performance may be different, depending on an orientation error of about 2° and lower than 5°, respectively in static and dynamic conditions. Finally, our third goal is to use a reliable technology in terms of both wireless communication and sensor technology, to objectively assess motor conditions of patients with neurological deficits. Among several possible pathologiew with relevant movement disorders, we focus on Parkinson's disease. In fact, PD may hyghly benefit from the use of magneto-inertial sensors for the diagnosis and assessment of its motor symptoms. As a matter of fact, motor symptoms in PD are not only hyghly relevant, but they are also very representative of the evolution of the pathology. For this reason they are strictly related to diagnosis, assessment and monitoring; indeed, a very important part of the widely used PD assessment clinical scale (i.e. the UPDRS scale), administred by physician, is focused on the evaluation of motor disorders. The clinical analysis, which is occasionally administred by the doctor, presents some limits: PD has fluctuations during different days, but also in the same day, whhich do not guarantee the efficacy of the medical assessment in the hospital. Hence, we decide to continuously monitor PD patients using M-IMUs: in detail, we use these typology of sensors to evaluate PD's cardinal motor symptoms in different tasks of its clinical scale. As result, our main contribution in this topic is to exploit a M-IMU sensor network to discriminate fluctuations in subjects with Parkinson's disease (i.e. ON and OFF status), and to detect statistically significant differences between PD and healthy subjects with a few number of sensor and performing easy tasks. After a deep analysis of some of the UPDRS tasks administred by the physician to the patients, we evidenced statistically significant results to assess PD. The first analysis regards patients during the execution of arm prono-supination task and evaluating the total power as a kinematic feature on only one sensor positioned on the index, thumb or wrist. These sensor locations and kinematic index can detect statistically significant differences between PD and healthy subjects (index, thumb, wrist: $p < 0.0001$). Moreover, we also found that using one M-IMU only on the trunk while performing a sit to stand task and evaluating trunk acceleration during trunk flexion it is possible to differentiate OFF and ON with respect to healthy subjects ($p < 0.05$).

IMPEDANCE IN HUMAN-MACHINE INTERACTION

Ph.D student Simona Valentini
Tutor Dino Accoto

The physical interaction between a human being and a technological artefact implies a power flow from or toward the human body. Power can be defined as the product between a generalized effort and a generalized flow. For example, in Mechanics the effort variable is a force/torque and the flow is a velocity. In the electric domain, the current represents the flow variable and the voltage the effort. In the frequency domain these quantities can be combined to obtain a dynamic property of the compound human-machine named impedance. Depending on what kind of interaction is established, the impedance to be addressed can be mechanical (either related to the robotic system or to the human body) or electrical. In this thesis three biomedical scenarios in which it is crucial to take into proper consideration the effects of impedance on the human-machine interaction have been explored. The first application case regarded the interaction of the human locomotor apparatus with an exoskeleton assisting cyclic motions. In the interaction with a human being the robot has to synchronously adapt to the intended motion of the user, who in turn should be allowed to exploit the robotic physical support and to reduce the effort needed

to perform a task. In the design of wearable robots that physically interact with a human, mechanical impedance has to be properly considered in order to implement control strategies capable of achieving a smooth, natural and non-constraining interaction. In order to minimize the perturbation induced by the robot on the natural efficient pendular nature of legs, a Switching Controller has been proposed that intermittently injects energy parcels into the human-robot system feeding the natural intrinsic oscillatory dynamics of the system, with the minimum required amount of energy. Rather than rigidly imposing a pre-defined trajectory, the presented controller delivers intermittent assistive torques to produce functional motion and to minimize unwanted perturbations to user's desired kinematic status. The proposed Switching Controller was experimentally validated on 8 healthy subjects performing knee flexion-extension motions in unassisted and assisted conditions. Electromyographic activity of main flexor-extensor knee muscles showed that the proposed controller favours extensor muscles during extension, with a statistically significant reduction in muscular activity. In the second scenario, the interaction between bone tissues and a surgical drilling tool has been analyzed. In particular it is reported the design of the end-effector of a surgical robot for the treatment of intervertebral disc degeneration through the injection of drugs in the disc following a transpedicular route. This surgical approach implies that the intervertebral disc is reached by means of a perforation of the vertebral peduncle. The robot was conceived to support and not to substitute the surgeon in performing the procedure. Therefore, it acts as a passive holder that guides the orientation of the drilling trajectory based on preoperative planning, the surgeon maintain the full control of the procedure advancing the driller along a guided path. Such approach preserves the haptic feedback that the surgeon receives from the interaction with the tissues. The impedance of bone tissues influences the pushing force and the feed rate during drilling. In order to provide the surgeon with supporting information for the identification of the tissues that are being crossed, a driller embedded with force and position sensors has been designed. The analyses of force and feed rate in the frequency domain have led to the definition of a parameter related to the mechanical properties of the bone layers encountered during drilling (i.e. cortical bone, cancellous bone, bone marrow). Taking inspiration from mechanical impedance of viscoelastic bodies, such parameter has been defined as the ratio between the Fourier transform of the force and the feed rate, averaged over a moving time window. An algorithm has been developed that allows the implementation of a real-time system to provide the surgeon with visual and audio information while performing bone drilling along guided trajectories. Finally, a third application scenario regarded the interaction with the nervous system by means of neural interfaces for prosthetic applications. Invasive interfaces with the peripheral nervous system currently rely on electric means for both nerves stimulation and signals recording. Recent studies showed that the quality of the signal-to-noise ratio of the afferent channel might be negatively affected by physiological reactions, including fibrosis. The formation of a fibrotic capsule around implanted electrodes leads to an increase in the electric impedance of the nervous tissue that impairs the long term efficacy of the implant. The possibility to stimulate the peripheral nervous tissue by means of electromagnetic (EM) waves has been investigated. EM stimulation does not require a direct contact with the tissue to be stimulated, therefore is capable of overcoming fibrotic capsules. A versatile calculation framework has been developed to investigate the properties of the electric field generated by a plurality of miniature coils with arbitrary shape and spatial orientation, arranged in cuff configuration. The capability of the miniature coils to elicit a neuronal response in specific portions of the peripheral nerve has been investigated.

POST-TRANSLATIONAL MODIFICATION OF RELEVANT PROTEINS IN TISSUE-SPECIFIC AUTOIMMUNITY

Ph.D student Chiara Vinci
Tutor Ahuva Nissim

Introduction: Autoimmune diseases are often associated with increased production of reactive oxygen species (ROS). ROS may post-translationally modify proteins generating neoepitopes which may be a key aspect in the

development of autoimmunity. Type 1 diabetes (T1D) and rheumatoid arthritis (RA) are autoimmune diseases that share some factors, such as association with the HLA-DRB1*04 and increased oxidative stress. My group has previously reported the presence of insulin oxidized by ROS (oxPTM-INS) in T1D patients and that antibodies to oxPTM-INS (oxPTM-INS-Ab) are detected in newly diagnosed T1D patients. My group has also reported an autoimmune reactivity against ROS modified type II collagen in rheumatoid arthritis patients (oxPTM-CII). Hypothesis: This study is based on the hypothesis that ROS released during chronic inflammation are able to post-translationally modify proteins leading to the formation of neoepitopes. The main hypothesis is that these oxPTM play a key role in autoimmune response and thus influence the diseases pathobiology. Objectives: The main objective of this study was to increase extend the understanding of oxPTM in autoimmunity and in arthritis. Specific aims: 1 - Testing the reactivity to oxPTM-INS in a longitudinal cohort of patients prior to diagnosis of T1D. 2 - Mapping oxPTM-INS neoepitopes. 3 - Testing reactivity to oxPTM-CII in large cohorts of patients with inflammatory arthritis. 4 - Mapping the oxPTM-CII neoepitopes. Methods: Modification of CII and insulin were confirmed by PAGE and, in the case of insulin, mass spectrometry. Serum samples from subjects with inflammatory arthritis (including RA and spondyloarthritis) and T1D were used to evaluate the presence of oxPTM-CII-Ab and oxPTM-INS-Ab. The correlation between these antibodies with clinical, biochemical and HLA genotype was assessed. The epitope mapping for oxPTM-CII and oxPTM-CII was studied. Results: 1 - Antibodies to at least one oxPTM-INS were present in over the 90% of children progressing to T1D (progr-T1D). •OH-INS-Ab were more common in progr-T1D children than in children non progressing to T1D positive for standard diabetes antibody marker (NP-AAB+) (82.6% vs 19%; p <0.001) and allowed discrimination between progr-T1D and NP-AAB+ children with 74% sensitivity and 91% specificity. None of the children non progressing to T1D negative for standard diabetes antibody marker NP-AAB- children were positive for oxPTM-INS-Ab. The comparison of plasma and serum from the same patients has confirmed all the previous data. In addition, we have shown that the correlation between plasma and serum analysis is very high. 2 - Mass spectrometry analysis confirmed previous data and has identified more amino acids modifications: cysteine oxidation and amino acid conversion. Comparing 2D gel-western blot analysis of insulin and oxPTM-INS performed using the most reactive serum samples from T1D patients was leading to the identifications of some interesting protein spots. 3 - In cohort 3 a stronger binding to oxPTM-CII was observed in serum samples from axSpA (74%) compare to PsA (33%), UA (35%) and FM (16%), (p <0.0001). Interestingly, binding of axSpA samples was similar to binding of serum samples from ERA (91.7%). Binding to ROS-CII was directed to a range of ROS-CII fragments between 25 and 150 kDa. In cohort 4 binding of AS serum samples to oxPTM-CII was significantly higher than binding to native CII (p <0.0001) with a percentage of autoreactivity of 30% to CII and 67.5% to at least one oxPTM-CII. 4 - Comparing 2D gel-western blot analysis of CII and oxPTM-CII performed using the most reactive serum samples from ERA patients was leading to the identifications of some interesting protein spots. Conclusions: For the first time I have demonstrated reactivity to oxPTM-CII in axSpA patients and these data may support a further understanding on axSpA pathogenesis. Moreover, oxPTM-CII might mark diseased-tissue specific targets. I have shown that oxPTM-INS auto-reactivity is present before the diagnosis of T1D in over 90% of cases, for this reason oxPTM-INS-Ab may become a biomarker to predict children progressing to T1D and for early diagnosis of T1D.

Awards

Awards

Annamaria Altomare
Early Career Investigator award at the Digestive Disease Week (DDW) 2018 for the research project "Type-1 Cannabinoid receptor effect on human colonic motility in patients with slow transit constipation and controls"

Lorenzo Ardito
"Borsa Zegna 2018/2019" research grant awarded by the Ermenegildo Zegna Founder's Scholarship program to conduct research in the topic of Digital Transformation.

Advanced Robotics and Human Centred Technologies Research Unit
Internal call "University Strategic Projects" grant awarded for the project: User-centred design of a robotic device for improving working conditions and user subjective perspective during patient-handling movements (SAFE MOVER)

Silvia Irina Briganti
Best oral presentation, Collegium of the postgraduate training courses, Campus Bio-Medico Univeristy

Carotti S., Zalfa F., Panasiti V., Zingariello M., Roberti V., Sancillo L., Perrone G., Rana R.A., Marine-Christophe J., Bagni C., Morini S.
Best poster at the 72th National Congress of the Italian Society of Anatomy and Histology

Michele Cicala
Honorary fellowship received by the American Gastroenterological Association

Rossella Del Toro
Italian Society of Diabetology Award

Luca Faramondi
CIPRNet Young CRITIS Award 13th edition of the International Conference on Critical Information Infrastructures Security (CRITIS)

Endocrinology and Diabetes Research Unit
Internal call "University Strategic Projects" grant awarded for the project: Oxidative post-translational modifications of Insulin as biomarkers of type 1 DIAbetes prediction, progression and complications

Giulio Iannello, Paolo Soda
Student travel award at IEEE International Conference on Bioinformatics and Biomedicine (BIBM), for the paper:

D'Amico N. C., Sicilia R., Cordelli E., Valbusa G., Bossi Zanetti I., Fazzini D., Scotti G., Iannello G., Soda P.
Radiomics and machine learning in the prediction of response to CyberKnife radiosurgery for acoustic neuroma: a pilot study.
IEEE International Conference on Bioinformatics and Biomedicine (BIBM). Madrid, Spain, 3-6 Dec. 2018. ISBN: 978-1-5386-5489-7 DOI 10.1109/BIBM.2018.8621276

Giulia Leanza
Italian Society of Diabetology Award

Ernesto Maddaloni
Italian Society of Diabetology Award

Measurements and Biomedical Instrumentation Research Unit
Internal call "University Strategic Projects" grant awarded for the project: HOPE (HOspital to the PatiEnt).

Anda Mihaela Naciu
Award "Premio Giovani", SIOMMMS (Società Italiana dell'Osteoporosi del Metabolismo Minerale e delle Malattie dello Scheletro)

Nicola Napoli
Alcmeone Award, Società Italiana di Diabetologia

Paolo Persichetti
AAWPS Award promoted by the American Alpine Workshop Plastic Surgery

Radiation Oncology Research Unit

Internal call "University Strategic Projects" grant awarded for the project: CoLlAborative multi-sources Radiopathomics approach for personalized Oncology in non-small cell lung cancer (CLARO)

Daniele Santini

Award for Professional Merits - International Grand Prix of Venice

Francesco Segreto

GiovedìScienza 2017 award promoted by the Centro Scienza Onlus Association.

Gaia Tabacco

Travel Grant EASD

Bruno Vincenzi

"Check-up Salute" prize

2018 Research papers awarded by Department of Medicine and Surgery as "UCBM Paper of the month"

January

Annibali O., Crescenzi A., Tomarchio V., Pagano A., Bianchi A., Grifoni A., Avvisati G.
PD-1 /PD-L1 checkpoint in hematological malignancies.
Leuk Res. 2018 Apr; 67:45-55. PubMed PMID: 29428449. IF 2,319

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June

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Eur Urol. 2018 Jun; 73(6):934-940. PubMed PMID: 27780643. IF 17,581

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Rocco G., Pennazza G., Santonico M., Longo F., Rocco R., Crucitti P., Antonelli Incalzi R.
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August

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Ther Adv Med Oncol. 2018 Aug 29;10: 1758835918794623. PubMed PMID: 30181783. IF 6,238

September

Frezza A.M., Jones R.L., Lo Vullo S., Asano N., Lucibello F., Ben-Ami E., Ratan R., Teterycz P., Boye K., Brahmi M., Palmerini E., Fedenko A., Vincenzi B., Brunello A., Desar I.M.E., Benjamin R.S., Blay J.Y., Broto J.M., Casali P.G., Gelderblom H., Grignani G.,-Gronchi A., Hall K.S., Mir O., Rutkowski P., Wagner A.J., Anurova O., Collini P., Dei Tos A.P., Flucke U., Hornick J.L., Lobmaier I., Philippe T., Picci P., Ranchere D., Renne S.L., Sbaraglia M., Thway K., Wagrodzki M., Wang W.L., Yoshida A., Mariani L., Kawai A., Stacchiotti S.

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JAMA Oncol. 2018 Sep 1; 4(9):e180219. PubMed PMID: 29800950. IF 20,871

October

D'Angelillo R.M., Ramella S.

Are we ready for histology-driven stereotactic ablative radiotherapy?

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November

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JAMA Oncol. 2019 Mar 1;5(3):343-350.PubMed PMID: 30476968. IF 20,871

December

Efficace F., Breccia M., Avvisati G., Cottone F., Intermesoli T., Borlenghi E.,

Carluccio P., Rodeghiero F., Fabbiano F., Luppi M., Romani C., Sborgia M., D'Ardia S., Nobile F., Cantore N., Crugnola M., Nadali G., Vignetti M., Amadori S., Lo Coco F.

Health-related quality of life, symptom burden, and comorbidity in long-term survivors of acute promyelocytic leukemia.

Leukemia. 2019 Jul;33(7):1598-1607.PubMed PMID: 30573776. IF 10,023

2018 Publications

Full List

ADVANCED ROBOTICS AND HUMAN CENTRED TECHNOLOGIES

Head L. Zollo (E. Guglielmelli until 30th September)

Articles

Tamilia E., Park E.H., Percivati S., Bolton J., Taffoni F., Peters J.M., Grant P.E., Pearl P.L., Madsen J.R., Papadelis C.
Surgical resection of ripple onset predicts outcome in pediatric epilepsy.
Ann Neurol. 2018 Sep; 84(3):331-346. PubMed PMID: 30022519. IF 10,25

di Biase L., Summa S., Tosi J., Taffoni F., Marano M., Cascio Rizzo A., Vecchio F., Formica D., Di Lazzaro V., Di Pino G., Tombini M.
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Scotto di Luzio F., Simonetti D., Cordella F., Miccinilli S., Sterzi S., Draicchio F., Zollo L.
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A wearable system for real-time continuous monitoring of physical activity.
J Healthc Eng. 2018 Mar 20; 2018:1878354. PubMed PMID: 29849993. IF 1,261

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Bertomeu-Motos A., Blanco A., Badesa F.J., Barios J.A., Zollo L., Garcia-Aracil N.
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Sci Rep. 2018 Jul 17; 8(1):10823. PubMed PMID: 30018334. IF 4,122

Giannatiempo S., Carpino G., Petitti T., Zobel B.B., Grasso R.F., Guglielmelli E.
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Design of a wearable mechatronic device to measure the wrist rigidity in Parkinson's disease patients
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ALLERGOLOGY, IMMUNOLOGY, RHEUMATOLOGY

Head A. Afeltra

Articles

Margiotta D.P.E, Basta F., Batani V., Afeltra A.
Belimumab and low-doses of mycophenolate mofetil as induction therapy of class IV lupus nephritis: case series and literature review.
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ANESTHESIA, INTENSIVE CARE AND PAIN MANAGEMENT

Head F.E. Agrò

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AUTOMATION AND CONTROL THEORY

Head R. Setola

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BIOCHEMISTRY AND MOLECULAR BIOLOGY

Head M. Maccarrone

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BREAST CARE

Head V. Altomare

Articles

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CARDIOVASCULAR SCIENCE

Head G. Di Sciascio

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Head V. Piemonte

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Head G. Iannello

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Head G. Pennazza

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Head L. De Gara

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Head M. Cicala

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GENERAL SURGERY

Head R. Coppola

Articles

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Head R. Antonelli Incalzi

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GYNAECOLOGY AND OBSTETRICS

Head R. Angioli

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HEART SURGERY

Head M. Chello

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HEMATOLOGY, STEM CELL TRANSPLANTATION, TRANSFUSION MEDICINE AND CELLULAR THERAPY

Head G. Avvisati

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Head T. Petitti

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INTERNAL MEDICINE AND HEPATOLOGY

Head A. Picardi

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Head: M. Ciccozzi

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Head V.M. Fazio

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Head A.M. Persico

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Head V. Di Lazzaro

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Head G. Di Pino

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Head S. Filippi

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Head M.G. De Marinis

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Head G. Tonini

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Head S. Ramella

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