Bologna
Metropolitan Research Hub

Cluster 1 – Health
Topics 2026

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Bologna
IRCCS Istituto di Ricovero e Cura a Carattere Scientifico

POLICLINICO DI
SANT'ORSOLA

SERVIZIO SANITARIO REGIONALE
EMILIA - ROMAGNA
Istituto Ortopedico Rizzoli di Bologna
Istituto di Ricovero e Cura a Carattere Scientifico

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Bologna

Istituto delle Scienze Neurologiche
Istituto di Ricovero e Cura a Carattere Scientifico

SUMMARY

ABOUT US

Bologna: an ideal ecosystem for health research

The Bologna metropolitan area represents an ideal environment for health research activities to thrive. This is thanks to the presence of the University of Bologna (UNIBO), a university with a long tradition of excellence in multi-disciplinary research, and three research hospitals. Each has been recognized by the Italian Minister of Health as "Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS)": Istituto Ortopedico Rizzoli (IRCCS IOR), Azienda Ospedaliero-Universitaria di Bologna (IRCCS AOU), and Istituto delle Scienze Neurologiche di Bologna (IRCCS ISNB). This denomination indicates medical institutions of excellence, devoted to biomedical and health systems research, alongside clinical activity.

The following sections will provide an overview of the four institutions.

Alma Mater Studiorum – University of Bologna (UNIBO)

The oldest university in the Western world, it paves the way for innovation through an increasingly rich course curriculum, cutting-edge research and an ever increasingly broad international perspective.

5 CAMPUSES AND A BRANCH IN BUENOS AIRES, A TEACHING CURRICULUM TAILORED TO THE NEEDS OF PRESENT-DAY SOCIETY
Over 250 degree programmes among its 31 departments and 5 schools are offered to over 97,000 students. 7,500 graduates are enrolled in PhDs and other 3rd-cycle programmes.

RANKED IN THE TOP 200 ON THE TWO MOST PRESTIGIOUS INTERNATIONAL UNIVERSITY RANKINGS, CONSIDERED THE LEADING UNIVERSITY IN EUROPE FOR STUDENT MOBILITY (ERASMUS+).

INVESTING IN THE 17 SUSTAINABLE DEVELOPMENT GOALS. Reviewing its 2022-2027 Strategic Plan taking full account of them, in order to meet the major modern society challenges.

INVESTING IN A MULTIDISCIPLINARY CROSS-CULTURAL APPROACH AND IN THE INSEPARABLE CONNECTION BETWEEN RESEARCH AND TEACHING. Leading and participating in European research and academic cooperation projects, Bologna has formed knowledge alliances with industry and public/private organizations. It is a hub of international networks. Beyond its close European links, it enjoys multiple connections with America, Africa, Asia, Australia.

RESEARCH AND INNOVATION: A PRIORITY OF THE UNIVERSITY MISSION.
INNOVATION: An active portfolio of over 800 patents and plant varietis. A total of 58 spin-off and start up companies, including Almacube, which is a business incubator that managed 16 incubated companies in 2022.
The **scientific community of UNIBO** counts 6,850 scholars: 3,382 between teachers and researchers, 2,430 PhD students, and 1,298 research fellows. A total of **50 facilities** are involved in research: 31 Departments, 12 Research and Training Centres, 7 Interdepartmental and Industrial Research Centres.

The Alma Mater develops and supports research collaborations with universities, research institutions and the industry, with **90 framework agreements with universities, public entities and research centres, and 49 with private enterprises**, to establish long-term collaborations that allow a wide range of strategically planned activities and initiatives. Furthermore, it has joined **80 between regional, national, and international associations and networks to promote research activities and collaborations**.

UNIBO is a Euraxess Contact Point. The Quality Assurance System of the University of Bologna has been assessed by ANVUR.

As reported in the 2022 edition of QS World University Rankings and US News Best Global Universities, **UNIBO is acknowledged as 1st and 2nd Best comprehensive University in Italy, 166th and 125th worldwide respectively**. In both Indexes, the UNIBO ranking by subjects related to Life Sciences & Medicine such as: Clinical Medicine, Molecular Biology and Genetics, Biotechnology and Applied Microbiology, Chemistry, Radiology, Nuclear Medicine and Medical Imaging, Oncology, Biological Sciences, Medicine, Computer Science and information, Engineering, is 1st, 2nd or 3rd in Italy, 44th to 142th worldwide.

The international exposure of the UNIBO is also checked by the CENSIS rankings of Italian Universities 2022/2023. Among the cluster of mega-universities, **UNIBO is 1st for "internationalization" and best in Italy in the overall ranking**. UNIBO employs 478 researches with H-index >20, of which more than 300 in the Biology, Medicine, Chemistry, engineering and Computational Science areas, with an ever-increasing attention to gender balance as shown by the adoption of a dedicated Gender Equality Plan. First in Italy, **14 Departments of the university have been awarded as Departments of Excellence.**

HEALTH RESEARCH AREAS

The University of Bologna is a comprehensive research university active in many areas of knowledge. This page collects the descriptions of our University's competences on the main research topics identified by the Horizon Europe funding framework programme.
The main competency areas for Health & Digital Health are the following:
Ambient Assisted Living
Big Data and Omics Medicine
Brain Ageing and Neurodegeneration
Cancer
Digital medicine and eHealth
Epidemiology, Biobanking & Cohorts
Health, non-communicable diseases and the environment
Multimorbidity and ageing
Pharmaceutical biotech
Rare diseases and undiagnosed disorders
Regenerative medicine and tissue engineering
Skeletal health and diseases
Social and ethical aspects of health
Systems and personalised medicine

RESEARCH & INNOVATION COMPETITIVE FUNDING

Very active at National and European levels in all the research areas. Activities related to competitive funding programmes are supported by the Research Division: more than 10 years' experience and about 50 employees assisting the research groups during the whole project lifecycle. Assistance is carried out in strict cooperation with the Knowledge Transfer

Office (for Innovation Management, IP protection and exploitation) and the uptake and commercialization of project results.

Overall, in **Horizon 2020**, UNIBO has been involved in **356 funded projects (98 as coordinator) with more than 150 M€ of funding**, 26 PI ERC and more than 2300 partners involved, of which 1600 from the private sector. In the framework of the Societal Challenge 1 – Health, Demographic Change & Wellbeing, the Innovative Medicine Initiative and related funding frameworks, UNIBO is **participating in 31 projects** with a total EU contribution of over **14 M€, becoming the 1st Italian University for H2020 SC1 participations,** among them, several projects on precision medicine.

Overall, in **Horizon Europe, 238 proposals** have already been invited for funding, with a total **contribution of 115 M€.** In the framework of the **Cluster 1 – Health**, UNIBO has been involved in **17 funded projects (3 as coordinator) with more than 8 M€ of funding**.

Azienda Ospedaliero-Universitaria di Bologna St. Orsola-Malpighi (IRCCS AOUBO)

The **IRCCS Azienda Ospedaliero-Universitaria di Bologna** (IRCCS AOUBO) **is Bologna's first hospital, with over 400 years of history**.
It is a research hospital and the main **official venue of the School of Medicine and Surgery** of the University of Bologna being the University's reference center for healthcare activities crucial for academic education and clinical research. **IRCCS AOUBO is a multi-specialistic and highly specialized hospital**, distributed over 32 pavilions, with a total of 1,498 beds. The hospital is staffed with 5,944 employees, including university researchers and physicians.
Every year the IRCCS admits approximately 56,000 patients (last data from 2023) and performs an estimated 1,100,000 outpatient visits, thus managing thousands of patients from Emilia-Romagna , other Italian regions, and European and non-European countries.
Healthcare and research activities are carried out and developed through 13 Departments of Integrated Activities (DAI) and a transversal organisation of pathways of care and homogeneous activities aimed at strengthening and improving all the distinctive activities of the hospital.
IRCCS AOUBO ranks **5th among the best Italian hospitals** in the **"Best Hospital 2024"** ranking, published by the American magazine "Newsweek", and the 66th in the global ranking. IRCCS AOUBO is an excellence research centre dedicated to translational research with the aim of improving patient care pathways and clinical practices. **In 2020, the hospital was awarded the status of IRCCS - "IRCCS - Istituto di Ricovero e Cura a Carattere Scientifico - Scientific Institute for Research, Hospitalization and Healthcare" by the Italian Ministry of Health, as the result of high specialization and excellence in care and biomedical research focusing on two specific areas**:
1- Assistance and research in transplantation and the critical patient
2- Integrated medical and surgical management for the treatment of oncological diseases.

The research activities addressing the two specific areas are declined in **eight research lines**. In addition to the two main areas, IRCCS AOUBO's is characterized by **multi-specialistic research activities** also covering **preclinical research**, which is carried out in dedicated research platforms and laboratories, and clinical research, including all phases of **translational research** (**clinical trials from T1 to T4**). IRCCS AOUBO hosts more than **60 disease registries** and a large number of **datasets for observational and clinical studies** and

is member of **12 European Reference Networks (ERNs) focusing on rare diseases and conditions** that require highly specialised treatment and concentrated knowledge and resources.

HEALTH RESEARCH AREAS

IRCCS AUOBO follows eight **IRCCS AOUBO's Research Lines:**

1. **Translational and clinical approaches for early diagnosis and prevention of complications in solid organ and hematopoietic stem cell transplantation**
   This line includes clinical and laboratory research projects directed at the diagnosis, prevention, and treatment of complications after transplantation for both solid organ, tissue, and hematopoietic stem cell recipients. of new drugs with adjuvant or therapeutic function in the transplantation process, impact of lifestyle on the outcome of the transplanted patient.
2. **Optimizing the use of transplantation through prevention, diagnosis, treatment, and risk factor analysis of severe organ failure**
   The line of research for optimizing the use of organ transplantation consists of the following areas:
   - Development of screening and prevention programs for diseases leading to organ failure;
   - Implementation of advanced imaging techniques and biomarkers for early detection of organ disease;
   - Use of artificial intelligence and machine learning for clinical data analysis and identification of patients at risk;
   - Research on drug therapies, organ support systems, and surgical interventions to delay or prevent
   - Terminal organ failure
3. **Research of strategies for the reconditioning and regeneration of cells, tissues, and organs and for the optimization of donor resources**
   The discrepancy between need and supply of organs is one of the major constraints on access to transplantation. Included in this line of research are projects that aim to optimize the overall donor process and increase organ availability through, for example, the use and development of perfusion techniques and other treatments to optimize the function of the harvested organ. Also included in this line are both basic and translational research projects that aim to develop cell protection, repair, and regeneration strategies to be applied to organs harvested for transplantation, as well as to pathological native organs.
4. **Development of multidisciplinary approaches and technologies directed toward the personalization of therapeutic strategies in patients with organ failure**
   Activities in this line of research aim to develop personalized diagnostic and treatment pathways that apply the principles of precision medicine. This line aims to implement a holistic approach to patient care by developing projects that will be based on the integration of multidisciplinary expertise that will enable the development of technologies and care designs centered on identifying and meeting the health and quality-of-life improvement needs of the patient with transplantation or severe organ failure.
5. **Research of diagnostic, prognostic, and predictive markers by advanced caretterization of solid and hematologic malignancies and their microenvironment using omics and AI techniques**
   Using advanced "omics" technologies (such as genomic, transcriptomic, proteomic, and methylome analyses), also integrating them with artificial intelligence, this line of

research aims to identify molecular markers in both solid and hematologic cancers. These markers will be used for early diagnostics, assessment of aggressiveness, in predicting response to therapies, and to select specific treatments for each patient. Thus, the goal is to develop more precise medicine tailored to the individual characteristics of each tumor, thus improving treatment options and quality of life for patients.

6. **Development of advanced and high complexity immunologic molecular-based therapies in solid and hematologic cancers, including conducting phase 1/2 clinical trials**
   Research activities include therapeutic strategies, including conducting phase 1/2 studies, innovative and high complexity in medical and surgical management in solid and hematologic cancers, with multidisciplinary perspective using advanced surgical techniques (multidisciplinary compartmental surgery, specialty organ transplantation), pharmacologic (molecular-based, immunologic with bispecific and immunoconjugated antibodies), radiotherapeutic (metabolic radiotherapy), advanced interventional (electrochemotherapy, biomaterials, telemedicine, liquid biopsy) and artificial intelligence (radiotherapy planning, radiomic analysis of CT, MR and PET images).
7. **Clinical development of therapies for solid neoplastic and hematologic diseases of rarely observedand/or highly complex patients including through multidisciplinary approaches**
   The line of research is aimed at the development in the clinical setting of innovative, high-complexity, biologically driven personalized therapeutic strategies in solid and hematologic cancers, particularly those of rare observation. Of particular importance are the development of targeted therapies, as well as the optimization of these therapies including through the study and characterization of drug-related toxicity and through multidisciplinary approaches.
8. **CAR-T journey: from producing new constructs to developing systems for predicting outcomes and complications after infusion**
   This line of research is aimed at:
   - to the production of nonprofit, GMP advanced cell therapy (ATMP) constructs at the erected cell factory of IRCCS AOU of Bologna for new indications (hematological, oncological, immunological)
   - to the development of systems for predicting risk of complications and response after CAR-T therapy with the goal of risk-adapted multidisciplinary clinical management.

RESEARCH & INNOVATION COMPETITIVE FUNDING

As a demonstration of the excellence of the research conducted in the IRCCS AOUBO and the ability to attract and manage funding from competitive tenders, **as of 31.12.2024** there have been **101 national and international funded projects** (in progress) of which 20 European projects. In 2024, n. 33 new projects were funded **for a total funding of more than 10M€.** Among others, **2024 sees the launch of 6 new European projects.** Specifically related to EU research in health fields, in IRCCS AOUBO are ongoing n=35 projects. The staff IRCCS AOUBO in the last three years (2022-2024) realized **5036 scientific publications.**

IRCCS Istituto Ortopedico Rizzoli (IRCCS IOR)

Istituto Ortopedico Rizzoli (IRCCS IOR) is an International benchmark in orthopaedics development since its foundation in 1896. IOR has been recognized by the Italian Ministry

of Health as a scientific research hospital for the high standard of its research and its impact on an international level since 1981. the high level of care it offers is made possible thanks to the ongoing scientific research and translation of results into clinical practice. It is the only one public Italian Research Hospital (IRCCS) certified in "Orthopaedics" by the Italian Ministry of Health and it is clinically active throughout the entire orthopaedics and trauma field. The integration of clinical wards (3 departments) and 9 Research biomedical and technological laboratories offers a full overview of pathologies and the constant ability to trial new treatment possibilities. The research and Innovation Department (RIT) of the health technology network of Regione Emiia Romagna is also deputed to industrial research and technology transfer. IOR has promoted and is the legal and operational headquarters of the IRCCS Musculoskeletal System Network (RAMS) and it also participates in the activities of the IRCCS Aging and Alliance Against Cancer Networks. IOR is a participating unit of the ERN on adult solid tumors (ERN EURACAN) and the ERN Coordination Center on rare skeletal diseases (ERN BOND).
IOR is also a key component of the regional health care system of Emilia-Romagna and a teaching hospital for the University of Bologna. **The Rizzoli Institute is ranked 9th among the World's Best Specialized Hospitals in 2024 and 1st in Italy.** IOR is located in different sites of Emilia Romagna Regione (Bentivoglio Orthopedics from 2009), Argenta Orthopedic Rehabilitation Center from 2022, Castel San Giovanni-Piacenza Orthopedic and Rehabilitation Center from 2024) and Sicily (Rizzoli Orthopedic Department Bagheria from 2012).
The Rizzoli Institute is the Regional HUb for:

- **musculoskeletal tumours,**
- **vertebral surgery,**
- **paediatric orthopaedics,**
- **foot surgery,**
- **upper limb surgery,**
- **prosthesis revision and replacement,**
- **surgical treatment of severe infectious bone diseases.**

It is the regional reference center for Rare Skeletal Disorders.
At IOR is active the Emilia-Romagna Musculoskeletal Tissue Bank, the first of its kind in Italy. It provides over 50 per cent of the musculoskeletal tissue used for implants and transplants in the national context.
RIPO, the Orthopaedic Prosthetic Implant Register, was set up at IOR in 1990. RIPO has been flanked by the Orthopaedic Prosthetic Explant Register, REPO, since 2002.
Preclinical, translational, clinical and management-organization research is focussed on the prevention, diagnosis and therapeutic strategies of acute/traumatic, degenerative, oncological, infective, inflammatory, congenital and rare diseases of the musculoskeletal system.
In order to provide highly innovative clinical responses to orthopedic pathologies in adults and children, the main excellent scientific research activities that have had an impact on clinical and healthcare activities include: new surgical techniques, robotic surgery, customization of surgical and postoperative care (prostheses, cutting guides and custom instruments, digital surgical planning, robotic surgery and fast track rehabilitation); medical devices (electromedical equipment, software, biomaterials, nanotechnologies and scaffolds); osteointegration and osteointegrated prostheses and bionic prostheses; orthoplasty and microsurgery; orthobiology and regenerative medicine using mesenchymal stem cells from different sources, autologous and homologous growth factors; oncological

diagnostics and osteoncology on bone and soft tissue tumors (new drugs and personalized therapies, mutational and genomic oncology, anatomo-pathological classification of tumors); bone and periprosthetic infections; in silico medicine; predictive biomarkers of pathologies and their prognosis; bioprinting; advanced imaging, interventional radiology (ablation and cryotherapy techniques); advanced models with bone tissue: bone tissue grown in the laboratory has allowed a significant advancement of preclinical studies by increasing their translational value (advanced models for the study of biomaterials and osteointegration, 3D bone metastasis models).
IOR is the Coordination Center for ERN Bond, the European Reference Network on bone disorders, and Appointed Unit for ERN EURACAN, the European Reference Network on adult cancers solid tumors. ERN are virtual networks which gather healthcare facilities from all over Europe in order to deal with complex or rare diseases that require highly specialized care. ERN also ensure a valuable concentration of knowledge and resources. These networks are established under the EU directive on patient's rights in Healthcare (2011/24/EU).
Finally, IOR has always been a national point of reference for musculoskeletal oncological pathologies of the axial and appendicular skeleton, of adult and pediatric age and participates in national networks on topics consistent with the pathologies treated. Since 2023 it has been recognized as a Provider for sarcomas of the bone and soft tissues of adults and children within the national network of rare tumors.

HEALTH RESEARCH AREAS

The strength of the IOR is the close integration between assistance and scientific research activities carried out by 9 Research Laboratories (Complex Structures and Simple Departmental Structures) where different professional figures are employed to support multidisciplinarity in biomedical and technological research.
IOR follows four **Rizzoli's Translational Research Lines** that include a set of research and clinical activities which ensure unity of translational clinical-scientific paths. These lines are related to specific areas defined in the institute's Strategic Plan.
LINE 1: **Musculoskeletal Oncology** The activities intend to address: 1- definition of the biological and genetic characteristics underlying tumor genesis and progression; 2- identification of diagnostic, prognostic-predictive and therapeutic markers; 3- implementation of oncology registries and biobanking activities; 4- validation of innovative techniques and approaches in the field of personalized medicine, in the fields of radiology, surgery, anesthesiology, rehabilitation and medical oncology; 5- promotion of network activities at internal, regional, national and international level.
LINE 2: **Regenerative and Reconstructive Orthopedics** The activities intend to address: 1- development and evaluation of new biomaterials, coatings, scaffolds, medical devices; 2) enhancement of the use of grafts, transplant surgery, autologous transplants or from the Musculoskeletal Tissue Bank; 3) evaluation of the cellular component also in relation to the tissue of origin (e.g. bone marrow, adipose tissue); use of secretome and extracellular vesicles/exosomes; "one step" isolation systems; 4) deepening of knowledge on the role of the microenvironment at the site of treatment; 5) development of innovative preclinical study models.
LINE 3: Innovative technologies for surgery of musculoskeletal system diseases The activities intend to address: 1. Evaluation of software for anatomical-biomechanical modeling of clinical cases, virtual reality and Artificial Intelligence tools; 2. Effectiveness of the main advanced technologies, including robotics, surgical navigation, bioprostheses and post-amputation bionic limbs, personalized instrumentation, augmented reality; 3. Evaluation and implementation of techniques for the multi-instrumental quantitative evaluation of treatments;4. Development of "digital twins" with new sequences from various imaging

devices, to support precision clinical decisions, integrating medical imaging data with clinical, genetic and functional data.

LINE 4: **Orthopedic pathologies of inflammatory - infectious - degenerative - genetic nature**

The activities intend to address: 1. study of etiopathogenesis, prevention, diagnosis, therapy of musculoskeletal diseases of infectious, inflammatory, environmental, idiopathic, metabolic and degenerative origin, also related to aging; 2. definition of new qualitative and quantitative diagnostic techniques to predict fragility (in the pre-fragility phase) , risk of fractures, osteoporosis and osteosarcopenia; 3. evaluation of pharmacological therapies and diagnostic and rehabilitative methods, definition of the biological bases of the individual response to treatments; 4. in-depth study of the innovative preventive, diagnostic and therapeutic aspects of bone, periprosthetic and postsurgical infections; 5. identification of the genetic-molecular, epidemiological, diagnostic/therapeutic aspects of rare musculoskeletal diseases.

IOR also has expertise on digital treatment of diagnostic images, computer-aided surgery, human movement analysis, telemedicine.

RESEARCH & INNOVATION COMPETITIVE FUNDING

Active projects: As of 01/31/2025, the Rizzoli Orthopedic Institute has 104 active funded research projects, of which 51 are funded by competitive calls (including 9 European projects, 10 from the Ministry of Health, 15 PNRR/PNC). Focusing on the projects funded by participation in competitive calls from 2020 to 2024, the Rizzoli Orthopedic Institute presents an average of approximately 80 projects each year to apply for the relevant funding. Below is a breakdown of the funding attracted thanks to participation in competitive calls.

From 2022 IOR is competent Authority of the Joint Action Jardin EU4H-2022-JA-05 aimed to develop strategies for systematic dissemination of information on the ERNs, with a specific emphasis on people living with rare diseases as well as the healthcare professionals community (In line with the general objective of the call in the framework of the European Union Programme for Action in the field of Health (EU4Health), area of action "Enhanced European Reference Networks.

Istituto delle Scienze Neurologiche di Bologna (IRCCS ISNB)

The **Istituto delle Scienze Neurologiche di Bologna (IRCCS ISNB)** is an excellence centre devoted to **translational research** from bench to bedside.

Currently, there are more than 300 researchers in over 40 clinical units devoted to adult and pediatric neurology, neurosurgery, neuroradiology, emergency neurology, neurorehabilitation. More than 1.000 square meters are dedicated to **neuroscience research laboratories**, and a **Neuroscience Biobank** which collects biological samples (blood, CSF, DNA etc.), cell lines and brain and skeletal muscle biopsies/tissues. The Institute is fully equipped with infrastructures and equipment for analysis in the field of cellular and molecular biology, including: platforms for next-generation sequencing (Illumina MiSeq, Illumina NextSeq 500, NovaSeq 6000); capillary electrophoresis sequencer (ABI-PRISM 3100); Luminex platform for multiplex protein assays; Simoa technology for ultra-sensitive protein detection; mass spectrometry; high field 3T MR scanner (Siemens Magnetom Skyra), equipped with a 64-channel head/neck coil, angiography equipment solution; Latest generation robotic surgical system; Micro-exoscopy for neurosurgery with intraoperative fluorescence technology; Digital biopsy tool with confocal technology.

The overall **scientific production** in the last 10 years includes 2.131 contributions in neuroscience journals for a total normalised IF of 8.634. Since 2013 the Institute has collected research grants for more than € 62 M from public (Regional Government of Emilia-Romagna, Ministry of Health, Ministry of Economy, EU) and private institutions (research and bank foundations and research associations).

The Institute is engaged in four **Rare Diseases networks**, being recognized as European Reference Centers, within the European Reference Network (ERN) for Rare Diseases (Neurological, Neuromuscular, Epilepsy and Adult solid Tumors), is part of the Italian IRCCS Paediatric Network (among 11 IRCCS), and coordinates the Italian IRCCS Neuroscience and Rehabilitation Network (among 30 IRCCS – Research Hospitals) which involves more than 500 researchers directly engaged in the scientific activities, mainly supported by the Ministry of Health, part of eight National Virtual Institutes (IVN) of pathology: Dementia, PD and Movement Disorders, SM and Neuro-immunological disorders, Rare Diseases Cerebrovascular Disorders, Motoneuron diseases, Epilepsy and Neuroncology. The Institute is member of the Enhancing NeuroImaging Genetics through Meta-Analysis (ENIGMA) Consortium.

HEALTH RESEARCH AREAS

The Institute pursues a comprehensive understanding of neurological diseases by integrating clinical and basic research, with the final aim of developing tools for prevention, early diagnosis and personalized treatment.

Research at ISNB is structured along 4 lines, approved by the Italian Ministry of Health, which includes:

- **Line 1 – Neurological and neuropsychiatric diseases of adulthood and brain ageing**: genetic basis, pathogenetic mechanisms, deep phenotyping and personalized therapy;
- **Line 2 – Neurological and neuropsychiatric diseases of the developmental age**: genetic basis, pathogenetic mechanisms, deep phenotyping and personalized therapy;
- **Line 3 – Emergency neurology**;
- **Line 4 – Neurosurgery, oncology of the nervous system, oncological neuropathology**.

In the context of the brain-body connection the Institute has focused its research activity on **biomarkers of neurodegenerative diseases** in easily accessible tissue such as the skin. As a result it has been developed a new biomarker for neurodegenerative disorders characterized by the abnormal aggregation of alpha-synuclein. The Institute has an internationally recognized leadership in the study of biomarkers (liquoral, blood - liquid biopsy- and imaging), genetics and epigenetics of neurodegenerative diseases and their link to aging. An asset of Institute is the capability to correlate biomarkers of neurodegenerative disorders with in vivo functional connectivity MRI measures.

The **Rehabilitation Bioengineering Laboratory**, advances neurorehabilitation by integrating bioengineering, neuroscience, and clinical research. The lab develops and validates innovative technologies, including robotic systems, brain-computer interfaces, and AI-driven tools to enhance motor and cognitive rehabilitation. Virtual reality applications, wearable sensors, and human-machine interfaces support mobility, cognitive training, and assistive technology development, improving independence and quality of life for individuals with disabilities. By pioneering **intelligent rehabilitation solutions**, the lab

contributes to the future of neurorehabilitation, promoting accessibility, inclusivity, and improved patient outcomes.

The laboratory hosts researchers from the Department of Electrical, Electronic, and Information Engineering "Guglielmo Marconi" (DEI) at the University of Bologna, alongside clinical engineers and researchers from the Institute of Neurological Sciences of Bologna (ISNB).

A major redevelopment project covering 1,500 square meters in Pavilion A is currently underway, with a focus on **neurorehabilitation**. This initiative aims to integrate cutting-edge research with clinical practice, fostering advancements in rehabilitation and patient care.

RESEARCH & INNOVATION COMPETITIVE FUNDING

The Institute, is currently participating in **4 EU Horizon projects** (MAIA, ORCHESTRA, ENLIGHTENME, TRIGGER), 1 EPPermed JTC project (SEI-MITO), 2 JPND projects (PRIONOMICS, STEPUP), 2 ERAPERMED projects (BRAVA, ARTIPRO), 1 IHI project (SYNTHIA), 4 EU4Health Joint Actions (NCD Initiative, EUnetCCC, JANE-2, TEHDAS2), 1 EU4HEALTH-ERN2 (EURACAN 23-27); ISNB has coordinated the PROPAG-AGEING project. The Institute is one of the partners of the AIFA-Ministry of Health INTERCEPTOR project.

ISNB takes part in **national calls funded by the Italian Ministry of Health**: Ricerca finalizzata, (7 funded projects from the last Call, of which 6 as coordinator) and PNRR (10 projects, of which 5 as coordinator), and is awarded research funding by other private national and local organisations such as AIRC, TELETHON, and Banking Foundations.
In 2024 ISNB was involved in 53 ongoing funded nationally and internationally.

Since 2022 ISNB has participated in 69 for-profit clinical trials to evaluate the safety and efficacy of new drugs for use in patients. The Institute is currently undergoing the accreditation procedure for Phase I clinical trials, expected to be completed in 2025.

RESEARCH INFRASTRUCTURES

UNIBO

BIOBANKS & REGISTRIES

The excellence in clinical activity that for decades has characterized **the Bologna research activity in the area of Life Sciences**, provides big opportunities for observational research. Several longitudinal collections of clinical data, biological samples and digital images are available and continuously enriched. They cover frequent clinical conditions with still unsolved diagnostic and therapeutic questions (e.g., inflammatory bowel diseases), as well as rare diseases (e.g., mitochondrial neurological diseases).
Longitudinal collections frequently include data on diet and lifestyle habits, and focus on longevity and healthy ageing. In addition, data on psychological and psychiatric status are collected in specific cohorts of patients.
Clinical expertise that characterises all relevant research groups and departments are complemented by ICT excellence. It provides up-to-date support in data storage, protection and linkage, as well as innovative data-mining and analysis.

START-UPs

Name	Description
Bioverse **Medtech** **Active since 2020**	Bioverse mainly develops and sells biomedical devices and electro-medical equipment designed especially for emergencies and low resource contexts. Bioverse's mission is to reduce the health assistance gap using the Reverse and Frugal Innovation approach.
eSteps **Medical & Sports** **Active since 2020**	eSteps works on contrasting the increase of motor impairment of the lower limbs, offering monitoring solutions before, during and after hospitalization with telemonitoring programmes. Telemonitoring is also applied to sports, with state-of-the-art technology, personalised and sustainable solutions centred around the patient/athlete.
Lite Sport **Sports** **Active since 2020**	LITE produces and sells provenly versatile and effective equipment, designed specifically to improve physical performance. The sensors and software systems that LITE implements in its equipment allow to monitor the workload and training performance in order to plan workout routines based on individual needs obtaining more effective results.

SPIN-OFF COMPANIES

Name	Description
Bionys **Health & Wellness** ***Active since 2024***	BIONYS s.r.l. is a spin-off company engaged in the development, production, and marketing of high technological value products and services based on bio- and nano-technologies. The core business activities of Bionys s.r.l. are the development of innovative diagnostic and therapeutic platforms for medicine and other fields where such innovative products and services may be applicable.
byFlow **Nano-biotech/ bioanalytical chemistry** ***Active since 2010***	B2B company focused on innovative know-how, technologies and methodologies in the R&D sector. byFlow offers novel analysis, technologies, and methods based on analytical separation techniques, particularly flow field-flow fractionation (FFF) in the field of bio/nanoanalytical chemistry. The methods are coupled with multiangle laser scattering (MALS) and fluorescence detection, mass spectrometry, and immunoassays.
Develop Players **Education and Welfare** ***Active since 2021***	Develop Players creates "serious games" (i.e. games developed for learning purposes) with the aim of helping students with specific learning diseases achieve better results at school and in their private life. We also provide courses to schools to equip teachers with better tools to help their students with school difficulties.
Insimili	InSimili develops and markets a high-tech product that aims to improve the drug selection process. By limiting the number of wrongly selected drugs, thus reducing

Health & Wellness ***Active since 2021***	failures in the clinical phase, we intend to make this process faster and more effective. Our customers are small, medium and large pharmaceutical companies, contract research organisations (CROs) and companies operating in the field of biotechnology, which perform in vitro testing for drug selection.
Mhealth Technologies **MedTech/ IoT/ Wearable sensors** ***Active since 2014***	Mhealth Technologies offers wearable solutions to monitor, assess and rehabilitate the motor function. MHT solutions provide relevant results for the physician and effective feedback for users. In this way, users become proactive in their health management.
Mysurable **Cloud/ Health Tech** ***Active since 2018***	Mysurable develops and manages innovative cloud-based technology solutions to measure age-related changes in the functional status of individuals.
OACP **Diagnostics products/ Biotech** ***Active since 2017***	Oncology and Cytogenetic Products provides innovative molecular biology reagents to the oncology diagnostics (FISH/ISH techniques) and COVID-19 diagnostics sectors.
O-DAMP **High-tech personal safety devices** ***Active since 2024***	The company deals with the research, development, production and marketing of hi-tech personal safety devices.
Personal Genomics **Research & Development/ Biotech** ***Active since 2011***	Personal Genomics provides genomic services based on new generation DNA sequencing (NGS). It carries out genomic analysis and interpretation of NGS data for the consumer, research and for the clinical markets, offering the best tools applicable to personalized medicine and pharmacogenomics. Main Personal Genomics objective consists in applying the prevention and treatment of diseases in a personalized way for each individual, based on his genetic heritage.
Stem Sel **Pharma** ***Active since 2013***	Prototype development, engineering, production, and commercialization of an instrumentation (and related consumables) to select and sort human stem cells from adult, "discarded" tissues for applications in regenerative medicine.
Studium Genetics **Health & Wellness** **Active since 2022**	Studium Genetics is a molecular diagnostics company focused on precision medicine. With our groundbreaking genomic and epigenomic testing, we generate reliable and meaningful clinical data about the unique biology of each patient with cancer or neurological disorders. Backed by physicians and institutions, we are shifting the standard of care towards a more innovative and personalized treatment.
Targeting Gut Disease **Pharma** ***Active since 2015***	TGD performs research and development of raw materials based on essential oils for dietary supplements with anti-inflammatory, immunomodulatory, and eubiotic properties. It advises on the development of in vitro, pre-clinical and clinical studies to demonstrate the efficacy of nutraceuticals and fortified foods.

IRCCS AOUBO

In IRCCS AOUBO have established ten research platforms in order to support researchers in cross-cutting scientific fields and to foster interdisciplinary collaborations:

- **Biobank of Research:** The AOUBO Biobank is a public non-profit organisation that collects, preserves and distributes human biological materials and associated data for future research and diagnosis, guaranteeing quality and safety according to international standards in compliance with regulations on consent and protection of sensitive data.
- **Computational Genomics:** The "Computational Genomics Platform" manages the bioinformatics infrastructure for analysing and interpreting genetic variants, providing researchers with advanced tools. Its goal is to integrate genomic data with other 'omics' disciplines for personalised medicine, monitor new sequencing technologies and develop state-of-the-art analysis strategies.

- **Biology and Molecular Medicine:** This structure supports oncology and transplantology research at IRCCS AOUBO, offering scientific expertise and specialised laboratories. These include the NGS Core Lab, dedicated to next-generation sequencing, and the Intestinal Microbiomics Laboratory, which studies the microbiome and its role in health and disease, including cancer. The latter also explores faecal transplantation (FMT) as an innovative therapeutic strategy, facilitating the identification of new biomarkers and microbiome-based treatments.
- **Organ Perfusion and Regeneration – RESTORE:** The RESTORE platform aims to combine clinical expertise in organ transplantation with scientific expertise in cellular, molecular biology and tissue regeneration. The main objectives include the development of protocols for cell, tissue and organ assessment, protection and regeneration, reducing the risks of dysfunction in transplantation and increasing the availability of suitable organs. The platform also conducts basic research on cells and organs derived from animal models and patients, with the aim of applying personalised approaches in the treatment of transplant patients.
- **Preclinical and traslational research in oncology-PRO:** This platform is strategic for developing clinical and translational research projects in oncology.
  The PRO platform has as its targeted goals the identification of predictive factors in the responses to targeted therapies and immuno-therapy through in vitro and in vivo study of: i) mechanisms of development of resistance, ii) identification of molecular processes responsible for metastatic dissemination (e.g. circulating tumor cells), iii)the development of nanotechnology for imaging and targeting of neoplastic cells and for pre- and intraoperative evaluation of neoplasms.
- **Clinical Farmacology:** The Clinical Pharmacology Platform develops personalised therapies for patients through innovative methods that analyse drug concentrations in tissues and biological fluids. It uses pharmacometric models, population pharmacokinetics and Monte Carlo simulations to optimise drug dosage. In addition, he applies pharmacogenetic techniques to identify genetic variants that influence drug metabolisation, especially for cancer and transplant patients. Since 2020, it has been advising on **Therapeutic Drug Monitoring (TDM)** of antibiotics, optimising therapies in real time. The platform promotes the use of personalised approaches to improve therapeutic outcomes and reduce the risk of failure and toxicity.
- **Advanced Imaging:** The IRCCS AOUBO offers an advanced imaging platform that supports research projects and the creation of artificial intelligence models for analysing medical images, with the aim of developing multicentre research networks, particularly at regional level. This is because advances in oncology are currently influenced by new therapies, surgical techniques, and in particular by the evolution of medical imaging. Recent technological innovations, such as low-dose CT tomography, 3 Tesla MRI, multi-parametric ultrasound, and digital PET, have improved diagnostics and treatment, allowing for more precise and rapid tissue characterisation. These techniques not only optimise clinical management, but also support research by integrating the use of multiple radiopharmaceuticals and advanced analyses such as radiomics and machine learning.
- **Immunobiology of transplantation:** The IRCCS AOUBO stands out for its research in transplantation, including organs, cells and advanced therapies such as CAR-T. Research focuses on manipulating the immune system to promote immunotolerance and reduce complications. The Laboratory of Immuno-Biology of Transplantation (IBT) has three main units:
  - Immune System Biology: study of immune cells and advanced techniques for transplantation.
  - Nanobiology: analysis of cellular nanovesicles.
  - Omics: genetic and epigenetic sequencing.

The aim is to personalise treatments, improve diagnosis and develop personalised medicine models for transplant patients.

- **Robotic surgery and innovative technology:** The Surgical and Interventional Platform is focused on the evolution of surgical and interventional technologies, with the aim of developing a sustainable model that integrates innovations efficiently into the healthcare system. The ultimate goal is to improve efficiency and sustainability in the use of surgical technologies.

IRCCS IOR

Nine Research Laboratories on technological and biomedical research:

- **Computational Bioengineering**
- **Movement Analysis and Functional Evaluation of Prosthetics**
- **Medical Technology**
- **Biomedical Sciences and Technologies**
- **Immunorheumatology and Tissue Regeneration**
- **Experimental Oncology**
- **Surgical Sciences and Technologies**
- **Pathologies Infections associated with the Implant**
- **Preclinical Studies for Regenerative Medicine of the Musculoskeletal System**

The **Biological Resource Centre** (**CRB)** is an organization providing biobanking services: the conservation of biological material and related information for research purposes. All activities take place in the same institution in order to guarantee the interoperability between the individual biobanks, homogenizing the procedures for the collection, processing and store of human biological materials in addition to standardizing the methods of collecting and storing information.

The Biological Resources Centre of IOR was born in 2017 within the Scientific Direction to coordinate the activities of three biobanks (collecting and storing biological samples and The CRB-IOR's targets are:

- to collect and store biological samples and information to support both basic and translational research,
- to coordinate and harmonize procedures following national and international guidelines,
- to manage sensitive data in compliance with privacy police protecting the rights of patients and citizens,
- to work in a regional, national and international network thanks to its participation in the European infrastructure BBMRI-ERIC, the National Node BBMRI.it and the participation of individual biobanks in other thematic networks.

The CBR-IOR is composed of the following **three biobanks** and **connected registries**: REM - Multiple Exostoses Disease Registry; RED - Ehlers Danlos Syndrome Registry; ROI - Osteogenesis Imperfecta Registry; ROM - Ollier Disease and Maffucci Syndrome Registry; ReLF - Li Fraumeni and Li Fraumeni Like Syndrome Registry; Primary Malignant Bone Tumor Registry.

- **Genetic Biobank (BIOGEN)**, developing research activity in the field of hereditary diseases;
- **Rheumatology Biobank (RheumaBank)**, enhancing basic and clinical research studies with the aim of having a better understanding of this autoimmune disease;

- **Musculoskeletal Tumor Biobank (BIOTUM)**, collecting samples and associated data from patients suffering from benign and malignant neoplasms of the musculoskeletal system.

The biological samples and the related information are managed by a shared software, protected with individual passwords and usable only by authorized personnel, that allows the complete tracing of the biological material (LIMS ModulBIO).

Bionic limbs Center: the platform with *Scuola Superiore Sant'Anna* Pisa is aimed to develop shared research structures in the field of the development of prosthetic and orthotic devices that combine the most advanced ICT technologies with innovative functionalizing surgeries of the stump, aimed at obtaining better control of prostheses and orthoses; more generally develop collaborative research in the field of rehabilitation of patients with neurological or neuromuscular deficit resulting from trauma.

3D lab *Rizzoli su Misura*: thanks to recent technological advances in the orthopedic field, and not only, accurate preoperative planning through 3D reconstructions of lesions and production of bone or joint substitutes through digital manufacturing are possible in order to improve patient treatments in the direction of personalized surgical approaches. Starting from CT or MRI images, it is possible to create biomodels useful in the diagnostic phase, as well as plan surgeries and design custom-made prostheses based on the patient's morphological characteristics and the type of surgery, in a constant comparison between the various technologists and the surgeon who will perform the surgery.

The Electron Microscopy Platform (PME) is a research infrastructure designed to support the scientific activity of researchers at IOR and other public and private institutions that require collaboration, consultancy or services.

Applied and Translational Research center (ATRc) is a function of the Scientific Direction, aimed to rapidly advance scientific research (i.e. on orthobiology) by transferring its results to clinical practice in the shortest possible time, in order to improve the quality of life of patients suffering from muscular-skeletal pathologies.

IRCCS ISNB

The **translational and basic neurosciences research** at ISNB is developed thanks to the following Laboratories: Neurogenetics (exome and genome NGS sequencing), Molecular and cell biology (iPSCs, gene editing, organoids), Neuropathology of neurodegenerative diseases (pathological and, Neuroimmunology and Neuromuscular disorders, Proteomics and Metabolomics (mass spectrometry), Brain Aging (geroscience: epigenetics, -omics), and Neuroimaging (pipelines of structural and functional MR imaging analysis, radiomics, connectomics).

The following Research laboratories, transversal to the Institute's activities, have recently been set up in partnership with UNIBO, thanks to a collaboration agreement signed between the two institutions, the creation of new spaces, the recruitment of health researchers and collaborators:

- **Laboratory of data science and bioinformatics**,
- **Laboratory of proteomics, metabolomics and bioanalytical chemistry**,
- **Laboratory for bioengineering of rehabilitation**,

- **Laboratory of experimental neuropsychology**,
- **Laboratory of brain ageing**.

In 2022, the **Institute's Biobank** was established as a non-profit infrastructure, functional part of the IRCCS - ISNB, and aimed at collecting, processing, storing and distributing human-derived biological samples (biosamples) of different types, in association with personal, clinical and genetic data of the donors. The samples and data in the Biobank are used for research purposes in the field of neurology, for diagnostic purposes, or for the development of targeted therapies. Furthermore, as part of a development project led by the IRCCS IOR, it is planned to extend the institute's Biobank infrastructure at the Bologna Technopole.

RESEARCH RESULTS

UNIBO

UNIBO is the owner of **383 health-related active patents**, connected to **54 inventions**, listed below.

Area	Titles	Publication #	Pub. Year
Neuroscience and Neurodegenerative Diseases	A flavonoid agonist of the Trkb receptor for BDNF improves hippocampal neurogenesis and hippocampus-dependent memory in the Ts65Dn mouse model of DS	US2019315709	2019
	Dual inhibitors for the treatment of neurodegenerative disorders and Alzheimer's disease	WO2015189830	2015
	Method for classifying a lesion as a uterine leiomyoma or as a uterine leiomyosarcoma	WO2013107910	2013
	Method for detecting a target genome	EP22747141.4	2024
	Method for determining a head and neck squamous cell carcinoma	WO2017153834	2017
	Method for estimating a conforming position of an eye, device for ophthalmic examinations implementing such method, and related electronic kit for updating an ophthalmic device	US2014093731	2014
	Method for estimating chronological age from DNA methylation levels in human dental tissue	US10889560	2021
	Method for evaluating the capacity of a serum to neutralize a virus	US20100189775	2010
	Method for the diagnosis of non-celiac gluten sensitivity	WO2017153834	2017
	Method for the molecular diagnosis of rare molecular subtypes in gastrointestinal stromal tumors (GIST)	WO2014167494	2014
	Method for the prognosis of melanoma	WO2020/070248	2020
Diagnostic and Monitoring Tools	Compositions, devices, and methods for in vitro control of the chemical microenvironment in cell cultures	WO2015189830	2015
	Device for cell cultures	WO2015189830	2015
	Device for sampling and detecting a pathogen in the air	WO2015189830	2015
	Diagnostic biomarker for inflammatory myopathy	WO2015189830	2015
	Impedance system for assessing muscle mass	WO2015189830	2015
	Integrated device for rapid dosing, mixing, and nebulization of chemical substances in suspension for cleaning and sanitizing surfaces and environments	WO2015189830	2015
	Locator device for the pituitary fossa	WO2015189830	2015
	Microstructured device and method of production thereof	WO2015189830	2015
	Ocular device for controlled release of an ophthalmic active ingredient, methods for producing such an ocular device, and its use for the treatment or prevention of ocular diseases and disorders	WO2015189830	2015
	Simulated blood composition	WO2015189830	2015
	System for detecting ionizing radiation emitted by sources such as radiopharmaceuticals, radioactive samples, and similar, detection sensors, and detection method	WO2015189830	2015
	System for monitoring manual activity levels for hand and wrist and monitoring method	WO2015189830	2015
Orthopedic and Prosthetic Devices	Device for ankle mobilization	WO2010128485	2010
	Device for interfacing filamentous or fibrous structures with real or simulated biological tissue	WO2010128485	2010
	Device for positioning organic tissue and related apparatus	WO2010128485	2010
	Device for the collection and analysis of a biological fluid	WO2010128485	2010
	ESR-type prosthetic implant and method for adjusting the prosthetic implant	WO2010128485	2010

	Heart valve prosthesis with integrated electronic circuit for measuring intravalvular electrical impedance, and system for monitoring the functionality of the prosthesis	WO2010128485	2010
	Improved orthopedic device	WO2010128485	2010
Cancer and Tumor Treatments	Bacteriophages and their uses for targeting GD2-expressing tumor cells	WO2009144755	2009
	Biomaterial coated gold nanostructures for photoacoustic imaging and photothermal therapy of tumor lesions	WO2015189830	2015
	Bionanofenretinide as a new antitumor formulation	WO2014167494	2014
	Gold nanocylinders conjugated with highly specific aptamers for bladder cancer	WO2015189830	2015
	Herpes simplex virus (HSV) with modified tropism, uses and process of preparation thereof	WO2009144755	2009
	Herpesvirus with modified glycoprotein B	WO2015189830	2015
	Herpesvirus with modified glycoprotein D	WO2015189830	2015
	Herpesvirus with modified glycoprotein H for propagation in a cell	WO2015189830	2015
	Nanoparticles to improve the analytical signal	WO2014167494	2014
	New constructs for gene therapy	WO2015189830	2015
	Retargeted herpesvirus with a glycoprotein H fusion	WO2015189830	2015
Additional Health-Related Patents	Method for estimating a conforming position of an eye, device for ophthalmic examinations implementing such method, and related electronic kit for updating an ophthalmic device	US2014093731	2014
	Method for estimating chronological age from DNA methylation levels in human dental tissue	US10889560	2021
	Method for evaluating the capacity of a serum to neutralize a virus	US20100189775	2010
	Method for the diagnosis of non-celiac gluten sensitivity	WO2017153834	2017
	Method for the interactive parallel processing of data on a cluster with the graphic input/output on a visualization device	WO2014076730	2014
	Method for the molecular diagnosis of rare molecular subtypes in gastrointestinal stromal tumors (GIST)	WO2014167494	2014
	Method for the molecular diagnosis of rare molecular subtypes in gastrointestinal stromal tumors (GIST)	WO2014167494	2014
	Method for the prognosis of melanoma	WO2020/070248	2020
	Pharmaceutical composition and pharmaceutical kit for the treatment of hepatocellular carcinoma	WO2009013569	2009
	Portable device based on immobilized cells for the detection of analytes	WO2010/092539A1	2010
	Silica nanoparticles doped with multiple dyes featuring highly efficient energy transfer and tunable stokes-shift	WO2012/049657	2012
	Use of a coordination complex or compound for the measurement of temperature	WO2012056415	2012

IRCCS AOUBO

The research activities of IRCCS AOUBO are also carried out through the promotion and technology transfer of its patents, including those in co-ownership with other institutions, such as University of Bologna. Thanks to the multidisciplinary nature of the research in IRCCS AOUBO, the portfolio of patents and other intellectual property titles includes innovations spanning various scientific-technological fields, many of which are also protected internationally.

1) METHOD FOR CLASSIFYNG A LESION AS A UTERINE LEIOMYOMA OR AS A UTERINE LEIOMYOSAR-COMA
2) DEVICE FOR PLACEMENT OF ORGANIC TISSUE AND RELATED APPARATUS
3) BLOOD SERUM FOR USE IN THE TREATMENT OF NEURODEGENERATIVE OPHTHALMOLOGICAL DIS-EASES

4) METHOD FOR EX VIVO DIAGNOSIS OF GLIOMAS BASED ON NEXT GENERATION SEQUENCING
5) ADJUVANT BEVERAGE
6) METHOD AND KIT FOR DIAGNOSIS OF GLUTEN SENSITIVITY NOT ASSOCIATED WITH CELIAC DISEASE
7) DIAGNOSTIC BIOMARKER OF INFLAMMATORY MYOPATHY
8) NATURAL CONTRAST MEDIUM FOR CHOLANGIOPANCREATOGRAPHIC MAGNETIC RESONANCE IMAGING

IRCCS IOR

Rizzoli Institute has a long experience in **patenting innovative devices and methods in the orthopedic field and houses a Technology Transfer Office (TTO)**, whose functions also include patent valorization through market and potential stakeholder research, participation in events with a high level of industry attendance, raising funds for its divulgation activities, and publishing technical data sheets on professional intellectual property divulgation websites.

To date, the **IOR portfolio** counts 9 patents, 6 of them are co-owned with other partners and 3 are fully owned by the Institute:

- METHOD FOR DIAGNOSING INCREASED LOCAL AND/OR SYSTEMIC BONE REABSORPTION
- NEW MOLECULES FOR BONE TISSUE REGENERATION
- ARTICULATED FOOT-ANKLE ORTHOSIS WITH FLOATING ROTATION AXIS
- EXOSOMES AND DERIVED USES
- DEVICE FOR RECONSTRUCTION OF A CRUCIATE LIGAMENT
- MATERIAL AND SYSTEM FOR THE THERAPEUTIC TREATMENT OF JOINTS
- POSITIONING DEVICE FOR ULTRASOUND PROBE
- DEVICE FOR MOBILIZATION OF THE ANKLE
- VERTEBRAL PROSTHESIS

IOR's TTO has been awarded by the Ministry of Economic Development's call for proposals for the enhancement of patents of Public Research Institutions through Proof of Concepts (PoC) projects, in order to increase the level of technological maturity of the IOR's inventions. This opportunity will push the IOR's intellectual property dissemination activities by modernizing the TTO communication style and adapting it to the latest industry standards.

IRCCS ISNB

ISNB has recently implemented a **Technology Transfer Office (TTO)** responsible for all the activities related to TT, namely: protection of research results; IPR management and exploitation; development of new partnerships with companies and other institutions (public and/or private). These collaborations intend to foster innovation by leveraging the strengths of each party involved.
In this initial stage the main objective for ISNB is to develop a specific set of expertise and resources to support researchers in each step of the TT process, from the identification of generated inventions to their protection, development and exploitation.

BOLOGNA IN THE EUROPEAN HEALTH RESEARCH NETWORKS

The Bologna research metropolitan hub is an active part of several European networks and associations, most of them greatly relevant to Health. Some of the main networks in which the four institutions take part are listed below.

Name	*Membership* / Description
Alliance Against Cancer (ACC) (Home - Alleanza contro il cancro**)**	*AOUBO Ordinary member* *IRCCS AOUBO is part of the Italian "Alliance Against Cancer (ACC)" network and is node of the "Rete Nazionale dei Tumori Rari (RNTR). ACC, the National Oncology Network founded in 2002 by the Ministry of Health. ACC mission is to lead technological and organizational innovation from basic research to clinical practice, raising and unifying the level of care, treatment, and rehabilitation of cancer patients throughout the country.*
Big Data Association (Associazione Big Data**)**	*Member (AOUBO, ISNB)* *The IRCCS AOUBO has joined research networks including the Big Data Association, established in 2018. The purpose of the association is the promotion of a community founded in Emilia-Romagna by research centres and infrastructures of excellence in the field of supercomputing (High Performance Computing) and the treatment of Big Data.*
Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)	*Full member (UNIBO)* BBMRI-ERIC is a European research infrastructure for biobanking, bringing together researchers, biobankers, industry, and patients to boost biomedical research.
CLUST-ER (Clust-ER Health)	*Full member (UNIBO, AOUBO, IOR, ISNB)* *The Clust-ER Industrie della Salute e del Benessere (Clust-ER Health) is the association recognized and supported by the Emilia-Romagna Region, created to encourage the development of innovation projects and policies in the Health and Wellness sector, recognized as a strategic sector for regional development, and to maximize the social and economic effects of these projects in the regional territory.*
Cutting Edge Cancer Research Services Across Europe (canSERV)	*Associate Member (UNIBO, AOUBO)* canSERV is an EU-funded project providing interdisciplinary and customised oncology services across the entire cancer continuum.
European Reference network for rare adult solid cancers (ERN EURACAN)	*Full members (AOUBO, IOR, ISNB)* *EURACAN is the European Reference Networks for all rare adult solid cancers.The EURACAN network comprises 106 highly specialised cancer centres grouped as Full Members and Affiliated Partners across 26 European countries.*
European Reference network for Rare Lung Diseases (ERN-LUNG**)**	*AOUBO Healthcare provider* *ERN-LUNG is a patient-centric network of European healthcare providers and patient organisations, committed Europe-wide and globally to reducing morbidity and mortality from rare lung diseases in people of all ages through patient care, advocacy, education, research and knowledge-sharing.*
European Refe rence network forRare Endocrine Conditions (Endo-ERN**)**	*AOUBO Reference center* *The European Reference Network on rare endocrine conditions (Endo-ERN) aims to improve access to high-quality healthcare for patients with rare hormonal disorders.*

European Reference network for Rare and Undiagnosed Skin Disorders (ERN-Skin)	*AOUBO Reference Centre* *The ERN-Skin covers the medical field of rare, complex and undiagnosed skin disorders in children and adults.*
European Reference network for Rare Congenital Malformations and Rare Intellectual Disability (ERN-ITHACA)	*AOUBO Full Member* *ERN ITHACA is the European Reference Network for rare malformative conditions, intellectual disabilities and neurodevelopmental disorders.*
European Reference Network for all patients with one of the rare genetic tumour risk syndromes (ERN GENTURIS)	*AOUBO Full Member* *ERN GENTURIS is the European Reference Network for all patients with one of the rare genetic tumour risk syndromes (genturis).*
European Reference network for Rare kidney diseases (ERN-RARE Kidney)	*AOUBO Reference center* *ERKNet is the European Reference Network for Rare Kidney Diseases, including pediatric and adult nephrology centers in 24 European countries.*
European Reference network for Rare uro-recto-genital diseases and complex conditions (ERN- eUROGEN)	*AOUBO Full Member* *ERN eUROGEN is the European Reference Network (ERN) for rare uro-recto-genital diseases and complex conditions.*
European Reference network for uncommon and rare diseases of the heart (ERN - GUARD-Heart)	*AOUBO Full Member* *ERN GUARD is the European Reference Network focused on genetically transmitted heart disease The mission of ERN GUARD-Heart is to facilitate access to diagnosis and treatment of rare and complex diseases of the heart in adult and paediatric patients across the European Union.*
European Reference network for Rare hepatological diseases (ERN - RARE-LIVER)	*AOUBO Full member* *ERN RARE-LIVER is a Europe-wide network for centres of excellence in the clinical management of rare liver disease in adults and in children.*
European Reference network for Rare Haematological diseases (ERN – EuroBloodNet)	*AOUBO Full Member* *ERN-EuroBloodNet is the European Reference Network on Rare Hematological Diseases.*
European Reference network for Rare hereditary metabolic disorders – (MetabERN)	*AOUBO Healthcare provider* *MetabERN is a Europe-wide network of centres of excellence in the field of Hereditary Metabolic Disorders*
European Reference network for Rare neurological diseases – (ERN-RND)	*ISNB Member* *The **ERN**-RND is a **European Network** established by the EU to support patients and families affected by rare **neurological** diseases (RND)*

European Reference network for Rare neuromuscular diseases –(ERN-NMD)	*ISNB Member* ***EURO-NMD** is a European Network for the thematic grouping of rare neuromuscular diseases (NMDs), a broad group of related disorders.*
European Reference network for Rare epilepsies –(EpiCARE)	*ISNB Member* *EpiCARE home page: EpiCARE is the **European Network** for rare and complex epilepsies.*
Italian IRCCS paediatric network (IDEA)	*ISNB Member* *The Italian Paediatric Associati) was founded in 2017 at the Ministry of Health with the aim of promoting and protecting health in childhood and adolescence,*
Italian IRCCS Neuroscience and Rehabilitation Network (RIN)	*ISNB Member* *ISNB coordinates the Italian IRCCS Neuroscience and Rehabilitation Network (n. 30 IRCCS – Research Hospitals) which involves more than 500 researchers directly engaged in the scientific activities, mainly supported by the Ministry of Health*
Italian IRRCS RAMS	*Coordinator (IOR)* *IRCCS Network on research on musculoskeletal diseases*
Italian IRCCS AGING	*Full Member (IOR)* *IRCCS network on research on aging – related diseases*
Europe's digital infrastructure for brain research (EBRAINS)	*ISNB Associate* *EBRAINS is a collaborative digital European Research Infrastructure that enhances and accelerates progress in neuroscience and brain health.*
Enhancing NeuroImaging Genetics through Meta-Analysis Consortium (ENIGMA)	*ISNB Member* *The ENIGMA Consortium brings together researchers in imaging genomics to understand brain structure, function, and disease, based on brain imaging and genetic data.*
European Life Sciences Infrastructure (ELIXIR)	*Node Institute (Unibo)* ELIXIR is an intergovernmental organisation that brings together life science resources from across Europe. These resources include databases, software tools, training materials, cloud storage and supercomputers.
European Health Telematics Association (EHTEL)	*Working member (UNIBO)* EHTEL (the European Health Telematics Association) is a unique pan-European multidisciplinary stakeholder organisation, which brings together corporate, institutional, and individual actors dedicated to the improvement of healthcare delivery through digital health.
European Infrastructure For Translational Medicine (EATRIS)	*Associate Member (Rizzoli Orthopaedic Institute)* EATRIS is the European infrastructure for translational medicine. It brings together resources and services for research communities to translate scientific discoveries into benefits for patients.
European Paediatric Translational Research	*Full member (UNIBO)* EPTRI is a pan-European initiative involving hundreds of research units gathered together to boost the paediatric research ecosystem and provide services for the development of medicines for children.

Infrastructure (EPTRI)	
European Reference Network for all patients with one of the rare genetic tumour risk syndromes (ERN GENTURIS)	*Full member (AOUBO)* ERN GENTURIS is the European Reference Network (ERN) for all patients with one of the rare genetic tumour risk syndromes (genturis).
European Reference network for rare adult solid cancers (ERN EURACAN)	*Full members (University Hospital of Bologna, Rizzoli Orthopaedic Institute, Institute of Neurological Sciences)* EURACAN is the European Reference Networks for all rare adult solid cancers.The EURACAN network comprises 106 highly specialised cancer centres grouped as Full Members and Affiliated Partners across 26 European countries.
European Technology Platform Nanomedicine (ETPN)	*Full member (UNIBO)* ETPN is an initiative to strengthen Europe's capabilities in nanomedicine, focusing on the application of nanotechnology in healthcare.
European Working Group of Myelodysplastic Syndrome and Severe Aplastic Anemia in children and adolescents (EWOG-MDS/SAA)	*Full member (UNIBO)* An international cooperative study group dedicated to improving care and outcomes for children and adolescents with myelodysplastic syndromes and severe aplastic anemia.
GUILD - Deans of Health	*Full member (UNIBO)* The Deans of Health group is composed of representatives with a strategic remit for health research in members' medical schools.
Healthcare Information and Management Systems Society (HIMSS)	*Associate Member (UNIBO)* HIMSS is a global advisor and thought leader supporting the transformation of the health ecosystem through information and technology.
HL7 Italia	*Full member (UNIBO)* An affiliate of HL7 International, responsible for localizing health IT standards in Italy and promoting modernization of Italian health IT.
Innovation Life Sciences Hub	*AOUBO member* *Innovation Life Sciences Hub is the first virtual hub of excellence with the goal of pooling research, products and services by encouraging the exchange of know-how and sharing of results. Promoted by the University of Pittsburgh Medical Center, it aggregates 25 entities including italian regions and other international universities and research centers and enterprises.*
Microbiome Support Association	*Full member (UNIBO)* Promotes microbiome understanding and applications as key drivers of food security, One Health, and human well-being1516.
ISOC	*Full Member IOR* *International Society of Orthopedic Centers with the mission to facilitate the exchange of ideas and best practices among the premier specialty orthopaedic institutions in the world and to collaborate on patient care, education, and research-based programs to advance improvements in orthopaedic care on a global scale.*
DARE FOUNDATION	*Full Member (UNIBO, AOUBO, IOR, ISNB)* *Digital Lifelong Prevention. Artificial intelligence, high-performance computing, big data analytics, wearables and digital twins – to significantly improve the speed, accuracy and effectiveness of healthcare prevention.*

Netval	*Full Member (IOR)* *Valorisation of public research, also and above all through the creation of a community of professional TTO managers*
INCIPIT	*Full Member IOR* *network composed by the main Italian Paediatric Hospitals and Scientific Institutes for Research, Hospitalization and Health Care (IRCCS) and other Institutions, aimed to promote and support the conduction of all types of clinical trials in the paediatric population by all kinds of sponsor (academic investigators, pharmaceutical industries, contract research organisations*
Italian Sarcoma Group	*Full Member IOR* *non-profit association recognized by the Ministry of Health aimed at improving research and care of patients of all ages affected by soft tissue and bone sarcomas and gastrointestinal stromal tumors (GIST).*
AIEOP	*Full Member IOR* *Italian Association of Pediatric Hematology and Oncology. .* *The main objective of THE NETWORK is to improve the care and assistance of children affected by tumors, hematological disorders or immunodeficiencies and to promote research in this field.*
Virtual Physiological Human Institute for Integrative Biomedical Research (VPHI)	*Full member (UNIBO)* The VPH Institute is an international non-profit organisation incorporated in Belgium, whose mission is to ensure that the Virtual Physiological Human is fully realised, universally adopted, and effectively used both in research and clinic.

OUR EXPERTISE AND INTERESTS ON THE 2026 TOPICS

This section presents the expertise and research assets of our researchers, organised by the topic of their interest.

Destination 1. Staying healthy in a rapidly changing society

HORIZON-HLTH-2026-01-STAYHLTH-02: Behavioural interventions as primary prevention for Non-Communicable Diseases (NCDs) among young people

Research Group	**Prof. Antonio Cicchella** Dep. Quality of Life Studies
Expertise in relation to the topic	Expertise in hormonal research in children and adolescents, growth and physical performance. Physical testing in children, motion analysis in children with special reference to walking biomechanics in neuromuscular diseases. ▪ Cicchella A, Stefanelli C, Massaro M. Upper Respiratory Tract Infections in Sport and the Immune System Response. A Review. Biology (Basel). 2021 Apr 23;10(5):362. doi: 10.3390/biology10050362. PMID: 33922542; PMCID: PMC8146667. ▪ Cicchella A. Recommendations for Resuming PA after Prolonged Rest in Children and Adolescents: A Systematic Integrative Review of Relevance for Immunity. J Funct Morphol Kinesiol. 2022 Jun 2;7(2):47. doi: 10.3390/jfmk7020047. PMID: 35736018; PMCID: PMC9224580. ▪ Cicchella A. Response to the Commentary: "Methodological Considerations for Analysing the Relation of Physical Activity with Leptin Levels in Children: Comment on the Study by Cicchella et al. (2013)" by David Jiménez-Pavon. Percept Mot Skills. 2016 Feb;122(1):220-6. doi: 10.1177/0031512516631052. Epub 2016 Feb 1. PMID: 27420317.

Research Group	**Prof. Antonello Lorenzini** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	PhD in Biochemistry and Physiopathology of Aging. Our group focuses on **nutrition and healthy lifestyles**. Regarding the Horizon calls, we emphasized our active collaboration with Prof. Lars Fadnes' group at the University of Bergen to expand the scope of their "**Food for Healthy Life**" **calculator** (F4HL: http://v2.food4healthylife.org/). This calculator currently allows, after analyzing an individual's diet, to prioritize the changes needed to make the diet healthier and therefore capable of extending the individual's longevity. Towards the goal of expanding the calculator's capabilities so that it will also produce **risk estimates of NCDs**, the collaboration has already produced

	three umbrella reviews (1, 2, 3), and it has others in progress. The calculator could form the basis of a preventive tool for projects dedicated to the prevention of NCDs both in young people (12-25 years) and in adults. A second project, which can be easily linked to the previous one, is a project on **Artificial intelligence**, it is a project born in Bologna between the PI's group and the CINECA supercomputing consortium. This collaboration aims to develop a tool that uses **Natural Language Processing (NLP)** to semi-automate the construction of meta-analyses from scientific literature, with particular emphasis on optimizing text and data mining in the biomedical and specifically in the epidemiological field. The first manuscript related to this tool has been submitted (4) and we have two other publications in progress that exploit this new tool. ▪ Umbrella Review of Systematic Reviews and Meta-Analyses on Consumption of Different Food Groups and Risk of Type 2 Diabetes Mellitus and Metabolic Syndrome. Banjarnahor RL, Javadi Arjmand E, Onni AT, Thomassen LM, Perillo M, Balakrishna R, Sletten ISK, Lorenzini A, Plastina P, Fadnes LT.J Nutr. 2025 May;155(5):1285-1297. doi: 10.1016/j.tjnut.2025.03.021. Epub 2025 Mar 22.PMID: 40122387 ▪ Umbrella Review of Systematic Reviews and Meta-Analyses on the Consumption of Different Food Groups and the Risk of Overweight and Obesity. Kristoffersen E, Hjort SL, Thomassen LM, Arjmand EJ, Perillo M, Balakrishna R, Onni AT, Sletten ISK, Lorenzini A, Fadnes LT. Nutrients. 2025 Feb 13;17(4):662. doi: 10.3390/nu17040662.PMID: 40004990 ▪ Umbrella Review of Systematic Reviews and Meta-analyses on Consumption of Different Food Groups and Risk of All-cause Mortality. Onni AT, Balakrishna R, Perillo M, Amato M, Javadi Arjmand E, Thomassen LM, Lorenzini A, Fadnes LT.Adv Nutr. 2025 Apr;16(4):100393. doi: 10.1016/j.advnut.2025.100393. Epub 2025 Feb 15.PMID: 39956388 ▪ TextAlchemy: an NLP tool to accelerate and semi-automate data extraction, validated in the nutritional field. Rooshan Saleem Butt, Matteo Perillo, Michele Visciarelli, Giorgio Pedrazzi, Marco Amato, Andrea Galassi, Rajiv Balakrishna, Anindita Tasnim Onni, Lars Thore Fadnes, Paolo Torroni, Roberta Turra, Antonello Lorenzini; *submitted*.

Research Group	**Prof. Stefania Toselli** Dep. Life Quality Studies
Expertise in relation to the topic	As a physical anthropologist, I have solid experience in assessing and monitoring body weight status, body composition, body image perception, and lifestyle behaviors in children and adolescents. My methodological skills include anthropometric and body composition assessments (using anthropometry, BIA, and plethysmography), the use of validated tools for behavioral and psychosocial evaluation (KIDMED, IPAQ, body image questionnaires, and silhouette scales), and the design of evidence-based behavioral and educational interventions.

Operationally, my work focuses on the design, implementation, and evaluation of multilevel interventions that combine nutritional counseling, motivational interviewing, structured physical activity, and family education, supported by systematic data collection and continuous outcome monitoring.
I am currently developing second-level behavioral protocols for overweight and obese children and adolescents, based on EOSS (Edmonton Obesity Staging System) criteria and metabolic stabilization, in close collaboration with Local Health Authorities (ASL) and primary care pediatricians. In addition, I aim to integrate digital health tools, including remote monitoring systems, mobile applications for tracking diet, physical activity, and sleep, and digital platforms for motivational counseling, to enhance accessibility, personalization, engagement, and adherence to intervention programs.
This experience is supported by peer-reviewed scientific publications demonstrating my ability to conduct applied research and to implement structured, evidence-based prevention programs in clinical and community settings. The integration of clinical, behavioral, and digital competencies provides a solid and scalable contribution to the objectives of Cluster 1 "Health," particularly in the areas of child and adolescent health promotion, lifestyle behavior change, and the prevention of non-communicable diseases (NCDs).

Selected Publications:

- NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. Lancet. 2024 Mar 16;403(10431):1027-1050. doi: 10.1016/S0140-6736(23)02750-2. Epub 2024 Feb 29.
- NCD Risk Factor Collaboration (NCD-RisC).Diminishing benefits of urban living for children and adolescents' growth and development. Nature. 2023 Mar;615(7954):874-883. doi: 10.1038/s41586-023-05772-8. Epub 2023 Mar 29.
- Esposito F, Sanmarchi F, Marini S, Masini A, Scrimaglia S, Adorno E, Soldà G, Arrichiello F, Ferretti F, Rangone M, Celenza F, Guberti E, Tiso D, Toselli S, Lorenzini A, Dallolio L, Sacchetti R. Weekday and Weekend Differences in Eating Habits, Physical Activity and Screen Time Behavior among a Sample of Primary School Children: The "Seven Days for My Health" Project. Int J Environ Res Public Health. 2022 Apr 1;19(7):4215. doi: 10.3390/ijerph19074215.
- Toselli S, Belcastro MG. Participation in sports, body composition, and fitness characteristics in children according to ethnic background. Scand J Med Sci Sports. 2017 Dec;27(12):1913-1926. doi: 10.1111/sms.12843. Epub 2017 Feb 24.
- Toselli S, Zaccagni L, Celenza F, Albertini A, Gualdi-Russo E. Risk factors of overweight and obesity among preschool children with different ethnic background.

	Endocrine. 2015 Aug;49(3):717-25. doi: 10.1007/s12020-014-0479-4. Epub 2014 Nov 25. ▪ Gualdi-Russo E, Toselli S, Masotti S, Marzouk D, Sundquist K, Sundquist J.Health, growth and psychosocial adaptation of immigrant children. Eur J Public Health. 2014 Aug;24 Suppl 1:16-25. doi: 10.1093/eurpub/cku107.

Research Group	**Prof. Alessia Tessari** Dep. Psychology
Expertise in relation to the topic	Our group offers a combination of rigorous evidence-based behavioral science, deep expertise in the cognitive design of digital health technologies (including gamification and AI integration), and a robust network for successful implementation and evaluation in real-world settings. In particular, the research group's expertise is at the intersection of health science, behavioral change, and cutting-edge technology, providing a holistic framework for effective primary prevention of Non-Communicable Diseases (NCDs). We specialize in the design, implementation, and rigorous evaluation of tailored interventions (including Randomized Controlled Trials and clinical protocols) focused on health promotion and NCD primary prevention. Our core expertise lies in studying the effects of various types of physical activity on cognitive processes across the lifespan to develop highly effective physical training programs. We design interventions to improve biomedical markers and psychosocial well-being, translating scientific knowledge into lasting healthy habits and behavioral change, particularly among young people. We also have proven expertise in developing user-centric and friendly Digital Tools for effective self-monitoring and engagement. This includes the strategic use of gamification elements to motivate sustained use. We also specialize in the cognitive design and usability of digital tools, ensuring they are intuitive and effective. For example, we co-designed and developed a user-friendly assistive AI with end-users and stakeholders (Horizon 2020 MAIA project). Our focus on cognitive design and usability is essential for creating tools that empower young people for self-management, essential for successful interventions. We maintain active, established collaborations that ensure real-world impact through: collaborations with local and European companies to enhance the accessibility and usability of digital apps; partnerships with several regional and extra-regional local health authorities for seamless implementation and scaling of prevention programs. ▪ Ventura et al. (2023). Co-designing an interactive artificial intelligent system with post-stroke patients and caregivers to augment the lost abilities and improve their quality of life: a human-centric approach. *Frontiers in Public Health*, *11*, 1227748. ▪ Ottoboni et al. (2022). A Multifunctional Adaptive and Interactive AI system to support people living with stroke,

	acquired brain or spinal cord injuries: A study protocol. *PloS one*, *17*(4), e0266702. ▪ Ottoboni et al. (2021). The effect of structured exercise on short-term memory subsystems: new insight on training activities. *International Journal of Environmental Research and Public Health*, *18*(14), 7545. ▪ Russo et al. (2021). The positive impact of physical activity on working memory abilities: Evidence from a large Italian pre-adolescent sample. *Journal of Human Sport and Exercise*, *16*(Proc2), 277-288. ▪ O'Brien et al. (2021). Multisensory perception, verbal, visuo-spatial and motor working memory modulation after a single open-or closed-skill exercise session in children. *Journal of Cognitive Enhancement*, *5*(2), 141-154. ▪ Masini et al. (2020). Active breaks: A pilot and feasibility study to evaluate the effectiveness of physical activity levels in a school based intervention in an Italian primary school. *International journal of environmental research and public health*, *17*(12), 4351.

Research Group	**Prof. Milena Raffi** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	The University of Bologna research group develops and evaluates behavioural and educational interventions for the primary prevention of non-communicable diseases (NCDs) among children and adolescents. Building on the EU4Health-funded DUSE project, the team applies an interdisciplinary, multi-level approach combining health education, behavioural science, and community engagement. **Expertise and methodological capacity:** • Behavioural change and health literacy in young populations • Educational design addressing diet, physical activity and emotional well-being • Participatory and co-creation approaches with schools, families, and health professionals • Quantitative and qualitative assessment of behavioural and psychosocial outcomes • Digital and gamified learning tools for health education **Activities offered for this call:** • Design and piloting of school-based behavioural interventions • Co-creation workshops with teachers and youth • Evaluation of intervention impact through mixed-methods research (pre/post behavioural assessments, validated lifestyle questionnaires, focus groups) • Development of training packages for educators and dissemination of results through open-access materials and policy briefs **Sought role:** Partner or WP leader for behavioural intervention design, implementation and evaluation.

	Keywords: Behavioural interventions, health education, youth, NCDs prevention, lifestyle change, schools, co-creation, gamification, nutrition, physiology. **Funding (main projects related to the topic)** • **2023** Counteracting Diabetes USing interdisciplinary Educative programs – DUSE. European program EU4H (Grant Agreement n. 101128641). • **2023** Standing posture during optic flow stimulation; the ideal predictor for early screening of microvascular complications in type 2 diabetes? Italian program PRIN. • **2020** Coordinator of European project "Exercise for diabetes: beneficial effect of new educational and physical activity programs – BE-NEW". Developed in the framework of Erasmus+ Knowledge Alliances Project BE-NEW 622371-EPP-1-2020-1-IT-SPO-SCP **Publications (main articles related to the topic)** • Arampatzakis V, Sevetlidis V, Derri V, Raffi M, Pavlidis G. (2025). Towards Reshaping Children's Habits: Vitalia's AR-Gamified Approach. Information, 16(7), 606. • Laffi A, Persiani M, Piras A, Meoni A, Raffi M. (2025). Effectiveness of Wearable Technologies in Supporting Physical Activity and Metabolic Health in Adults with Type 2 Diabetes: A Systematic–Narrative Hybrid Review. Healthcare, 13(19), 2422. • Negri V, Mingotti A, Tinarelli R, Laffi A, Raffi M, Piras A. (2025) Enhancing Diabetic Retinopathy Diagnosis with Machine Learning: A Random Forest Approach Using Muscle Response Data. IEEE Medical Measurements & Applications (MeMeA), Chania (GR), 2025, pp. 1-6 • Piras A, Raffi M (2023) A Narrative Literature Review on the Role of Exercise Training in Managing Type 1 and Type 2 Diabetes Mellitus. Healthcare 2023, 11:2947. • Piras A, Perazzolo M, Scalinci SZ, Raffi M (2022) The effect of diabetic retinopathy on standing posture during optic flow stimulation. Gait & Posture 95: 242 - 248.

Research Group	**Dr Gabriele Egidy Assenza** IRCCS, Azienda Ospedaliera-Universitaria di Bologna
Expertise in relation to the topic	Dr Egidy Assenza and his research team bring a strong foundation in clinical and translational research, with experience in complex patient cohorts (children and adult with congenital heart disease) and interdisciplinary work, and are now positioned to extend their expertise into the domain of behavioural and multi-domain interventions.
	Specific Activities and Tasks – Topic-Specific (Behavioural + Multi-Domain) The research group is capable of collaborating to carry out the following activities/tasks within the realm of behavioural and multi-domain interventions:

A. Intervention Design & Development

- Conduct formative
- Co-design multi-domain intervention packages combining behavioural change
- Tailor the intervention to the specific population
- Define the behavioural "active ingredients" and map out a logic model or causal chain: behavioural change → engagement/adherence → physiological/functional outcomes.

B. Behavioural Monitoring & Adherence Support

- Deploy tools and methods for monitoring behaviour (wearables, smartphone apps, self-report questionnaires, diaries)
- Implement adherence support mechanisms: regular feedback, coaching, group sessions, peer support, digital reminders.
- Use behavioural science frameworks (e.g., COM-B, behaviour change technique taxonomy) to structure the intervention and monitor fidelity.

C. Multi-Domain Measurement & Outcomes Evaluation

- Partecipate in pre- and post- intervention assessments of domain-specific outcomes:
    - Cognitive / executive function / memory / processing speed via neuropsychological battery.
    - Physical/physiological outcomes: gait, balance, endurance/fitness, muscle strength, cardiovascular/vascular risk measures.
    - Nutritional / metabolic biomarkers: maybe diet adherence, body composition, lipids, glucose, inflammation markers.
    - Psychosocial / behavioural outcomes: mood, quality of life, social engagement, functional status, behavioural change metrics.
- Use multi-domain composite outcome measures (global cognition, functional status) as well as domain-specific.
- Include intermediate/mediator variables (behavioural engagement, adherence, lifestyle change) and possibly biomarker mediators.

D. Experimental Study Design & Implementation

- Conduct pilot feasibility studies of the multi-domain behavioural intervention
- Progress to randomised controlled trials (RCT) or cluster-RCTs, with appropriate control groups
- Longitudinal follow-up of
- Use mixed methods (quantitative + qualitative) for process evaluation
- Possibly use adaptive intervention designs or personalised interventions

E. Implementation & Scale-Up, Real-world Translation

- Assess feasibility of implementing the intervention in various Monitor cost-effectiveness, scalability, acceptability in routine practice.
- Collaborating in the development of implementation manuals, training materials for staff, fidelity monitoring tools.
- Use data to inform policy or service redesign

3. Experimental Activities / Methodology

Here are detailed methodological capacities and activities the group can carry out:

- Participant recruitment and baseline **characterization** (12-25 year-old patient with congenital heart disease).
- Behavioural intervention delivery
- Use of digital/technological platforms
- Neuropsychological testing and functional assessments
- Physical/physiological assessments
- Outcome measurement and statistical analysis
- Process evaluation and qualitative research
- Pilot feasibility work and sample size estimation
- Randomised controlled trial design
- Longitudinal follow-up and maintenance analysis
- Implementation science methodology

4. Demonstration of Expertise & Background

While Dr Egidy Assenza's principal published domain has been cardiology and congenital heart disease, his research profile and institutional environment reflect strong methodological, clinical and research leadership capabilities.

5. Summary Statement

In summary, Dr Egidy Assenza and his team have the methodological, clinical and translational research credentials to serve as a credible lead or partner in the field of behavioural and multi-domain interventions. Their strengths lie in rigorous clinical research, complex patient populations, and institutional support. By combining behavioural science, multi-domain intervention design, advanced measurement/monitoring and implementation pathways, they are particularly suited to deliver high-impact research in this emerging field.

Destination 2. Living and working in a health-promoting environment

HORIZON-HLTH-2026-01-ENVHLTH-01: Towards a better understanding and anticipation of the impacts of climate change on health

Research Group	**Prof. Igor Diemberger** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	Prof. Igor Diemberger, MD, PhD, FESC, FEHRA, FAIAC is Head of the Cardio-Thoracic-Vascular Day-Hospital Service at the IRCCS University Hospital S. Orsola (since 2021) and holds a joint 50:50 clinical–academic role as Consultant Cardiologist and Electrophysiologist (since 2009). His clinical work is tightly integrated with translational research, focusing on the epidemiology, diagnosis, and management of cardiac arrhythmias, implantable and wearable cardiovascular technologies, and biomarkers. He is internationally recognised for expertise in conduction-system pacing, cardiac resynchronization therapy (CRT), remote monitoring of cardiac implantable electronic devices (CIEDs), and the development of multimodal digital biomarkers. He also coordinates the PhD Programme in Health and Technologies at the University of Bologna, strengthening advanced training at the interface between engineering, digital innovation, and medicine. Prof. Diemberger directs a multidisciplinary research group dedicated to translating emerging technologies and digital-health solutions into validated clinical applications for hospital-based and home-monitoring environments. The group's activities encompass workflow integration, regulatory-aligned clinical validation (including MDR and CE-mark readiness), usability and acceptability studies, and secure real-world data infrastructures. Alongside clinical and digital expertise, the team includes laboratory specialists supporting biomarker research, biosignal characterisation, and analysis of device-derived physiological measurements. Its methodological strengths span large prospective cohort studies, medical-device validation, diagnostic-accuracy research, and implementation-science approaches to digital cardiology and telemedicine. With long-standing involvement in major European collaborative programmes, Prof. Diemberger plays a key role in advancing multicentre cardiovascular research, digital-health innovation, and precision-medicine implementation. His contributions include multicentre study design, clinical validation of novel digital tools, and integration of advanced diagnostics into routine care pathways. Within the Horizon Europe TRIGGER consortium, the group contributes to clinical and translational workstreams linking climate-related exposures to cardiovascular health outcomes. Activities include the design and coordination of patient-facing study protocols, recruitment and longitudinal follow-up within the Bologna Climate-Health Connection Lab, and the clinical validation of digital-health and multimodal physiological monitoring tools in real-world settings. In line with TRIGGER's co-

	creation framework, the group supports citizen-engagement activities that ensure patient involvement in study design, feedback processes, and dissemination, integrating lived experience into climate-cardiology research. The team also contributes to data-driven models assessing how environmental stressors influence cardiovascular risk and symptom dynamics, reinforcing TRIGGER's mission to translate climate-health insights into proactive prevention and early-warning strategies. This work complements participation in BIOTOOL-CHF, where the group advances precision-cardiology approaches through biomarker-guided risk stratification. The research group operates within a high-volume tertiary arrhythmia and device-therapy centre, supported by robust infrastructures and international clinical-research networks. Collaborations span engineering departments and industrial partners to advance sensing technologies, AI-enabled risk stratification, and telemedicine platforms. The group enables progression from TRL-5 to TRL-7 through clinical validation, patient-centred co-design, and cross-sector data integration. ORCID: https://orcid.org/0000-0002-3823-3809

Research Group	**Prof. Daniel Remondini** Dep. Physics and Astronomy
Expertise in relation to the topic	Expertise in modeling and analysis of biological and biomedical data with a "One health" approach, as developed within the EU VEO project (WP2 "Advanced datamining tools" co-leader) or in E-MUSE MSCA project on novel food development and analysis. Application of Artificial Intelligence methods (e.g. NLP tools for protein sequence analysis): Language models learn to represent antigenic properties of human influenza A(H3) virus, Francesco Durazzi, Marion P. G. Koopmans, Ron A. M. Fouchier & Daniel Remondini, Scientific Reports | (2025) 15:21364 Application of network theory approaches for the analysis of metagenomic data (human, animal, environmental): Metagenomics data: tell me which metrics and I will tell you which communities, Alessandro Fuschi, Alessandra Merlotti, Daniel Remondini, ISME Commun. 2025 Jul 24;5(1):ycaf125. doi: 10.1093/ismeco/ycaf125; Time-series sewage metagenomics distinguishes seasonal, human-derived and environmental microbial communities potentially allowing source-attributed surveillance. Becsei Á, Fuschi A, …, Remondini D, Aarestrup FM, Munk P. Nat Commun. 2024;15(1):7551. doi: 10.1038/s41467-024-51957-8 Application of mathematical modelling for epidemic evolution characterization integrating multiple data types (genomic, clinical, demographic, mobility): Human mobility and sewage data correlate with COVID-19 epidemic evolution in a 3-year surveillance of the metropolitan area of Bologna, Francesco Durazzi, Enrico Lunedei, Giulio Colombini, Giulia Gatti, Vittorio

	Sambri, Alessandra De Cesare,Cecilia Crippa, Frédérique Pasquali, Gastone Castellani, Daniel Remondini, Armando Bazzani and Bologna MODELS4COVID Study Group, Durazzi et al. BMC Infectious Diseases (2025) 25:1467; Modelling antimicrobial resistance transmission to guide personalized antimicrobial stewardship interventions and infection control policies in healthcare setting: a pilot study, F. Durazzi, …, Daniel Remondini & Evelina Tacconell, Sci. Rep. (2023) 13:15803 https://doi.org/10.1038/s41598-023-42511-5

Research Group	**Prof. Alessandro Silvani** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	I have expertise in translational research on sleep and the brain-heart axis and currently chair the Scientific Committee of the European Sleep Research Society (ESRS). In the Italian national NRPP project "Age-IT", I lead the task of prospectively recording sleep, heart rate, and physical activity with wearable sensors during daily life in caregivers of patients with dementia, with the goal of predicting their coping with the care burden. In the national CNP project "Digital Lifelong Prevention (DARE)", I lead a work package and a task dedicated to the prospective recording of sleep, heart rate and physical activity with wearable sensors during daily life in people > 65 years of age to improve the estimation of their risk of falling beyond the state of the art. Within these projects, we have already recorded 500+ subjects in the last year with multi-wearable sensor setups over 1 week. The experience and research network at my institution associated with these ongoing activities may be readily translated to monitoring sleep, heart rate, and physical activity, which are important health-related objective readouts, and link the results to data on climate.

Research Group	**Prof. Laura Mercolini** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	The Pharmaco-Toxicological Analysis Laboratory (PTA Lab), Department of Pharmacy and Biotechnology (FaBiT), Alma Mater Studiorum – University of Bologna, develops and validates patient-centric analytical workflows that enable high-frequency, longitudinal follow-up in diverse and vulnerable populations. The laboratory integrates minimally invasive volumetric/dried microsampling (e.g., VAMS, qDBS, mfDBS, capillary-generated DBS) with advanced (U)HPLC-MS/MS and UHPLC-HRMS platforms to support quantitative determination of pharmacological treatments, hormones and immune-inflammatory mediators, together with untargeted high-resolution profiling (metabolomics/exposomics). Methods are established under EMA/FDA/ICH bioanalytical guidance, with clearly documented development, calibration and validation plans, and quality assurance spanning pre-analytical, analytical and post-analytical phases. Within ENVHLTH-01, these capabilities are directly applicable to elucidating and anticipating climate-related health impacts. PTA

Lab's workflows allow decentralised and home-based sampling (blood, plasma, serum, urine, oral fluid) suitable for air-quality perturbations, heat/cold-wave studies and other environmental stressors, supporting equitable participation and high-frequency follow-up in multi-centre European cohorts. Analytical outputs include validated targeted panels (e.g., cytokines/chemokines surrogates, endocrine markers, pharmacotherapy levels) and broad HRMS fingerprints capturing small-molecule perturbations. Data can be generated with controlled metadata, internal standardisation, batch alignment and longitudinal QC, enabling downstream integration with clinical outcomes, wearable-derived physiology and geocoded exposure layers.
The identification of climate-linked biological signatures and putative susceptibility markers can be achieved through advanced data processing and interpretation of raw measurements. The research group possesses the expertise to implement HRMS and multivariate statistics, complemented by sensitive analyses across time windows, exposure strata and relevant subgroups. Prior experience with decentralised sampling in infectious-disease contexts and established logistics for large-scale sample flow (kit provisioning, return, chain-of-custody, turnaround) support timely evidence generation and inter-site comparability. This combination of analytical depth, operational scalability and regulatory-ready validation aligns with the topic's expected outcomes and provides a solid foundation for the bioanalytical and data-integration components of collaborative climate-health studies.

Relevant publications

- Protti M, Mandrioli R, Mercolini L. Quantitative microsampling for bioanalytical applications related to the SARS-CoV-2 pandemic: Usefulness, benefits and pitfalls. J Pharm Biomed Anal. 191 (2020) 113597. https://doi.org/10.1016/j.jpba.2020.113597
- Protti M, Mandrioli R, Santos HM, Lodeiro C, Capelo-Martínez JL, Mercolini L. How microsampling is impacting pharmacokinetic and toxicokinetic studies: volumetric absorptive microsampling (VAMS). Bioanalysis. 17 (2025) 997-1009. https://doi.org/10.1080/17576180.2025.2546782
- Carvalho LB, Teigas-Campos PAD, Jorge S, et al. Normalization methods in mass spectrometry-based analytical proteomics: A case study based on renal cell carcinoma datasets. Talanta. 266b (2024) 124953. https://doi.org/10.1016/j.talanta.2023.124953
- Protti M, Cirrincione M, Palano S, et al. Targeted quantitative metabolic profiling of brain-derived cell cultures by semi-automated MEPS and LC-MS/MS. J Pharm Biomed Anal. 236 (2023) 115757. https://doi.org/doi:10.1016/j.jpba.2023.115757
- Protti M, Mercolini L, Mandrioli R. Review: the role of automation in improving the performance and throughput of microsample bioanalysis. Anal Chim Acta. 1359 (2025) 344018. https://doi.org/10.1016/j.aca.2025.344018

	Relevant projects ▪ "Therapeutic monitoring of second-generation antidepressant drugs in patients with food disorders, performed by means of mini-invasive techniques: a pilot study", 2018. Funding: Servizio Sanitario Regionale Emilia Romagna (707/2018/ SPER /AUSLBO). ▪ "Linking tryptophan catabolism to amyotrophic lateral sclerosis: from the pathogenesis to the pharmacological treatment", 2017. Funding: Ministry for Education, University and Research (MIUR) with PRIN (Scientific Projects with High National Impact) funds (Ref. 20173EAZ2Z). ▪ "Finding new targets to counteract brain progenitor cells dysregulation in AGC1 deficiency hypomyelination: a multi-disciplinary approach" 2019-2022. Funding: Fondazione Telethon (Ref. GGP19067). ▪ "Dried microsamples: multi-matrix, long-term stability study of doping-relevant peptides", 2019. Funding: World Anti-Doping Agency (WADA, Ref. 19A08LM). ▪ "Analysis of lithium plasma levels by peripheral blood microsampling in the monitoring of patients with bipolar disorder" 2022-2024. Funding: Servizio Sanitario Regionale Emilia Romagna (849-2022-SPER-AUSLBO).

Research Group	**Prof. Silvana Di Sabatino** Affiliation: Dept of Physics and Astronomy
Expertise in relation to the topic	Full Professor of atmospheric physics at the Department of Physics and Astronomy of the University of Bologna, where she teaches atmospheric boundary-layer physics, dynamic meteorology, and synoptic meteorology. She holds a PhD from the University of Cambridge (UK) in environmental fluid mechanics. Her current research relates to the study of the relationship between local-scale land-air turbulent processes and meso-scale dynamics, and the assessment of land-use changes in the future climate. Recently, she worked on nature-based solutions as a means to promote the shift in the usage of typical engineering practice to combat the effects of hydro-meteorological risks. She has a long-standing record of international research collaborations and leading roles in international experimental campaigns in the US (e.g. MATERHORN project). She has been a steering committee member of several international and national initiatives (e.g. COST Action 732, International Association of Urban Climate, Harmonisation within Atmospheric Dispersion Modelling for Regulatory Purposes initiative, Italian Association of Atmospheric Science and Meteorology - AISAM). She is the founding editor and co-Editor-in-Chief of the Bulletin of Atmospheric Science and Technology (Springer Nature), Associate editor of Environmental Fluid Dynamics (Springer Nature) and serves on the editorial board of Boundary-Layer Meteorology (Springer Nature). She has co-authored more than 100 scientific publications, of which over 80 are in peer-reviewed journals. She has had leading roles in several national and EU projects, e.g. LLP RESCUE, iSCAPE, H2020-OPERANDUM, H2020-I-CHANGE, LIFE-

	CLIMAXPO, HEU-ALBATROSS, HEU-LAND4CLIMATE, HEU-RISKADAPT, HEU-TRIGGER. Currently, she is the co-coordinator of HEU-ALBATROSS and the coordinator of the H2020-TRIGGER. The latter is of particular relevance for the actual proposal as it concerns the same topics and is directly related to the activities requested in the call. In addition, Silvana is a founding member of the European Climate-Health Cluster mentioned in the call.

Research Group	**Dr Francesco Nonino** IRCCS Istituto delle Scienze Neurologiche
Expertise in relation to the topic	The Unit of Epidemiology and Statistics of the IRCCS Institute of Neurological Sciences includes professionals with expertise in the clinical, statistical, epidemiological, neuroimaging, and biomedical editing fields. **Record linkage** - The Unit has developed a long-standing experience on record linkage between clinical and administrative data. Validated algorithms have been developed and tested on a living cohort of about 2,000 subjects with Parkinson's disease or atypical Parkinsonism in the province of Bologna since 2015, performing studies on the epidemiology of Parkinson's disease, epilepsy, multiple sclerosis. Such record linkage model can be applied to chronic, degenerative or inflammatory, neurological conditions within studies on the environmental determinants of diseases. Namely, the Unit has recently won a competitive grant (Funded by the Fondazione del Monte di Bologna e Ravenna, grant n. 2025.0163) to investigate potential environmental determinants of neurological conditions such as stroke, amyotrophic lateral sclerosis, epilepsy, Parkinson's disease and obstructive sleep apnea syndrome, through clinical and instrumental parameters. The project is developed in collaboration with the Unit of Epidemiology, Health Promotion and Risk Communication Unit of the AUSL of Bologna. Another project developed by the Unit of Epidemiology and Statistics and funded by the Scientific Direction of the IRCCS ISNB is investigating the environmental determinants of neurological conditions in relation to urban green areas. **Evidence synthesis** - By hosting the editorial staff of the Cochrane Review Group on Multiple Sclerosis and Rare Diseases of the Central Nervous System and the direction of the Italian Center of the Cochrane Collaboration, the Unit developed advanced experience in evidence synthesis (systematic reviews, scoping reviews, umbrella reviews and evidence mapping). Therefore, its contribution in the project could be relevant in creating a robust evidence base on which to develop advancements within the topic of interest and in pooling data from different centers. **Methodological support in consensus processes** – The Unit has developed a robust experience within the GRADE Working Group in the contextualization of scientific evidence within multi-stakeholder panels. Methodological support can be provided for the production of evidence-based guidance (national and international clinical practice guidelines and HTA reports). This competence may be exploited to pilot the results of a study as

	evidence informing the work of a decision-making panel. Members of the Units saff are involved in a GRADE project group on planetary health, investigating the effects on the planetary boundaries of interventions aimed at improving human health. **Selected references** ▪ Zenesini C, Cascini S, Picariello R, et al. Hypertension, Diabetes and Depression as Modifiable Risk Factors for Dementia: A Common Data Model Approach in a Population-Based Cohort, with Study Protocol and Preliminary Results. JClinMed. 2025, 14, 6622 doi: 10.3390/jcm14186622 ▪ Muccioli L, Zenesini C, Licchetta L, et al. Causes of hospitalization and mortality in persons with epilepsy: The EpiLink Bologna cohort, Italy. Eur J Neurol. 2025;32(2):e16576. ▪ Ridley B, Nonino F, Baldin E, Casetta I, Iuliano G, Filippini G. Azathioprine for people with multiple sclerosis. Cochrane Database Syst Rev. 2024;12(12):CD015005. ▪ Piggott T, Moja L, Jenei K, et al. GRADE Concept 7: Issues and Insights Linking Guideline Recommendations to Trustworthy Essential Medicine Lists. J Clin Epidemiol. 2024 Feb;166:111241 ▪ Ridley B, Minozzi S, Gonzalez-Lorenzo M, et al. Immunomodulators and immunosuppressants for progressive multiple sclerosis: a network meta-analysis. Cochrane Database Syst Rev. 2024;9(9):CD015443. ▪ Gonzalez-Lorenzo M, Ridley B, Minozzi S, et al. Immunomodulators and immunosuppressants for relapsing-remitting multiple sclerosis: a network meta-analysis. Cochrane Database Syst Rev. 2024;1(1):CD011381. ▪ Belotti LMB, Di Martino M, Zenesini C, et al. Impact of adherence to disease-modifying drugs in multiple sclerosis: A study on Italian real-world data. Mult Scler Relat Disord. 2023;80:105094. ▪ Tugwell P, Welch V, Magwood O, et al. Protocol for the development of guidance for collaborator and partner engagement in health care evidence syntheses. Syst Rev. 2023 Aug 2;12(1):134.

HORIZON-HLTH-2026-01-ENVHLTH-04: Towards climate resilient, prepared and carbon neutral populations and healthcare systems

Research Group	**Prof. Igor Diemberger** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	Prof. Igor Diemberger, MD, PhD, FESC, FEHRA, FAIAC is Head of the Cardio-Thoracic-Vascular Day-Hospital Service at the IRCCS University Hospital S. Orsola (since 2021) and holds a joint 50:50 clinical–academic role as Consultant Cardiologist and Electrophysiologist (since 2009). His clinical work is tightly integrated with translational research, focusing on the epidemiology, diagnosis, and management of cardiac arrhythmias, implantable and wearable cardiovascular technologies, and biomarkers. He is internationally recognised for expertise in conduction-system pacing, cardiac resynchronization therapy (CRT), remote

monitoring of cardiac implantable electronic devices (CIEDs), and the development of multimodal digital biomarkers. He also coordinates the PhD Programme in Health and Technologies at the University of Bologna, strengthening advanced training at the interface between engineering, digital innovation, and medicine. Prof. Diemberger directs a multidisciplinary research group dedicated to translating emerging technologies and digital-health solutions into validated clinical applications for hospital-based and home-monitoring environments. The group's activities encompass workflow integration, regulatory-aligned clinical validation (including MDR and CE-mark readiness), usability and acceptability studies, and secure real-world data infrastructures. Alongside clinical and digital expertise, the team includes laboratory specialists supporting biomarker research, biosignal characterisation, and analysis of device-derived physiological measurements. Its methodological strengths span large prospective cohort studies, medical-device validation, diagnostic-accuracy research, and implementation-science approaches to digital cardiology and telemedicine.

With long-standing involvement in major European collaborative programmes, Prof. Diemberger plays a key role in advancing multicentre cardiovascular research, digital-health innovation, and precision-medicine implementation. His contributions include multicentre study design, clinical validation of novel digital tools, and integration of advanced diagnostics into routine care pathways.

Within the Horizon Europe TRIGGER consortium, the group contributes to clinical and translational workstreams linking climate-related exposures to cardiovascular health outcomes. Activities include the design and coordination of patient-facing study protocols, recruitment and longitudinal follow-up within the Bologna Climate-Health Connection Lab, and the clinical validation of digital-health and multimodal physiological monitoring tools in real-world settings. In line with TRIGGER's co-creation framework, the group supports citizen-engagement activities that ensure patient involvement in study design, feedback processes, and dissemination, integrating lived experience into climate-cardiology research. The team also contributes to data-driven models assessing how environmental stressors influence cardiovascular risk and symptom dynamics, reinforcing TRIGGER's mission to translate climate-health insights into proactive prevention and early-warning strategies. This work complements participation in BIOTOOL-CHF, where the group advances precision-cardiology approaches through biomarker-guided risk stratification.

The research group operates within a high-volume tertiary arrhythmia and device-therapy centre, supported by robust infrastructures and international clinical-research networks. Collaborations span engineering departments and industrial partners to advance sensing technologies, AI-enabled risk stratification, and telemedicine platforms. The group enables

	progression from TRL-5 to TRL-7 through clinical validation, patient-centred co-design, and cross-sector data integration. ORCID: https://orcid.org/0000-0002-3823-3809

Research Group	**Prof. Mattia Casula** Dep. Political and Social Sciences
Expertise in relation to the topic	I am an Associate Professor in Political Science at the Department of Political and Social Sciences. Over the years, I have specialized in public policy and public administration analysis, focusing on the roles of public and private actors, including citizens, in the delivery and co-design of public services. My research has primarily examined topics at the sub-national level, such as EU structural funds, regional development policy, transformative innovation policy, migration and integration policy, health policy, and the use of knowledge and science to support these policies. My studies analyze the dynamics of implementation among the public, private, and third sectors when EU or national policies are executed at regional and local levels. In doing so, I also try to develop new, innovative tools to guarantee effective do-design and co-created processes. This work enhances our understanding of how public and private actors engage in policy making—both in design and implementation—which is essential for building a sustainable, civic, and democratic Europe and fostering common European values, especially in a context in which traditional policies, such as health ones, are strongly impatted by emerging issues such as climate change, management of pandemics, and increasing inequalities.. Thus, my contribution to the Call should involve an analysis, from both theoretical and empirical perspectives, of the public-private relationships that emerge during these processes in the specified fields. More in detail, my contribution is to offer SSH input, particularly on processes of co-creation and implementation of public services in the social and healthcare sectors. I act as a partner, not a coordinator, to support those involved in the design and implementation of healthcare services. In the past I work in several national and European projects in these fields. List of my publications: https://orcid.org/0000-00027081-8153

Research Group	**Prof. Francesco Paolucci** Dep. Sociology and Business Law
Expertise in relation to the topic	Professor of Health Economics and Policy at the University of Newcastle, Australia, and the University of Bologna, Italy. He was appointed advisor to the Chilean Minister of Health on healthcare reform and represented the Emilia-Romagna Region on the technical committee for the distribution of funds for the National Health System. He is an associate editor for the world's leading journals in health policy and economics and strong record of international research collaborations. He has Published over 110 academic peer-reviewed articles, book chapters and reviews. Prof. Paolucci is currently chief investigator on grants funded by the Australian Research Council, the National Health Medical

Research Council, and the European Commission (Horizon2020). So far, he has been awarded various industry grants from public and private agencies. His engagement is extensively in academics, conducting innovative research activities, training programs, journal reviews, and supervision of post-graduate theses nationally and abroad.

Area of Contribution

His area of expertise is on public policy and healthcare financing. It involves activities aimed at improving the efficiency and equity of healthcare resource allocations. Activities include designing and implementing economic evaluations, such as cost-effectiveness and cost-utility analysis, to quantify the value of medical technologies and interventions. In addition, contributes to stakeholders' preference elicitation studies (such as discrete choice experiments or DCE) to understand how different stakeholders value health outcomes and treatment attributes. These activities support evidence-based decision-making by integrating clinical effectiveness, cost-effectiveness, costs, and value of preferences to guide policy and priority setting in healthcare systems.

Related Projects

- **Health Economic Evaluation of Biomarker-based Diagnostic Toolkit to Personalize Pharmacological Approached in Congestive Heart Failure (BIOTOOL-CHF) Project** [*$2,600,000 | 2023 | European Commission, European Union*]
- **Old and lonely? Preferences for peer support interventions among older adults in Australia** *[$5,000,000 | 2022 | Australian Commonwealth Government]*
- **Identify barriers, facilitators and system capabilities for telehealth uptake and develop an evidence-informed integrated model of telehealth implementation across and within HNE Mental Health** *[$125,766 |2021| Hunter Medical Research Institute]*
- ***Economic Development, Health and Nutrition for Sustainable Development*** *[$10,000 |2019| Australia Africa Universities Network (AAUN)]*
- **Healthcare programs evaluation** *[$113,000 | 2015 | 360]*

Related Publications

- Antonini M, et al., **'Are we ready for the next pandemic? Public preferences and trade-offs between vaccine characteristics and societal restrictions across 21 countries**', Social Science and Medicine, 366 (2025)
- Wilson J, et al., **'Measuring factors associated with telehealth use by people who use mental health services: A psychometric analysis of a theoretical domains framework questionnaire**', JOURNAL OF TELEMEDICINE AND TELECARE (2024)
- Schilling C, et al., **'An Economic Model for Estimating Trial Costs with an Application to Placebo Surgery Trials**', APPLIED HEALTH ECONOMICS AND HEALTH POLICY, 21, 263-273 (2023)
- Sequeira AR, Mentzakis E, Archangelidi O, Paolucci F, **'The economic and health impact of rare diseases: A meta-analysis'**, HEALTH POLICY AND TECHNOLOGY, 10, 32-44 (2021)

Destination 3. Tackling diseases and reducing disease burden

HORIZON-HLTH-2026-01-DISEASE-02: Innovative interventions to prevent the harmful effects of using digital technologies on the mental health of children and young adults

Research Group	**Prof. Antonio Cicchella** Dep. Quality of Life Studies
Expertise in relation to the topic	I have previously presented a project as coordinator (not funded), about the implementation of a system for monitoring and promotion of physical activity and well being, by means of "health" totems installed in public park (boxes with access by app, having inside devices for measuring basic health parameters : ecg, blood pressure, body balance, hand grip, jumping capacities , walking and running, able to collect data on health status and connected with an app able to suggest the physical activity to be done and to monitor the progresses. I have expertise in physical activity monitoring and promotion in children and adolescents, with special reference to physical performance tests and children development. I have a background in healthy and disease in children, with special focus on neuromuscular diseases. ▪ Cicchella A. Recommendations for Resuming PA after Prolonged Rest in Children and Adolescents: A Systematic Integrative Review of Relevance for Immunity. J Funct Morphol Kinesiol. 2022 Jun 2;7(2):47. doi: 10.3390/jfmk7020047. PMID: 35736018; PMCID: PMC9224580. ▪ Cicchella A. Static Body Balance in Children and Expert Adults Ballroom Dancers: Insights from Spectral Analysis of Shifts. Biology (Basel). 2021 Dec 8;10(12):1291. doi: 10.3390/biology10121291. PMID: 34943206; PMCID: PMC8698350.

Research Group	**Prof. Sara Garofalo** Dep. Psychology
Expertise in relation to the topic	Our research teams combine complementary expertise from multiple research units of the Department of Psychology, with a strong track record in Italian and European-funded projects. Our interdisciplinary team integrates **cognitive neuroscience, data science, and psychometric tools development and validation** to address human cognition and brain functioning in both clinical and non-clinical human populations of all ages. The **Neuroscience of Motivation, Decision and Learning (MoDeL) group (**https://psicologia.unibo.it/en/research/research-groups/model-neuroscience-of-motivation-decision-and-learning**)**, operating within the **Center for Studies and Research in Cognitive Neuroscience (CsrNC), has a large expertise in the investigation** of the neural and cognitive mechanisms underlying adaptive and maladaptive learning processes, decision-making,

	and motivation. Using a multimodal approach - combining behavioural, psychophysiological (e.g., skin conductance, EMG, eye-tracking), electrophysiological (EEG), and non-invasive neurostimulation techniques (TMS, tDCS) - the group explores the neuro-behavioral underpinning of reward-based learning and how these processes contribute to vulnerability to anxiety, addiction, and compulsive behaviours. The **Laboratory of Psychometrics and Neuropsychology** (https://psicologia.unibo.it/en/research/research-groups/boost-perception), operating within the **Cognitive Enhancement Service for Developmental Age (SPEV) and founder of the** University **spin-off Develop-Players**, brings applied expertise in designing and validating interventions to support cognitive and emotional development. The group unites psychologists and computer scientists to create scientifically validated digital tools and games aimed at children with atypical neurodevelopment, fostering self-regulation and adaptive engagement with technology. Together, these teams offer an integrated research-to-intervention framework combining neuroscience, clinical practice, advanced data science, and digital innovation.

Research Group	**Prof. Elisa Magosso** Dep. Electrical, Electronic and Information Engineering
Expertise in relation to the topic	**ACTIVITIES/TASKS** • Implementation of **experimental protocols** involving the simultaneous acquisition of **multiple biological signals** such as: brain electrical activity (high-density EEG, 64-128 channels); muscle activation (EMG); cardiac activity (ECG); Eye movements (EOG); autonomic arousal (GSR); body part motion and orientation (IMUs). The group has the availability of non-medical devices suitable for data acquisition on healthy participants. • **Analysis of biological signals** via advanced methods, such as: o brain origin signals (fNIRS, MEG, EEG) through artifact removal and filtering, time–frequency analysis (e.g., wavelet transforms), cortical source reconstruction, brain connectivity estimation, graph-theoretical metrics; o Heart Rate Variability (HRV); o Cortico-muscular connectivity and autonomic–cerebral interaction (e.g., Granger Causality, information-theoretic measures); o Implementation of custom analysis pipelines in MATLAB and Python. • Development and application of **Artificial Intelligence techniques**, in particular deep learning methods (e.g., convolutional neural networks), combined with **explainability techniques** ensuring transparent and interpretable models, for: o Classification, and characterization of cognitive and motor states, (e.g., attentional states, perceptual states, motor intention and execution);

	○ Extraction of features and biomarkers characterizing neurological conditions and assessing the effects of rehabilitative interventions in patients; ○ Implementation of AI pipelines with integrated explainability, designed to be: applicable to small datasets, adaptable for single-subject analyses, capable of processing multimodal data. • Development of **biologically inspired neural network models**, simulating the interconnections among multiple brain areas, for simulating and interpreting the neural mechanisms underlying perceptual and motor behaviour in healthy and pathology (e.g. Parkinson, stroke). **PUBLICATIONS** ▪ Magosso E. et al "Audiovisual integration in hemianopia: A neurocomputational account based on cortico-collicular interaction" Neuropsychologia 2016. ▪ Magosso E. et al "EEG Alpha Power Is Modulated by Attentional Changes during Cognitive Tasks and Virtual Reality Immersion", Comput. Intell. Neurosci. 2019. ▪ Borra D., Fantozzi S., Magosso E. "Interpretable and lightweight convolutional neural network for EEG decoding: Application to movement execution and imagination", Neu. Netw. 2020. ▪ Borra D., Magosso E., et al. "A Bayesian-optimized design for an interpretable convolutional neural network to decode and analyze the P300 response in Autism", J. Neu. Eng. 2022. ▪ Magosso E., Borra D. "The strength of anticipated distractors shapes EEG alpha and theta ▪ oscillations in a Working Memory task", NeuroImage 2024. ▪ Borra D., […], Magosso E. "Revealing EEG signatures of intervention in disorder of consciousness using artificial intelligence: methodology and feasibility", Comput. Methods Programs Biomed. Accepted. **PROJECTS (participation)** ▪ H2020-JTI (2015-2021):"CASTLE: CAbin Systems design Toward passenger welLbEing; ▪ PRIN: "Visual awareness lost and found: neural and cognitive mechanisms (2015); "Performing actions in a changing environment" (2017); "Multisensory integration of locomotion-related visual and somatomotor signals"(2022); ▪ H2020 FET (2021-2025): "MAIA: Multifunctional, adaptive and interactive AI system for Acting in multiple contexts ▪ PNRR-PE12 (2022-2025): "MNESYS: A multiscale integrated approach to the study of the nervous system in health and disease"; ▪ - PNC-I.1 (2023-2026) "DARE: Digital lifelong prevention"

Research Group	**Prof. Elvis Mazzoni** Dep. Psycologhy
Expertise in relation to the topic	The **SEFoRA Lab** and the related group **DEduTech-2Life (Developmental Technologies for life-cycle education and lifelong**

	learning) have relevant and wide experience in the following fields: • Functional and dysfunctional use of Digital and Emergent Technologies in human life cycle, with particular interest on Technoference and Parental Phubbing dynamics. • Use of Digital and Emerging Technologies to support transitions characterizing the entire life cycle. • Developmental Robotics: Robots and Artificial Intelligence to build knowledge, foster inclusion and develop skills in children, adolescents, emerging adults, and adults. The laboratory has already participated in previously European project and programme related to the use of emerging and digital technologies, such as human-robot interaction (Sestosenso project) and the use of social media in Youth (Catch-EyoU project). Particularly Prof. Elvis Mazzoni and Prof. Martina Benvenuti have relevant publication in the field of the functional and dysfunctional Internet use in the lifecycle with research with different population covering all the life periods. Currently, the researches are focused particularly on the period 0-6 with a specific attention on the dynamics and effects of technoference and parental phubbing. The laboratory could contribute to the **analysis of dysfunctional effects in the use of digital technologies and also in the development of tools** related to the idea of digital minimalism i.e. the use of those applications and functions of digital devices functional to the developmental tasks of specific life periods. The SEFoRA Lab team offer an integrated research-to-intervention framework combining developmental and educational psychology approaches, and digital innovation—directly aligned with the objectives of developing and testing **innovative interventions to prevent harmful effects of digital technology use on mental health**.

Research Group	**Prof. Catia Prandi** Dep. Computer Science and Engineering
Expertise in relation to the topic	Thanks to my background in **Computer Science and Human-Computer Interaction**, my work leverages **participatory approaches, digital literacy, and citizen science** as frameworks for civic engagement and youth empowerment. I am currently investigating how co-designed technologies can serve as tools to raise awareness about wellbeing - including digital wellbeing and mental health - among children and young adults. In this context, I am coordinating two projects. I am the local PI of a PRIN 2022 project titled "Improving Digital Wellbeing with and for Teens", where we co-designed a mobile app for students (15–19) and a website for teachers to create personalized learning paths on digital wellbeing. In addition, I lead the INCISIVE project (Citizen Science e tecnologie pervasive: un approccio partecipato per il benessere delle giovani generazioni), funded by Unibo 5x1000, where 85 high school students (16–18) engaged in reflecting on mental health

	while co-designing an app prototype tailored to their needs and interests. Additionally, As the scientific coordinator of the "CitizER science" project (Emilia Romagna region), I held several 3-hours workshops with students from middle schools to high schools, reflecting with them about digital wellbeing and how to co-design Citizen science gamified apps for the good of their peers. Publications: ▪ Fusing Gratitude Journaling and Citizen Science: A Youth-Centered Co-Design Framework for Mental Well-Beingand Data Literacy, T Zambon, C Ceccarini, C Prandi, Proceedings of the 16th Biannual Conference of the Italian SIGCHI Chapter, 1-8, 2025 ▪ Towards Digital Well-being Education in High-School, L Scibetta, F Ballarini, C Ceccarini, A Monge Roffarello, C Prandi, ...Proceedings of the Extended Abstracts of the CHI Conference on Human Factors, 2024 ▪ Digital Wellbeing for Teens: Designing Educational Systems (DIGI-Teens 2024), C Ceccarini, C Prandi, A Monge Roffarello, L De Russis, Proceedings of the 2024 International Conference on Advanced Visual Interface ▪ The design of Tecnico GO!: catering for students' well-being during the COVID-19 pandemics, V Nisi, C Prandi, S Ma, M Ferreira, H Nicolau, A Esteves, N Nunes, Multimedia Tools and Applications 82 (29), 46129-46151, 2023

Research Group	**Prof. Paola Bonifacci** Dep. Psychology
Expertise in relation to the topic	Head of the Laboratory for the Assessment of Learning Disorders (LADA) and leads the Research Group "Cognitive Processes, Learning Disorders and Bilingualism" at the Department of Psychology, University of Bologna. Her research focuses on learning processes and the cognitive and behavioural mechanisms of neurodevelopmental disorders, with particular attention to emotional and family-related factors. She has extensive experience in coordinating national and international projects involving universities, public health services and local institutions, including a long-standing collaboration with the Municipality of Bologna. As Principal Investigator, she coordinated multidisciplinary projects such as ADLAB on language and learning disorders in bilingual children across nine regional health centres in Emilia-Romagna, research on Klinefelter Syndrome, and the Family Language Policy project, as well as a European research network on bilingualism and teachers' beliefs (UNA Europa Seed Funding). Her methodological expertise includes experimental designs, psychometric assessment, digital tools for learning evaluation and eye-tracking technologies, applied in clinical and real-life contexts. These approaches support the development and validation of interventions and digital tools in health-oriented projects. Prof. Bonifacci has authored 64 peer-reviewed

publications in international journals (h-index = 22) and regularly participates in international conferences and scientific networks. Within European research programmes, she contributes to work package design, intervention evaluation, outcome measurement, and the integration of clinical and family perspectives into project implementation and policy-related deliverables.

Selected publications:

- Bonifacci, P., Ravaldini, V., Cangelosi, M., & Tobia, V. (2024). Socioeconomic status, linguistic skills and language background differentially relate to preschoolers' emotional and behavioural profile. *Child and Adolescent Psychiatry and Mental Health*, 18 (133)
- Bonifacci, P., Compiani, D., Vassura, C., Affranti, A., Peri, B., Ravaldini, V., & Tobia, V. (2024). Home Learning Environment and Screen Time Differentially Mediate the Relationship Between Socioeconomic Status and Preschoolers' Learning and Behavioural Profiles. *Child Psychiatry & Human Development*.
- Bonifacci, P., Tobia, V., Sansavini, A., & Guarini, A. (2023). Eye-Movements in a Text Reading Task: A Comparison of Preterm Children, Children with Dyslexia and Typical Readers. *Brain Sciences*, 13(3), 425.
- Bonifacci, P., Colombini, E., Marzocchi, M., Tobia, V., Desideri, L. (2022). Text-to-speech applications to reduce mind wandering in students with dyslexia. *Journal of Computer Assisted Learning, 38(2), 440–454*
- Bonifacci, P., Tobia, V., Marra, V., Desideri, L., Baiocco, R., & Ottaviani, C. (2020). Rumination and Emotional Profile in Children with Specific Learning Disorders and Their Parents. *International Journal of Environmental Research and Public Health*, *17*(2), 389.
- Bonifacci, P., Atti, E., Casamenti, M., Piani, B., Porrelli, M., Mari, R. (2020). Which Measures Better Discriminate Language Minority Bilingual Children With and Without Developmental Language Disorder? A Study Testing a Combined Protocol of First and Second Language Assessment. *Journal of Speech, Language, and Hearing Research, 63*(6),1898-1915.
- Bonifacci, P., Massi, L., Pignataro, V., Zocco, S., & Chiodo, S. (2019). Parenting Stress and Broader Phenotype in Parents of Children with Attention Deficit Hyperactivity Disorder, Dyslexia or Typical Development. *International journal of environmental research and public health*, *16*(11), 1878.
- Desideri, L., Ottaviani, C., Malavasi, M., Di Marzio, R., Bonifacci, P. (2019). Emotional processes in human-robot interaction during brief cognitive testing. *Computers in Human Behavior,* 90, 331-342.
- Bonifacci, P., Storti, M., Tobia, & V., Suardi, A. (2016). Specific Learning Disabilities: A look inside children's and parents' psychological wellbeing and relationships. *Journal of Learning Disabilities*, 49(5) 532–545.

Research Group	**Group proposal: Proff. Annalisa Guarini, Elvis Mazzoni, Paola Bonifacci, Sara Garofalo** Dep. Psycologhy
Expertise in relation to the topic	Our proposal would combine complementary expertise from multiple research units of the Department of Psychology, with a strong track record in Italian and European-funded projects. Our interdisciplinary team integrates cognitive neuroscience, general psychology, developmental psychology, clinical psychology, and digital innovation to address the mental health impacts of digital technology use in children and young adults. The **Laboratory of Psychometrics and Neuropsychology** (https://psicologia.unibo.it/en/research/research-groups/boost-perception), operating within the **Cognitive Enhancement Service for Developmental Age (SPEV) and founder of the** University **spin-off Develop-Players**, brings applied expertise in designing and validating digital interventions to support cognitive and emotional development. The group unites psychologists and computer scientists to create scientifically validated digital games aimed at children with atypical neurodevelopment, fostering self-regulation and adaptive engagement with technology. The **Neuroscience of Motivation, Decision and Learning (MoDeL) group (**https://psicologia.unibo.it/en/research/research-groups/model-neuroscience-of-motivation-decision-and-learning**)**, operating within the **Center for Studies and Research in Cognitive Neuroscience (CsrNC), has a large expertise in the investigation** of the neural and cognitive mechanisms underlying adaptive and maladaptive learning processes, decision-making, and motivation. Using a multimodal approach - combining behavioural, psychophysiological (e.g., skin conductance, EMG, eye-tracking), electrophysiological (EEG), and non-invasive neurostimulation techniques (TMS, tDCS) - the neuro-behavioral underpinning of reward-based learning and how these processes contribute to vulnerability to anxiety, addiction, and compulsive behaviours, all of which are digital-use-related conducts. The **Laboratory for the Assessment of Learning Disorders (LADA) and the associated Psychological Service** has long-standing expertise in the field of learning processes and neurodevelopmental disorders, with extensive experience in research and applied projects carried out in collaboration with schools, local authorities, and private companies. It brings strong research expertise in integrating digital technologies with learning assessment systems, focusing on their impact on efficiency, effectiveness, and perceived well-being. The laboratory adopts experimental, psychometric, and technological approaches (eye-tracking) to develop evidence-

based methodologies and innovative tools that support inclusive education and adaptive learning environments.

The laboratory can contribute to the project by working on the **clinical and effectiveness aspects of technology use**, adopting a family-centered approach that takes into account the outcomes and sustainability of the proposed tools within a systemic and multidimensional framework.

The Research Group **Wellbeing at School, Bullying and Cyberbullying Prevention Programs** (https://psicologia.unibo.it/en/research/research-groups/wellbeing-at-school-bullying-and-cyberbullying-prevention-programs-1), based within the **Developmental Psychology Lab** and linked to the **SERES Psychological Service**, has extensive experience in prevention and intervention initiatives in school settings. The team has participated in several national and international projects aimed at promoting school wellbeing and preventing bullying and cyberbullying. The group collaborates closely with local institutions, including the Municipality of Bologna and the Regional School Office, which ensures access to a wide network of schools and facilitates data collection and stakeholder involvement. The team also has specific expertise in developing digital applications (APPs) to support parenting and promote psychological wellbeing. Together, these teams offer an integrated research-to-intervention framework combining neuroscience, clinical practice, advanced data science, and digital innovation.

The **SEFoRA Lab** and the related group **DEduTech-2Life (Developmental Technologies for life-cycle education and lifelong learning)** have relevant and wide experience in the following fields:

- Functional and dysfunctional use of Digital and Emergent Technologies in human life cycle, with particular interest on Technoference and Parental Phubbing dynamics.
- Use of Digital and Emerging Technologies to support transitions characterizing the entire life cycle.
- Developmental Robotics: Robots and Artificial Intelligence to build knowledge, foster inclusion and develop skills in children, adolescents, emerging adults, and adults.

The laboratory could contribute to the **analysis of dysfunctional effects in the use of digital technologies and also in the development of tools** related to the idea of digital minimalism i.e. the use of those applications and functions of digital devices functional to the developmental tasks of specific life periods.Together, these teams offer an integrated research-to-intervention framework combining neuroscience, developmental and educational psychology approaches, clinical practice, and digital innovation—directly aligned with the objectives of developing and testing **innovative interventions to prevent harmful effects of digital technology use on mental health**.

HORIZON-HLTH-2026-01-DISEASE-03: Advancing research on the prevention, diagnosis, and management of post-infection long-term conditions

Research Group	**Prof. Davide Martelli** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	Prof. Davide Martelli is an internationally recognized expert in neuroimmunology and autonomic physiology, with a specific focus on how the sympathetic nervous system regulates immune responses during and after infection. He discovered the *splanchnic anti-inflammatory pathway*, a key component of the inflammatory reflex that modulates systemic inflammation. His current research investigates how prolonged activation of this reflex contributes to immune dysregulation and post-infection long-term conditions. Prof. Martelli has developed a comprehensive experimental platform that integrates *in vivo* physiological monitoring, genetic mouse models, and ex vivo immune profiling. His laboratory employs transgenic lines lacking β2-adrenergic receptors, neuropeptide Y1 (NPY1) receptors, or both, enabling precise dissection of sympathetic–immune interactions. These models allow mechanistic exploration of how neural circuits influence immune trajectories after infection and how maladaptive neuro-immune signaling contributes to chronic sequelae. Recent studies from his group have provided evidence that *non-selective β-blockers enhance infection resolution* in animals and humans (Scientific Reports, in press, 2026), directly supporting the translational relevance of targeting sympathetic pathways in infection recovery. Furthermore, Prof. Martelli's group has established preliminary data for *cell-based immunotherapies*, where immune cells "educated" by sympathetic signals propagate anti-inflammatory effects upon adoptive transfer. His expertise is supported by a solid publication record in top-tier journals (*Brain, Behavior and Immunity; Journal of Physiology; Scientific Reports; Autonomic Neuroscience*) and leadership in international collaborations with the Florey Institute (Australia) and the University of São Paulo (Brazil). His ongoing projects, including a PRIN2022 grant and participation in the Italian PNRR "INF-ACT" program on emerging infectious diseases, provide the infrastructure and translational partnerships necessary to investigate and intervene in post-infectious chronic conditions. Prof. Martelli's group thus offers unique expertise and experimental capacity to elucidate the neuro-immune mechanisms underpinning post-infection syndromes and to develop innovative interventions targeting maladaptive autonomic–immune interactions.

Research Group	**Prof. Laura Mercolini** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	The Research Group of Pharmaco-Toxicological Analysis Laboratory (PTA Lab), led by Prof. Laura Mercolini, has a long-standing track record in quantitative bioanalysis of drugs for therapeutic drug monitoring (TDM) and in the measurement of disease and susceptibility markers, hormones and

neurotransmitters. Building on this foundation, the group has developed a strong focus on longitudinal monitoring of patients by integrating advanced (U)HPLC-MS/MS and UHPLC-HRMS platforms with innovative microsampling technologies. This portfolio is directly aligned with the objectives of HORIZON-HLTH-2026-01-DISEASE-03, which require robust, patient-centric analytical strategies to characterise, prevent and manage post-infection long-term conditions across different infectious diseases.

PTA Lab can contribute to this topic by designing and validating targeted and untargeted analytical workflows for antibacterial and antiviral agents, metabolites and exposure biomarkers in multiple biological matrices (e.g., blood, plasma, serum, urine, saliva). The group has consolidated expertise in volumetric and dried microsampling (VAMS, qDBS, mfDBS, capillary-generated DBS and related approaches), enabling minimally invasive, frequent and decentralised sampling in both hospital-based and home-based settings. These approaches are particularly suited for large, multi-centre cohorts and for vulnerable populations, supporting high-frequency follow-up without overburdening patients and healthcare systems. Analytical investigations include targeted quantification of pharmacological treatments and key biochemical pathways, as well as HRMS-based omics (metabolomics, exposomics) aimed at identifying biochemical signatures of post-infection sequelae, patient stratification patterns, and markers predictive of disease progression or treatment response.

Within consortia addressing post-infection long-term conditions (e.g., chronic pulmonary and systemic sequelae after tuberculosis or long-term complications of herpesvirus/CMV infection in immunocompromised or other high-risk patients), PTA Lab can act as a centralised bioanalytical and microsampling hub. The group is able to:

- Co-design sampling schemes and standard operating procedures for longitudinal studies;
- Implement microsampling-based sampling strategies for outpatients or remote settings;
- Perform high-throughput quantitative analysis of drugs, inflammatory and immunological biomarkers, and metabolic signatures;
- Support data integration with clinical and imaging outcomes, in collaboration with clinical and basic-science partners (e.g., microbiology, immunology, neurology/neuro-immunology groups).

All methods are developed and validated in accordance with EMA/FDA/ICH bioanalytical guidelines, ensuring standardisation, regulatory compliance and comparability across sites. The group has ongoing collaborations with international analytical laboratories and is well positioned to support cross-laboratory method transfer and harmonisation in large European consortia.

Relevant publications

	▪ Protti M, Mandrioli R, Mercolini L. Quantitative microsampling for bioanalytical applications related to the SARS-CoV-2 pandemic: Usefulness, benefits and pitfalls. J Pharm Biomed Anal. 191 (2020) 113597. https://doi.org/10.1016/j.jpba.2020.113597 ▪ Protti M, Mandrioli R, Santos HM, Lodeiro C, Capelo-Martínez JL, Mercolini L. How microsampling is impacting pharmacokinetic and toxicokinetic studies: volumetric absorptive microsampling (VAMS). Bioanalysis. 17 (2025) 997-1009. https://doi.org/10.1080/17576180.2025.2546782 ▪ Carvalho LB, Teigas-Campos PAD, Jorge S, et al. Normalization methods in mass spectrometry-based analytical proteomics: A case study based on renal cell carcinoma datasets. Talanta. 266b (2024) 124953. https://doi.org/10.1016/j.talanta.2023.124953 ▪ Protti M, Cirrincione M, Palano S, et al. Targeted quantitative metabolic profiling of brain-derived cell cultures by semi-automated MEPS and LC-MS/MS. J Pharm Biomed Anal. 236 (2023) 115757. https://doi.org/doi:10.1016/j.jpba.2023.115757 Protti M, Mercolini L, Mandrioli R. Review: the role of automation in improving the performance and throughput of microsample bioanalysis. Anal Chim Acta. 1359 (2025) 344018. https://doi.org/10.1016/j.aca.2025.344018 **Relevant projects** ▪ "Therapeutic monitoring of second-generation antidepressant drugs in patients with food disorders, performed by means of mini-invasive techniques: a pilot study", 2018. Funding: Servizio Sanitario Regionale Emilia Romagna (707/2018/ SPER /AUSLBO). ▪ "Linking tryptophan catabolism to amyotrophic lateral sclerosis: from the pathogenesis to the pharmacological treatment", 2017. Funding: Ministry for Education, University and Research (MIUR) with PRIN (Scientific Projects with High National Impact) funds (Ref. 20173EAZ2Z). ▪ "Finding new targets to counteract brain progenitor cells dysregulation in AGC1 deficiency hypomyelination: a multi-disciplinary approach" 2019-2022. Funding: Fondazione Telethon (Ref. GGP19067). ▪ "Dried microsamples: multi-matrix, long-term stability study of doping-relevant peptides", 2019. Funding: World Anti-Doping Agency (WADA, Ref. 19A08LM). ▪ "Analysis of lithium plasma levels by peripheral blood microsampling in the monitoring of patients with bipolar disorder" 2022-2024. Funding: Servizio Sanitario Regionale Emilia Romagna (849-2022-SPER-AUSLBO).

Research Group	**Prof. Marina Tadolini** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	**Expertise:** Clinical management of tuberculosis (TB) and MDR-TB; post-treatment follow up for at least 12 months after the end of TB treatment; TB Prevalence surveys at natinoal level (high burden countries); early TB diagnosis in vulnerable population; Longitudinal

	cohort studies of TB patients with associated clinical, bacteriological, radiological and socioeconomic data; characterization of subclinical/asymptomatic TB; Implementation and outreach activities in vulnerable populations (recent migrants from high incidence countries); evaluation of new biomarkers and diagnostic tests; TB prevention strategy (TB infection screening and treatment); Coordination of international TB experts' platform for evaluation of new preventive and therapeutic strategies, including for MDR-TB (Global TB consilium in the framework of Global TB Network initiative); **Publications:** ▪ Fumagalli G, Mencarini J, Sini I, Allavena L, Tadolini M, Mantero M, Blasi F, Riccardi N, Pontarelli A, Piccioni P, Calcagno A, Sotgiu G, Shah D, Codecasa LR, Parrella R; StopTB Italia ODV. Post-tuberculosis lung disease: a guide for clinicians. Infection. 2025 Sep 25. doi: 10.1007/s15010-025-02645-2. Epub ahead of print. PMID: 40996670. ▪ Nasiri MJ, Silva DR, Rommasi F, Zahmatkesh MM, Tajabadi Z, Khelghati F, Sarmastzadeh T, Centis R, D'Ambrosio L, Bombarda S, Dalcolmo MP, Galvão T, de Queiroz Mello FC, Rabahi MF, Pontali E, Solovic I, Tadolini M, Marconi L, Tiberi S, van den Boom M, Sotgiu G, Migliori GB. Vaccination in post-tuberculosis lung disease management: A review of the evidence. Pulmonology. 2025 Dec 31;31(1):2416801. doi: 10.1016/j.pulmoe.2023.07.002. Epub 2024 Oct 24. PMID: 37679219. **Tasks that could be carried out:** retrospective cohort study from patients who have completed TB treatment with clinical, bacteriological, radiological and socioeconomic data

HORIZON-HLTH-2026-01-DISEASE-04: Development of novel vaccines for viral pathogens with epidemic potential

Research Group	**Prof. Francesco Paolucci** Dep. Sociology and Business Law
Expertise in relation to the topic	Professor of Health Economics and Policy at the University of Newcastle, Australia, and the University of Bologna, Italy. He was appointed advisor to the Chilean Minister of Health on healthcare reform and represented the Emilia-Romagna Region on the technical committee for the distribution of funds for the National Health System. He is an associate editor for the world's leading journals in health policy and economics and strong record of international research collaborations. He has Published over 110 academic peer-reviewed articles, book chapters and reviews. Prof. Paolucci is currently chief investigator on grants funded by the Australian Research Council, the National Health Medical Research Council, and the European Commission (Horizon2020). So far, he has been awarded various industry grants from public and private agencies. His engagement is extensively in academics, conducting innovative research activities, training

programs, journal reviews, and supervision of post-graduate theses nationally and abroad.

Area of Contribution

His area of expertise is on public policy and healthcare financing. It involves activities aimed at improving the efficiency and equity of healthcare resource allocations. Activities include designing and implementing economic evaluations, such as cost-effectiveness and cost-utility analysis, to quantify the value of medical technologies and interventions. In addition, contributes to stakeholders' preference elicitation studies (such as discrete choice experiments or DCE) to understand how different stakeholders value health outcomes and treatment attributes. These activities support evidence-based decision-making by integrating clinical effectiveness, cost-effectiveness, costs, and value of preferences to guide policy and priority setting in healthcare systems.

Related Projects

- **Health Economic Evaluation of Biomarker-based Diagnostic Toolkit to Personalize Pharmacological Approached in Congestive Heart Failure (BIOTOOL-CHF) Project** [*$2,600,000 | 2023 | European Commission, European Union*]
- **Old and lonely? Preferences for peer support interventions among older adults in Australia** *[$5,000,000 | 2022 | Australian Commonwealth Government]*
- **Identify barriers, facilitators and system capabilities for telehealth uptake and develop an evidence-informed integrated model of telehealth implementation across and within HNE Mental Health** *[$125,766 | 2021 | Hunter Medical Research Institute]*
- ***Economic Development, Health and Nutrition for Sustainable Development*** *[$10,000 | 2019 | Australia Africa Universities Network (AAUN)]*
- **Healthcare programs evaluation** *[$113,000 | 2015 | 360]*

Related Publications

- Antonini M, et al., **'Are we ready for the next pandemic? Public preferences and trade-offs between vaccine characteristics and societal restrictions across 21 countries**', Social Science and Medicine, 366 (2025)
- Wilson J, et al., **'Measuring factors associated with telehealth use by people who use mental health services: A psychometric analysis of a theoretical domains framework questionnaire**', JOURNAL OF TELEMEDICINE AND TELECARE (2024)
- Schilling C, et al., **'An Economic Model for Estimating Trial Costs with an Application to Placebo Surgery Trials**', APPLIED HEALTH ECONOMICS AND HEALTH POLICY, 21, 263-273 (2023)
- Sequeira AR, Mentzakis E, Archangelidi O, Paolucci F, **'The economic and health impact of rare diseases: A meta-analysis'**, HEALTH POLICY AND TECHNOLOGY, 10, 32-44 (2021)

Research Group	**Prof. Daniel Remondini** Dep. Physics and Astronomy
Expertise in relation to the topic	Expertise in modeling and analysis of biological and biomedical data with a "One health" approach, as developed within the EU VEO project (WP2 "Advanced datamining tools" co-leader) or in E-MUSE MSCA project on novel food development and analysis. Application of Artificial Intelligence methods (e.g. NLP tools for protein sequence analysis): Language models learn to represent antigenic properties of human influenza A(H3) virus, Francesco Durazzi, Marion P. G. Koopmans, Ron A. M. Fouchier & Daniel Remondini, Scientific Reports | (2025) 15:21364 Application of network theory approaches for the analysis of metagenomic data (human, animal, environmental): Metagenomics data: tell me which metrics and I will tell you which communities, Alessandro Fuschi, Alessandra Merlotti, Daniel Remondini, ISME Commun. 2025 Jul 24;5(1):ycaf125. doi: 10.1093/ismeco/ycaf125; Time-series sewage metagenomics distinguishes seasonal, human-derived and environmental microbial communities potentially allowing source-attributed surveillance. Becsei Á, Fuschi A, …, Remondini D, Aarestrup FM, Munk P. Nat Commun. 2024;15(1):7551. doi: 10.1038/s41467-024-51957-8 Application of mathematical modelling for epidemic evolution characterization integrating multiple data types (genomic, clinical, demographic, mobility): Human mobility and sewage data correlate with COVID-19 epidemic evolution in a 3-year surveillance of the metropolitan area of Bologna, Francesco Durazzi, Enrico Lunedei, Giulio Colombini, Giulia Gatti, Vittorio Sambri, Alessandra De Cesare,Cecilia Crippa, Frédérique Pasquali, Gastone Castellani, Daniel Remondini, Armando Bazzani and Bologna MODELS4COVID Study Group, Durazzi et al. BMC Infectious Diseases (2025) 25:1467; Modelling antimicrobial resistance transmission to guide personalized antimicrobial stewardship interventions and infection control policies in healthcare setting: a pilot study, F. Durazzi, …, Daniel Remondini & Evelina Tacconell, Sci. Rep. (2023) 13:15803 https://doi.org/10.1038/s41598-023-42511-5

Research Group	**Prof. Pier Luigi Martelli** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	The Bologna Biocomputing Group develops algorithms, methods and software tools by exploiting and integrating data from multi-disciplinary data sets. The group has a large experience in the application of machine learning models to the interpretation of omic data that can be used to stratify and cluster disease and phenotypes and to characterize the biological significance of molecules that can act as biomarkers

	We curated tools for the characterization of the structure and function of proteins and their variants, as well as databases of associations among variations/genes, diseases and phenotypes. Specifically, the group can support the phases of: ▪ Identification of host receptors guided by the analysis of the role of macromolecules in the context of biological complexity and target structural and functional characterization. ▪ Structural and functional characterization of host receptors and viral proteins, and of their interactions. The tools developed by the group are available at http://www.biocomp.unibo.it/predictors. The group is active in the ELIXIR ESFRI, it has contacts with managers of centralized data and tool repositories and it has direct connections with computing and cloud providers.

HORIZON-HLTH-2026-01-DISEASE-09: Multisectoral approach to tackle chronic non-communicable diseases: implementation research maximising collaboration and coordination with sectors and in settings beyond the healthcare system (GACD)

Research Group	**Prof. Antonio Cicchella** Dep. Quality of Life Studies
Expertise in relation to the topic	Expertise in exercise sciences connect with health and especially: hormones and exercise in children and adoloscents, physical activity growth and metabolic syndrome, obesity and physical activity, exercise and infections, exercise and addictive behaviours. ▪ Sun J, Zhao R, Chen J, Yao K, Chen T, Lu T, Cicchella A. Psychological and behavioral characteristics of overweight and obese Chinese college students with high stress. BMC Psychol. 2025 Sep 29;13(1):1080. doi: 10.1186/s40359-025-03457-7. PMID: 41024172; PMCID: PMC12482486. ▪ Sun J, Zhao R, Cicchella A. Mental and Physical Health of Chinese College Students After Shanghai Lockdown: An Exploratory Study. Healthcare (Basel). 2025 Jul 30;13(15):1864. doi: 10.3390/healthcare13151864. PMID: 40805895; PMCID: PMC12346089. ▪ Sun J, Chen J, Cicchella A. Correlation of Adiponectin and Leptin with Anthropometrics and Behavioral and Physical Performance in Overweight and Obese Chinese College Students. Biology (Basel). 2024 Jul 27;13(8):567. doi: 10.3390/biology13080567. PMID: 39194505; PMCID: PMC11352017. ▪ Cicchella A. Recommendations for Resuming PA after Prolonged Rest in Children and Adolescents: A Systematic Integrative Review of Relevance for Immunity. J Funct Morphol Kinesiol. 2022 Jun 2;7(2):47. doi: 10.3390/jfmk7020047. PMID: 35736018; PMCID: PMC9224580. ▪ Cicchella A, Jürimäe T, Stefanelli C, Purge P, Lätt E, Saar M. Correlations of skinfold thicknesses and circumferences at exactly defined body sites with leptin in 10-12-year-old boys

	with different BMIs. Coll Antropol. 2014 Jun;38(2):459-65. PMID: 25144974.

Research Group	**Prof. Antonello Lorenzini** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	PhD in Biochemistry and Physiopathology of Aging. Our group focuses on **nutrition and healthy lifestyles**. Regarding the Horizon calls, we emphasized our active collaboration with Prof. Lars Fadnes' group at the University of Bergen to expand the scope of their "**Food for Healthy Life**" **calculator** (F4HL: http://v2.food4healthylife.org/). This calculator currently allows, after analyzing an individual's diet, to prioritize the changes needed to make the diet healthier and therefore capable of extending the individual's longevity. Towards the goal of expanding the calculator's capabilities so that it will also produce **risk estimates of NCDs**, the collaboration has already produced three umbrella reviews (1, 2, 3), and it has others in progress. The calculator could form the basis of a preventive tool for projects dedicated to the prevention of NCDs both in young people (12-25 years) and in adults. A second project, which can be easily linked to the previous one, is a project on **Artificial intelligence**, it is a project born in Bologna between the PI's group and the CINECA supercomputing consortium. This collaboration aims to develop a tool that uses **Natural Language Processing (NLP)** to semi-automate the construction of meta-analyses from scientific literature, with particular emphasis on optimizing text and data mining in the biomedical and specifically in the epidemiological field. The first manuscript related to this tool has been submitted (4) and we have two other publications in progress that exploit this new tool. ▪ Umbrella Review of Systematic Reviews and Meta-Analyses on Consumption of Different Food Groups and Risk of Type 2 Diabetes Mellitus and Metabolic Syndrome. Banjarnahor RL, Javadi Arjmand E, Onni AT, Thomassen LM, Perillo M, Balakrishna R, Sletten ISK, Lorenzini A, Plastina P, Fadnes LT.J Nutr. 2025 May;155(5):1285-1297. doi: 10.1016/j.tjnut.2025.03.021. Epub 2025 Mar 22.PMID: 40122387 ▪ Umbrella Review of Systematic Reviews and Meta-Analyses on the Consumption of Different Food Groups and the Risk of Overweight and Obesity. Kristoffersen E, Hjort SL, Thomassen LM, Arjmand EJ, Perillo M, Balakrishna R, Onni AT, Sletten ISK, Lorenzini A, Fadnes LT. Nutrients. 2025 Feb 13;17(4):662. doi: 10.3390/nu17040662.PMID: 40004990 ▪ Umbrella Review of Systematic Reviews and Meta-analyses on Consumption of Different Food Groups and Risk of All-cause Mortality. Onni AT, Balakrishna R, Perillo M, Amato M, Javadi Arjmand E, Thomassen LM, Lorenzini A, Fadnes LT.Adv Nutr. 2025 Apr;16(4):100393. doi: 10.1016/j.advnut.2025.100393. Epub 2025 Feb 15.PMID: 39956388 ▪ TextAlchemy: an NLP tool to accelerate and semi-automate data extraction, validated in the nutritional field. Rooshan Saleem Butt, Matteo Perillo, Michele Visciarelli, Giorgio Pedrazzi,

	Marco Amato, Andrea Galassi, Rajiv Balakrishna, Anindita Tasnim Onni, Lars Thore Fadnes, Paolo Torroni, Roberta Turra, Antonello Lorenzini; *submitted*.

Research Group	**Prof. Alessia Tessari** Dep. Psychology
Expertise in relation to the topic	Our group offers a combination of rigorous evidence-based behavioral science, deep expertise in the cognitive design of digital health technologies, and a robust network for successful implementation in real-world settings. We focus on healthy aging and well-being across the lifespan, particularly for vulnerable populations (e.g., Alzheimer's, retirees), and younger populations. This expertise is built on three interconnected pillars: 1. Translational Research on Longevity and Lifestyle We develop and implement scientific protocols utilizing physical activity as a critical determinant to counteract Non-Communicable Diseases (NCDs) and promote psycho-cognitive well-being (impacting central nervous system and mitigating depression). Research focuses on managing the stress of major life transitions (like retirement), which exposes individuals to higher risks of chronic conditions. 2. Digital Implementation and Technological Development We provide essential tools and methodologies for Digital Implementation, ensuring scalability and contextual relevance. Our expertise lies in the use of ICT, Virtual Reality (VR), and gamification for well-being (demonstrated by projects like REWIRE and MAIA). We specialize in designing optimal usability and human-technology interaction, and in adapting digital tools (e.g., self-monitoring apps) to specific socio-cultural, political, and economic contexts. This includes developing tools to calculate individual risk indices. 3. Implementation Research and Community Contexts We apply a robust Action-Research framework to systematically integrate evidence-based interventions outside of clinical settings, specifically in community and organizational contexts. We design implementation strategies to promote physical activity in real-world environments (schools, urban spaces). Our experience is bolstered by strong connections with real-world stakeholders, including local health authorities, trade unions, companies, and centers managing complex social security/employment procedures, alongside solid relationships with various EU universities and technology firms. ▪ Ventura et al. (2023). Co-designing an interactive artificial intelligent system with post-stroke patients and caregivers to augment the lost abilities and improve their quality of life: a human-centric approach. *Frontiers in Public Health*, *11*, 1227748. ▪ Ottoboni et al. (2022). A Multifunctional Adaptive and Interactive AI system to support people living with stroke, acquired brain or spinal cord injuries: A study protocol. *PloS one*, *17*(4), e0266702. ▪ Ottoboni et al. (2021). The effect of structured exercise on short-term memory subsystems: new insight on training activities.

	International Journal of Environmental Research and Public Health, *18*(14), 7545. ▪ O'Brien et al. (2021). Multisensory perception, verbal, visuo-spatial and motor working memory modulation after a single open-or closed-skill exercise session in children. *Journal of Cognitive Enhancement*, *5*(2), 141-154. ▪ O'Brien, J., Ottoboni, G., Tessari, A., & Setti, A. (2017). One bout of open skill exercise improves cross-modal perception and immediate memory in healthy older adults who habitually exercise. *PloS one*, *12*(6), e0178739.

Research Group	**Prof. Roberto Mandrioli** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	*Activities/tasks the research group will be able to carry out* High- sensitivity, high-accuracy determination of drugs or treatment/exposu-re/vulnerability/diagnosis biomarkers in different biofluids (blood, plasma, urine, saliva, sweat) by HPLC-MS/MS and related techniques. Analytical determinations that can provide objective data suitable for taking informed therapeutic/diagnostic decisions. Development and/or application of devices for invasive or non-invasive biofluid sampling. Microsampling for repeated/frequent testing. *Expertise* Development, validation and application of high-performance analytical methods for the analysis of bioactive molecules in different biological fluids. Development and implementation of original devices, and use and adaptation of commercial devices, for microsampling and application of the resulting micromatrices for therapeutic drug monitoring, forensic analysis, ADME studies. Analytical techniques: HPLC-MS, HPLC-MS/MS, UHPLC-HRMS, CZE-MS, ATR-FTIR. Recent publications: ▪ R. Mandrioli *et al.* Novel microsampling approach using fabric-phase sorptive extraction (FPSE) for cannabinoid analysis in blood. Microchem. J. 210, 113855 (2025); ▪ M. Protti *et al.* Quantitative urine spot microsamples for the chiral analysis of clenbuterol by capillary electrokinetic chromatography. Microchem. J. 210, 112940 (2025); ▪ J. Millán-Santiago *et al.* Volumetric absorptive microsampling for the therapeutic drug monitoring of psychiatric patients treated with cariprazine. JPBA 236, 115740 (2023). Other publications: https://www.unibo.it/sitoweb/roberto.mandrioli/publications. Relevant projects: Member of project "Advancing peptide analysis in dried blood spots: application potential and stability study of doping-relevant peptides" (2020 WADA Research Grants Section A: Ref. 20A12LM). Relevant patents: "Device for the microsampling, storage and transport of a biological matrix", Italian patent request n. 102025000025819.

Research Group	**Prof. Olivia Manfrini** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	Olivia Manfrini is a Professor of Cardiology at the University of Bologna. She coordinates the activities of the Laboratory of Epidemiology and Clinical Cardiology at DIMEC, which was established with the aim of identifying and analyzing disparities in cardiovascular (CV) health, understanding their causes, and developing targeted solutions. The research group's work is based on an awareness of the importance of Big Data in clinical research. From its earliest stages, the laboratory recognized the potential of large-scale analysis to understand and address issues of clinical interest. In line with this principle, one of the Laboratory's first and main activities was the establishment and launch of the ISACS (International Survey of Acute Coronary Syndromes) registry (NCT01218776). This multicenter, international observational study was designed in 2010 to collect data on acute coronary syndromes (ACS) in Eastern European countries, which at that time had their economy in transition, providing a solid basis for analyzing cardiovascular inequalities. Over the years, our group has integrated advanced statistical analysis and machine learning techniques in collaboration with specialized centers. These tools have enabled us to conduct in-depth studies on crucial topics, including: ▪ Sex and gender differences in the presentation, treatment, and outcomes of ACS. ▪ The impact of clinical management on the prognosis of elderly and frail patients with ACS. ▪ Inequalities in CV heath linked to disadvantaged socioeconomic conditions. ▪ The management of complex patients with CV diease, such as those undergoing chemotherapy or affected by SARS-CoV-2. The group currently coordinates and processes data on more than 100,000 patients from centers located in Serbia, Macedonia, Croatia, Romania, Kosovo, Bosnia-Herzegovina, Italy, and Montenegro. The global perspective that has always inspired our project has allowed us to build a solid network of international collaboration that is open to new partnerships, united by a passion for research, ethics, and data rigor. ▪ Rahaman T, Cenko E, Manfrini O, Maas A, Bergami M, Gale CP, Gulati M, Bugiardini R. Sex Disparities in Ischemic Heart Disease Mortality Across United States: The Southern Burden of Excess Body Weight and Diet. **J Am Heart Assoc. 2025** Nov 3:e043914. doi: 10.1161/JAHA.125.043914. ▪ Bugiardini R, Rahaman T, Manfrini O, Maas A, Bergami M, Badimon L, Mendieta G, Vavlukis M, Merkely B, Vasiljevic Z, Gale CP, Gulati M, Cenko E. Diet and sex inequities in ischemic heart disease mortality across Europe: findings from the global burden of disease study. **Cardiovasc Res. 2025** Nov 3:cvaf176. doi: 10.1093/cvr/cvaf176. ▪ Rahaman T, Cenko E, Manfrini O, Maas A, Bergami M, Gale CP, Gulati M, Bugiardini R. Sex Disparities in Ischemic Heart Disease

	in South Asia: The Role of Dietary Factors. **JACC Asia. 2025** Aug 25:S2772-3747(25)00386-2. doi: 10.1016/j.jacasi.2025.07.012. ▪ Maas A, Cenko E, Vaccarino V, Göttgens I, Bergami M, Manfrini O, Badimon L, Mendieta G, Oertelt-Prigione S, Vasiljevic-Pokracic Z, Dorobantu M, Vavlukis, Merkely B, Gulati M, Bugiardini R. Changing Clinical Perspectives on Sex and Healthcare Disparities In Ischaemic Heart Disease. **Lancet Reg Health Eur. 2025;** 56: 101370 doi: 10.1016/j.lanepe.2025.101370. ▪ Cenko E, Yoon J, Bergami M, Gale CP, Vasiljevic Z, Vavlukis M, Kedev S, Miličić D, Dorobantu M, Badimon L, Manfrini O, Bugiardini R. Coronary revascularization and sex differences in cardiovascular mortality after myocardial infarction in 12 high and middle-income European countries. **Eur Heart J Qual Care Clin Outcomes. 2024** May 7:qcae035. doi: 10.1093/ehjqcco/qcae035. ▪ 6. Manfrini O, Cenko E, Bugiardini R. Gender Differences in Residual Risk Factors for Major Adverse Cardiovascular Events Following ACS and How to Bridge the Gap. **Curr Atheroscler Rep. 2020** Sep 3;22(11):65. doi: 10.1007/s11883-020-00882-4. PMID: 32880760

Research Group	**Dr Pierpaolo Palumbo** Dep. Electrical, Electronic, and Information Engineering
Expertise in relation to the topic	We are a group of biomedical engineers with consolidated expertise in the field of biomedical data analysis and predictive models. We are particularly interested in collaborating in research projects on allergies and autoimmune conditions. We are accustomed to work across disciplines and sectors and inclined to serve disadvantaged populations in either high- or low- and middle-income countries. Our experience in predictive models ranges from risk factor identification to model development, validation, and impact analysis. We have developed health risk assessment models for non-communicable diseases. We have validated risk screening models proposed by international medical societies. We have applied causal machine learning techniques on observational data to evaluate the efficacy of different interventions, derive personalised efficacy profiles, and evaluate the potential impact of risk predictive models informing intervention policies. We have acquired domain specific knowledge on – among others – geriatric affections (falls and late-life depression), lower-limb amputations, and metal allergies. Selected publications • Palumbo, P. (2025). Qini Curves for Potential Impact Assessment of Risk Predictive Models Informing Intervention Policies. Value in Health • Topic Group on "Falls among the elderly" of the ITU/WHO Focus Group "Artificial Intelligence for Health" (2023). Fall risk stratification of community-living older people. Commentary on the world guidelines for fall prevention and management. Age and Ageing, 52(10)

	• Belvederi Murri, M. et al. (2022). Risk Prediction Models for Depression in Community-Dwelling Older Adults. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 30(9), 949–960 • Palumbo, P. et al. (2022). The Degree of Safety against Falls Provided by 4 Different Prosthetic Knee Types in People with Transfemoral Amputation: A Retrospective Observational Study. Physical Therapy • Cattelani, L. et al. (2019). Risk Prediction Model for Late Life Depression: Development and Validation on Three Large European Datasets. IEEE Journal of Biomedical and Health Informatics, 23(5), 2196–2204 • Palumbo, P et al. (2019). Simulating the effects of a clinical guidelines screening algorithm for fall risk in community dwelling older adults. Aging Clinical and Experimental Research, 31(8), 1069–1076 • Klenk, J. et al. (2017). Conceptualizing a Dynamic Fall Risk Model Including Intrinsic Risks and Exposures. Journal of the American Medical Directors Association, 1–7 • Palumbo, P. et al.(2016). Predictive Performance of a Fall Risk Assessment Tool for Community-Dwelling Older People (FRAT-up) in 4 European Cohorts. Journal of the American Medical Directors Association, 17(12), 1106–1113 • Palumbo, P.et al. (2015). Fall Risk Assessment Tools for Elderly Living in the Community: Can We Do Better? PLOS ONE, 10(12) • Palumbo, P. et al. (2015). A probabilistic model to investigate the properties of prognostic tools for falls. Methods of Information in Medicine, 54(2) https://scholar.google.com/citations?user=HSrKkzgAAAAJ

Research Group	**Prof. Anna Vittoria Mattioli** Dep. Life Quality Studies
Expertise in relation to the topic	Full Professor of Advanced Medical and Surgical Technology and Methodology at the University of Bologna and a cardiologist with internationally recognized expertise in sex- and gender-specific mechanisms of cardiovascular diseases (CVD). Her research focuses on lifelong cardiovascular prevention, women's cardiovascular health, and lifestyle-driven modulation of cardiometabolic risk through nutrition, exercise, and digital health tools. She has coordinated and participated in several national and EU-funded projects on precision prevention, active ageing, and digital cardiovascular risk monitoring (e.g., HEAL ITALIA, Lively Ageing, WEARbeing), integrating biomedical, technological, and population-level research. As Vice-President of the National Institute for Cardiovascular Research (INRC) and incoming Coordinator of the Gender Cardiovascular Diseases Working Group of the Italian Society of Cardiology, she promotes translational research on hormonal, inflammatory, and metabolic pathways mediating sex and gender differences in cardiovascular diseases.

	Her current research investigates the interplay between biological and environmental determinants of cardiovascular risk, including the exposome, environmental stressors, menopause transition, and maternal–fetal interactions. These studies contribute to defining **sex-specific phenotypes and endotypes** of cardiovascular disease and their implications for precision prevention and treatment. Through **IPPOCRA-Tech**, a university spin-off, she has developed a **non-invasive, AI-based device capable of simultaneously monitoring the five vital signs**, enabling real-time assessment of physiological stress responses and supporting large-scale, data-driven implementation research. With over 300 peer-reviewed publications and international recognition (FESC, FACC), Prof. Mattioli combines clinical and translational expertise to advance **sex- and gender-sensitive mechanistic and implementation research** on chronic non-communicable diseases. Her work directly contributes to the GACD objectives by fostering cross-sectoral integration of biomedical, digital, and environmental data to improve prevention and management strategies for cardiovascular health.

Research Group	**Dr Lidia Strigari** IRCCS Sant'Orsola
Expertise in relation to the topic	The Department of Medical Physics, led by Lidia Strigari, has extensive experience in multidisciplinary and multisectoral research aimed at understanding, monitoring, and improving health outcomes in chronic non-communicable diseases (NCDs). Its expertise encompasses the integration of biomedical imaging, computational modelling, patient-specific data analysis, and health system analytics to support implementation research that maximises collaboration across sectors and extends beyond traditional healthcare settings. The Department has pioneered approaches that combine quantitative imaging biomarkers, physiological modelling, and digital twin technologies to capture disease heterogeneity and predict individual responses to interventions. These capabilities enable the simulation and evaluation of interventions not only within clinical environments but also across community and social contexts, supporting a genuinely multisectoral approach. By linking clinical, behavioural, environmental, and socio-economic data, the Department develops integrated frameworks that inform policy and practice, facilitating evidence-based decision-making in the prevention and management of NCDs. Furthermore, the Department has a strong track record in conducting and participating in complex research projects involving multiple stakeholders, including academic institutions, public health agencies, industry partners, and patient organisations. This experience ensures effective collaboration and knowledge exchange across sectors, fostering the co-design of interventions that are culturally relevant, contextually appropriate, and scalable. High-performance computational infrastructures, advanced analytics, and reproducible workflows allow the Department to model interventions, assess outcomes, and

	generate actionable insights that accelerate the translation of research into practice. Within the scope of HORIZON-HLTH-2026-01-DISEASE-09, the Department can provide methodological expertise in implementation research, multisectoral collaboration, and data-driven intervention design. Its capabilities support the optimisation of interventions across healthcare and non-healthcare settings, the development of monitoring frameworks for complex NCD interventions, and the evaluation of impact in real-world contexts, thereby advancing European and global strategies for the prevention and management of chronic diseases.

Research Group	**Prof. Marco Caprini & Dr Francesco Formaggio** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	Research Focus Our group investigates mechanisms underlying chronic non-communicable diseases (NCDs) with a strong emphasis on neuroscience, targeting both central and peripheral nervous system dysfunctions. We develop advanced in vitro and in vivo models to study neuroinflammation, neuropathic pain, and neurodegeneration. Experimental Activities and Methodologies • Cellular Models: Primary cultures of neurons and glial cells (astrocytes, microglia); differentiation of iPSCs into neurons and glia. • Tissue and Animal Models: Ex vivo tissue preparations and in vivo models for chronic pain and neurodegenerative conditions. • Advanced Techniques: Electrophysiology (patch-clamp, multielectrode arrays), calcium imaging, confocal and electron microscopy. • Bioprinting: Development of 3D bioprinted human models in neuroscience Demonstration of Expertise **Relevant Publications** • Formaggio F. et al., Neurobiology of Disease, 2025: Calcium dysregulation in Fabry neuropathy. • Formaggio F. et al., J. Mater. Chem. B, 2025: 3D-bioprinted dermal-like scaffold for nerve regeneration. • Lucarini I., Formaggio F. et al., Adv. Healthc Mater, 2025: Silicon nanowire mats for advanced bioelectrical recordings. **Recent projects** • Fondazione Del Monte (2024–2026): Bioprinting of human 3D models for chronic pain. • Collaborative project: PRIN BASICPROMED (2023–2025): Biological characterization of bioprinted samples via confocal microscopy. • Collaborative project: PNRR MNESYS (2022–2025): Electrophysiological characterization of iPSC-derived neurons in Angelman syndrome.

HORIZON-HLTH-2026-01-DISEASE-11: Understanding of sex and/or gender-specific mechanisms of cardiovascular diseases: determinants, risk factors and pathways

Research Group	**Prof. Davide Agnoletti** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	The Cardiovascular Internal Medicine Unit of the University of Bologna (DIMEC, IRCCS Policlinico S. Orsola) is an ESH Hypertension Excellence Center with a consolidated clinical–research program on hypertensive disorders of pregnancy (HDP) and sex-specific vascular aging. HDP, which complicate about 10% of pregnancies and remain a leading cause of maternal, fetal, and neonatal morbidity, are used by our group as a natural, women-only model to study the trajectory from pregnancy-related hypertension to later cardiovascular disease, in line with the framework shown in the project presentation on *HORIZON-HLTH-2026-01-DISEASE-11*. In a single-center cohort, we showed that prenatal care delivered by a multidisciplinary team including internists specialized in hypertension and obstetric medicine is associated with a lower incidence of preeclampsia compared with standard obstetric management, demonstrating the clinical value of embedding internal medicine into cardio-obstetrics (Piani *et al.*, *Eur J Intern Med* 2023;117:148–150. doi:10.1016/j.ejim.2023.08.017). This model is exactly the one promoted at European level by the ESH Working Group "Hypertension in Women", with whom our Unit actively collaborates and which recently issued the 2024 Position Statement on the management of HDP (Thomopoulos *et al.*, *J Hypertens* 2024;42:1109–1132. doi:10.1097/HJH.0000000000003739). This confirms our international connections inside the ESH cardio-obstetric network. Our group is expert in characterization of vascular structure and function through a triad of non-invasive methods: 1. Applanation tonometry with carotid–femoral PWV, augmentation index, and central BP to quantify aortic stiffness; (Agnoletti D, *et al. Atherosclerosis*. 2012;224(1):108-112. doi:10.1016/j.atherosclerosis.2012.06.055)(Agnoletti D, *et al. Journal of Human Hypertension*. 2017;31(3):189-194. doi:10.1038/jhh.2016.58). 2. Carotid ultrasonography wall-tracking system to measure local carotid stiffness, strain, and distensibility; 3. Endothelial function testing (FMD/microvascular reactivity) to capture early endothelial dysfunction. This multilevel phenotyping is applied to women with HDP without preeclampsia, and overt preeclampsia, allowing sex-specific comparisons over gestation and postpartum. In parallel, we identified two circulating markers that refine risk stratification: first-trimester CD93, reduced in women who later develop preeclampsia (Piani *et al.*, *High Blood Press Cardiovasc Prev* 2023;30:591–594. doi:10.1007/s40292-023-00608-y), and the serum uric acid/creatinine ratio (SUA/sCr), independently

	associated with preeclampsia, preterm birth, and neonatal composite outcome (Piani *et al.*, *J Hypertens* 2023;41:1333–1338). Putting together vascular phenotyping, biomarkers, and an ESH-anchored international network, the Bologna Unit is uniquely positioned to contribute to Horizon actions on sex- and gender-specific mechanisms of cardiovascular disease in pregnancy and postpartum.

Research Group	**Dr. Arianna Giorgetti** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	The research group of legal medicine has access to a unique casuistry of post-mortem cases involving cardiovascular diseases (CVD) and sudden cardiac death (SCD). This resource allows direct study of sex- and gender-specific mechanisms by analyzing human cardiac tissues and biological fluids collected during routine forensic investigations. Our research group is specialized in: ▪ Detailed macroscopical and pathological examination of the cardiac tissues, with possible comparison with the clinical history, including histopathology. This could provide material for *molecular analysis* to identify fibrosis, inflammation, and conduction system alterations with sex-stratified evaluation; ▪ Forensic toxicology screening of biological fluids for drugs of abuse, new psychoactive substances (NPS), that represent a public health threat in the EU, with an insight into the mechanisms of drug toxicity; ▪ Environmental toxicology, including PFAS and micro/nanoplastics determination, enabling exploration of their differential impact on cardiovascular risk in men and women; ▪ Studies on metabolism and biomarkers, specifically for drugs of abuse; ▪ Studies on the impact of gender in toxicology. Integration of pathological, molecular, and toxicological data with sex- and gender-sensitive metadata to identify determinants and risk factors underpinning cardiovascular disease mechanisms. Our team's experience is supported by prior forensic toxicology and environmental toxicology projects, as well as genomics models, demonstrating capability in analyzing complex samples for emerging contaminants and psychoactive substances. Please check our previous expertise here: ▪ Expertise in analytics for drugs of abuse and application in real samples: Giorgetti A et al., Drug Test Anal. 2022 Feb;14(2):202-223. doi: 10.1002/dta.3170. ▪ Studies of drug toxicity in postmortem samples: Giorgetti A et al., Int J Legal Med. 2024 Sep;138(5):1801-1811. doi: 10.1007/s00414-024-03263-7; Goirgetti A et al., Forensic Toxicol. 2020 38:314-326 doi: 10.1007/s11419-019-00514-w; Esposito M et al., Forensic Sci Med Pathol. 2025 Oct 21. doi: 10.1007/s12024-025-01096-3. ▪ Environmental toxicology and integration with histopathological assessment. Giorgetti A et al., Environ Res.

	2025 Aug 15;279(Pt 2):121846. doi: 10.1016/j.envres.2025.121846. ▪ Gender-specific studies in forensic toxicology: Pelletti G et al. Forensic Sci Int. 2022 Dec;341:111479. doi: 10.1016/j.forsciint.2022.111479. ▪ Genomics on a postmortem caseuistry: Beccacece A et al., Genes (Basel). 2023 Jun 15;14(6):1265. doi: 10.3390/genes14061265. Projects of the group ▪ Projects of great national interest in Italy (PRIN) 2022. Project title: "Early Life Exposure to per- and polyfluoroalkyl substaNces (PFAS) and heAlth risks - ELENA", sector Life Sciences LS7. Code of the project: P20223ZH85. ▪ Fondazione del Monte di Bologna (Italy) Research Call 2024. Project title: Analysis of Microplastics in PLACenta Samples and Study of Possible Effects on Metabolism (MicroPLACEM) (Macro-Thematic Area: Women's and Children's Health)

Research Group	**Prof. Sabrina Valente** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	<u>Experimental activities and methodology:</u> • Expertise in cell biology such as human vascular wall adult stromal/stem including isolation and culture, morphological, phenotypical and molecular characterization, multi-lineage differentiation in adipogenic, osteogenic, chondrogenic, leiomyogenic, and angiogenic cells and immunomodulatory assay • Cell culture: maintenance and in vitro manipulation of various primary cells and cell lines (tumor and non-tumor cells), co-culture cells of different type of cells (direct contact and with transwell), organ culture • 3D cell culture: generation of spheroids using single and multi-cell types; cell-biomaterial scaffolds; in vitro angiogenesis on Matrigel (tube formation) • Cellular analysis: viability, morphology, proliferation and migration; scratch wound healing assay; flow cytometry (immunophenotype characterization and cell cycle analysis) • Microscopy: light, fluorescent, confocal, and Transmission and Scanning electron microscopy • Histology on cells, spheroids, tissues, and engineering cell-scaffolds: histological staining, immunocytochemistry, immunohistochemistry, immunofluorescence, including sample processing, sectioning, microscope observation, image acquisition and analysis • Ultrastructure on cells, spheroids, tissues, and engineering cell scaffolds: sample processing, resin embedding, ultramicrotome sectioning, ultrastructural examination, immunogold labeling • Molecular biology: RNA isolation, RT-PCR, Real Time-PCR, Western Blot • Biochemical (ELISA) and cell viability assays (Alamar Blue, PrestoBlue, MTT, TUNEL assay and LIVE/DEAD)

	• Morphometric and semi-quantitative analysis • Biomaterial-cell interactions between various types of cells and scaffolds • Image analysis and acquisition software <u>Relevant publications:</u> ▪ Ciavarella C, et al. A 3D Composite Model Using Electrospinning Technology to Study Endothelial Damage. Biomolecules. 2025;15(6):865. doi: 10.3390/biom15060865. ▪ Astolfi G, et al. Human glial Müller and Umbilical Vein Endothelial cell coculture as an in vitro model to investigate retinal oxidative damage. A morphological and molecular assessment. Microsc Res Tech. 2023;86(4):439-451. doi: 10.1002/jemt.24284. ▪ Valente S, et al. Phenotypic, morphological, and metabolic characterization of vascular-spheres from human vascular mesenchymal stem cells. Microsc Res Tech. 2022;85(2):447-459. doi: 10.1002/jemt.23918. ▪ Valente S, et al. Exploring the human mesenchymal stem cell tubule communication network through electron microscopy. Ultrastruct Pathol. 2015;39(2):88-94. doi: 10.3109/01913123.2014.960545. ▪ Valente S, et al. Human cadaver multipotent stromal/stem cells isolated from arteries stored in liquid nitrogen for 5 years. Stem Cell Res Ther. 2014;5(1):8. doi: 10.1186/scrt397. ▪ Gualandi C, et al. Poly(butylene/diethylene glycol succinate) multiblock copolyester as a candidate biomaterial for soft tissue engineering: Solid state properties, degradability and biocompatibility. Journal of Bioactive and Compatible Polymers. 2012; 27(3):244-264. doi: 10.1177/0883911512440536. ▪ Pasquinelli G, et al. Multidistrict human mesenchymal vascular cells: pluripotency and stemness characteristics. Cytotherapy. 2010;12(3):275-87. doi: 10.3109/14653241003596679.

Research Group	**Prof. Nicola Facchinello** Dep. Pharmacy and Biotechnologies
Expertise in relation to the topic	**Expertise in relation to the topic** Our research group applies advanced zebrafish models to investigate how biological sex influences cardiovascular development, disease susceptibility, and regenerative capacity. The zebrafish is uniquely suited to dissect sex- and hormone-specific mechanisms of cardiovascular disease (CVD), as its transparent embryos allow real-time visualization of cardiac structure, physiology, and regeneration in vivo. **Key Expertise and Experimental Activities** • Sex-specific cardiovascular modeling: Generation of genetic zebrafish lines carrying human disease mutations by CRISPR/cas9 technology to examine how male and female hormonal and genetic environments differentially affect cardiac development and pathology. • Hormonal pathway manipulation: Application of glucocorticoid and sex-steroid modulation to assess the

	interaction between stress hormone signaling and sex-specific cardiac outcomes, contributing to the understanding of structural, hormonal and biological determinants of CVDs. • In vivo imaging and functional analysis: Use of fluorescent transgenic lines and high-resolution imaging to monitor heart morphology, contractility, and inflammatory and regenerative responses in a sex-aware manner. • Molecular and transcriptomic profiling: Integration of RNA-seq and hormonal pathway analysis to identify sex-specific gene expression patterns and signaling cascades relevant to cardiomyopathy, fibrosis, and repair. • Risk model validation: Experimental exploration of sex-dependent determinants and biomarkers supporting the development of tailored CVD risk models, aligning with the Horizon Europe goals of identifying and validating sex/gender-specific determinants, risk factors, and pathways. **Demonstration of Expertise and Background** Our group has a strong publication record on zebrafish cardiovascular biology and molecular signaling, including in Nature Metabolism, Journal of Cell Biology, and Cell death Disease. Representative works include: • *Facchinello N. et al.*, Nat Metab (2022) "Oxidative pentose phosphate pathway controls vascular mural cell coverage by regulating extracellular matrix composition." • *Facchinello N. et al.*, J Cell Biol (2021) "LPHN2 inhibits vascular permeability by differential control of endothelial cell adhesion." • *Brañas Casas R. et al. Facchinello N.* Cell Death Dis (2024) "Zebrafish polg2 knock-out recapitulates human POLG-disorders; implications for drug treatment." • Vencato S., *et al.,* Biomed Pharmacother (2025) "Givinostat inhibits in vitro differentiation of cardiac fibroadipogenic precursors from a mouse model of arrhythmogenic cardiomyopathy." Our ongoing Telethon-funded project on CDKL5 deficiency and participation in HORIZON-EIC-2022-PATHFINDER (AI-driven cardiogenomics) further demonstrate our translational and collaborative capacity in disease modeling and cardiovascular genetics.

Research Group	**Prof. Davide Pacini** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	Full Professor in MEDS-13/C Heart Surgery and is the Head of SCUOLA DI SPECIALIZZAZIONE in CARDIOCHIRURGIA at DIMEC (Dept of Medical and Surgical Sciences). His daily clinical activity is carried out as Director of the Cardiac Surgery Unit at the Sant'Orsola Hospital in Bologna. He has performed more than 4,000 cardiac and vascular procedures, including: Coronary surgery in open circulation and beating heart; Valve replacement and repair and arrhythmia surgery; Heart transplants and cardiocirculatory support; Pulmonary thromboendarterectomy; Major aortic surgery and minor vascular surgery (carotid

	thromboendoercectomy, peripheral arterial thrombectomies); Beating heart mitral valve repair without open circulation (NeoChord); Hybrid left ventricular aneurysm repair; Endovascular surgery. These skills are combined with impressive research activity, which has led him to author 437 publications in high-impact journals and 9,710 citations, for a personal h-index of 55. Over the last 2 years, in collaboration with ANFI - ASA staff, he has been developing research on a porcine model of cardiocirculatory death for the re-functionalization of hearts donated by DCD. He and his team of young colleagues have acquired the skills to work on the porcine model and implement a vast range of interventions useful and/or necessary for carrying out in vivo experiments on wild or pathological induced swine models.

Research Group	**Prof. Domenico Tupone** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	I am a neuroscientist whose research expertise focuses primarily on **autonomic regulation, thermoregulation, and neural control of homeostasis**, particularly in relation to **hibernation, sleep, and inducible torpor-like states**. Within this broad framework, my recent work has focused on studying the physiological autonomic alterations that follow the onset of **subarachnoid hemorrhage (SAH)**. My studies are not centered directly on the clinical or pathological aspects of SAH itself (such as its causes or surgical management), but rather on the neurophysiological mechanisms that leads to autonomic dysfunction following SAH and how to their treatment, that may have relevance for brain protection and recovery after SAH. In particular, my research explores: ▪ The **neural circuits** involved in the alteration of body temperature, metabolism, and cardiovascular activity during SAH. ▪ **Therapeutic hypothermia and hibernation-like states** as potential neuroprotective strategies for conditions such as stroke, cardiac arrest, or SAH. ▪ The **identification of new pharmacological** interventions for the treatment of specific autonomic alterations following ischemic or hemorrhagic events. We have expertise in the chronic instrumentation of rats for studies on central thermoregulatory control and sleep, including measurements of brain and core temperatures, muscle EMG, EEG, diaphragmatic EMG, and cardiovascular variables in freely behaving and anesthetized rodent models. Our laboratory has a high level of proficiency and consistency in electrophysiological, optogenetic, chemogenetic, and immunohistochemical techniques. **Relevant Publications** ▪ Morrison SF, Cano G, Hernan SL, Chiavetta P, **Tupone D.** Inhibition of the hypothalamic ventromedial periventricular

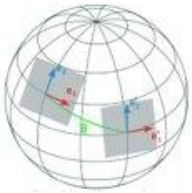
	area activates a dynorphin pathway-dependent thermoregulatory inversion in rats. Curr Biol. **2025.** ▪ Migliorino E, Nonino F, Amici R, **Tupone D,** Aspide R. Neurogenic Fever after Subarachnoid Hemorrhage in Animal Models: A Systematic Review. Int J Mol Sci. **2023**. ▪ **Tupone D,** Cetas JS. In a model of SAH-induced neurogenic fever, BAT thermogenesis is mediated by erythrocytes and blocked by agonism of adenosine A1 receptors. Sci Rep. **2021**. ▪ **Tupone D,** Cetas JS, Morrison SF. Hibernation, Hypothermia and a Possible Therapeutic "Shifted Homeostasis" Induced by Central Activation of A1 Adenosine Receptor (A1AR). Nihon Shinkei Seishin Yakurigaku Zasshi. **2016.** **Funding** ▪ **08/01/2023 - 07/31/2025** Progetti di Ricerca di Interesse Nazionale (PRIN) Italy, **Tupone (PI).** Title: Central control of neurogenic fever in subarachnoid hemorrhage. ▪ **2016** Awards "Programma per giovani Ricercatori "Rita Levi Montalcini". **Tupone (PI)**

Research Group	**Prof. Domenico Ventrella** Dep. Veterinary Medical Sciences
Expertise in relation to the topic	The ASA Unit conducts both self-funded and externally supported research activities through research contracts and/or competitive grants. Upon request, the Unit can also organize and support specialized interventional and surgical training sessions, performed *in vivo* on animal models, as part of postgraduate educational programmes targeting Medical Doctors and Veterinary Surgeons. The Main Areas of Activity are: Translational medicine and experimental surgery on healthy or experimentally induced pathological *in vivo* and/or *ex vivo* preclinical (porcine) models; Reproductive and metabolic physiology in selected species (mainly pig, laboratory species, wildlife, and teleost fish); Complementary and alternative methods to animal experimentation. The ASA Unit, classified as a third-level facility within the ANFI Service, is coordinated by Dr. Domenico Ventrella and supported by a multidisciplinary research team comprising professors, researchers, research fellows, PhD students, and scholarship holders. With over 20 years of expertise in the development and validation of porcine models (both healthy and experimentally induced, including innovative pathological models) suitable for preclinical trials and research support services, the team provides specialized skills and technical resources to: pharmaceutical, nutraceutical, biotechnological, and medical device industries, as well as governmental bodies, foundations, and academic institutions. The Unit is actively committed to the progressive implementation of the 3Rs principles (Reduction, Replacement, and Refinement) in preclinical animal research. This includes the continuous refinement and characterization of animal models, the adoption of *ex vivo* and *in vitro* approaches whenever feasible, and the

	promotion of the One Health perspective, integrating human, animal, and environmental health. The ASA Unit has advanced expertise in the development of specific extraction and analytical methods for physiological and endocrinological biomarkers, employing techniques such as RIA, ELISA, and related assays. Additional competencies include: Electrophysiological investigations (ERG, PERG, EEG, cerebral oximetry – NIRS, etc.); Ocular OCT imaging; Pharmacokinetic analyses; Functional studies on male gametes; Cardiocirculatory research, including extracorporeal membrane oxygenation (ECMO) and extracorporeal circulation (ECC) circuit models. These skills enable the Unit to design and conduct independent and collaborative studies across multiple biomedical and veterinary research fields. Biological Material Services The ASA Unit also provides specialized services for the isolation, recovery, preparation, and shipment of biological tissues, including sterile samples, intended for bioengineering, toxicological, or cell culture applications (e.g., isolation of primary cell lines). The ASA Unit is equipped with state-of-the-art infrastructures, including: ▪ Dedicated animal housing facilities for pigs, suitable for both acute and recovery experiments (including biosafety level 2 GMO studies); ▪ Two fully equipped surgical theatres for large and small pigs, with seven parallel operating stations, each equipped with anesthesia machines, monitoring systems, and automatic ventilators; ▪ Transesophageal echocardiography probe; ▪ Defibrillator; ▪ Angiograph for interventional and vascular procedures; ▪ Recovery cages allowing continuous physiological monitoring; ▪ Laboratories for cell and tissue isolation, biological sample processing, male gamete evaluation, image analysis, and RIA/ELISA assays. The ASA Unit maintains active collaborations with all departmental facilities, providing integrated support for a wide range of research and diagnostic activities, including: ▪ First- and second-level diagnostic imaging (radiology, ultrasonography, fluoroscopy, computed tomography); ▪ Endoscopic procedures; ▪ Minimally invasive surgery (laparoscopy and thoracoscopy); ▪ Pathology services, equipped for histological, histochemical, cytological, immunohistochemical, and molecular biology analyses; ▪ Biochemistry and molecular biotechnology laboratories.

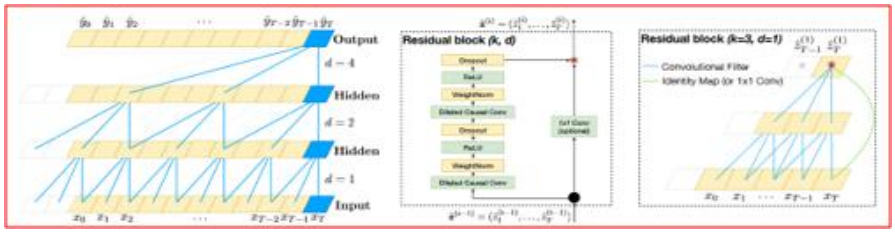
Research Group	**Prof. Rita Fioresi** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	**Mathematics of Machine Learning and Deep Learning (DL)**

- Mathematics and foundations of machine learning and graph neural networks (e.g. Sheaf Neural Networks, Data Manifolds, etc.)
- Mathematical modelling and bio-inspired DL models
- Geometry based DL techniques: Graph Neural Networks, Geometric Deep Learning, Generative AI via Continuous flow Matching for non-euclidean domains.



Analysis of medical images and data

- Generation and analysis of synthetic biomedical data
- Genetic sequence modelling with Temporal Convolutions
- Attribution Physiological signal time series modeling with Temporal Convolutions for personalized medicine (wearable devices)



- Multimodal data: physiological signals, physiometric data, etc. (PPG, ECG, ...) methods and attention mechanisms

Publications

- Pietro Demurtas, Jacopo Bertozzi, Irene Di Silvestro, Kevin Carlin, Andre Ghetti, Brian Krause, Giovanni Perini, Ferdinando Zanchetta & Rita Fioresi, Gene selection for prediction of transcriptome signal based on a machine learning approach, Discover Applied Sciences, Springer, 2025.
- Catarina P. Coutinho; Ferdinando Zanchetta; Michele Carbonelli; Marco Battista; Alice Galzignato; Chiara La Morgia; Giulia Amore; Martina Romagnoli; Giacomo Savini; Luigi Brotto; Paolo Nucci; Leonardo Caporali; Francesco Bandello; Valerio Carelli; Maria Lucia Cascavilla; Rita Fioresi; Piero Barboni, Machine Learning Applied to Visual Fields of Dominant Optic Atrophy Patients, 2025.
- Mehrab, Aneeqa; Lapenna, Michela; Zanchetta, Ferdinando; Simonetti, Angelica; Faglioni, Giovanni; Malagoli, Andrea; Fioresi, Rita, Kolmogorov–Arnold and Long Short-Term Memory Convolutional Network Models for Supervised Quality Recognition of Photoplethysmogram Signals, «ENTROPY», 2025.
- Petkovic J.; Fioresi R., Spontaneous Emergence of Robustness to Light Variation in CNNs With a Precortically Inspired Module, «NEURAL COMPUTATION», 2024, 36.
- Grementieri, L; Fioresi, R, Model-Centric Data Manifold: The Data Through the Eyes of the Model, «SIAM JOURNAL ON IMAGING SCIENCES», 2022

Projects as PI

- **CaLiForNIA MSCA-DN (2023-2027)**mathematical models for machine learning

	• **CaLIGOLA MSCA-SE (2022-2026)** vision models and quantum computing • **CaLISTA COST Action (2022-2026):** topological data analysis

Research Group	**Prof. Arrigo F. G. Cicero** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	Associate Professor of Human Nutrition at the University of Bologna, where he also directs the **School of Specialization in Food Sciences** and coordinates the **Laboratory of Lipidology and Cardiovascular Prevention** at the Dept. of Medical and Surgical Sciences. His clinical and academic work integrates **nutrition science, cardiovascular prevention, lipid metabolism, and clinical pharmacology**, focusing on **lifelong health promotion and reduction of non-communicable disease burden**. Areas of Expertise Prof. Cicero's expertise covers the main thematic areas of the **Joint Action CR/CV&NCD-g-25-17**, including: ▪ **Epidemiological research** through long-term population studies (he is currently the Scientific Lead of the Brisighella Heart Study (BHS) and clinical registries (among others, Uric and Cardiovascular Disease: Uric Acid Right for heArt Health – URRAH -Project). ▪ **Cardiovascular disease prevention across the lifespan**, with emphasis on modifiable risk factors. ▪ **Nutritional and lifestyle interventions** targeting healthy ageing, dietary quality, and metabolic resilience. ▪ **Development and clinical testing of nutraceuticals, functional foods and diets**, assessing their impact on lipid profile, inflammation, endothelial function, and oxidative stress. ▪ **Preventive pharmacotherapy** in high cardiovascular risk patients. ▪ **Implementation of innovative diagnostic tools** for early detection of vascular dysfunction. ▪ **Health education and literacy** programs for improving awareness and adherence to preventive measures. ▪ **Evidence synthesis and policy translation** to inform national and EU-level guidelines on preventive health. Major Research Projects and Leadership Roles Prof. Cicero has also served as **Principal Investigator or Co-Investigator** in numerous national and international studies on **nutraceutical efficacy, lipid-lowering interventions, and vascular health**, conducted according to **Good Clinical Practice (GCP)**. Selected research programmes and funding: ▪ **PRIN and PNRR-funded projects** on diet-related prevention of metabolic and cardiovascular diseases. ▪ "Innovative and sustainable processes for the development of Vitamin D nutraceutical from fish waste: extraction, formulation and clinical study for the evaluation of its bioavailability and clinical consequence" (VITADWASTE; PRIN 2022M9JL3%) (Local PI) ▪ Cardiometabolic risk of obese subjects: genetic, laboratory and clinical determinants in general population and

	outpatients" (PNRR-MCNT2-2023-12377884) (National Coordinator) ▪ "ON Foods—Research and innovation network on food and nutrition Sustainability, Safety and Security—Working ON Foods) (PNRR Project code PE00000003, Concession Decree No. 1550 of 11 October 2022 adopted by the Italian Ministry of University and Research) (Local PI) Relevance to the EU Joint Action CR/CV&NCD-g-25-17 Prof. Cicero's expertise and research portfolio are highly synergistic with the **objectives, scope, and activities** of the Joint Action "Support lifelong prevention for a healthy life, including through screening, with focus on cardiovascular diseases", specifically: ▪ **Development and implementation of population-level interventions** addressing diet, nutrition, and physical activity to prevent cardiovascular diseases, obesity, and diabetes. ▪ **Contribution to EU-level guidance and protocols** for early detection and management of cardiovascular risk. ▪ **Transfer and scaling-up of best practices** in cardiovascular prevention and health literacy. ▪ **Piloting innovative and cost-effective approaches** integrating nutraceuticals, dietary patterns, and behavioural change interventions into preventive frameworks. ▪ **Support for equity in prevention**, focusing on vulnerable and ageing populations through education, access to care, and adherence promotion. Link for publication HERE.

HORIZON-HLTH-2026-01-DISEASE-15: Scaling up innovation in cardiovascular health

Research Group	**Prof. Antonello Lorenzini** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	PhD in Biochemistry and Physiopathology of Aging. Our group focuses on **nutrition and healthy lifestyles**. Regarding the Horizon calls, we emphasized our active collaboration with Prof. Lars Fadnes' group at the University of Bergen to expand the scope of their "**Food for Healthy Life**" **calculator** (F4HL: http://v2.food4healthylife.org/). This calculator currently allows, after analyzing an individual's diet, to prioritize the changes needed to make the diet healthier and therefore capable of extending the individual's longevity. Towards the goal of expanding the calculator's capabilities so that it will also produce **risk estimates of NCDs**, the collaboration has already produced three umbrella reviews (1, 2, 3), and it has others in progress. The calculator could form the basis of a preventive tool for projects dedicated to the prevention of NCDs both in young people (12-25 years) and in adults. A second project, which can be easily linked to the previous one, is a project on **Artificial intelligence**, it is a project born in Bologna between the PI's group and the CINECA supercomputing consortium. This collaboration aims to develop a tool that uses **Natural Language Processing (NLP)** to semi-automate the construction of meta-analyses from scientific literature, with

	particular emphasis on optimizing text and data mining in the biomedical and specifically in the epidemiological field. The first manuscript related to this tool has been submitted (4) and we have two other publications in progress that exploit this new tool. ▪ Umbrella Review of Systematic Reviews and Meta-Analyses on Consumption of Different Food Groups and Risk of Type 2 Diabetes Mellitus and Metabolic Syndrome. Banjarnahor RL, Javadi Arjmand E, Onni AT, Thomassen LM, Perillo M, Balakrishna R, Sletten ISK, Lorenzini A, Plastina P, Fadnes LT.J Nutr. 2025 May;155(5):1285-1297. doi: 10.1016/j.tjnut.2025.03.021. Epub 2025 Mar 22.PMID: 40122387 ▪ Umbrella Review of Systematic Reviews and Meta-Analyses on the Consumption of Different Food Groups and the Risk of Overweight and Obesity. Kristoffersen E, Hjort SL, Thomassen LM, Arjmand EJ, Perillo M, Balakrishna R, Onni AT, Sletten ISK, Lorenzini A, Fadnes LT. Nutrients. 2025 Feb 13;17(4):662. doi: 10.3390/nu17040662.PMID: 40004990 ▪ Umbrella Review of Systematic Reviews and Meta-analyses on Consumption of Different Food Groups and Risk of All-cause Mortality. Onni AT, Balakrishna R, Perillo M, Amato M, Javadi Arjmand E, Thomassen LM, Lorenzini A, Fadnes LT.Adv Nutr. 2025 Apr;16(4):100393. doi: 10.1016/j.advnut.2025.100393. Epub 2025 Feb 15.PMID: 39956388 ▪ TextAlchemy: an NLP tool to accelerate and semi-automate data extraction, validated in the nutritional field. Rooshan Saleem Butt, Matteo Perillo, Michele Visciarelli, Giorgio Pedrazzi, Marco Amato, Andrea Galassi, Rajiv Balakrishna, Anindita Tasnim Onni, Lars Thore Fadnes, Paolo Torroni, Roberta Turra, Antonello Lorenzini; *submitted*.

Research Group	**Prof. Anna Vittoria Mattioli** Dep. Life Quality Studies
Expertise in relation to the topic	Full Professor of Advanced Medical and Surgical Technology and Methodology at the University of Bologna and a cardiologist with internationally recognized expertise in sex- and gender-specific mechanisms of cardiovascular diseases (CVD). Her research focuses on lifelong cardiovascular prevention, women's cardiovascular health, and lifestyle-driven modulation of cardiometabolic risk through nutrition, exercise, and digital health tools. She has coordinated and participated in several national and EU-funded projects on precision prevention, active ageing, and digital cardiovascular risk monitoring (e.g., HEAL ITALIA, Lively Ageing, WEARbeing), integrating biomedical, technological, and population-level research. As Vice-President of the National Institute for Cardiovascular Research (INRC) and incoming Coordinator of the Gender Cardiovascular Diseases Working Group of the Italian Society of Cardiology, she promotes translational research on hormonal, inflammatory, and metabolic pathways mediating sex and gender differences in cardiovascular diseases.

	Her current research investigates the interplay between biological and environmental determinants of cardiovascular risk, including the exposome, environmental stressors, menopause transition, and maternal–fetal interactions. These studies contribute to defining **sex-specific phenotypes and endotypes** of cardiovascular disease and their implications for precision prevention and treatment. Through **IPPOCRA-Tech**, a university spin-off, she has developed a **non-invasive, AI-based device capable of simultaneously monitoring the five vital signs**, enabling real-time assessment of physiological stress responses and supporting large-scale, data-driven implementation research. With over 300 peer-reviewed publications and international recognition (FESC, FACC), Prof. Mattioli combines clinical and translational expertise to advance **sex- and gender-sensitive mechanistic and implementation research** on chronic non-communicable diseases. Her work directly contributes to the GACD objectives by fostering cross-sectoral integration of biomedical, digital, and environmental data to improve prevention and management strategies for cardiovascular health.

Destination 4. Ensuring access to innovative, sustainable and high-quality health care

HORIZON-HLTH-2026-01-CARE-03: Identifying and addressing low-value care in health and care systems

Research Group	**Dr. Pierpaolo Palumbo** Dep. Electrical, Electronic, and Information Engineering
Expertise in relation to the topic	We are a group of biomedical engineers with consolidated expertise in the field of biomedical data analysis and predictive models. We are interested in participating in the topic 2026-01-CARE-03 by developing data models and/or tools to identify and/or address low-value care and by performing digital and artificial intelligence-based analyses. Our experience ranges from risk factor identification to model development, validation, and impact analysis. We have developed health risk assessment models for non-communicable diseases. We have validated risk screening models proposed by international medical societies. We have applied causal machine learning techniques on observational data to evaluate the efficacy of different interventions, derive personalised efficacy profiles, and evaluate the potential impact of risk predictive models informing intervention policies. We believe this expertise can be used to identify overuse, misuse, underuse, and unwarranted variations in healthcare services utilization and design intervention policies in a context of health system performance assessment. <u>Selected publications</u> ▪ Palumbo, P. (2025). Qini Curves for Potential Impact Assessment of Risk Predictive Models Informing Intervention Policies. Value in Health ▪ Topic Group on "Falls among the elderly" of the ITU/WHO Focus Group "Artificial Intelligence for Health" (2023). Fall risk stratification of community-living older people. Commentary on the world guidelines for fall prevention and management. Age and Ageing, 52(10) ▪ Belvederi Murri, M. et al. (2022). Risk Prediction Models for Depression in Community-Dwelling Older Adults. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 30(9), 949–960 ▪ Palumbo, P. et al. (2022). The Degree of Safety against Falls Provided by 4 Different Prosthetic Knee Types in People with Transfemoral Amputation: A Retrospective Observational Study. Physical Therapy ▪ Cattelani, L. et al. (2019). Risk Prediction Model for Late Life Depression: Development and Validation on Three Large European Datasets. IEEE Journal of Biomedical and Health Informatics, 23(5), 2196–2204 ▪ Palumbo, P et al. (2019). Simulating the effects of a clinical guidelines screening algorithm for fall risk in community dwelling

	older adults. Aging Clinical and Experimental Research, 31(8), 1069–1076 ▪ Klenk, J. et al. (2017). Conceptualizing a Dynamic Fall Risk Model Including Intrinsic Risks and Exposures. Journal of the American Medical Directors Association, 1–7 ▪ Palumbo, P. et al.(2016). Predictive Performance of a Fall Risk Assessment Tool for Community-Dwelling Older People (FRAT-up) in 4 European Cohorts. Journal of the American Medical Directors Association, 17(12), 1106–1113 ▪ Palumbo, P.et al. (2015). Fall Risk Assessment Tools for Elderly Living in the Community: Can We Do Better? PLOS ONE, 10(12) ▪ Palumbo, P. et al. (2015). A probabilistic model to investigate the properties of prognostic tools for falls. Methods of Information in Medicine, 54(2) ▪ https://scholar.google.com/citations?user=HSrKkzgAAAAJ

Destination 5. Developing and using new tools, technologies and digital solutions for a healthy society

HORIZON-HLTH-2026-01-TOOL-03: Integrating New Approach Methodologies (NAMs) to advance biomedical research and regulatory testing

Research Group	**Prof. Marilisa Cortesi** Dep. Electrical Electronic and Information Engineering
Expertise in relation to the topic	**Development of computational models of cell behaviour, with particular focus on 3D cell cultures (scaffold-based, organotypic models) and digital twins**. Custom programmable solutions that can be adapted to different settings and applications and experimentally validated. Expertise recognised by the European Union that funded my Marie Skłodowska-Curie Global Fellowship (Horizon 2020). See the following publications as examples of our work. ▪ Cortesi, Marilisa, et al. "An in-silico study of cancer cell survival and spatial distribution within a 3D microenvironment." Scientific Reports 10.1 (2020): 12976. ▪ Cortesi, Marilisa, et al. "Development and validation of an in-silico tool for the study of therapeutic agents in 3D cell cultures." *Computers in Biology and Medicine* 130 (2021): 104211 ▪ Cortesi, Marilisa, et al. "A comparative analysis of 2D and 3D experimental data for the identification of the parameters of computational models." *Scientific Reports* 13.1 (2023): 15769. ▪ Cortesi, Marilisa, and Emanuele Giordano. "Driving cell response through deep learning, a study in simulated 3D cell cultures." *Heliyon* 10.9 (2024). ▪ Cortesi, Marilisa, et al. "Development and validation of a computational tool to predict treatment outcomes in cells from high-grade serous ovarian cancer patients." *Bioengineering & Translational Medicine* (2025): e70082. **Development of custom software tool for the analysis of *in vitro* data.** Image analysis tools (also AI based) to quantify features of interest from microscopy images (shape/size of organoids or cells, individual cells behaviour). Advanced analysis methods for cell tracking and time series analysis. Experimental validation of such tools, as shown by the references below. ▪ Cortesi, Marilisa, et al. "AIM: a computational tool for the automatic quantification of scratch wound healing assays." Applied Sciences 7.12 (2017): 1237. ▪ Cortesi, Marilisa, et al. "Reliable measurement of E. coli single cell fluorescence distribution using a standard microscope set-up." Journal of biological engineering 11.1 (2017): 8. ▪ Cortesi, Marilisa, et al. "I-AbACUS: a reliable software tool for the semi-automatic analysis of invasion and migration transwell assays." Scientific Reports 8.1 (2018): 3814. ▪ Cortesi, Marilisa, et al. "Development of an electrical impedance tomography set-up for the quantification of mineralization in biopolymer scaffolds." Physiological Measurement 42.6 (2021): 064001.

	▪ Cortesi, Marilisa, et al. "Accurate Identification of Cancer Cells in Complex Pre-Clinical Models Using a Deep-Learning Neural Network: A Transfection-Free Approach." Advanced Biology 8.11 (2024): 2400034. ▪ Cortesi, Marilisa, et al. "A novel approach for the quantification of single-cell adhesion dynamics from microscopy images." bioRxiv (2024): 2024-10.

Research Group	**Prof. Ivana Kurelac** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	The group is focusing on development of liquid biopsy approaches for high grade serous ovarian cancer (HGSOC), with the aim to provide biomarkers for early detection, neoadjuvant chemotherapy response prediction and relapse detection. We are tightly collaborating with gynecological surgeons from our institution, allowing collection of HGSOC derived material (fresh, snap frozen, FFPE, peripheral blood and ascites) from >40 patients per year. We possess expertise in canonical methods for peripheral blood liquid biopsy: circulating tumor cell (CTC) enrichment (Parsortix, EasySep, CD45 negative selection, Cell Search, access to DEPArray cell isolation system), cell free DNA extraction, analysis of the circulating entities by molecular approaches (expression profiling, TP53 next generation sequencing and mitochondrial DNA); as well as expertise in histopathological and molecular analyses of the matched ascites and solid tumor tissue. Importantly for the HORIZON-HLTH-2026-01-TOOL-03 call, in collaboration with engineering group led by Dr. Pietro Ferraro from ISASI Institute, Naples (https://www.isasi.cnr.it/en/computational-microscopy/), we are involved in **development of innovative, label-free and molecular marker-free approaches for detection of cancer cells in body fluids** by artificial intelligence-guided tomographic CTC detection based on their morphologic characteristics. **Tasks and activities the group will be able to carry out within the proposal: provision of material for NAM development and testing, validation of the NAM by comparison with currently available technologies.** Relevant publications: https://doi.org/10.1101/2025.10.13.681971 https://doi.org/10.3389/fmolb.2025.1537407 **https://doi.org/10.1002/VIW.20200034** https://doi.org/10.1038/s41598-023-32110-9 https://doi.org/10.1364/DH.2024.W1A.2 **Relevant funding:** MORFEO (Morphological Biomarkers for early diagnosis in Oncology)", funded by Italian Ministry of University and Research (567,943.00 euro, PRIN 2017 - #2017N7R2CJ)

Research Group	**Prof. Sabrina Valente** Dep. Medical and Surgical Sciences
Expertise in relation to the topic	Experimental activities and methodology: • Expertise in cell biology such as human vascular wall adult stromal/stem including isolation and culture, morphological, phenotypical and molecular characterization, multi-lineage differentiation in adipogenic, osteogenic, chondrogenic, leiomyogenic, and angiogenic cells and immunomodulatory assay • Cell culture: maintenance and in vitro manipulation of various primary cells and cell lines (tumor and non-tumor cells), co-culture cells of different type of cells (direct contact and with transwell), organ culture • 3D cell culture: generation of spheroids using single and multi-cell types; cell-biomaterial scaffolds; in vitro angiogenesis on Matrigel (tube formation) • Cellular analysis: viability, morphology, proliferation and migration; scratch wound healing assay; flow cytometry (immunophenotype characterization and cell cycle analysis) • Microscopy: light, fluorescent, confocal, and Transmission and Scanning electron microscopy • Histology on cells, spheroids, tissues, and engineering cell-scaffolds: histological staining, immunocytochemistry, immunohistochemistry, immunofluorescence, including sample processing, sectioning, microscope observation, image acquisition and analysis • Ultrastructure on cells, spheroids, tissues, and engineering cell scaffolds: sample processing, resin embedding, ultramicrotome sectioning, ultrastructural examination, immunogold labeling • Molecular biology: RNA isolation, RT-PCR, Real Time-PCR, Western Blot • Biochemical (ELISA) and cell viability assays (Alamar Blue, PrestoBlue, MTT, TUNEL assay and LIVE/DEAD) • Morphometric and semi-quantitative analysis • Biomaterial-cell interactions between various types of cells and scaffolds • Image analysis and acquisition software Relevant publications: ▪ Ciavarella C, et al. A 3D Composite Model Using Electrospinning Technology to Study Endothelial Damage. Biomolecules. 2025;15(6):865. doi: 10.3390/biom15060865. ▪ Astolfi G, et al. Human glial Müller and Umbilical Vein Endothelial cell coculture as an in vitro model to investigate retinal oxidative damage. A morphological and molecular assessment. Microsc Res Tech. 2023;86(4):439-451. doi: 10.1002/jemt.24284. ▪ Valente S, et al. Phenotypic, morphological, and metabolic characterization of vascular-spheres from human vascular mesenchymal stem cells. Microsc Res Tech. 2022;85(2):447-459. doi: 10.1002/jemt.23918.

	▪ Valente S, et al. Exploring the human mesenchymal stem cell tubule communication network through electron microscopy. Ultrastruct Pathol. 2015;39(2):88-94. doi: 10.3109/01913123.2014.960545. ▪ Valente S, et al. Human cadaver multipotent stromal/stem cells isolated from arteries stored in liquid nitrogen for 5 years. Stem Cell Res Ther. 2014;5(1):8. doi: 10.1186/scrt397. ▪ Gualandi C, et al. Poly(butylene/diethylene glycol succinate) multiblock copolyester as a candidate biomaterial for soft tissue engineering: Solid state properties, degradability and biocompatibility. Journal of Bioactive and Compatible Polymers. 2012; 27(3):244-264. doi: 10.1177/0883911512440536. ▪ - Pasquinelli G, et al. Multidistrict human mesenchymal vascular cells: pluripotency and stemness characteristics. Cytotherapy. 2010;12(3):275-87. doi: 10.3109/14653241003596679.

Research Group	**Prof. Francesco Formaggio** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	The research group led by Dr. Francesco Formaggio specializes in advanced 3D bioprinting technologies applied to human tissue modeling, with a particular focus on neurobiology, pain mechanisms, and personalized medicine. The group has developed robust methodologies for generating innervated human skin models using patient-derived induced pluripotent stem cells (iPSCs), enabling the study of chronic pain and rare neuropathies such as Fabry disease. Key experimental capabilities include: ▪ Differentiation of iPSCs into dorsal root ganglion (DRG) sensory neurons. ▪ 3D bioprinting of multi-cellular constructs combining neurons, fibroblasts, and keratinocytes. ▪ Confocal and two-photon microscopy-based structural and functional characterization of bioprinted tissues. ▪ Disease modeling using patient-specific mutations. Beyond fibroblasts and keratinocytes, the group has the expertise and infrastructure to bioprint a wide range of cell types, including immortalized cell lines, astrocytes, and other neuronal subtypes, enabling the reconstruction of diverse tissue architectures. This versatility supports applications in neuroscience, oncology, dermatology, and regenerative medicine. Importantly, the bioprinting system used by the group is custom-built and highly modular, allowing for: • The use of custom bioinks tailored to specific cell types and tissue functions. • Integration of diverse biomaterials beyond those supported by commercial platforms. • Fine control over printing parameters, such as temperature, pressure, and nozzle configuration, which are often fixed or limited in off-the-shelf bioprinters. This flexibility enables the creation of physiologically relevant and highly specialized tissue models that are not achievable with standard commercial systems.

	Relevant Publications ▪ Formaggio F. et al. (2025) – Bioprinted human skin innervated with patient-derived sensory neurons for Fabry disease modeling, J. Mater. Chem. B. This study demonstrates the successful bioprinting of a human skin model innervated with DRG neurons derived from Fabry patients. It validates the approach for studying somatosensory pathways and pain-related mutations in a controlled 3D environment. Funded Projects as Principal Investigator ▪ 2024–2026 – Bioprinting of a 3D Human Model for the Study of Chronic Pain In Vitro Funded by Fondazione Del Monte di Bologna e Ravenna (€25,000) Dr. Formaggio coordinates the development of a bioprinted human skin model using iPSCs from Fabry patients to generate DRG neurons. The project focuses on reconstructing the primary somatosensory pathway and analyzing patient-specific mutations. ▪ 2025–2027 – Bioprinting of a 3D Human Model for Chronic Pain Investigation In Vitro Funded by Bando Ricerca scientifica e alta tecnologia 2024 (€5,000) This project expands the previous work by integrating fibroblasts and keratinocytes with DRG neurons in a bioprinted construct, aiming to refine the model's complexity and translational relevance. Collaborative Projects ▪ 2023–2025 – BASICPROMED – Bioprinting of Structurally Homogeneous, Compositionally Complex Tumor Spheroids for Pharmaceutical Testing Funded under PRIN – Projects of Relevant National Interest, ERC Sector LS – Life Sciences Dr. Formaggio contributes to the biological characterization of bioprinted tumor spheroids using confocal microscopy, supporting the development of personalized medicine platforms. Project leads: Simone Bonetti and Emanuela Saracino (CNR-Bologna) Dr. Francesco Formaggio's research group offers a unique combination of expertise in bioprinting, stem cell biology, and neurophysiology, with proven experience in developing complex human tissue models and characterizing them using advanced imaging techniques. The group's custom bioprinting platform provides unmatched flexibility in terms of bioink formulation, biomaterial integration, and printing conditions, making it ideally suited for European projects focused on personalized medicine, neuroscience applications, and broader tissue engineering.

Research Group	**Prof. Roberto Feuda** Dep. Biological, Geological, and Environmental Sciences
Expertise in relation to the topic	The research group offers internationally recognised expertise in **genomics, molecular and developmental biology**, with a strong focus on the **developmental genomics**. This is supported by publications in *Cell*, *Science*, *Science Advances*, *Nature Communications*, *Genome Biology and Evolution*, and *BMC Biology*.

Molecular & Developmental Neurobiology: The group has extensive experience dissecting **neurogenic gene regulatory networks**. Core capabilities include:
– single-cell and single-nucleus transcriptomics in *Drosophila*, mosquitoes, and Human embryonic Stem cells
– lineage and trajectory inference (RNA velocity, CellRank, pseudotime);
– spatial validation (HCR, in situ hybridisation);
– embryonic and larval manipulations in model and emerging systems.

Genomics & Single-cell Technologies: **The group routinely generates and analyses** large-scale genomic and transcriptomic datasets**, with practical experience across major platforms such as Parse Biosciences and 10x Genomics.**

Evolutionary Genomics: **The PI has over a decade of expertise in** comparative genomics**, including the origins of sensory systems (GPCRs), evolutionary dynamics of neuronal gene families.**

Model Systems & Experimental Breadth: **The laboratory works across a wide phylogenetic range: including** *Drosophila melanogaster* **and human embryonic stem cells for neuronal development and mosquitoes (***Aedes*, *Anopheles*, *Toxorhynchites***) for sensory and neuronal evolution. This breadth is supported by multiple Royal Society and HFSP-funded programmes on neuron development, ctenophore genomics, and sensory evolution.**

Methods, Infrastructure & Collaborative Capacity: **The group can carry out: high-throughput sequencing (bulk, single-cell), temporal developmental sampling and modelling, GRN reconstruction (ATAC-seq, RNA-seq, motif inference), and analysis of protein evolution. Photopigment biochemistry and functional assays are enabled through long-standing collaborations (EMBL, UCL, Bristol, Francis Crick Institute). The team has strong computational infrastructure and extensive experience coordinating multi-institutional international projects (HFSP, Royal Society URF, Leverhulme).**

Track Record: **The PI has produced** 36 publications**, >2,000 citations, and an** h-index of 20**; led** >£1.8M **in PI grants and** $1.5M **as HFSP coordinator; delivered invited talks at EMBL, EPFL, Caltech, and Euro Evo-Devo; and supervised PhD students and postdocs who now hold positions in academia and industry. This record demonstrates a consistent ability to deliver high-impact, complex, multidisciplinary research aligned with the Topic.**

Research Group	**Prof. Giampaolo Zuccheri** Dep. Pharmacy and Biotechnology
Expertise in relation to the topic	Expertise in making and developing *in vitro* 3D tumor cell models. We are developing our solution towards organ-on-chip (or body-on-chip) that synergizes bioprinting with microstructured culture devices. The tumor microenvironment and the tumor macro-heterogeneity can be modeled while having a large number of 3D models to also sustain robust quantitative analysis of the outcome of treatments with chemicals, nanomaterials or any medicinal products. There are no technical preclusions in integrating microbiome in the devices. [*patent application in progress*] - capability of making 3D in-vitro cell models (homotypical or heterotypical cell cultures) to test the uptake of chemical substances in the cells and the ensuing effects on the models. We can make large numbers of 3D models (spheroid-like) to be able to get statistically robust data, structural data, compositional/biochemical data We have experience in making such models with staminal mouse CNS cells. https://doi.org/10.1007/s00018-023-04748-1 - multi-organ models or body-on-chip can be obtained by arranging multi-type cell spheroids sharing culture medium in the same container or by fluidically connecting different spheroid arrays in a physiologically-relevant manner. Profiles of the biodistribution of drugs in different 3D models can be obtained. - 3D models can be grown with or without extracellular matrix and with control of the local mechanical properties of culture (stiff or soft supports). - line cells can be genetically modified to characterize patient mutations, express markers (such as fluorescent proteins), or to test for the pollutant effect in the presence of specific desired mutations in the cell line. - the 3D models can be characterized by fluorescence microscopy, including lightsheet fluorescence microscopy to characterize the uptake of model pollutants in the depth of a biological model and the cell behavior (and over time). An established partnership with a research group specializing in inflammation could allow the implementation of targeted characterization assays for inflammation.

Research Group	**Dr Alessandra Maresca** IRCCS Istituto delle Scienze Neurologiche di Bologna
Expertise in relation to the topic	**PI of the Laboratory of Molecular and Cellular Biology at the Program of Neurogenetics** Expertise in studying pathogenic mechanisms and testing drugs using iPSCs-based models derived from patients affected by mitochondrial diseases caused by genetic defects in both nuclear and mitochondrial DNA (mtDNA). Specifically, reprogramming of somatic cells in iPSCs, with appropriate quality control check including mtDNA deep sequencing. For cells carrying heteroplasmic mtDNA pathogenic variants, we have developed a protocol to increase the mutant load in the iPSCs generated, to be sure to obtain a model with

	mitochondrial dysfunction and reproduce the pathological features of patients. We have experience in differentiating 3D cortical brain organoids to be functionally characterized. Specifically, we can evaluate: morphology and growth rate, expression of specific markers by immunofluorescence analysis, histology and histoenzymatic staining for COS/SDH activities, bioenergetics function looking at the mitochondrial respiration and mitochondrial complexes assembly, ROS production, release of molecules in the cell medium (cytokines, mtDNA), molecular analysis for quantification of mtDNA copy number and heteroplasmy, single cell mtDNA sequencing and RNA sequencing, bulk RNA sequencing, and different cellular assays od dissociated organoids (i.e. cell death). We have also preliminary data of MRI on cortical organoids. Relevant grant on this topic: • "Retinal ganglion cells and ORganoids from Inherited Optic Neuropathies: light on pathogenesis to fight blindness (REORION Project)" RF-2018-12366703 funded by Ministry of Health, P.I. Prof. Valerio Carelli • "Cure MERRF: from fibroblasts to organoids speeding basic science into clinical trials for mitochondrial diseases" GGP20115, funded by Telethon Foundation, P.I. Prof. Valerio Carelli • "iPSC-driven repositioning of Sildenafil for treating Mitochondrial Disorders-SildeMITO", funded by AFM Telethon, PI Alessandro Prigione (Dusseldorf University) • "THERAPY4ALL: Towards therapies for mitochondrial diseases" PNRR-MR1-2023-12377223, funded by Ministry of Health, P.I. Prof. Valerio Carelli Relevant publications: 1:doi:10.1016/j.xcrm.2023.101383. 2: doi:10.1186/s10020-022-00519-z. 3: doi:10.1016/j.celrep.2022.111124. 4: doi: 10.1016/j.stemcr.2021.06.016. 5: doi: 10.3389/fneur.2021.648916. 6: doi: 10.1016/j.scr.2020.101939 7: doi:10.1016/j.celrep.2018.01.089. 8: 10.1101/2025.05.15.25325571 (pre-print).

Research Group	**Dr Cecilia Garofalo** IRCCS Istituto delle Scienze Neurologiche di Bologna
Expertise in relation to the topic	My expertise in research concerns Molecular and Cellular Oncology in solid tumors like Breast cancer and sarcomas, and now my new field of research is brain tumors. In particular, my main interest is to study detailed molecular characterization through integrated omics approaches as tools for diagnostic and prognostic improvement and elements of prediction of response/resistance to new therapeutic target therapies, particularly when combined with clinical trials.

The scientific and technical competencies reflect the profile of a molecular oncology researcher specializing in translational research on solid tumors with particular focus on biomarkers, mechanisms of treatment resistance, liquid biopsy, and the development of innovative targeted therapies. These competencies align with advanced understanding of molecular mechanisms of cancer, particularly in identifying and overcoming treatment resistance through biomarker development, signaling pathway analysis, and preclinical therapeutic experimentation.
Specifically:
-Study of the molecular biology of solid tumors, including mechanisms of tumor invasiveness and dissemination.
-Development of pharmacogenomic biomarkers for chemotherapies aimed at identifying therapeutic responses and resistance.
-Investigation of signaling pathway activities such as those related to insulin and IGF receptors, focusing on their role in drug resistance and tumor progression.
-Preclinical testing of novel specific inhibitors and therapeutic combinations for sarcomas, including the use of drugs like trabectedin and metformin and identification of new antitumor agents considered for the alternative treatment regimen for patients not responsive to conventional chemotherapy
-Advanced expertise in molecular techniques such as next-generation sequencing (NGS) for identifying pathognomonic gene fusions in sarcomas.
-Application of pharmacogenomic methods to define predictive biomarkers for response to oncologic therapies.
-Experience in handling and analyzing tumor cell lines for preclinical studies in sarcomas.
-Knowledge of molecular mechanisms underlying cell signaling and interactions between hormone receptors and oncogenic signaling pathways.
- Development of molecules for a better diagnosis of tumors with known molecular alterations characterizing the pathology and the identification of new genetic alterations to introduce diagnostic, prognostic, predictive, and required bases for new target therapies.

Relevant Projects:

- High Throughput Screening per il riposizionamento di farmaci nel trattamento dei Glioblastoma: un nuovo approccio terapeutico.
- Predictive Biomarker of treatments in advanced/metastatic Leiomyosarcoma.
- Role of Circadian Clock genes in Liposarcoma treatments.
- Role of Insulin Receptor in sarcoma

Relevant publications:

- Minopoli M, et al **Crosstalk between Macrophages and Myxoid Liposarcoma Cells Increases Spreading and Invasiveness of**

	Tumor Cells. Cancers (Basel). 2021 Jun 30;13(13):3298. doi: 10.3390/cancers13133298. ▪ Racanelli D, et al N**ext-Generation Sequencing Approaches for the Identification of Pathognomonic Fusion Transcripts in Sarcomas: The Experience of the Italian ACC Sarcoma Working Group.** .Front Oncol. 2020 Apr 15;10:489. doi: 10.3389/fonc.2020.00489. eCollection 2020.PMID:32351889 ▪ Ratti C, et al **Trabectedin overrides osteosarcoma differentiative block and reprograms the tumor immune enviroment enabling effective combination with immune checkpoint inhibitors** Clin Cancer Res. 2017 Jun 9. pii: clincanres.3186.2016. doi: 10.1158/1078-0432.CCR-16-3186. [Epub ahead of print] PubMed PMID: 28600479. ▪ Garofalo C, et al. **Preclinical Effectiveness of selective inhibitor of IRS1/2 NT157 in osteosarcoma cell lines.** Front Endocrinol (Lausanne). 2015 May 13;6:74. doi:10.3389/fendo.2015.00074. eCollection 2015. PubMed PMID: 26029165; PubMed Central PMCID: PMC4429561. ▪ Amaral AT*, Garofalo C*, et al **Trabectedin efficacy in Ewing sarcoma is greatly increased by combination with anti-IGF signaling agents.** Clin Cancer Res. 2015 Jan 21. pii: clincanres.1688.2014. [Epub ahead of print] PubMed PMID: 25609059.

Research Group	**Prof. Elisa Michelini** Dep. Chemistry
Expertise in relation to the topic	A battery of biosensors, cell-based assays relying on 3D cell models and sustainable supports (paper, threads, microfluidic chips) is available for analysis of molecular pathways and receptor activation (e.g., for hormonal activity, (anti)inflammatory activity, oxidative stress, anti-tumoral activity, antimicrobial activity etc.). Development and prototyping (TRL3-4) of portable biosensors (paper sensors and smartphone-based devices for real time low-cost on-site analysis. Prototypes have been developed and applied to detect contaminants such as toxins, biogenic amines, pesticides, heavy metals and xenobiotics, pathogens, endocrine disrupting chemicals (hormones, BPA, pharmaceuticals…) and bioactivities (general toxicity, inflammatory activity, oxidative stress, genotoxicity etc) in water, food and clinical samples (serum, saliva, sweat, exhaled breath condensate). **References** 1. Maiorano E, Calabretta MM, Lunedei E, **Michelini E**. All-in-One Sustainable Thread Biosensor for Chemiluminescence Smartphone Detection of Lactate in Sweat. Biosensors (Basel). 2025 Aug 13;15(8):530. doi: 10.3390/bios15080530. 2. Nazir F, Gregucci D, Calabretta MM, Cambrea C, Vahidi P, Lavrnić S, Toscano A, **Michelini E**. An All-in-One Sustainable Smartphone Paper Biosensor for Water Toxicity Monitoring Combining Bioluminescence Detection with Artificial Intelligence. Anal Chem. 2025 Aug 26;97(33):18092-18100. doi: 10.1021/acs.analchem.5c02369.

	3. Calabretta MM, Ferri M, Tassoni A, Maiello S, **Michelini E**. Novel bioassays based on 3D-printed device for sensing of hypoxia and p53 pathway in 3D cell models. Anal Bioanal Chem. 2024 Dec;416(29):6819-6826. doi: 10.1007/s00216-024-05606-0. 4. Calabretta MM, Gregucci D, Guardigli M, **Michelini E**. Low-cost and sustainable smartphone-based tissue-on-chip device for bioluminescence biosensing. Biosens Bioelectron. 2024 Oct 1;261:116454. doi: 10.1016/j.bios.2024.116454. 5. **Michelini E**, Calabretta MM, Cevenini L, Lopreside A, Southworth T, Fontaine DM, Simoni P, Branchini BR, Roda A. Smartphone-based multicolor bioluminescent 3D spheroid biosensors for monitoring inflammatory activity. Biosens Bioelectron. 2019 Jan 1;123:269-277. doi: 10.1016/j.bios.2018.09.012

HORIZON-HLTH-2026-01-TOOL-06: Support to European Research Area (ERA) action on accelerating New Approach Methodologies (NAMs) to advance biomedical research and testing of medicinal products and medical devices

Research Group	**Dr Lidia Strigari** IRCCS Sant'Orsola
Expertise in relation to the topic	The Department of Medical Physics, led by Lidia Strigari, has consolidated expertise in developing and validating New Approach Methodologies (NAMs) that advance biomedical research and support the testing of medicinal products and medical devices. Its core strengths integrate chemical-physical modelling, computational simulation, image-based in silico trials, and biomedical digital twins, fully aligned with the objectives of the HORIZON-HLTH-2026-01-TOOL-06 call. The Department has long-standing experience in developing predictive chemical-physical models of radiation–matter interactions, particle transport, and tissue responses using advanced Monte Carlo platforms such as FLUKA and GEANT4. These models are complemented by pharmacokinetic and pharmacodynamic simulations that incorporate physiological and imaging-derived parameters, enabling quantitative predictions of drug, radiopharmaceutical and device performance. The group also develops models that reproduce diffusion processes, molecular binding dynamics, tumour microenvironment behaviour, and mechanisms of therapeutic resistance, providing robust NAMs that reduce reliance on animal experimentation. In the field of in silico image-based trials, the Department is a national leader in creating virtual patient cohorts constructed from PET/CT, CT total-body, and MRI data. These virtual populations enable controlled testing of diagnostic and therapeutic innovations, preclinical validation of clinical trial designs, and simulation of treatment responses across anatomically and functionally varied scenarios. The group routinely employs digital phantoms, radiomic and image-derived biomarkers, and spatiotemporal modelling to evaluate device performance, predict therapeutic outcomes and validate AI algorithms within reproducible computational environments.

	The Department is also active in developing biomedical digital twins to model patient-specific responses to radiopharmaceuticals, immunotherapy, and combined treatment regimens. These digital twins integrate imaging, clinical variables and multi-omic datasets to generate dynamic, mechanistic representations of individual patients. This approach supports personalised treatment optimisation, prediction of toxicity thresholds, and in silico testing of alternative therapeutic strategies, contributing directly to the next generation of NAMs for regulatory and clinical use. All activities are supported by high-performance computing infrastructures and clinically validated computational pipelines that adhere to FAIR and GDPR principles. The Department routinely employs advanced tools for image preprocessing, normalisation and quantification, including MATLAB, Python, R and SPM12, ensuring the reproducibility and regulatory readiness of all models and simulations. In the context of the HORIZON-HLTH-2026-01-TOOL-06 action, the Department of Medical Physics can provide scientific and methodological leadership in the development, harmonisation and verification of NAMs based on physical and computational modelling. It can contribute to European frameworks for validating digital twins and in silico trials, support the standardisation of imaging-based modelling protocols, and collaborate with regulatory stakeholders to accelerate the transition from animal-based approaches to predictive, simulation-driven methodologies for testing medicines and medical devices.

Destination 6. Maintaining an innovative, sustainable, and competitive EU health industry

HORIZON-HLTH-2026-01-IND-03: Regulatory science to support translational development of patient-centred health technologies

Research Group	**Prof. Davide Martelli** Dep. Biomedical and Neuromotor Sciences
Expertise in relation to the topic	Prof. Davide Martelli is an internationally recognized expert in the neurophysiological regulation of immunity and the translational development of neuro-immune interventions. His research bridges fundamental autonomic physiology with translational immunology to design *patient-centred health technologies* capable of modulating immune responses in a controlled and reproducible manner. Prof. Martelli leads a research program at the University of Bologna that investigates the sympathetic control of immune function and its therapeutic exploitation. His laboratory combines *in vivo* physiological recordings, targeted sympathetic nerve manipulation, and *ex vivo* immune assays to uncover neural–immune mechanisms that can be harnessed for therapeutic purposes. Using a suite of *genetic mouse models*—including β2-adrenergic receptor knockouts, neuropeptide Y1 receptor knockouts, and β2/NPY1 double knockouts—his group can precisely dissect the contribution of specific neural pathways to immune modulation. This experimental expertise supports the development and regulatory validation of *neuro-immune therapeutic platforms*, including pharmacological and bioelectronic approaches, as well as *cell-based strategies* where immune cells conditioned by sympathetic signaling acquire transferable anti-inflammatory properties. Such biologically inspired interventions align with the goals of translational regulatory science aimed at ensuring efficacy, reproducibility, and safety in patient-centred innovations. Prof. Martelli has coordinated and contributed to numerous competitive research projects, including Italian PRIN grants and multiple *Australian National Health and Medical Research Council (NHMRC)* projects investigating autonomic control of immunity. He also maintains active *international collaborations with leading institutions in Brazil* (University of São Paulo and Federal University of Rio de Janeiro), focusing on cross-species and translational models of neuro-immune regulation. These collaborations reinforce the global applicability and regulatory relevance of his work. His scientific excellence is demonstrated by more than 45 peer-reviewed publications in high-impact journals (*Brain, Behavior and Immunity; Journal of Physiology; Scientific Reports; Autonomic Neuroscience*) and by his editorial appointments in *Neuroimmunomodulation* and *Frontiers in Physiology*. Through this combined expertise, Prof. Martelli's group provides a robust foundation for advancing *regulatory science in neuro-immune therapeutics*, contributing mechanistic data, validation pipelines, and translational insight to support the safe implementation of innovative patient-centred health technologies.

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