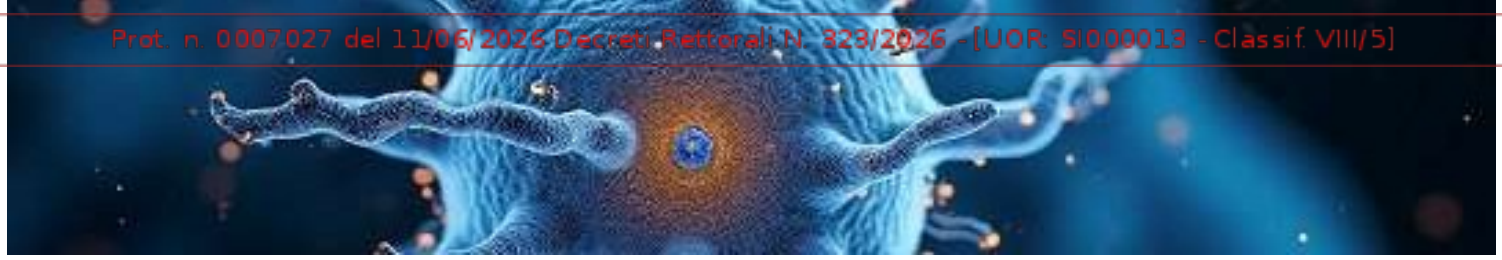

RESEARCH PROGRAMME

42nd cycle - PhD in Science and Technology for Advanced Therapies

a.y. 2026-2027

List of Research Topics

CU 1

Multisensing platforms based on ultra-sensitive organic (bio)sensors for precision medicine

Multimodal Artificial Intelligence for Biomarker Discovery and Characterization of Complex Diseases

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Technological improvements in Hadrontherapy

CU 2

Advanced genomic engineering of blood cells with polyfunctional editors

Dissecting the emergence of stemness during blood development using human pluripotent stem cells

Engineering Lentiviral Vectors to Modulate Adaptive and Innate Immunity In Vivo

Innovative Strategies for Hematopoietic Stem/Progenitor Cell Mobilization in Early-Life Gene Therapy

Enhancing Human Hematopoietic Stem and Progenitor Cell Fitness in Gene Editing

Deciphering hematological alterations in DADA2 for future gene therapy applications

RAREFIND - International Training for Doctoral Research on Advanced Gene and Cell Therapies

Tunable human striatal grafts for functional circuit reconstruction in Huntington’s disease

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Native RNA Sequencing and Targeted Transcriptomics for Precision Medicine

From encoded libraries to targeted products

Extracellular Vesicle-Based Biomarkers for Diagnosis and Monitoring of Lysosomal Storage Disorders

Dissecting molecular barriers to viral gene delivery

From brain snRNAseq-profiled biomarkers to peripheral predictive trajectories

Scholarship code

C42.CU1.01

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Multisensing platforms based on ultra-sensitive organic (bio)sensors for precision medicine

Reference Person:	**Andrea Spanu**
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Host University/Institute:	**IUSS Pavia**
	Scienze, Tecnologie e Società
Location:	**Pavia, Italy**

Research Keywords:	Organic conformable sensors
	Multisensing systems
	Wearable sensors and biosensors
Reference ERCs:	PE7_4 (Micro- and nano-) systems engineering
	PE7_11 Components and systems for applications (in e.g. medicine, biology, environment)
	PE8_13 Industrial bioengineering
Available positions:	**1**

Description of the research topic

Precision medicine approach has completely re-defined the medical field, challenging the old one-size-fits-all approach that modern medicine embraced since its inception. In particular, the paradigm is now shifting towards more customizable diagnostic and therapeutic approaches to adapt to the distinct characteristics of each individual patient.

In this context and given the extreme complexity of the "human body system", ultrasensitive and potentially conformable sensors and biosensors represent an innovative and powerful technological approach. These systems can be envisioned for off-body analysis, like spot measurements of different body fluids or the in vitro study of cells from a patient, as well as for on -body measurements, like the continuous, non-invasive monitoring of physiological and biochemical parameters from the surface of the skin. This PhD research project will focus on the design, fabrication, and validation of low-cost, conformable sensors and biosensors based on organic technologies for the detection of biochemical and bioelectrical parameters.

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The work will include the development of multisensing platforms for the detection of several analites like metabolites, electrolytes, neurotransmitters, hormones, and electrical signals (e.g., extracellular electrical activity, ECG, EEG, EMG), depending on the specific use case. The research will involve interdisciplinary collaborations across bioengineering, materials science, microelectronics, and clinical science. The goal of the program is to contribute to the next generation of diagnostic tools that are personalized, predictive, and preventive, thus aligned with the core principles of precision medicine.

Research team and environment

Our team has more than 20 yrs of experience in organic bioelectronics, an interdisciplinary field that combines organic electronics, material science, biology and biomedicine. In particular, organic bioelectronics offers a vast portfolio of different materials and convenient fabrication techniques (including printing techniques like ink-jet, screen printing and spray coating), which enables novel applications in biosensing, cellular interfacing in vitro and in vivo, pharmacology, and tissue engineering. For more information, please refer to https://www.iusspavia.it/en/research/laboratories/flexiblebioelectronics-and-wearable-devices-lab-flow-lab

Suggested skills for this research topic

Preferred background in physics, electronic engineering, biomedical engineering, chemistry, material science. Lab experience in fabrication and characterization of electronic devices and/or material science is not mandatory but appreciated.

Scholarship code

C42.CU1.02

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Multimodal Artificial Intelligence for Biomarker Discovery and Characterization of Complex Diseases

Reference Person: **Christian Salvatore**

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Host University/Institute: **IUSS Pavia**

Scienze, Tecnologie e Società

Location: **Pavia, Italy**

Research Keywords: artificial intelligence

neuroimaging

complex diseases

Reference ERCs: PE6_11 Machine learning, statistical data processing and applications using signal processing (e.g. speech, image, video)

LS5_17 Imaging in neuroscience

PE6_7 Artificial intelligence, intelligent systems, natural language processing

Available positions: **1**

Description of the research topic

Complex diseases represent a major challenge for modern healthcare systems due to their heterogeneous manifestations, multifactorial mechanisms, and variable clinical progression. These conditions, including neurological, oncological, cardiovascular, inflammatory, and metabolic diseases, require advanced tools for early diagnosis, disease monitoring, patient stratification, and personalized treatment strategies.

The aim of this research is to develop and evaluate artificial intelligence methods for the computational characterization of complex diseases through the integration of multimodal biomedical data, including medical imaging, omics data, clinical and laboratory variables, functional assessments, and behavioral, textual, or language-derived features.

The project will address key methodological challenges such as automated segmentation of anatomical or pathological structures, biomarker identification, disease classification,

progression prediction, and patient subgroup discovery. Particular attention will be devoted to multimodal learning strategies capable of integrating heterogeneous data sources into clinically meaningful disease signatures.

Advanced machine learning and deep learning approaches will be explored, including representation learning, explainable artificial intelligence, and large language models for the analysis and interpretation of clinical, cognitive, and textual data. The proposed methods will be evaluated on real-world datasets collected in collaboration with clinical and research institutions, with the ultimate goal of supporting personalized approaches to the assessment and management of complex diseases.

Research team and environment

The research will be conducted at IUSS Pavia within the Artificial Intelligence Research Group – Ailice Labs (https://www.ailice.ai), an interdisciplinary research environment focused on the development of artificial intelligence methods for healthcare and neuroscience applications.

The research group combines expertise in machine learning, biomedical data analysis, neuroimaging, and explainable AI. The team includes university faculty members, researchers, and PhD students working on AI-driven approaches for medical data analysis and clinical decision support.

The project will benefit from collaborations with hospitals, research institutions, and industrial partners involved in digital health and medical AI, including the IUSS spin-off DeepTrace Technologies. These collaborations enable access to biomedical datasets and facilitate the translation of research results into clinically relevant tools.

Suggested skills for this research topic

The ideal candidate should hold a degree in Computer Science, Computer Engineering, Biomedical Engineering, Physics, Applied Mathematics, or related disciplines.

Strong programming skills in Python are required. Prior experience in machine learning, deep learning, or biomedical data analysis is highly desirable. Knowledge of medical image analysis, neuroimaging data processing, or multimodal data integration represents an advantage.

Familiarity with deep learning frameworks (e.g. PyTorch or TensorFlow), scientific computing libraries, and data analysis tools is expected. Experience with neuroimaging analysis tools (e.g., FSL, SPM, or related software) is a plus.

The candidate should demonstrate analytical thinking, problem-solving ability, and the capability to work independently as well as within interdisciplinary research teams involving computer scientists, clinicians, and neuroscientists.

Good proficiency in English is required for research communication and scientific writing.

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C42.CU1.03

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Hadrontherapy Radiobiological study of radioresistant tumors, New instrumental technologies

Reference Person:	**Angelica Facoetti**
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Host University/Institute:	**Fondazione CNAO**
	Centro Nazionale di Adroterapia
Location:	**Pavia, Italy**

Research Keywords:	radioresistance
	radiobiology
	Hypoxia
Reference ERCs:	LS3_1 Cell cycle, cell division and growth
	LS3_2 Cell senescence, cell death, autophagy, cell ageing
	LS3_3 Cell behaviour, including control of cell shape, cell migration
Available positions:	**1**

Description of the research topic

Radiotherapy remains a cornerstone of cancer treatment; however, its clinical efficacy is often hindered by the intrinsic radioresistance of certain tumors. Much like conventional X-ray therapy, the success of hadrontherapy is governed by a complex interplay of biological factors at the subcellular, cellular, and microenvironmental levels. These include the classic "Rs" of radiobiology: DNA damage repair mechanisms, cell cycle redistribution, tumor repopulation, and the reoxygenation of surviving cells. Furthermore, inherent radiosensitivity and the increasingly vital role of the immune system's reactivation in the antitumor response must be addressed.

By conducting 2D and 3D in vitro studies alongside radiobiological modeling at the CNAO facility, this research aims to identify predictive biomarkers and biological parameters that

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can be translated into clinical practice. Ultimately, the project seeks to establish the scientific foundation for personalizing radiation type, dose delivery, and fractionation.

The final goal of these radiobiological studies is to focus on the specific biological profile of each cancer, allowing us to maximize therapeutic efficacy according to different radiation types while minimizing toxicity to healthy tissues. This transition is essential to truly unlocking the potential of next-generation particle therapy and ensuring the highest standard of individualized oncological care.

Research team and environment

Biologist, physics, medical doctor, bioengineering

Suggested skills for this research topic

Laboratory skills: Proficiency in maintaining and manipulating 2D and 3D in vitro models (spheroids and organoids); hands-on experience with DNA damage and repair assays (e.g., gamma-H2AX immunofluorescence, Comet assay), western blotting, and flow cytometry, familiarity with confocal or fluorescence microscopy, flexibility to work in a hybrid environment involving physicists, clinicians, and biologists. Radiation therapy skills: degree in physics, medicine, biotechnology, or biology oe equivalent

English language proficency.

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C42.CU1.04

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Technological improvements in Hadrontherapy

Reference Person:	**Marco Pullia**
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Host University/Institute:	**Fondazione CNAO**
	Centro Nazionale di Adroterapia Oncologica
Location:	**Pavia, Italy**

Research Keywords:	Accelerator design and simulations
	Dose delivery systems
	Range verification
Reference ERCs:	PE6_12 Scientific computing, simulation and modelling tools
	PE2_3 Experimental particle physics with accelerators
	PE7_11 Components and systems for applications (in e.g. medicine, biology, environment)
Available positions:	**1**

Description of the research topic

In general terms, CNAO is interested in the development of techniques to improve the accuracy of the treatment both on the side of the beam production, of the dose delivery and on the side of the delivered dose verification.

The main developments can be grouped in a few categories like

“accelerator simulation and developments” (e.g. resonant slow extraction, mixed beams (accelerating He and C together: C ions deliver the treatment while He is used for range verification), use of crystals for extraction, faster extraction schemes),

“range verification” (e.g. using mixed beams (development of the detector), ionoacoustics, nanodroplets or prompt gammas),

“beam diagnostics” (eg development of ultra-thin detectors usable also during treatments, beam tomography, Schottky beam measurements),

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"development of dose delivery systems" (eg 4D dose delivery, particle arc therapy, minibeams).

In all cases the continuous discussion of the technical aspects with the "users", let it be the biological or clinical side, is fundamental and the transdisciplinary approach to complex medical technology problems is a key research objective

Research team and environment

The thesis is in the framework of the technical research unit at CNAO and of its national and international collaborations. The research team includes physicists, engineers and technicians but it has continuous collaborations, contacts and discussion with all the CNAO groups ranging from medical doctors to TSRM, from medical physicist to radiobiologists and bio engineers.

Suggested skills for this research topic

A good knowledge of English is mandatory

Some knowledge in particle matter interaction is useful

Some knowledge in accelerator physics is welcome

Some knowledge of basic signal processing or of electronics may be of help for some subjects

Scholarship code

C42.CU2.01

CU2 - GENE AND CELL THERAPIES

Advanced genomic engineering of blood cells with polyfunctional editors

Reference Person: **Daniele Canarutto**

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Host University/Institute: **Fondazione Telethon ETS**

San Raffaele Telethon Institute for Gene Therapy

Location: **Milan, Italy**

Research Keywords: gene editing

hematology

Reference ERCs: LS7_2 Medical technologies and tools (including genetic tools and biomarkers) for prevention, diagnosis, monitoring and treatment of diseases

Available positions: **1**

Description of the research topic

Gene editing allows for targeted genome modifications, yet is constrained in its clinical application by cellular responses and requirement of chemotherapy for engraftment of edited cells. RNA programmable CRISPR based editors can be customized for dual independent biological activity: permanent editing at a target site coupled with transient modulation of endogenous genes of interest. In this project, the candidate will aim to exploit polyfunctional editors to address the aforementioned limitations, as follows:

i) Design and develop novel polyfunctional editors for stealthy, efficient, and simultaneous permanent and transient modification of hematopoietic stem and progenitor cells (HSPCs) and T-cells. DNA-binding domains, effector domains, and linkers will both be screened from existing databases and designed ex novo, combined, and tested for efficacy and tolerability in primary cells.

ii) Define and validate relevant biological targets of polyfunctional editors, to transiently increase cell fitness, ameliorate cellular response to manipulation, and favor engraftment.

iii) Model therapeutic strategies in HSPC exchange settings, with the ultimate goal of achieving chemotherapy-free and therapeutically relevant levels of engraftment of genetically engineered cells.

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The candidate will acquire skills in the fields of cell biology, molecular biology, murine experiments, and bioinformatics, leveraging on recent advances from the hosting lab in the field of genetic engineering of HSPCs and T-cells. Altogether, this project aims to develop safer, more precise genome editing strategies in HSPCs, advancing toward clinically relevant therapeutic applications.

Research team and environment

SR-Tiget represents a multi-disciplinary environment, blending scientific expertise in developing innovative gene and cell therapies, access to preclinical models to evaluate efficacy and safety, and competence in conducting early-phase clinical trials. This bench-to-bedside capacity fosters alliances with industrial partners and start-up companies, crucial for securing resources to address regulatory hurdles and manufacturing needs to bring therapies to registration and make them available to patients. Our unit, Novel Gene Therapy Strategies, focuses on improving methods for therapeutic genetic manipulation of hematopoietic stem cells and exploring novel approaches. Current main goals include: clinical translation of gene editing of hematopoietic cells, enhancing HDR-mediated gene editing, exploring novel applications of emerging editing systems, and developing non-genotoxic conditioning.

https://research.hsr.it/en/institutes/san-raffaele-telethon-institute-for-gene-therapy.html

Suggested skills for this research topic

Candidates should exhibit enthusiasm and interest for the fields of gene therapy and gene editing. Good knowledge of molecular and cellular biology is required, with particular focus on the mechanisms of gene transfer and gene integration, cellular DNA repair pathways, and hematopoietic stem cells biology. Previous work experience in hematopoietic stem cells engineering is particularly welcome. Skill requirements encompass bench molecular biology, expertise in flow cytometric assays and analysis, expertise in primary cells culture and cell lines culture, previous work with in vivo murine models and, preferably, with immuno-compromised hematochimeric murine models of hematopoiesis, data analysis, data generation and data presentation.

Scholarship code

C42.CU2.02

CU2 - GENE AND CELL THERAPIES

Dissecting the emergence of stemness during blood development using human pluripotent stem cells

Reference Person:	**Andrea Ditadi**
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Host University/Institute:	**Fondazione Telethon ETS**
	San Raffaele Telethon Institute for Gene Therapy
Location:	**Milan, Italy**

Research Keywords:	Hematopoietic development
	Hematopoietic stem cells
	Gene expression regulation
Reference ERCs:	LS3_13 Stem cells
	LS7_4 Regenerative medicine
	LS3_15 Development of cell-based therapeutic approaches for tissue regeneration
Available positions:	**1**

Description of the research topic

Hematopoietic stem cells (HSCs) supply blood cells for the entirety of a person's life through their ability to self-renew, i.e. to generate indefinitely more cells with the same characteristics. HSC transplantation is the only curative therapy for many hematologic diseases. However, limited donor availability and graft quality remain critical challenges worldwide. Generating large amounts of transplantable HSCs ex vivo from human pluripotent stem cells (hPSCs) would transform access to curative therapies and provide a renewable platform for disease modeling, immunotherapy, and drug testing. Through recently published work and our own exciting preliminary data, the long-standing goal of differentiating hPSCs in HSCs is becoming reality. Yet, the process remains inefficient, with the frequency of true HSCs estimated at less than one in one million cells. Identifying bona fide HSCs is therefore essential to guide specific protocol design for HSC generation.

This effort is hampered by our limited knowledge of HSC development in human embryos as as well as our inability to accurately identify uniquely HSCs in vitro. HSCs are functionally

defined by multipotency, self-renewal, and bone marrow homing, assessed by xenograft, the gold standard for proving their presence but not for identifying them. Surface marker panels enrich for HSCs but lack precision, and multi-omics analyses are now revealing molecular heterogeneity within these phenotypically homogenous populations.

The activities of project are design to enable the precise identification and scalable generation of HSCs in vitro from hPSCs. Specifically, we aim to:

1. Define conserved and context-specific regulatory programs of HSC emergence and self-renewal.

2. Link clonal functional identity with transcriptomic and epigenomic signatures across human development and hPSC-derived hematopoiesis.

3. Establish a molecular framework to inform protocols for de novo HSC generation.

Research team and environment

The Ditadi lab is a young, international and dynamic group that focuses on an ambitious and fundamental research program integrating developmental, cell and molecular biology.

We are located at the Ospedale San Raffaele (OSR, https://research.hsr.it/en/index.html), within the San Raffaele-Telethon Institute for Gene Therapy (SR-TIGET), an internationally recognized leading center in the field of cell and gene therapy and HSC biology. We have therefore access to extensive expertise and resources for state-of-the-art pre-clinical and clinical HSC research technology, including facilities and infrastructures (Next-Generation Sequencing, Cell Sorting and Imaging, Animal Facilities, GLP laboratories), and direct access to clinically relevant human samples. This ensures that our projects benefit from close collaborations with active clinicians and are expected to accelerate the development of techniques that could be translated to the clinic.

Suggested skills for this research topic

Essential requirements

- A M.S. in biotechnology and/or molecular biology and/or genetics
- Previous experience in cell culture.
- Experience in basic molecular biology techniques.
- Experience in multiple basic molecular biology techniques (cloning, DNA extraction and genotyping, RNA analysis via qPCRs, etc).
- Fluency in English.

Preferred requirements

- A background in stem cell biology would be advantageous.

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- Experience with mouse work and/or genome engineering would be an asset
- Organizational and social skills
- Ability to work independently as well as in a team.
- Ability to work in a multi-cultural, multi-ethnic environment with sensitivity and respect for diversity.
- Ability to manage competing priorities in a fast-paced environment.
- Excellent communication skills and self-motivation.

Scholarship code

C42.CU2.03

CU2 - GENE AND CELL THERAPIES

Engineering Lentiviral Vectors to Modulate Adaptive and Innate Immunity In Vivo

Reference Person:	**Mario Leonardo Squadrito**
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Host University/Institute:	**Fondazione Telethon ETS**
	San Raffaele Telethon Institute for Gene Therapy
Location:	**Milan, Italy**

Research Keywords:	Lentiviral vector engineering
	In vivo gene therapy
	Cancer immunology
Reference ERCs:	LS7_5 Applied gene, cell and immune therapies
	LS6_3 Regulation of the immune response
	LS9_1 Bioengineering for synthetic and chemical biology
Available positions:	**1**

Description of the research topic

In vivo gene therapy aims to genetically modify specific cell types directly within the body through the delivery of gene transfer vectors. Compared to ex vivo approaches, in vivo gene therapy does not require the isolation and manipulation of target cells outside the body, enabling simpler, faster and potentially more scalable therapeutic interventions. However, in vivo vector delivery can also trigger immune activation, including cytokine release and inflammatory responses, which may limit gene transfer efficiency and reduce the therapeutic benefit. Understanding how gene transfer vectors interact with the immune system is therefore a critical challenge for the development of next-generation gene therapies.

This project focuses on the use of engineered lentiviral vectors as tools to study and actively modulate immune responses in vivo. Lentiviral vectors represent powerful platforms for stable gene delivery and can be designed to target specific cell populations. In this project, LVs will be used both as gene delivery vehicles and as experimental tools to investigate how the immune system responds to foreign antigens, including viral antigens and tumor-associated neoantigens.

Scholarship code

C42.CU2.03

The student will investigate how innate and adaptive immune cells respond to antigen expression delivered by lentiviral vectors in vivo. Using advanced molecular biology and gene engineering strategies, the project aims to identify genetic payloads that can modulate immune activation in a controlled and cell-type-specific manner. These payloads may include immunoregulatory cytokines, regulatory RNAs, or synthetic genetic elements capable of tuning immune responses.

The project will combine experimental approaches in molecular biology, viral vector engineering, mouse models, and bioinformatics analysis. By integrating these methodologies, the research aims to generate new knowledge on vector-immune system interactions and to identify innovative strategies to improve the safety and efficacy of in vivo gene therapy. Ultimately, the project will contribute to the development of novel gene therapy platforms capable of precisely modulating immune responses in dstinct diseases.

Research team and environment

Our research group focuses on the development of innovative gene delivery technologies to engineer cells directly in vivo. The laboratory combines expertise in molecular biology, viral vector engineering, computational design of therapeutic payloads, and preclinical models of disease.

A central objective of the group is to develop advanced gene transfer platforms capable of targeting immune cells such as monocytes, macrophages, and lymphocytes. Using engineered lentiviral vectors, we aim to achieve efficient, cell-specific genetic modification while maintaining high safety standards. Our research integrates experimental biology with computational approaches to design optimized therapeutic molecules, including engineered cytokines, regulatory RNAs, and synthetic gene circuits.

The student will work in a highly collaborative and interdisciplinary environment, interacting with experts in immunology, gene therapy, bioinformatics, and translational research.

Suggested skills for this research topic

Applicants should have a background in biology, biotechnology, molecular biology, immunology, or related disciplines. Previous laboratory experience in molecular biology techniques is desirable but not strictly required.

The ideal candidate should demonstrate strong motivation, curiosity, and the ability to learn new experimental and computational approaches. During the project, the student will acquire skills in molecular cloning, viral vector production, and the design of gene expression constructs. Training will also include work with mouse models, allowing the student to gain experience in in vivo experimentation and analysis of immune responses.

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Basic knowledge of data analysis and willingness to learn bioinformatics approaches, including the use of R for biological data analysis, will be considered an advantage. Organizational skills, attention to detail, and the ability to work both independently and within a team are important.

Scholarship code

C42.CU2.04

CU2 - GENE AND CELL THERAPIES

Innovative Strategies for Hematopoietic Stem/Progenitor Cell Mobilization in Early-Life Gene Therapy

Reference Person:	**Serena Scala**
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Host University/Institute:	**Fondazione Telethon ETS**
	San Raffaele Telethon Institute for Gene Therapy
Location:	**Milan, Italy**

Research Keywords:	Hematopoietic stem cell mobilization
	Hematopoietic stem cells
	Gene therapy
Reference ERCs:	LS3_13 Stem cells
	LS4_11 Haematopoiesis and blood diseases
	LS7_4 Regenerative medicine
Available positions:	**1**

Description of the research topic

Hematopoietic stem/progenitor cell (HSPC) gene therapy (GT) has proven its efficacy in the treatment of several genetic disorders. This strategy relies on the collection of autologous HSPC, their genetic modification ex vivo, and subsequent re-infusion into the patient. Currently, HSPC collection is performed through bone marrow (BM) aspirates or leukapheresis following the administration of mobilizing agents. However, these procedures remain challenging for very young infants. With expanded newborn screening, more patients will be diagnosed early in life, emphasizing the need for improved HSPC mobilization strategies for very young individuals.

By leveraging single-cell transcriptomic datasets of BM-resident and trafficking HSPC populations, we have recently identified a set of candidate genes potentially involved in the regulation of HSPC retention and mobilization. Building on these findings, the project aims to validate and further expand the repertoire of molecular targets for HSPC mobilization. In addition to functional validation of candidate genes, the project will integrate advanced molecular profiling approaches, including single-cell omics technologies and bioinformatics

analyses, to better characterize the molecular networks governing HSPC trafficking and to identify additional pathways that could be therapeutically exploited.

The student will contribute to both the experimental and analytical components of the project. Functional studies will assess the role of candidate genes in HSPC mobilization using in vitro adhesion assays and in vivo approaches. In particular, pharmacological inhibition and molecular perturbation will be applied in optimized adhesion assays to evaluate the contribution of target genes to HSPC interaction with the BM niche. In parallel, the project will include the establishment and characterization of an innovative pediatric xenotransplantation model designed to recapitulate early-life hematopoiesis and to evaluate mobilization strategies in a physiologically relevant context.

This multidisciplinary project integrates molecular biology, single-cell technologies, bioinformatics, and preclinical modeling, providing an ideal environment for training in translational research. The results will contribute to developing improved HSPC mobilization protocols suitable for infants, supporting both gene therapy and hematopoietic stem cell transplantation, and offering insights into fundamental mechanisms of HSPC trafficking.

Research team and environment

The research will be conducted at SR-TIGET, a joint venture between Fondazione Telethon and Ospedale San Raffaele, which provides an outstanding scientific and translational research environment. The research team includes both junior and experienced scientists, including PhD students, fellows, post-doctoral researchers (two biologists and a bioinformatician), and a senior technician, all with expertise in flow cytometry, functional assays, molecular techniques and single-cell omics for rare cell populations. As a highly collaborative and international environment, the institute and the team actively participates in major scientific conferences and congresses, fostering collaborations at the interface of basic and clinical research.

Suggested skills for this research topic

A strong PhD candidate should be highly motivated and demonstrate genuine enthusiasm for scientific discovery, with a clear interest in basic and translational research. The candidate should be able to work effectively both independently and as part of a collaborative team, contributing positively to a dynamic research environment. A Master's degree in Biology or Biotechnology and proficiency in English are required. Previous hands-on experience with molecular biology and cell biology techniques is highly desirable, as it will support the ability to design, perform, and interpret experiments. Strong organizational skills, curiosity, and commitment to scientific rigor will further contribute to the candidate's success in a PhD training program.

Scholarship code

C42.CU2.05

CU2 - GENE AND CELL THERAPIES

Enhancing Human Hematopoietic Stem and Progenitor Cell Fitness in Gene Editing

Reference Person:	**Eugenio Montini**
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Host University/Institute:	**Fondazione Telethon ETS**
	San Raffaele Telethon Institute for Gene Therapy
Location:	**Milan, Italy**

Research Keywords:	HSPC Fitness in Gene Editing
	Stem Cell Gene Editing
	DNA Damage Response in HSPCs
Reference ERCs:	LS7_5 Applied gene, cell and immune therapies
	LS2_2 Gene editing
	LS7_4 Regenerative medicine
Available positions:	**1**

Description of the research topic

Gene editing (GE) in hematopoietic stem and progenitor cells (HSPCs) enables precise modification of specific genomic sequences, unlike gene addition approaches that introduce an additional gene copy. Programmable nucleases generate targeted DNA breaks that allow gene disruption or precise sequence correction. In clinical applications, patient HSPCs are edited ex vivo and reinfused after conditioning to enable durable engraftment and long-term therapeutic benefit.

However, programmable nucleases functions activate the DNA damage response, which triggers cell-cycle arrest, senescence, loss of stem-cell properties, and reduced capacity to durably reconstitute hematopoiesis.

One strategy currently used to mitigate these effects is the transient inhibition of p53, a key tumor-suppressor an important regulator of the cellular DNA-damage response. Although p53 inhibition can improve cell survival and expansion, it raises concerns about increased

genotoxic risk, highlighting the need for alternative approaches that enhance editing outcomes while preserving genomic integrity.

In this project, we propose a strategy based on the transient delivery of alternative factors that support HSPC survival and maintain stem-cell properties during the gene-editing process, without the risks associated with inhibition of the p53 pathway.

Candidate factors have been identified in large-scale integration-site analyses on patients treated with lentiviral HSPC gene therapy and that are recurrently associated with the expansion and persistence of hematopoietic clones in vivo. These findings indicate that specific pathways can enhance human HSPC fitness, defined here as the ability to survive stress, preserve stem-cell properties, engraft efficiently, and sustain long-term hematopoiesis.

Candidate genes will be prioritized based on recurrence in human clonal tracking datasets, known roles in stemness and self-renewal, and functions in stress or inflammatory responses relevant to HSPC biology.

We will first test whether transient mRNA expression of these factors improves survival, editing yield, and preservation of primitive HSPC features during ex vivo gene editing. The most promising candidates will then be evaluated in vivo for their effects on engraftment and long-term hematopoietic reconstitution.

This project will identify biologically grounded regulators of human HSPC fitness that can be transiently harnessed to improve the safety and efficacy of therapeutic gene editing.

Research team and environment

The project will be conducted at the San Raffaele Telethon Institute for Gene Therapy (SR-TIGET) in Milan, an international center of excellence in gene and cell therapy research and clinical translation. The work will be carried out within the Safety of Gene Therapy and Insertional Mutagenesis Unit, which integrates molecular biology, stem cell biology, and computational analysis to study clonal dynamics and genomic safety in hematopoietic stem cell gene therapy. The research team includes scientists with expertise in HSPC biology, gene editing, and vector integration analysis, supported by advanced core facilities for genomics, bioinformatics, and preclinical models.

Suggested skills for this research topic

The ideal candidate should hold a Master's degree in molecular biology, genetics, biotechnology, or a related life sciences field. Previous experience with basic molecular biology techniques (e.g., PCR, cloning, cell culture) is desirable. Exposure to stem cell biology, gene editing technologies (such as CRISPR-Cas systems), or genomic analysis will be considered an advantage but is not required. Interest in hematopoietic stem cell biology and gene therapy is essential. The candidate should demonstrate strong motivation, curiosity,

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C42.CU2.05

and the ability to work both independently and within a multidisciplinary research team. Good organizational and problem-solving skills are expected. Proficiency in spoken and written English is required; knowledge of Italian is not required.

Scholarship code

C42.CU2.06

CU2 - GENE AND CELL THERAPIES

Deciphering hematological alterations in DADA2 for future gene therapy applications

Reference Person:	**Alessandro Aiuti**
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Host University/Institute:	**Fondazione Telethon ETS**
	San Raffaele Telethon Institute for Gene Therapy (SR-TIGET)
Location:	**Milan, Italy**

Research Keywords:	INBORN ERRORS OF IMMUNITY
	DISEASE PATHOGENESIS
	GENE THERAPY
Reference ERCs:	LS7_5 Applied gene, cell and immune therapies
	LS4_11 Haematopoiesis and blood diseases
Available positions:	**1**

Description of the research topic

The research project aims to characterize the clinical evolution and mechanisms underlying the hematological manifestations of Adenosine Deaminase 2 Deficiency (DADA2), in the view of a gene therapy approach with hematopoietic stem/progenitor cells (HSPCs). DADA2 is a rare monogenic autoinflammatory disease caused by biallelic mutations in the ADA2 gene and associated with vasculitis, immunodeficiency, and hematological abnormalities. Despite recent advances in diagnosis and treatment, the cellular mechanisms driving hematological involvement remain poorly understood, particularly in patients presenting with severe cytopenias and bone marrow failure. Currently, these manifestations represent the main indications to HSPC transplantation.

The first aim is the establishment and characterization of a DADA2 patient cohort through the integration of clinical, hematological, immunological, and genetic data to define the phenotypic spectrum of the disease and identify patients for further investigation in subsequent studies.

The second objective will focus on the longitudinal characterization of hematological disease progression and on the immuno-hematological profiling of the bone marrow

Scholarship code

C42.CU2.06

microenvironment. The PhD candidate will be involved in experimental activities aimed at investigating the bone marrow niche and the immune mechanisms responsible for damage to HSPCs using multiparametric flow cytometry, multi-omics and in vitro functional assays technologies available at the Institute. The project will investigate alterations affecting HSPCs and the role of infiltrating T cells in the development and progression of bone marrow failure, with the goal of identifying risk factors and pathogenic mechanisms.

The third objective will evaluate the clinical translatability of gene therapy approaches based on autologous HSPC genetically corrected using a lentiviral vector carrying the ADA2 gene, which have thus far been tested in preclinical models. The candidate will perform phenotypic and functional analyses of the HSPC compartment under steady-state conditions and following pharmacological mobilization of CD34+ cells into peripheral blood, in order to assess stem cell fitness and suitability for future gene therapy applications.

The research activity will include an experimental laboratory component integrated with the clinical research activities related to patient diagnosis, longitudinal follow-up, data analyses, also in collaboration with other centers.

Research team and environment

SR-TIGET provides a multidisciplinary research environment that integrates unique expertise in gene therapy development, access to advanced multi-omics technologies and preclinical models, and extensive experience in the design and conduct of clinical studies. The Project Supervisor (Alessandro Aiuti) is Head of the Unit of Pathogenesis and Therapy of Primary Immunodeficiencies and of the Clinical Research Unit. These Units conduct research aimed at elucidating the pathogenic mechanisms underlying primary immunodeficiencies through the application of state-of-the-art genetic and immunological technologies.

The PhD candidate will carry out the experimental activities in the laboratory of Dr. Alessandra Mortellaro, Group Leader at SR-TIGET, whose research focuses on the development of hematopoietic stem cell-based gene therapy approaches for the treatment of DADA2.

https://research.hsr.it/en/institutes/san-raffaele-telethon-institute-for-gene-therapy.html

Suggested skills for this research topic

The ideal candidate should have a solid background in biomedical sciences, with particular emphasis on immunology, hematology, and human genetics, as well as a strong interest in the study of the pathogenic mechanisms underlying immune-mediated diseases and rare disorders. Previous experience in biomedical research and the ability to interpret clinical and biological data will be highly valued. A strong interest in translational research integrating experimental and clinical aspects is required, together with an interest in investigating the cellular and molecular processes involved in immune regulation and hematopoiesis. The candidate should also demonstrate critical thinking and analytical skills, the ability to work

independently as well as within multidisciplinary teams. Excellent communication skills and proficiency in scientific English will be essential.

Scholarship code

C42.CU2.07

CU2 - GENE AND CELL THERAPIES

RAREFIND - International Training for Doctoral Research on Advanced Gene and Cell Therapies

Reference Person:	**Alberto Auricchio**
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Host University/Institute:	**Fondazione Telethon ETS**
	TIGEM (Telethon Institute of Genetics and Medicine) and SR-TIGET (San Raffaele Telethon Institute for Gene Therapy
Location:	**Milan, Pozzuoli (Naples), Italy**
Research Keywords:	gene therapy
	cell therapy
	rare genetic disorders
Reference ERCs:	LS2_14 Genetic diseases
	LS7_5 Applied gene, cell and immune therapies
	LS2_2 Gene editing
Available positions:	**11 (reserved for MSCA COFUND Rarefind grant holders)**

Description of the research topic

The RAREFIND project is an innovative doctoral training program designed to meet the growing need for specialized education in advanced gene and cell therapies. Coordinated by Fondazione Telethon (FTELE) with the School of Advanced Studies (IUSS) as implementing partner, RAREFIND offers a dynamic interdisciplinary and intersectoral training environment. The program encourages international mobility and promotes excellence in research across FTELE's leading institutes, TIGEM and SR-TIGET, both recognized for their pioneering contributions to genetic research and therapy development. RAREFIND aims to train 22 doctoral candidates (DCs) through cutting-edge research projects on gene therapy, gene editing, and related fields. Participants, selected through a rigorous and competitive process, will receive comprehensive education combining scientific expertise with transferable skills. They will gain hands-on experience in leading laboratories, collaborate closely with non-academic entities, and benefit from secondments and specialized training. This approach ensures exposure to a broad range of perspectives, preparing DCs to advance the development of personalized therapies for rare genetic diseases.

Scholarship code

C42.CU2.07

A key pillar of the program is its emphasis on career development. RAREFIND offers tailored mentorship, targeted professional skills training, and opportunities to engage with leaders from academia, industry, and regulatory bodies. This holistic approach ensures that graduates are equipped not only for academic research careers but also for leadership roles in biotechnology, pharmaceutical companies, and other sectors in gene and cell therapies. By integrating translational research with real-world applications, RAREFIND accelerates the transformation of scientific discoveries into therapeutic solutions, strengthening Europe's biomedical landscape.

Research team and environment

Research will be conducted in Italy at the two FTELE research institutes, TIGEM (www.tigem.it) and SR-TIGET (research.hsr.it/en/institutes/san-raffaele-telethon-institute-for-gene-therapy.html). The research teams at TIGEM and SR-TIGET comprises world-renowned scientists and experts in the field of advanced gene and cell therapies, with proven track records of groundbreaking research, evidenced by high-impact publications and significant contributions to the understanding and treatment of genetic disorders. FTELE institutes are part of a vibrant regional and national research and innovation ecosystem in Italy, which includes top-tier universities, research hospitals, research institutions and biotech companies. This ecosystem offers ample opportunities for collaboration, networking, and access to cutting-edge resources.

Suggested skills for this research topic

The ideal candidate should hold a Master's degree in biological sciences, medicine, biotechnology, or related disciplines, with a strong background in molecular biology, genetics, and cell therapy. Experience with experimental techniques (e.g. gene editing, cell culture, omics technologies, or bioinformatics) is highly desirable. Candidates should demonstrate strong analytical thinking, problem-solving abilities, and a capacity to work in interdisciplinary and international environments bridging basic, translational, and clinical research. Previous research experience, as well as the ability to communicate scientific results effectively, is essential. Soft skills such as teamwork, adaptability, and motivation for innovation in personalized medicine are key. Proficiency in English (spoken and written) is required, while knowledge of additional languages is not mandatory but may facilitate collaboration in international settings.

Scholarship code

C42.CU2.08

CU2 - GENE AND CELL THERAPIES

Tunable human striatal grafts for functional circuit reconstruction in Huntington's disease

Reference Person:	**Annalisa Buffo**
	annalisa.buffo@unito.it
Host University/Institute:	**Università degli studi di Torino**
	Dipartimento di Neuroscienze Rita Levi Montalcini e Neuroscience Institute Cavalieri Ottolenghi
Location:	**Turin, Italy**

Research Keywords:	Chemogenetics
	Medium spiny neurons
	Cell replacement therapy
Reference ERCs:	LS3_13 Stem cells
	LS5_5 Neural networks and plasticity
	LS5_11 Neurological and neurodegenerative disorders
Available positions:	**1**

Description of the research topic

Huntington's disease (HD) is a fatal genetic neurodegenerative disorder, leading to progressive loss of striatal medium spiny neurons (MSNs) and motor and cognitive decline. Although gene therapy approaches are promising, especially at early stages, they cannot restore neurons and circuitry lost at overt disease stages. Cell replacement therapy therefore represents a valuable therapeutic option.

Our group has contributed to establish striatal donor approaches in toxin-based rat models of HD. We have shown that human striatal progenitors survive transplantation, acquire striatal identity in vivo, and generate MSNs, interneurons, and astrocytes (Besusso et al, Sci Rep 2020; Schellino et al., Stem Cell Res Ther 2023; Scaramuzza et al., Pharmacol Res 2025). These grafts integrate into host circuits and influence behavioral outcomes. However, circuit reconstruction remains partial, functional recovery is limited, and the contribution of distinct graft components to therapeutic actions is unclear, although such knowledge is key for improving both proper connectivity and functional rescue.

Scholarship code

C42.CU2.08

This PhD project aims to develop tunable human striatal grafts with enhanced therapeutic potential for HD. The central hypothesis is that selective modulation of the activity of graft components can improve maturation, connectivity, and functional outcomes, while clarifying the role of specific graft cell types in recovery. Towards this aim, we will specifically investigate modulation of the whole MSN population, as well as targeting of D1- or D2-type MSNs. This will require the development of tools for selective control of graft activity, including viral vectors and/or engineered donor cell lines enabling MSN- or D1/D2-specific expression of chemogenetic actuators with improved sensitivity, selectivity, and safety. These tools will be used in in vitro, ex vivo, and in vivo approaches. In vitro studies will use 3D graftoids and organoids to model network assembly and maturation, supported by multielectrode array recordings, imaging, histology, and molecular analyses. In vivo transplantation studies will be coupled to behavioral assessment and ex vivo recordings of graft maturation and host integration.

Overall, the project will establish a platform for controllable striatal grafts, moving beyond graft survival and differentiation alone toward a model in which graft function can be actively shaped and optimized according to therapeutic needs and disease stage.

Research team and environment

The project will be conducted in the Buffo lab at the Neuroscience Institute Cavalieri Ottolenghi and Dept of Neuroscience, University of Turin. The lab investigates the reparative potential of neural stem cells and glia, with recognized expertise in stem cell biology, neural plasticity, single-cell genomics, imaging, genome editing, in vivo models, and behavior. The candidate will join a dynamic, multidisciplinary, and internationally connected research environment, supported by advanced core facilities. The position is fully funded within the ERC SyG CUSTOM-MADE and benefits from an exceptional collaborative network with the laboratories of Elena Cattaneo (University of Milan), Jenny Emnéus (University of Copenhagen), and Malin Parmar (University of Lund).

More at: https://nico.ottolenghi.unito.it/en/research-groups/physiopathology-of-neural-stem-cells/

Suggested skills for this research topic

The ideal candidate should hold a Master's degree in neuroscience, biology, biotechnology, biomedical sciences, or a related discipline. We are seeking a highly motivated applicant with a strong interest in neural repair, circuit neuroscience, and experimental neurobiology. A solid background in neurobiology is expected. Prior experience in electrophysiology, stem cell biology, in vivo experimentation, and/or behavioral neuroscience will be considered an advantage. The candidate should be able to work effectively and collaboratively within a research team and have good spoken and written English. The successful applicant will actively contribute to defining and prioritizing key experimental questions within the whole project scope, formulating testable hypotheses, and developing the work plan. We value

candidates who are organized, collaborative, adaptable, curious and resilient. Experimental work may occasionally require flexible hours.

Scholarship code

C42.CU2.09

CU2 - GENE AND CELL THERAPIES

CROSSTALK BETWEEN THE NUCLEAR ENVELOPE, GENE EXPRESSION, AND NUCLEAR INTEGRITY IN LAMINOPATHIES

Reference Person:	**Marco Foiani**
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Host University/Institute:	**Consiglio Nazionale delle Ricerche**
	Istituto di Genetica Molecolare (IGM)
Location:	**Pavia, Italy**

Research Keywords:	Nuclear structure and dynamics
	Gene expression regulation
	Nuclear lamina
Reference ERCs:	LS1_3 DNA and RNA biology
	LS2_1 Genetics
	LS3_7 Mechanobiology of cells, tissues and organs
Available positions:	**1**

Description of the research topic

The mission of the Institute of Molecular Genetics is to study the mechanisms involved in genome replication and stability evolving, over the years, to frame the study of genome integrity in the broader context of the Structure/Function relationship that binds the integrity of the nucleus, gene expression and in a wider sense cellular metabolism. The quality of publications documented the excellence of research carried out in the Institute.

The proposed research will focus on the causal relationship between the nuclear envelope, gene expression regulation and loss of nuclear integrity in normal and laminopathic cells.

The main topics will include:

(i) Nuclear envelope structure and intermolecular interactions in normal and laminopathic cells and in aging cells;

(ii) Chromatin regulation through transposable elements and miRNAs in normal and laminopathic cells;

(iii) Mechanosignaling response in terms of gene regulation and nuclear stability in normal and laminopathic cells

(iv) Development of innovative therapeutic approaches for laminopathic cells and aging disorders.

Research team and environment

The candidate will be placed in a stimulating and welcoming research group, active for years in the field of studies on lamin and nuclear envelope stability, their involvement in diseases and related molecular mechanisms. The group is highly qualified and productive and constitutes an extremely favorable environment for the inclusion of young researchers. The project will be conducted in a top-level institute equipped with all the necessary instrumentation to apply the most modern methodological approaches. The size of the institute, not too big but not too small, ensures a friendly and supportive environment together inserted in a highly competitive scientific context. The research group is involved in international collaborations and networking activities, a condition providing a stimulating and open mind approach to young researchers.

Suggested skills for this research topic

Academic background: the ideal applicant should hold a Master Degree in one of the following disciplines: biology, biological sciences, molecular biology, genetics, biotechnology.

Technical expertise: a background in nucleic acid extraction and analysis, protein analysis, basis of biostatistics and bioinformatics and mammalian cell culturing would be appreciated. Experience in confocal microscopy is highly appreciated. Soft skills: ability to work in a research team and to communicate to the scientific community.

A B2 level of spoken and written English is also required.

Scholarship code

C42.CU2.10

CU2 - GENE AND CELL THERAPIES

In vitro models to test advanced therapies for infection and tissue regeneration

Reference Person: **Lia Rimondini**

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Host University/Institute: **Università del Piemonte Orientale**

DIPARTIMENTO DI SCIENZE DELLA SALUTE

Location: **Novara, Italy**

Research Keywords: Tissue regeneration

3D and 4D in vitro models

Advanced therapies

Reference ERCs: PE11_1 Engineering of biomaterials, biomimetic, bioinspired and bio-enabled materials

LS7_4 Regenerative medicine

LS3_12 Organoids

Available positions: **1**

Description of the research topic

The candidate will develop advanced 3D in vitro models of skin and mucosal tissues to study chronic infection, inflammation, and tissue regeneration. The work will include cell co-culture systems, organoid-based models, and the use of organ-on-chip platforms or more complex dynamic culture systems that better reproduce tissue microenvironments. These models will be used to evaluate advanced therapies aimed at controlling chronic infections and promoting tissue repair.

Research team and environment

The INNOVATION Lab is a multidisciplinary research group led by Prof. Lia Rimondini and based in Novara, Italy, at CAAD – Interdepartmental Center for Translational Research on Autoimmune and Allergic Diseases, UPO – Università del Piemonte Orientale. The group brings together researchers with backgrounds in biology, biotechnology, medicine and dentistry, working in tissue engineering, biomaterials, regenerative medicine and

bioengineering. The laboratory focuses on advanced in vitro models, biomaterials, cell–material interactions, antimicrobial strategies and regenerative platforms for tissue repair. CAAD provides a high-level research infrastructure equipped with advanced technologies for omics sciences, experimental biology and translational biomedical research.

Websites:

INNOVATION Lab: https://www.theinnovationlab.it/

CAAD / Innovation Lab: https://ipazia-caad.uniupo.it/innovation-lab/

Suggested skills for this research topic

The candidate should be able to perform and interpret the related biological, microbiological, and functional analyses, including assays aimed at evaluating cell viability, proliferation, migration, wound closure, inflammatory response, extracellular matrix remodeling, bacterial adhesion, biofilm formation, and antibacterial activity.

Experience in tissue engineering, host–pathogen interactions, 3D and 4D cell culture systems, organoids, bioreactors, and, where relevant, the use of biomaterials, scaffolds, dressings, or medical-device-related platforms would be highly desirable.

Scholarship code

C42.CU2.11

CU2 - GENE AND CELL THERAPIES

Epitranscript regulation of ncRNAs involved in 3D chromatin architecture

Reference Person:	**Dafne Campigli Di Giammartino**
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Host University/Institute:	**Istituto Italiano di Tecnologia**
	IIT, Center for Human Technologies
Location:	**Genova, Italy**

Research Keywords:	epitranscriptomics
	3D chromatin
	cancer stem cells
Reference ERCs:	LS1_3 DNA and RNA biology
	LS2_4 Gene regulation
	LS2_3 Epigenetics
Available positions:	**1 (reserved for MSCA Doctoral Network IN2ACT)**

Description of the research topic

3D chromatin architecture plays a crucial role in facilitating interactions between regulatory elements and gene loci, thereby influencing cellular function and identity. Long non-coding RNAs (lncRNAs) are key mediators in this spatial organization and recent advances suggest that epitranscript modifications such as N6-methyladenosine (m6A) on ncRNAs can modulate their function and stability, impacting chromatin dynamics. Building on these insights, and on the preliminary data produced in-house, this PhD project will focus on the implementation of a dCas13 protein fused with an m6A eraser to reverse m6A modification on previously selected ncRNAs that were found to be enriched in highly connected chromatin regions, with the final goal of uncovering novel molecular mechanisms that influence chromatin architecture and gene expression regulation in cancer stem cells.

Research team and environment

Research activities in the group of Dr Campigli Di Giammartino aim at understanding how non-coding elements (such as enhancers and non-coding RNAs) and their

epigenetic/epitranscriptomic modifications regulate 3D genome architecture, gene expression and cell identity. To address this question, we use cutting-edge chromatin conformation assays (e.g.Hi-C, Hi-ChIP, Micro-C) in conjunction with other -omics techniques (e.g. ChIPseq, RNA-seq etc.) and in combination with CRISPR-based genetic and epigenetic engineering tools in mouse stem cells as well as in human tumor stem cells. The laboratory is an integral part of the IIT RNA Flagship program, it collaborates closely with laboratories of the Human Technopole Functional Genomics unit and is an active member of the international FANTOM6 project on non-coding RNAs and chromatin regulation, providing the lab with a lively global research community.

Suggested skills for this research topic

Research experience (e.g. through Master thesis work or research internships) in cellular and molecular biology techniques are required. Familiarity with the non-coding RNA fileld, CRISPR technologies and/or previous experience in producing NGS data (such as ChIP-seq, RNA-seq) will be considered a strong advantage.

Proficiency in the English language is required, as well as good communication skills, both oral and written. Successful candidates will need to provide an English test (e.g. IELTS, TOEFL, Cambridge English). You may be exempt if you are a national of a majority native-English speaking country, or have qualifications / degree that has been taught and assessed in English. The supervisor can also confirm during the interview that a candidate has the required level of English."

Scholarship code

C42.CU3.01

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Native RNA Sequencing and Targeted Transcriptomics for Precision Medicine

Reference Person:	**Francesco Nicassio**
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Host University/Institute:	**Istituto Italiano di Tecnologia**
	IIT, Center for Genomic Science of IIT@SEMM (CGS)
Location:	**Milan, Italy**

Research Keywords:	Long-Read Transcriptomics
	Precision Medicine
	Epitranscriptomics
Reference ERCs:	LS2_7 Transcriptomics
	LS1_3 DNA and RNA biology
	LS7_2 Medical technologies and tools (including genetic tools and biomarkers) for prevention, diagnosis, monitoring and treatment of diseases
Available positions:	**1 (reserved for MSCA Doctoral Network IN2ACT)**

Description of the research topic

Recent advances in RNA biology have highlighted the critical role of transcript diversity, RNA modifications, and non-coding RNAs in human health and disease. However, most transcriptomic approaches still rely on short-read sequencing technologies that require reverse transcription and amplification, limiting the accurate characterization of full-length RNA molecules. Native RNA sequencing based on Oxford Nanopore Technologies (ONT) enables the direct analysis of full-length RNA while preserving information on RNA processing and epitranscriptomic modifications.

This PhD project aims to develop and validate advanced methodologies for native RNA sequencing, addressing key barriers that currently limit its application in biomedical and clinical research. The project will focus on three objectives. First, protocols for sample preparation and library construction will be optimized to improve data quality, sensitivity, and reproducibility across biological and clinical specimens. Second, targeted enrichment

strategies will be developed to enable the analysis of low-abundance transcripts while preserving native RNA features, including RNA modifications and transcript isoform diversity. Third, the project will explore proof-of-principle diagnostic applications based on direct RNA sequencing for biomarker discovery and precision medicine.

The research will combine molecular biology, genomics, biotechnology, and computational analysis. The candidate will gain expertise in long-read sequencing, transcriptomics, RNA biology, bioinformatics, and quantitative data analysis, with particular attention to developing robust workflows suitable for clinical translation.

The project will be carried out within the international and interdisciplinary framework of INT2ACT, a Marie Skłodowska-Curie Doctoral Network dedicated to Innovative Nucleic Acids Technologies for Analysis, Detection and Treatment, in collaboration with leading academic and industrial partners in RNA sequencing, biotechnology, and translational genomics. Through this environment, the candidate will contribute to the development of next-generation technologies for transcriptome analysis and precision medicine.

Expected outcomes include improved native RNA sequencing protocols, advanced targeted transcriptomics approaches, analytical frameworks for studying RNA modifications and transcript diversity, and technological foundations for future diagnostic applications based on direct RNA sequencing.

Research team and environment

The PhD project will be carried out at the Center for Genomic Science of the Istituto Italiano di Tecnologia (IIT) in Milan, in the lab of Dr. Francesco Nicassio. The research team combines expertise in RNA biology, non-coding RNAs, epitranscriptomics, long-read sequencing, cancer genomics, and computational biology. The lab is internationally recognized for developing and applying Oxford Nanopore sequencing technologies to study transcriptome complexity and RNA modifications in biomedical and clinical contexts.

The project is embedded within the INT2ACT Marie Skłodowska-Curie Doctoral Network and benefits from collaborations with leading academic and industrial partners, including Johns Hopkins University, baseclick GmbH, and Flomics Biotech. The candidate will have access to state-of-the-art sequencing platforms, computational infrastructure, and international training opportunities in both academia and industry.

Further information:

https://int2act.eu/

https://genomics.iit.it

Suggested skills for this research topic

The ideal candidate should hold a Master's degree in Biology, Biotechnology, Molecular Biology, Genomics, Bioinformatics, Biomedical Sciences, or related disciplines. Previous

research experience in RNA biology, transcriptomics, genomics, cancer biology, or molecular medicine is highly desirable.

Experience with molecular biology techniques, including nucleic acid manipulation, cell culture, gene perturbation (e.g. CRISPR), and sequencing technologies is advantageous. Familiarity with RNA sequencing, transcriptome analysis, RNA stability studies, long-read sequencing, and computational analysis of biological datasets is desirable. Knowledge of bioinformatics tools and programming languages such as R or Python will be considered a plus.

Candidates should demonstrate strong analytical thinking, scientific curiosity, problem-solving abilities, and the capacity to work in multidisciplinary and international research environments. Proficiency in spoken and written English is required.

Scholarship code

C42.CU3.02

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

From encoded libraries to targeted products

Reference Person: **Samuele Cazzamalli**

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Host University/Institute: **Philogen**

Philochem R&D (Philochem AG Zürich)

Location: **Otelfingen (ZH), Switzerland**

Research Keywords: Targeting

Encoded Libraries

Industrial PhD

Reference ERCs: LS7_2 Medical technologies and tools (including genetic tools and biomarkers) for prevention, diagnosis, monitoring and treatment of diseases

LS1_11 Chemical biology

PE5_18 Medicinal chemistry

Available positions: **5 (reserved for Philochem Company's employees)**

Description of the research topic

Conventional therapeutic drugs are not designed to accumulate at the site of disease.

In this project, we aim to develop disease-targeted products for imaging and therapy using large, encoded libraries.

The project focuses on the generation of encoded libraries based on peptides, small organic ligands, or antibodies, and/or their screening against proteins of pharmaceutical interest.

The ligands derived in the project will be conjugated to bioactive payloads such as cytokines, antibodies, radionuclides, cytotoxic drugs (examples) to generate diagnostic or therapeutic products for applications in oncology or in other pathological conditions.

Part of the project is also dedicated to improving library screening methodologies to allow multiplexed binding kinetic measurements and improve hit identification.

Scholarship code

C42.CU3.02

The students will learn how to produce libraries, screen them, synthesize small molecules and peptides, or produce antibody-based products. The students will also learn how to express recombinant target proteins and run in vitro and in vivo biological assays.

Artificial Intelligence and Machine Learning are also utilized to valorize library screening results and improve hit nomination workflows.

Research team and environment

Philochem AG (Otelfingen, near Zurich) is the discovery R&D center of the Philogen Group, focused on targeted oncology. The team is multidisciplinary (chemistry, biology and analytical sciences) and works end-to-end from target/ligand discovery to selection of preclinical candidates. Core platforms include antibody phage display and DNA-encoded combinatorial libraries, complemented by modern analytical capabilities such as mass-spectrometry methods that support drug discovery and development. The research environment is a state-of-the-art lab setting with a young, collaborative culture, fast decision-making, high individual responsibility, and close interaction with Philogen's GMP manufacturing and clinical development organizations. (www.philochem.ch)

Suggested skills for this research topic

Ideal candidates have an MSc/PhD (or near completion) in chemistry, chemical biology, biochemistry, biotechnology or related fields. Hands-on experience in encoded library technologies (DNA-encoded libraries and/or antibody/phage display) and affinity screening is a plus. Skills in peptide/small-molecule synthesis, NGS-ready library handling, and bioconjugation to payloads (e.g., cytokines, radionuclides, cytotoxics) are valued, plus recombinant protein expression/purification and in vitro/in vivo assay work. Experience with kinetic binding (SPR/BLI) and interest in multiplexed kinetics and better hit identification are a plus. Data/AI: Python/R, statistics, ML to interpret screening data and streamline hit nomination. Soft skills: rigorous experimental design, teamwork across chemistry/biology/data science, clear documentation, and proactive problem-solving. English proficiency is sufficient; German and Italian are beneficial but not required.

Scholarship code

C42.CU3.03

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Extracellular Vesicle-Based Biomarkers for Diagnosis and Monitoring of Lysosomal Storage Disorders

Reference Person:	**Giovanni Duro**
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Host University/Institute:	**Consiglio Nazionale delle Ricerche**
	Institute for biomedical research and innovation (IRIB)
Location:	**Palermo, Italy**

Research Keywords:	pharmacodynamics biomarkers
	Lysosomal Storage Disorders
	Small Extracellular Vesicles
Reference ERCs:	LS1_9 Molecular mechanisms of signalling processes
	LS3_5 Cell signalling and signal transduction, exosome biology
	LS7_2 Medical technologies and tools (including genetic tools and biomarkers) for prevention, diagnosis, monitoring and treatment of diseases
Available positions:	**1**

Description of the research topic

The aim of this PhD project is to isolate and characterize extracellular vesicles (EVs) from the plasma of patients affected by Pompe, Gaucher, and Fabry diseases in order to evaluate their potential role as emerging molecular biomarkers. The analysis of EV composition, biological functions, and diagnostic potential will represent the core objective of this three-year research project. To date, only a limited number of studies have investigated the role of EVs in rare diseases. Increasing evidence suggests that EV release may represent an alternative pathway to lysosomal degradation. However, the EV pool derived from the plasma of patients with lysosomal dysfunction remains largely unexplored. A deeper understanding of EV biology in lysosomal storage diseases (LSDs) could therefore provide new insights into disease mechanisms and support the development of innovative diagnostic strategies. This project will focus on the characterization of EVs isolated from different subject groups, including healthy individuals, carriers, and affected patients. Their molecular composition, biological

effects, and potential involvement in different cellular compartments will be investigated for each disease analyzed. Particular attention will be given to EV-mediated intercellular communication and its possible contribution to disease progression. Furthermore, the project will explore key molecular mechanisms involved in LSDs, including enzymatic deficiencies and lysosomal dysfunction. The identification of specific biomarkers within EVs, such as microRNAs (miRNAs), represents a promising and innovative approach. These molecules may reflect the underlying pathological processes and could support early diagnosis, monitoring of therapeutic response, and the development of personalized treatment strategies. Importantly, EV-based biomarkers could reduce the need for invasive diagnostic procedures, as some LSDs, including Fabry and Pompe diseases, often require tissue biopsies. The project will rely on a multidisciplinary approach involving neurologists, geneticists, biochemists, and biomedical engineers. All research activities will be conducted in accordance with current ethical regulations, and informed consent will be obtained from all participating patients.

Research team and environment

The research team operates within the SAGEMAL project, promoted by the National Research Council of Italy at the Institute for Biomedical Research and Innovation in Palermo. The project investigates the molecular and biochemical mechanisms underlying lysosomal storage diseases, a heterogeneous group of inherited metabolic disorders caused by deficiencies of specific lysosomal enzymes and characterized by the intracellular accumulation of undegraded substrates. The group's research focuses on the characterization of genetic alterations and enzymatic defects associated with several disorders, including Fabry, Gaucher, and Pompe diseases. Using integrated approaches that combine molecular genetics and biochemical analyses, the team aims to clarify pathogenic mechanisms, evaluate the functional impact of mutations, and identify novel biomarkers to improve early diagnosis, therapeutic monitoring, and the detection of still undiagnosed patients. https://www.irib.cnr.it/progetti/sagemal/

Suggested skills for this research topic

We are looking for a highly motivated candidate for the PhD project "Extracellular Vesicle-Based Biomarkers for Diagnosis and Monitoring of Lysosomal Storage Disorders". The ideal candidate should combine expertise in extracellular vesicle biology and lysosomal storage diseases. Essential skills include traditional laboratory techniques (PCR, nucleic acid and protein extraction) and advanced methods for isolation and characterization of extracellular vesicles. The project is ambitious and multidisciplinary, requiring the ability to independently plan, execute, and analyze experiments, integrate molecular and clinical data, and contribute to translational biomarker strategies. The candidate should be proactive, detail-oriented, eager to advance innovative non-invasive approaches for early diagnosis and monitoring of lysosomal storage disorders, and possess a good command of the English language to communicate results effectively.

Scholarship code

C42.CU3.04

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Dissecting molecular barriers to viral gene delivery

Reference Person:	**Anna Kajaste-Rudnitski**
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Host University/Institute:	**Università degli studi di Pavia**
	DBB-Dipartimento di Biologia e Biotecnologie "L. Spallanzani"
Location:	**Pavia, Italy**

Research Keywords:	Cell-autonomous innate immunity
	Viral gene delivery
	human induced pluripotent stem cells
Reference ERCs:	LS7_5 Applied gene, cell and immune therapies
	LS6_1 Innate immunity
	LS5_11 Neurological and neurodegenerative disorders
Available positions:	**1**

Description of the research topic

This PhD project regards the investigation of cell-autonomous barriers to efficient gene delivery using viral vectors in the context of clinically relevant target tissues. The objective is to identify molecular mechanisms that prevent efficient viral vector transduction using advanced molecular biology and virology approaches coupled with cell biology involving culture and differentiation of iPSC-derived cells and the use of state-of-the-art transcriptomic and proteomic approaches.

Research team and environment

The AKR lab offers a competitive and highly motivating environment suitable for ambitious and hardworking candidates that are fully dedicated to experimental research. The team is currently composed of two postdocs, two PhD students, a lab manager and several BSc and MSc students. The AKR lab is located within the Golgi-Spallanzani building at the Department of Biology and Biotechnology of the University of Pavia with access to dedicated molecular biology and BSL2 level cell culture laboratories and all necessary infrastructures, including imaging and FACS facilities at the Centro Grandi Strumenti.

Scholarship code

C42.CU3.04

Suggested skills for this research topic

The candidate is expected to have a track record in experimental work in the fields on molecular biology and cell biology. Specifically, skills in viral vectors production and use (LV and AAV) and the culture and differentiation of iPSC-derived cells are required together with experience in FACS and Confocal imaging as well as molecular biology techniques including Western blotting, qPCR, cloning and nucleic acid extraction. Techniques to study DNA damage responses and antiviral immunity are a significant plus. Required soft skills include good writing and presentation skills, excellent teamworking capacity and fluent English.

Scholarship code

C42.CU3.05

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

From brain snRNAseq-profiled biomarkers to peripheral predictive trajectories

Reference Person:	**Cristina Lanni**
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Host University/Institute:	**Università degli studi di Pavia**
	Dipartimento di Scienze del Farmaco
Location:	**Pavia, Italy**

Research Keywords:	snRNA-seq
	Proteomics
	Neurodegeneration trajectories
Reference ERCs:	LS7_10 Preventative and prognostic medicine
	LS5_11 Neurological and neurodegenerative disorders
Available positions:	**1**

Description of the research topic

This translational project aims to identify novel amyloid-independent mechanisms of early Alzheimer's disease (AD) progression. By integrating single-nucleus RNA-sequencing (snRNA-seq) from human hippocampal dentate gyrus samples with longitudinal plasma proteomics from the "InveCe.Ab" cohort (a single-step multidimensional population-based study of 70-74-year old living in Abbiategrasso - ClinicalTrials.gov, NCT01345110), the study will trace disease trajectories and validate accessible peripheral biomarkers on already collected and ethical committee cleared samples.

Research team and environment

The PhD candidate will join the Lab of Biology and Pharmacology of Aging, Cancer and Neurodegeneration within the Department of Drug Sciences at the University of Pavia, fully equipped for advanced cell cultures, biochemical, and molecular biology techniques. Research activities are further supported by departmental shared utilities and the Centro Grandi Strumenti (CGS), which provides cutting-edge access to imaging, confocal microscopy, flow cytometry, TEM, NMR, and microCT.

The project will be directly supervised by PI Cristina Lanni, an expert in neurodegeneration whose research focuses on Alzheimer's disease mechanisms, peripheral biomarkers, and the gut-brain-glymphatic axis. This project is further reinforced by a solid track record of national and international fundings. Within this solid framework, the candidate will operate in an interdisciplinary, well-funded environment well suited for performing translational neuroscience research.

Suggested skills for this research topic

The ideal candidate must possess solid hands-on experience in molecular biology and applied biochemistry techniques. Additionally, preference will be given to candidates with a proven background in analyzing transcriptomic and proteomic datasets, ideally acquired during their master thesis or previous research experiences, to successfully drive the multi-omics integration and validation phases of the project.