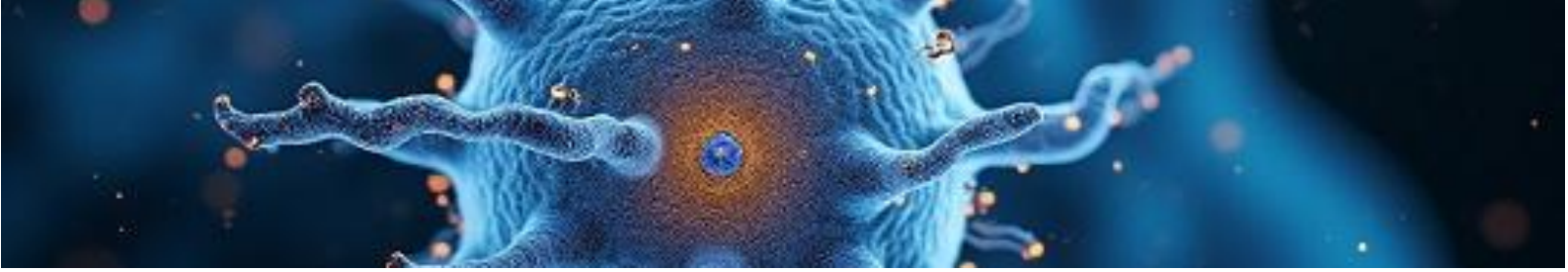
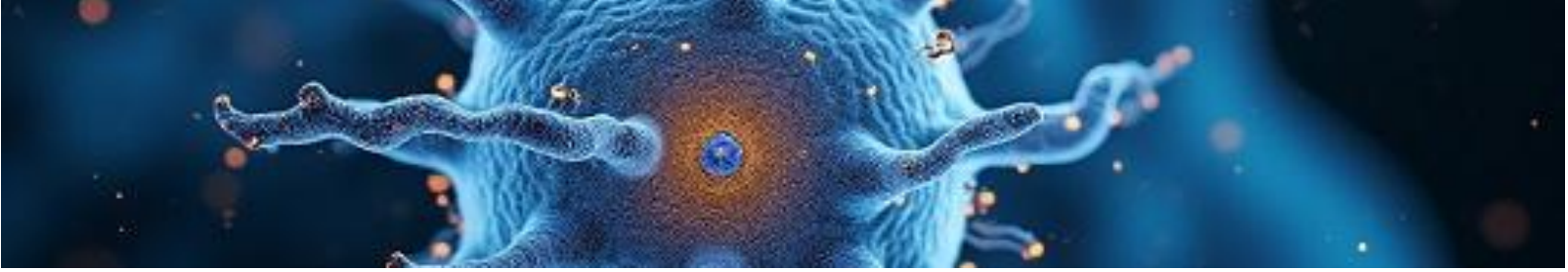


RESEARCH PROGRAMME

41° cycle - PhD in Science and Technology for Advanced Therapies

a.y. 2025-2026



List of Research Topics

CU 1

Optimization of Dose Distribution and LETd in Upright Carbon Ion Radiotherapy

Radiobiological Insights into Hypoxia-Driven Resistance in Hadron Therapy

Artificial Intelligence Approaches for Automated Segmentation of Brain Imaging

Conformable sensors for analytic applications in precision diagnostics

CU 2

Epitope Editing to Generate an Immunotherapy Stealth Hematopoiesis

3D Genome Dynamics of RNA Factory Assembly in Human Cardiomyocyte Programming

Mechanisms controlling nuclear integrity and gene expression

Uncovering and targeting drivers of T cell dysfunction for enhanced cancer immunotherapy

Identification and optimization of novel genome editing tools

Validation of a translational systemic AAV-based gene therapy for Wolfram syndrome

Decoding CAR-T Therapy: The Role of cfDNA and EVs in Predicting Success and Toxicity

Unveiling Endothelial Mechanisms to Advance Hemophilia A Therapies

Directing the timing of maturation across neuron types derived from human pluripotent stem cells

Development of a selection strategy to boost the efficacy and safety of genome editing in HSPCs

Next generation versatile and effective AAV-mediated large gene delivery

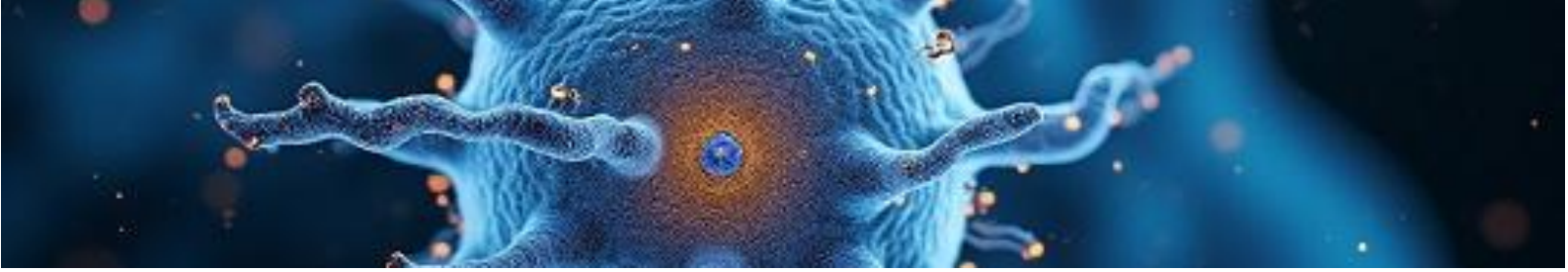
Novel Targeted Gene Editing and Delivery Technologies for Engineering Human Hematopoietic Stem Cells

Unlocking in vivo gene therapy in hematopoietic stem cells

Expanding AAV gene therapy by editing

Engineering chromatin dynamics to fine-tune enhancer-promoter interactions in neurodevelopment

HSPCs gene editing based enrichment strategies for the treatment of inborn metabolic disorders



CU 3

Molecular Mechanisms of Coenzyme Q biosynthesis

Molecular Mechanisms of Coenzyme Q biosynthesis

Development of new anti-cancer drugs based on high-affinity, highly selective ligands

Neuronal network dynamics in health and disease

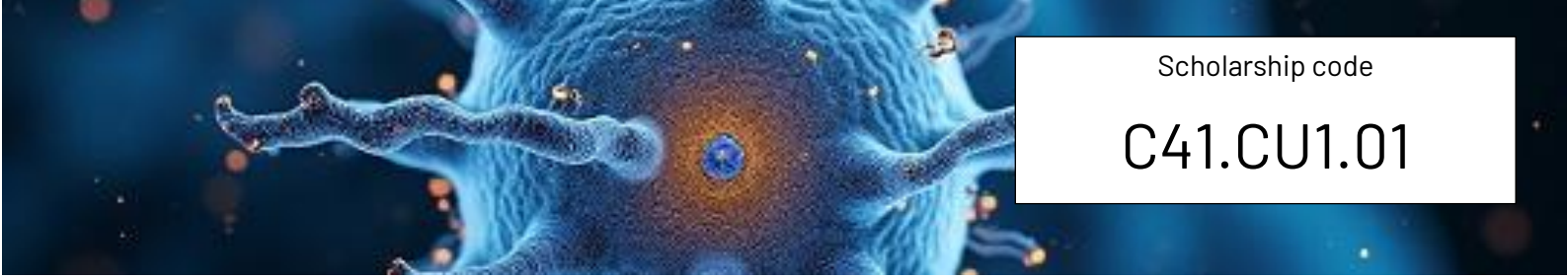
Development and optimization of industrial processes for the production of therapeutic proteins

Targeting Autism in lysosomal storage Disorders: from bed to bench side

Epidemiological studies in birth cohorts and in vitro/vivo models for non-communicable diseases

Vaccines for Cancer & Infection using mRNA Tech, ExtraVesicles, and Microbiota-Driven Innate Memory

Macromolecules of Biotechnological and Pharmaceutical Interest



Scholarship code

C41.CU1.01

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Optimization of Dose Distribution and LETd in Upright Carbon Ion Radiotherapy

Reference Person: Mario Ciocca

(mario.ciocca@cnao.it)

Host University/Institute: Fondazione CNAO

Dipartimento Medico, Unità di fisica medica

Location: Pavia, Italy

Research Keywords: Medical physics

Dosimetry of scanning ion beams

Treatment planning in particle beam radiotherapy

Reference ERCs: PE2_6 Nuclear, hadron and heavy ion physics

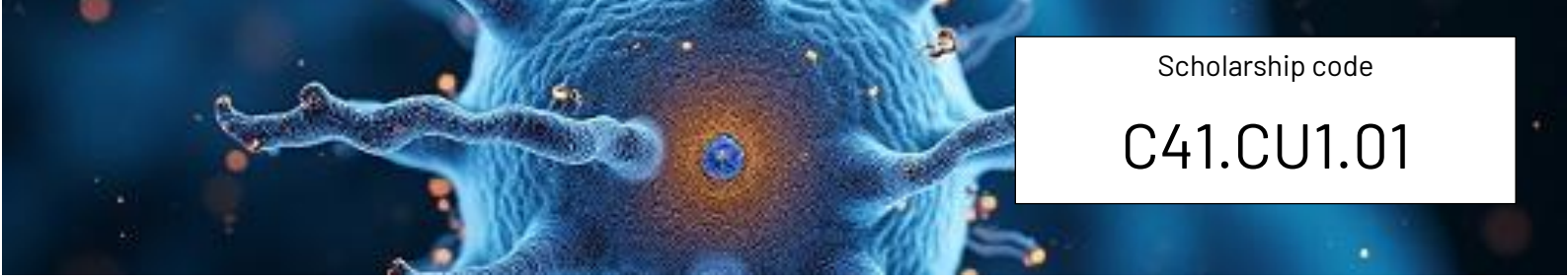
LS7_2 Medical technologies and tools (including genetic tools and biomarkers) for prevention, diagnosis, monitoring and treatment of diseases

Available positions: 1

Description of the research topic

Carbon ion therapy offers significant advantages over conventional radiation modalities due to its favorable physical and biological properties. In particular, carbon ions exhibit a sharp Bragg peak, minimal lateral scattering, and an increased relative biological effectiveness (RBE). However, these benefits come with added complexity in terms of treatment planning, especially regarding LETd (dose-weighted Linear Energy Transfer) distributions and plan robustness.

For particle therapy—and in particular for heavy ions—upright patient positioning has recently emerged as a powerful strategy to enhance treatment planning capabilities. This approach enables the generation of optimized plans that resemble those achievable with gantry-based geometries, while drastically reducing the technological and infrastructural footprint typically required for rotating beamlines. At the same time, upright positioning



Scholarship code

C41.CU1.01

supports further improvement in the quality of dose distributions, treatment robustness, and LETd control (Fredriksson, Med Phys 2023).

This project aims to investigate the potential of upright carbon ion therapy for the treatment of head & neck and abdominal tumors, two anatomical districts characterized by complex geometry and proximity to critical organs-at-risk. The first objective is to explore how different beam delivery modalities—specifically, fixed-beam configurations versus static arc-beam strategies enabled by upright positioning—affect the trade-off between dose conformity, plan robustness, and LETd distribution. In-silico optimization and analysis will be performed on a cohort of patients, with a focus on head and neck and pancreas cancer patients, with the goal of identifying planning strategies that achieve an optimal biological and physical balance.

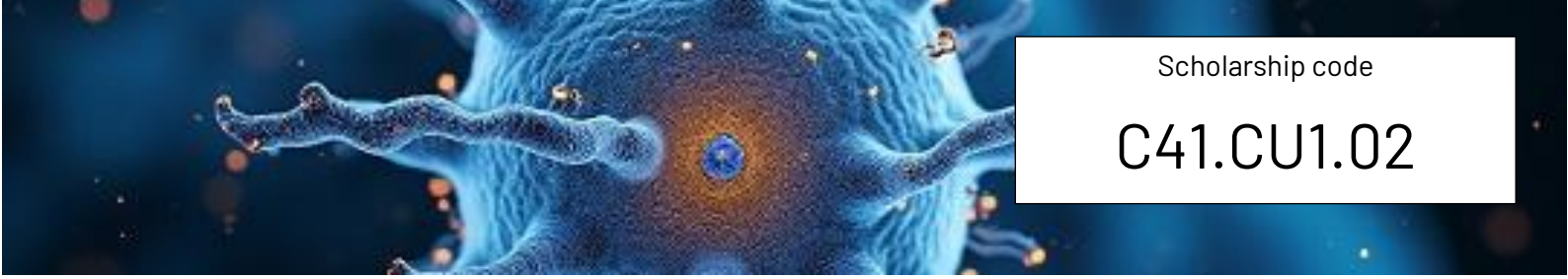
The second part of the project will focus on the clinical feasibility and technical validation of the optimized plans. Following the installation of the upright treatment chair at CNAO, the candidate will evaluate plan deliverability and perform end-to-end testing using both geometric and anthropomorphic phantoms. This phase will provide crucial data on the practical implementation of biologically optimized upright treatments and lay the groundwork for future clinical translation.

Research team and environment

The Unit of Medical Physics at Fondazione CNAO includes 9 physicists experts in Medical Physics (MPE), one post-doc senior researcher expert in FLUKA Monte Carlo simulation, plus several physicists in training and doctorate students. The Unit has in charge the tasks of dosimetry, treatment planning and quality control of scanning high-energy ion beams (protons and carbon ions), as well as CT and MRI scanners. Research activities are mainly focused on robust and LET-based ion plan optimization, radiobiological modelling for RBE estimation in hadrontherapy, 4-D dosimetry, advanced treatment tecniques like as upright patient positioning, BNCT, new ion species for hadrontherapy like as helium ions. See also: https://fondazionecnao.it/

Suggested skills for this research topic

Preferably, Master Degree in Physics and Master's Thesis in medical physics applied to hadrontherapy. Profinciency in English.



Scholarship code

C41.CU1.02

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Radiobiological Insights into Hypoxia-Driven Resistance in Hadron Therapy

Reference Person: Angelica Facoetti

(angelica.facoetti@cnao.it)

Host University/Institute: Fondazione CNAO

Dipartimento Ricerca e Sviluppo

Location: Pavia, Italy

Research Keywords: Hypoxia

Radioresistance

Hadrontherapy

Reference ERCs: LS4_12 Cancer

LS3_3 Cell behaviour, including control of cell shape, cell migration

Available positions: 1

Description of the research topic

Hadron therapy, encompassing both protons and heavier ions such as carbon and helium, has emerged as a powerful modality for cancer treatment, offering precise dose localization and enhanced relative biological effectiveness (RBE) compared to conventional photon radiotherapy. However, despite the physical and biological advantages of hadron therapy, tumour hypoxia remains a major barrier to treatment efficacy, contributing to radioresistance and promoting tumour progression through complex biological mechanisms.

Hypoxia is a common feature of solid tumours and is associated with significant changes in cellular behaviour, including altered DNA repair, metabolic rewiring, stem cell enrichment, and increased invasion and metastatic potential. While high-LET radiation is less dependent on oxygen for inducing lethal DNA damage, hypoxic tumour regions may still exhibit reduced sensitivity due to adaptive responses and selection of resistant phenotypes. The interplay between oxygen availability and hadron-induced cellular damage is not yet fully understood,

particularly in the context of fractionated treatment and dynamic tumour microenvironments.

This PhD project aims to dissect the biological mechanisms of hypoxia-induced resistance in the context of hadron therapy, exploring how oxygen deficiency influences cellular response, damage repair, and long-term tumour behaviour following exposure to different irradiation modalities such as protons and carbon ions.

This project aims to explore how hypoxia influences tumour cell response to different irradiation types, examining both short and long-terms effects. By comparing cellular behaviours in normoxic and hypoxic conditions across different models, the study will investigate beam-specific biological responses and identify potential biomarkers for resistance, with the goal of informing more personalized and effective hadron therapy strategies. In addition, this project will evaluate the development and feasibility of using sensors in cell cultures to correlate metabolic signals with hypoxia.

This research will contribute to a deeper understanding of how hypoxia shapes the biological response to hadron therapy and will help identify novel therapeutic targets. Ultimately, the project aims to support the development of personalized approaches to hadron therapy, especially for tumours in which hypoxia is a major driver of treatment failure.

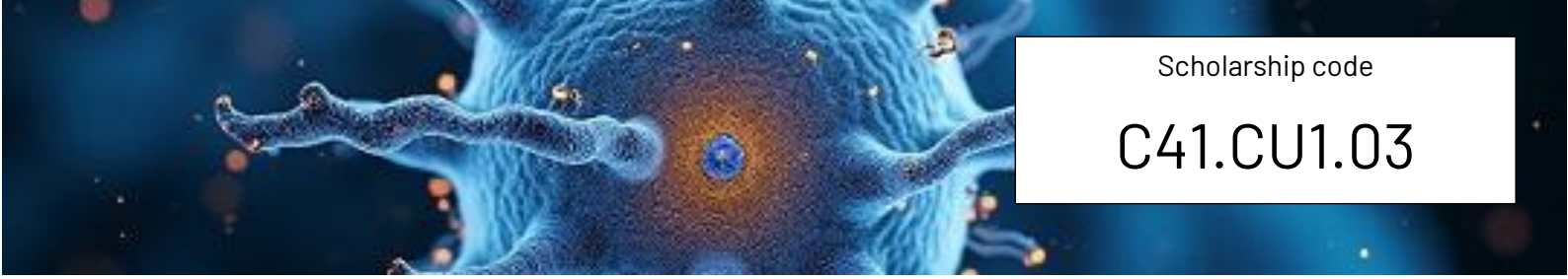
Research team and environment

The research will be conducted within the Radiobiology Laboratory of CNAO (National Center for Oncological Hadrontherapy) in Pavia, Italy. The laboratory is part of a multidisciplinary research environment focused on studying the biological effects of particle therapy, particularly proton and carbon ion beams, which are used clinically at CNAO for the treatment of radioresistant tumors.

The Radiobiology team includes researchers with expertise in cellular biology, radiation biology, and biophysics. The lab is equipped for in vitro experiments, including cell culture , molecular assays, and imaging techniques. The research activity benefits from close collaboration with clinicians, physicists, and engineers, fostering a translational approach that bridges basic research and clinical application.

Suggested skills for this research topic

A solid background in cell biology is recommended. Familiarity with radiobiology concepts, including mechanisms of radiation-induced cell death and hypoxia-related resistance, is essential. Experience with 2D and 3D (spheroids) in vitro assays (e.g., clonogenic survival, immunofluorescence, MTT assay, vitality, migration/invasion assays) and basic laboratory techniques will be valuable. Knowledge of particle therapy (e.g., protons, carbon or helium ions) and radiation physics is highly recommended, as is the ability to analyze and interpret experimental data using software tools such as ImageJ, GraphPad Prism.



Scholarship code

C41.CU1.03

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Artificial Intelligence Approaches for Automated Segmentation of Brain Imaging

Reference Person:	Christian Salvatore
	(christian.salvatore@iusspavia.it)
Host University/Institute:	IUSS Pavia
	Scienze, Tecnologie e Società
Location:	Pavia, Italy

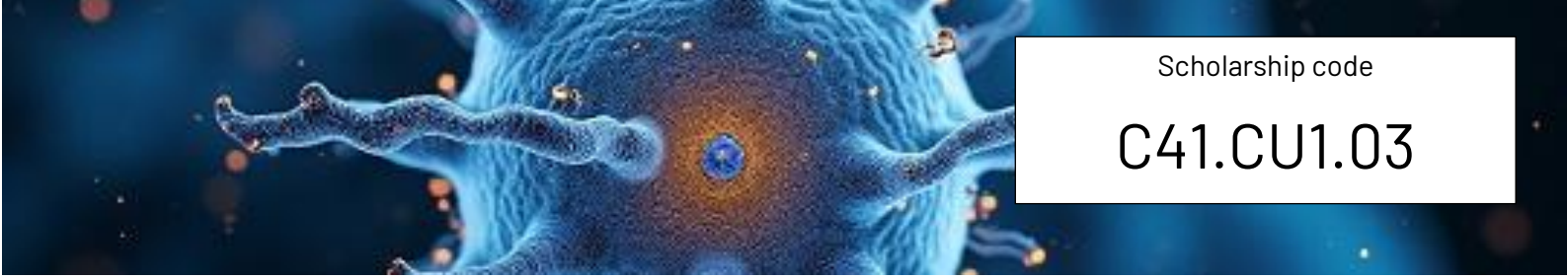
Research Keywords:	Imaging
	Machine learning
	Brain
Reference ERCs:	PE6_11 Machine learning, statistical data processing and applications using signal processing (e.g. speech, image, video)
	LS5_17 Imaging in neuroscience
	PE6_7 Artificial intelligence, intelligent systems, natural language processing

Available positions:	1

Description of the research topic

The goal of this research is to develop and evaluate AI-based approaches for the automated segmentation of brain imaging data, with applications in both clinical diagnostics and neuroscientific research.

This project will focus on the design, implementation, and validation of detection and segmentation models capable of delineating anatomical regions or pathological structures from various brain imaging modalities, e.g., MRI, CT, or PET. Key challenges include handling heterogeneity in image quality and ensuring robustness across populations and imaging centers.



Scholarship code

C41.CU1.03

The research will integrate advanced neural architectures (e.g., U-Net and its variants, YOLO etc.), training strategies incorporating anatomical priors, and uncertainty estimation methods to assess model confidence and guide clinical usage.

A further emphasis will be placed on explainability and interpretability, crucial for the adoption of AI tools in healthcare contexts.

Beyond methodological innovation, the project aims to evaluate the proposed models on real-world datasets and benchmark their performance against existing tools.

Ultimately, the project aspires to contribute to the development of AI systems that support clinicians in delivering faster, more accurate, and personalized care.

Research team and environment

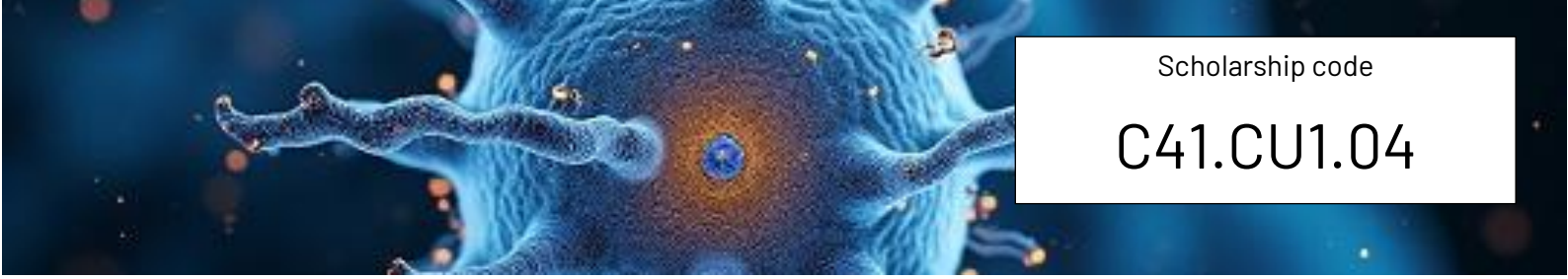
The research will be conducted at IUSS Pavia, specifically within the Artificial Intelligence Research Group - Ailice Labs (ailice.ai), an interdisciplinary environment focused on advancing AI applied to healthcare and neuroscience. The team is composed of university professors, researchers and PhD students, combines expertise in machine learning, computational imaging, neuroAI, and clinical data analysis, fostering cross-disciplinary innovation. Ailice Labs collaborates with hospitals and academic institutions, such as the IUSS spinoff DeepTrace Technologies, to ensure translational impact.

Suggested skills for this research topic

The ideal candidate should have completed an academic degree in Computer Science, Computer Engineering, Biomedical Engineering, Physics, or related disciplines.

Good-to-strong programming skills in Python is essential. Prior knowledge in medical image analysis, machine learning, or neuroimaging, as well as experience with machine-learning algorithms and common deep-learning frameworks is highly desirable. Familiarity with tools such as FSL or SPM is a plus.

The candidate should demonstrate problem-solving abilities, independence, and a collaborative attitude within interdisciplinary environments.



Scholarship code

C41.CU1.04

CU1 - HADRON THERAPY AND ADVANCED BIOPHYSICAL THERAPIES

Conformable sensors for analytic applications in precision diagnostics

Reference Person:	Annalisa Bonfiglio
	(annalisa.bonfiglio@iusspavia.it)
Host University/Institute:	IUSS Pavia
	Classe di Scienze Tecnologie e Società
Location:	Pavia, Italy

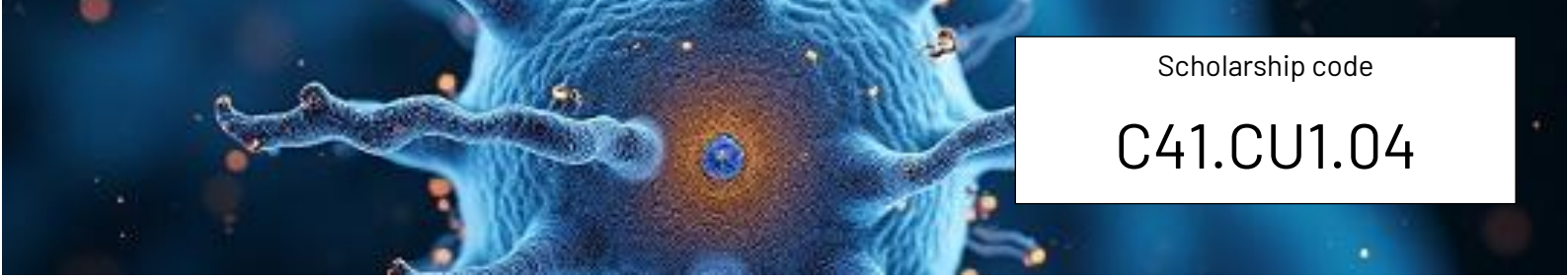
Research Keywords:	(Bio)sensors
	Wearable devices
	Conformable monitoring systems
Reference ERCs:	PE7_4 (Micro- and nano-) systems engineering
	PE7_11 Components and systems for applications (in e.g. medicine, biology, environment)
	PE4_8 Electrochemistry, electrodialysis, microfluidics, sensors

Available positions: 1

Description of the research topic

Precision medicine aims to tailor diagnostic and therapeutic strategies to the unique characteristics of each patient. In this context, conformable sensors—soft, flexible, and skin- or tissue-adaptive devices—represent a transformative technological frontier. These systems can seamlessly interface with the human body, spanning a very large dimensional range (from single cells to the whole body) enabling the continuous, non-invasive, and high-resolution monitoring of physiological and biochemical parameters over time.

This PhD research project will focus on the design, fabrication, and validation of conformable sensors for applications in precision medicine, with a particular emphasis on devices capable of multiplexed, real-time data acquisition. The work will include the development of biocompatible materials and microfabrication techniques for wearable or implantable platforms, integration with wireless and low-power communication systems,



Scholarship code

C41.CU1.04

and the implementation of data analytics pipelines to convert raw signals into clinically meaningful insights.

Potential target biomarkers include metabolites (e.g., glucose, lactate), electrolytes (e.g., sodium, potassium), and vital signs (e.g., temperature, hydration, ECG), depending on the intended clinical use. Use cases may range from early diagnosis and therapeutic monitoring in chronic diseases (e.g., diabetes, cardiovascular disorders) to real-time feedback in digital health systems.

The research will involve interdisciplinary collaboration across bioengineering, materials science, microelectronics, and clinical domains. The ultimate goal is to contribute to the next generation of diagnostic tools that are personalized, predictive, and preventive, aligned with the core principles of precision medicine.

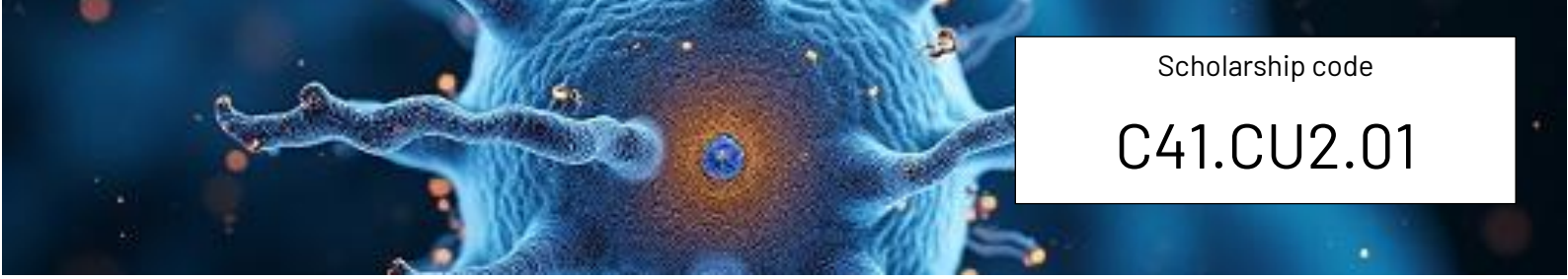
Research team and environment

Our team has more than 20 yrs of experience organic bioelectronics, an interdisciplinary field that combines organic electronic materials—such as conjugated polymers and small molecules—with biological systems to enable electronic sensing, stimulation, and signal transduction at the biotic–abiotic interface. These materials are soft, flexible, and often biocompatible, making them ideal for interfacing with tissues, cells, and biomolecules. Organic bioelectronics enables novel applications in biosensing, neural recording, drug delivery, and tissue engineering by translating biological signals (e.g., ionic, chemical) into electronic ones and vice versa, with high sensitivity and specificity.

For more infos, please refer to https://www.iusspavia.it/en/research/laboratories/flexible-bioelectronics-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 also appreciated.



Scholarship code

C41.CU2.01

CU2 - GENE AND CELL THERAPIES

Epitope Editing to Generate an Immunotherapy Stealth Hematopoiesis

Reference Person: Pietro Genovese

(pietro_genovese@dfci.harvard.edu)

Host University/Institute: Boston Children's Hospital

Gene Therapy Program

Location: Boston, MA, United States

Research Keywords: Gene editing

Cancer adoptive Immunotherapy

Hematology

Reference ERCs: LS2_2 Gene editing

LS4_11 Haematopoiesis and blood diseases

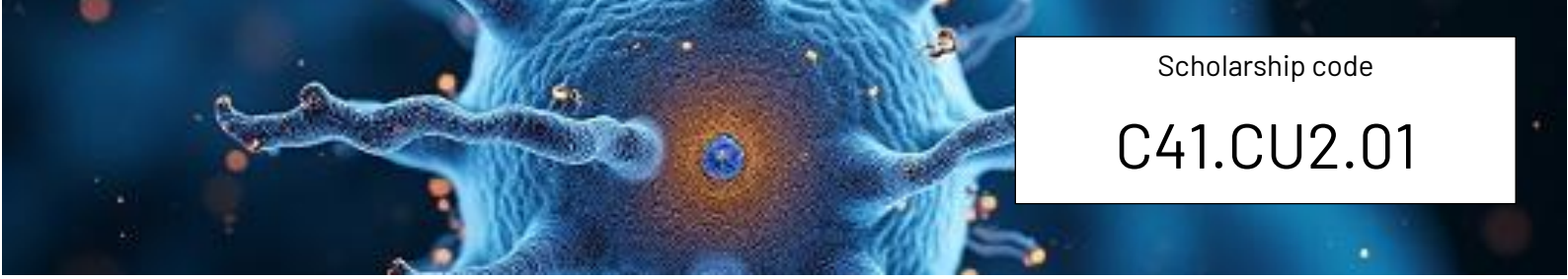
LS7_5 Applied gene, cell and immune therapies

Available positions: 1 (reserved for Boston Children's Hospital's employees)

Description of the research topic

Acute myeloid leukemia (AML) remains a formidable clinical challenge, with relapse and therapy resistance undermining long-term outcomes in over half of patients, despite hematopoietic stem/progenitor cell (HSPC) transplantation. Current immunotherapies—such as monoclonal antibodies and CAR-T cells—face a major obstacle in AML: most potential targets are shared with healthy hematopoietic cells, resulting in unacceptable toxicity.

This research proposes a novel paradigm called epitope editing, aimed at creating an "immunotherapy stealth" hematopoiesis. The strategy involves introducing minimal, precise amino acid substitutions into the extracellular domains of key cytokine receptors (FLT3, KIT, and CD123) expressed on HSPCs. These modifications abrogate antibody binding without impairing receptor function, enabling healthy HSPCs to resist immunotherapy while maintaining physiological hematopoiesis.



Scholarship code

C41.CU2.01

The PhD project focuses on optimizing base-editing technologies—specifically adenine base editors delivered via mRNA electroporation—to multiplex these edits efficiently and safely in $CD34^+$ HSPCs. Candidate cells will be assessed for editing efficiency, immunotherapy resistance, and hematopoietic potential both in vitro and via xenotransplantation in immunodeficient mice.

This approach may unlock sustained, high-intensity immunotherapies post-HSCT by shielding healthy cells from off-target toxicity. If successful, it offers a platform applicable across a range of hematologic malignancies, reshaping the therapeutic landscape for high-risk AML and beyond.

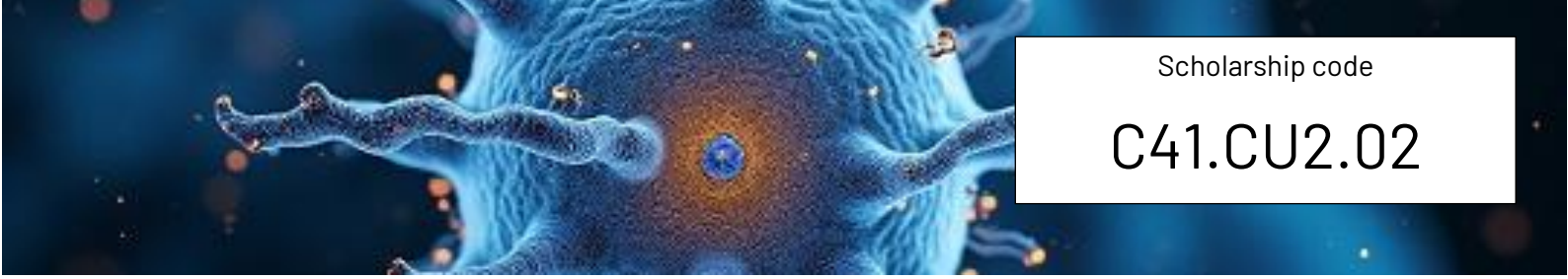
Research team and environment

The work will be conducted in the Genovese Lab, a team of young and eclectic scientists interested in exploiting gene-engineering tools to study biological functions and solve problems with a direct impact on human health. The Genovese Lab exploits a variety of cutting-edge gene editing technologies (CRISPR/Cas, TALEN, ZFN, base editors, and epigenetic transcriptional regulators) to develop new therapeutic strategies for inherited and oncologic diseases. We couple advanced molecular and cell biology approaches, such as viral vector design, chimeric antigen receptors (CAR), next-generation sequencing, and ex vivo manipulation of stem cells and primary lymphocytes, with suitable preclinical models of disease to develop novel therapeutics based on precision medicine.

Genovese Lab website: https://labs.dana-farber.org/genoveselab

Suggested skills for this research topic

We seek a driven, team-oriented PhD candidate with an M.Sc., M.D., or residency in life sciences, strong in immunology and cancer biology. The ideal candidate will be enthusiastic about molecular biology techniques, including tumor models and human sample analysis. Essential skills include multitasking, organization, communication, and expertise in tumor biology, immunology, and flow cytometry. Preferred experience includes gene editing, cloning, protein engineering, NGS, and a strong publication record. English fluency is required.



Scholarship code

C41.CU2.02

CU2 - GENE AND CELL THERAPIES

3D Genome Dynamics of RNA Factory Assembly in Human Cardiomyocyte Programming

Reference Person: Alessandro Bertero

(alessandro.bertero@unito.it)

Host University/Institute: Università degli studi di Torino

Dipartimento di Biotecnologie Molecolari e Scienze per la Salute

Location: Turin, Italy

Research Keywords: 3D genomics

Human induced pluripotent stem cells

Cardiac development and regeneration

Reference ERCs: LS1_3 DNA and RNA biology

LS3_13 Stem cells

LS4_10 The cardiovascular system and cardiovascular diseases

Available positions: 1

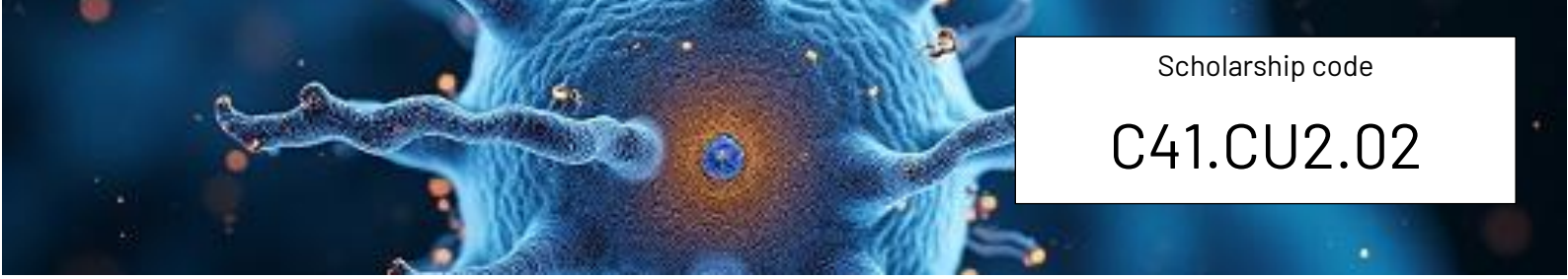
Project: TRANS-3, ERC Starting Grant, Agreement n. 101076026

Description of the research topic

How is the choreography of gene expression orchestrated during human development? Beyond DNA sequence, 3D genome architecture organizes enhancers, genes, and noncoding elements into functional nuclear neighborhoods. Among these, RNA factories—membraneless compartments that coordinate transcription, splicing, and RNA processing—are emerging as master regulators of cell identity. Yet, how they assemble, and which factors control their formation, remains largely unknown.

This PhD project will investigate the formation and function of RNA factories during the differentiation of human iPSCs into cardiomyocytes, with a focus on transcription factors that link chromatin architecture and RNA metabolism.

Anchored in the ERC-funded TRANS-3 project, we propose that GATA4—a pioneer factor essential for heart development and frequently mutated in congenital heart disease (CHD)—



Scholarship code

C41.CU2.02

acts as an organizer of inter-chromosomal RNA hubs by bridging regulatory DNA and RNA. The project will also examine MEF2C, TBX5, and other core factors involved in cardiac reprogramming.

To dissect these processes, the candidate will apply a cutting-edge toolbox including:

- ChIP-seq and RNA immunoprecipitation (RIP) to profile chromatin and RNA-binding sites (Bertero et al., Nature 2018, PMID: 29489750; Genes Dev 2015, PMID: 25805847)
- Hi-C to define 3D genome topology (Bertero et al., Nat Commun 2019, PMID: 30948719)
- Trans-C, a computational method to map inter-chromosomal contacts (Hristov et al., Genome Res 2024, PMID 39322282)
- o-MAP, an RNA-guided proximity labeling approach for identifying nuclear microenvironments (Kania et al., bioRxiv 2024, PMID 39574693)
- iPS2-seq, a high-throughput single-cell screening strategy (Balmas et al., SSRN 2024; https://dx.doi.org/10.2139/ssrn.4854180)

Using genome-edited iPSC lines, the project will examine how disease-linked mutations affect spatial genome regulation and RNA factory dynamics.

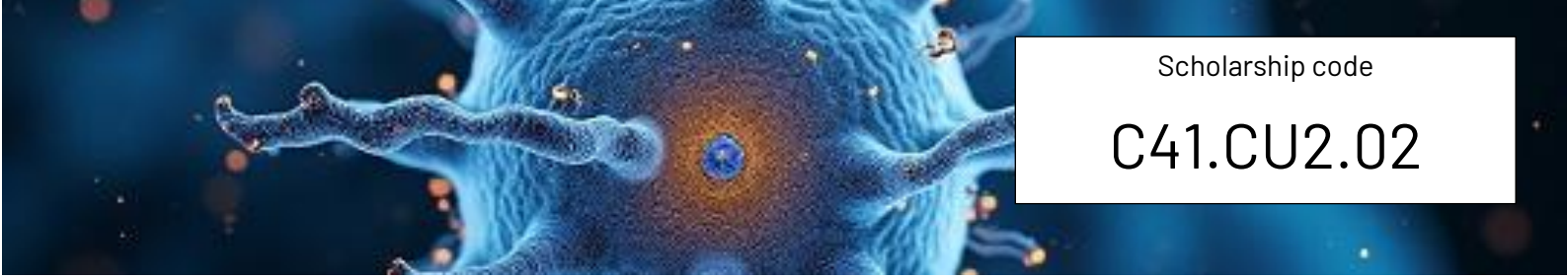
In addition to shedding light on CHD mechanisms, this work will guide improved protocols to program iPSCs into mature cardiomyocytes—a key step for effective cell therapies (Pawlowski et al., Stem Cell Rep 2017, PMID: 28344001).

This project is ideal for curious and motivated students excited by RNA biology, genome architecture, and stem cell technologies, and eager to bridge basic discovery with future therapeutic applications.

Research team and environment

The Genome Architecting Lab at the University of Turin investigates how 3D chromatin structure shapes heart development and disease, and leverages this knowledge to engineer stem cell programming for regenerative medicine. We are funded by an ERC Starting Grant, which will cover the PhD project in full, and our PI, Prof. Alessandro Bertero, is a recipient of the Armenise-Harvard Career Development Award and FEBS Excellence Award. The group includes 12+ scientists with multidisciplinary backgrounds in stem cell biology, single-cell genomics, imaging, genome editing, and bioengineering. We are based at the Molecular Biotechnology Center (MBC), an international research hub in the city center, equipped with advanced core facilities and award-winning modern lab spaces. We offer a collaborative, stimulating environment and support training, conference travel, and other formative opportunities. Torino offers excellent quality of life with accessible living costs.

More at: www.berterolab.com

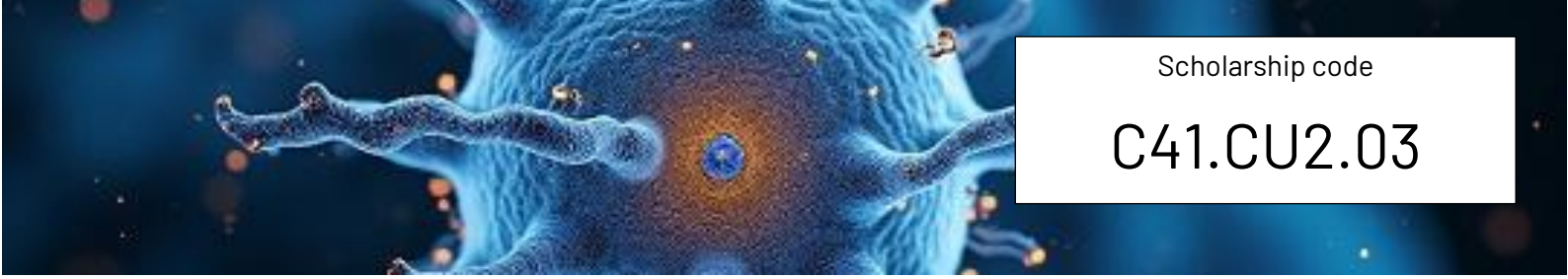


Scholarship code

C41.CU2.02

Suggested skills for this research topic

We are looking for highly motivated candidates with training in molecular biology, biotechnology, or related fields. Prior experience in wet lab research beyond thesis work is strongly preferred. Ideal applicants will have knowledge in one or more of the following areas: 3D chromatin biology, pluripotent stem cells, or cardiovascular development. The ability to work both at the bench and to write basic data analysis code is essential; the candidate will collaborate with professional bioinformaticians to frame biologically grounded, computationally tractable questions. Scientific publications, poster/oral presentations, and a record of project ownership are strong assets. Fluency in English and a desire to become an independent, critical-thinking researcher are key. We value candidates who are adaptable yet organized, team-oriented, intellectually curious, and resilient. Please note that stem cell work may occasionally require flexible hours.



Scholarship code

C41.CU2.03

CU2 - GENE AND CELL THERAPIES

Mechanisms controlling nuclear integrity and gene expression

Reference Person:	Marco Foiani
	(marco.foiani@cnr.it)
Host University/Institute:	Consiglio Nazionale delle Ricerche
	Istituto di Genetica Molecolare (IGM)
Location:	Pavia, Italy

Research Keywords:	Genome instability
	Gene expression
	Cell metabolism
Reference ERCs:	LS1_3 DNA and RNA biology
	LS2_1 Genetics
	LS3_7 Mechanobiology of cells, tissues and organs

Available positions: 1

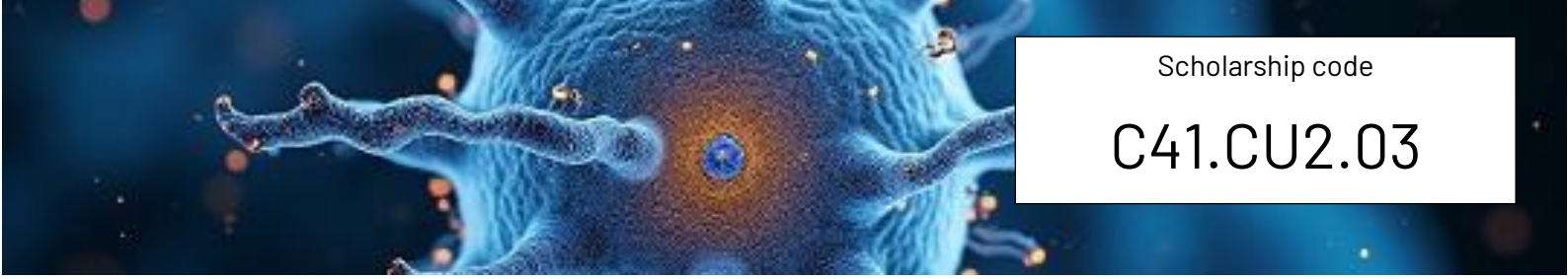
Description of the research topic

The mission of the Institute of Molecular Genetics-CNR 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 a comprehensive view of the complex network of interactions contributing to the maintenance of genome stability in eukaryotes. The main topics will include:

(i) Mechanical regulation of genome integrity programs and its implication in cancer, neurological disorders and aging.

(ii) Role of epigenetics programs, acting via chromatin organization, in cell- and tissue-specific programs and their contribution to human diseases.



Scholarship code

C41.CU2.03

(iii) Multy-disciplinary approaches to study the interplay between genome organization and cell mechanics in regulating cell-state homeostasis in cancer and in genetic diseases.

(iv) Emerging crosstalk between non-coding RNAs, chromatin and transcription/pre-mRNA splicing and DNA repair pathways in the context of genome stability.

(v) Development of innovative therapeutic approaches for cancer and genetic and neurological diseases.

Research team and environment

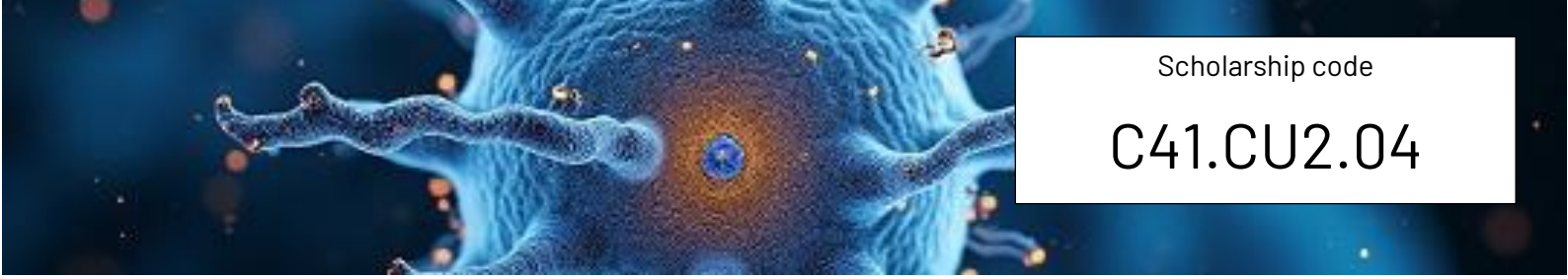
The candidate will be placed in a stimulating and welcoming research group, active for years in the field of studies on genomic instability and related molecular mechanisms. The group is highly qualified and productive and constitutes an extremely favorable environment for the inclusion of young researchers. 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.

Suggested skills for this research topic

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

Technical expertise: a background in nucleic acids metabolism, protein analysis, basis of biostatistics and bioinformatics and bacterial and mammalian cell culturing would be appreciated. Soft skills: ability to work in a research team and to communicate to the scientific community.

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



Scholarship code

C41.CU2.04

CU2 - GENE AND CELL THERAPIES

Uncovering and targeting drivers of T cell dysfunction for enhanced cancer immunotherapy

Reference Person: Angelo Lombardo

(lombardo.angelo@hsr.it)

Host University/Institute: Fondazione Telethon

San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)

Location: Milan, Italy

Research Keywords: Cancer immunotherapy

Target discovery

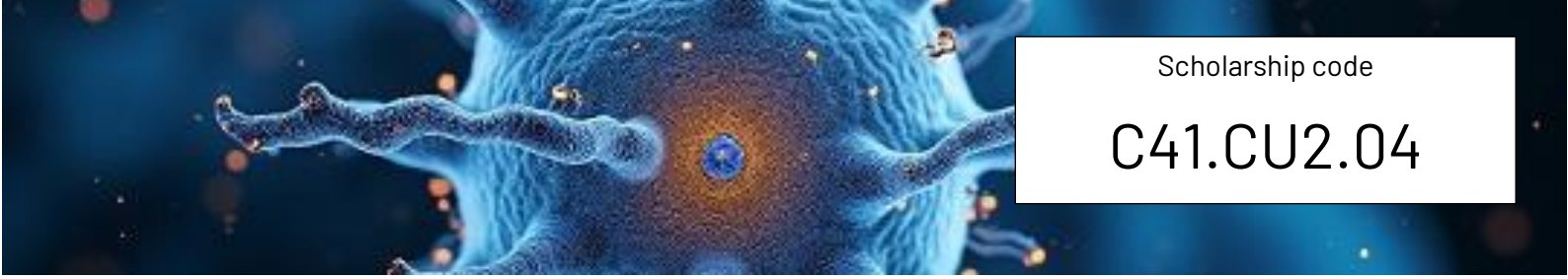
T cell engineering

Reference ERCs: LS7_5 Applied gene, cell and immune therapies

Available positions: 1

Description of the research topic

T cell-based immunotherapies have emerged as a powerful strategy in cancer treatment by harnessing the immune system's capacity to recognize and eliminate tumor cells. Approaches such as chimeric antigen receptor T cells and T cell receptor-engineered lymphocytes have demonstrated remarkable clinical success, particularly in hematologic malignancies. However, their efficacy against solid tumors remains significantly limited, primarily due to immunosuppressive mechanisms within the tumor microenvironment. Among these, adenosine and transforming growth factor-beta are key immunosuppressive mediators that impair T cell proliferation, activation, and persistence, ultimately contributing to tumor immune evasion. Importantly, these inhibitory conditions can be recapitulated in vitro, providing a controlled platform to investigate the molecular pathways underlying T cell dysfunction. Identifying factors that enable T cells to resist such immunosuppression could inform the development of novel strategies to enhance the efficacy of T cell-based therapies. This project aims to design and implement functional screens leveraging genome and/or epigenome editing to identify coding and non-coding genes that promote T cell persistence and function under immunosuppressive conditions.



Scholarship code

C41.CU2.04

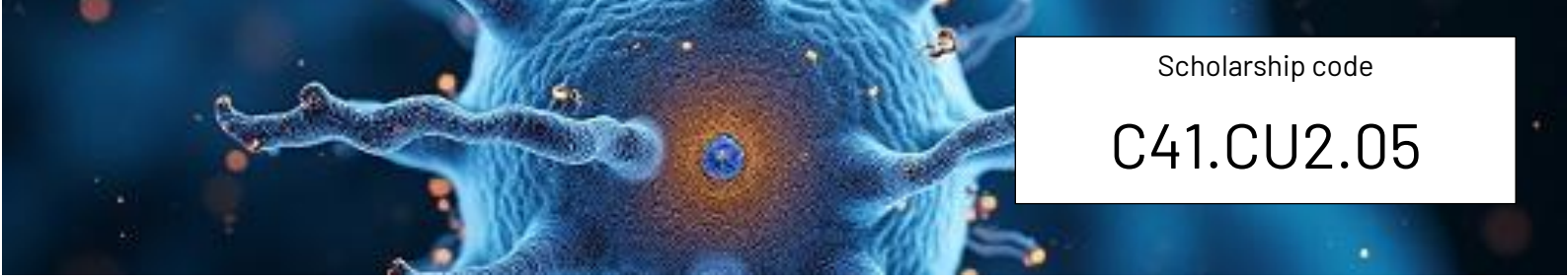
The findings are expected to reveal novel actionable targets to improve the performance of T cell-based immunotherapies.

Research team and environment

The research team, led by Prof. Angelo Lombardo at SR-Tiget (Milan, IT), operates within a world-renowned institute for gene and cell therapy. In this context, we develop and apply innovative gene and epigenetic editing strategies for therapeutic purposes. Specifically, our group pioneered targeted gene correction in clinically relevant cells and established a platform for efficient and durable gene silencing using engineered epigenetic repressors (Amabile, Cell 2016; Cappelluti, Nature 2024). We are leveraging this approach to treat diseases where gene silencing can be beneficial, engineer immune cells for cancer immunotherapy, and investigate the stability and specificity of silencing across cell types and developmental stages. Our research relies on protein engineering, advanced gene delivery systems, disease-relevant models, and genome-scale loss-of-function screens, and is conducted in a highly collaborative environment that fosters innovation, translation, and training.

Suggested skills for this research topic

The ideal candidate should have a background in molecular and cellular biology, with a strong interest in immunology and cancer research. Experiences in T cell biology, flow cytometry, and genome or epigenome editing are desirable. Basic knowledge of bioinformatics tools and the ability to analyze high-throughput data will be considered a strong asset. The candidate should be highly motivated, detail-oriented, and capable of working both independently and as part of a multidisciplinary team. Strong communication skills, proficiency in spoken and written English, and a proactive attitude toward learning and problem-solving are essential.



Scholarship code

C41.CU2.05

CU2 - GENE AND CELL THERAPIES

Identification and optimization of novel genome editing tools

Reference Person: Anna Cereseto

(anna.cereseto@unitn.it)

Host University/Institute: Università di Trento

Dipartimento di Biologia Cellulare, Computazionale e Integrata (CIBIO)

Location: Trento, Italy

Research Keywords: Genome editing

RNA guided nucleases

Directed evolution

Reference ERCs: LS2_2 Gene editing

Available positions: 1

Project: FIS, MUR-FIS00002542
CUP: E53C23001540001

Description of the research topic

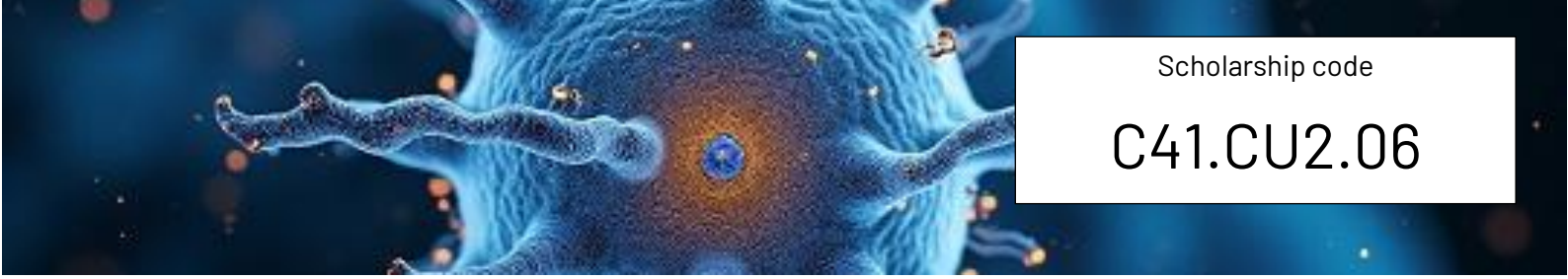
The aim of the project is the identification of novel genome editing tool starting from a very large metagenomic databank. We will focus on RNA guided nucleases (RGN) with reduced molecular size to increase compatibility for in vivo delivery (LNP and AAV vectors). The RGN will be optimized for editing activity through AI tools and directed evolution using a lab platform (EPICA). Finally the RGN (eventually adapted to epigenome editors) will be tested for specific genomic loci editing with clinical relevance for gene therapy development.

Research team and environment

https://www.cibio.unitn.it/79/laboratories

Suggested skills for this research topic

Expertise in molecular biology. English proficient user (C).



Scholarship code

C41.CU2.06

CU2 - GENE AND CELL THERAPIES

Validation of a translational systemic AAV-based gene therapy for Wolfram syndrome

Reference Person: Vania Broccoli

(vania.broccoli@cnr.it)

Host University/Institute: Consiglio Nazionale delle Ricerche

Istituto di Neuroscienze

Location: Milan, Italy

Research Keywords: Gene therapy

Neurological disease

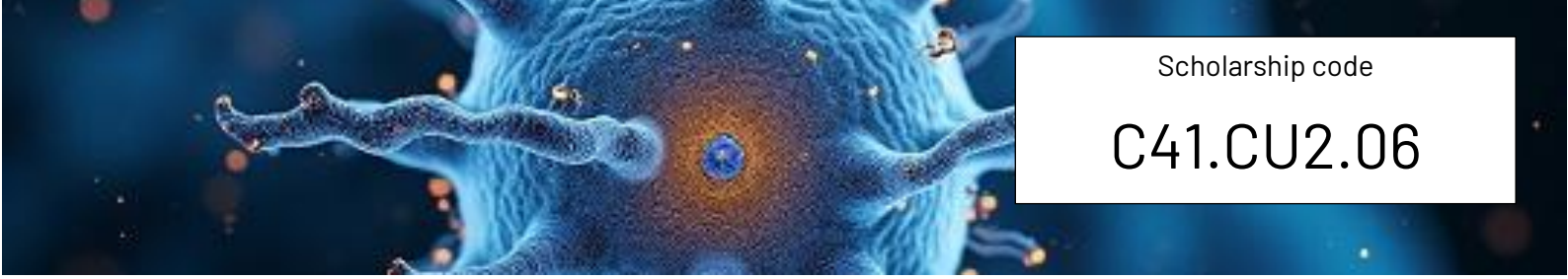
Reference ERCs: LS7_5 Applied gene, cell and immune therapies

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

Wolfram syndrome 1 (WS1) is a rare genetic disorder caused by mutations in the WFS1 gene leading to a spectrum of clinical dysfunctions, in particular infantile diabetes, visual loss and neurodegeneration . Currently, no therapeutic options are available to arrest or delay the progression of these pathological manifestations. WS1 is caused by mutations in the WFS1 gene, which encodes for Wolframin, a multi-transmembrane protein resident in the endoplasmic reticulum. We have previously showed that Wfs1-deficient mice develop progressive neuronal loss both in the retina and bran with progressive demise of pancreatic beta-cells. We have also established an AAV system for the regulated expression of Wfs1 to establish a gene replacement therapy with translational potential. The project will define the vector design, AAV capsid and delivery strategies to achieve high and simultaneous gene expression in multiple affected tissues and organs after systemic delivery. Treated Wfs1-mutant mice will be evaluated for gene-transfer efficiency, cell functional recovery, neurodegeneration protection and symptomatic rescue. This project will build the foundation for establishing the first gene-based therapeutic strategy for treating the severe pathological conditions in WS1.



Scholarship code

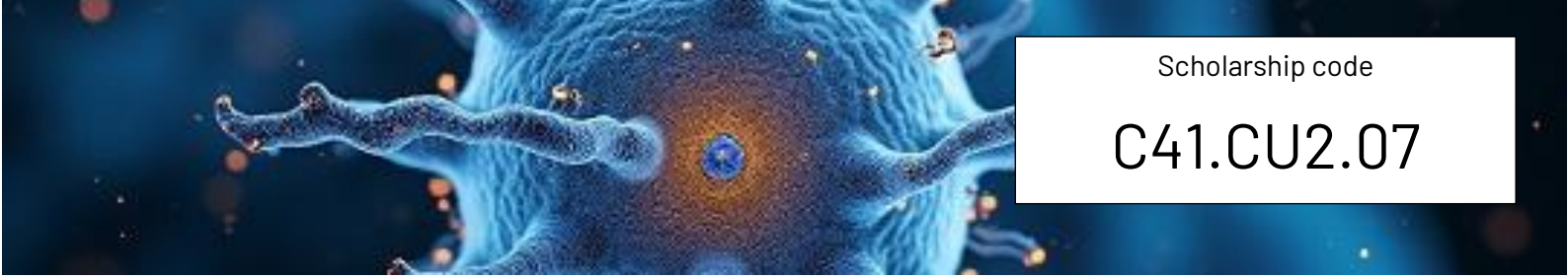
C41.CU2.06

Research team and environment

Broccoli's Laboratory offers an interdisciplinary environment with a variety of interests in developing translational gene-based precision therapies for incurable diseases. Deep expertise in genome editing, disease mouse models, patient stem cell biology and vectorology are available in the lab. Collaborative initiatives and dynamic environment are nurtured in order to promote innovative and creative approaches for defining and testing novel therapeutic strategies.

Suggested skills for this research topic

High interest in gene-based translational approaches to treat neurological diseases. previous experience in neuroscience will be a plus.



Scholarship code

C41.CU2.07

CU2 - GENE AND CELL THERAPIES

Decoding CAR-T Therapy: The Role of cfDNA and EVs in Predicting Success and Toxicity

Reference Person:	Daniela Cesana
	(cesana.daniela@hsr.it)
Host University/Institute:	Fondazione Telethon
	San Raffaele Telethon Institute for Gene Therapy (SR-TIGET)
Location:	Milan, Italy

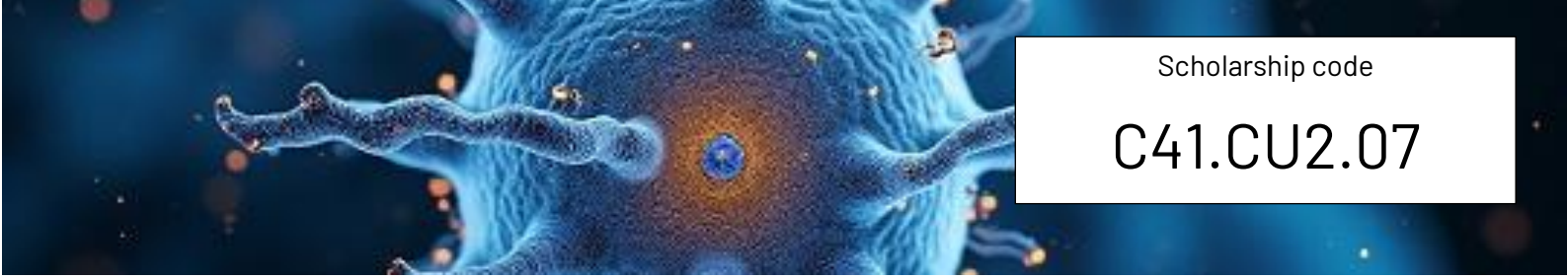
Research Keywords:	CAR-T therapy
	Efficacy and toxicity
	Predictive models
Reference ERCs:	LS7_5 Applied gene, cell and immune therapies
	LS7_2 Medical technologies and tools (including genetic tools and biomarkers) for prevention, diagnosis, monitoring and treatment of diseases

Available positions: 1

Description of the research topic

Chimeric Antigen Receptor (CAR) T-cell therapy has transformed the landscape of hematological malignancy treatment, delivering impressive clinical results. Yet, therapeutic outcomes remain highly variable, shaped by both the inherent characteristics of the engineered T-cell product and patient-specific factors, which can influence both the infusion and post-treatment stages. In this evolving context, liquid biopsies are emerging as a powerful, non-invasive tool for monitoring the dynamic biological changes in patients. Among the key components of liquid biopsies, cell-free DNA (cfDNA) and extracellular vesicles (EVs) provide a valuable snapshot of tissue-specific alterations, offering insights that go beyond traditional diagnostics.

cfDNA is released into the bloodstream by dying cells, carrying with it epigenetic and genetic signatures that can be traced back to the originating tissue or cellular source. Through DNA methylation profiling, it is possible to unearth hidden signals of tissue damage



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C41.CU2.07

and immune activity over time. Meanwhile, EVs, lipid-based particles secreted by a wide variety of cells under both physiological and pathological conditions, play an essential role in intercellular communication. They transport diverse cargo, influencing numerous biological processes not just locally, but also at distant sites within the body.

This thesis project aims to explore the diagnostic and predictive power of cfDNA and EVs in patients undergoing CAR-T cell therapy for hematological and solid cancers. Utilizing state-of-the-art molecular techniques, the candidate will investigate both the methylation landscape and vector integration profiles in cfDNA collected from treated patients over time, to assess the dynamics of CAR-T cell activity and the levels of tissue damage induced by disease progression and therapy. Additionally, the project will delve into the diagnostic and therapeutic potential of EVs.

We expect to uncover distinct patterns of cfDNA and EV release that correlate with CAR-T cell engraftment, persistence, treatment efficacy, and adverse events. Ultimately, this work will pave the way for establishing cfDNA and EVs as dynamic biomarkers to predict both therapeutic success and potential toxicity in CAR-T therapy, providing new insights into the biological mechanisms that dictate the outcome of this groundbreaking immunotherapy.

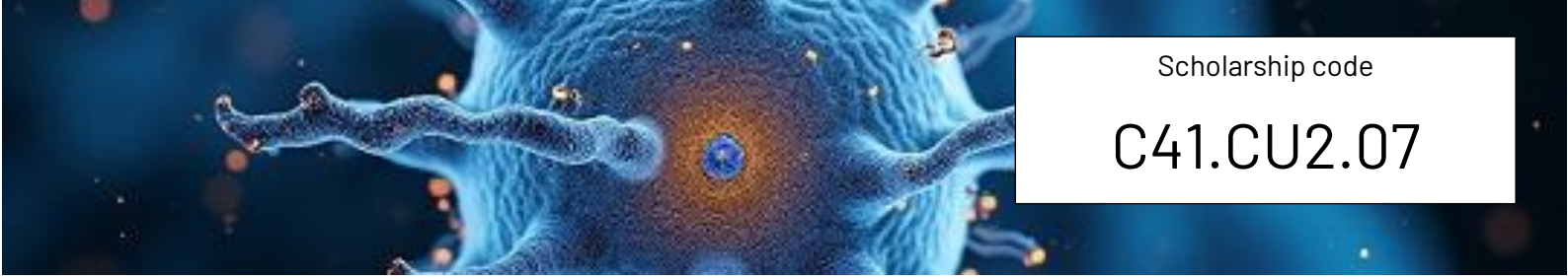
Research team and environment

My unit consists of 1 PhD student in Computer Science and Engineering, 1 fellow, 1 senior technician, and 1 Master student in Bionformatics. The candidate will have the opportunity to work in a leading scientific institute where gene therapy approaches are directly applied in clinical practice. This environment offers a unique chance to assess the translational relevance of scientific hypotheses in cohorts of GT-treated patients. The project benefits from exclusive resources, including patented technologies, optimized techniques for genomic DNA integration site retrieval, and well-established bioinformatics platforms for data analysis. The candidate will also work alongside world-renowned experts in GT, CAR-T immunotherapies, clonal tracking, and bioinformatics, providing an exceptional collaborative research environment.

https://research.hsr.it/en/institutes/san-raffaele-telethon-institute-for-gene-therapy/safety-of-gene-therapy-and-insertional-mutagenesis/daniela-cesana.html

Suggested skills for this research topic

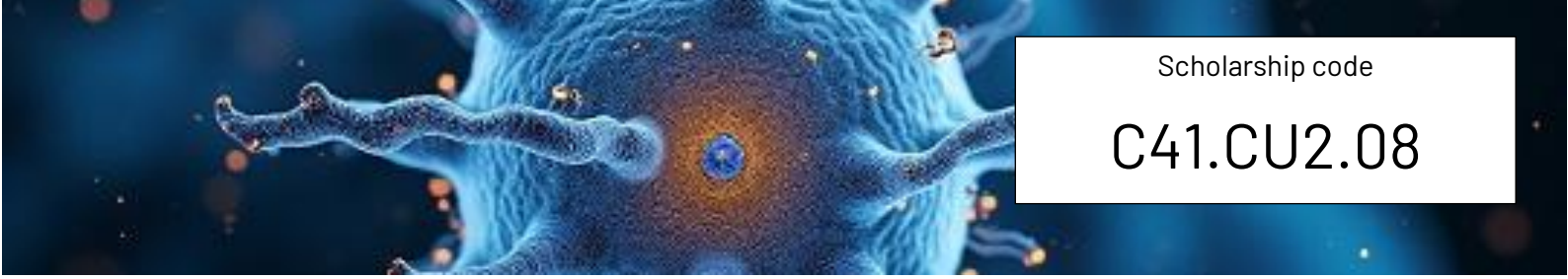
The candidate should have a good background in molecular biology techniques and gene therapy, with the ability to handle tasks such as library preparation and sequencing. The ideal candidate will be familiar with or open to learning advanced techniques such as DNA and cfDNA extraction, PCR, real-time PCR, digital PCR, cloning, and bacterial cultures. Familiarity with cell culture, vector production, immune-staining, and fluorescence cell sorting, will be advantageous. The candidate should also be a strong team player, capable of collaborating closely with bioinformaticians and must have an aptitude for learning state-



Scholarship code

C41.CU2.07

of-the-art data analysis techniques. Good communication skills are essential, and the candidate must be proficient in English, as he/she will be expected to present the progress of the project both within the Institute and at international scientific meetings.



Scholarship code

C41.CU2.08

CU2 - GENE AND CELL THERAPIES

Unveiling Endothelial Mechanisms to Advance Hemophilia A Therapies

Reference Person: Antonia Follenzi

(antonia.follenzi@med.uniupo.it)

Host University/Institute: Università del Piemonte Orientale

Dipartimento di Scienze della Salute

Location: Novara, Italy

Research Keywords: Hemophilia A

Endothelial dysfunction

Coagulation FVIII

Reference ERCs: LS7_5 Applied gene, cell and immune therapies

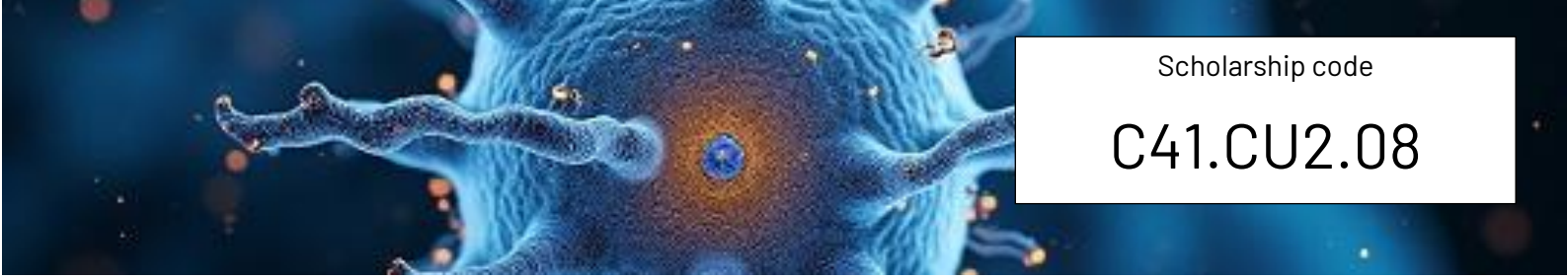
LS7_4 Regenerative medicine

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

Hemophilia A (HA) is an inherited bleeding disorder caused by the absence or dysfunction of coagulation factor VIII (FVIII). The clinical hallmark of HA is prolonged bleeding, which may occur spontaneously or following injury, trauma, or surgery. In addition to bleeding episodes, HA is associated with broader complications such as cardiovascular disease, hemarthrosis, and intracranial hemorrhages (ICHs). It is well established that FVIII is primarily secreted by endothelial cells (ECs). This fact is critical in understanding how FVIII deficiency may affect EC function and, more broadly, vascular homeostasis. Hemostasis and angiogenesis are tightly linked physiological processes; while extensively studied independently, coagulation factors (CFs) have long been viewed solely as components of the clotting cascade. However, emerging evidence suggests that CFs, including FVIII, play important roles in modulating endothelial behavior. Our previous findings demonstrated



Scholarship code

C41.CU2.08

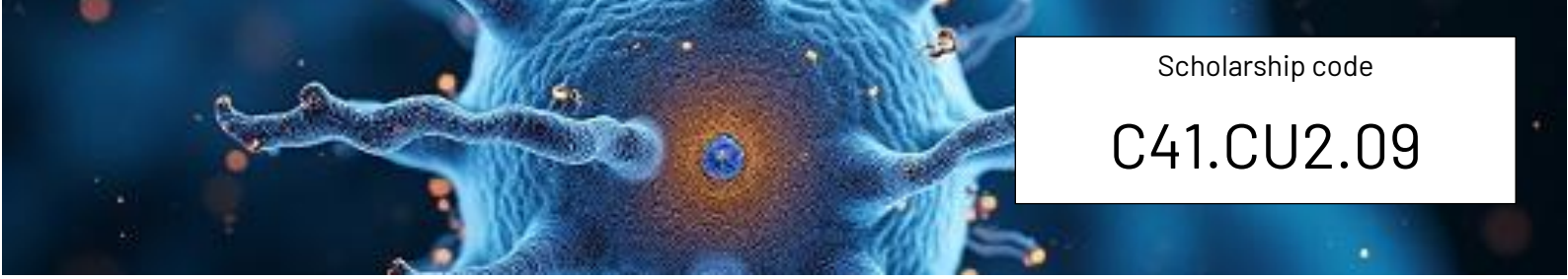
that FVIII is essential for healthy EC function. In HA-derived ECs, we observed impaired angiogenesis, reduced migration, and compromised barrier integrity—all of which were rescued upon FVIII supplementation. Moreover, FVIII was found to activate key intracellular signaling pathways and influence the extracellular matrix (ECM), highlighting its broader regulatory functions. In this project, we aim to dissect the mechanistic role of FVIII in maintaining vascular integrity. Using advanced molecular techniques, we will analyze gene and protein expression profiles affected by FVIII absence and identify the cell surface receptors mediating its effects. Additionally, we will develop a 3D endothelial cell model to study how FVIII modulates ECM interactions and affects cellular mechanical responses to the microenvironment. Ultimately, this research will elucidate novel mechanisms by which FVIII supports vascular health, offering insights that could guide the development of next-generation therapies for Hemophilia A.

Research team and environment

The Histology Lab, led by Prof. Antonia Follenzi, includes senior collaborators (Prof. Merlin, Borsotti and Olgasi), 2 assistant professors, 5 postdocs, 7 PhD students, several Master's students in Medical Biotechnology, and 2 lab technicians. Research focuses on gene and cell therapy for Hemophilia A, the extracoagulative roles of FVIII, Nanomedicine strategies for targeted cancer treatment, and Generation and analysis of induced pluripotent stem cells (iPSCs) from patients with Amyotrophic Lateral Sclerosis (ALS) to investigate disease mechanisms. The School of Medicine at the University of Eastern Piedmont (UPO) includes two departments—Health Sciences and Translational Medicine—working with the university hospitals in Novara and Alessandria. Additionally, the Center for Autoimmune and Allergic Diseases (CAAD) strengthens UPO's position in the biomedical sciences by offering cutting-edge infrastructure, core facilities, and specialized services to support research and innovation.

Suggested skills for this research topic

The ideal candidate for our project should hold a Master degree in Biology or Medical Biotechnology, with a solid foundation in cell and molecular biology. Prior laboratory experience is appreciated, and familiarity with key experimental techniques is desirable. We are looking for a curious, motivated, and proactive individual who is enthusiastic about learning new methodologies and collaborating within an international research team. Strong communication skills and proficiency in English are essential, as English is the working language of the lab. Knowledge of computer science or data analysis tools is considered a strong plus.



Scholarship code

C41.CU2.09

CU2 - GENE AND CELL THERAPIES

Directing the timing of maturation across neuron types derived from human pluripotent stem cells

Reference Person:	Gabriele Ciceri
	(gabriele.ciceri@gmail.com)
Host University/Institute:	Fondazione Telethon
	San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)
Location:	Milan, Italy

Research Keywords:	Developmental timing
	Neuronal maturation
	Human pluripotent stem cells differentiation
Reference ERCs:	LS3_13 Stem cells
	LS5_1 Neuronal cells
	LS3_9 Cell differentiation, formation of tissues and organs

Available positions: 1

Description of the research topic

The assembly of brain networks relies on the execution of basic developmental steps in space and time. Basic steps are broadly conserved, yet brain development displays variations in speed and duration across species, regions and cell types. It takes almost two decades to build a mature cerebral cortex in humans. In contrast, neurons in other regions develop much faster. Such dramatic temporal differences are thought to underly the emergence of complex brain properties and alterations of neuronal maturation timing are linked to brain disorders.

How temporal information is encoded in the developing brain is unclear, despite its crucial role for coordinating the growth and acquisition of mature function. it turns out that the timing of development is largely driven by cell-intrinsic programs, like “clocks” that are retained in vitro during the differentiation of human pluripotent stem cell (hPSC). Our

research has recently identified an epigenetic clock that prolong the time to reach maturity and can be manipulated to speed up neuronal maturation.

The proposed project will investigate mechanisms underlying “slow” and “fast” maturation and dissect how their modulation enables the coordinated maturation of distinct neuron types. We will leverage our unique expertise in cutting-edge hPSC differentiations into several region-specific neuron types. This system enables to precisely map and contrast maturation rates across cell type, to perturb candidate pathways and engineer cells in order to accelerate, delay or revert the maturation process. The final goal is to establish a transformative stem cell-based platform to control maturation timing on demand for disease modeling applications.

The project will tackle a fundamental, yet unexplored frontiers in stem cell biology and will combine advanced technologies of hPSC-based differentiation, cellular/genetic engineering, molecular profiling and assays of neuronal functionality.

Ciceri et. al. An epigenetic barrier sets the timing of human neuronal maturation. Nature, 2024

Ciceri G & Studer L. Epigenetic control and manipulation of neuronal maturation timing. Curr Opin Genet Dev, 2024

Why human brain cells grow so slowly. Nature Video :

https://www.youtube.com/watch?v=llJkc6tulus

https://www.the-scientist.com/human-neurons-play-the-waiting-game-71900

Mechanisms guiding the slow pace of maturation in human neurons uncovered. Nature, 2024

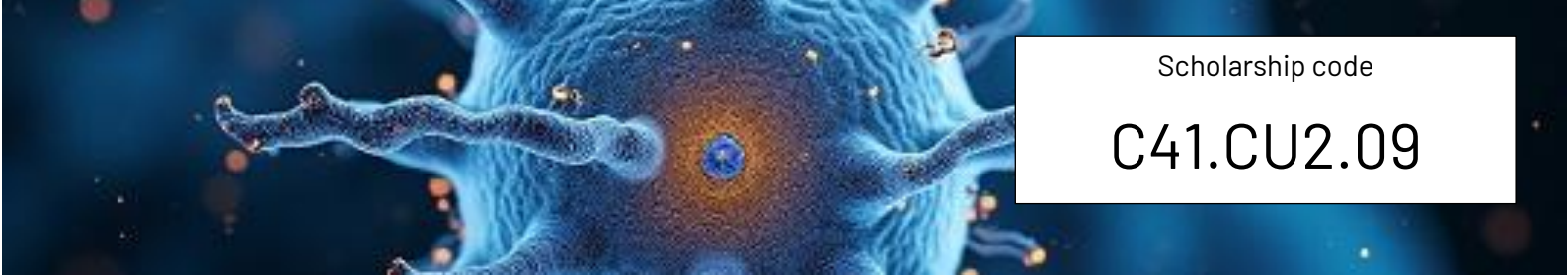
https://neuronline.sfn.org/training/module-2-neuronal-differentiation

Research team and environment

The project will be carried out at San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), which has pioneered discoveries in cell/gene engineering and fosters research on emerging concepts in stem cell biology, tissue engineering and cellular aging. SR-Tiget is part of San Raffaele Hospital, a vibrant biomedical campus which host multidisciplinary research, including experimental neuroscience, and state-of-the-art scientific infrastructure.

The PI, Gabriele Ciceri, has a strong track-record in neuroscience and stem cell biology and international PhD and postdoc research experience with world leaders. The newly established and rapidly growing team is supported by prestigious international award from the Harvard-Armenise foundation, in addition to Telethon Foundation.

https://scholar.google.com/citations?user=3bHGsMEAAAAJ&hl=en&oi=ao



Scholarship code

C41.CU2.09

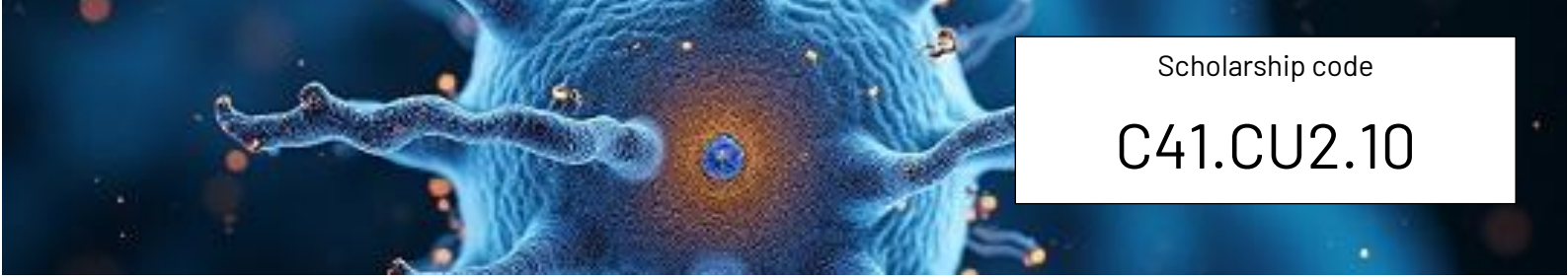
Orcid 0000-0002-8481-9771

https://x.com/gabriele_ciceri

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

Suggested skills for this research topic

We are looking for highly motivated and creative doctoral students to work on a new concept at the intersection of stem cell biology, neuroscience, and gene/cell engineering: "what drives timing during brain maturation". International and national candidates holding a master's degree in life science or equivalent are welcome to apply. Candidates are expected to have great communication and writing skills in English. Genuine interest in the topic, strong initiative and organization, teamwork and planning skills are very positively valued. Previous knowledge in developmental biology and neuroscience as well as documented experience in standard molecular biology and cell culture techniques or bioengineering are preferable.



Scholarship code

C41.CU2.10

CU2 - GENE AND CELL THERAPIES

Development of a selection strategy to boost the efficacy and safety of genome editing in HSPCs

Reference Person: Anna Villa

(villa.anna@hsr.it)

Host University/Institute: Fondazione Telethon

San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)

Location: Milan, Italy

Research Keywords: Genome Editing

Stem Cell

Genome Integrity

Reference ERCs: LS7_4 Regenerative medicine

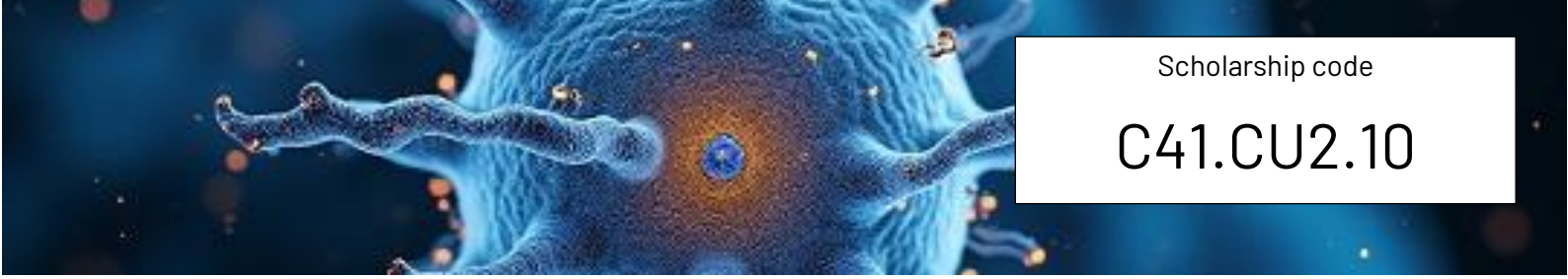
LS7_5 Applied gene, cell and immune therapies

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

CRISPR-Cas9 gene editing has the potential to revolutionize gene therapy by the avoidance of dysregulated corrective transgene expression. We have recently applied homology directed repair (HDR) mediated GE to treat a severe form of primary immunodeficiency caused by defects in Recombination Activating Gene 1 (RAG1), a tightly regulated molecule of the VDJ recombination, the process responsible for T and B cell receptor rearrangement. We designed a strategy to potentially cure most of the mutations causing the broad spectrum of RAG1 clinical manifestations by precise and targeted correction of the genetic defect (Castiello et al, Science Trans Med 2024). In this project we propose to refine our RAG1 gene correction strategy by applying novel selection strategy to enrich the proportion of HDR-edited cells. We will test novel vector based on the Selection by Means of Artificial Transactivators (SMArT-2) platform, combining a codon optimized RAG1 sequence (coRAG1)



Scholarship code

C41.CU2.10

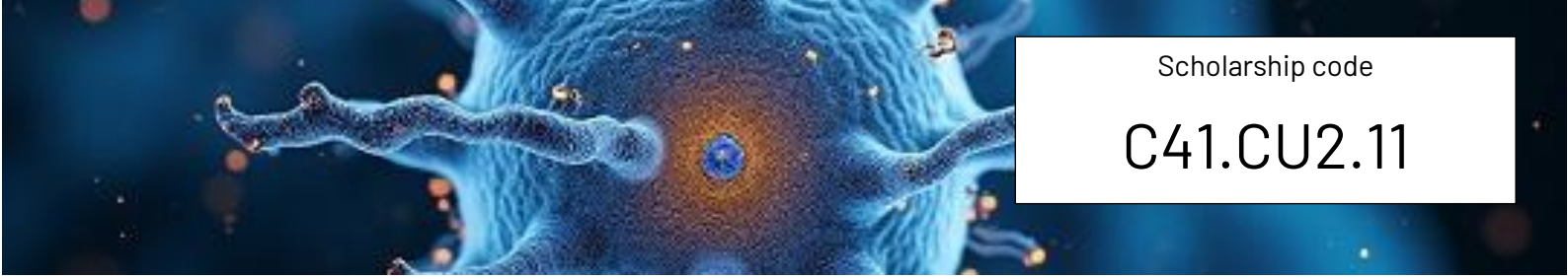
with a P2A and a GFP selector cassette. These novel platforms will be tested in surrogate cellular models to assess RAG1 expression during cell cycle regulation and then applied to human CD34 cells. Ex vivo and in vivo studies will be performed to test stemness, in vitro and in vivo fitness and engraftment capacity. Artificial thymic organoid (ATO) will be exploited to complement in vivo studies and analyze T cell differentiation from gene edited CD34+ cells. Single cell transcriptomic and proteomics will be conducted in CD34 cells edited in different selector platforms. Finally, safety studies with conventional and novel techniques will be performed to study genome integrity upon selection in various applied strategies.

Research team and environment

Our team is focused on the pathophysiology and development of novel cellular therapies to cure severe combined immunodeficiencies and inherited bone defects (https://research.hsr.it/en/institutes/san-raffaele-telethon-institute-for-gene-therapy/pathogenesis-and-treatment-of-immune-and-bone-diseases.html). We have conducted extensive studies to define pathophysiology of immune dysregulation in inherited immune defects and in parallel developed innovative cell therapy. Our team is part of San Raffaele Telethon Institute for Research (SR-Tiget), a very exciting Institute globally recognized for its pioneering work in the research and clinical application. Training courses on flow-cytometry, confocal microscopy, animal handling, statistics and GLP studies are available to students and staff. Attendance to seminar and national/international meetings is promoted. Weekly lab and clinical meetings favour discussion within team and with other teams on research activities.

Suggested skills for this research topic

The candidates should hold a Life Science degree. Highly motivated candidates with good skills in molecular and cellular biology are encouraged to apply. Experience in animal model management is a plus. The candidates should have ability to work in team; research planning and organization, and communication skills are required. The successful candidate is expected to be ambitious, hardworking, well-organized, team-oriented, and able to work independently. Good verbal and written English communication skills are essential.



Scholarship code

C41.CU2.11

CU2 - GENE AND CELL THERAPIES

Next generation versatile and effective AAV-mediated large gene delivery

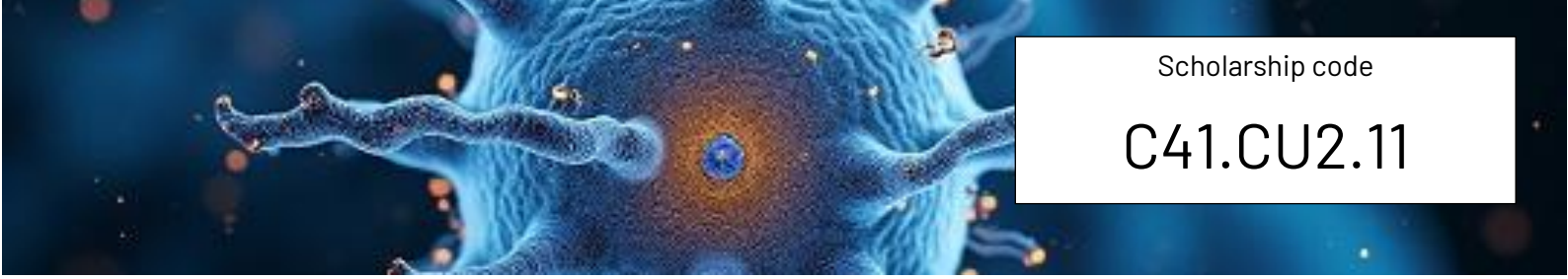
Reference Person:	Ivana Trapani
	(trapani@tigem.it)
Host University/Institute:	Fondazione Telethon
	Telethon Institute of Genetics and Medicine (TIGEM)
Location:	Pozzuoli (NA), Italy
Research Keywords:	AAV
Reference ERCs:	LS7_5 Applied gene, cell and immune therapies
Available positions:	1
Project:	NextGeneTx , HORIZON-ERC, ERC-2024-STG, N. 101164722

Description of the research topic

The research project focuses on overcoming one of the most critical limitations of in vivo gene therapy using adeno-associated virus (AAV) vectors: their restricted cargo capacity, which is less than 5 kilobases. This limitation currently prevents AAV-based therapies from being applied to a wide range of inherited diseases caused by mutations in large genes. To address this challenge, the project will build on a recently developed AAV-based platform that exploits inteins—short protein elements capable of mediating protein splicing in a traceless manner — focusing on increasing both the efficiency and the safety of the approach.

Research team and environment

The PhD project will be carried out at TIGEM (Telethon Institute of Genetics and Medicine), a leading research center in the field of human genetics and gene therapy, located in Pozzuoli (Naples), Italy. The student will join the research group led by Dr. Ivana Trapani. The lab offers a multidisciplinary and collaborative environment, with access to state-of-the-art facilities for molecular biology, in vivo studies, and advanced imaging. TIGEM fosters scientific training through seminars, journal clubs, and international collaborations. More



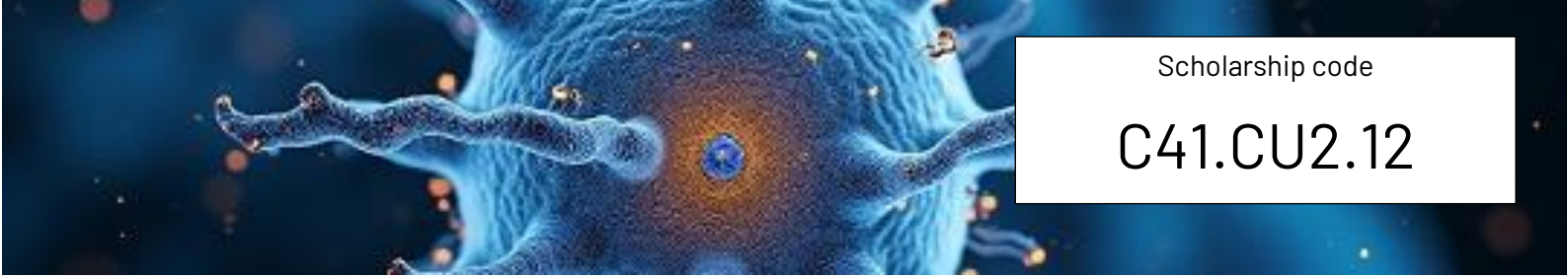
Scholarship code

C41.CU2.11

information on TIGEM and the Trapani lab can be found at: https://www.tigem.it/research/research-faculty/trapani

Suggested skills for this research topic

- Excellent skills in molecular biology and cloning.
- Strong experience in gene therapy or genome editing is highly desirable.
- Experience in retinal research is a plus but not mandatory.
- English proficiency
- A proactive, collaborative, and independent mindset.



Scholarship code

C41.CU2.12

CU2 - GENE AND CELL THERAPIES

Novel Targeted Gene Editing and Delivery Technologies for Engineering Human Hematopoietic Stem Cells

Reference Person: Luigi Naldini

(naldini.luigi@hsr.it)

Host University/Institute: Fondazione Telethon

San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)

Location: Milan, Italy

Research Keywords: Gene editing

Gene delivery

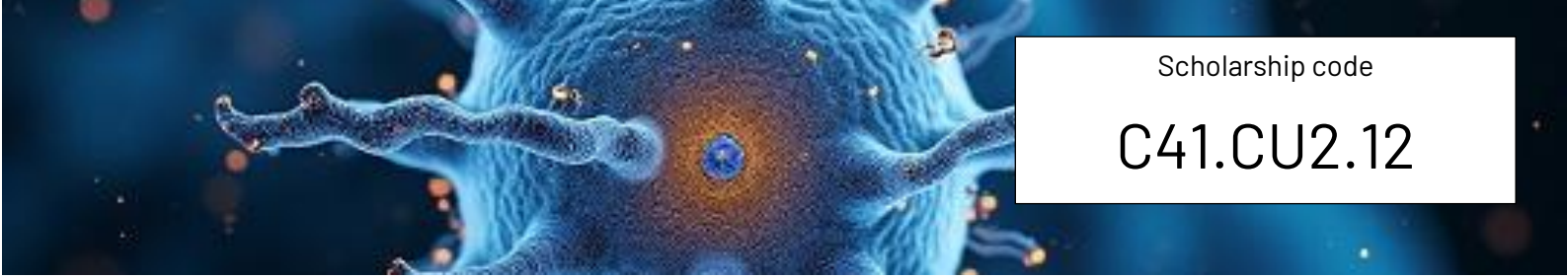
Hematopoietic stem cells

Reference ERCs: LS7_5 Applied gene, cell and immune therapies

Available positions: 1

Description of the research topic

Ex vivo therapeutic gene addition into hematopoietic stem and progenitor cells (HSPCs) by means of lentiviral vectors has proven to be an effective strategy to treat a wide variety of genetic disorders. However, the multi-copy and semi-random genome-wide integration of the vector in the target cell genome may still pose concerns of residual genotoxicity and hamper faithful reconstitution of expression of the integrated transgene. To overcome these issues, targeted integration approaches based on programmable nucleases and homology-directed repair (HDR) have been developed, enabling site-specific insertion of therapeutic sequences in HSPCs, enabling in situ gene correction and safe harbour landing. Yet, these methods still face major hurdles, such as genotoxicity from DNA double-strand breaks (DSBs) and the cytotoxicity of current editing system delivery (e.g., electroporation). This project aims to develop innovative strategies for (i) targeted integration of gene-sized payloads, and (ii) non-toxic delivery of the editing machinery to HSPCs. To achieve the first goal, the candidate will explore: i) shifting the integration profile of viral vectors from semi-random to site-specific; ii) improving the specificity, efficiency, and tolerability of retrotransposon- and prime editing-based systems in human HSPCs. Readouts will include integration site mapping (LAM-PCR, targeted sequencing), quantification of targeted



events, transgene expression, and functional assays (e.g., CFU, multilineage differentiation). If editing reaches double-digit efficiencies in vitro, xenotransplantation studies in immunodeficient mice will be conducted to benchmark performance against HDR-based strategies. To achieve the second goal, the candidate will leverage recent advances from the hosting lab to test lipid nanoparticles (LNPs) for ex vivo delivery of editing tools and DNA templates to HSPCs. DNA template design will be optimized to enhance nuclear delivery. In parallel, functionalization of LNPs with lipid-conjugated ligands to target specific HSPC subsets will be explored, aiming to reduce reagent use and enable future in vivo applications. Readouts will include editing efficiency, cell viability, delivery assessment (fluorescent cargo), and functional output (e.g., engraftment in immunodeficient mice). Altogether, this project aims to develop safer, more precise genome editing strategies in HSPCs, advancing toward clinically relevant therapeutic applications.

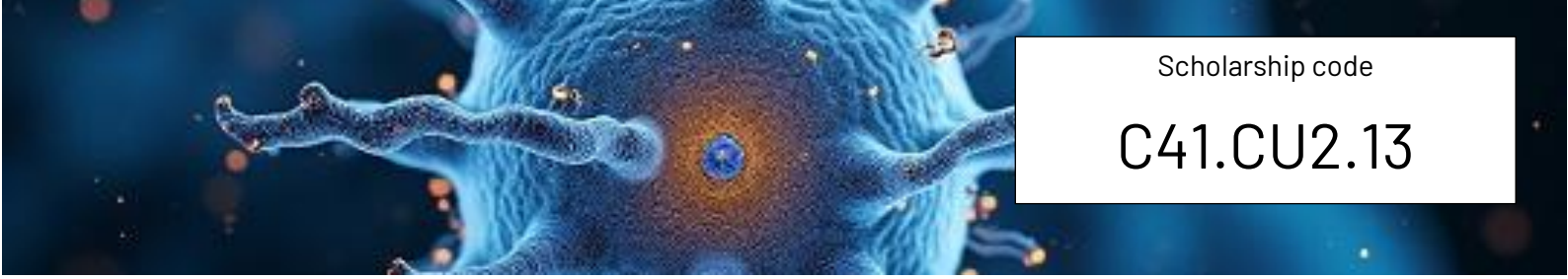
Research team and environment

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

C41.CU2.13

CU2 - GENE AND CELL THERAPIES

Unlocking in vivo gene therapy in hematopoietic stem cells

Reference Person: Michela Milani

(milani.michela@hsr.it)

Host University/Institute: Fondazione Telethon

San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)

Location: Milan, Italy

Research Keywords: In vivo gene therapy

Lentiviral vector engineering

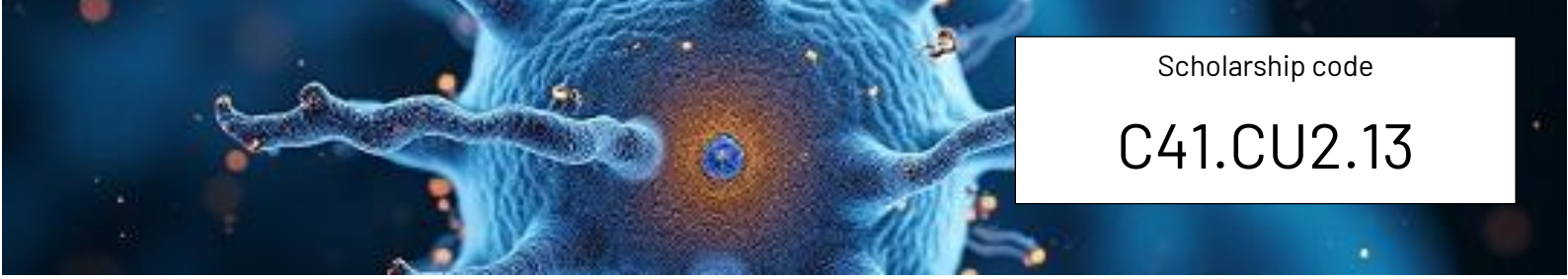
Hematopoietic stem and progenitor cells

Reference ERCs: LS7_4 Regenerative medicine

Available positions: 1

Description of the research topic

Lentiviral vector (LV) mediated ex vivo gene therapy in hematopoietic stem and progenitor cells (HSPCs) fulfilled the promise of a cure for different genetic diseases. However, ex vivo manipulation of HSPC, collection of a proper number of cells, and the risks associated with patient conditioning and transplant still pose challenges to broad access to HSPC gene therapy. The overarching goal of this project is to overcome these hurdles by implementing an in vivo gene therapy approach. As a paradigmatic disease model to investigate the feasibility of this approach, we chose Fanconi anemia (FA), a rare genetic disorder belonging to the DNA repair deficiency syndromes. In FA, the HSC compartment is directly affected, posing additional constraints for ex vivo culture, collection of HSPCs, and patient conditioning. For these reasons, FA is an ideal candidate for in vivo LV-mediated gene transfer. To investigate the feasibility of this approach, we studied HSPC biodistribution in newborn, 2-week-old, or adult mice. We discovered a unique window of opportunity in the formers due to early post-natal persistence of the hepatic fetal hematopoietic niche and extensive trafficking of HSC to the bone marrow (BM). Indeed, we successfully targeted bona fide HSC by intravenous (i.v.) administration of GFP-expressing LV to newborn mice. We obtained stable, life-long GFP expression in up to 8% of all blood lineages, paralleled by a comparable expression in HSPCs harvested from the BM, which could engraft long-term in



Scholarship code

C41.CU2.13

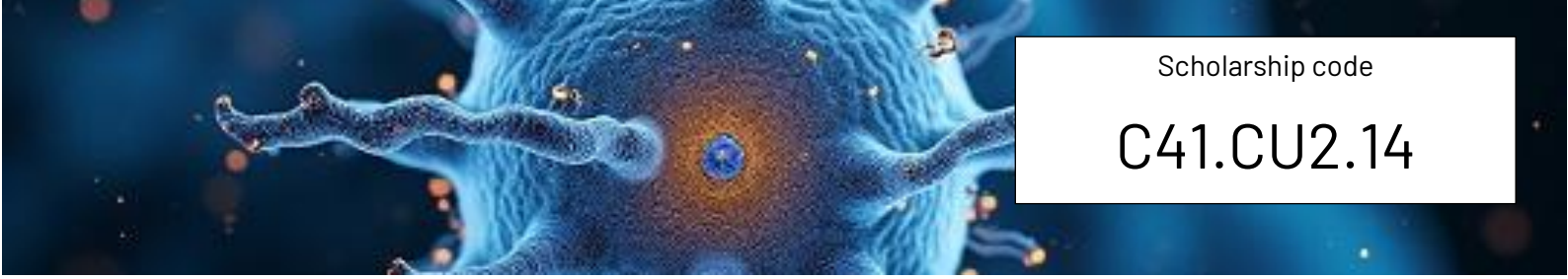
busulfan-conditioned mice. We also increased gene transfer efficiency by up to 15% by applying a G-CSF/Plerixafor mobilization regimen, modeling the clinical use, and extending the possibility of effectively targeting HSPCs in vivo to juvenile mice. Based on this preliminary data, the general objective of this project is to generate Universal Switchable-LV retargeted toward HSPCs to obtain stable and efficient in vivo gene transfer in the FA mouse model. Moreover, the specificity of these vectors may be easily redirected toward the antigen of interest by changing the binding moiety. We will test these engineered LV in vitro on primary human cells and in vivo in newborn FA mice or humanized mice. All together, these data will provide the basis for possible clinical translation of this approach for FA and will be seminal to pave the way to expand further the plethora of genetic diseases that would benefit from in vivo gene therapy.

Research team and environment

SR-Tiget has the mission to perform cutting-edge research on gene and cell therapy and to translate its results into therapeutic advances for genetic diseases. Over the years, SR-Tiget has made pioneering contributions to the gene and cell therapy field with relevant discoveries in vector design, gene transfer and gene editing strategies, and stem cell biology. Our team has a strong experience in lentiviral vector engineering and in vivo gene therapy approaches, combined with the long-standing expertise in HSPC biology present at SR-Tiget. In addition, we are collaborating with key experts in the relevant fields. We have access to a state-of-the-art cytometry facility, a specific-pathogen-free animal facility, a biosafety level 2 culture room for the production and handling of LV, a process-development lab for the production of purified batches of LV, and a Vector integration core for LV integration site analysis.

Suggested skills for this research topic

We are looking for a highly motivated Ph.D. student to join our Team. The ideal candidate has an academic background in molecular biology and molecular medicine. He/she should have experience in basic molecular biology techniques, such as nucleic acid purification, quantification, and PCR, and in cell culture. Previous experience in flow cytometry and/or mouse handling is a plus. Proficient knowledge of English is mandatory. We are looking for a dedicated, passionate candidate, able to work independently and in a team when needed.



Scholarship code

C41.CU2.14

CU2 - GENE AND CELL THERAPIES

Expanding AAV gene therapy by editing

Reference Person: Alberto Auricchio

(auricchio@tigem.it)

Host University/Institute: Fondazione Telethon

Telethon Institute of Genetics and Medicine (TIGEM)

Location: Pozzuoli (NA), Italy

Research Keywords: Gene therapy

Reference ERCs: LS7_5 Applied gene, cell and immune therapies

Available positions: 1

Description of the research topic

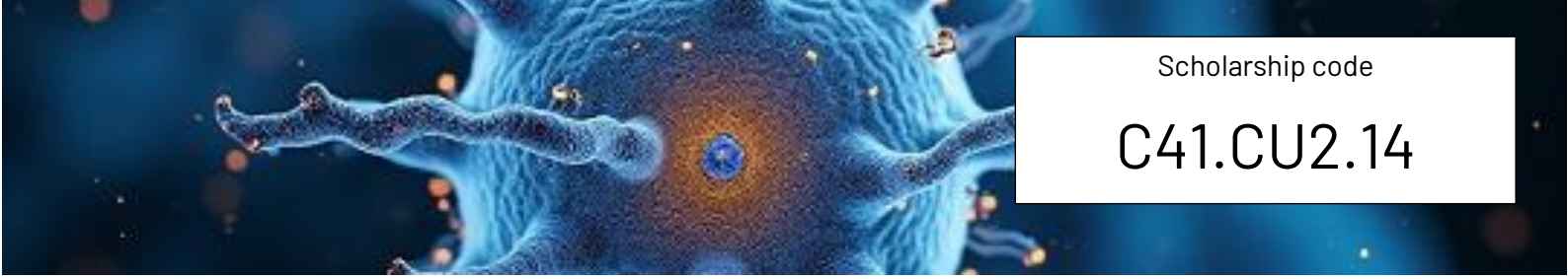
Gene therapy is entering a new era, with AAV-based treatments showing great promise for genetic diseases. However, challenges remain—especially in achieving safe, long-lasting effects in growing tissues and addressing dominant mutations that traditional gene replacement can't fix.

The project aims to overcome these challenges by developing precise tools to insert therapeutic DNA exactly where it's needed in the genome. It explores two innovative strategies: one using engineered Cas proteins to guide accurate DNA repair, and another avoiding DNA cutting by employing novel integration systems like transposases or bacterial proteins.

These approaches are being tested in models of retinal and liver diseases, with the goal of creating therapies that are safer, more effective, and more durable. The project also focuses on non-viral delivery methods to reduce risks further.

Research team and environment

The PhD project will be carried out at TIGEM (Telethon Institute of Genetics and Medicine), a leading research center in the field of human genetics and gene therapy, located in Pozzuoli (Naples), Italy. The student will join the research group led by Prof Alberto Auricchio. The lab offers a multidisciplinary and collaborative environment, with access to state-of-the-art facilities for molecular biology, in vivo studies, and advanced imaging. TIGEM fosters



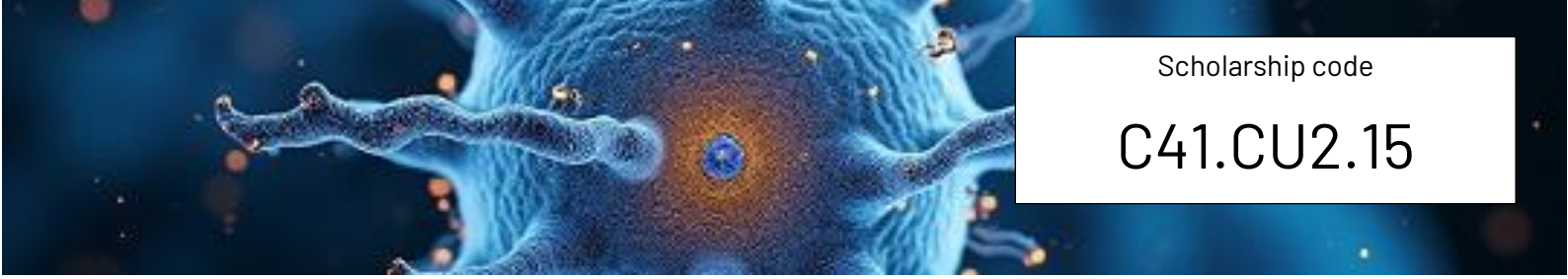
Scholarship code

C41.CU2.14

scientific training through seminars, journal clubs, and international collaborations. More information on TIGEM and the Auricchio lab can be found at: https://www.tigem.it/research/research-faculty/auricchio

Suggested skills for this research topic

The ideal PhD candidate should have a strong academic background in molecular biology, genetics, biotechnology, or a closely related field. They should demonstrate foundational laboratory skills such as molecular cloning, cell culture, and basic genomic techniques like PCR and sequencing. While prior experience with genome editing tools such as CRISPR-Cas or transposases is advantageous, it is not mandatory, as comprehensive training will be provided. The candidate must be highly motivated, curious, and capable of working both independently and collaboratively within a multidisciplinary team. Strong analytical thinking, problem-solving abilities, and clear scientific communication skills are essential. Proficiency in English is required for effective communication and documentation.



Scholarship code

C41.CU2.15

CU2 - GENE AND CELL THERAPIES

Engineering chromatin dynamics to fine-tune enhancer-promoter interactions in neurodevelopment

Reference Person: Michele Gabriele

(gabriele.michele@hsr.it)

Host University/Institute: Fondazione Telethon

San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)

Location: Milan, Italy

Research Keywords: Chromatin dynamics

Enhancer-promoter interactions

Genome engineering

Reference ERCs: LS2_4 Gene regulation

LS2_3 Epigenetics

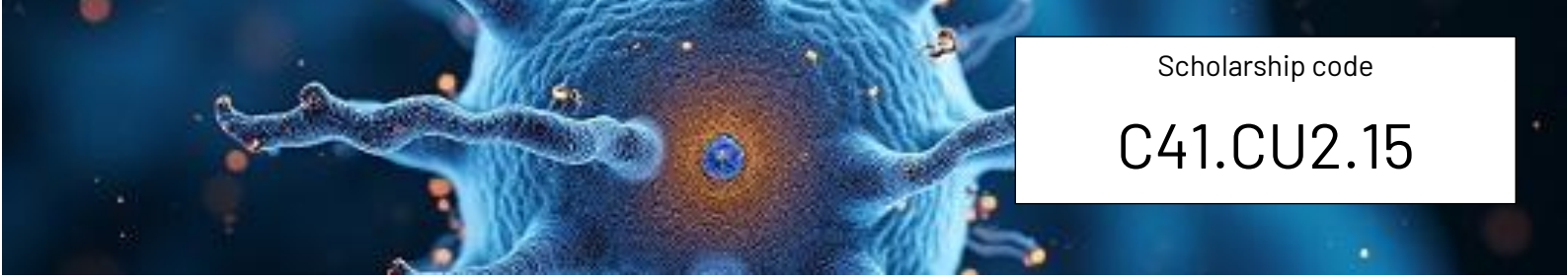
LS2_11 Bioinformatics and computational biology

Available positions: 1

Description of the research topic

Mutations in transcriptional enhancers and their regulators are a primary cause of neurodevelopmental disorders and many tumors. Despite the importance of enhancers, we still do not fully understand their mechanism, nor do we fully understand the molecular mechanisms by which mutations in DNA non-coding regulatory elements and chromatin regulators, such as chromatin loopers or histone modifiers, affect gene expression regulation. Therefore, identifying these molecular mechanisms and understanding the causal relationship between chromatin dynamics and gene expression will open the way to new therapeutic approaches based on targeting enhancer-promoter interactions (EPIs) and/or gene therapy.

To fill these knowledge gaps and develop a strategy to engineer EPIs, the candidate will employ a multidisciplinary approach that encompasses super-resolution live-cell imaging, 3D genome architecture, single-cell approaches, and genome editing to engineer the



Scholarship code

C41.CU2.15

frequency and duration of chromatin contacts, with the aim of tuning EPIs whose dysregulation is linked to pathologies. Specifically, the candidate will engineer endogenous regulatory loci of the genome to observe EPIs and nascent transcription in real time in living cells during neuronal differentiation. This approach allows the measurement of the 3D distance, frequency, and duration of long-range interactions between regulatory elements and the consequences on nascent transcription, thereby identifying the biophysical mechanisms of EPIs. This experimental platform will be used to engineer dysregulated EPIs with synthetic chromatin loopers to manipulate the dynamics of regulatory elements with the aim of fine-tuning gene expression.

In this multidisciplinary project, the candidate will acquire competences in pluripotent stem cell culture and neuronal differentiation, gene editing with CRISPR/Cas9, molecular cloning, execution and library preparation of 3D genome architecture, epigenomics and single-cell next-generation sequencing assays and their data analysis, use of super-resolution live-cell imaging, and application of biophysical approaches to study chromatin dynamics in living cells.

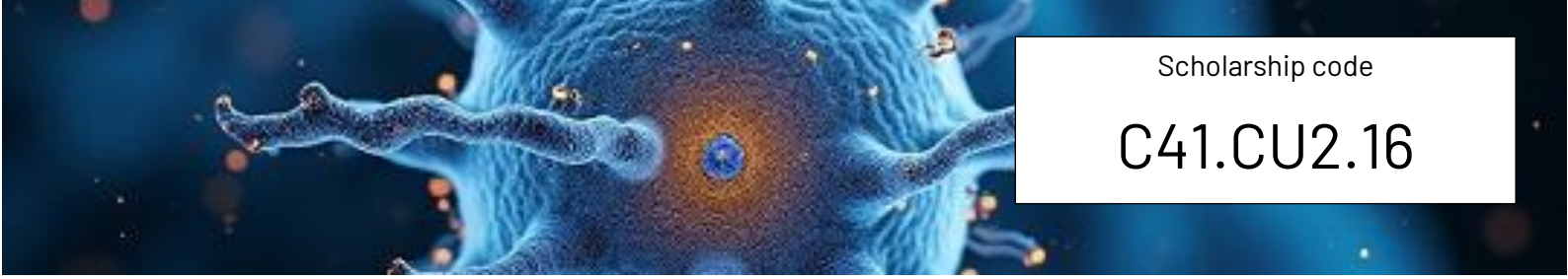
Research team and environment

The new laboratory "3D genome dynamics in differentiation and pathology" led by Gabriele Michele was recently opened at the SR-Tiget (https://www.gabrielelab.com/research). The candidate will have the opportunity to join an emerging group and contribute to establishing its lab environment. The current small size of the laboratory provides the candidate with the opportunity to collaborate and be trained directly with Dr. Gabriele, who recently returned to Italy after completing his postdoctoral work at MIT. The lab has access to all the core facilities and services of the San Raffaele Telethon Institute of Gene Therapy.

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

Suggested skills for this research topic

Previous experience with the mentioned methodologies is appreciated, but not required. Suggested familiarity with NGS methods and experience with Python, Jupyter, and bash scripting is recommended. The candidate should be passionate about multidisciplinary approaches and curious about learning how to apply biophysics to molecular and cellular biology. A positive attitude towards collaborating with others and interacting with colleagues from different disciplines is required. Proficiency in English is a requirement.



Scholarship code

C41.CU2.16

CU2 - GENE AND CELL THERAPIES

HSPCs gene editing based enrichment strategies for the treatment of inborn metabolic disorders

Reference Person: Daniele Canarutto

(canarutto.daniele@hsr.it)

Host University/Institute: Fondazione Telethon

San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)

Location: Milan, Italy

Research Keywords: Homology directed repair

HSPCs gene therapy

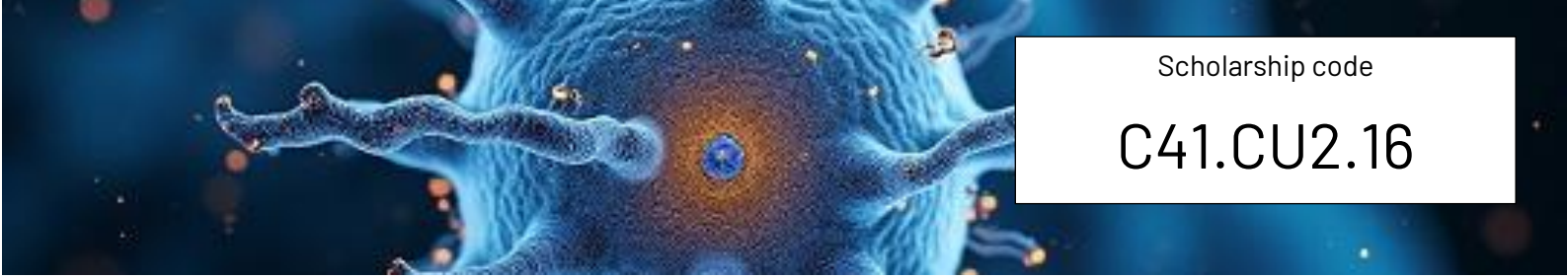
Precision gene editing

Reference ERCs: LS7_5 Applied gene, cell and immune therapies

Available positions: 1

Description of the research topic

Ex vivo gene addition in hematopoietic stem and progenitor cells (HSPCs) is a clinically validated approach that has successfully treated several inborn errors of metabolism (IEMs). However, this strategy carries safety concerns related to random genomic integration and potential activation of nearby oncogenes, particularly when strong viral promoters are used to drive therapeutic gene expression. Targeted gene editing using nucleases and homology-directed repair (HDR) represents a safer alternative, allowing site-specific integration of therapeutic transgenes. Yet, it remains inefficient due to the genotoxicity associated with the quality and quantity of the vectors used. This project aims to develop innovative gene editing and selection strategies for enriching precise edits to overcome the current limitations of HDR. The research will focus on four main objectives: (1) optimizing donor template delivery by improving viral vector design (AAV, IDLV) and refining cell culture conditions to preserve HSPC stemness and clonal diversity; (2a) enriching for precisely edited cells using fluorescence-activated cell sorting (FACS)-based positive selection, where a transiently expressed selector is activated only upon successful HDR-mediated integration; (2b) establishing a purging selection approach that targets an essential haploinsufficient gene, allowing only cells with precise HDR that express gene of interest



Scholarship code

C41.CU2.16

(GOI) to survive while eliminating those repaired by error-prone non-homologous end joining (NHEJ). (3) Simplifying the selection process using a Cas9-based epigenome editor that simultaneously mediates gene editing and transiently transactivates selector or genes to promote functionality and selection of edited HSPCs. (4) Therapeutic potential of this editing and selection platform will be demonstrated in two rare diseases: X-linked adrenoleukodystrophy (X-ALD) and Pompe disease, both requires supra-physiological levels of enzyme production. Key experimental readouts will include editing efficiency, clonal diversity assessments, transgene expression profiling, and functional validation through xenotransplantation into immunodeficient mice to assess long-term engraftment and lineage differentiation. Altogether, this project seeks to establish a safe, efficient, and scalable genome editing platform for HSPCs, advancing the clinical translation of gene therapy for inborn errors of metabolism.

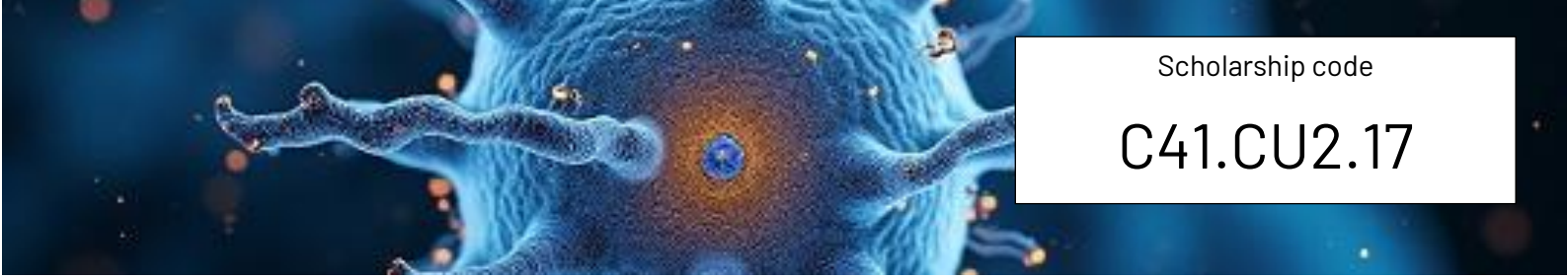
Research team and environment

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

C41.CU2.17

CU2 - GENE AND CELL THERAPIES

Gene therapy and genome editing in the retina

Reference Person: Alberto Auricchio

(auricchio@tigem.it)

Host University/Institute: Fondazione Telethon

Telethon Insitute of Genetics and Medicine (TIGEM)

Location: Pozzuoli (NA), Italy

Research Keywords: Gene editing

Adeno associated vectors

Inherited retinal diseases

Reference ERCs: LS7_5 Applied gene, cell and immune therapies

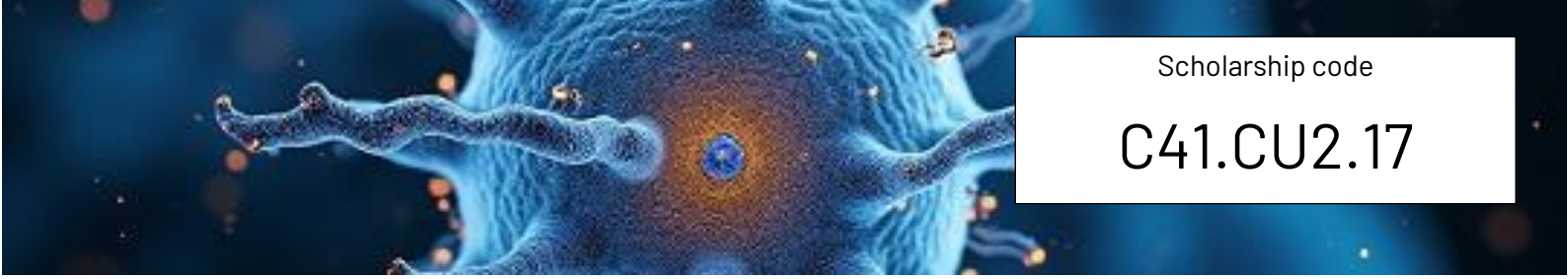
Available positions: 2

Description of the research topic

Inherited retinal diseases (IRD) are a major cause of blindness worldwide, primarily due to mutations in genes expressed in retinal photoreceptor cells (PR). Recent advancements in gene therapy using adeno-associated viral vectors (AAV) have led to the approval of Luxturna, the first gene therapy for an ocular disease, treating a rare form of inherited childhood blindness. However, many genes involved in IRD are too large for AAV vectors. Our research aims to overcome this challenge to develop therapies for common IRDs. Traditional gene replacement is ineffective for dominant IRDs due to gain-of-function mutations. Therefore, new approaches using AAV and CRISPR-Cas9 are being evaluated to block mutant alleles and replace them with wild-type copies, potentially offering new treatments for severe blinding conditions.

Research team and environment

The Telethon Institute of Genetics and Medicine (TIGEM) is a renowned research institute dedicated to understanding the genetic basis of human diseases and developing innovative therapies. Located in Pozzuoli, Italy, TIGEM focuses on translational research, bridging the gap between basic science and clinical applications. The institute is known for its cutting-



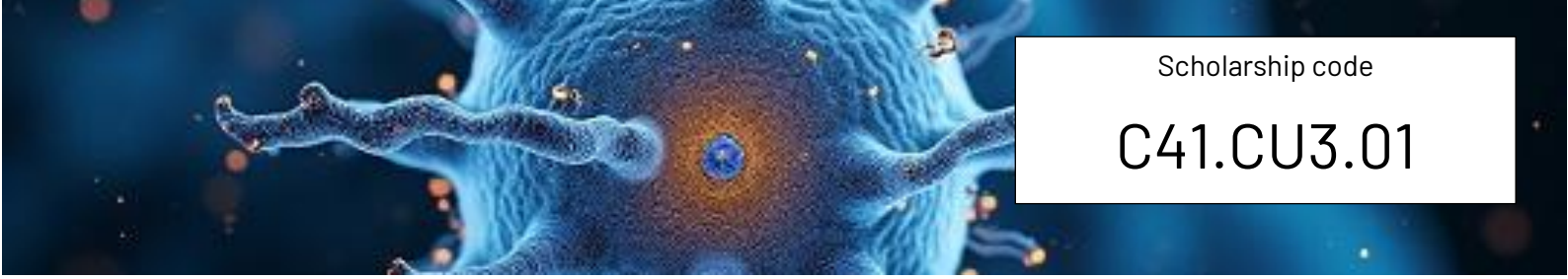
Scholarship code

C41.CU2.17

edge work in gene therapy, particularly using adeno-associated viral vectors (AAV) and CRISPR-Cas9 technologies (www.tigem.it)

Suggested skills for this research topic

The ideal candidate for this graduate program should have a Bachelor's or Master's degree in molecular biology, genetics, or a related field. They should have practical laboratory experience and basic labporatory skills (molecular biology, cloning, histology etc..). The candidate should possess good analytical skills and the ability to interpret data accurately. Strong problem-solving abilities and attention to detail are important. Soft skills such as effective communication, teamwork, and adaptability are essential for working in a collaborative research environment. Proficiency in English is required.



Scholarship code

C41.CU3.01

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Molecular Mechanisms of Coenzyme Q biosynthesis

Reference Person: Andrea Mattevi

(andrea.mattevi@unipv.it)

Host University/Institute: Università degli studi di Pavia

Dipartimento di Biologia e Biotecnologie

Location: Pavia, Italy

Research Keywords: Enzyme biochemistry

Redox biology

Inhibitor discovery

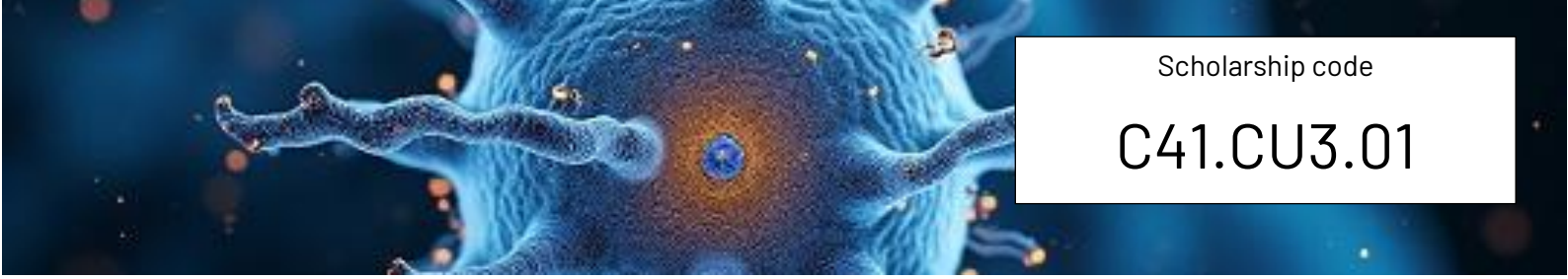
Reference ERCs: LS1_1 Macromolecular complexes including interactions involving nucleic acids, proteins, lipids and carbohydrates

Available positions: 1

Project: MetaQ, ERC Advanced Grant 2022, n. 101094471

Description of the research topic

Coenzyme Q (CoQ), a crucial lipid-soluble molecule involved in the mitochondrial electron transport chain, is synthesized through a complex and highly regulated pathway. This biosynthetic process is orchestrated by a network of specialized proteins that assemble into a multi-enzyme complex on the matrix side of the inner mitochondrial membrane, forming a dynamic and spatially organized structure known as the COQ metabolon. This metabolon serves as a scaffold that facilitates substrate channeling, enzyme stabilization, and the efficient production of CoQ. Our long-term research objective is to uncover and define the molecular and structural mechanisms that govern the assembly, regulation, and functional dynamics of this biosynthetic metabolon. The PhD candidate will play a pivotal role in this project and will be primarily responsible for the development, optimization, and execution of expression systems for the various COQ proteins. This includes heterologous expression in appropriate systems, purification using advanced chromatographic techniques, and the implementation of in vitro enzymatic assays to assess protein function and interaction. In addition to bench work, the candidate will also contribute to



Scholarship code

C41.CU3.01

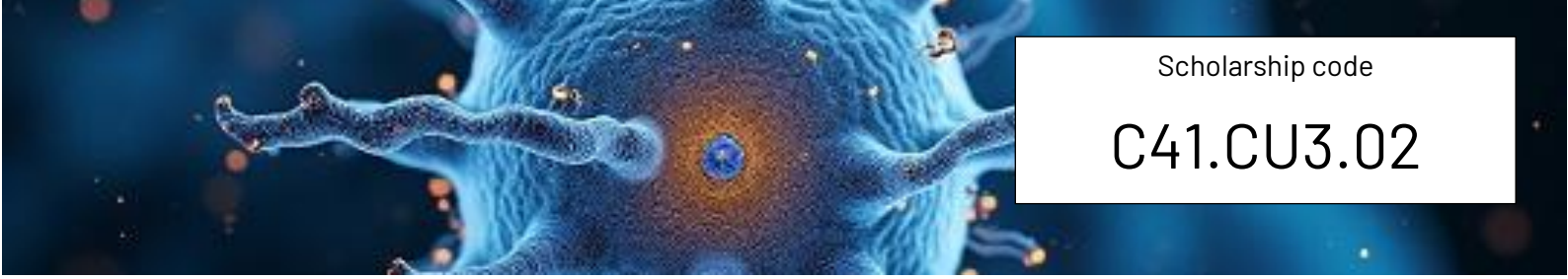
experimental design, data interpretation, and collaborative efforts with structural biology and bioinformatics teams.

Research team and environment

Structural and Molecular Biology group coordinated by Andrea Mattevi

Suggested skills for this research topic

Protein biochemistry, enzymology, analytical chemistry, and biophysics.



Scholarship code

C41.CU3.02

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Molecular Mechanisms of Coenzyme Q biosynthesis

Reference Person: Andrea Mattevi

(andrea.mattevi@unipv.it)

Host University/Institute: Università degli studi di Pavia

Dipartimento di Biologia e Biotecnologie

Location: Pavia, Italy

Research Keywords: Enzyme biochemistry

Redox biology

Inhibitor discovery

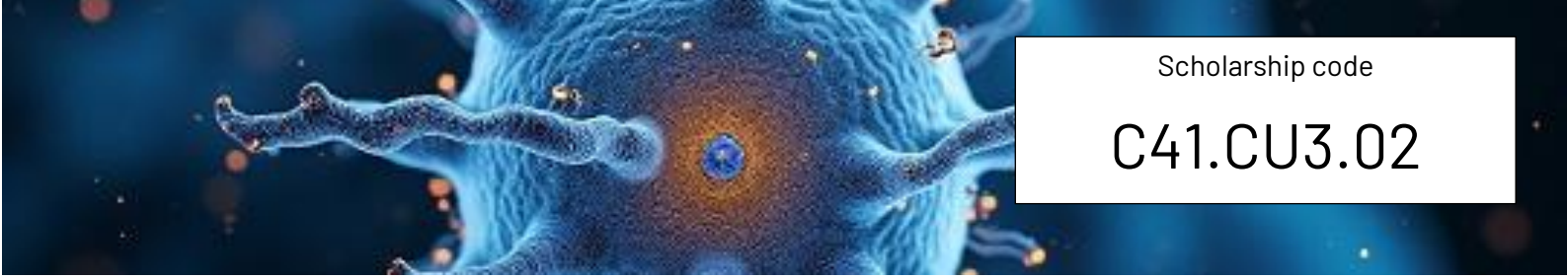
Reference ERCs: LS1_1 Macromolecular complexes including interactions involving nucleic acids, proteins, lipids and carbohydrates

Available positions: 1

Project: MetaQ, ERC Advanced Grant 2022, n. 101094471

Description of the research topic

Coenzyme Q (CoQ), a crucial lipid-soluble molecule involved in the mitochondrial electron transport chain, is synthesized through a complex and highly regulated pathway. This biosynthetic process is orchestrated by a network of specialized proteins that assemble into a multi-enzyme complex on the matrix side of the inner mitochondrial membrane, forming a dynamic and spatially organized structure known as the COQ metabolon. This metabolon serves as a scaffold that facilitates substrate channeling, enzyme stabilization, and the efficient production of CoQ. Our long-term research objective is to uncover and define the molecular and structural mechanisms that govern the assembly, regulation, and functional dynamics of this biosynthetic metabolon. By understanding how the constituent COQ proteins interact, associate, and co-function within this complex, we aim to uncover new biological insights that could be leveraged for therapeutic development, particularly in the context of CoQ deficiencies and mitochondrial disorders. The PhD's project will pivot toward the identification and screening of small molecule inhibitors that specifically target either the structural integrity of the metabolon or key proteins responsible for substrate trafficking, metabolon organization, and catalytic activation.



Scholarship code

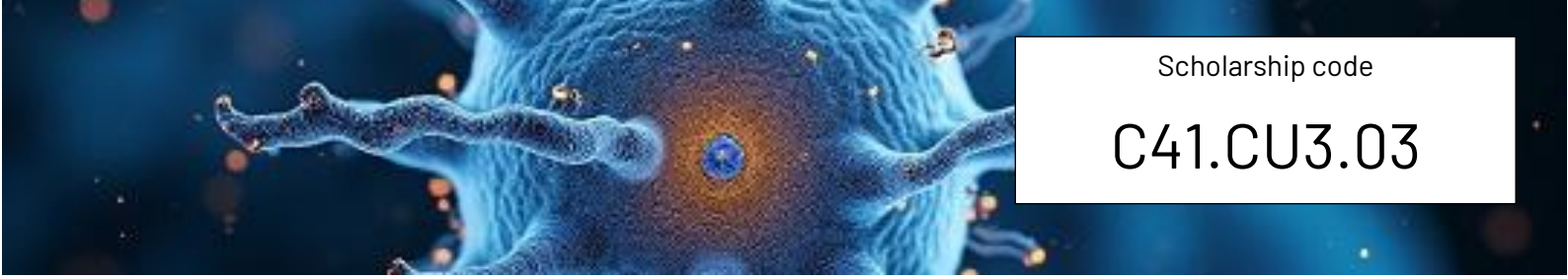
C41.CU3.02

Research team and environment

Structural and Molecular Biology group coordinated by Andrea Mattevi

Suggested skills for this research topic

Protein biochemistry, enzymology, analytical chemistry, and biophysics.



Scholarship code

C41.CU3.03

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Development of new anti-cancer drugs based on high-affinity, highly selective ligands

Reference Person:	Samuele Cazzamalli
	(samuele.cazzamalli@philochem.ch)
Host University/Institute:	Philogen
	R&D (Philochem AG Zürich)
Location:	Otelfingen (ZH), Switzerland

Research Keywords:	Targeted therapies
	Oncology
	Encoded Libaries
Reference ERCs:	PE5_18 Medicinal chemistry
	PE8_13 Industrial bioengineering

Available positions:	4 (reserved for Philochem Company's employees)

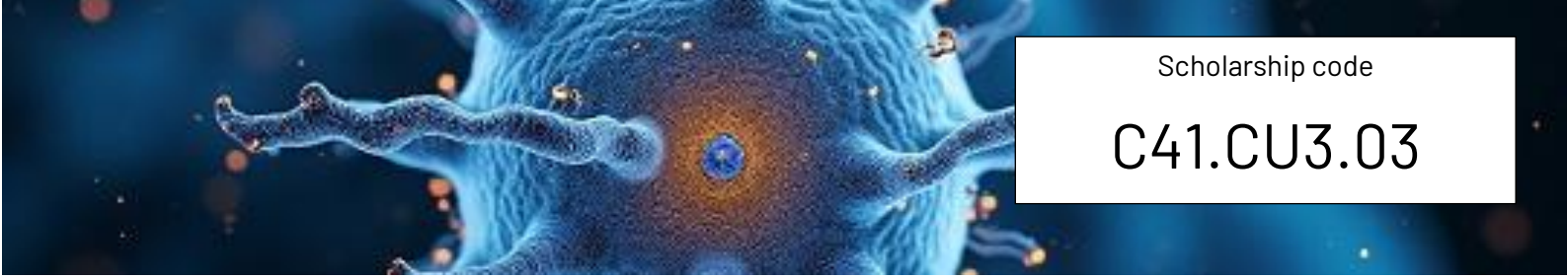
Description of the research topic

Conventional anti-cancer chemotherapy relies on the use of antiproliferative drugs that lack tissue selectivity and are therefore associated with high systemic toxicity.

This research project focuses on the development of new anti-cancer drugs conjugated with small organic molecules, peptides, or antibodies that exhibit high affinity and selectivity for tumor-associated proteins. This strategy enables a high accumulation of the active compound at the tumor site without affecting healthy organs, resulting in increased efficacy and reduced toxicity.

During the project, the candidate will work on identifying tumor "target" proteins, generating new selective conjugates, and evaluating them in vitro. Finally, the most promising conjugates will be tested in vivo using animal models.

Research team and environment



Scholarship code

C41.CU3.03

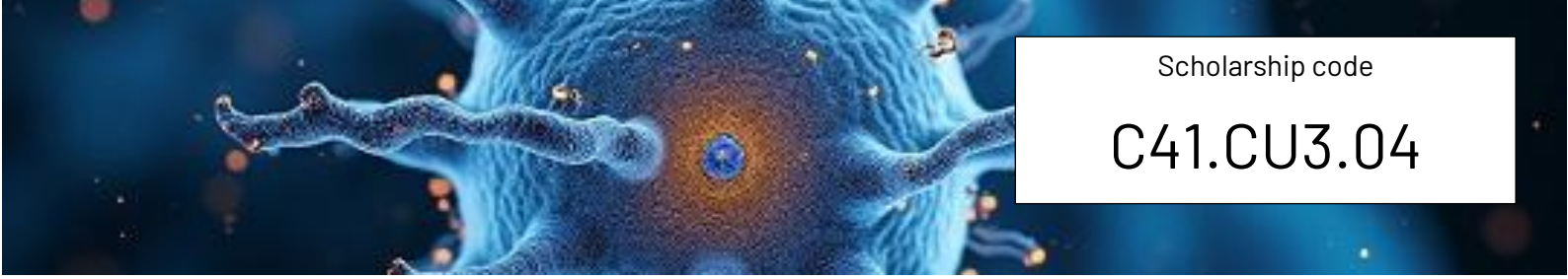
Philogen (www.philogen.com) is a Swiss-Italian biotechnology company, founded in 1996, with a mission to innovate the treatment of cancer and other serious conditions.

Philochem AG (www.philochem.ch) is the Swiss subsidiary of the Philogen group, acting as an R&D unit and developing drug prototypes based on disease-targeted small molecules, peptides, and antibodies.

The Philogen group is experienced in running industrial PhD programs (open since 2017) in collaboration with leading universities, including IUSS Pavia.

Suggested skills for this research topic

- Master Degree in chemistry, medicinal chemistry, or related disciplines.
- Experience in synthesis (small organic ligands and/or peptide chemistry; bioconjugation chemistry is considered a plus) and characterisation of organic compounds OR in protein production and characterization
- Experience with modern analytic techniques (e.g., HPLC, LC-MS OR FPLC, SDS-page) and interpretation of results obtained by spectroscopic techniques (e.g., NMR).
- Good knowledge of data analysis and editing Software (i.e., Excel, Word, Power point, Prism, R, MatLab, Illustrator).
- Experience in performing literature searches using chemistry databases (PubMed, SciFinder, Reaxys) and in applying the results to solve synthetic challenges in the lab.
- Fluency in oral and written English.



Scholarship code

C41.CU3.04

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Neuronal network dynamics in health and disease

Reference Person: Claudia Lodovichi

(claudia.lodovichi@cnr.it)

Host University/Institute: Consiglio Nazionale delle Ricerche

Istituto di Biofisica

Location: Pisa, Italy

Research Keywords: Imaging in vivo

Electrophysiology in vivo

Neuronal circuit dynamics

Reference ERCs: LS5_16 Systems and computational neuroscience

LS5_5 Neural networks and plasticity

PE3_16 Physics of biological systems

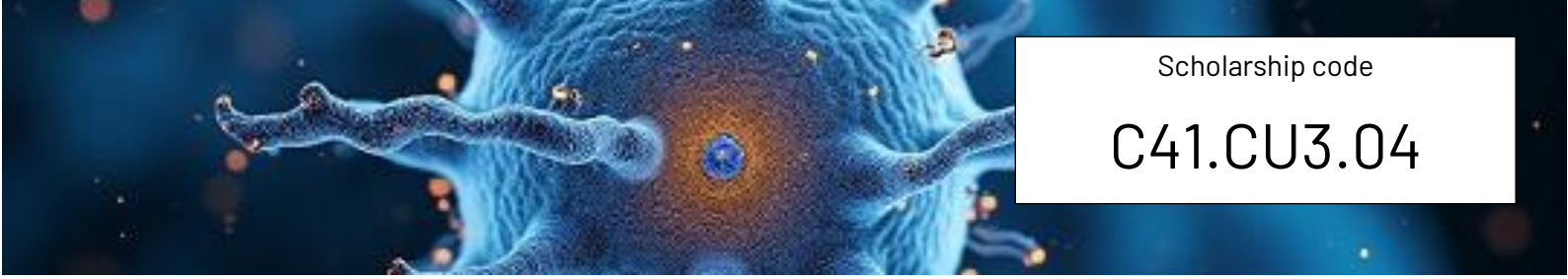
Available positions: 1

Description of the research topic

The project aim at studying neuronal network activity in physiological conditions and in mouse model of brain disorders in vivo, using electrophysiological recording and functional two photon imaging, in awake behaving mice. We will analyze the role of inhibition in regulating neuronal network dynamics, how this changes according to the status of the subject, along the circadian rhythm and how these processes get altered in brain diseases.

Research team and environment

In the lab we are interested in understanding how sensory (and cognitive) information is encoded in the brain, and how these processes get disrupted in pathological conditions. To address these questions, we analyze brain activity, at systems level, in vivo, by using multiphoton imaging and electrophysiology in awake behaving mice. Due to the key role of inhibition in regulating brain activity, we investigate how changes in the inhibitory tone affect the computation of the brain, taking into account the status of the subject and the circadian rhythm.

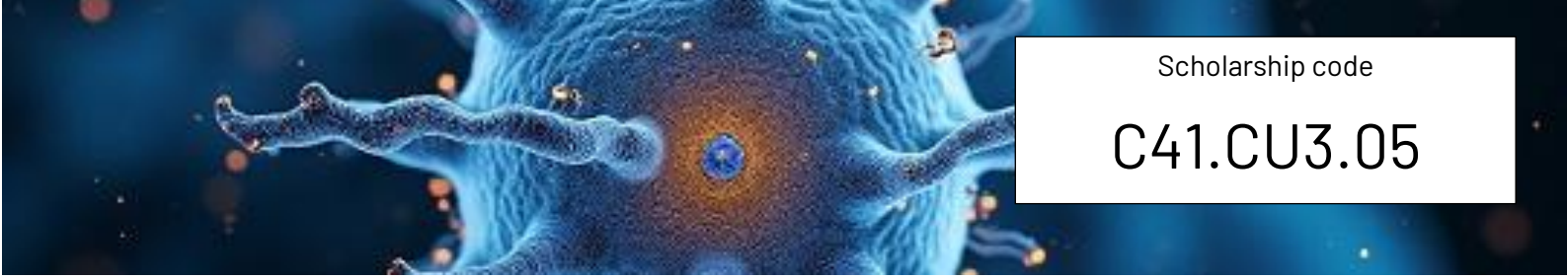


Scholarship code

C41.CU3.04

Suggested skills for this research topic

Master in neuroscience, physics, biological science, engineering, math, medical degree. Ability/ willing to work in vivo. Programming in mat lab and python is required, so having already some knowledge is appropriate.



Scholarship code

C41.CU3.05

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Development and optimization of industrial processes for the production of therapeutic proteins

Reference Person: Lorenzo Ghezzi

(lorenzo.ghezzi@philogen.com)

Host University/Institute: Philogen SpA

Development & Industrialization

Location: Siena, Italy

Research Keywords: Biopharmaceutical process

GMP manufacturing

Process development and improvement

Reference ERCs: PE8_13 Industrial bioengineering

PE8_10 Manufacturing engineering and industrial design

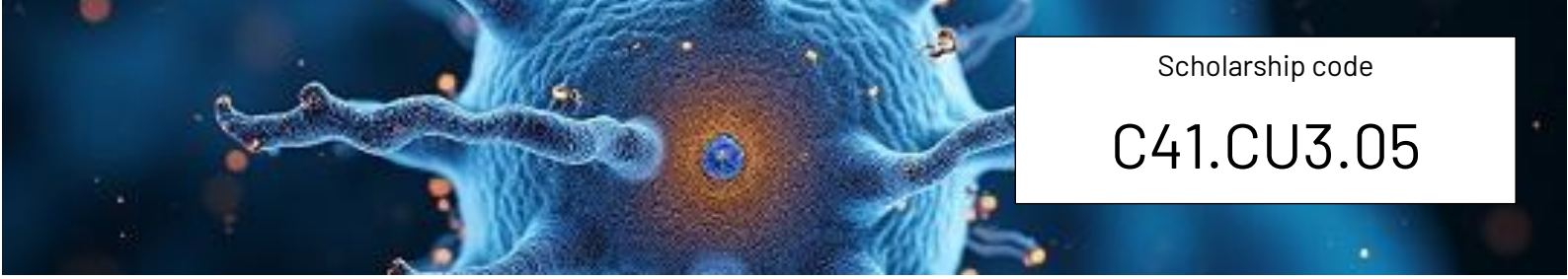
Available positions: 1 (reserved for Philogen Company's employees)

Description of the research topic

The new frontier in anti-cancer drug development lies in conjugating them with small organic molecules, peptides or antibodies that have a high affinity for and selectivity towards tumour-associated proteins, thereby increasing their efficacy. This research project focuses on developing and optimizing industrial biotechnological processes for producing recombinant therapeutic proteins. During the project, the candidate will work on developing and optimising cell fermentation and chromatographic purification, to determine the optimal production conditions for the protein of interest, seeking the best compromise between yield and purity. The identified process will then be transferred to industrial GMP production.

Research team and environment

Philogen (www.philogen.com) is a Swiss-Italian biotechnology company, founded in 1996, with a mission to innovate the treatment of cancer and other serious conditions.



Scholarship code

C41.CU3.05

Philochem AG (www.philochem.ch) is the Swiss subsidiary of the Philogen group, acting as an R&D unit and developing drug prototypes based on disease-targeted small molecules, peptides, and antibodies.

The Philogen group is experienced in running industrial PhD programs (open since 2017) in collaboration with leading universities, including IUSS Pavia.

Suggested skills for this research topic

• Master's degree in health biology, biotechnology, or related disciplines.

• Experience in cell culture (the ability to handle cells in suspension is considered a plus).

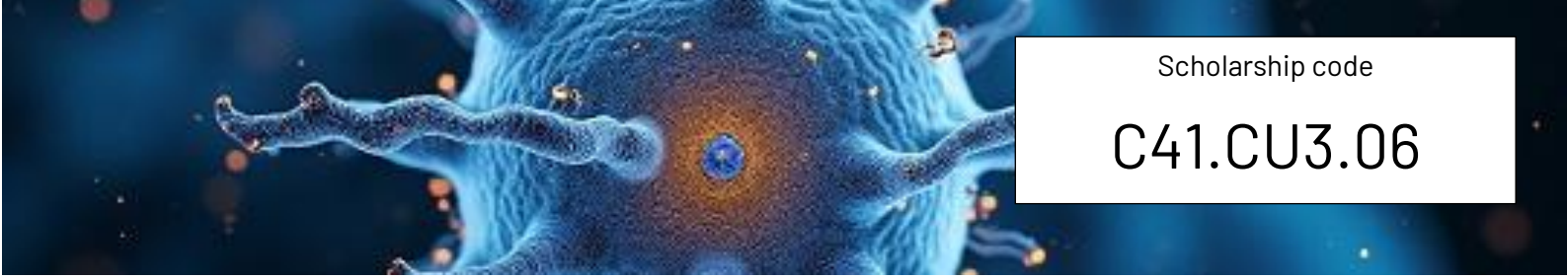
• Experience in protein purification through chromatographic and non-chromatographic methodologies (e.g., FPLC, TFF).

• Experience with modern analytic techniques (e.g., HPLC, SDS-page, ELISA, UV-Vis).

• Good knowledge of data analysis and editing Software (i.e., Excel, Word, Power point).

• Experience in performing literature searches using scientific databases (e.g., PubMed) and in applying the results to solve process challenges in the lab.

• Fluency in oral and written English.



Scholarship code

C41.CU3.06

CU3 – BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Targeting Autism in lysosomal storage Disorders: from bed to bench side

Reference Person: Elvira De Leonibus

(elvira.deleonibus@cnr.it)

Host University/Institute: Consiglio Nazionale delle Ricerche

Istituto di Biochimica e Biologia Cellulare (IBBC)

Location: Monterotondo (RM), Italy

Research Keywords: Lysosomal storage disorders

Drug-Repurposing

Neurobehavioral Dysfunctions

Reference ERCs: LS5_3 Neural development and related disorders

LS5_11 Neurological and neurodegenerative disorders

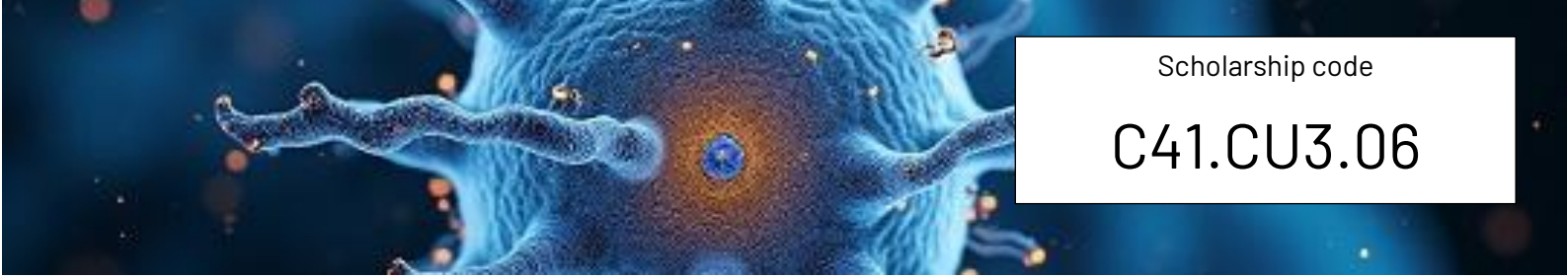
LS7_7 Pharmacology and toxicology

Available positions: 1

Description of the research topic

This PhD project explores the neurobiological basis of complex behavioral symptoms observed in rare pediatric disorders, with a focus on lysosomal dysfunction and its impact on neural circuits regulating motivation, cognition, and sleep. Neurodevelopmental disorders linked to lysosomal defects often present early-life behavioral disturbances such as hyperactivity, stereotypies, and profound sleep impairment, followed by progressive cognitive decline. The lack of effective treatments for these symptoms highlights the urgent need for targeted therapeutic approaches that go beyond the standard palliative care.

Recent evidence from animal models indicates that alterations in neurotransmitter signaling and disruptions in sleep–wake transitions may originate from developmental imbalances in specific brain circuits, independently of classical neurodegeneration. This project aims to dissect the contribution of these circuits in modulating rest-activity



rhythms and behavioral states and to repurpose FDA-approved treatments to improve the symptomatology and the disease progression. Advanced tools such as in vivo electrophysiology, optogenetics, and molecular profiling will be used to identify causal mechanisms and therapeutic targets.

In parallel, the student will help develop and validate an integrated preclinical platform designed for sustainable, high-throughput drug screening. This system will combine behavioral and physiological data from mouse models with automated analysis pipelines and machine learning to identify early biomarkers of disease and treatment efficacy.

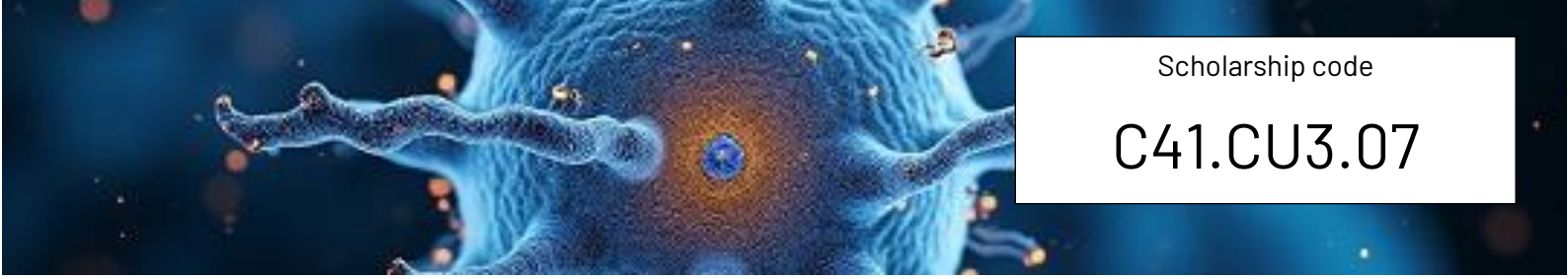
The project is positioned at the intersection of neuroscience, rare disease research, and translational medicine. It is embedded within an international collaborative framework and aligned with global efforts (e.g., IMPC and EMMA) to accelerate the development of personalized therapies. The PhD candidate will receive multidisciplinary training in behavioral neuroscience, neuropharmacology, data analysis, and in vivo modeling, preparing he/she for a career in academic or applied biomedical research.

Research team and environment

The PI is a Research Director at IBBC-CNR (Elvira De Leonibus – IBBC) with extensive experience in mentoring PhD students, postdocs, and early-career researchers (ORCID: 0000-0002-1871-2440). The team includes senior scientists and young researchers (e.g., Lattao, Marotta, D'Elia), fostering a dynamic, collaborative environment. The project is embedded in a translational neuroscience hub with strong links to the Mouse Clinic and the IMPC (https://www.mousephenotype.org), and benefits from new technological platforms for in vivo phenotyping and digital behavioral profiling. The PhD candidate will receive interdisciplinary training in neurobiology, pharmacology, data science, and preclinical research. IBBC is located in the Monterotondo Research Campus, which hosts the EMBL outstation (https://www.embl.org/about/info/embl-in-italy/) and offers a stimulating international scientific environment.

Suggested skills for this research topic

The ideal candidate holds a degree in biomedical sciences, preferably with a background in neurobiology, neuroscience, or related fields. A strong motivation to pursue experimental research, critical thinking skills, and the ability to work both independently and collaboratively within a team are essential. Prior experience with animal models, behavioral neuroscience, or neuropharmacology—whether through laboratory work or certified training courses—is considered an asset. The candidate should be open to interdisciplinary approaches and eager to develop new technical and analytical skills. Proficiency in English is required; no additional languages are necessary.



Scholarship code

C41.CU3.07

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Epidemiological studies in birth cohorts and in vitro/vivo models for non-communicable diseases

Reference Person: Gaspare Drago

(gaspare.drago@irib.cnr.it)

Host University/Institute: Consiglio Nazionale delle Ricerche

Istituto per la Ricerca e Innovazione Biomedica (CNR-IRIB)

Location: Palermo (PA), Italy

Research Keywords: Exposome

Birth cohort

Biomarkers

Reference ERCs: LS7_9 Public health and epidemiology

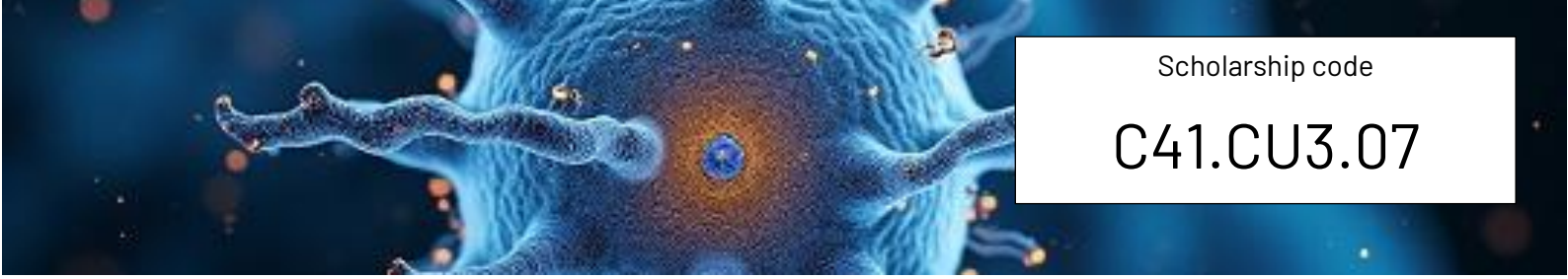
LS4_8 Impact of stress (including environmental stress) on physiology

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 relationship between environmental exposures and human health is one of the most critical issues in biomedical research. Growing evidence suggests that early life exposure to environmental hazards, along with the adoption of unhealthy lifestyles, may raise the risk for non-communicable diseases (NCDs) later in life. The complex interaction underlying the risk of chronic diseases – starting from intrauterine life – requires a greater knowledge of the events between environmental insults and the risk of future pathology. In this context, the concept of the exposome – defined as the totality of environmental exposures an individual experiences throughout his/her life, from conception onwards – has emerged as a key framework for understanding the environmental contribution to disease etiology. Birth cohort studies represent a valuable research model for investigating the impact of



Scholarship code

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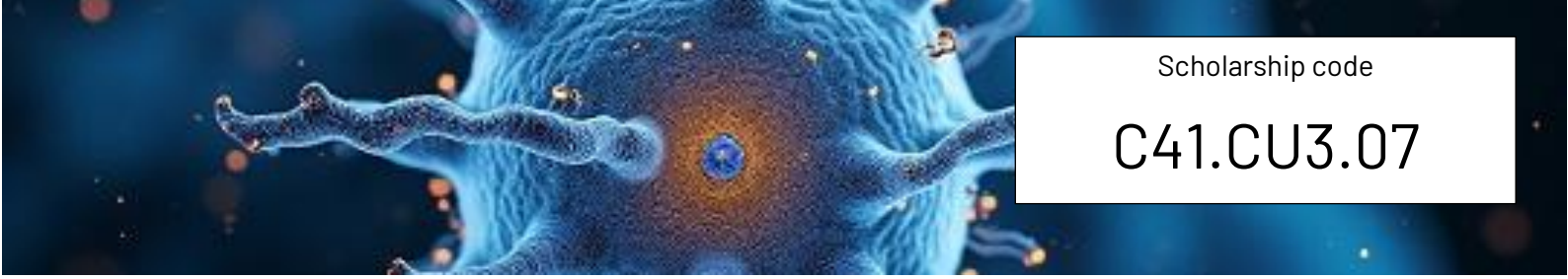
environmental factors over time. By following mother-child pairs from gestation through early life, these studies enable the identification of associations between early exposures and later health outcomes, including developmental and metabolic conditions. These cohorts often include extensive biological sample collections, clinical assessments, and detailed environmental exposure data, forming a solid foundation for studying the human exposome. In parallel, advances in omics technologies and experimental models are making it possible to explore the biological mechanisms underlying observed associations. The integration of longitudinal epidemiological and omics data – such as genomics, epigenomics, metabolomics, and proteomics – along with in vitro and in vivo models, enables researchers to move beyond correlation, toward understanding causal pathways and biological responses to environmental stressors. Exploring the interactions between environmental, biological, and behavioral factors – and their impact on human health – through experimental models and advanced techniques enables the validation of epidemiological data, the elucidation of pathogenic mechanisms, and the identification of clinically relevant biomarkers. This integrative approach has broad practical implications: it can inform early risk assessment, guide the discovery of predictive biomarkers for chronic diseases, support evidence-based regulatory decisions on environmental contaminants, and foster the development of targeted prevention strategies and personalized interventions.

Research team and environment

The PhD project will be carried out at IRIB-CNR (Institute for Biomedical Research and Innovation) in Palermo, within a multidisciplinary team including the Environmental Epidemiology and Molecular Immunology groups. The epidemiology group has solid expertise in longitudinal studies on environmental and lifestyle risk factors affecting maternal and child health. Since 2018, it coordinates the neonatal environment and health outcomes (NEHO) birth cohort, investigating maternal exposure to pollutants, circulating microRNA alterations, and children's growth trajectories. The Molecular Immunology group conducts in vitro and in vivo studies on pollutant-induced innate immune modulation and cell signaling. In collaboration with the epidemiology group, it contributes to identifying early biomarkers and elucidating molecular mechanisms linking environmental exposures to chronic disease risk.

Suggested skills for this research topic

The ideal candidate holds a Master's degree in biology, biotechnology, or related disciplines, including medicine. Experience in data analysis, basic laboratory techniques, handling of biological samples, as well as familiarity with bioinformatics tools and multi-omics data analysis, may represent preferential qualifications, as they are relevant to the activities required for the position. An interest in interdisciplinary research combining molecular and epidemiological approaches is important. The ability to work in a team and manage tasks independently is desirable. Proficiency in English (spoken and written) is required for



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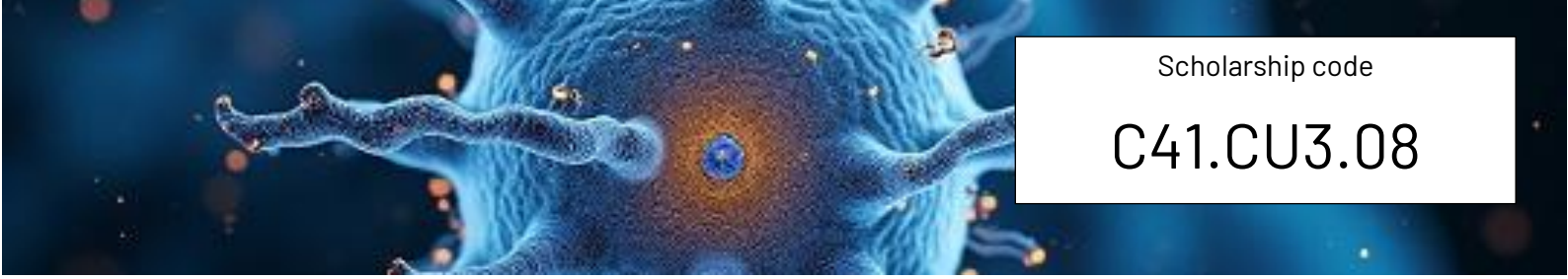
communication and publication. Knowledge of Italian is not mandatory but may be helpful for integration and fieldwork.



Scholarship code

C41.CU3.08

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Vaccines for Cancer & Infection using mRNA Tech, ExtraVesicles, and Microbiota-Driven Innate Memory

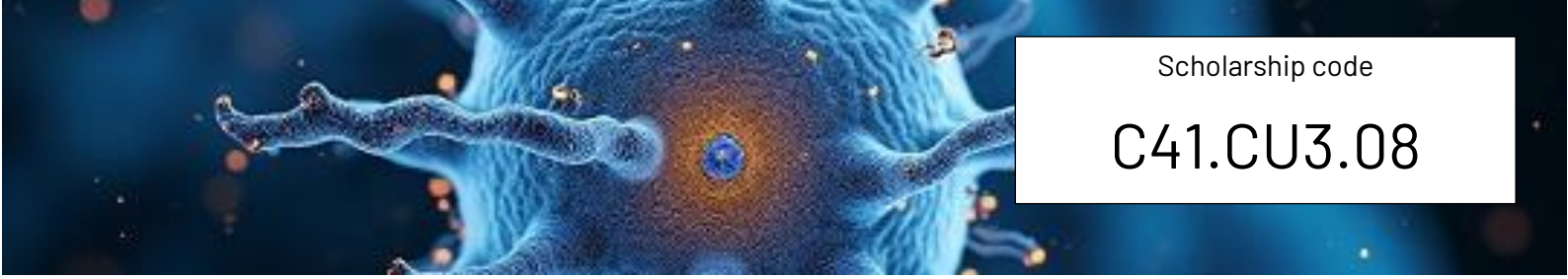
Reference Person:	Paola Italiani
	(paola.italiani@cnr.it)
Host University/Institute:	Consiglio Nazionale delle Ricerche
	Istituto di Biochimica e Biologia Cellulare (IBBC)
Location:	Naples, Italy

Research Keywords:	Immunotherapy based on innate immune cells
	Innate Immune Memory
	Advances in vaccinology against cancer/infection
Reference ERCs:	LS6_1 Innate immunity
	LS6_11 Innovative immunological tools and approaches, including therapies
	LS6_10 Vaccine development

Available positions: 1

Description of the research topic

The PhD candidate will be engaged in three research activities, all designed to generate novel insights for the development of advanced vaccines targeting cancer and infectious diseases. The project aims to develop personalized vaccines based either on idiotype mRNA-modified Dendritic Cells or on lipid nanoparticles carrying patient-specific idiotypic mRNA, as novel therapeutic strategies to improve treatment of B-cell lymphomas and Chronic Lymphocytic Leukemias. The candidate will be involved in all phases of vaccines' development, with a focus on determining their interaction with monocytes and monocyte-derived macrophages (MDM). This interaction will be assessed as to inflammation, MDM polarization, and triggering of Innate Immune Memory (IMM). Known molecular mechanisms and new regulatory ones will be investigated and identified.



Scholarship code

C41.CU3.08

The study will then be extended to evaluate these mechanisms upon stimulation with BCG (Bacillus Calmette-Guérin) vaccine or infection with Mycobacterium tuberculosis (Mtb). The communication between innate immune cells and BCG or Mtb via Mycobacterial extracellular vesicles (MEVs) and Macrophage-derived extracellular vesicles (MDEVs) will be investigated. By exploring composition and immunomodulatory effects of EVs, the study aims to: identify immunomodulatory molecules within MEVs that may contribute to immune evasion or manipulation; determine host-derived cargo from MDEVs that could act as antimicrobial or bacterial-physiology modulators; provide foundational data supporting the development of EV-based immunotherapies or vaccine adjuvants.

The IIM involvement serves as a "trait d'union" for a third pivotal player in anti-tumor and infection immunity: the microbiota. The candidate will investigate how the microbiota and its modulation influence IIM induction in DCs and MDM, clarifying its role in cancer control, infection resistance, and vaccine efficacy. The candidate will study ex-vivo the IIM in DCs and MDM isolated from cancer patients or BCG-vaccinated individuals, exposed to selected microbiota bacteria. The goal is to identify specific microbial strains—or personalized combinations—that can act as IIM inducers promoting a functional phenotype optimized against cancer and infections. This study could lay the groundwork for addressing key open questions: What is the impact of the microbiota on IIM? How can we leverage microbiota-induced IIM mechanisms to improve cancer prognosis and/or infectious disease outcomes?

Research team and environment

The research team of Laboratory of Innate Immunity, Inflammation and Nanoimmunosafety at CNR-IBBC headed by Dr Paola Italiani has a twenty years' experience in immunology (especially in innate immunity and inflammation), in comparative immunology, in molecular and cell biology, pharmaco-toxicology, and nanosafety, in project management in academy and in collaboration with industry, and in higher education and training.

Chemists from IRIB-CNR (Italy) and Immunologists from Shenzhen Institute of Advances Technologies (Cina) and from Butantan Institute, Vaccine Development Laboratory (Brasile) will be involved in the research team as external collaborators.

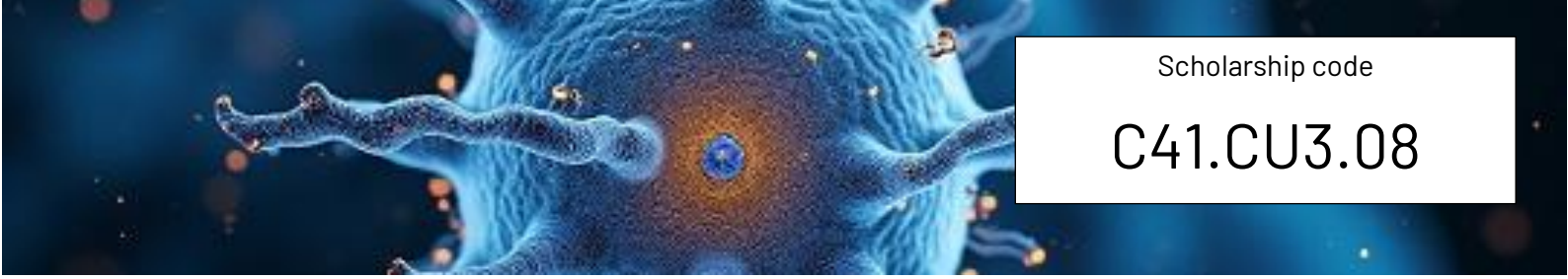
The team can count on well-equipped laboratory (e.g., real-time PCR, ELLA, Bioanalyser) and cell culture room, and on the access to FACS facility, CyTOF facility, Advanced Microscopy facility (Euro-bioimaging).

Teams' webpage:

http://www.ibbc.cnr.it/research-applications/innate-immunity-and-inflammation/

Suggested skills for this research topic

We are seeking a highly motivated and enthusiastic PhD candidate to join our dynamic and multidisciplinary research team dedicated to advance our understanding in the field of Immunology. Ideal candidate should have the following background and skills:



Scholarship code

C41.CU3.08

• Strong academic background in Immunology, Molecular Biology, or related biomedical sciences

• Practical prior experience with key laboratory techniques (e.g., PCR, ELISA, Western blotting, flow cytometry, etc.) or human primary cell/line cell culture will be considered an asset;

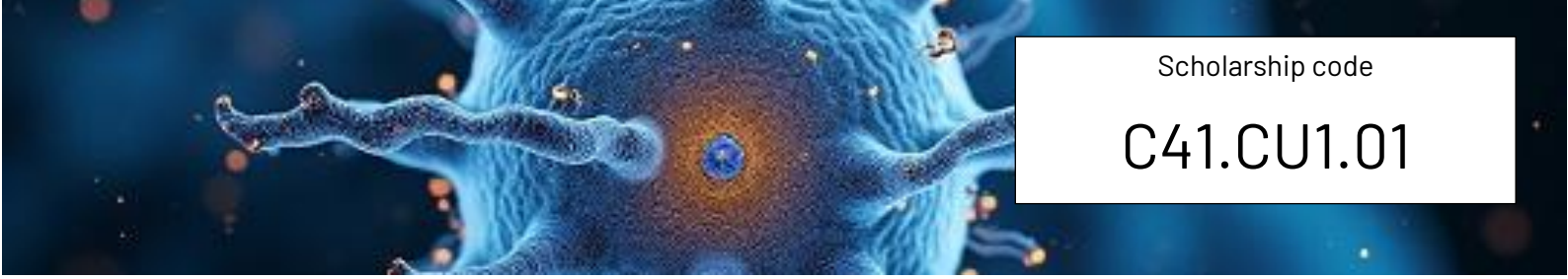
• High level of motivation, curiosity and critical thinking skills:

• Willingness and ability to learn new techniques and work across disciplines;

• Excellent communication and teamwork skills;

• Availability for research internships abroad, as part of international collaborations and training programs;

• Fluent written and spoken English proficiency; no additional languages are necessary.



Scholarship code

C41.CU1.01

CU3 - BIOMOLECULAR AND BIOTECHNOLOGICAL SCIENCES

Macromolecules of Biotechnological and Pharmaceutical Interest

Reference Person:	Federico Forneris
	(federico.forneris@unipv.it)
Host University/Institute:	Università degli studi di Pavia
	Dipartimenti vari
Location:	Pavia, Italy
Research Keywords:	Biological macromolecules
	Pharmaceutics and biocatalysis
	Life science research
Reference ERCs:	LS1_4 Protein biology
	PE5_17 Organic chemistry
	LS7_7 Pharmacology and toxicology
Available positions:	3

Description of the research topic

The main topic of this PhD fellowship can be related to one of the basic research subjects addressed in the Biomolecular Sciences and Biotechnologies curriculum. Depending on the choice of research supervisor (which will be done by the selected PhD fellow) topics will include:

Structural enzymology (Prof. A. Mattevi, http://www-9.unipv.it/biocry/)

Structure-function studies of extracellular protein ensembles (Prof. F. Forneris, https://fornerislab.unipv.it/)

Bio-inorganic chemistry (Prof. E. Monzani, https://chimica.dip.unipv.it/en/research/research-teams-and-topics/inorganic-chemistry/bioinorganic-chemistry)

Biocatalysis (Prof. D. Ubiali, https://scienzedelfarmaco.dip.unipv.it/en/research/our-people-and-divisions/medicinal-chemistry/biocatalysis-laboratory),

Pharmaceutical technology (Prof. B. Conti, https://scienzedelfarmaco.dip.unipv.it/en/research/research-areas/pharmaceutical-technology/pharmaceutical-technology-law-ptl),

Molecular basis of heritable skeletal disorders (Prof. A. Rossi, https://medicinamolecolare.dip.unipv.it/en/research/research-teams-and-topics/biochemistry/molecular-basis-osteochondrodysplasias-antonio),

Neuropharmacology (Prof. C. Lanni, https://scienzedelfarmaco.dip.unipv.it/en/research/our-people-and-divisions/pharmacology/biology-and-pharmacology-aging-inflammatory),

Molecular ematology (Prof. M. Torti, https://dbb.dip.unipv.it/en/research/research-teams-and-topics/cellular-biology-and-biochemistry-vascular-system/platelet),

Molecular microbiology (Prof. S. Buroni, https://dbb.dip.unipv.it/en/research/research-teams-and-topics/molecular-microbiology/molecular-microbiology-laboratory),

Pharmaceutical analysis (Prof. E. De Lorenzi, https://scienzedelfarmaco.dip.unipv.it/en/research/our-people-and-divisions/medicinal-chemistry/organic-chemistry-pharmaceutical-and),

Molecular biology and gene therapy (Prof. A.K. Kajaste-Rudnitski, https://dbb.dip.unipv.it/en/research/research-teams-and-topics/molecular-mechanisms-innate-immunity-and-nucleic-acid-sensing-0).

Candidates are invited to get in touch with potential supervisors to further discuss possible research projects.

Research team and environment

Research activities will be carried out in one of the supervisor's laboratories of the University of Pavia. Details are provided in the websites of the different departments:

Department of Biology and Biotechnology (Profs. Mattevi, Forneris, Torti, Buroni, Kajaste-Rudnitski): https://dbb.dip.unipv.it/en/research

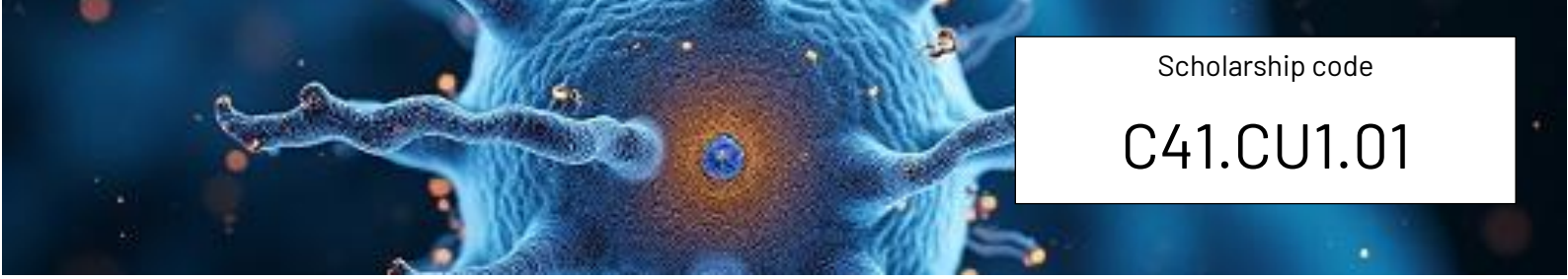
Department of Chemistry (Prof. Monzani): https://chimica.dip.unipv.it/en/research

Department of Drug Sciences: https://scienzedelfarmaco.dip.unipv.it/en/research

Department of Molecular Medicine: https://medicinamolecolare.dip.unipv.it/en/research

Suggested skills for this research topic

Prospective candidates will be selected based on their previous theoretical and practical experiences related to the research activities carried out in the prospective supervisor's host laboratories. Typically, successful candidates hold an M.S. in disciplines such as Biology, Biotechnology, Chemistry, Pharmacy, Physics, Bioinformatics, Biomedical



Scholarship code

C41.CU1.01

Engineering and had opportunities for practical laboratory training during internship activities lasting at least 6 months. Evidence of international mobility during previous training will be considered. Candidates must be able to understand and sustain scientific conversations in English.