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# PROJECT	DEPARTMENT	TITLE AND ABSTRACT	SITE
1 **G. DAMIA** **Lab of Preclinical Gynecological Preclinical**	**Experimental Oncology**	**Characterization of breast cancer models that metastasize to the brain** Brain metastases (BrM) from solid tumors contribute significantly to morbidity and/or mortality in cancer patients. Although there have been advances in recent years in the diagnosis and treatment of patients with BrM—including the development of targeted therapies capable of crossing the blood-brain barrier (BBB)—mortality rates and recurrence of BrM remain high. The project in which the PhD student will be involved is part of a broader research project aimed at identifying new integrative biomarkers capable of specifically predicting brain metastases from breast cancer and identifying the key factors, pathways, and bacteria involved in the formation of brain metastases. Specifically, this research project has two fundamental objectives: ii) to characterize, from a molecular perspective (i.e., transcriptomics, genomics, epigenomics, and metagenomics), two preclinical models of breast cancer that metastasize to the brain, which will be compared both with the parental line and with a breast cancer subline that metastasizes to bone; i) to generate new preclinical models of breast cancer capable of metastasizing to the brain, derived from brain metastases in women with breast cancer. A better understanding of these models could lead to the identification of the cellular pathways involved in the metastasis process and the potential identification of drug targets **Requirements:** • Experience with cell cultures and working with animals is preferred	Milano
2 **D. DIBITETTO** **Molecular Oncology and DNA Damage Response Unit**	**Experimental Oncology**	**A novel therapeutic approach to eradicate BRCA-deficient cancers** BRCA-deficient tumors are characterized by pronounced genomic instability and frequently develop resistance to platinum-based chemotherapy and PARP inhibitors. This project aims to investigate a novel therapeutic strategy based on the combined inhibition of DNA-PK and POLθ. The selected candidate will integrate cell and molecular biology with biochemical approaches to dissect the mechanistic effects of dual targeting of these DNA repair pathways. In addition, the project will assess whether this therapy enhances tumor immunogenicity compared to conventional treatments. By evaluating changes in immune signaling, the study will explore the potential for	Milano

		improved anti-tumor immune responses. Ultimately, this work aims to lay the foundation for more effective and durable treatment strategies to eradicate BRCA-deficient cancers. **Requirements:** • Fluent English • The ideal candidate should have a strong background on relevant cellular and molecular biology techniques (e.g. cell culture, gene editing by CRISPR etc)	
3 **L. DIOMEDE** **Center for Toxicology and Preclinical Biochemistry/Laboratory of Human Pathology and Model Organisms**	**Biochemistry and Molecular Pharmacology**	**Mitochondrial transfer as a potential strategy to restore bioenergetic function and counteract mitochondrial dysfunction associated with pathological conditions.** The project aims to develop an innovative therapeutic approach involving the transfer of healthy mitochondria into damaged cells, in order to restore their bioenergetic function and treat mitochondrial dysfunction associated with pathological conditions. Among these, particularly relevant is ischemia-reperfusion injury associated with organ transplantation, as well as that occurring in certain metabolic and degenerative diseases. In addition to optimizing procedures for maintaining mitochondrial viability during isolation and storage, the candidate will define the most suitable conditions for *in vitro* transfer in 2D and 3D cellular models and, *in vivo*, using the invertebrate nematode *C. elegans* as an animal model. The data obtained will form the basis for future preclinical studies. **Requirements:** • Basic knowledge of subcellular structure isolation and cellular and subcellular labeling techniques • Solid experience in 2D cell culture • Previous experience in *C. elegans* culture and maintenance techniques is required • Experience with fluorescence microscopy is preferred, while the ability to use confocal microscopy would be considered an additional advantage.	Milano
4 **R. FRAPOLLI** **Laboratory of Anticancer Pharmacology / Preclinical Experimental Therapy Unit**	**Experimental Oncology**	**Eribulin in leiomyosarcomas: from a cytotoxic drug to a potential adjuvant** Eribulin is an antitumor drug that has shown efficacy in some patients affected by uterine leiomyosarcoma, a tumor histotype that is still characterized by a poor prognosis. It is an antimitotic agent that also acts on the tumor microenvironment by remodeling the extracellular matrix and the tumor vasculature. This project aims to study the consequences of such	Milano

		remodeling on the distribution and efficacy of antitumor drugs administered subsequently to eribulin. In parallel, new therapeutic combinations designed to improve the efficacy of eribulin in leiomyosarcoma will be investigated.The candidate will be responsible for in vivo pharmacological studies, pharmacokinetic analyses using HPLC, HPLC–MS/MS, and Imaging Mass Spectrometry, as well as the collection and preparation of samples for histological analyses **Requirements:** • Basic knowledge of analytical techniques. Experience with cell culture/laboratory animals is a preferential title	
5 **C. GHILARDI** **Tumor Microenvironment Laboratory / Molecular Anticancer Therapy Unit**	**Experimental Oncology**	**Efficacy of eribulin in uterine leyomiosarcoma (uLMS): mode of action on cancer cells and tumor microenvironment** Effective therapies for advanced uLMS are still a major challenge. Eribuline (ERI) has shown promising activity on a subset of uLMS, although its clinical efficacy is hindered by intrinsic and acquired resistance. The current knowledge of the mechanism of action of ERI supports the idea that this drug may act on both the neoplastic cells and the TME, but the relevance of these mechanisms in uLMS remains to be defined. This project aims to unravel the molecular mechanisms behind the different responses to ERI in uLMS to identify biomarkers for patient stratification and the rational design of new effective combinations. The candidate will be responsible for developing in vitro models of uLMS to investigate the molecular mechanisms underlying the effects of eribulin on both neoplastic cells and the tumor microenvironment. **Requirements:** • Experience with cell cultures, functional assays, and the evaluation of responses to drug treatments in vitro • molecular biology techniques (e.g., nucleic acid and protein extraction, PCR, Western blot), is preferred	Milano
6 **A. NOBILI** **UNFUNDED PHD POSITION**	**Health Policies**	**Optimising Antibiotic Use in Primary Care: Strategies to Reduce Antibiotic Resistance** The project aims to evaluate and improve antibiotic prescribing practices within community medicine, analysing real-world data from primary care. In Italy, it is estimated that approximately 30% of antibiotic prescriptions in primary care are inappropriate, contributing to increased resistance and risk of treatment failure. The objective is to identify factors influencing inappropriate use and to	Milano

		propose targeted interventions (training, audit, feedback) to optimise the quality and quantity of prescriptions. The candidate, a general practitioner, will play an active role in data collection, analysis, and implementation of strategies, collaborating with the Mario Negri Institute and engaging colleagues in the community. The impact of digital tools and the correlation between prescribing and the emergence of resistance will also be evaluated. **Requirements:** • Knowledge of statistical analysis techniques and clinical database management • Interest in pharmacological research and community medicine • Experience in clinical practice as a general practitioner • Familiarity with guidelines on antibiotic use • Experience with clinical audits and training colleagues is a preferential element	
7 **L. PASINA** **Laboratory of Clinical Pharmacology and Appropriate Prescribing** **UNFUNDED PHD POSITION**	**Health Policies**	**Pharmacological therapies for oral lichen planus and risk of malignant transformation: a retrospective observational cohort study** The project investigates the role of pharmacological therapies in oral lichen planus (OLP), a chronic inflammatory disease with the potential for malignant transformation.The primary objective is to identify, in a retrospective cohort (2000–2025), the most effective treatment regimen for preventing oral cancer. The study will analyze clinical, demographic, and behavioral data to control for major confounding factors.The rate of malignant transformation and time to disease progression will also be assessed. Attention will be paid to the association between therapeutic strategies and cancer risk. The project also aims to identify predictive factors useful for individual risk stratification. The candidate's role is to collect, statistically analyze, and interpret clinical data. The expected results will contribute to the development of more effective and personalized therapeutic strategies. **Requirements:** • Knowledge of statistical analysis techniques and clinical database management	Milano

		• Interest in pharmacological research and specialized medicine • Experience in clinical dental practice • Familiarity with the pharmacological management of oral lichen planus • Experience with clinical audits and training of colleagues is an advantage	
8 **A. PASSONI Laboratory of Metabolites and Proteins in Translational Research / Unit of Spectrometry Applied to One-Health**	**Environmental Health Science**	**Deciphering sarcoma metabolic heterogeneity through untargeted mass spectrometry imaging** The project is focused on the biochemical characterization of sarcoma tissues using mass spectrometry-based approaches. Mass spectrometry imaging (MSI) in untargeted mode will be used to study the spatial distribution of metabolites and lipids within the tumor microenvironment. The PhD candidate will be involved in the development and optimization of the MSI method, from sample preparation to data processing. A significant part of the project will be dedicated to untargeted data analysis, including feature extraction, segmentation, and biochemical studies. **Requirements:** • Master's degree in Chemistry, or related disciplines. Previous experience with mass spectrometry techniques, particularly imaging (MSI), is considered a strong advantage, as well as familiarity with the full analytical workflow (sample preparation, acquisition, and data analysis) • Experience in handling complex datasets and use of dedicated mass spectrometry software is appreciated	Milano
9 **L. PERICO Laboratory for Targeted Therapies for Autoimmune Diseases**	**Molecular Medicine**	**Mitigating mitochondrial RNA release during aging to control inflammation and senescence, preserving organ function and enhancing healthspan (MIRACLE)** The MIRACLE project investigates the role of cytoplasmic mitochondrial RNA (mtRNA) release — triggered by aging-associated mitochondrial dysfunction — as a primary driver of chronic low-grade inflammation and cellular senescence in the heart and kidneys. Preliminary data show that mtRNA accumulates in cardiac tissues of aged mice, associated with inflammatory cell infiltration and senescence markers. Through the combination of multidisciplinary approaches, the candidate will be actively involved in the characterization of the molecular mechanisms of mtRNA release *in vitro* (cardiomyocytes and renal tubular cells), *in vivo*	Bergamo

		(mouse aging models), and in human-derived fibroblasts from young, middle-aged, and elderly donors. The candidate will also be responsible for assessing the therapeutic potential of various treatment approaches, including: (A) SIRT3 activation to preserve mitochondrial integrity; (B) gene transfer to express the mitochondrial degradosome (mtEXO) in the cytosol to degrade cytosolic mtRNA; (C) a trispecific antibody (TriKe) to eliminate HLA-E+ senescent cells via NK cell activation. The candidate will actively contribute to all experimental phases, from cell and molecular biology to the development and validation of therapeutic tools. **Requirements:** • Master's degree in biology, biotechnology, pharmacy, or related disciplines. • Knowledge of basic cell and molecular biology techniques (Western Blot, RT-PCR, immunofluorescence, cell culture) • Experience with laboratory animal models and/or flow cytometry is a preferential title • Good written and spoken English.	
10 **A.D. RE CECCONI Muscle Pathophysiology Laboratory**	**Neuroscience**	**Exploring the Dual Role of Musclin Against Muscle and Bone Wasting in Cancer** Cancer cachexia (CC) causes progressive loss of both muscle and bone mass in up to 80% of advanced cancer patients, with no effective therapies currently available. This project investigates musclin, a myokine involved in muscle and skeletal homeostasis whose levels are early reduced during CC. Preliminary data indicate that the musclin–Npr3 axis represents a promising therapeutic target. We identified a stable musclin-derived peptide (MP-D) displaying anti-atrophic and anti-osteoclastogenic effects. The project aims to optimize MP-D and evaluate its efficacy in preventing muscle and bone wasting in animal models of cachexia and bone metastasis. The candidate will be responsible for experimental design, *in vitro* and *in vivo* analyses, and functional validation of the peptide. **Requirements:** • Experience with cell culture and laboratory animals is a preferential title.	Ranica (BG)
11 **G. TARABOLETTI Tumor Microenvironment Laboratory**	**Experimental Oncology**	**Novel compounds targeting pharmacoresistance mechanisms in breast cancer** Therapy resistance represents the leading cause of disease progression in patients with breast cancer. This project aims to develop novel compounds capable of counteracting the onset of therapy resistance. Specifically, it will investigate compounds that inhibit pathways activated by	Bergamo

		growth factors and hormones, which drive resistance to hormone therapy in estrogen receptor–positive breast cancer and to chemotherapy in triple-negative breast cancer. The candidate will analyze the pathways involved and assess, in vitro and in vivo, the ability of the selected pathway inhibitors to prevent or overcome pharmacoresistance. **Requirements:** • Experience in cell culture and in the main molecular biology techniques • Willingness to perform experimental work in in vivo preclinical tumor models would be an advantage • Interest in cancer pharmacology and good data-analysis skills	
12 **P. TRIONFINI** **Laboratory of Cell Reprogramming and Gene Therapy**	**Molecular Medicine**	**Study of the molecular mechanisms underlying atypical hemolytic uremic syndrome (aHUS) associated with mutations in DGKE, with the aim of developing a personalized therapy.** The project aims to develop a patient-specific in vitro diagnostic and mechanistic model for the characterization of aHUS associated with mutations in DGKE. The candidate will be required to generate endothelial cells derived from induced pluripotent stem cells (iPSCs) obtained from a patient with a homozygous truncating mutation, from a compound heterozygous patient, and from healthy heterozygous parents. Once the patient-specific cells have been obtained, complement deposition, endothelial phenotype through omics approaches (proteomics and metabolomics), and endothelial function through angiogenic assays will be analyzed. Finally, through comparison with endothelial cells derived from a healthy subject, potential therapeutic targets will be identified. **Requirements:** • Experience in cell culture, particularly of induced pluripotent stem cells, and in basic biochemical techniques such as Western blotting.	Bergamo
13 **P. TRIONFINI** **Laboratory of Cell Reprogramming and Gene Therapy**	**Molecular Medicine**	**Development of cell-based therapies for the treatment of Hemophilia A and for the prevention of kidney damage.** The project aims to develop universal allogeneic cell therapies for the treatment of various diseases, with the goal of reducing the high costs associated with personalized, patient-specific therapies. In particular, the candidate will genetically modify hypoimmunogenic induced pluripotent stem cells (iPSCs) already available in the host laboratory, in	Bergamo

		order to enhance their ability to evade the immune system. From these cells, liver organoids will be generated and their therapeutic efficacy will be evaluated in murine models of Hemophilia A. Furthermore, the hypoimmunogenic iPSCs will be differentiated into mesenchymal cells, whose regenerative and reparative capacity will be tested in a model of kidney injury. **Requirements:** • experience in cell culture, particularly of induced pluripotent stem cells, and in optical and fluorescence microscopy.	
14 **T. RAVIZZA e A. Epilepsy and Therapeutic Strategies Laboratory Glio-Neuronal Communication and Biomarkers Unit**	**Acute Brain and Cardiovascular Injury**	**Functional and molecular studies on the liver–brain–gut axis: bile acids as a new therapeutic target in the progression of neurological damage** The project aims to investigate whether bile acids represent a key mechanism of communication between intestinal dysbiosis and neuronal hyperexcitability underlying neurological deficits and the generation of epileptic seizures following acute brain injury. Bile acids, through the activation of G protein–coupled receptors expressed in both the intestine and the brain, may influence: the integrity of the blood–brain barrier, neuronal and glial function, and neuroinflammatory processes. These mechanisms are involved in the progression of neurological damage. Project objectives: To characterize the bile acid profile in blood and brain during the development of neurological deficits and drug-resistant epilepsy in murine models of acute brain injury, and in cohorts of individuals with drugresistant epilepsy. To evaluate the role of specific dysregulated bile acids in neurological deficits and in the progression of brain damage toward the generation of epileptic seizures in murine models. This project will help to clarify the pathogenetic role of intestinal dysbiosis in neurological dysfunctions following acute brain injury; identify bile acids as key mediators of the gut–brain axis; and validate new therapeutic targets. **Requirements:** • a preferred qualification is prior experience in animal experimentation (though not mandatory); however • willingness to work with mouse models of disease is required.	Milano

15 **M.B. VIOLATTO** **Laboratory of Nanobiology and Nanotoxicology** **Unit of Toxicology and Preclinical Pharmacology**	**Biochemistry and Molecular Pharmacology**	**Role of the protein corona of liposomal formulations in modulating liver tropism and therapeutic efficacy in murine models of liver diseases.** The tropism of several drugs linked to nanocarriers is strongly influenced by their interaction with circulating proteins. Moreover, variations in the chemical composition of the nanocarrier coating can dramatically impact the formation of the protein corona and consequently the interaction with organs and cells. From this perspective, this project will evaluate how well identified features of the surface of nanocarrier, clinically transferable, might drive the interaction with biological matrices of different complexity. The study will be performed according to a well-defined timeframe: Year 1: interaction of the formulations in biological fluids and cells; Year 2: stability in circulation, biodistribution and targeting, and possible toxic effects in healthy mice; Year 3: biodistribution and specific targeting in pathological models and therapeutic effect. **Requirements:** • handling and treatment of murine models; histological analyses • fundamentals of molecular biology • imaging techniques	Milano

Summary of the PhD in Clinical and Experimental Pharmacology (A.Y. 2024-25, 40th cycle) of the Istituto di Ricerche Farmacologiche Mario Negri IRCCS (IRFMN)

COURSE FEATURES

Name	Clinical and Experimental Pharmacology
Number of positions	15
Legal duration	3 years
Beginning of the course	01/11/2026
Site of the course	Milano, Bergamo or Ranica (BG)
Language	Italian and English
Research stay abroad	6 months (optional)
Selection criteria	Assessment of qualifications and oral interview
Study grant	Research Fellowship (social security included)
How to apply	Online, on the website indicated below

DEADLINES	DATES
Call open	17/06/2026, at 10:00 (CEST)
Expiration of the call	17/07/2026, at 10:00 (CEST)
Pre-selection (based on titles)	by 04/09/2026
Interviews (Italian or English)	22-29/09/2025
Final ranking	by 30/09/2026

Website: https://www.marionegri.it/education/phd-course-clinical-and-experimental-pharmacology

FAQ PhD in Clinical and Experimental Pharmacology; IRFMN A.Y. 2025/26

Q1 **To whom could I ask for clarification on the PhD Course in Clinical and Experimental Pharmacology?**

A1 Communications and requests related to the Course should be sent to the Course secretariat email address: dottoratoirfmn@marionegri.it

Q2 **Is it possible to participate in the selection process for the PhD Course in Clinical and Experimental Pharmacology even if I do not yet hold a MSc Degree?**

A2 It is possible, however candidates may be admitted under reserve. The title required for access to the PhD Course must be obtained by the date of enrolment, and in any case not after the starting date of the Course.

Q3 **I carried out the online enrolment for admission to the PhD course but I did not upload the signed and dated identity document as required by the call. Can I modify the application?**

A3 It is not possible to modify the submitted application. You must resubmit a new one with all attachments.

Q4 **What kind of document should be uploaded in the "Previous research experience" section of the form?**

A4 You should upload a document with a brief description of any internship/research experience (duration > 1 month), highlighting where it was carried out, how long it lasted, in which field of research, the scientific skills acquired at a cultural and methodological level. Four to five lines per experience will suffice.

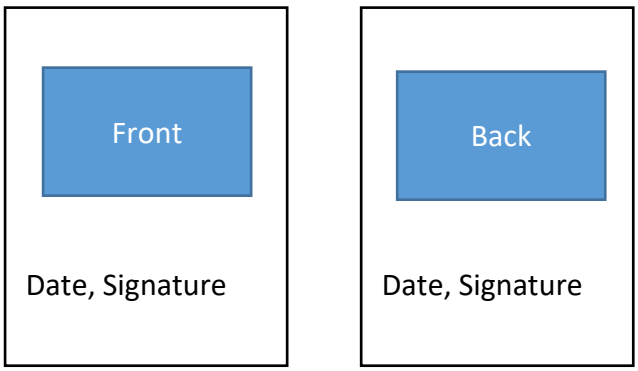
Q5 **Does the reference letter have to be redacted in a particular format?**

A5 It must contain the date, signature and qualification of the drafter and the organisation to which it belongs. Furthermore, it must be written on the organisation letterhead.

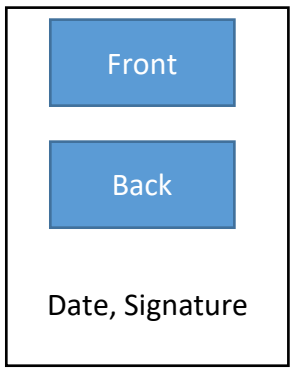
Q6 **How should the ID document with date and signature at the bottom be scanned?**

A6 Scan the ID document back and front. The signature and date can be affixed either digitally (using common pdf reading and editing programs) or manually by affixing them on the scan printout and rescanning the document.
In case you do not have a scanner, you can scan the document front and back by overlaying it with a dated and signed sheet as "background" using common scanner apps. Below are examples.

a.



b.



Q7 In what format should the Curriculum Vitae be provided?

A7 The Curriculum Vitae should be in European format and should contain, in addition to personal information, the following information: Work Experience; Education and Training; Language Skills; Digital Skills; Publications, Conferences and Seminars; Other. Additional information about the Europass CV and the online form can be found at the following link: https://europa.eu/europass/en

Q8 How can I correctly indicate my graduation score?

A8 The graduation score should be indicated in this way: score earned/maximum score attainable, or as a percentage. The following are some examples:

105/110
110/110 L
3.85/4
95%

Q9 I am experiencing problems uploading files to the online application form. How can this be solved?

A9 All documents to be attached to the application form should be in pdf and named without special characters or spacing, avoiding particularly long wording. Below are some examples suitable for the case:

- CV
- ID
- Title
- Publications
- Recommendation Letter