PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
promosso da: AIRC Fondazione CARIPLO | con il supporto di: SEMM European School of Molecular Medicine | UNIVERSITÀ DEGLI STUDI DI MILANO

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	FIERMONTE GIUSEPPE
Institute of Affiliation	Università degli Studi di Bari Aldo Moro
Title of the proposed project:	Human Genetically Defined PDAC Organoids to Identify Early Diagnostic Biomarkers
Short description of the project	Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies, largely due to late diagnosis and the lack of effective early detection strategies. PDAC development is driven by the progressive accumulation of genetic alterations, most commonly involving KRAS, TP53, CDKN2A, and SMAD4. However, the molecular and metabolic events associated with the sequential acquisition of these alterations remain poorly understood. Our laboratory has established human induced pluripotent stem cell (iPSC)-derived pancreatic organoid models carrying inducible oncogenic KRAS alone or in combination with mutant TP53, providing a unique platform to study early stages of pancreatic tumorigenesis. Building on these preliminary models, the PhD candidate will generate and characterize additional organoid lines with CDKN2A and SMAD4 downregulation, creating a genetically defined series that recapitulates the stepwise evolution of PDAC. The project will investigate how the progressive accumulation of these driver events reshapes cellular identity, signaling pathways, and metabolic programs during malignant transformation. To achieve this, the candidate will apply integrated multi-omics approaches, including transcriptomic profiling by RNA sequencing and characterization of the secretome through extracellular vesicle analysis, small RNA sequencing, and metabolomic profiling. A major objective of the project will be the identification of molecular and metabolic biomarkers associated with early PDAC development. Candidate biomarkers will be prioritized through integrative computational analyses and validated using publicly available patient datasets to assess their clinical relevance. This interdisciplinary project combines stem cell biology, cancer genetics, organoid technology, and multi-omics approaches to address fundamental questions in pancreatic cancer initiation. The resulting models are expected to provide novel insights into the earliest stages of PDAC development, reveal candidate biomarkers for early detection, and establish a versatile platform for future mechanistic and therapeutic studies.
Main research area for the project	Cancer biology
5 key words for the project	Mitochondria, Oxidative stress and/or Reactive Oxygen Species (ROS), Metabolism/Metabolomics, Glucose metabolism and/or Warburg effect, Cell metabolism

LAB INFO	
Main topic/s of the lab	Molecular Mechanisms of Cancer Initiation: Stem Cell Models, Metabolism and Biomarker Discovery

Short description of the lab activity	The laboratory focuses on understanding the molecular mechanisms underlying cancer initiation and progression, with particular emphasis on the interplay between genetic alterations, cellular metabolism, and gene regulation. A major research area is the study of pancreatic ductal adenocarcinoma (PDAC), one of the most aggressive and lethal human malignancies, using innovative human stem cell–based models that enable investigation of the earliest stages of tumor development. To address fundamental questions in cancer biology, the lab has developed advanced induced pluripotent stem cell (iPSC)-derived organoid platforms that faithfully recapitulate human tissue architecture and disease progression. These models are engineered to carry clinically relevant oncogenic alterations and provide a unique opportunity to investigate how specific combinations of driver mutations reshape cellular identity, signaling pathways, and tumor phenotypes in a controlled genetic background. Particular attention is devoted to the study of key cancer-associated genes and their cooperative roles in tumor initiation and evolution. Another major focus of the laboratory is cancer metabolism. Research activities aim to elucidate how oncogenic mutations reprogram metabolic networks to support cell growth, survival, and adaptation to hostile microenvironments. Through state-of-the-art metabolomics, stable isotope tracing, and mass spectrometry approaches, the lab investigates metabolic vulnerabilities that may represent novel therapeutic opportunities. These studies are integrated with transcriptomic and computational analyses to obtain a comprehensive view of the molecular pathways driving disease progression. The group is also interested in extracellular communication mechanisms, particularly the role of extracellular vesicles (EVs) and secreted metabolites in cancer development. By combining extracellular vesicle isolation technologies with RNA sequencing and metabolomic profiling, the laboratory seeks to identify biomarkers that reflect the molecular state of tumor cells and could be exploited for early diagnosis and patient stratification. Methodologically, the lab combines stem cell biology, genome engineering, organoid technology, multi-omics profiling, bioinformatics, and functional validation studies. This highly interdisciplinary approach enables the investigation of complex biological processes from multiple perspectives and facilitates the translation of basic discoveries into clinically relevant applications. Overall, the laboratory aims to uncover the molecular and metabolic determinants of cancer initiation, identify novel biomarkers for early detection, and reveal new therapeutic vulnerabilities that can ultimately improve patient outcomes.
Recent bibliography	- An in vivo "turning model" reveals new RanBP9 interactions in lung macrophages. CELL DEATH DISCOV 2025 Apr; 11: 171 - RANBP9 and RANBP10 cooperate in regulating non-small cell lung cancer proliferation. J EXP CLIN CANC RES 2025 Aug; 44: 259

	- MAFB: a key regulator of myeloid commitment involved in hematological diseases. CELL DEATH DISCOV 2025 Jun; 11: 276 - Reversal of MYB-dependent suppression of MAFB expression overrides leukaemia phenotype in MLL-rearranged AML. Cell Death Dis 2023 Nov; 14: 763 - SPINK2 silencing suppresses leukemic proliferation and restores myeloid commitment via MECOM downregulation in acute myeloid leukaemia. Cell Death Discov 2026 Mar; 12:
Group composition	2 Post-Doc, 2 PhD student, 3 Lab technicians
Institutional page link	https://www.uniba.it/en/