PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
promosso da: AIRC Fondazione CARIPLO | con il supporto di: IEMM Istituto Europeo di Medicina Molecolare, UNIVERSITÀ DEGLI STUDI DI MILANO

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	**PELLEGATA NATALIA SIMONA**
Institute of Affiliation	Università degli Studi di Pavia
Title of the proposed project:	Dissecting the molecular underpinnings of clinically relevant NET cell states to improve patients' outcome
Short description of the project	The AIRC-funded project explores the molecular basis of cancer cell plasticity in neuroendocrine tumors (NETs), especially in paragangliomas (PPGLs). It investigates how cells transition between pseudohypoxic and dedifferentiated states, processes linked to aggressive disease and poor prognosis. By decoding these dynamics, the project aims to reveal state-specific vulnerabilities and therapeutic opportunities, addressing a critical unmet clinical need. The candidate will combine experimental and computational approaches to dissect cell state transitions using the well-established PC12 model (PPGL). Guided by a bioinformatician, the physician scientist will analyze RNA-seq datasets to identify transcriptional programs driving the pseudohypoxic-to-dedifferentiated switch, applying differential expression and pathway analyses. Findings will be validated with qRT-PCR and extended to additional aggressive NETs (SCLC). The physician scientist will conduct CRISPR-based genome editing to modulate the expression of candidate transcription factors (TFs) driving cell plasticity such as ASCL1 and YAP1, along with novel TFs emerging from the RNASeq analyses, and will assess the impact of these factors on cell identity, differentiation, epithelial-mesenchymal traits, proliferation, migration, invasion, and metabolism across engineered cell lines. Advanced co-culture systems (primary tumor cells-cells from the tumor microenvironment) will be used to investigate inter-cellular interactions, elucidating how cellular heterogeneity and plasticity contribute to tumor progression and therapeutic vulnerability. These studies will enable the physician scientist to integrate multi-layered datasets spanning genomics, functional assays, and phenotypic analyses, to link molecular alterations to biological outcomes. This interdisciplinary training in molecular biology, genomics, bioinformatics, and translational cancer research will provide the candidate with a strong and versatile scientific skill set. In parallel, he/she will develop key competencies in experimental design, data interpretation, and scientific communication, necessary for careers in clinical or translational research, while empowering them to tackle complex biomedical challenges and contribute to the development of innovative precision medicine strategies aimed at improving outcomes for patients with aggressive NETs.
Main research area for the project	Cancer Biology
5 keywords for the project	Animal models - Drug response and/or resistance - Epithelial mesenchyme transition (EMT) – Metastasis - Neuroendocrine cancers

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LAB INFO	
Main topic/s of the lab	Translational cancer research
Short description of the lab activity	The PI of the host lab is an expert in cancer genetics, molecular and translational oncology, with a long-standing focus on neuroendocrine tumors (NETs) and on the mechanisms driving tumor progression and therapeutic response and resistance. She leads the Translational Cancer Genetics Laboratory (TCG Lab) at the University of Pavia, where research is centered on uncovering the molecular and functional basis of cancer development and aggressiveness, with particular emphasis on clinically challenging solid tumors, including NETs. The lab integrates multidisciplinary approaches combining cancer genetics, genomics, epigenetics, functional biology, cell metabolism to identify key pathways that regulate tumor behavior and plasticity. Experimental activities leverage clinically relevant in vitro models, including tumor cell lines, 3D/4D hydrogels to grow primary tumor organoids (with time-dependent features), 3D co-cultures, as well as in vivo xenografts, coupled with high-throughput genomic and transcriptomic analyses to characterize disease-relevant processes and therapy resistance/response. These experimental strategies are complemented by bioinformatic interrogation of large-scale datasets, enabling the identification of novel biomarkers and therapeutic targets in a data-driven manner. A major objective of the TCG Lab is to bridge mechanistic discoveries with clinical application. The group focuses on identifying actionable vulnerabilities of aggressive tumors and validating innovative therapeutic strategies, including single-agent and combinatorial treatments, in preclinical models. As an example of our multi-layers studies, please refer to a recently posted article on a drug combination with promising antitumor activity in paragangliomas (PPGL) where extensive in vitro testing in advanced models (including primary patient-derived cells) and in vivo evaluation were complemented by omics characterization of therapy response pathways to reveal a clinically actionable vulnerability in aggressive PPGLs and identify a prognostic gene signature with broad translational potential (https://www.biorxiv.org/content/10.1101/2025.02.18.638668v1). Through this translational framework, the TCG lab contributes to precision oncology by improving disease stratification, advancing early diagnostic markers, and developing tailored therapeutic approaches aimed at improving patient outcomes in aggressive NETs.
Recent bibliography	Angpt2/Tie2 autostimulatory loop controls tumorigenesis. EMBO MOL MED 2022 May; 14: e14364 Combined Targeting of Pathogenetic Mechanisms in Pancreatic Neuroendocrine Tumors Elicits Synergistic Antitumor Effects. CANCERS 2022 Nov; 14: Obesity and cancer-extracellular matrix, angiogenesis, and adrenergic signaling as unusual suspects linking the two diseases.

	CANCER METAST REV 2022 Sep; 41: 517 Mutation of the Cell Cycle Regulator p27kip1 Drives Pseudohypoxic Pheochromocytoma Development. CANCERS 2021 Jan; 13: Anti-secretory and anti-proliferative actions of next-generation dual subtype 2 and 5 somatostatin receptor ligands in neuroendocrine tumor models. Front Oncol 2026; 16: 1766563
Group composition	The research group consists of the Principal Investigator (PI), four PhD students, one early-career scientist, and four MSc students. The PI is responsible for defining the research strategy, overseeing the progress of all projects, supervising and mentoring junior researchers, and securing external funding. Each PhD student leads an individual research project while contributing to the supervision and training of MSc students. The early-career scientist supports ongoing research activities, provides technical and scientific expertise, and assists in mentoring junior group members. MSc students carry out their thesis projects under the supervision of the PI and the PhD students.
Institutional page link	https://dbb.dip.unipv.it/en/research/research-teams-and-topics/cancer-genetics/translational-cancer-genetics-laboratory-tcg
Lab website link	https://geneticslabunipv.wixsite.com/tcglab