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	**PAGANI MASSIMILIANO**
Institute of Affiliation	IFOM - Istituto Fondazione di Oncologia Molecolare, ETS
Title of the proposed project:	Mapping the Spatial Microenvironment and Cellular Plasticity in Metastatic Colo-rectal cancer
Short description of the project	Solid tumors represent complex entities shaped by diverse interactions occurring between malignant and stromal cells in a highly structured and heterogeneous ecosystem known as the tumor microenvironment (TME). Rather than acting as mere bystanders, non-tumoral tissue-resident cells critically shape tumor pathogenesis and therapeutic outcomes. Crucially, the cellular composition of the TME depends on the organ of origin and individual patient characteristics, shifting our perception of cancer from a purely genetic disease to a dynamic landscape of malignant and normal cell interactions. Among the most heterogeneous cancer types reside colon adenocarcinomas (CRC). Initially considered as a condition driven solely by a streamlined sequence of genetic alterations occurring in epithelial cells of the colon mucosa, recent findings have uncovered the prominent role of nongenetic cellular plasticity as a mean to promote metastasis and immune evasion in CRC. Several molecular studies have employed RNA sequencing at single-cell resolution to show an enrichment in proportions for specific TME cell phenotypes with putative function in the establishment of a pro-metastatic environment including specific pro-inflammatory cancer-associated fibroblasts (CAFs), tumor-associated macrophages (TAMs), and immunosuppressive regulatory T cells (Tregs) that correlate with worse prognosis. However, the exact spatial relationships, co-existence patterns, and ranges of interaction between these immune and cancer cells remain poorly understood. This doctoral project utilizes high-throughput technologies capable of retaining spatial resolution in situ to explore cancer cell plasticity. The study aims to identify key cellular states in primary CRC that initiate metastasis and link their functionality to the surrounding TME niche. By bridging phenotypic information with the original spatial architecture, the project will chart the spatial relationships between tumor, stromal, and immune cells (with particular emphasis on Tregs and TAMs). Ultimately, this research will highlight biologically meaningful and therapeutically actionable communication axes that elicit invasive phenotypes, providing ideal translational training for a physician-scientist.
Main research area for the project	Cancer Biology
5 keywords for the project	Treg cells – Microenvironment - Colorectal and/or Intestinal ca. – Metastasis - Transcriptome/Transcriptomics

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LAB INFO	
Main topic/s of the lab	Tumor immunology - cancer epigenetics
Short description of the lab activity	The Molecular Oncology and Immunology laboratory focuses its research on human colorectal cancer (CRC) to address its biological heterogeneity and the undelying mechanisms that promote metastatic progression. The lab's research interests are broadly divided into two complementary pillars: tumor immunology and cancer epigenetics. In Tumor Immunology, the lab investigates the intricate relationship between the human immune system and tumor progression. The primary focus is understanding how the tumor microenvironment (TME), specifically immunosuppressive populations like regulatory T cells (Tregs), promotes immune evasion and metastasis. The lab leverages high-resolution multi-omic strategies and advanced spatial transcriptomics to dissect the molecular, epigenetic, and spatial architecture of these immune cells. By mapping cell-cell communication networks directly in situ, the group aims to identify novel therapeutic targets capable of reversing local immunosuppression and reactivating robust anti-tumor immune responses. In Cancer Epigenetics, the lab studies the non-genetic elements that coordinate aberrant transcriptional programs driving cancer metastasis. Rather than focusing purely on genetic mutations, the group investigates how cellular plasticity and the reactivation of fetal or regenerative gene modules allow primary cancer cells to colonize distant organs. Central to this effort is the mapping of the metastatic "enhancerome", the complex network of genomic regulatory regions and upstream transcription factors that dictate aggressive cancer phenotypes. To bridge the gap between computational predictions and clinical application, the laboratory utilizes cutting-edge, translationally relevant experimental platforms. These include patient-derived tumor explants (PDTE) to study intact human tumor architecture ex vivo, and patient-derived organoid (PDO) originating from both primary tumors and metastatic sites. Together, these systems serve as advanced preclinical models to validate hypothesis and screen for novel therapeutic compounds.
Recent bibliography	An atlas of transcribed enhancers across helper T cell diversity for decoding human diseases. SCIENCE 2024 Jul; 385: eadd8394 Open-ST: High-resolution spatial transcriptomics in 3D. CELL 2024 Jul; 187: 3953 Clonally expanded EOMES+ Tr1-like cells in primary and metastatic tumors are associated with disease progression. Nat Immunol 2021 Jun; 22: 735 Epigenomic landscape of human colorectal cancer unveils an aberrant core of pan-cancer enhancers orchestrated by YAP/TAZ. Nat Commun 2021 Apr; 12: 2340

	A 3D morphogenetic blueprint for metastatic outgrowth in breast cancer. Cell 2026 Jun; 189: 3701
Group composition	Total members 18: Senior Scientists 3, Postdocs 7, PhD Students 4, Graduate Students 3, Master Students 1
Institutional page link	https://www.ifom.eu/it/
Lab website link	https://www.ifom.eu/it/ricerca-cancro/ricerca-lab/ricerca-lab-pagani.php