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

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	TRIPODO CLAUDIO
Institute of Affiliation	IFOM - Istituto Fondazione di Oncologia Molecolare, ETS
Title of the proposed project:	Perturbed hematopoiesis as a systemic driver of cancer evolution
Short description of the project	The PhD project will investigate how perturbed hematopoiesis shapes cancer evolution by modifying the host environment in which malignant clones expand, compete and adapt. The working hypothesis is that inherited or acquired alterations of hematopoiesis, including beta-globin defects, stress/extramedullary hematopoiesis and clonal hematopoiesis driven by lesions such as Dnmt3a or Tet2, generate systemic selective pressures that influence tumor growth, immune escape, tissue invasion, metastatic competence and treatment response. The project will use experimental cancer models in hematopoietically normal and perturbed hosts, with priority given to solid tumors but with the possibility of extending selected concepts to hematological malignancies when biologically appropriate. Tumor evolution will be assessed through longitudinal sampling, quantitative pathology, flow or mass cytometry, molecular profiling, single-cell and spatial transcriptomics, multiplex imaging and, where feasible, clonal tracking strategies. Particular attention will be given to how altered erythroid, myeloid and lymphoid output reshapes dendritic-cell function, T-cell priming, inflammatory set points, stromal organization and vascular or invasive-front niches. A specific exploratory axis will address whether iron availability, erythroid stress programs and macrophage iron-handling states contribute to tumor adaptation, and whether targeting iron metabolism, inflammatory myeloid circuits or hematopoiesis-derived immune suppression can modify tumor evolutionary trajectories. Host-conditioned tissue states will be integrated with tumor-intrinsic programs of proliferation, plasticity, DNA-damage response and immune evasion. The expected outcome is a spatially and mechanistically resolved framework linking abnormal hematopoiesis to cancer evolution, with candidate biomarkers and therapeutic vulnerabilities relevant to risk stratification, prevention of progression and precision treatment.
Main research area for the project	Cancer biology
5 keywords for the project	Hematopoiesis – Microenvironment - Transgenic mice - T cells/TCR - Ferroptosis

LAB INFO	
Main topic/s of the lab	Experimental pathology, digital pathology, spatial multi-omics and quantitative tissue analysis

Short description of the lab activity	The Advanced Pathology Laboratory at IFOM, coordinated by Prof. Claudio Tripodo, investigates how cancer progression is shaped by the spatial organization of tumor cells, stromal tissues, immune niches and systemic hematopoietic responses. The laboratory works at the interface of experimental pathology, tumor immunology, digital pathology and spatial biology, with the goal of understanding tumors as evolving tissue ecosystems rather than as isolated malignant cell populations. A central research focus is tumor heterogeneity. The lab studies how genetic, epigenetic and phenotypic diversification generates tumor subclones and regional tumor states with different proliferative, invasive, immune-evasive and therapy-resistant properties. These states are mapped in their native tissue context using quantitative histopathology, multiplex imaging, single-cell and spatial transcriptomics, and AI-assisted whole-slide image analysis. A second major area is stromal remodeling. The lab investigates how tumors reshape extracellular matrix, vascular structures, fibroblastic compartments and invasive-front regions to support growth, tissue invasion and metastatic dissemination. Particular attention is given to the way stromal architecture constrains or enables immune-cell access, lymphoid organization and local immune competence. The laboratory also studies tumor–immune interactions, including the formation of immunosuppressive niches, the exclusion or dysfunction of T cells, the organization of tertiary lymphoid structures and the role of myeloid and dendritic-cell states in tumor control or progression. These studies are designed to identify tissue configurations that explain differential immune surveillance and response to immunotherapy. A further research line addresses cancer-associated hematopoietic adaptation. The lab explores how tumors perturb bone marrow and extramedullary hematopoiesis, and how altered hematopoietic output feeds back on cancer progression through inflammatory, myeloid, erythroid and immune-regulatory circuits. This includes experimental and translational studies of perturbed hematopoiesis, stress erythropoiesis and clonal hematopoiesis as systemic modifiers of solid tumor evolution. Across these programs, the laboratory develops spatially resolved biomarkers that connect tissue morphology, cellular neighborhoods, molecular programs and clinical behavior. Its translational work uses FFPE samples, digital pathology, spatial multi-omics and computational tissue analysis to identify resistant tumor regions, host-conditioned aggressive states and candidate therapeutic vulnerabilities. The overall aim is to convert advanced tissue maps into mechanistic hypotheses and clinically useful tools for diagnosis, risk stratification and precision oncology.
Recent bibliography	Patterns of Oncogene Coexpression at Single-Cell Resolution Influence Survival in Lymphoma. CANCER DISCOV 2023 May; 13: 1144 Aggressive B-cell lymphomas retain ATR-dependent determinants of T-cell exclusion from the Germinal Center Dark Zone. J CLIN INVEST 2025 Sep; 135:

	B-cell Receptor Silencing Reveals the Origin and Dependencies of High-Grade B-cell Lymphomas with MYC and BCL2 Rearrangements. Blood Cancer Discov 2025 Jul; 6: 364 Tissue fluidification promotes a cGAS-STING cytosolic DNA response in invasive breast cancer. Nat Mater 2023 May; 22: 644 Spatially-resolved transcriptomics reveal macrophage heterogeneity and prognostic significance in diffuse large B-cell lymphoma. Nat Commun 2024 Mar; 15: 2113
Group composition	Olga Blazevits (Staff Scientist), Silvia Ripa (Post Doc), Emanuele Frigo (Physician Scientist), Emanuele Savino (Phd Student SEMM), Giada Lucia Cicio (Technician), Alice Ghiselli Ricci (Data Scientist), Maryam Mohammadi (Bioinformatician).
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