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

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	**MARCENARO EMANUELA**
Institute of Affiliation	Università degli Studi di Genova
Title of the proposed project:	Reprogramming NK cell dysfunction in breast and ovarian cancers to enhance immunotherapy efficacy
Short description of the project	The proposed PhD project aims to define the phenotypic, functional, and spatial heterogeneity of Natural Killer (NK) cells within the tumor microenvironment (TME) of women's cancers, focusing on breast and ovarian malignancies. Despite being key effectors of anti-tumor immunity, NK cells are frequently functionally impaired in solid tumors, where tumor-immune interactions and immune checkpoint pathways drive immune escape and heterogeneous responses to immunotherapy. Building on ongoing work in tumor immunology and NK-cell biology, including previous characterization of NK-cell receptor repertoires in breast and gynecological cancers, this project will integrate multi-omics (transcriptomics and proteomics) and functional approaches to define NK-cell states associated with immune dysfunction and clinical outcome. The candidate will combine multiparametric flow cytometry, in vitro functional assays, bulk and single-cell RNA sequencing, and spatial transcriptomics to generate a spatially resolved map of NK-cell biology across tumor tissue, blood, and clinically relevant compartments. A central goal is to decode receptor-ligand networks, immune checkpoint landscapes, and NK-cell spatial organization within tumor and stromal niches, to identify functionally relevant subsets and predictive biomarkers of response or resistance to immunotherapy. Mechanistic insights will be validated in vivo using tumor models to interrogate NK-tumor cell interactions in a physiologically relevant context and to test strategies aimed at restoring NK-cell function, including blocking monoclonal antibodies targeting immune checkpoints such as PD-1 and NKG2A. The project will be conducted at the Molecular Immunology Laboratory (DIMES), University of Genoa, in close collaboration with IRCCS AOU San Martino Hospital, where clinical samples will be collected. The candidate will be involved in translational research and may participate in clinical observation within breast and gynecological oncology units. This program will train a physician-scientist at the interface of tumor immunology, multi-omics, and translational oncology, aiming to develop more precise NK-cell-based immunotherapeutic strategies for women's cancers.
Main research area for the project	Immunology
5 keywords for the project	Breast ca. – Immunotherapy - NK and/or NKT cells - Cervix or endometrial ca. - Ovarian ca.

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AVAILABLE POSITIONS

LAB INFO	
Main topic/s of the lab	Tumor Immunology, Natural Killer (NK) Cell Biology, Cancer Immunotherapy, Translational Oncology.
Short description of the lab activity	The proposed PhD project will be carried out within the Molecular Immunology Laboratory, Department of Experimental Medicine (DIMES), University of Genoa, a multidisciplinary research environment encompassing complementary expertise in tumor immunology and cancer immunotherapy. Within the laboratory, Prof. Emanuela Marcenaro coordinates several research projects focused on tumor immunology and cancer immunotherapy and investigates the cellular and molecular mechanisms regulating anti-tumor immune responses, with particular emphasis on Natural Killer (NK) cells and their interaction with the tumor microenvironment. Building on a longstanding tradition of excellence in NK-cell biology and cancer immunology, the laboratory has contributed to the identification and functional characterization of key receptors and immune-regulatory pathways involved in tumor immune surveillance. This work has paved the way for the development of innovative immunotherapeutic approaches, including monoclonal antibodies targeting NK-cell inhibitory receptors that have progressed to clinical evaluation. Current research activities focus on understanding the mechanisms of tumor immune escape, deciphering the immune landscape of solid and hematological malignancies, and identifying novel biomarkers and therapeutic targets to improve cancer patient management. Particular attention is devoted to breast, ovarian, and other gynecological cancers, leveraging close interactions with clinical departments and translational research networks. The laboratory integrates state-of-the-art experimental and computational approaches, including: • High-dimensional flow cytometry and immune profiling; • Functional characterization of NK cells and other immune populations; • Isolation and analysis of primary immune and tumor cells from peripheral blood, tumor tissues and biological fluids; • Genomic, transcriptomic and multi-omics approaches; • Spatial characterization of the tumor microenvironment; • Advanced 3D culture systems and zebrafish xenograft models; • Bioinformatic and statistical analysis of large-scale datasets. A major strength of the laboratory is its strong translational orientation. Through established collaborations with oncologists, surgeons, pathologists and clinical researchers, the group has access to clinically annotated patient cohorts and biological samples, enabling the translation of mechanistic discoveries into clinically relevant applications. Ongoing studies aim to identify biomarkers of disease progression and treatment response, as well as novel targets for next-generation immunotherapies. The laboratory offers a highly collaborative and multidisciplinary environment where basic, translational and clinical research are tightly integrated.

	Physician-scientists joining the group will have the opportunity to develop expertise in tumor immunology, biomarker discovery and cancer immunotherapy while working at the interface between laboratory research and clinical medicine.
Recent bibliography	Untimely TGFβ responses in COVID-19 limit antiviral functions of NK cells. NATURE 2021 Dec; 600: 295 NKG2A and HLA-E define an alternative immune checkpoint axis in bladder cancer. CANCER CELL 2022 Sep; 40: 1027 The landscape of combining immune checkpoint inhibitors with novel Therapies: Secret alliances against breast cancer. CANCER TREAT REV 2024 Nov; 130: 102831 PD-1+ NK cell subsets in high grade serous ovarian cancer: an indicator of disease severity and a target for combined immune-checkpoint blockade. J Exp Clin Cancer Res 2025 Aug; 44: 258 Lactate-mediated NK cell dysfunction as a prognostic marker and therapeutic target in breast cancer. CELL DEATH DISCOV 2026 Mar; 12:
Group composition	In addition to the Principal Investigator, the laboratory currently includes 1 Associate Professor, 3 Postdoctoral Researchers, 2 PhD Students and 1 Early-Stage Researcher. The group also hosts Master's students, medical residents and visiting researchers, fostering a dynamic and interdisciplinary training environment.
Institutional page link	https://dimes.unige.it/
Lab website link	https://rubrica.unige.it/personale/UkNHWlJh