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

Principal Investigator	Marcenaro Emanuela
Hosting institution	Università degli Studi di Genova
Proposal title	Decoding Natural Killer Cell Function in the Tumor Microenvironment of Women's Cancers: from Bench to Bedside
Keywords	Breast ca.; Immunotherapy; NK and/or NKT cells; Combination therapy; Ovarian ca.
PhD project description	The proposed PhD project aims to dissect the phenotypic and functional diversity of Natural Killer (NK) cells in the tumor microenvironment (TME) of women's cancers, with a primary focus on breast and ovarian tumors. NK cells play a crucial role in immune surveillance, yet their activity is often impaired in solid tumors. Understanding the molecular and cellular mechanisms that shape NK cell dysfunction in the TME will support the identification of actionable immune targets. The candidate will integrate flow cytometry, in vitro functional assays, and next-generation sequencing approaches (bulk and/or single-cell RNA-seq) to characterize NK cells from tumor tissue, blood, and peritoneal fluids. Special attention will be given to receptor-ligand interactions, immune checkpoint expression, and the impact of tumor-derived signals on NK cell effector programs. In recent years, we have introduced transcriptomic analyses to complement our established immunophenotyping pipeline, and the PhD student will play a central role in this transition, contributing to the design and execution of multi-omics studies. The research will be hosted at the Molecular Immunology Lab, Department of Experimental Medicine (DIMES), University of Genoa, in close collaboration with IRCCS Ospedale Policlinico San Martino, where clinical samples will be collected. The candidate will be involved in two ongoing translational research projects focused on the immunobiology of high-grade serous ovarian carcinoma and breast cancers. Approximately 80% of the time will be dedicated to laboratory work; the remaining 20% will involve training and clinical observation in units such as Breast Surgery or Gynecologic Oncology, depending on the availability and agreement of the respective unit supervisors. The candidate will be directly supervised by the PI and supported in manuscript preparation, data dissemination, and participation in international grant applications. This project offers a unique opportunity to gain expertise at the interface of tumor immunology, genomics, and translational oncology.
Main topics of the lab	Our research aims to dissect NK-mediated immune regulatory mechanisms, identify novel immunotherapeutic targets, and translate findings into clinical applications.
Short description of the lab activity	Research Activities. The Molecular Immunology Laboratory at the Department of Experimental Medicine (DIMES), University of Genoa, is led by Prof. Emanuela Marcenaro, Full Professor of Histology and

	specialist in Clinical Pathology. The lab focuses on the immunological and molecular mechanisms underlying the interaction between immune cells and tumors, with a particular emphasis on the phenotype, function, and immune evasion strategies of human Natural Killer (NK) cells. Prof. Marcenaro's scientific career developed within the research team of Prof. Alessandro Moretta, a pioneer in the field of NK cell biology and anti-tumor immunotherapy. She has significantly contributed to the identification and functional characterization of numerous NK cell receptors and the generation of monoclonal antibodies (mAbs), several of which were patented for clinical use—such as anti-NKG2A antibodies (international patent no. PT2476705 E), currently employed in clinical trials. Research Focus and Objectives. The group integrates cutting-edge immunological, cellular, and molecular biology techniques to investigate both solid and hematological malignancies, with particular focus on breast, ovarian, and gynecological cancers. The overarching goal is to dissect the immune contexture of the tumor microenvironment and to identify new diagnostic and therapeutic targets, by: • Characterizing NK cell phenotypes and their functional responses in different tumor settings; • Studying tumor immune evasion mechanisms and tumor-infiltrating immune cells; • Identifying predictive biomarkers of disease progression and therapeutic response using multiparametric flow cytometry, functional assays, and genomic/transcriptomic approaches; • Employing 3D culture systems and in vivo zebrafish xenograft models; • Processing primary and immortalized cell lines in both adhesion and suspension; • Purifying lymphocyte subsets from peripheral blood, tumor tissues, and biological fluids; • Performing spatial biomarker analysis and big data analysis. Feasibility and Translational Relevance. The feasibility of the group's projects is supported by: • The strong scientific background of the PI and research team; • Complementary expertise in tumor immunology, NK cell biology, and immunotherapy; • Access to a wide panel of validated monoclonal antibodies (some originally developed in the lab); • Established technical platforms and methodologies; • National and international collaborations with leading research institutes and clinical units (including surgeons, pathologists, and oncologists); • Access to clinical samples from ongoing observational and translational studies. These elements ensure not only the robustness and innovation of the group's scientific investigations, but also their potential for meaningful clinical translation. The team is actively involved in clinical research and contributes to the development of novel immunotherapeutic strategies aimed at improving precision medicine approaches and patient outcomes.
Main research area	Immunology
Group composition	In addition to the Principal Investigator (PI), the lab currently includes 3 PhD students, 3 postdoctoral researchers, 1 early-stage researcher, and 1 associate professor. We also host several master's students and research interns involved in various ongoing projects. This

	multidisciplinary team collaborates closely to foster an enriching scientific environment combining mentorship, innovation, and translational impact.
Institutional page link	https://dimes.unige.it/
Lab website link	
Social media link	
Lab bibliography	Untimely TGFb responses in COVID-19 limit antiviral functions of NK cells. Witkowski M, Tizian C, Ferreira-Gomes M, Niemeyer D, Jones TC, Heinrich F, Frischbutter S, Angermair S, Hohnstein T, Mattiola I, Nawrath P, McEwen S, Zocche S, Viviano E, Heinz GA, Maurer M, Kölsch U, Chua RL, Aschman T, Meisel C, Radke J, Sawitzki B, Roehmel J, Allers K, Moos V, Schneider T, Hanitsch L, Mall MA, Conrad C, Radbruch H, Duerr CU, Trapani JA, Marcenaro E, Kallinich T, Corman VM, Kurth F, Sander LE, Drosten C, Treskatsch S, Durek P, Kruglov A, Radbruch A, Mashreghi MF, Diefenbach A NATURE 2021 Dec; 600: 295