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	**LUGLI ENRICO**
Institute of Affiliation	Humanitas Mirasole S.p.A.
Title of the proposed project:	Biomarkers of anti-tumor response in solid tumors treated with combination immunotherapy targeting immunosuppression
Short description of the project	Immune checkpoint blockade revolutionized cancer therapy but a number of patients fail to respond because of primary or secondary mechanisms of resistance, in many cases involving a suppressive architecture of the tumor microenvironment. Our lab has previously identified intratumoral and systemic T-cell characteristics associated with improved progression and enhanced response to cancer immunotherapy. Immunosuppressive T cell populations, particularly those with effector characteristics, play a critical role in blocking anti-tumor immune responses and are associated with poor prognosis across multiple solid tumor types. Preclinical data suggest that combining immunosuppressive T-cell depletion with anti-PD-1/PD-L1 immunotherapy enhances anti-tumor activity, yet its immunodynamic effects in humans are still unknown. At the Humanitas Research Hospital in Milan, we designed an innovative clinical trial targeting immunosuppressive T cell populations in combination with immune checkpoint blockade immunotherapy in metastatic solid tumor patients, with a major focus on translational endpoints and biomarker discovery. Serial multi-tissue biopsies and blood samples will be collected pre- and post-treatment to capture immune changes. Multiomics cellular, molecular and spatial technologies will profile circulating immune subsets, the spatial architecture of tumors and systemic changes to identify biomarkers undergoing modulation with, and predicting response to combination immunotherapy. Following results from this trial, we anticipate to conduct follow-up clinical and laboratory studies where the cohort of most sensitive tumors will be expanded and the combined immunotherapy optimized for improved efficacy. The successful MD candidate will have clinical expertise in solid tumor oncology and basic laboratory expertise in cellular immunology, molecular biology, biochemistry or related fields. Access to Humanitas facilities (flow cytometry, genomics, histology, microscopy, metabolomics and advanced bioinformatics) will be granted.
Main research area for the project	Immunology
5 keywords for the project	Cytotoxic T Lymphocytes (CTL) - Treg cells - Combination therapy - Clinical trials - Tumor-Infiltrating Lymphocytes (TIL)

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LAB INFO	
Main topic/s of the lab	Adaptive immunity, multiomics profiling of patients' samples, combination immunotherapy targeting the tumor microenvironment
Short description of the lab activity	Patients' follow up, blood and biopsies collection during combination immunotherapy, multiomics profiling (high-dimensional flow cytometry, single cell omics, proteomics, multimodal data integration), reporting results in scientific manuscripts
Recent bibliography	Multimodal single-cell profiling of intrahepatic cholangiocarcinoma defines hyperactivated Tregs as a potential therapeutic target. J HEPATOL 2022 Nov; 77: 1359 CD4+ Regulatory T Cells in Human Cancer: Subsets, Origin, and Molecular Regulation. CANCER IMMUNOL RES 2024 Apr; 12: 393 NaCl enhances CD8+ T cell effector functions in cancer immunotherapy. NAT IMMUNOL 2024 Oct; 25: 1845 Lymph-node-derived stem-like but not tumor-tissue-resident CD8+ T cells fuel anticancer immunity. NAT IMMUNOL 2025 Aug; 26: 1367 Distinct in vivo dynamics of donor-derived stem cell memory CAR T cells post-allogeneic HSCT relapse. CELL 2026 Jun; 189: 3686
Group composition	The lab involves 18 people (1 project leader, 5 postdocs, 6 PhD students, 3 technicians and 3 bioinformaticians) with expertise in cellular and molecular biology, technology development and bioinformatics.
Institutional page link	https://www.humanitas-research.com/
Lab website link	https://www.humanitas-research.com/groups/enrico-lugli-group/