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	**PELICCI PIER GIUSEPPE**
Institute of Affiliation	Istituto Europeo di Oncologia I.R.C.C.S. S.r.l.
Title of the proposed project:	Targeting metabolic vulnerabilities of circulating tumor cells to prevent metastatic relapse.
Short description of the project	Metastatic relapse remains the leading cause of cancer-related mortality despite major advances in surgery, systemic therapies, and (neo)adjuvant treatment strategies. Circulating tumor cells (CTCs), the obligate intermediates of metastatic dissemination, represent an attractive therapeutic target. However, the biology of viable CTCs remains poorly understood because their isolation and functional characterization are technically challenging, and no therapies targeting CTC-specific vulnerabilities are currently available. We developed a clinically relevant platform enabling large-scale isolation and functional interrogation of viable metastasis-derived CTCs (mCTCs) from patient-derived xenograft models. Using integrated clonal tracking, transcriptomic, metabolomic, and functional analyses, we identified a previously unrecognized adaptive state that enables CTC survival during hematogenous dissemination. This state is characterized by metabolic rewiring, suppression of mitochondrial activity, and activation of antioxidant programs. Importantly, disruption of this adaptive mechanism using a repurposed clinically available drug selectively impairs CTC fitness, reduces metastatic colonization, and markedly suppresses metastatic relapse in preclinical models (in preparation). The PhD project will investigate whether this metabolic vulnerability represents a general and therapeutically exploitable feature of metastatic dissemination. The candidate will: (i) determine the conservation of this adaptive program across multiple tumor types: breast cancer, melanoma, and lung cancer; (ii) evaluate the efficacy of CTC-targeting strategies alone and combined with chemotherapy and immune checkpoint blockade in models of minimal residual disease and metastatic cancer; and (iii) translate these findings to patients by developing microfluidic and imaging-based assays for functional characterization and pharmacological interrogation of human CTCs. This project integrates cancer biology, metastasis research, functional genomics, translational medicine, and early drug development. Clinical activities (20% of the training program) may be carried out at the Division of New Drugs for Innovative Therapies at IEO, directed by Prof. Giuseppe Curigliano. The project is embedded within a translational collaboration between the two laboratories, providing exposure to preclinical and clinical drug development.
Main research area for the project	Cancer Biology

5 keywords for the project	Oxidative stress and/or Reactive Oxygen Species (ROS) – Genomics - Circulating tumor cells – Metastasis - Metabolism/Metabolomics

LAB INFO	
Main topic/s of the lab	cancer biology, metastatic dissemination, therapy resistance, breast cancer, leukemia, genomics, transcriptomics
Short description of the lab activity	The ultimate goal of our lab research is the identification of novel tools to improve cancer patient treatment, rooted in the biological mechanisms underlying therapy resistance and metastatic dissemination, which represent two of the main challenges in cancer research nowadays. To this end, we combine preclinical in vitro and in vivo biological-experimental and computational approaches, focusing on two tumor models: breast cancer —as an example of solid tumor— and acute myeloid leukemia —as an example of hematological tumor. The ground hypothesis lies in the increasing experimental evidence indicating that the stress cells undergo during metastatization and upon chemotherapy, albeit different, results in the selection of tumor cells with similar traits enabling them to survive, proliferate (and disseminate). At the same time, such features represent vulnerabilities: If cancer cells rely on such mechanisms to survive in hostile stressful conditions of the tumor microenvironment, interfering with such processes is likely to kill them. A comprehensive understanding of these mechanisms is thus of pivotal importance to identify novel potentially targetable cancer vulnerabilities. In this scenario, our current research activities aim at i. unveiling mechanisms inducing the acquisition by cancer cells of features enabling dissemination and therapy resistance, in breast cancer and leukemia, by investigating —and integrating— genomic and transcriptomic information, exploiting gold standard and innovative model systems; ii. identifying novel approaches exploitable in the future in a therapeutic setting, by leveraging immunotherapy-based approaches and nanoparticles-delivered RNA-based treatment strategies; iii. investigating epigenetics-related molecular mechanisms of aging possibly predisposing to cancer.
Recent bibliography	High-resolution Nanopore methylome-maps reveal random hyper-methylation at CpG-poor regions as driver of chemoresistance in leukemias. Commun Biol 2023 Apr; 6: 382 A rare subset of primary tumor cells with concomitant hyper-activation of extracellular matrix remodeling and dsRNA-IFN1 signaling metastasizes in breast cancer. CANCER RES 2023 Jul; 83: 2155 Caloric restriction leads to druggable LSD1-dependent cancer stem cells expansion. NAT COMMUN 2024 Jan; 15: 828 Mechanical load inhibits cancer growth in mouse and human hearts. SCIENCE 2026 Apr; 392: eads9412

	MiTo: tracing the phenotypic evolution of somatic cell lineages via mitochondrial single-cell multi-omics. NAT COMMUN 2026 May;
Group composition	Our group includes six staff scientists, eight post-doctoral fellows, eight PhD students, three technicians, two undergraduate students, with both experimental and computational expertise.
Institutional page link	https://www.research.ieo.it/
Lab website link	https://www.research.ieo.it/research-and-technology/principal-investigators/pier-giuseppe-pelicci/