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

Principal Investigator	Cea Michele
Hosting institution	Università degli Studi di Genova
Proposal title	Targeting Metabolic Reprogramming to Improve Therapeutic Outcomes in Multiple Myeloma
Keywords	Drug response and/or resistance; Epithelial mesenchyme transition (EMT); Biomarkers; Myeloma; Metabolism/Metabolomics
PhD project description	Multiple myeloma (MM) remains an incurable malignancy due to drug resistance and disease relapse. Increasing evidence indicates that metabolic reprogramming plays a crucial role in enabling MM cells to evade therapy and survive within the bone marrow microenvironment. This PhD project aims to investigate the clinical and therapeutic relevance of metabolic rewiring in MM, with the goal of identifying novel metabolic vulnerabilities that can be targeted to overcome resistance and improve patient outcomes. The student will integrate in vitro studies, patient-derived samples, and multi-omics approaches (metabolomics, transcriptomics) to define key metabolic pathways associated with resistance to both standard-of-care and emerging therapies. Focus will be given to the interaction between MM cells and the immune microenvironment under metabolic stress conditions, such as fasting or pharmacological NAD+ depletion. To identify actionable metabolic targets, the project will also incorporate a functional CRISPR-Cas9 knockout screen focused on metabolic and stress response genes. This approach will allow the discovery of genes essential for MM cell survival under therapeutic and nutrient-restricted conditions, providing mechanistic insights and guiding the development of combination strategies. In collaboration with clinical departments, the student will access longitudinal bone marrow and peripheral blood samples from MM patients undergoing therapy, including those enrolled in clinical trials investigating metabolic interventions. These samples will enable validation of laboratory findings and correlation with treatment response and minimal residual disease (MRD) status. The project offers a unique opportunity to work in a highly translational setting, fostering strong interaction between laboratory research and clinical practice. The student will be based at IRCCS Ospedale Policlinico San Martino-University of Genoa, within a multidisciplinary team of hematologists, molecular biologists, and data scientists. Clinical duties, if applicable, may be carried out at the Clinic of Hematology and Bone Marrow Transplantation Unit, one of the leading centers for MM treatment in Europe.
Main topics of the lab	Our lab investigates metabolic and immune vulnerabilities in multiple myeloma to develop innovative, mechanism-based therapies that overcome drug resistance and improve patient outcomes.
Short description of the	Our laboratory is dedicated to uncovering the metabolic and

lab activity	immunologic mechanisms that sustain multiple myeloma (MM) progression, therapy resistance, and immune evasion. We apply an integrative and translational approach that combines functional genomics (including CRISPR-Cas9 screening), metabolomics, transcriptomics, and advanced in vitro and in vivo models. A key focus is on targeting metabolic vulnerabilities, such as NAD^+ metabolism, redox homeostasis, and mitochondrial function, to enhance the efficacy of standard and emerging MM therapies. We are particularly interested in how metabolic stress, including fasting-mimicking strategies or pharmacologic interventions, modulates the tumor–immune microenvironment and can be harnessed to improve responses to immunotherapies such as bispecific antibodies and CAR-T cells. By bridging basic science and clinical research, our goal is to develop innovative, mechanism-based therapeutic strategies with direct impact on patient care. The lab operates within a multidisciplinary environment, with strong collaborations between molecular biologists, hematologists, immunologists, and bioinformaticians, and access to clinical samples from MM patients enrolled in therapeutic trials.
Main research area	Cancer biology
Group composition	he research group is composed of a multidisciplinary team of 9 members: 1 Principal Investigator 1 Senior Researcher 2 Postdoctoral Fellows 1 PhD Student 1 Research Technician 1 Bioinformatician 2 Clinical Collaborators (associated members) The team combines expertise in molecular biology, hematology, immunology, and functional genomics, and works in close collaboration with clinical departments and core facilities to advance translational research in multiple myeloma.
Institutional page link	https://dimi.unige.it/
Lab website link	
Social media link	
Lab bibliography	Amino acid depletion triggered by -asparaginase sensitizes MM cells to carfilzomib by inducing mitochondria ROS-mediated cell death. Soncini D, Minetto P, Martinuzzi C, Becherini P, Fenu V, Guolo F, Todoerti K, Calice G, Contini P, Miglino M, Rivoli G, Aquino S, Dominietto A, Cagnetta A, Passalacqua M, Bruzzone S, Nencioni A, Zucchetti M, Ceruti T, Neri A, Lemoli RM, Cea M Blood Adv 2020 Sep; 4: 4312