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

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	**GIACOMINI ARIANNA**
Institute of Affiliation	Università degli Studi di Brescia
Title of the proposed project:	Novel small molecule FGF traps as drug candidates for cancer therapy: from biophysical screening to in vivo validation
Short description of the project	The fibroblast growth factor (FGF)/FGF receptor (FGFR) signalling pathway is a key driver of tumor progression, promoting cancer cell proliferation, survival, angiogenesis, and resistance to therapy. Aberrant activation of this pathway is frequently observed across multiple cancer types and represents a major mechanism of escape from anti-angiogenic treatments. Although FGFR tyrosine kinase inhibitors have shown clinical efficacy, their use is often limited by systemic toxicity, on-target/off-tumor effects, and acquired resistance. To overcome these limitations, our research focuses on an innovative therapeutic strategy based on small-molecule FGF traps. We previously identified NSC12, the first orally available pan-FGF trap capable of inhibiting tumor growth and angiogenesis in several preclinical cancer models (Ronca and Giacomini et al., Cancer Cell, 2015). Despite these promising results, NSC12 displays suboptimal pharmacological properties that prevent its further development. In collaboration with Prof. Mor's laboratory at the University of Parma, we recently generated a novel series of non-steroidal NSC12 derivatives with improved chemical and pharmacological properties. Preliminary structure-activity relationship studies identified molecular determinants regulating FGF binding and selectivity, providing a framework for the rational optimization of next-generation compounds. The aim of this project is to develop highly selective small-molecule FGF traps with enhanced affinity, drug-like properties, and anti-tumor activity. We will integrate computational drug design, medicinal chemistry, biophysical characterization of ligand-FGF interactions, and functional validation in FGF-dependent biological systems by using in vitro, ex vivo and in vivo models. Lead compounds will be evaluated for (i) anti-angiogenic activity, (ii) anti-tumor activity in relevant human models, including aggressive non-Hodgkin lymphomas, and (iii) toxicity. By targeting extracellular FGF ligands rather than intracellular FGFR kinase activity, this project proposes a first-in-class therapeutic strategy expected to overcome the limitations of current FGFR inhibitors. Successful completion will provide novel drug candidates and establish a broadly applicable platform for treating FGF-driven malignancies.
Main research area for the project	Cancer biology
5 key words for the project	Lymphomas, Target therapy, FGF and/or receptor, Small molecule inhibitors

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LAB INFO	
Main topic/s of the lab	Hematological malignancies, with particular focus on multiple myeloma and aggressive non-Hodgkin lymphomas
Short description of the lab activity	The research group led by Prof. Arianna Giacomini at the Department of Molecular and Translational Medicine, University of Brescia, focuses on identifying and validating new therapeutic targets for hematological cancers, with particular focus on multiple myeloma and aggressive non-Hodgkin lymphomas. Their research aims to: - Identify molecular pathways that drive tumor growth, survival and dissemination. - Develop innovative targeted therapies, including inhibitors of the FGF/FGFR signaling pathway and carbonic anhydrase IX (CAIX). - Investigate novel therapeutic strategies, such as FGF-trapping molecules, to interfere with the tumor microenvironment and angiogenesis. - Translate laboratory discoveries into potential clinical applications for patients with hematological malignancies. Ongoing research projects: NON-HODGKIN LYMPHOMAS: - Blocking the FGF/FGFR system as a new therapeutic strategy for c-Myc-driven aggressive B-cell non-Hodgkin lymphoma MULTIPLE MYELOMA: - Therapeutic potential of Carbonic Anhydrase IX inhibitors in multiple myeloma - Role of the long non-coding RNA MIAT on the growth and progression of multiple myeloma
Recent bibliography	- Halting the FGF/FGFR axis leads to anti-tumor activity in Waldenström's Macroglobulinemia by silencing MYD88. BLOOD 2021 May; 137: 2495 - Chemical modification of NSC12 leads to a specific FGF-trap with antitumor activity in multiple myeloma. EUR J MED CHEM 2021 Oct; 221: 113529 - Discovery of novel FGF trap small molecules endowed with anti-myeloma activity. PHARMACOL RES 2024 Aug; 206: 107291 - The FGF/FGFR/c-Myc axis as a promising therapeutic target in multiple myeloma. J EXP CLIN CANC RES 2024 Nov; 43: 294 - FGF/FGFR inhibitors downmodulates c-Myc oncoprotein and hampers the growth of adrenocortical carcinoma. BIOMED PHARMACOTHER 2025 Nov; 192: 118677
Group composition	Prof. Giacomini's research group currently comprises three postdoctoral fellows, one PhD student, one Master's student enrolled in the Medical Biotechnologies program, and one Bachelor's student in Biotechnologies.
Institutional page link	https://www.unibs.it/it
Social media links	https://www.instagram.com/giacomini_bloodcancerlab/