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	**ORSO FRANCESCA**
Institute of Affiliation	Università degli Studi del Piemonte Orientale "Amedeo Avogadro"
Title of the proposed project:	DEMO-BRCA: Deciphering the Epigenetic and Microenvironmental Modifiers of BRCA1/2-Driven Tumor Onset
Short description of the project	Germline mutations in BRCA1/2 significantly elevate the lifetime risk of developing a spectrum of aggressive malignancies. While BRCA1/2 mutations are notoriously tied to breast and ovarian cancers, they also elevate risks for pancreatic and prostate malignancies. The striking variation in age of onset and tissue specificity among carriers indicates that secondary microenvironmental and epigenetic modifiers govern penetrance. Defective DNA repair in these carriers drives a premature aging phenotype-marked by systemic chronic inflammation, cellular senescence, and immune exhaustion-while tissue-specific triggers, such as local microbial dysbiosis act as critical oncogenic catalyst. MicroRNAs (miRNAs) serve as critical epigenetic rheostats; however, how the alteration of specific miRNA networks interacts with underlying BRCA1/2 deficiencies to drive cellular transformation remains poorly understood. We hypothesize that BRCA1/2 mutations establish a baseline state of accelerated tissue aging, which disrupts host miRNA expression profiles. This altered non-coding RNA landscape interacts synergistically with local microbial dysbiosis to epigenetically reprogram pre-malignant cells, ultimately dictating tissue-specific tumor onset and explaining incomplete penetrance. In collaboration with the Gynecology Division, University of Torino, Ospedale Mauriziano, Italy, we plan to: • Perform small RNA-sequencing alongside single-cell RNA-seq/ATAC-seq on pre-malignant tissues from young mutation carriers and controls to identify dysregulated miRNA signatures associated with accelerated cellular senescence, epithelial identity shifts, and immune exhaustion. • Utilize patient-derived organoid models to determine how microbial dysbiosis, bacterial genotoxins, and microbial-derived estrogen metabolites modulate host miRNA networks, and evaluate how these non-coding RNAs drive localized genomic instability. • Analyze longitudinal blood/plasma samples from mutation carriers to correlate shifts in circulating miRNAs with the onset of cellular senescence and early-stage tumorigenesis across different organs. The project will elucidate how miRNAs translate tissue-specific microbial stress and premature aging into oncogenic signals, aiming to uncover non-invasive, miRNA-based predictive biomarkers for multi-organ tumor onset and identify targeted RNA-based prevention strategies for high-risk carriers.
Main research area for the project	Cancer biology
5 keywords for the project	Breast ca. - Aging and cancer – microRNA – Organoids - Cell metabolism

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LAB INFO	
Main topic/s of the lab	Molecular Oncology
Short description of the lab activity	The laboratory focuses on studying microRNAs (miRNAs) involved in age-related pathologies, with a primary emphasis on cancer. Specifically, our research aims to identify miRNAs driving the progression of breast cancer and osteosarcoma. Ultimately, we seek to develop innovative miRNA-based therapeutics and diagnostic tools to improve the clinical management of these malignancies. Given their stable presence in various bodily fluids, miRNAs serve as promising non-invasive biomarkers for both oncology and aging-related diseases. Currently, our main research efforts are dedicated to understanding the driving factors behind the rising incidence of breast cancer in young women over the past decade, with the goal of identifying specific miRNA biomarkers for the prevention and early detection of early-onset breast cancer.
Recent bibliography	ESDN inhibits melanoma progression by blocking E-selectin expression in endothelial cells via STAT3. CANCER LETT 2021 Jul; 510: 13 Dihydroorotate dehydrogenase inhibition reveals metabolic vulnerability in chronic myeloid leukemia. CELL DEATH DIS 2022 Jun; 13: 576 Stroma-derived miR-214 coordinates tumor dissemination. J EXP CLIN CANC RES 2023 Jan; 42: 20 Emerging roles of 3D-culture systems in tackling tumor drug resistance. Can Drug Res 2023; 6: 788 The chimeric aptamer axl-miR-214sponge inhibits breast cancer and melanoma dissemination. Mol Ther 2025 Nov; 33: 5804
Group composition	2 Post-doc fellows 1 PhD student 3 Master students
Institutional page link	https://upobook.uniupo.it/francesca.orso
Social media link	https://www.linkedin.com/in/francesca-orso-b34135163/