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	**BRANCOLINI CLAUDIO**
Institute of Affiliation	Università degli Studi di Udine
Title of the proposed project:	Targeting Epigenetic and 3D Genome Vulnerabilities in Uterine Leiomyosarcoma
Short description of the project	Uterine leiomyosarcoma (uLMS) is a rare and highly aggressive uterine cancer characterized by poor prognosis, high rates of metastasis, and limited therapeutic options. Although recurrent genetic alterations have been identified, these alone do not fully explain the disease's aggressive behavior or resistance to treatment. This project hypothesizes that uLMS progression is driven by extensive remodeling of enhancer networks and three-dimensional chromatin architecture, which establish oncogenic gene expression programs that promote tumor growth, metastasis, and therapy resistance. To investigate this hypothesis, the project in collaboration with the Dipartimento Mamma-Bambino (Azienda Ospedaliera Universitaria Friuli Centrale), will integrate patient-derived models with advanced multi-omics approaches and CRISPR-based epigenome engineering. First, a biobank of normal myometrium, uterine leiomyoma, and uLMS tissues, together with primary cell cultures and patient-derived organoids, will be established to provide robust experimental models. Second, the epigenetic and three-dimensional chromatin landscape of uLMS will be characterized using whole-genome sequencing, RNA sequencing (scRNA-seq), ChIP-seq (H3K27ac), and HiChIP. These complementary techniques will identify active enhancers, super-enhancers, chromatin interactions, and regulatory networks that are uniquely altered in malignant tissues. The final phase of the project will functionally validate candidate oncogenic distal regulatory elements using CRISPR interference (dCas9-KRAB) to silence selected enhancers. The effects on cell proliferation, invasion, apoptosis, drug sensitivity, and gene expression will determine whether these regulatory elements are essential for maintaining the malignant phenotype and therefore represent potential therapeutic targets. The expected outcome is the first comprehensive atlas of enhancer activity and chromatin organization in uLMS, providing new insights into the epigenetic mechanisms underlying tumor development and progression. Beyond advancing the understanding of uLMS biology, the project will generate valuable patient-derived resources, identify novel biomarkers for diagnosis and prognosis, and uncover enhancer-dependent molecular vulnerabilities that could support the development of innovative epigenetic therapies and precision medicine strategies for this devastating disease.
Main research area for the project	Cancer biology
5 key words for the project	Histone modifications, Gene expression and/or profile, Epigenetics, Soft tissue tumors, CRISPR/Cas9

LAB INFO	
Main topic/s of the lab	Epigenetics-Senescence-Apoptosis
Short description of the lab activity	Neoplastic transformation occurs when cells acquire alterations that enable them to evade the restrictive mechanisms normally active in our tissues, primarily senescence and cell death. This is driven by the accumulation of DNA mutations and epigenetic changes. The laboratory is interested in elucidating the epigenetic mechanisms underlying neoplastic transformation and drug resistance. One model we use is the axis formed by MEF2 transcription factors and their epigenetic regulators, the class IIa HDACs. Our main tumour model is uterine leiomyosarcoma, a rare and aggressive cancer with limited treatment options. In this context, through a collaboration with the Department of Gynaecology at the University of Udine, the laboratory applies advanced epigenomic and genomic characterisation techniques to sophisticated cell models derived from patients with LMS. The most important results recently published by the lab are: 1. Identification of new compounds with antineoplastic activity against uterine leiomyosarcoma cells 2. Characterisation of the role of HDAC4 in regulating the epigenetic environment at sites of DNA damage 3. Insight into the regulation of super-enhancers during oncogene-induced senescence 4. Elucidation of the epigenetic mechanisms underlying the action of epigenetic drugs 5. Definition of the role of MEF2 and class IIa HDACs in regulating the proliferative aggressiveness of uterine leiomyosarcoma cells
Recent bibliography	- Changes in chromatin accessibility and transcriptional landscape induced by HDAC inhibitors in TP53 mutated patient-derived colon cancer organoids. BIOMED PHARMACOTHER 2024 Apr; 173: 116374 - Transcription of endogenous retroviruses in senescent cells contributes to the accumulation of double-stranded RNAs that trigger an anti-viral response that reinforces senescence. CELL DEATH DIS 2024 Feb; 15: 157 - HDAC4 influences the DNA damage response and counteracts senescence by assembling with HDAC1/HDAC2 to control H2BK120 acetylation and homology-directed repair. NUCLEIC ACIDS RES 2024 Aug; 52: 8218 - Identification of a novel minor-groove DNA binder that represses mitochondrial gene expression and induces apoptosis in highly aggressive leiomyosarcoma cells. CELL DEATH DISCOV 2025 Nov; 11: 524 - Transcriptomic and genomic studies classify NKL54 as a histone deacetylase inhibitor with indirect influence on MEF2-dependent transcription. Nucleic Acids Res 2022 Mar; 50: 2566
Group composition	Martina Minisini – Postdoctoral Researcher Martina Mascaro – Postdoctoral Researcher Alessio Bertozzo – PhD Student, Bioinformatician Emanuele Cricchi – PhD Student Gabriele

	Bandolini – PhD Student Francesca D'Este – Research Technician (Advanced Microscopy) Raffaella Picco – Bioinformatician
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