PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
promosso da: AIRC Fondazione CARIPLO | con il supporto di: SIF/MMC European Group on Molecular Medicine | UNIVERSITÀ DEGLI STUDI DI MILANO

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	BARDELLI ALBERTO
Institute of Affiliation	Università degli Studi di Torino
Title of the proposed project:	Targeting Metastatic Prowess with Translational Oncology
Short description of the project	The candidate will join IFOM (The AIRC Institute of Molecular Oncology) and the Bardelli laboratory in the heart of Milan, an internationally recognised hub for translational oncology, with long-standing expertise in genomics, patient-derived models, multiomics and artificial intelligence applied to colorectal (CRC) and other cancers. The project will dissect the biological basis of intrinsic tumour aggressiveness through the "born to be bad" (BBB) versus "born to be good" (BBG) framework. BBB tumours are micrometastatic from the outset, persist as minimal residual disease (MRD) after surgery and recur, whereas BBG tumours remain localised and are cured by surgery alone. No clinical biomarker currently distinguishes these phenotypes, and patients are often treated alike. The candidate will work across three integrated objectives: (i) liquid biopsy/ctDNA-guided clinical trials - building on studies such as PEGASUS, that tailor adjuvant therapy in resected colon cancer according to MRD status; (ii) functional drug screening on patient-derived "avatars" (2D lines, 3D organoids and xenopatients) to dissect mechanisms of primary and acquired resistance, including drug-tolerant persister cells, and to identify new and repurposed therapies; (iii) translation of laboratory programmes into early-phase clinical trials, with particular emphasis on DNA-repair vulnerabilities as therapeutically actionable determinants of tumour evolution and immune responsiveness. According to candidate preferences, training will combine wet-lab techniques (organoid manipulation, drug-screening assays, in vivo modelling) and dry-lab skills (bioinformatics, machine learning, AI-based "pathomics") to foster a true physician-scientist profile able to bridge laboratory research, clinical trials and new drug development. A defining feature will be weekly clinical activity in a high-level oncology setting, ensuring continuous communication between laboratory and hospital and a genuine bench-to-bedside loop. The PhD environment is international and multidisciplinary, bringing together physicians, molecular biologists and bioinformaticians, and prepares graduates for future leadership in precision oncology.
Main research area for the project	Genomic medicine
5 key words for the project	Genomics, Chemotherapy and/or chemotherapic drugs, colorectal and/or intestinal ca., Clinical trials, Liquid biopsy

LAB INFO	
Main topic/s of the lab	Genomics of Cancer and Targeted Therapies
Short description of the lab activity	Our research is focused specifically on precision oncology for CRC, in particular on the characterization of tumor heterogeneity

	and mechanisms of tumor evolution during therapy administration, with the final aim to identify novel vulnerabilities and therapeutic strategies to prevent or delay the onset of resistance, thus improving survival of cancer patients. In addition, we recently unveiled that cancer cells, alike bacteria in response to antibiotic stress, adaptively down-modulate DNA mismatch repair and homologous recombination proteins, and switch to an error prone-mediated DNA replication process in presence of increased DNA damage when exposed to targeted therapy. Furthermore, immune checkpoint inhibitors have been shown to induce durable responses in a subset of approximately 5% patients with metastatic CRC that carry defective mismatch repair or are microsatellite unstable (MSI). We discovered that inactivation of MMR genes in microsatellite stable (MSS) immune refractory CRCs leads to immune surveillance and response to immune therapy and proposed that this could be pursued for therapeutic purposes. These results led to the ongoing clinical trial ARETHUSA. By using CRC 2D cell lines, 3D patients-derived organoids and xenopatients we defined the mechanisms of primary and secondary resistance to targeted therapies, including how metastatic CRC escape from EGFR, BRAF, TRK, and HER2 inhibition. The use of cancer cell models that replicate the same molecular traits exhibited by tumors of interest in the body, along with the ability to derive them from human samples, enables a detailed study of various aspects of tumor biology, such as the signals driving uncontrolled proliferation. These models also allow for the evaluation of the effectiveness of different anticancer therapies, including immunotherapy. In essence, these models serve as patient-specific "avatars", making it possible to experiment with different treatment approaches to identify the most effective therapeutic options for each individual patient. In addition to analyzing the genetic profiles of tumors and identifying correlations-referred to as pharmacogenomic associations-between drug activity profiles and the genetic profiles of malignant cells, the laboratory is dedicated to exploring the relationship between the genome and various "omics" disciplines (the study of different molecules derived from genome transcription and their interactions with it), including transcriptomics, methylomics, proteomics, metabolomics, and more. This approach involves an in-depth investigation of the molecular foundations of cancer and resistance to various treatments, with a particular focus on the mechanisms underlying its development.
Recent bibliography	- Genetic and pharmacological modulation of DNA mismatch repair heterogeneous tumors promotes immune surveillance. CANCER CELL 2023 Jan; 41: 196 - Circulating tumor DNA to guide rechallenge with panitumumab in metastatic colorectal cancer: the phase 2 CHRONOS trial. NAT MED 2022 Aug; 28: 1612

	- Cancer drug-tolerant persister cells: from biological questions to clinical opportunities. NAT REV CANCER 2024 Oct; 24: 694 - Cisplatin and temozolomide combinatorial treatment triggers hypermutability and immune surveillance in experimental cancer models. CANCER CELL 2025 Jul; 43: 1296 - Pharmacological inhibition of PMS2 induces MMR deficiency and response to immune checkpoint blockade. CANCER DISCOV 2026 Apr; :
Group composition	Postdocs: 12 PhD Students: 7 Technicians: 3 Staff Scientists: 2
Institutional page link	https://www.mbc.unito.it/it/genomics-cancer-and-targeted-therapies
Lab website link	https://www.mbc.unito.it/it/genomics-cancer-and-targeted-therapies
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