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

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	**GAGLIARDI PAOLO ARMANDO**
Institute of Affiliation	Università degli Studi di Torino
Title of the proposed project:	Multiplexed single-cell measurements of ERK/JNK/p38 dynamics to predict colorectal cancer response to chemotherapy
Short description of the project	Even genetically identical cancer cells can show heterogeneous responses to therapy. Some cells die rapidly, others die only after prolonged treatment, while others enter drug-tolerant states and survive despite therapy. An intriguing possibility is that intrinsic cellular variability and microenvironmental cues place cancer cells in distinct dynamic signaling states that ultimately shape therapeutic response. However, signal transduction is highly dynamic and remarkably variable at the single-cell level. For example, epithelial mammary cells display pulsatile MAPK/ERK activity when monitored by live microscopy using fluorescent biosensors, and the frequency of ERK pulses correlates with cell survival or death upon treatment with doxorubicin. The field of fluorescent biosensors is rapidly expanding and now includes reporters for stress-response pathways such as JNK and p38-MAPK, both of which are critically involved in cancer cell responses to drug-induced stress. We hypothesize that multiplexed live-cell biosensor measurements can reveal dynamic signaling states that predict therapeutic response in colorectal cancer. We will combine fluorescent reporters for MAPK/ERK, JNK and p38-MAPK in colorectal cancer models ranging from established cell lines to cancer organoids treated with clinically relevant chemotherapeutic agents, including 5-FU, irinotecan, oxaliplatin and combination regimens such as FOLFIRI. This approach will generate single-cell temporal measurements from thousands of cells, linking pathway dynamics to cell fate decisions such as mitosis, apoptosis, arrest, and survival. Computational analysis will be used to extract temporal and spatial features of signaling across the three pathways and identify dynamic fingerprints associated with sensitivity, delayed response, or drug tolerance. Finally, pharmacological and genetic perturbations of critical pathway nodes will test whether these signaling states can be shifted to enhance chemotherapy-induced cell death or prevent the emergence of tolerant cells. The long-term goal is to identify rational combinations of colorectal cancer chemotherapeutic agents with modulators of MAPK, JNK, or p38 signaling to improve therapeutic efficacy.
Main research area for the project	Cancer biology
5 key words for the project	Cell signaling, Chemotherapy and/or chemotherapic drugs, MAP Kinases, In vitro imaging and/or live cell imaging, Fluorescence imaging system

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LAB INFO	
Main topic/s of the lab	Cancer Cell Dynamics
Short description of the lab activity	The lab activity follows two main research lines: 1) Decoding ERK Signaling Dynamics to Improve Therapies for KRAS-Mutated Cancers We investigate how cancer cells dynamically process signals through the MAPK/ERK pathway in the presence of KRAS mutations. Using fluorescent biosensors, live-cell imaging, and single-cell analysis, we uncover how KRAS mutations distort ERK activity patterns and collective signaling waves that shape cell survival, proliferation, and drug response. We study how next-generation KRAS inhibitors modulate these dynamics and why resistance frequently emerges. By integrating experimental data with computational analyses, we identify drug combinations that specifically target altered signaling behaviors. Ultimately, we aim to enhance the effectiveness of KRAS-targeted therapies and develop biomarkers that capture signaling dynamics in clinically relevant samples. 2) Targeting ERK Survival Waves to Boost Chemotherapy Effectiveness We investigate how dying tumour cells transmit protective ERK signalling waves that help neighbouring cells resist chemotherapy. Using fluorescent biosensors, automated live-cell imaging, and single-cell analysis, we quantify how apoptosis triggers these collective ERK activation events across multiple cancer types and treatments. We dissect the secreted factors and signalling pathways that enable ERK waves to propagate, identifying molecular nodes that can be selectively blocked. By combining chemotherapies with inhibitors of ERK wave propagation, we aim to enhance cell killing and overcome community-driven chemoresistance. Finally, we validate these combinations in patient-derived organoids to establish a translational framework for improving therapeutic response across diverse cancers.
Recent bibliography	- Spatiotemporal control of ERK pulse frequency coordinates fate decisions during mammary acinar morphogenesis. DEV CELL 2022 Sep; 57: 2153 - Optogenetic actuator - ERK biosensor circuits identify MAPK network nodes that shape ERK dynamics. MOL SYST BIOL 2022 Jun; 18: e10670 - Collective ERK/Akt activity waves orchestrate epithelial homeostasis by driving apoptosis-induced survival. DEV CELL 2021 Jun; 56: 1712 - CODEX, a neural network approach to explore signaling dynamics landscapes. MOL SYST BIOL 2021 Apr; 17: e10026 - Automatic detection of spatio-temporal signaling patterns in cell collectives. J CELL BIOL 2023 Oct; 222:
Group composition	The lab consists of 3 current members, and we carry out our research activity in the laboratories of the Italian Institute of

	Genomic Medicine (IIGM) at the Candiolo Cancer Institute, as part of the colaboration between the Department of Oncology and IIGM. The lab will be completed by an additional member in the autumn, to bring the team to 4 scientists: 1) Paolo Armando Gagliardi, PI, Associate Professor in Biochemistry, Department of Oncology, University of Torino. 2) A PhD student in Translational Oncology, University of Torino. 3) A researh assistant. 4) A postdoc researcher (expected start in October 2026).
Institutional page link	https://www.iigm.it/team/cancer-cell-dynamics-lab/?lang=en
Lab website link	https://sites.google.com/view/cancer-cell-dynamics-lab
Social media links	https://www.linkedin.com/in/paolo-armando-gagliardi-87980656/