

AVAILABLE POSITIONS

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Institute of Affiliation	Italian Institute of Technology (IIT)

PROJECT INFO	
Title of the proposed project:	Isoform-Level Transcriptional Heterogeneity and Tumor Cell States in Cancer
Short description of the project	Transcriptional heterogeneity is a central feature of cancer biology and contributes to tumor adaptation, therapy resistance and clinical outcome. While single-cell RNA sequencing has transformed our ability to resolve cancer cell states, most analyses still operate at gene-level resolution, overlooking the contribution of transcript isoforms, non-coding RNAs and RNA processing events to tumor identity and vulnerability. This PhD project will investigate isoform-level transcriptional heterogeneity in cancer, using breast cancer as a primary disease model. The student will combine long-read transcriptomics, patient-derived breast cancer organoids, bulk and single-cell cancer datasets, and computational analysis of transcript isoform usage to define how distinct RNA architectures are associated with tumor cell states. The project will build on in-house long-read sequencing resources based on Oxford Nanopore Technology and generated from breast cancer models, including patient-derived organoids and subtype-relevant experimental systems. A major goal will be to move beyond gene-level expression and ask whether specific isoforms or transcript-level configurations contribute to the definition of biologically meaningful cancer states, including proliferative, plastic, stress-adapted or therapy-tolerant populations. The project will also explore the relationship between transcript-level heterogeneity and cancer-relevant genes, including genes involved in tumor progression, cell-state regulation and selective vulnerability. In this framework, isoform usage and non-coding RNA expression will be interpreted as part of broader regulatory programs that may help explain tumor heterogeneity and nominate candidate biomarkers or functional vulnerabilities. The ideal candidate will be interested in cancer genomics, RNA biology and computational biology, and will work at the interface between transcriptomics, single-cell data analysis and patient-relevant cancer models.
Main research area for the project	B2 - Cancer Omics and Precision Oncology
Second research area for the project	B3 - Computational and Systems Biology
3 key words for the project	Single-cell RNA-seq; Long-Read transcriptomics; Breast cancer organoids

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LAB INFO	
Main topic/s of the lab	RNA biology, cancer genomics, long-read transcriptomics, non-coding RNAs, single-cell multi-omics and functional genomics in cancer.
Short description of the lab activity	The Genomic Science laboratory at IIT investigates how RNA-based regulatory mechanisms shape cancer cell identity, plasticity and therapeutic vulnerability. The lab combines advanced genomic technologies, including long-read RNA sequencing, single-cell and multi-omic profiling, CRISPR-based perturbation platforms and computational genomics, to study gene regulation in cancer and patient-relevant model systems. A major focus of the group is to understand how transcript isoforms, non-coding RNAs and RNA regulatory programs contribute to tumor heterogeneity, adaptation and therapy response.
Recent bibliography	• <i>Nadalin F., Marzi M.J., Pirra Piscazzi M., Fuentes-Bravo P., Procaccia S., Climent M., Bonetti P., Rubolino C., Giuliani B., Papatheodorou I., Marioni J.C., Nicassio F.</i> - Multi-omic lineage tracing predicts the transcriptional, epigenetic and genetic determinants of cancer evolution - Nature Communications, DOI 10.1038/s41467-024-51424-4 • <i>Maestri S., Furlan M., Mulroney L., Tarrero L.C., Ugolini C., Pozza F.D., Leonardi T., Birney E., Nicassio F., Pelizzola M.</i> - Benchmarking of computational methods for m6A profiling with Nanopore direct RNA sequencing- <i>Briefings in Bioinformatics</i>, vol. 25, (no. 2) DOI 10.1093/bib/bbae001 • Other publications at https://genomics.iit.it/publications
Group composition	The group currently includes: • Technologist (Matteo J Marzi) • Researcher Computational (Benedetto Polimeni) • Technician Experimental (Sara Bisi) • Technician Computational (Alessandro Poletti) • Post Doc Computational (Camilla Ugolini) • Post Doc Experimental (Verdiana Martello) • PhD Fellow Experimental (Giada Tria) • PhD Fellow Experimental (Chiara Finocchiaro) • PhD Fellow Computational (Pablo Angulo Lara) • PhD Fellow Computational (Fatemeh Kordevani) • Research Fellow (Sara Mimani) • Research Fellow (Sofia Denaro)
Institutional page link	https://www.iit.it/it/
Lab website link	https://genomics.iit.it