European School of Molecular Medicine

2025 summer call PhD selections

AVAILABLE POSITIONS

Principal Investigator	Francesco Nicassio
Affiliation	Italian Institute of Technology (IIT)
Title of the proposed project:	Unveiling the RNA Code in Cancer: Long-Read Technologies and AI Models
Short description of the project	Understanding transcriptional heterogeneity is critical to decode cancer vulnerabilities and develop effective biomarkers. This PhD project will leverage long-read **Oxford Nanopore Technology** (ONT) and its applications to RNA and transcriptomics — including full-length cDNA, single-cell cDNA, and native RNA sequencing — to investigate how transcript isoforms and RNA modifications shape the identity and adaptability of cancer cells, with implications for both diagnosis and therapy. The project will exploit a proprietary and unpublished dataset that represents one of the largest and most comprehensive long-read transcriptomic resources ever generated for a single cancer type. Derived from 2D breast cancer models and patient-derived organoids (PDOs), this dataset integrates multiple omics layers and enables isoform-level reconstruction of both coding and non-coding RNAs, alongside single-molecule detection of RNA modifications such as m^6A, pseudouridine, m^5C, and inosine. A key goal is to bridge bulk and single-cell resolution to capture cancer subtypes and plastic cell states driving tumor progression and treatment resistance. Based on the candidate's background and interests, the project may explore one or more of the following directions: • **Functional transcriptomics,** dissecting isoform-specific regulation and RNA modification patterns underlying tumor plasticity and drug response; • **Single-cell and single-molecule analysis**, integrating long-read bulk and single-cell data to resolve dynamic transcriptional states at high resolution; • **AI-based modeling**, developing deep learning approaches to extract cancer-relevant signatures and to integrate multi-omic data for robust classification and subtype prediction. The project allows for contributions to methodological innovation, including novel strategies for transcript annotation, regulatory network inference, or benchmarking of RNA modification detection tools. The PhD will be hosted in the **Nicassio Lab**, a hybrid environment with strong integration of wet-lab and computational expertise. The lab is internationally recognized for its pioneering work on gene expression regulation, non-coding RNA biology, and Nanopore-based transcriptomics, and is a core member of the RNA Flagship Program at IIT, a national initiative promoting RNA-based biomedical innovation.
Main research area for the project	Computational Biology
Second research area for the project	Genomic Medicine

3 key words for project	Long-read transcriptomics, RNA modifications, Non coding RNA
Main topic/s of the lab	Gene regulation, non-coding RNA biology, long-read transcriptomics, RNA modifications, cancer omics
Short description of the lab activity	The **Nicassio Lab** investigates gene expression regulation and RNA biology in cancer, with a specific focus on non-coding RNAs, transcriptional plasticity, and RNA modifications. A central aim is to decode how these molecular layers contribute to tumor heterogeneity, therapeutic response, and disease evolution. Our group is internationally recognized for its pioneering role in applying new omic technologies to transcriptome and non-coding biology. Recently, we have developed tools and strategies for **long-read sequencing** to analyze gene regulatory networks, identify **regulatory non-coding RNAs**, and map isoform diversity and **RNA modifications** at single-molecule resolution. Our expertise in using **Oxford Nanopore Technologies (ONT)** for RNA biology places us at the forefront of functional transcriptomics and epitranscriptomics in cancer. The lab operates as a **hybrid experimental–computational environment**, integrating molecular biology, sequencing technologies, and advanced bioinformatics, including deep learning models for transcript and modification analysis. This setup enables us to carry out both large-scale data generation and the development of novel analytical tools, addressing biological questions with high precision and innovation. We maintain a strong translational focus, with projects aimed at uncovering RNA-based biomarkers and regulatory signatures in **breast cancer** and other solid tumors. Our activities span from **single-cell multi-omics** to **CRISPR-based functional screening**, supporting the discovery and validation of new non-coding drivers of cancer. The lab is a coordinating node of the **RNA Technology Flagship at IIT,** a national initiative fostering cutting-edge RNA research and therapeutic innovation. It is also embedded in multiple international networks, including FANTOM6, the LongTREC and INT2ACT **MSCA consortia**, and collaborations with **EMBL**, **RIKEN**, and **AstraZeneca**. The team includes researchers with diverse expertise (experimental, computational, clinical) and hosts regular visiting scientists and collaborators. PhD students joining the lab will benefit from close mentorship, exposure to international collaborations, and the opportunity to work on high-impact scientific questions using state-of-the-art technologies.

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Recent bibliography	1. Nadalin F, Marzi M.J., Piscazzi M.P., Fuentes-Bravo P., Procaccia S., Climent M., Bonetti P., Rubolino C., Giuliani B., Papatheodorou I., Marioni J.C., **Nicassio F.** Multiomic lineage tracing predicts the transcriptional, epigenetic and genetic determinants of cancer evolution. **Nat Commun.** 2024; 15:7609. 2. Maestri S., Furlan M., Mulroney L., Coscujuela Tarrero L., Ugolini C., Dalla Pozza F., Leonardi T., Birney E., **Nicassio F., Pelizzola M.** Benchmarking of computational methods for m6A profiling with Nanopore direct RNA sequencing. **Brief Bioinform.** 2024; 25. 3. Giambruno R., Zacco E., Ugolini C., Vandelli A., Mulroney L., D'Onghia M., Giuliani B., Criscuolo E., Castelli M., Clementi N., Mancini N., Bonaldi T., Gustincich S., Leonardi T., Tartaglia G.G., **Nicassio F.** Unveiling the role of PUS7-mediated pseudouridylation in host protein interactions specific for the SARSCoV2 RNA genome. **Mol Ther Nucleic Acids.** 2023; 34:102052. 4. Ugolini C, Mulroney L, Leger A, Castelli M, Criscuolo E, Williamson MK, Davidson AD, Almuqrin A, Giambruno R, Jain M, Frigè G, Olsen H, Tzertzinis G, Schildkraut I, Wulf MG, Corrêa IR, Ettwiller L, Clementi N, Clementi M, Mancini N, Birney E, Akeson M, **Nicassio F,** Matthews DA, Leonardi T. Nanopore ReCappable sequencing maps SARS-CoV-2 5' capping sites and provides new insights into the structure of sgRNAs **Nucleic Acids Res.** 2022 Mar 4:gkac144. doi: 10.1093/nar/gkac144 5. Tordonato C., Marzi M.J., Giangreco G., Freddi S., Bonetti P., Tosoni D., Di Fiore P.P., **Nicassio F.** miR-146 connects stem cell identity with metabolism and pharmacological resistance in breast cancer. **J Cell Biol.** 2021; 220.
Group composition	The Nicassio lab includes **13 active members**, comprising a senior technologist, three postdoctoral researchers, three PhD students, one research fellow, two lab technicians, one undergraduate student, and two external collaborators. The team integrates experimental and computational expertise and is organized into two synergistic units: **Functional Non-coding Genomics** and **Computational RNA Biology**.
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