

DEPARTMENT: Center for Genomic Science of IIT@SEMM – Milan – Istituto Italiano di Tecnologia (IIT) - <https://cgs.iit.it>

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Project Title: Transcriptional and Epigenetic mechanisms provided by Noncoding RNAs in human cancer.

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Background: The spatial and temporal heterogeneity characterizing cancer presents a major hurdle to both basic and translation research. Within the same tumor, cancer cells can behave differently with some of them acquiring the ability to adapt in response to harsh or even hostile conditions, produced either by the host or following cancer treatment. In recent years, it has become increasingly evident that non-coding mechanisms play an important role in gene regulation. Short (microRNAs) and long non-coding RNAs (lncRNAs) as well as non-coding DNA elements (enhancer, silencer), have emerged as key elements in the adaptive response mechanisms and in the transcriptional/epigenetic reprogramming of cancer cells, which occur during cancer evolution and in the most aggressive cases of the disease, such as metastatic spread or tolerance/resistance to therapy. These RNA elements are also extremely attractive for applied medicine, as they could be exploited to provide a new generation of targets for therapeutic/theranostic applications with unprecedented sensitivity and specificity.

Aim: This project is aimed at investigating the role noncoding RNAs and DNA elements play in the adaptive response of breast cancer cells following anticancer therapies and in the context of advanced 3D models and primary tumor organoids. The candidate will use cutting-edge genomic approaches to achieve a high-resolution characterization of the transcriptional/epigenetic landscape of cancer cells, focusing on their evolutionary trajectories that will be characterized in time and space. The ultimate goal will be to gain insight into the genetic and epigenetic factors that hinder the success of established anticancer therapies.

Methodology: The project is highly interdisciplinary. We will use as model system stroma-enhancer cancer organoids, a sort of "cancer avatars", which mimic the 3D spatial tissue organization and maintain the genetic and phenotypic heterogeneity of their tissue of origin. The candidate will exploit cutting-edge approaches, including state-of-the-art genomic platforms (i.e. RNAseq, ATACseq, DNaseq, Genomic Barcoding, Single-Cell sequencing), genetic interrogation by multiplexed CRISPR/cas9 system (CRISPRi/a, CROP-seq, Perturb-seq approaches) and novel emerging methodologies that will be developed as part of the project (e.g. Spatially-resolved omics).

Hosting Lab: The “*Non-Coding Genome*” lab adopts genomic approaches to the study of the dynamics of non-coding RNAs (microRNAs and long noncoding RNAs) and of the control of gene expression and cell behavior, in particular during cancer evolution (therapy resistance, metastatic spread). To date, the "Noncoding Genome" lab consists of 10 people (1 senior staff member, 5 post docs, 3 PhD students, 1 undergraduate student). The **Center for Genomic Science** of IIT@SEMM is an outstation of the Istituto Italiano di Tecnologia (IIT). Its scientific mission is the development and application of genomic technologies (Next-generation sequencing, bioinformatics and beyond) towards a better understanding of biological processes and diseases, with emphasis on Cancer and RNA biology. The center benefits from close ties with the European Institute of Oncology (IEO-hospital, Milan), one of the largest cancer hospitals in Italy, which hosts our lab spaces and provides us with complementary infrastructure as well access to clinical data and biological samples for cancer studies. The Center is part of the RNA initiative ([iRNA@IIT](#)), a scientific action promoted by the IIT and aimed at generating ground-breaking interdisciplinary knowledge in the fields of RNA biology, RNA technologies and RNA-based therapeutics.

Links

<https://www.iit.it/people-details/-/people/francesco-nicassio>

<https://genomics.iit.it/research/micrnas-and-non-coding-rnas-in-development-and-disease>

<https://www.iit.it/web/irna>