European School of Molecular Medicine

2025 summer call PhD selections

AVAILABLE POSITIONS

Principal Investigator	Lorenzo Calviello
Affiliation	Human Technopole
Title of the proposed project	**CiliaRNA - RNA regulation and local translation in the ciliary organelle**
Short description of the project	Cilia have mostly been described in the literature as highly structured and complex protein-membrane organelles. With RNA localization emerging as a fundamental property of many subcellular compartments and organelles, the role of RNA and ribonucleoparticles (RNPs) in cilia remains vastly overlooked. Moreover, active protein synthesis has been recently observed inside the cilium itself, either in its mature form or during ciliogenesis. The identity and functions of RNAs, and ribosomes participating in local translation, as well as their contribution to ciliary functions, remain largely unknown. In this project, we will combine cell biology, transcriptomics, proteomics and cryoEM approaches to shed light on a vastly unexplored aspect of a fundamental organelle in eukaryotic cells. With a growing number of genetic disorders affecting primary and motile cilia (ciliopathies), this project will contribute towards understanding the functions of hundreds of ciliopathies-associated proteins, whose roles outside core ciliary functions remain to be investigated. Merging in vivo structural dynamics of the ciliary organelle with high-resolution functional transcriptomics, we propose an integrative biology framework for the exploration of cilia RNA biology and its regulation, at the interface between RNA and protein.
Main research area for the project	Molecular and cellular biology
Second research area for the project	Genomic Medicine
3 key words for project	
Main topic/s of the lab	Advanced analytical methods in transcriptomics Integrative -omics in mRNA biology Computational analysis of translation profiles De novo discovery from RNA to Protein
Short description of the lab activity	The Calviello Group is a multidisciplinary research group in the Genomics Research Centre –Functional Genomics Programme, adjunct with the Computational Biology Research Centre. The group studies post-transcriptional gene regulation, employing computational and experimental methods revolving around the -omics of translation, a fundamental process which dictates the functions of transcribed genome, and impacts the cytoplasmic fate of mRNAs and proteins. Some areas of investigations include: • **Quantification of translation control across cell types and states** RNA cis-regulatory elements and RNA-binding proteins (RBP) can modulate the rate of protein synthesis from the mRNA, providing an additional mode of gene expression control. Moreover, decades of detailed molecular investigations in protein synthesis have

	uncovered multiple connections between nascent RNA processing, translation, and mRNA decay. Despite the vast amounts of datasets illustrating these processes in a transcriptome-wide fashion and with great accuracy, an analytical framework able to quantify and predict regulation at different steps of the gene expression cascade is missing. • **Characterizing the role of heterogeneous RNPs and their dynamics along the mRNA** Tight control of cytoplasmic gene expression is orchestrated by the action of multiple ribonucleoprotein (RNP) complexes. One prominent example is the human ribosome, which undergoes drastic changes as it scans through the mRNA and engages in protein synthesis. Recent advancements in profiling RNP complexes have revealed hundreds of regulatory factors interacting with the ribosome throughout the translation cycle. However, our knowledge of the functions of heterogeneous ribosomal complexes remains very limited. • **Alternative RNA processing and its contribution to protein synthesis and cell physiology** RNA-sequencing (RNA-seq) data has enabled researchers to quantify the expression of thousands of genes, from more canonical example of protein coding genes to cryptic transcripts of unknown function. Moreover, different transcript isoforms from the same genes can exhibit tissue-specific functions, highlighting the need for transcript-level investigation into gene regulation. For hundreds of genes, computational analysis of Ribo-seq data has provided evidence for translation and co-translational mRNA decay in a transcript isoform-specific fashion, providing a powerful window into the cytoplasmic fate of thousands of transcripts. However, the functional relevance for the presence of multiple transcript isoforms is largely unexplored. • **Proteogenomics applications between RNA and protein** RNA sequencing technologies are essential to detect expressed transcripts, thus providing useful priors to identify synthesized proteins. As shown by different studies, careful analysis of the profiling of ribosomes (Ribo-seq) can reveal protein synthesis events with high confidence and aid the discovery of new proteins being translated from upstream Open reading Frames (uORFs), long non-coding RNAs (lncRNAs) and alternative transcript isoforms. Despite these recent promising results, integrating transcriptomics with the complex world of proteome dynamics, while considering regulation via post-translational modifications, protein isoforms and subcellular localization and function, remains an unmet challenge in the post-genomics era.
Recent bibliography	Jowhar et al, A ubiquitous GC content signature underlies multimodal mRNA regulation by DDX3X, Molecular Systems Biology, 2024 Calviello et al, DDX3 depletion represses translation of mRNAs with complex 5'UTRs, NAR, 2021 Calviello et al, Quantification of translation uncovers the functions of the alternative transcriptome, Nature Structural and Molecular Biology, 2019

	Calviello et al, Detecting actively translated open reading frames in ribosome profiling data, Nature Methods, 2015
Group composition	1 Bioinformatician (AI approaches in transcriptomics) 1 Postdoc (Subcellular translation dynamics) 1 PhD Student (De novo discovery from RNA to protein) 1 PhD Student (Integrative classification of mRNA variants) 1 Senior Technician (Experimental protocol optimization)
Institutional page link	https://humantechnopole.it/en/research-groups/calviello-group/
Lab website link	https://calviellolab.github.io/
Social media links	https://x.com/translatomics | https://bsky.app/profile/translatomics.bsky.social