European School of Molecular Medicine

RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

* Name & Surname: Piero Carninci

* Affiliation -Human Technopole

PHD PROJECT DETAILS

* Title of the proposed project

Deciphering the role of lncRNA in regulating genome activity

* Short description of the project (up to 300 words)

While the fraction of mammalian genomes that encode for protein is limited to less than 2% of the genome, the vast majority of the genome is transcribed into a myriad of lncRNAs. These include long-non-coding RNAs, enhancer RNAs, non-coding RNAs deriving from retrotransposon elements, among a growing number RNAs. We are engaged in the identification and functional characterization of a number of lncRNAs. To infer functions of such lncRNAs, we have developed methods to comprehensively collect full-length versions of all the capped RNAs and their variants from human cells, leveraging on the cap-trapping methods (CFC-Sequencing). Since there is a growing number of lncRNAs that epigenetically regulate chromatin, we developed RADICL-seq, a method to massively screen for RNA-Chromatin interaction.
We will apply RADICL-seq, CFC-seq, HiC, cap-analysis gene expression (CAGE) and other methods, to broadly construct a chromatin-centered RNA-chromatin interaction maps for various cell models, including iPS differentiating into neurons and immune cells and tumor cells. We will create a comprehensive “RNA Interactome” including multiple cell types and states. We will analyze the data to assign function and probe possible mechanisms of actions of non-coding RNAs as component of structure of chromatin and regulators of chromatin activity. This will include lncRNAs as chromatin regulators, enhancer-RNAs as regulators of gene activity, intronic RNAs as structural RNAs, and RNA containing retrotransposon sequences as functional RNA motifs. We will refine our model, where RNAs-chromatin interactions follow complex patterns that vary upon cell differentiation/activation, showing remarkable cell

specificity. Learning from currently analyzed datasets, we will explore the ranges of RNA interactions with chromatin, from local to long-range contacts. We will select lncRNAs as candidates for demonstrating the lncRNA functions by perturbations towards the identification of novel regulatory RNA genes.

* Indicate the main research area for the project described above - Molecular and Cellular Biology

If needed indicate a second research area for the project described above
-Computational Biology

* Provide up to 3 key words for project:

long-noncoding RNA; functional genomics; chromatin

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

Mapping functions of non-coding regulatory elements of the genome.

* Short description of the lab activity (up to 500 words)

In recent years, genomic studies have identified multiple functions for non-coding genome and transcriptome, including regulation of gene expression in all cells, tissues and organs. However, we have still much to learn. Appropriate gene regulation, like gene expression dosage in each cell is a key factor in health and disease. To fully understand genome regulation, is mandatory to understand how non-coding regions act together in all different cells and tissues of the human body.
The genome produces a large variety of long non-coding RNAs (lncRNAs). The relatively few well studied lncRNAs are engaged in a variety of activities, including interactions with chromatin, other RNAs, proteins and may have regulatory or structural role. Together with lncRNAs, the genome is also regulated by many proteins, including transcription factors, epigenome modifiers and other DNA interacting proteins. Altogether, all these molecules form complexes that interact and regulate chromatin, promoters and enhancers in the human body with high cell specificity in health and diseases in different genetic background.
To address these challenges, the Carninci Group strive to develop and broadly use technologies to comprehensively study the non-protein-coding part of the genome, its function and interactome. The following are some of the focuses of the laboratory:

- We study the role, structure, modifications and interactome of SINE elements embedded in antisense lncRNAs, which are involved in the regulation of translation of the gene they target. These RNAs, called SINEUPs, are the first class of lncRNAs known to positively regulate protein synthesis and are revealing fundamental aspects of RNA biology.
- We develop and standardize transcription profiling technologies like the cap-analysis gene expression (CAGE), to develop a universal and finely quantitative transcriptome technology, which will ultimately be used to profile populations of single cells in tissues.
- We further develop approaches to detect interactomes of molecules, like for the RADICL-seq technology, which globally detects interactions of RNA with chromatin and identifies RNAs that are likely to regulate gene activity. –

Technologies developed in the Carninci Group are made broadly available to the Genomics Research Centre and the whole Human Technopole to broadly share inter-functional information from genomics data. Altogether, understanding the function of the non-coding regulatory genome is essential to develop genome medicine, to fully realize the potential of genomics for human health.

* Recent bibliography (max 5 references)

RADIP technology comprehensively identifies H3K27me3-associated RNA–chromatin interactions

X Shu, M Kato, S Takizawa, Y Suzuki, P Carninci
Nucleic Acids Research 52 (22), e104-e104

Decryption of sequence, structure, and functional features of SINE repeat elements in SINEUP non-coding RNA-mediated post-transcriptional gene regulation
H Sharma, MNZ Valentine, N Toki, HN Sueki, S Gustincich, H Takahashi, ...
Nature Communications 15 (1), 1400

Functional annotation of human long noncoding RNAs via molecular phenotyping
JA Ramilowski, CW Yip, S Agrawal, JC Chang, Y Ciani, IV Kulakovskiy, ...
Genome research 30 (7), 1060-1072

RADICL-seq identifies general and cell type–specific principles of genome-wide RNA-chromatin interactions
A Bonetti, F Agostini, AM Suzuki, K Hashimoto, G Pascarella, J Gimenez, ...
Nature Communications 11 (1), 1018

An atlas of human long non-coding RNAs with accurate 5′ ends
CC Hon, JA Ramilowski, J Harshbarger, N Bertin, OJL Rackham, J Gough, ...
Nature 543 (7644), 199-204

* Group composition: total members, and roles distribution (PhD, postdoc, technician, etc.)

Approx 12 members, 4 postdocs, 2 technicians/senior technicians, one scientist, 2 master students, 4 PhD students.

Institutional page link

https://humantechnopole.it/en/research-centres/genomics/

Lab website link, if any

https://humantechnopole.it/en/research-groups/carninci-group/

Social media links, if any

Twitter/X : @carninci

If you prepare a video to promote your lab/project, please include the link below