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MUR PNRR National Center for Gene Therapy and Drugs based on RNA Technology

Spoke 6: RNA drug development

veRNAdì

A webinar series about RNA

to share projects and competences,
increase networking, discuss issues
and new ideas, and disseminate results

Every last Friday of the month

https://rb.gy/y40y6

XIV veRNAdì: March 28 2025, 15:00

Genome regulation by non-coding transcription

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While the protein encoding fraction of mammalian genomes is limited to less than 2% of the genome, the majority of the genome is transcribed into a myriad of lncRNAs. These include long non-coding RNAs, enhancer RNAs, non-coding RNAs deriving from retrotransposons, among a growing number RNAs. In the past 20 years, the FANTOM projects had a central role in identification and initial functional characterization of a number of lncRNAs. To infer functions of such ncRNAs, 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 have broadly applied RADICL-seq, CFC-seq, HiC, cap-analysis gene expression (CAGE) and other methods, to broadly construct a chromatin-centered RNA-chromatin interaction maps, for iPS differentiating into neurons and monocytes activating into macrophages, as well other cells, to create an initial comprehensive "RNA Interactome" of 16 mammalian cells types/states. Our analysis, part of the FANTOM6 project, reveals an unprecedented role or RNA as component of structure of chromatin. We have found roles of lncRNAs as candidates chromatin regulators, but also roles for enhancer-RNAs, intronic RNAs and RNA containing retrotransposon sequences. Altogether, RNA-chromatin interactions follow complex patterns that vary upon cell differentiation/activation and shows cell specificity. Interactions range from local to long range contacts. A substantial fraction of the lncRNAs that are perturbed show measurable phenotypes in human cells, suggesting that a large fraction of yet uncharacterized RNAs are structural or regulatory RNAs.