大学院学生各位　To All Graduate Students

2023年度 基盤医学特論 開講通知 Information on Special Lecture Tokuron & Tokupro AY2023

特徴あるプログラム CIBoG/AI-MAILs オミクス解析学プログラム

CIBoG/AI-MAILs Omics Analysis

題目：Genomics regulation and long non-coding RNAs functions

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日時：2023年11月20日（月）17：00～18：30（Zoom）

Time and Date: 20th November, 2023 17:00-18:30(Zoom Lecture)

使用言語：英語　Language：English

概説：　We have been mapping genome elements over the years, broadly identifying promoters, enhancers, protein coding and lncRNAs in the FANTOM projects. LncRNAs constitute a large group of transcripts, for the majority of which the function is still unknown. Genetic evidence of conservation suggest function for some 19K, however a more direct assessment of lncRNA function is needed. We started the FANTOM6 project to directly test function of lncRNA by systematically knocking down several hundreds of lncRNAs in human primary fibroblasts and ES cells, suggesting function for >30% of lncRNA tested in each cell type. To build broader information on lncRNA function, we embarked in a broad map of the interactome of lncRNAs. Using our RADICL-seq (RNA and DNA Ligated and Sequenced) technology, complemented by a suite of complementary methods, we focus to broadly map RNA bound to chromatin, given their important role to regulate the epigenome/chromatin activity. Our data are revealing novel and unexpected pattern of interactions, which include interactome driven by enhancer RNAs, intronic RNAs, lncRNAs and RNAs from retrotransposon elements. RNAs display dynamic patterns of interaction and specific interactomes for each class of RNAs, suggesting a yet not described regulatory and structural role of RNAs.

An important subset of lncRNA is constituted by antisense RNAs. We have identified a new class of non-coding antisense RNAs, named SINEUPs, which counterintuitively up-regulate protein translation of the sense RNA that they overlap. Enhancement of protein translation is mediated by SINE elements and the specificity of action is mediated by the region antisense to the 5’UTRs of the target mRNAs. SINEUPs can be designed to target specifically any targeted mRNAs for therapies, including but not limited to haplo-insufficiencies. We are deciphering the structure/functional relationship behind the mechanism of action SINEUPs in protein translation.

Retrotransposition is considered to cause genetic disorders. We combined short- and long-DNA read sequencing of repeat elements with a new bioinformatics pipeline, which revealed that the presence of unexpected non-homologous recombination and retroelements acting as recombination hotspots are enriched in centromeres and cancer genes. Also, somatic recombination profiles are altered in Parkinson’s and Alzheimer’s diseases, indicating a link between retroelements recombination and genomic instability in neurodegeneration.

Moving transcriptome technologies at single cell level, we are involved in the Human Cell Atlas (HCA) project, with particular focus to Japanese and Asian genetic backgrounds, to comprehensively map transcription and its regulation in all human cells. Our approach capitalizes on CAGE, but at single cell level by adapting a template switch protocol to commercial instruments, as well as developing tools to identify promoters and enhancers usage at single cell level and linking expression to genetic variations and diseases.

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