2021 年度　生命科学技術国際卓越講義

World-leading Innovative Lectures
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Long non-coding RNAs in cellular networks and genome regulation

Prof. Piero Carninci

Head of Genomics Research Centre - Functional Genomics, Genomics ;
Research group leader, Carninci Group Team Leader for Laboratory for Transcriptome Technology
and Deputy Centre Director at the RIKEN

Date: Monday, December 6, 2021
Time: 9:30AM ～ 11:00AM
Venue: Zoom (meeting URL will be sent after registering)
Participants: Up to 500 participants

Please register by this QR code or clicking the following link

Registration Form

Abstract

Genome activity is controlled by regulatory sequences, such as promoters and enhancers. These elements can be mapped by identifying the transcription starting sites (TSSs) of the RNAs that they produce. We previously developed the Cap Analysis of Gene Expression (CAGE) technology, which identifies TSSs at single-base resolution and quantitatively measures their activity throughout the genome at high-throughput, providing broad insights into gene regulation.

The FANTOM5 project, centered on CAGE, has generated comprehensive maps of these regulatory elements and their networks using a comprehensive panel of human and mouse primary cells and other tissues. We identified more than 223K and 162K promoters and 65K and 44K enhancers, in human and mouse respectively, which show often tissue specificity. We also built a reliable atlas of human lncRNAs based in unambiguous identification of their promoters, predicting possible function for 19,175 of them. To further explore lncRNAs function, the FANTOM6 project established a large lncRNA knockdown data set by systematically knocking down several hundreds of lncRNAs in human primary fibroblasts and ES cells.

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 haploinsufficiencies. The map of precise TSSs identified by CAGE in FANTOM5 gives us information to flexibly design the antisense region for effective SINEUPs in each cell type, allowing to correct unbalanced gene expression in disease models.

Expanding these activities, we are working with Human Cell Atlas (HCA) project, aiming at the creation of a comprehensive map of all human cells at single cell level. We have developed single cell CAGE and bioinformatics pipeline for the 10X Genomics platform (Moody et al, Biorxiv, https://doi.org/10.1101/2021.04.04.438388) allowing CAGE at single cell level, which will be broadly used to study transcriptional regulation at single cell level.

Organizer:　World-leading Innovative Graduate Study Program for Life Science and Technology
Cooperation:　Graduate Program for Leaders in Life Innovation, The University of Tokyo

For Further Information Contact: Nana Sekine at WINGS-LST Office
Phone: 03-5841-0246　E-mail: wings-life@m.u-tokyo.ac.jp