Functional Genomics & Metabolism

Functional Genomics & Metabolism Seminar Series 2025

Pioneers in Metabolic Research and Genomics

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BMB Seminar Room

"Dynamics of 3D genome structure and function"

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Abstract
3D genome structure regulates gene expression by regulating the interactions between enhancers and promoters. CTCF and loop-extruding cohesins fold the genome into loops and domains known as Topologically Associating Domains (TADs). However, whether these domains were stable or dynamic was not clear. First, we will briefly discuss our recent work live-imaging work quantifying the dynamics of CTCF- and cohesin-mediated chromatin looping and the implications of our finding that these loops are both highly dynamic (~10-30 min median lifetime) and rare (~3%-6.5% looped fraction).
Second, motivated by understanding the degree of selectivity for interactions between enhancers and promoters, we will discuss more recent work and unpublished focused on quantifying the interactions between enhancers and promoters (E-P). Specifically, Hi-C has poor sensitivity and depth for capturing E-P interactions. To overcome this limitation, we have developed Region-Capture Micro-C (RCMC) to generate the deepest 3D genome structure maps reported so far. With RCMC, we find extensive multi-way looping interactions between enhancers and promoters that are largely independent of loop extrusion. Instead, our results suggest that E-P interactions form through a compartmentalization mechanism and we therefore refer to these fine-scale interactions as “microcompartments”. We will also discuss recent unpublished work on how E-P interactions dynamically form upon mitotic exit and recent applications of machine learning to impute 3D genome structure. Finally, we will integrate these observations to present our current view for how the cell regulates which enhancers interact with and activate which genes.