THE GIS
SPEAKER SERIES

Analysis of cell coordination at different scales: computational attempts

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Host: Shyam Prabhakar

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9.30am – 10.30am

GIS L2 – Seminar Room
60 Biopolis Street, Genome, Singapore 138672

About The Speaker

Dr. Peter Kharchenko has completed his PhD at Harvard University Biophysics program, studying gene regulation under the supervision of George Church, and then went on to do a postdoctoral fellowship in the group of Peter Park, focusing on chromatin configuration. Peter's own group at the Harvard Medical School has developed computational methods for genomic analysis of single cells, enabling statistical separation of distinct cellular states, detection of genomic aberrations in transcriptional data, and inference of cellular dynamics from snapshots of cellular state. His group has also applied these approaches to study the organization of different tissues and the impact of diseases ranging from cancer to schizophrenia. Peter then joined Altos Labs as a Principal Investigator in 2022, focusing his groups efforts on mechanisms of cell and tissue resilience. Peter is currently a Visiting Professor at Institute of Science and Technology, Austria.

About The Seminar

Coordinated cellular activity is fundamental to tissue function and is commonly perturbed in disease, yet scalable methods to quantify such coordination and its mechanisms remain limited. I will discuss these challenges and how my group has approached it at different scales: from analysis of population-scale transcriptional analysis of patient cohorts, down to local tissue contexts resolved by spatial transcriptomics. First, I will outline an interpretable tensor decomposition framework that we designed for analysis of population scale scRNA seq that captures multicellular expression programs - correlated state changes across cell types - and relates them to clinical or environmental covariates in patient cohorts. We can use such multicellular programs to look for factors potentially mediating this coordination and use genetic variation within population to evaluate causal hypothesis. Though the mechanisms underlying such organism-wide coordination are also likely to be indirect. In contrast, at the scale of small cellular neighborhoods within tissues, we expect more direct influences to be key. I will discuss how spatial transcriptomics can quantify coordination in situ and the challenges faced by such approaches. In particular, I will show that most current techniques are vulnerable to pervasive segmentation errors that misattribute transcripts across adjacent cells, generating spurious region specific signals, interaction changed genes, and ligand–receptor pairs. I will describe a practical mitigation strategy based on factorization of subcellular neighborhood composition vectors and probabilistic labeling to identify and remove admixture driven factors, thereby restoring biologically coherent signals and improving interpretability of downstream analyses.