NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Single-cell Atlas of Transcribed Cis-Regulatory Elements (tCRE) Reveals Disease-associated Regulatory Modules in Distinct Cell Populations

Date: 11 September 2023, Monday
Time: 2:30 pm to 3.30 pm
Venue: SBS CR4 (SBS-01n-24)
Host: Assoc. Prof. Koh Cheng Gee

Profiling of cis-regulatory elements (CREs) in single cells enables the interrogation of cell-type specific contexts of gene regulation and genetic predisposition to diseases. Here we demonstrated transcribed CREs (tCREs) are detectable from single-cell RNA-5′end-sequencing. As compared to CREs defined based on chromatin accessibility, we found tCREs are more accurate in predicting CRE interactions by co-activity, more sensitive in detecting shifts in alternative promoter usage and more enriched in disease heritability. We applied single-cell RNA-5′end-sequencing to 23 human tissues, defining an atlas of >250,000 proximal and distal tCREs across 180 distinct cell-types comprised of >400,000 single cells. This atlas allows us to define groups of cell-types specific CREs (i.e. regulatory modules) and thus to interrogate the regulatory factors driving the cell-types specific gene expression program (e.g. transcription factors, super-enhancers etc). We then linked the distal tCREs to genes by co-activity and quantified the cell-type specific usage of alternative proximal and distal tCRE of genes, facilitating the functional interpretation of diseases-associated noncoding variants with cellular contexts. To functionally interrogate CREs, we built a high-content screening platform and perturbed non-coding regulatory RNAs and DNA using antisense-oligonucleotides (ASO) and CRISPRi, respectively, and reported ~40% elements are functionally important in gene regulation and exhibit cell type specific activities.

Speaker:

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