Infectious Diseases Labs

A*STAR IDL

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Tuesday 21st January 2025
11:00 AM to 12:00 PM (SGT)

Venue: Codon A & B, Matrix Level 5

Toward a cell-type-specific understanding of complex diseases

High-throughput genotyping and sequencing have led to the discovery of thousands of disease-associated variants. Because most of these variants lie in non-coding regions, their functional mechanisms remain unclear. To identify genetic effects underlying complex diseases, it has become increasingly important to investigate the proper cell types and contexts. We demonstrate the power of cell-type-specific assays for three complex diseases. Coronary artery disease (CAD) is the leading cause of death globally. Approximately 40 - 60% of CAD severity can be attributed to genetic factors. GWAS meta-analyses have uncovered more than 100 significant loci, but most are difficult to interpret because they reside in non-coding regions. We found that coronary artery smooth muscle-specific genetic regulatory mechanisms are highly enriched in CAD GWAS signals. By jointly analyzing eQTL and GWAS datasets, we identified five risk genes. TCF21 and SMAD3 were subsequently validated by single-cell analysis in atherosclerotic mouse models. Age-related macular degeneration is one of the leading causes of blindness in elderlies. It has been estimated that genetic factors explain 45% - 70% of the variation in the severity of age-related macular degeneration. Retinal pigment epithelium (RPE) is vital in ocular development but is underrepresented in genetic regulation studies. By jointly analyzing RPE eQTL and AMD GWAS, we identified several risk genes including RDH5. In particular, we found that the eQTL regulatory SNP also regulates splicing. Experimental validation confirms that the minor allele leads to aberrant splicing and subsequently RNA non-sense-mediated decay. This result revealed the genetic mechanism of RDH5 regulation and confirmed RDH5 as a risk gene for age-related macular degeneration, making it a potential target for drug development. Autoimmune diseases are a group of illnesses that are individually rare but collectively affect 5% of the population. Leveraging ~1M PBMC single cells from the Asian Immune Diversity Atlas (AIDA), we showcase our recent results on leveraging single-cell sQTLs to disentangle autoimmune diseases.

Dr Boxiang Liu obtained a BA degree in Biophysics from Illinois Wesleyan University, a MS degree in Statistics and a PhD degree in Bioinformatics from Stanford University. He was a research leader at Baidu Research USA and joined the National University of Singapore as an Assistant Professor in 2022. His research group specializes in genetic regulation of molecular traits (QTLs) and single-cell multi-omics. He is the winner of President's Award in Natural Sciences and Mathematics, Stanford University CEHG fellowship, Charles B. Carrington Memorial Award, and the Chinese Government Outstanding Overseas Ph.D. Students. His research group focuses on using computational and statistical tools to understand the genetics of complex human diseases, with the long-term goal of validating known and identifying novel drug targets.

Hosted by: Dr Amit Singhal

Seminar is open to all. No registration required.

Questions? Contact us at **seminars@idlabs.a-star.edu.sg**

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