RNA Salon Singapore

With support from:

20 min talks from ECRs followed by snacks and networking

June 18th 4:00 - 6:00 pm

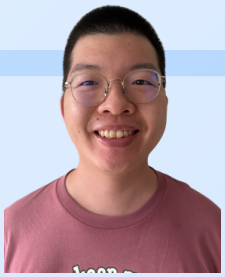
TR5, School of Biological Sciences, NTU

Mitochondrial immune checkpoint: two-step conversion of oxidative stress to dsRNA-dependent inflammation

Shen Haoqing, National University of Singapore

Synopsis: Mitochondria are emerging as central regulators of innate immunity, yet how mitochondrial stress is converted into inflammatory signals remains poorly understood. Here, we uncover a previously unrecognized mechanism by which mitochondrial oxidative stress induces a latent immunogenic dsRNA within mitochondria. We show that mitochondrial reactive oxygen species remodel the mitochondrial dsRNA landscape through a post-translational mechanism, generating a hidden reservoir of immunogenic dsRNA. Through genome-wide functional screening, transcriptomic profiling, and biochemical dissection, we further demonstrate that a second, molecularly distinct event determines whether this latent reservoir remains contained or escapes to ignite interferon responses, which we call it a mitochondria-centered two-step "Draw-and-Release" model. Finally, we show that pharmacologic mtROS scavenging reduces mt-dsRNA burden, suppresses interferon-stimulated gene expression, and alleviates liver inflammation in vivo. Together, our study establishes a mitochondria-centered checkpoint in which mitochondria bridge the conversion of oxidative stress to inflammation.

A rationally engineered CasRx platform for efficient, site-specific RNA editing



Chee Jiunn En, Nanyang Technological University

Synopsis: Type VI CRISPR-Cas systems that target RNA have recently been exploited for transcriptome engineering. Specifically, catalytically dead Cas13 proteins have been fused to ADAR2 deaminase domain for A-to-I editing of various RNA transcripts. Despite the promise of existing tools, they often struggle with balancing the trade-off between editing efficiency and specificity. To address the issue, we had developed a programmable A-to-I RNA editor that has both high editing efficiency and specificity. Through rational protein engineering, we created a mutant CasRx protein scaffold and identified a novel ADAR2 deaminase domain variant that together enhanced specificity without overly compromising editing efficiency. We benchmarked our RNA editor with the existing REPAIR system and found that our platform showed comparable on-target editing activity as REPAIRv1 while maintaining high specificity like REPAIRv2. To further improve the system, we have found ADAR2 from other species which showed significant improvement of on target activity and expanded motif preferences. Our versatile CasRx scaffold may also be adapted for other RNA engineering applications.

Bambu-Pipe: An end-to-end pipeline for transcript discovery and quantification from long-read single-cell and spatial transcriptomics data

Lee Chin Hao, Genome Institute of Singapore

Synopsis: We present Bambu-Pipe, a Nextflow pipeline that provides an end-to-end workflow for context-aware transcript discovery and quantification from long-read single-cell and spatial transcriptomics data. Combining single-cell and spatial profiling with long-read RNA-Seq enables the discovery and quantification of RNA isoforms at single-cell resolution, but reproducible analysis requires careful integration of multiple specialised tools. Bambu-Pipe addresses this challenge by combining read filtering, barcode and UMI demultiplexing, primer trimming, and genome alignment with transcript discovery and quantification using Bambu, supporting both per-cell and cluster-level quantification. The pipeline supports Oxford Nanopore and PacBio data across 10x single-cell and Visium spatial chemistries. Together, Bambu-Pipe provides a flexible, scalable, and accessible tool for isoform-level analysis of single-cell and spatial long-read RNA-Seq data.