Infectious Diseases Labs

ID LABS

Dr Cheryl Lee

Endogenous peptide lab
Duke-NUS Medical School, Singapore

Monday, 17th July 2023
11am to 12pm (SGT)

Venue: Cistron A & B @ Matrix L5

Mitochondrial peptide MOCCI finetunes Complex IV to modulate infection outcomes

Mito-SEPs are small open reading frame-encoded peptides that localize to the mitochondria. Through ribosome profiling and RNA-sequencing of human aortic endothelial cells, we observed that the expression of mito-SEPs is negatively correlated with inflammation. Using a pipeline developed in the lab to identify novel mito-SEPs, we identified mito-SEPs upregulated during inflammation, termed *i*-mito-SEPs. We report the discovery and deorphanization of Modulator of Cytochrome C oxidase during Inflammation (MOCCI), a 83 aa mitochondrial SEP (mito-SEP) that is specific to the inflamed state. MOCCI is a paralog of NADH:Ubiquinone Oxidoreductase Complex Assembly Factor 4 (NDUFA4), the 14th subunit of the mitochondrial respiratory chain complex IV (CIV). During inflammation, MOCCI replaces NDUFA4 in CIV, which leads to repressed CIV activity, lower membrane potential and reduced ROS production. Interestingly, knocking out of MOCCI in different cell types result in opposite inflammatory outcomes. The contradictory observations suggest that modulation of inflammatory pathways by CIV activity is cell type and context-dependent. We propose that mito-SEPs are important immunomodulators, of which one of the mechanisms is through altering mitochondrial electron transport chain activity.

Dr Cheryl Lee is a senior postdoc in the endogenous peptide lab in Duke-NUS Medical School, under the supervision of Asst Prof Lena Ho. She received her PhD from University of Cambridge, working on reproductive biology. During her PhD, she characterised the stem cell niche of placental cells and carried out a screen to identify factors that improve the stemness of trophoblast stem cells. When she returned to Singapore, she switched to studying vascular inflammation, as it is the leading cause of cardiovascular diseases. Through a screen to search for novel peptides involved in inflammation, she discovered a micro-peptide that controls the ETC, called MOCCI. Now her research centres around understanding how the ETC controls inflammation, particularly during viral infection

Hosted by Dr Amit Singhal

Webinar is open to all. No registration required

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