GCNI
Gerald Choa Neuroscience Institute
蔡永業腦神經科學研究所

香港中文大學
The Chinese University of Hong Kong

Research Seminar

"Human Stem Cell Models of Neurodegenerative Diseases"

by Dr. Christy Hung

Dr. Christy Hung is a group leader and Alzheimer's Research UK Senior Fellow at University College London and the Francis Crick Institute. Her primary research focus centres on understanding endolysosomal dysfunction in neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and Frontotemporal Dementia. Christy and her team are combining advanced imaging techniques, biochemical analyses, and human stem cell cultures to investigate the mechanisms underlying endolysosomal dysfunction.

28 Feb 2024 (Wed) 4-5pm

G02, G/F, Lo Kwee-Seong Integrated Biomedical Sciences Building (Area 39)

Abstract: A tidy brain is a healthy brain. Lysosome-mediated degradative systems, including the endosomal-lysosomal pathway and autophagy, are responsible for the clearance of protein aggregates. A growing body of evidence from cell biology, genetics, and genome-wide association studies has highlighted the significance of lysosomal dysfunction as a fundamental cellular impairment across multiple neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), and Frontotemporal Dementia (FTD).

My team found that APP and PSEN1 mutations, which are causal for early-onset familial AD, lead to significant defects in endolysosome function and autophagy in human iPSC-derived cortical neurons. Crucially, we have successfully rescued the defects in the lysosome and autophagy systems due to PSEN1 mutations by CRISPR knockout of APP. We further demonstrated that loss-of-function variations in SORL1, which are causal for sporadic AD, lead to significant defects in lysosome function and autophagy in human neurons. Importantly, we have successfully rescued these lysosomal and autophagy defects using extracellular antisense oligonucleotides targeting APP. Our data suggested that dysfunction of the lysosomal-autophagic system represents a convergent mechanism shared by familial and sporadic forms of AD.