



Jockey Club College of Veterinary
Medicine and Life Sciences

香港城市大學
City University of Hong Kong

in collaboration with Cornell University



Dissecting Molecular Mechanisms of Frontotemporal Lobar Degeneration

By

Dr. Xiaolai Zhou

Professor of Ophthalmology,

Zhongshan Ophthalmic Center (ZOC), Sun Yat-sen University (SYSU)

Hong Kong Time

Date: 3 November 2021 (Wednesday)

Time: 12:00pm – 1:00pm

Zoom: <https://cityu.zoom.us/j/97821451154>

Meeting ID: 978 2145 1154

****The seminar will be recorded and shared among JCC staff and students upon request.***

Abstract:

Frontotemporal lobar degeneration (FTLD) is a second most common early-onset dementia after Alzheimer's disease. Haploinsufficiency of progranulin (PGRN) caused by granulin (GRN) gene mutations is one of the leading causes of FTLD (FTLD-GRN). But the disease mechanisms underlying FTLD-GRN is unknown. Accumulating evidence suggests a critical role of PGRN in lysosomes. However, how PGRN is trafficked to lysosomes and what is the exact function of PGRN within lysosomes are unclear. Here we identified a novel pathway for lysosomal delivery of PGRN. We found that prosaposin (PSAP) interacts with PGRN and facilitates its lysosomal targeting in both biosynthetic and endocytic pathways via the cation-independent mannose 6-phosphate receptor and low-density lipoprotein receptor-related protein 1. Reversely, we further showed PGRN also facilitates the lysosomal trafficking of PSAP through its own cell surface receptor, sortilin. Finally, we demonstrated that lysosomal targeted PGRN is further processed into low-pH resistant granulin peptides and those granulin peptides positively regulate the enzymatic activities of multiple lysosomal hydrolases such as cathepsin D and glucocerebrosidase. Collectively, our results provide a novel understanding of the lysosomal trafficking and function of PGRN, and shed light on the molecular mechanisms FTLD caused by GRN mutations.

Biography:



Dr. Xiaolai Zhou is a Professor of Ophthalmology and a Principal Investigator of the Neuro-Ophthalmology Lab in the State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center (ZOC), Sun Yat-sen University (SYSU). Dr. Zhou received his M.D. from Hengyang Medical School, University of South China (2006) and M.S. in Ophthalmology from ZOC, SYSU (2009). He obtained his Ph.D. in Neurobiology in Dr. Kerstin Kriegelstein's lab (2013) in University of Freiburg, Germany, and conducted his postdoctoral training in Dr. Fenghua Hu's lab in Cornell University (2013-2017). Immediately after his postdoctoral training, Dr. Zhou joined Mayo Clinic (Jacksonville) as an Assistant Professor. In December 2020, Dr. Zhou accepted the 'Bairen' professorship of Sun Yat-sen University, set up his research lab in the State Key Laboratory of Ophthalmology in ZOC. Dr. Zhou worked on the molecular and genetic mechanisms of lysosomal dysfunction related-brain and -retinal degeneration. Specifically, his research focused on frontotemporal lobar degeneration and retinal degeneration caused by Progranulin (PGRN) gene mutation. Dr. Zhou's research has been published in peer-review journals, such as *Lancet Neurol.*, *Nat Commun.*, *Brain*, *Acta Neuropathol.*, *J Cell Biology*, *EMBO Rep*.

You are most welcomed to join!

Enquiries: Tatum Chan (3442 6762; chan.tatum@cityu.edu.hk)