SEMINAR

ALL ARE WELCOME

TEMASEK LIFESCIENCES LABORATORY

15 Mar 2022 (Tues), 4pm

Hosted by: Dr YU Fengwei

Join Zoom Meeting
https://us02web.zoom.us/j/87105731517
Meeting ID: 871 0573 1517 | Passcode: 177788

RNA Editing Restricts Hyperactive Ciliary Kinases

Dr Guangshuo OU
Tsinghua University, China



Protein kinase activity must be precisely regulated, but it remains unclear how a cell governs hyperactive kinases. Here, we generated a constitutively active mitogen-activated protein kinase DYF-5 (DYF-5CA) in C. elegans, which disrupted sensory cilia. Genetic suppressor screens identified that mutations of ADR-2, an RNA adenosine deaminase, rescued ciliary phenotypes of dyf-5CA. We found that dyf-5CA animals abnormally transcribed antisense RNAs that pair with dyf-5CA mRNA to form double-stranded RNA, recruiting ADR-2 to edit the region ectopically. RNA editing impaired dyf-5CA mRNA splicing, and the resultant intron retentions blocked DYF-5CA protein translation and activated nonsense-mediated dyf-5CA mRNA decay. The kinase RNA editing requires kinase hyperactivity. The similar RNA editing-dependent feedback regulation restricted other ciliary kinases NEKL-4/NEK10 and DYF-18/CCRK, suggesting a widespread mechanism underlying kinase regulation. We are cloning additional factors that regulate this feedback regulation.

Dr Guangshuo Ou is a professor and vice Dean in the School of Life Sciences, Tsinghua University. The Ou lab has been working on the cytoskeleton in the developing nervous system during the past decade. Guided by surprising results from forward genetic screens, the Ou lab has recently worked on RNA editing and cilia. Dr. Ou received his Ph.D.at the University of California Davis and was a postdoctoral fellow with Ron Vale at UCSF/HHMI.

Recent Publications:

1. Xie C, Jiang Y, Zhu Z, Huang S, Li W, **Ou G.** Actin filament debranching regulates cell polarity during cell migration and asymmetric cell division. Proc Natl Acad Sci U S A. 2021 Sep 14;118(37):e2100805118.

2. Li D, Liu Y, Yi P, Zhu Z, Li W, Zhang QC, Li JB, **Ou G.** RNA editing restricts hyperactive ciliary kinases. Science. 2021 Aug 27;373(6558):984-991.

3. Xie C, Li L, Li M, Shao W, Zuo Q, Huang X, Chen R, Li W, Brunnbauer M, Ökten Z, Chen L, **Ou G.** Optimal sidestepping of intraflagellar transport kinesins regulates structure and function of sensory cilia. EMBO J. 2020 Jun 17;39(12):e103955.