

in partnership with



Florian Engert

Professor of Molecular and Cellular Biology
Harvard University, USA

Host: Caroline Lei Wee (IMCB)



Tuesday, 19 March (Hybrid)

2:00 PM-3:00PM

IMCB Seminar Room 3-46, Level 3, Proteos, Biopolis
Singapore 138673 (or scan QR code for zoom registration)

Ketamine modulates a norepinephrine-astroglial circuit to persistently suppress futility-induced passivity

Mood-altering compounds hold promise for the treatment of many psychiatric disorders, such as depression, but connecting their molecular, circuit, and behavioral effects has been challenging. Here we find that, analogous to effects in rodent learned helplessness models, ketamine pre-exposure persistently suppresses futility-induced passivity in larval zebrafish. While antidepressants are thought to primarily act on neurons, brain-wide imaging in behaving zebrafish showed that ketamine elevates intracellular calcium in astroglia for many minutes, followed by persistent calcium downregulation post-washout. Calcium elevation depends on astroglial $\alpha 1$ -adrenergic receptors and is required for suppression of passivity. Chemo-/optogenetic perturbations of noradrenergic neurons and astroglia demonstrate that the aftereffects of glial calcium elevation are sufficient to suppress passivity by inhibiting neuronal-astroglial integration of behavioral futility. Imaging in mouse cortex reveals that ketamine elevates astroglial calcium through conserved pathways, suggesting that ketamine exerts its behavioral effects by persistently modulating evolutionarily ancient neuromodulatory systems spanning neurons and astroglia.

Florian Engert is Professor of Molecular and Cellular Biology at Harvard University, USA. He received his Ph.D. in physics from Ludwig Maximilian University of Munich 1997, and spent the following two years as a postdoctoral fellow at the Max Planck Institute for Neurobiology in Munich with Tobias Bonhoeffer. This was followed by two more years as a postdoc with Mu-ming Poo, first at the University of California, San Diego, and then at the University of California, Berkeley. In 2002, he accepted a position as an assistant professor at Harvard University, where he received tenure and was promoted to full professor in 2009. The general goal of his laboratory at present and in the intermediate future is the development of the larval zebrafish as a model system for the comprehensive identification and examination of neural circuits controlling various aspects of natural behaviors.