NUS National University of Singapore | Department of Anatomy
Yong Loo Lin School of Medicine

NUHS National University Health System

## RESEARCH SEMINAR

# THE CONDITIONAL KNOCKOUT APPROACH: CRE/LOX TECHNOLOGY IN HUMAN NEURONS

The use of human pluripotent stem cells to model human diseases has become a new standard in biomedical sciences. To this end, patient-derived somatic cells are studied in vitro to mimic human pathological conditions. Particularly, the human synapse is involved in many congenital disorders, hence a systematic understanding of its function and structure is essential for the quest of therapies. In my presentation I describe as an experimental strategy the 'Conditional Knockout Approach' which allows to engineer disease-relevant mutations in human neurons. In combination with Cre/Lox technology, this method enables me to investigate the molecular causes of human diseases independent of the genetic background or of genetic alterations induced by clonal selection. I generated knockouts in human genes encoding for major neuronal and synaptic components including Munc18-1 (STXBP1), L1CAM, and Synapsin-1, which impact synaptic transmission, axon development, and synaptic plasticity, respectively. Strikingly, in the case of Synapsin-1 we uncovered a novel presynaptic mechanism of plasticity in human neurons: After stimulation by neuromodulators synapsins acutely and bi-directionally control in a cAMP-dependent manner the reserve pool size of synaptic vesicles in human neurons by acting downstream of neuromodulator G-protein coupled receptors for serotonin and noradrenaline.

**Thursday**
**28 November 2019**
**3.00 pm – 4.00 pm**
**Seminar Room, MD10**
**Level 2, Anatomy Museum**

**Dr Christopher Patzke**
**Research Associate, Südhof-lab**
**Stanford University School of Medicine**
**Department of Molecular & Cellular Physiology**

Address enquiries : Ms Nuramalina at 6516 3200. All are welcome.