**KCTD13 INFLUENCE SYNAPTIC PRUNING OF THE BRAIN VIA THE MICROGLIA CELL**

**DongLiang Ma[2], Muhammad Danial Bin Mohd Mazlan[1], Eunice Chin[1] Sang Ho Song[1], George Augustine[1], Eyleen L. Goh[1]**

*[1] Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore*
*[2] Neuroscience Academic Clinical Programme, Duke-NUS Medical School, 20 College Road, Singapore 169856*

The potassium channel tetramerization domain containing 13 (*Kctd13*) gene is located within 16p11.2 locus where copy number variation is highly associated with risk of developing neuropsychiatric disorders, such as autism spectrum disorders. Recent studies have reported alterations to neuronal function in mouse models of *Kctd13* deletion. However, the underlying mechanisms are still unknown. Using CRISPR-Cas9 technology, we generated a novel transgenic knockout mouse model carrying loss-of-function mutation on *Kctd1*3 (*Kctd13*-KO) discovered in ASD subjects. We then examined the effects of *Kctd13*-KO on neuron functions and non-neuronal cells types such as astrocytes and microglia. Consistent with the emerging role that immune cells play in the pathophysiology of brain disorders, we found an increased microglial count in the hippocampus of *Kctd13*-KO mice. Microglia in *Kctd13*-KO animals express higher lysosomal marker CD68, and are more ramified than wild-type (WT) microglia. Cultured *Kctd13*-KO microglia also showed increased phagocytic activity as compared to WT microglia. Besides mediating inflammation during infection or clearing damaged cellular debris after brain insult, microglia also play a major role in synaptic pruning during postnatal development. We investigated these various functions of microglia and validated via pharmacological inhibition using selection antagonists. In addition, co-culturing WT neurons with *Kctd13*-KO microglia but not WT microglia, resulted in decreased frequency of miniature excitatory postsynaptic current, which can be rescued by expressing KCTD13 in *Kctd13* KO microglia. Thus, KCTD13 plays a role in maintaining synaptic functions via microglial and aberrations of which could lead to deficits seen in neuropsychiatric disorders.