ASHBi SEMINAR

Genetic Engineering and Neural-behavioral Phenotyping of a Macaque Model of Autism Spectrum Disorder

Dr. Yang Zhou

Principal Investigator, Montreal Neurological Institute-Hospital

Assistant Professor, Department of Neurology and Neurosurgery
Faculty of Medicine, McGill University

Date: Wednesday, 4h December 2019

Time: 11:00–12:00

Venue: Seminar Room 106, Faculty of Medicine Bldg. C

Mutation or disruption of the SHANK3 (SH3 domain and ankyrin repeat) gene at the 22q13.3 locus represents a highly penetrant, monogenic risk-factor for Autism Spectrum Disorder (ASD) and is a leading cause of Phelan–McDermid Syndrome (PMS). Recent advances in gene editing enabled the creation of genetically engineered non-human primate (NHP) models of brain disorders. Such NHP models might better approximate some neural and behavioral features of ASD than rodents and allow for gaining a better neurobiological understanding of ASD as well as developing treatment strategies. I will be presenting a collaborative effort during my postdoctoral training on a study of macaque monkeys carrying germline-transmissible SHANK3 mutation generated with CRISPR/Cas9-mediated gene editing. The founder mutants exhibited sleep disturbances, motor deficits, and increased repetitive behaviors, as well as social and learning impairments. Examining resting-state brain activity in founder monkeys with functional magnetic resonance imaging revealed altered local and global connectivity patterns indicative of circuit abnormalities. Our findings of altered brain connectivity and compromised behavioral performance in SHANK3 mutant macaques parallel some aspects of the gene-circuit-behavior dysfunction in human ASD and PMS.

Organizer: Prof. Tadashi Isa

[E-mail] isa.tadashi.7u@kyoto-u.ac.jp [Tel] 075-753-4351

Hosted by Institute for the Advanced Study of Human Biology (WPI-ASHBi)