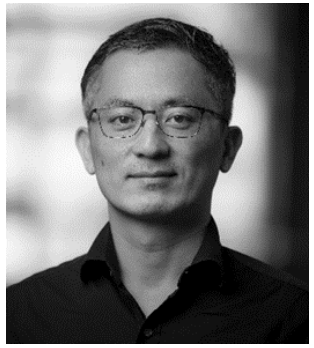
CRC 1451 - Project A09: Optogenetic modulation of cortical circuits improves motor control in Huntington's disease mice

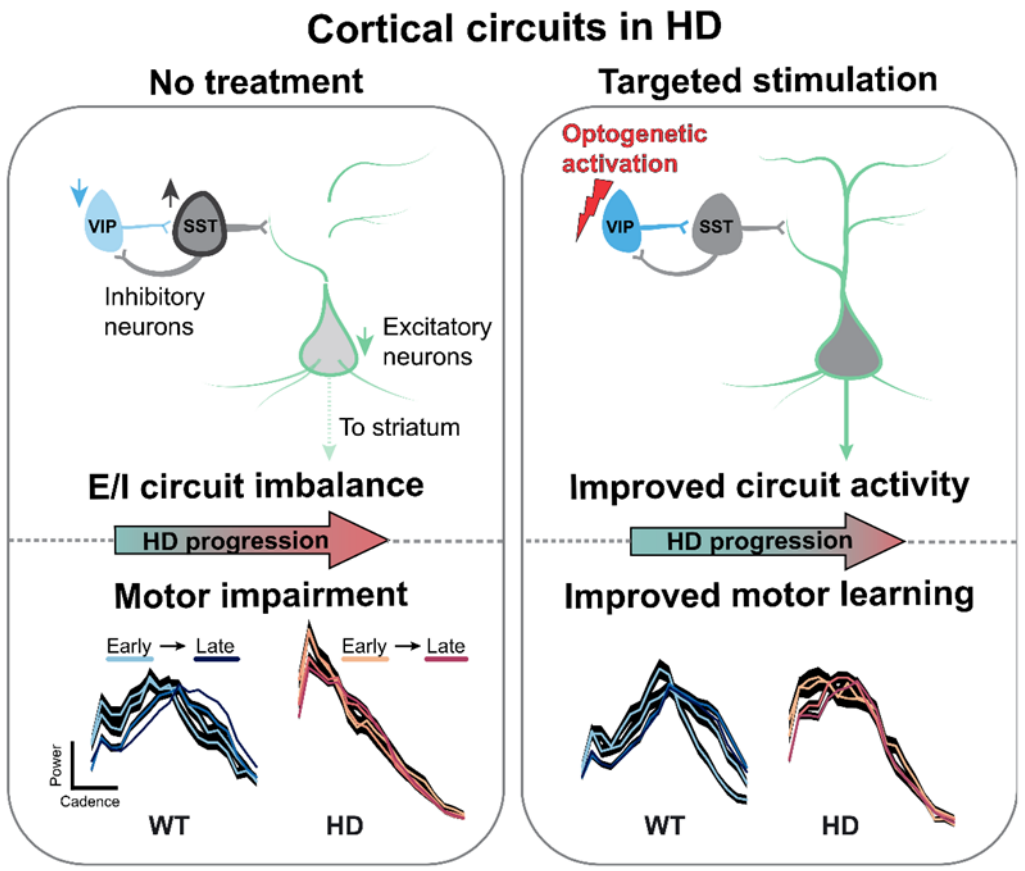
Huntington's disease (HD) is a devastating movement disorder without a current cure. It leads to impairments of the cortical circuit, yet how specific neuronal cell types are affected remains unexplored. In this study, we used longitudinal in vivo two-photon calcium imaging in the motor cortex of behaving HD mice to monitor the activity of excitatory corticostriatal projection neurons as well as three types of cortical inhibitory interneurons. We found that motor deficits were accompanied by neuron type-specific activity changes, including hypoactivity of vasoactive intestinal peptide (VIP) interneurons and corticostriatal neurons. Optogenetic activation of VIP cells restored healthy levels of cortical activity and resulted in lasting improvements of motor function. Our findings highlight cortical interneurons as a potential therapeutic target, and provide a platform for investigating other brain disorders with neural network imbalances.

Sonja Blumenstock is a project scientist interested in how neural circuits fail in neuro-degeneration. She combines high-resolution microscopy, neurostimulation and behavioural readouts to discover circuit biomarkers and therapeutic targets.



Takaki Komiyama is a Professor of Neurobiology and Neurosciences at the University of California San Diego. He is an expert in neural circuits for motor control.

Irina Dudanova is a PI in project A09. She studies molecular underpinnings and cellular mechanisms of neurodegenerative diseases with a focus on Huntington's disease.



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Restoring cortical disinhibition improves Huntington's disease phenotypes

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