DZNE German Center for Neurodegenerative Diseases within the Helmholtz Association

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

NEUROCURE Cluster of Excellence

EINSTEIN CENTER Neurosciences

Einstein Center for Neurosciences Berlin

Neuroscience Colloquium

Winter Semester 2017/2018

Lectures are held Thursdays, 5 p.m.
Venue: Paul-Ehrlich Lecturehall, Virchowweg 4, next to CCO

Ian Wickersham

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New circuit-specific and cell-type-specific transgene targeting techniques for neurons

Genetically-encoded tools like channelrhodopsin have revolutionized neuroscience, but they are usually useful only when selectively expressed in functionally meaningful subsets of neurons. In this talk I will present two advances from my lab for achieving this. First, I will describe a new class of double-deletion-mutant rabies viral vectors that leave transduced cells alive and healthy indefinitely. Recombinant rabies viral vectors have proven very useful in neuroscience for applications including retrograde targeting of projection neurons and monosynaptic tracing, but their cytotoxicity has usually limited their use to short-term experiments. The second-generation vectors described here have a second gene deleted in addition to the usual deletion of the glycoprotein gene. Deletion of the viral polymerase gene abolishes cytotoxicity and reduces transgene expression to trace levels but leaves vectors still able to retrogradely infect projection neurons and express recombinases, allowing downstream expression of other transgene products such as fluorophores and calcium indicators. In the second part of the talk, I will describe a novel approach to the problem of cell-type-specific transgene expression in wild-type animals. Directing expression of transgenes to specific cell types *in vivo* is critical for many branches of biology, but it typically requires creation of transgenic lines, which is impractical for most species. I show that using an endogenous protein as a scaffold for intracellular assembly of split transcription factors allows expression of transgenes specifically in cells that express the targeted protein. Our prototype system targets calretinin, a calcium binding protein characteristic of important interneuronal subtypes in cerebral cortex and elsewhere in the brain. The system can be delivered by adeno-associated viral vectors and causes expression of green fluorescent protein or channelrhodopsin specifically in calretinin-expressing interneurons in the cortex and hippocampus of wild-type mice and rats, allowing targeted electrophysiological recording or optogenetic control of these neurons' activity. Finally, I will show that the system is strongly species-independent, potentially allowing eventual adaptation for clinical use.

Location: Paul Ehrlich-Hörsaal,
Charité – Universitätsmedizin Berlin, Campus Mitte
Virchowweg 4, next to CCO

Date: **Thursday, February 1st, 5 p.m.**

Host: Niccolò Zampieri

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