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Life Sciences Seminar

The Importance of Signaling Pathway Downregulation for Central Nervous System Development and Homeostasis

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Host: Simon Hippenmeyer

During Central Nervous System development, neurons migrate, mature, and integrate into the following an intricate set of cues. Similarly, in the adult brain, homeostasis is achieved by responding to cues that regulate a myriad of processes, including adult neurogenesis. Cells respond to all these cues by triggering signaling pathways that, once the information is transduced, must be downregulated. Inappropriate regulation of signaling pathways cause neurons to mismigrate, lose responsiveness to new signals, and/or sustain the original signaling response, causing harm or death to the cell. The E3 Cullin-5 RING ligase (CRL5) is a crucial regulator of neuron migration and cell position in the retina, cortex, and cerebellum, by downregulating the Reelin/Dab1 signaling pathway. However, the role of CRL5 in the developing and adult hippocampus has remained elusive. Our work shows that CRL5 regulates lamination of hippocampal pyramidal neurons and participates in their dendritic arborization. We uncover that CRL5 downregulation of the small GTPase ARL4C, and its associated signaling effectors, participates in pyramidal neuron apical dendrite and dendritic tree formation and potentially in pyramidal neuron localization during hippocampal development. Moreover, CRL5 participates in dentate gyrus lamination and mossy fiber (i.e. granule cell axon) innervation. Particularly, we showed that depletion of Rbx2 affects mossy fiber pruning by deregulating the Semaphorin-3F signaling. Finally, we show that CRL5 also opposes Reelin/Dab1 signaling in the hippocampus to restrain the production of adult-born neurons in the dentate gyrus. Overall, we identified CRL5 as a novel regulator of hippocampal morphogenesis and homeostasis and uncovered several CRL5-regulated signaling pathways involved in these events.

Tuesday, May 14, 2019 01:30pm - 02:30pm

IST Austria Campus Seminar Room, Lab Building East

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