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INM-KOLLOQUIUM

"THE PHYSICAL REGULATION OF NEURONAL DEVELOPMENT AND REGENERATION"

Dr. Kristian Franze
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Dienstag, 11.12.2018, 11.00 Uhr

INM, Leibniz-Saal, Campus D2 5
Gastgeberin: Jun.-Prof. Dr. Franziska Lautenschläger

The microtubule (MT) cytoskeleton in neuronal axons is highly oriented with almost all MTs pointing with their growing end (+end) away from the cell body (+end out). Molecular motor proteins rely on this orientation to efficiently transport cellular cargo to the distal regions of the axon. However, the mechanisms underlying this unique MT configuration remain poorly understood. We here analyzed MT growth behavior with supervised machine learning in Drosophila melanogaster neurons, complemented by an analytical model of MT growth and shrinkage. +end out MTs grew for longer times than –end out MTs, leading to dramatic differences in average MT lengths with –end out MTs being short and unstable. This difference in MT growth times was caused by a dynactin gradient, which promoted growth in the periphery of the cell. These findings suggest a simple mechanism that organizes axonal MTs. First, +end out MTs are stabilized by distally located dynactin. Subsequently, the short –end out MTs are transported out of the axon, depolymerize, or reorient, leaving mostly +end out MTs in the axon.
Once MT polarity is established, axons keep growing to their target tissue. In order to move, neurons have to exert forces on and thus mechanically interact with their environment. However, we currently know very little about the mechanical regulation of neuronal growth. In vitro, Xenopus axon growth velocities, directionality, as well as fasciculation and maturation all significantly depended on substrate stiffness. Moreover, when grown on substrates incorporating linear stiffness gradients, axon bundles turned towards softer substrates. In vivo time-lapse atomic force microscopy revealed stiffness gradients in developing brain tissue, which axons followed as well towards soft. Interfering with brain stiffness and mechanosensitive ion channels in vivo both led to similar aberrant neuronal growth patterns with reduced fasciculation and pathfinding errors. Importantly, CNS tissue significantly softened after traumatic injuries. Ultimately, mechanical signals not only directly impacted neuronal growth but also indirectly by regulating neuronal responses to and the availability of chemical guidance cues, strongly suggesting that chemical and mechanical signaling pathways are intimately linked, and that their interaction is crucial for neuronal development and regeneration.

Wir laden 15 Minuten vor Beginn zu einem Get-together mit dem Referenten ein.

KONTAKT

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