Technology Offer

Taxol Induces Axonal Growth
File no.: MI 0202-3439 KEL

Background

It's not altogether clear why injured peripheral axons can regenerate relatively easily, whereas central axons have a much rougher time. Frank Bradke and colleagues from the Max Planck Institute of Neurobiology in Martinsried, Germany, decided to take a comparative look at microtubules in the business end of the axon: the tip or growth cone. Rather than growth cones, injured central axons have swellings at their tips called retraction bulbs that are the hallmark of a failed growth response. The Max Planck scientists lesioned the dorsal column or the sciatic nerve in 2- to 3-month-old mice and tracked axon tips with a fluorescent reporter. In central axons, retraction bulbs continue to increase in size after injury and contained disorganized microtubule networks compared with the sleek and organized regenerating peripheral axons. Disruption of microtubules with nocodazole caused retraction bulb formation in peripheral axons in vivo and in cell culture. In contrast, stabilizing microtubules with taxol prevented retraction bulbs.

Technology

Axons in the CNS do not regrow after injury, whereas lesioned axons in the peripheral nervous system (PNS) regenerate. Lesioned CNS axons form characteristic swellings at their tips known as retraction bulbs, which are the nongrowing counterparts of growth cones. Although much progress has been made in identifying intracellular and molecular mechanisms that regulate growth cone locomotion and axonal elongation, a comprehensive understanding of how retraction bulbs form and why they are unable to grow is still elusive. In a recent issue of the Journal of Neuroscience (22 Aug. 2007), Max Planck researchers report the analysis of the morphological and intracellular responses of injured axons in the CNS compared with those in the PNS. They show that retraction bulbs of injured CNS axons increase in size over time, whereas growth cones of injured PNS axons remain constant. Retraction bulbs contain a disorganized microtubule network, whereas growth cones possess the typical bundling of microtubules. Using in vivo imaging, the scientists find that pharmacological disruption of microtubules in growth cones transforms them into retraction bulb-like structures whose growth is inhibited. Correspondingly, microtubule destabilization of sensory neurons in cell culture induces retraction bulb formation. Conversely, microtubule stabilization prevents the formation of retraction bulbs and decreases axonal degeneration in vivo. Finally, microtubule stabilization enhances the growth capacity of CNS neurons cultured on myelin. Thus, the stability and
organization of microtubules define the fate of lesioned axonal stumps to become either advancing growth cones or nongrowing retraction bulbs. The data pinpoint microtubules as a key regulatory target for axonal regeneration.

**Literature**

Microtubule stabilization specifies initial neuronal polarization.
Harald Witte, Dorothee Neukirchen, and Frank Bradke. 

Disorganized Microtubules Underlie the Formation of Retraction Bulbs and the Failure of Axonal Regeneration
Ali Ertürk, Farida Hellal, Joana Enes, and Frank Bradke

For scientific questions, correspondence can directly be addressed to:

Frank Bradke, Ph.D.
Max Planck Institute of Neurobiology
Axonal Growth and Regeneration
Am Klopferspitz 18
82152 Martinsried, Germany
Email: fbradke@neuro.mpg.de

**Patent Information:** WO2006/094811A2