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The molecular mechanism of axonal transport in vivo and in vitro

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ABSTRACT OF THE TALK

Axonal transport is essential for the maintenance of neuronal function. Motor and sensory neurons appear particularly vulnerable to transport defects since mutations in this pathway induce the death of these neuronal populations in humans and mice. However, how defects in this process relate to disease, presently remains unclear.

A major focus of our laboratory is to understand the nature of the cellular machinery controlling sorting and long-range axonal transport in motor and sensory neurons. To fulfil this task, we have exploited the binding fragment of tetanus toxin (TeNT H_C), and more recently that of botulinum neurotoxin (BoNT) A and E. TeNT H_C enters motor neurons at the neuromuscular junction and is targeted to the soma located in the spinal cord. Its entry relies on a specialised clathrin-mediated pathway, which determines its sorting to axonal carriers shared with neurotrophins and their receptors Trks and $p75^{NTR}$. This route requires a specific subset of small GTPases and relies on Rab7 activity for long-range axonal transport powered by cytoplasmic dynein. Interestingly, mutations in components of the dynein motor complex and Rab7 have been shown to be associated with motor neuron disease and peripheral neuropathies in humans, suggesting the possibility that mutations in other components of these pathways may determine and/or predispose these pathologies.