Tubulin polyglutamylation is a general traffic-control mechanism in hippocampal neurons

By: Bodakuntla, S (Bodakuntla, Satish)[1,2]; Schnitzler, A (Schnitzler, Anne)[3]; Villablanca, C (Villablanca, Cristopher)[4,5]; Gonzalez-Billault, C (Gonzalez-Billault, Christian)[4,5]; Bieche, I (Bieche, Ivan)[3,6]; Janke, C (Janke, Carsten)[1,2]; Magiera, MM (Magiera, Maria M.)[1,2]

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Abstract

Neurons are highly complex cells that heavily rely on intracellular transport to distribute a range of functionally essential cargoes within the cell. Post-translational modifications of tubulin are emerging as mechanisms for regulating microtubule functions, but their impact on neuronal transport is only marginally understood. Here, we have systematically studied the impact of post-translational polyglutamylation on axonal transport. In cultured hippocampal neurons, deletion of a single deglutamylase, CCP1 (also known as AGTPBP1), is sufficient to induce abnormal accumulation of polyglutamylation, i.e. hyperglutamylation. We next investigated how hyperglutamylation affects axonal transport of a range of functionally different neuronal cargoes: mitochondria. lysosomes, LAMP1 endosomes and BDNF vesicles. Strikingly, we found a reduced motility for all these cargoes, suggesting that polyglutamylation could act as a regulator of cargo transport in neurons. This, together with the recent discovery that hyperglutamylation induces neurodegeneration, makes it likely that perturbed neuronal trafficking could be one of the central molecular causes underlying this novel type of degeneration.

This article has an associated First Person interview with the first author of the paper.

Keywords

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Author Information

Reprint Address: Janke, C; Magiera, MM (reprint author)

PSL Res Univ, Inst Curie, CNRS, UMR3348, F-91405 Orsay, France.

Reprint Address: Janke, C; Magiera, MM (reprint author)

Univ Paris Sud, Univ Paris Saclay, CNRS, UMR3348, F-91405 Orsay, France.

Addresses:

[1] PSL Res Univ, Inst Curie, CNRS, UMR3348, F-91405 Orsay, France

[2] Univ Paris Sud, Univ Paris Saclay, CNRS, UMR3348, F-91405 Orsay, France

[3] PSL Res Univ, Inst Curie, Dept Genet, F-75005 Paris, France

[4] Ctr Gerosci Brain Hlth & Metab GERO, Santiago 7800003, Chile

[5] Univ Chile, Fac Sci, Dept Biol, Santiago 7800003, Chile

[6] Univ Paris 05, Sorbonne Paris Cite, F-75005 Paris, France

E-mail Addresses:carsten.janke@curie.fr; maria.magiera@curie.fr

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