

The tubulin code – a mechanism to control microtubule properties

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The tubulin code is a concept predicting that functions of the microtubule cytoskeleton are regulated, or even determined, by a variety of biochemically complex tubulin posttranslational modifications [1,2]. While this concept looks at the first glimpse like a straight-forward regulatory system, only few functions could so far be attributed to specific tubulin modifications.

We use a combination of in-vitro and in-vivo approaches to determine how microtubule properties and functions are controlled in neurons. Neurons are particularly dependent on the microtubule cytoskeleton, which is essential for a multitude of their physiological functions. We have shown that deregulation of one posttranslational modification of tubulin, polyglutamylation, leads to neurodegeneration due to slight perturbations of organelle transport [3], indicating that this modification might only subtly, but significantly alter microtubule functions. We developed novel approaches to directly measure the molecular mechanisms that are controlled by polyglutamylation, which will be presented here.

The concept that arises from our work is that fine-tuning mechanisms might be key for understanding how physiological processes are kept in balance over longer periods of time and changing environmental conditions. Their perturbation might be a so-far underestimated trigger for late-onset diseases such as neurodegeneration and cancer.

[1] M. M. Magiera, P. Singh, S. Gadadhar, C. Janke, *Cell* 173, 1323 (2018).

[2] M. M. Magiera, P. Singh, C. Janke, *Cell* 173, 1552 (2018).

[3] M. M. Magiera S. Bodakuntla, J. Ziak, S. Lacomme, P. Marques Sousa, S. Leboucher, T.J. Hausrat, C. Bosc, A. Andrieux, M. Kneussel, M. Landry, A. Calas, M. Balastik, and C. Janke, *EMBO J* 37, e100440 (2018).