

COLLOQUIA IN PHYSIOLOGY AND VASCULAR BIOLOGY

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
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Monday 31.03.2014 11:00 c.t. **Carsten Janke** (host: H. Sitte)
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"Molecular mechanisms and biological functions of microtubule posttranslational modifications"

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Abstract:

Tubulin is subject to a range of posttranslational modifications. Two of these modifications, polyglutamylation and polyglycylation, are localized at the outer surface of microtubules and are therefore likely to regulate the interactions with microtubule associated proteins. Enzymes that catalyse polyglutamylation and polyglycylation are both members of an evolutionary conserved family of tubulin tyrosine ligase like proteins (TTLL), whereas reverse enzymes (until present only deglutamylases have been identified) are members of the cytosolic carboxy peptidase family (CCP).

Polyglutamylation is enriched on several, mostly specialized, cellular microtubules, such as neuronal microtubules, axomenes of cilia and flagella and centrioles of the centrosomes. Other microtubule structures that are glutamylated in a temporary manner are the mitotic spindle and the midbody during cell division. Polyglycylation, in contrast, has so far only been observed in cilia and flagella.

I will present an overview of our work starting with the discovery of the modification enzymes up to current functional studies. Our functional data demonstrate an important role of polyglutamylation in neurodegeneration. Glycylation plays a key role in stabilizing cilia and flagella, and is also important for primary cilia. We have also demonstrated that absence of glycylation enzymes can lead to amplified tumour development, which can be explained by dysfunction and loss of primary cilia.