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Microtubules are key cytoskeletal elements involved in a large number of functions in eukaryotic cells.

They assemble from a protein dimer of a- and b-tubulin, two highly similar and conserved proteins. Tubulins are subject to a large variety of posttranslational modifications (Fig. 1), which provide a rapid and reversible mechanism to diversify microtubule functions in cells. Our team is studying the mechanisms and functional roles of these modifications by using an interdisciplinary approach.

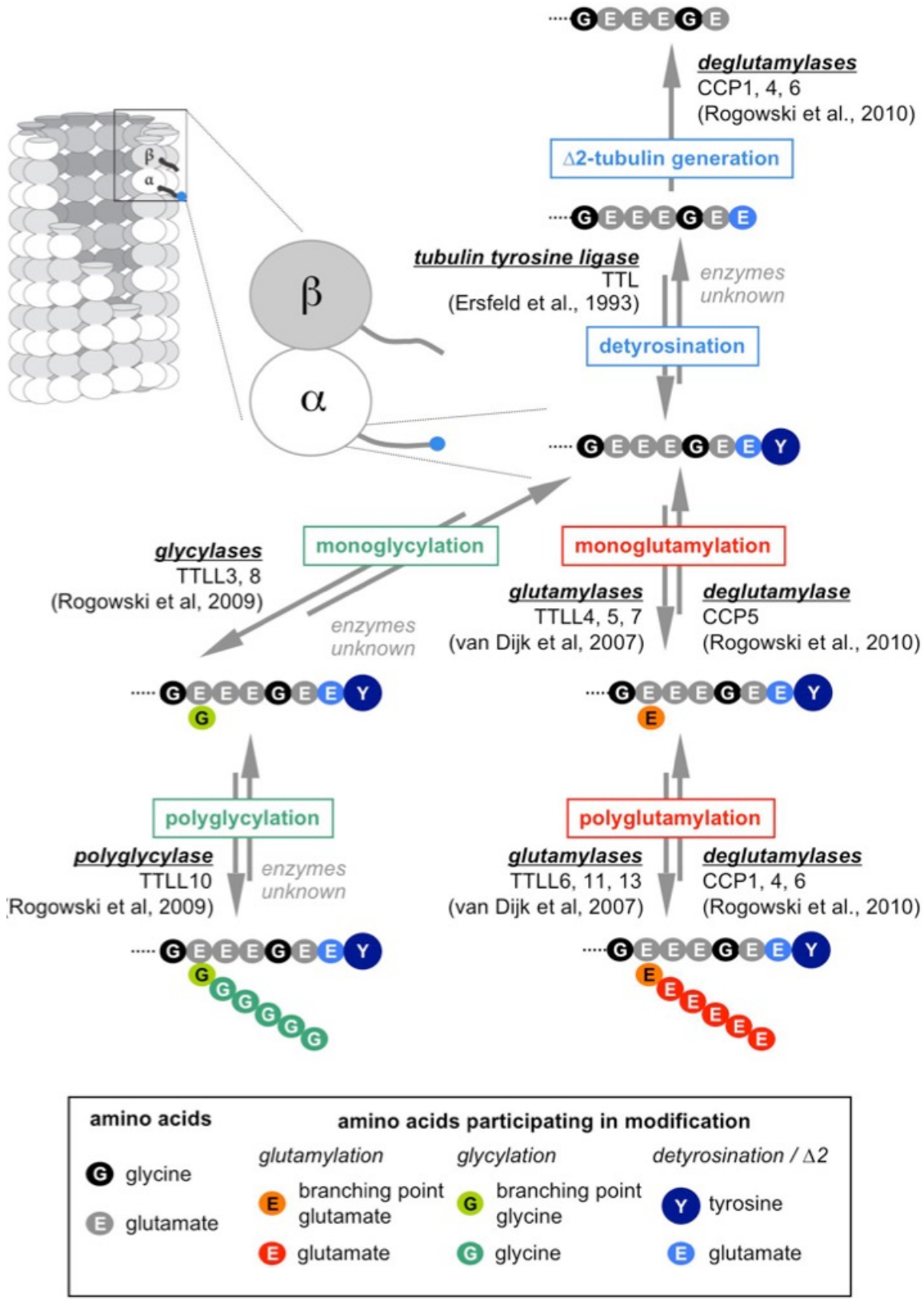
deglutamylases
CCP1, 4, 6
(Rogowski et al., 2010)
Δ2-tubulin generation
tubulin tyrosine ligase
TTL
(Ersfeld et al., 1993)
enzymes unknown
detyrosination
β
α
monoglycylation
monoglutamylation
glycylases
TTLL3, 8
(Rogowski et al, 2009)
enzymes unknown
glutamylases
TTLL4, 5, 7
(van Dijk et al, 2007)
deglutamylase
CCP5
(Rogowski et al., 2010)
polyglycylation
polyglycylase
TTLL10
(Rogowski et al, 2009)
enzymes unknown
polyglutamylation
glutamylases
TTLL6, 11, 13
(van Dijk et al, 2007)
deglutamylases
CCP1, 4, 6
(Rogowski et al., 2010)
amino acids
glycine
glutamate
amino acids participating in modification
glutamylation
branching point glutamate
glutamate
glycylation
branching point glycine
glycine
detyrosination / Δ2
tyrosine
glutamate

Figure 1: Schematic representation of tubulin post-translational modifications The three modifications that directly modify the C-terminal tail of tubulin, their mechanisms and enzymes involved in the modifications are depicted. Polyglutamylation and polyglycylation take place on both, α- and β-tubulin, whereas detyrosination is restricted to α-tubulin.

Our team has identified the enzymes involved in the posttranslational polyglutamylation (*1, 2*), deglutamylation (*3, 4*) and polyglycylation (*5*) of tubulin. Following the discovery of these enzymes, we are now investigating (i) the molecular mechanisms, and (ii) the biological functions of tubulin-modifying enzymes.

Polyglutamylation and polyglycylation take place within the C-terminal tails of the tubulin molecules. These tails are localized at the outer surface of the microtubule (Fig. 1), thus their posttranslational modification is most likely regulating the interactions of microtubules with their multiple binding partners, commonly known as microtubule-associated proteins (MAPs) and molecular motors. So far we have demonstrated that the microtubule-severing protein spastin is regulated by tubulin polyglutamylation (*6*), and that tubulin glycylation stabilizes ciliary axonemes by a yet unknown molecular mechanism (*5, 7*). Our functional studies have demonstrated an important role for both, polyglutamylation and polyglycylation for motile and primary cilia in mammals (*7, 8*), and we have found that polyglutamylation is directly linked to neurodegeneration in mice (*4*). We have further demonstrated a direct link between altered levels of a tubulin glycylase and colorectal cancer development (*8*).

In our ongoing projects, we are using biochemistry, biophysics and structural biology in conjunction with cell and mouse biology to identify the molecular mechanisms by which tubulin posttranslational modifications regulative microtubule behaviour and functions, and which are the cellular and developmental roles of these modifications and the corresponding enzymes. Our functional studies are focussed on the nervous system, cilia and flagella (including spermatogenesis), and cell division. Our team is closely collaborating with clinicians to delineate the implications of tubulin posttranlsational modifications in human pathologies.

Key publications

Year of publication 2017

Akendengue L., Trepout S., Grana M., Voegele A., Janke C., Raynal B., Chenal A., Marco S., Wehenkel A.M. (2017 Mar 30)
Bacterial kinesin light chain (Bklc) links the Btub cytoskeleton to membranes
SCIENTIFIC REPORTS : 7 : DOI : 10.1038/srep45668

Year of publication 2014

Olivia Tort, Sebastián Tanco, Cecilia Rocha, Ivan Bièche, Cecilia Seixas, Christophe Bosc, Annie

Andrieux, Marie-Jo Moutin, Francesc Xavier Avilés, Julia Lorenzo, Carsten Janke (2014 Oct 1)
The cytosolic carboxypeptidases CCP2 and CCP3 catalyze posttranslational removal of acidic amino acids.
Molecular biology of the cell : 3017-27 : DOI : 10.1091/mbc.E14-06-1072

Cecilia Rocha, Laura Papon, Wulfran Cacheux, Patricia Marques Sousa, Valeria Lascano, Olivia Tort, Tiziana Giordano, Sophie Vacher, Benedicte Lemmers, Pascale Mariani, Didier Meseure, Jan Paul Medema, Ivan Bièche, Michael Hahne, Carsten Janke (2014 Oct 1)
Tubulin glycylases are required for primary cilia, control of cell proliferation and tumor development in colon.
The EMBO journal : 2247-60 : DOI : 10.15252/embj.201488466

Year of publication 2013

Montserrat Bosch Grau, Gloria Gonzalez Curto, Cecilia Rocha, Maria M Magiera, Patricia Marques Sousa, Tiziana Giordano, Nathalie Spassky, Carsten Janke (2013 Aug 5)
Tubulin glycylases and glutamylases have distinct functions in stabilization and motility of ependymal cilia.
The Journal of cell biology : 441-51 : DOI : 10.1083/jcb.201305041

Year of publication 2010

Krzysztof Rogowski, Juliette van Dijk, Maria M Magiera, Christophe Bosc, Jean-Christophe Deloulme, Anouk Bosson, Leticia Peris, Nicholas D Gold, Benjamin Lacroix, Montserrat Bosch Grau, Nicole Bec, Christian Larroque, Solange Desagher, Max Holzer, Annie Andrieux, Marie-Jo Moutin, Carsten Janke (2010 Nov 12)
A family of protein-deglutamylating enzymes associated with neurodegeneration.
Cell : 564-78 : DOI : 10.1016/j.cell.2010.10.014

Benjamin Lacroix, Juliette van Dijk, Nicholas D Gold, Julien Guizetti, Gudrun Aldrian-Herrada, Krzysztof Rogowski, Daniel W Gerlich, Carsten Janke (2010 Jun 14)
Tubulin polyglutamylation stimulates spastin-mediated microtubule severing.
The Journal of cell biology : 945-54 : DOI : 10.1083/jcb.201001024