ABSTRACT

The spatio-temporal organization and dynamic behavior of microtubules accurately react to cellular needs during intracellular transport, signal transduction, growth, division, and differentiation. The cell generates centrosomal microtubules *de novo* with the help of γ-tubulin complexes (γTuRCs). The post-translational modifications fine-tune microtubule nucleation by targeting the proteins, interacting with γTuRCs. However, the exact signaling pathways, regulating centrosomal microtubule nucleation, remain mostly unknown.

In the presented thesis, we functionally characterized protein tyrosine phosphatase SHP-1 and E3 UFM-protein ligase 1 (UFL1) with its interacting protein CDK5RAP3 (C53) in the regulation of centrosomal microtubule nucleation. We also elucidated the role of actin regulatory protein profilin 1 in this process. We found that SHP-1 formed complexes with γTuRC proteins and negatively regulated microtubule nucleation by modulating the amount of γ-tubulin/γTuRC at the centrosomes in bone marrow-derived mast cells (BMMCs). We suggested a novel mechanism with centrosomal tyrosine-phosphorylated Syk kinase, targeted by SHP-1 during Ag-induced BMMCs activation, regulating microtubules.

We showed for the first time that UFL1/C53 protein complex is involved in the regulation of microtubule nucleation. The C53, which protein level is regulated by UFL1, could associate with centrosomes. Upon induced ER stress, C53 detached from centrosomes, which resulted in the increased microtubule nucleation and ER expansion. Our findings point to a new mechanism for ER stress relief by stimulation of microtubule nucleation.

We reported that profilin 1 extends its regulation functions not only to actin filament polymerization but also to microtubule nucleation. We suggest that profilin 1 plays a dual role as a coordinator of actin and microtubule organization in mammalian cells. Finally, we found that both plant and animal highly purified γ-tubulins lacking associated proteins have the intrinsic property of self-polymerization into filaments.