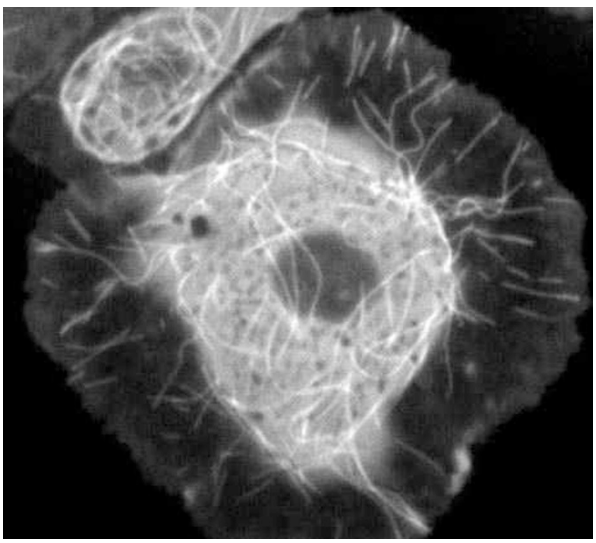
Nature Reviews Molecular Cell Biology | AOP, published online 11 November 2010; doi:10.1038/nrm3014

CYTOSKELETON

Keeping minus ends stable

Microtubules, which are made up of α- and β-tubulin heterodimers, have a minus end and a plus end. Most microtubule plus ends are dynamic and transition between growth and shrinkage in response to proteins that promote their assembly and disassembly. By contrast, microtubule minus ends are not usually dynamic and therefore might be stabilized by unknown proteins. Goodwin and Vale now show that Patronin (also known as Short spindle protein 4 (SSP4)) caps and stabilizes microtubule minus ends to organize the microtubule cytoskeleton.

A previous study in the Vale laboratory identified Patronin in an RNA interference (RNAi) screen for spindle morphology defects in *Drosophila melanogaster* S2 cells, in which Patronin depletion caused short mitotic spindles and microtubule fragments in interphase. Here, the authors further characterize Patronin function and observe that its depletion causes the unexpected appearance of short microtubules at the cell periphery and decreases the density of the interphase microtubule cytoskeleton. Some microtubules were seen to release from sites of nucleation, and these free microtubules moved towards the periphery of Patronin-depleted cells by treadmilling, a process in which tubulin is added to the plus end of microtubules and lost from the minus end at the same rate. In some cases, the rate of minus-end depolymerization was faster than the rate of plus-end polymerization (which is not altered by Patronin depletion), leading to the complete disappearance of microtubules. This finding is likely to account for the sparse interphase microtubule array in Patronin-depleted cells.



Patronin depletion in S2 cells expressing green fluorescent protein–tubulin results in numerous short microtubules that are disconnected from microtubule nucleation centres. Time-lapse imaging shows that these free microtubules move throughout the cytoplasm by treadmilling. Image courtesy of S. S. Goodwin and R. D. Vale, University of California, San Francisco, USA.

So, how are microtubule minus ends depolymerized in Patronin-depleted cells? Kinesin-13 family members are cytoskeletal motors that depolymerize microtubules and can bind to microtubule plus and minus ends *in vitro*. The authors individually expressed RNAi against the three *D. melanogaster* Kinesin-13 proteins (Kinesin-like protein 10A (KLP10A), KLP59C and KLP59D) in Patronin-depleted cells, and showed that only KLP10A depletion rescues the Patronin RNAi and short spindle phenotypes. KLP10A was observed along the depolymerizing minus ends of treadmilling microtubules in Patronin-depleted cells during interphase, supporting the conclusion that it actively depolymerizes microtubule minus ends in the absence of Patronin. Thus, *in vivo*, Patronin protects microtubule minus ends against KLP10A-induced depolymerization during interphase and mitosis.

Finally, the authors investigated *in vitro* the relationship of green fluorescent protein–Patronin with microtubules made from purified tubulin. Adding the motor domain of a KLP10A homologue to microtubules assembled *in vitro* caused them to depolymerize at both ends. Importantly, purified Patronin bound selectively to the minus ends of microtubules and inhibited KLP10A-mediated depolymerization there. Thus, *in vitro,* purified Patronin selectively binds to microtubule minus ends to protect them against Kinesin-13-induced depolymerization.

This study provides insight into how microtubule minus-end dynamics are regulated to ensure the efficient organization of the microtubule cytoskeleton. A closer look at microtubule minus ends might reveal additional proteins that serve to regulate their dynamics *in vivo*.

Katharine H. Wrighton

ORIGINAL RESEARCH PAPER Goodwin, S. S. & Vale, R. D. Patronin regulates the microtubule network by protecting microtubule minus ends. *Cell* **143**, 263–274 (2010)
FURTHER READING Akhmanova, A. & Steinmetz, M. O. Tracking the ends: a dynamic protein network controls the fate of microtubule tips. *Nature Rev. Mol. Cell Biol.* **9**, 309–322 (2008)