Roadworks on the motorways of the cell

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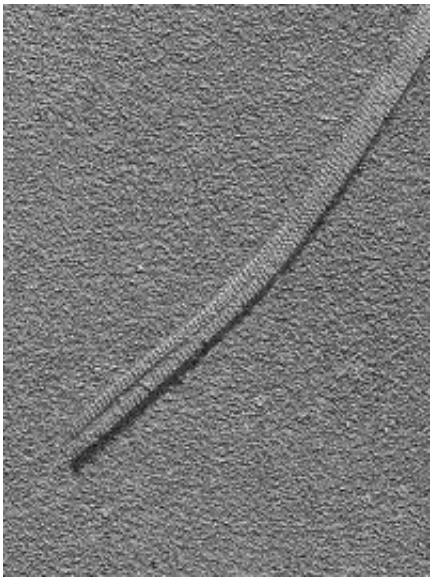

In the absence on Mal3p microtubules are unstable and can open at the seam. The image shows a microtubule with opening seam (bottom left), seen through the electron microscope. Credit: Image by Linda Sandblad, EMBL

A cell is a busy place. In a permanent rush hour, molecules are transported along a dynamic motorway system made up of filaments called microtubules. Microtubules constantly grow and shrink and are rapidly assembled wherever a cargo needs to go, but during this transportation process they need to be kept stable.

Researchers from the European Molecular Biology Laboratory (EMBL) have discovered for the first time that a protein stabilises microtubules by binding to their weakest part, the so-called lattice seam. The study,

which appears in this week's issue of the journal *Cell*, also suggests that the protein creates a special surface along the seam that offers an alternative track for transportation.

The basic building blocks of microtubules are proteins called tubulins. They assemble in a single line to form so-called protofilaments, of which several combine to build a large tubulin sheet. Investigating how this sheet folds into the tube-like structures of microtubules in yeast, researchers have now discovered that a protein called Mal3p is crucial. Combining molecular techniques with a unique Electron Microscope setup based at the ETH in Zürich, they found that Mal3p binds to the seam of the microtubule, which forms as the two sides of the tubulin sheet fold into a tube. The protein binds in a single line along the seam, seals the tube and stabilises it at its weakest point.

"It is the first time that we've found a protein that specifically binds to the microtubule seam," says Andreas Hoenger, former group leader at EMBL who has just moved to head a lab at the University of Colorado. "Until now the function of the seam has been unknown and it has been largely ignored as an odd and irrelevant part of the microtubule lattice. Our experiments now reveal it as a central spot where microtubule stability can be regulated."

Without Mal3p, microtubules are unstable and likely to disassemble, while in its presence they grow into long filaments. Mal3p could function as a key regulator of microtubule behaviour. Controlling its presence allows fast switches between growth and shrinkage of microtubules, which are essential for rapid and flexible cellular transport. Mal3p's location along the microtubule seam is crucial, because here it can confer stability without obstructing the traffic of motor proteins along the filament. Apart from its stabilising role Mal3P could also play a more active role in transportation.

"Motor proteins move along microtubules through direct interaction with tubulin. They transport cargo similarly to trucks driving on motorways," explains Damian Brunner, group leader at EMBL. "The line of Mal3p along the seam potentially creates an alternative track on the filament, along which a specialised type of motor protein could move, just like creating a railway track along a motorway. This dual system could make transport more diverse and efficient."

The new insights gained into cellular transport and the stabilisation of microtubules in yeast might help shed light on how similar processes work in humans. Mal3p is highly conserved across species and its human counterpart plays a role in various clinical conditions, such as colon cancer or neurodegenerative diseases.

Source: European Molecular Biology Laboratory