Research Sheds Light on Magic of Microtubule Growth

Transport within the cell relies on a system of tracks, the microtubules, which continuously grow or decay at one end, while the other end remains tethered and static. Researchers at the ISMB have now elucidated how some of the proteins that coordinate the building work on a growing end recognise the sites where they are needed.

Research into dynamic cellular systems such as the ever-changing microtubule cytoskeleton is complicated by the fact that structural methods typically require static and stable molecular complexes. The group of Carolyn Moores at Birkbeck Crystallography / ISMB, working together with Thomas Surrey at Cancer Research UK, has created a static model of the dynamically growing microtubule end, allowing them to pin down the structural interactions that hold the building site together.

Protein building blocks (tubulin proteins) that are added to the growing end normally carry the energy-rich substance GTP, which is split up into GDP and phosphate within seconds of incorporation. By offering building blocks with a non-cleavable analogue of GTP, the researchers could create a microtubule arrested in its growth but retaining the characteristics of a growing (GTP-carrying) end. Moores’ group at the ISMB could then obtain detailed images of this structure using electron microscopy at very low temperatures (cryo-EM).

Specifically, their work published in the latest issue of the journal “Cell” (Maurer et al) shows how a crucial group of proteins needed for the extension of the tip and its interaction with cellular features, the End-Binding (EB) proteins, bind to the building blocks that carry the uncleaved (and uncleavable) GTP. The researchers found that each of the EB proteins bridges two strings of tubulin subunits running the length of the tube structure, the so-called protofilaments.

Intriguingly, each microtubule has a “seam” where the protofilaments are connected in a different fashion, and the EB proteins appear to recognise that difference, as they don’t bridge the seam.

“The fascinating behaviour of growing microtubule ends has been tantalising biologists for some time,” says Moores.

With the help of this model system, further research will uncover more details of the wider context in the dynamic behaviour of the cytoskeleton made up of the microtubules.

“The biophysical experiments performed in the Surrey lab were essential in optimising sample preparation for our cryo-electron microscopy structural experiments, but we never anticipated the secrets of microtubule biology we would uncover when we started our collaboration.”

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