Structure watch

MONITORING MAPS

The dynamic turnover of microtubule filaments, which consist of protofilaments of α-tubulin–β-tubulin heterodimers that are bound head-to-tail, is controlled by microtubule-associated proteins (MAPs). MAPs can either stabilize or destabilize microtubules, but our understanding of the mechanistic basis of this is limited by a lack of structural insights into how MAPs associate with microtubules. Fourniol *et al.* have now used cryo-electron microscopy and single particle algorithms to visualize how the MAP doublecortin (DCX) binds microtubules.

DCX can both nucleate and stabilize microtubules, which allowed Fourniol *et al.* to visualize microtubules assembled into the same architecture that they would form *in vivo*. They confirmed that these microtubules are made of a standard 13-protofilament cylinder and that DCX binds at the region where four tubulin dimers meet; this allows it to stabilize interactions along both the longitudinal and lateral lattices. DCX does not bind along the 'seam' — an area of discontinuity in the lattice that is proposed to affect microtubule dynamics — and this suggests that the way in which DCX stabilizes microtubules is not through this region.

ORIGINAL RESEARCH PAPER Fourniol, F. J. *et al.* Template-free 13-protofilament microtubule-MAP assembly visualized at 8 Å resolution. *J. Cell Biol.* **191**, 463–470 (2010)

FIT FOR EXPORT

The export of proteins from the nucleus is driven by export transport factors, including exportins. The exportin CRM1 (also known as EXP1) mediates export of a broad range of substrates, and this requires it to bind to both RanGTP and the cargo protein through a nuclear export sequence (NES). The classic NES is characterized by four spaced hydrophobic residues that are separated by variable numbers of amino acid residues. Previously, it was unclear how CRM1 recognizes different cargo proteins that have unique spacings of their hydrophobic residues, and whether it has to alter its own conformation to do so.

Güttler *et al.* have now determined the crystal structure for RanGTP bound to CRM1 and two different cargo proteins, namely chimaera proteins containing the NES of the protein kinase A inhibitor (PKI) or HIV-1 Rev. Despite the unique spacing of their key residues, the NESs of both proteins can be accommodated in the same hydrophobic cleft of CRM1, which retains a defined conformation while recognizing distinct NESs. Instead, each NES adopts a unique conformation to allow it to fit into the hydrophobic pocket, and the distinct spacings of five key hydrophobic residues are compensated for by different conformations of the NES region being bound to CRM1. The PKI substrate forms an α-helical conformation, whereas the Rev peptide has a more extended conformation. Thus, this study calls for the classic definition of NES to be refined into a more structure-based view of the consensus site.

ORIGINAL RESEARCH PAPER Güttler, T. *et al.* NES consensus redefined by structures of PKI-type and Rev-type nuclear export signals bound to CRM1. *Nature Struct. Mol. Biol.* **17**, 1367–1376 (2010)

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