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Cryo-EM analysis revealed how microtubule-associated protein 4 (MAP4) controls microtubule stability and kinesin motility

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Tau-family microtubule-associated proteins (MAPs) control microtubule stability and microtubule-based motility through its C-terminal microtubule binding domain (MBD). MBD consists of three to five disordered repeat sequences produced by alternative splicing, altering the function of MAPs. Despite its importance, however, the regulatory mechanism of MAPs through MBD repeats are still poorly understood.

To investigate the regulatory mechanism by MAPs, we focused on the microtubule-associated protein 4 (MAP4), which is a member of the Tau-family MAPs. MAP4 has several isoforms with different number of the MBD repeat sequences, which alters microtubule stability and kinesin motility. Using cryo-electron microscopy (cryo-EM), we visualized complex structures of the microtubule, Kinesin-1, and MAP4 MBD 4 repeat (4R-MAP4) or MAP4 MBD 5 repeat (5R-MAP4). Both MAP4 MBD repeats formed complex along the microtubule protofilament, from Kinesin-1 at the minus-end side to the next kinesin-1 at the plus-end side. The strongest density of the MAP4 was observed around the inter-dimer interface of the tubulin. The difference between 4R-MAP4 and 5R-MAP4, and tau protein will be discussed.

KEY WORDS

MAP4, Tau, MAP, Microtubule, Cryo-EM, TEM