Mechanism of microtubule depolymerization by kinesin-13s

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Kinesins-13s are non-motile molecular motors that regulate microtubule dynamics by promoting microtubule depolymerization. This kinesin family is precisely localized and regulated in eukaryotic cell to participate in a broad range of processes such as spindle assembly and poleward microtubule flux during mitosis, cytokenesis, axonal branching and ciliogenesis. Kinesin-13s diffuse to microtubule ends where they stabilize curved protofilaments, leading to microtubule depolymerization. They contain a highly conserved ATPase motor domain that can depolymerize microtubules by itself. However the molecular mechanism of microtubule depolymerization by kinesin-13 is unknown. We report cryo-electron microscopy structures at high resolution (3 - 6 Å range) of motor domain constructs of the *Drosophila melanogaster* kinesin-13 KLP10A bound to straight and curved tubulin and in different nucleotide states. The cryo-EM data provides a pseudo atomic view of the microtubule depolymerization activity of kinesin-13s. In particular the structures reveal how the motor domain is adapted to perform an activity seemingly very different from processive kinesins. The structures show nucleotide induced conformational changes and how they are coupled with kinesin-13-specific structural elements to alter the conformation of tubulin. Integrated with single molecule fluorescence polarization experiments and completed with the study of a phosphoregulation on the KLP10A motor domain, this work provides a detailled view of the mechanism of microtubule depolymerization by kinesin-13s.