De novo identification of mammalian ciliary motility proteins using cryo-EM

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Abstract

Dynein-decorated doublet microtubules (DMTs) are critical components of the oscillatory molecular machine of cilia, the axoneme, and have luminal surfaces patterned periodically by microtubule inner proteins (MIPs). Here we present an atomic model of the 48-nm repeat of a mammalian DMT, derived from a cryoelectron microscopy (cryo-EM)map of the complex isolated from bovine respiratory cilia. The structure uncovers principles of doublet microtubule organization and features specific to vertebrate cilia, including previously unknown MIPs, a luminal bundle of tektin filaments, and a pentameric dynein-docking complex. We identify a

mechanism for bridging 48- to 24-nm periodicity across the microtubule wall and show that loss of the proteins involved causes defective ciliary motility and laterality abnormalities in zebrafish and mice. Our structure identifies candidate genes for diagnosis of ciliopathies and provides a framework to understand their functions in driving ciliary motility.

Figure:

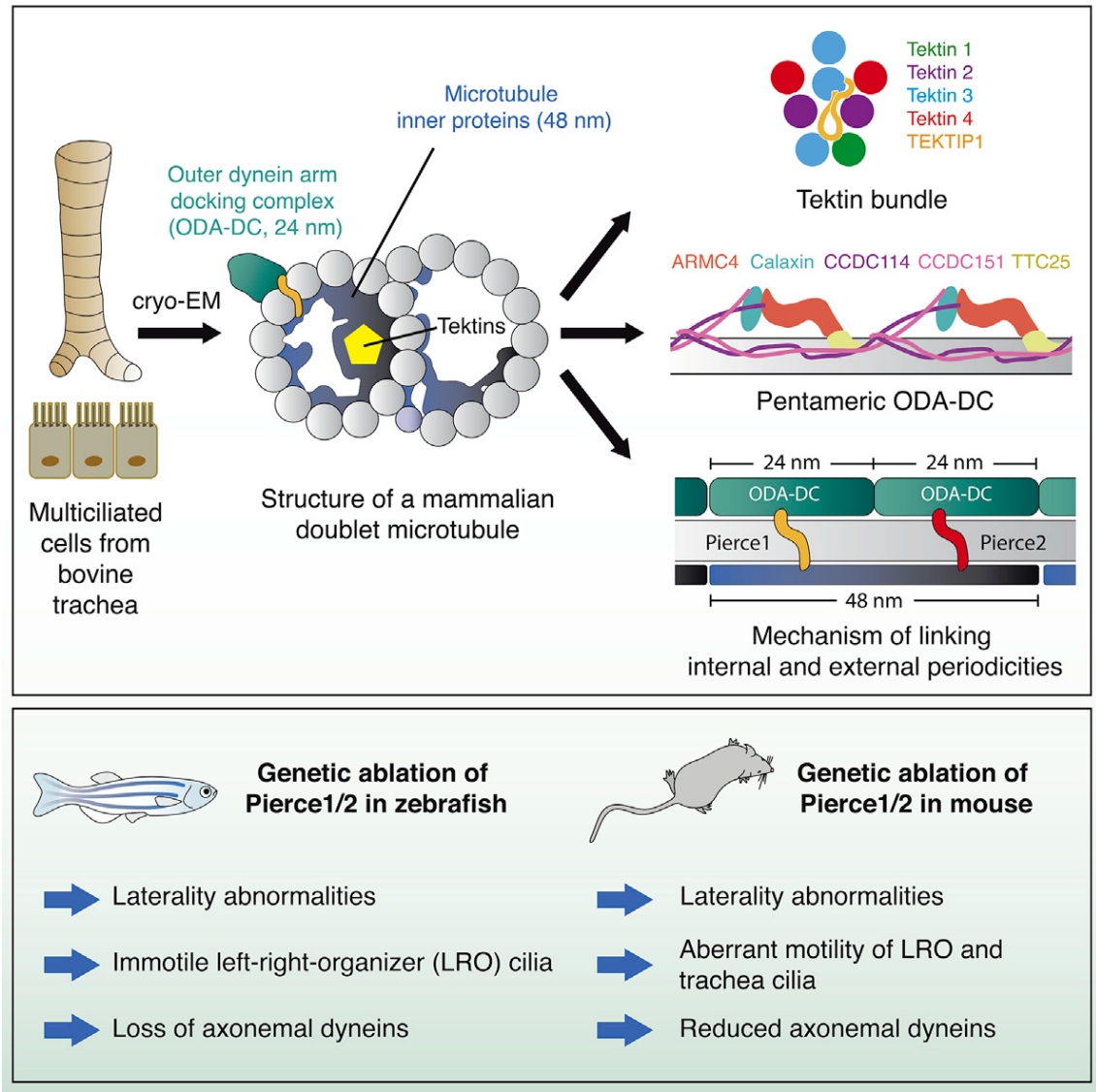

Figure Legend:

- Structure of the 48-nm repeat of a mammalian doublet microtubule from respiratory cilia
- Tektin filaments bind within the lumens of doublet microtubules
- A pentameric docking complex attaches axonemal dyneins to doublet microtubules
- Loss of connectivity across microtubule