

Abstract Submitted
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Dynein's C-terminal Domain Plays a Novel Role in Regulating Force Generation¹ ARNE GENNERICH, MATTHEW NICHOLAS, SIBYLLE BRENNER, Albert Einstein College of Medicine, CAITLIN LAZAR, SARAH WEIL, RICHARD VALLEE, PETER HOOK, Columbia University College of Physicians and Surgeons, GENNERICH LAB COLLABORATION, VALLEE LAB COLLABORATION — Cytoplasmic dynein is a microtubule motor involved in a wide range of low and high force requiring functions in metazoans. In contrast, yeast dynein is involved in a single, nonessential function, nuclear positioning. Interestingly, the single-molecule function of yeast dynein is also unique: whereas mammalian dyneins generate forces of 1-2 pN, *S. cerevisiae* dynein stalls at 5-7 pN. The basis for this functional difference is unknown. However, the major structural difference between mammalian and yeast dyneins is a ~30 kDa C-terminal extension (CT) present in higher eukaryotic dyneins, but missing in yeast. To test whether the CT accounts for the differences in function, we produced recombinant rat dynein motor domains (MD) with (WT-MD) and without (Δ CT-MD) the CT, using baculovirus expression. To define motor function, we performed single-molecule optical trapping studies. Dimerized WT-MD stalls at ~1 pN and detaches from microtubules after brief stalls, in agreement with previous studies on native mammalian dynein. In sharp contrast, but similar to yeast dynein, Δ CT-MD stalls at ~6 pN, with stall durations up to minutes. These results identify the CT as a new regulatory element for controlling dynein force generation.

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