A novel isoform of MAP4 organises the antiparallel microtubule array required for muscle cell differentiation

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Keywords: *microtubules, microtubule motors, MAP4, dynein, kinesin-1.*

Abstract

The microtubule cytoskeleton is critical for muscle cell differentiation and undergoes reorganisation into an array of antiparallel microtubules, which serves as template for contractile sarcomere formation. Here, we identify a previously uncharacterised isoform of microtubule-associated protein MAP4, oMAP4, as a microtubule organising factor that is crucial for myogenesis. We show that oMAP4 is expressed upon muscle cell differentiation and is the only MAP4 isoform essential for normal progression of the myogenic differentiation programme. Depletion of oMAP4 impairs cell elongation and cell-cell fusion, centrosomal protein reorganisation and expression of sarcomeric components. We find that oMAP4 is required for antiparallel microtubule organisation in muscle cells and that it prevents dynein- and kinesin-driven microtubule-microtubule sliding. Purified oMAP4 aligns dynamic microtubules *in vitro*. We propose a model in which the cooperation of dynein-mediated microtubule transport and oMAP4-mediated zippering of microtubules drives formation of an antiparallel microtubule array that provides critical support for the polarisation and elongation of myotubes.