

ABSTRACT

Hook proteins are evolutionarily conserved dynein adaptors that promote assembly of highly processive dynein-dynactin motor complexes. Mammals contain three Hook paralogs, namely Hook1, Hook2 and Hook3 that have distinct subcellular localisations and expectedly, distinct cellular functions. Here we demonstrate that Hook2 binds to, and promotes dynein-dynactin assembly specifically during mitosis. During the late G2 phase, Hook2 mediates dynein-dynactin localization at the nuclear envelope (NE), which is required for centrosome anchoring to the NE. Independent of its binding to dynein, Hook2 regulates microtubule nucleation at the centrosome- accordingly, Hook2-depleted cells have reduced astral microtubules and spindle positioning defects. Besides the centrosome, Hook2 localizes to, and recruits dynactin and dynein to the central spindle. Dynactin-dependent targeting of centralspindlin complex to the midzone is abrogated upon Hook2 depletion, accordingly Hook2 depletion results in cytokinesis failure. We find that the zebrafish Hook2 homolog promotes dynein-dynactin association and was essential for zebrafish early development. Together, these results suggest that Hook2 mediates assembly of the dynein-dynactin complex and regulates mitotic progression and cytokinesis.