Mitogen-activated protein/extracellular signal-regulated kinase kinase 1act/tubulin interaction is an important determinant of mitotic stability in cultured HT1080 human fibrosarcoma cells.

ABSTRACT

Activation of the mitogen-activated protein kinase (MAPK) pathway plays a major role in neoplastic cell transformation. Using a proteomics approach, we identified alpha tubulin and beta tubulin as proteins that interact with activated MAP/extracellular signal-regulated kinase kinase 1 (MEK1), a central MAPK regulatory kinase. Confocal analysis revealed spatiotemporal control of MEK1-tubulin colocalization that was most prominent in the mitotic spindle apparatus in variant HT1080 human fibrosarcoma cells. Peptide arrays identified the critical role of positively charged amino acids R108, R113, R160, and K157 on the surface of MEK1 for tubulin interaction. Overexpression of activated MEK1 caused defects in spindle arrangement, chromosome segregation, and ploidy. In contrast, chromosome polyploidy was reduced in the presence of an activated MEK1 mutant (R108A, R113A) that disrupted interactions with tubulin. Our findings indicate the importance of signaling by activated MEK1-tubulin in spindle organization and chromosomal instability.

Keyword: Mitotic stability; Fibrosarcoma; MEK; Tubulin.