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Microtubule dynamics and tumor invasion involving MCAK

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The mitotic centromere associated kinesin (MCAK, also known as Kif2c) belonging to the kinesin-13 family of microtubule motor proteins is best known for its involvement in regulation of microtubule dynamics, spindle formation, chromosome separation and depolymerisation of improperly attached microtubules at centromeres.[1,2] Its targeted and cell cycle-specific localization e.g. at centromeres, centrosomes and at the growing tips of micotubules, and its depolymerase activities are regulated by phosphorylation of different residues by kinases such as Aurora kinase B/C, Aurora kinase A, Cyclin-dependent kinase 1 and polo-like kinase.[1,3] Thus, Aurora B phosphorylation of the neck region has been proposed to control the long-range interactions with the C-terminal non-motor region of MCAK.[4] Knockdown and mutations or inactivation of MCAK or overexpression of kinases controlling MCAK activities can lead to mitotic and meiotic arrest,[5] and predispose to aneuploidy and chromosomal instability.[6] The complex regulation of MCAK activities by dimerization, conformational changes in dependence of differential phosphorylation of residues in the N- and C-terminal domain, and the susceptibility to degradation by phosphorylations have been well documented but also revealed complex temporal-spatial regulation.[3] Although previous reports showed that MCAK does not exclusively function in spindle and mitotic and meiotic divisions but is also involved in processes like directional growth, so far, it has been an enigma why overexpression of MCAK is a hallmark of several highly invasive tumors. Effects of altering phosphorylation status of MCAK in S196 in the neck domain have most excessively been studied in Xenopus and in vitro,[4] and revealed influences on localization and activity of MCAK in mitosis.[3] Ritter et al.[7] in this issue of *Cell Cycle* provide now exciting and compelling new evidence that phosphorylation of MCAK at serin 196 by Aurora kinase B is also a main player in control of catalytic activities of MCAK in mammalian cells and in mitosis, and moreover that MCAK is involved in directional migration and invasion of tumor cells. Thus, expressing phosphomimetic MCAK in HeLa cells decreased dramatically MCAK at centromeres. Furthermore, expression of MCAK 192A and MCAK 192D reduced the invasion of HeLa cells by about 50%, similar to knockdown of MCAK by RNAi. The study provides therefore new information linking overexpression of MCAK with lymphatic invasion and lymph node metastasis in gastric and colorectal cancer, and provides a basis for new approaches in therapeutic treatment of these cancers.

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