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TMCO1 mediates cancer cell migration through regulating microtubule assembling

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Abstract

Transmembrane and coiled-coil domains 1 (TMCO1) is highly conserved in amino acid sequence among species and ubiquitously expressed in all human tissues. Homozygous frameshift mutation in TMCO1 causes distinctive craniofacial dysmorphism, skeletal anomalies, and mental retardation. However, its physiological functions, particularly in cancer biology, are largely unknown. In this study, we have found that knock down of TMCO1 in HeLa cells, a human cervical cancer cell line, and U2OS cells, an osteosarcoma cell line, remarkably inhibited their migratory capability; TMCO1 was highly expressed in the cells of the invasive front of high grade lung cancer and metastatic cancer cells in the clinical specimens, and lung cancer cells at the metastatic bone site in our animal model; Immunohistostaining revealed that TMCO1 was co-localized with microtubules and was able to be co-sedimentated with microtubules in the presence of paclitaxel and GTP; and deficiency of TMCO1 in cells dramatically increased acetylation of tubulin. Further investigation demonstrated that TMCO1 impacted microtubule dynamics, which is closely correlated with cancer metastasis, TBA drug response and therapeutic prognosis. Our findings provide not only new mechanistic insights into cancer metastasis, but also critically evaluate the significance of TMCO1 as a novel target for therapeutic treatment of the disease.

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