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A splicing variant of merlin promotes metastasis in hepatocellular carcinoma

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Merlin (moesin-ezrin-radixin-like protein), encoded by the neurofibromatosis type 2 (*Nf2*) tumor suppressor gene, is a member of the band 4.1 family. As one of the most versatile tumor suppressors, it is capable of integrating several different mechanisms that regulate cell proliferation, motility, survival and signaling pathways. As we know, Merlin has at least five splicing forms. However, little is known about the functional importance of these splicing forms. To understand the roles of Merlin in the process of tumorigenesis and tumor metastasis, we studied Merlin and its splicing forms in hepatocellular carcinoma (HCC). Our data shows that Merlin is present at low levels in HCC specimen, particularly in metastatic tumors, where it is associated with a poor prognosis. Surprisingly, a splicing variant of Merlin that lacks exons 2, 3 and 4 (Δ^{2-4} Merlin) is amplified in HCC and portal vein tumor thrombus (PVTT) specimens and in the CSQT2 cell line derived from PVTT. Our studies show that Δ^{2-4} Merlin interferes with the capacity of wild-type Merlin to bind b-catenin and ERM, and it localizes in the cytoplasm rather than at the cell surface. Furthermore, Δ^{2-4} Merlin overexpression increases the expression levels of b-catenin and stemness-related genes, induces the epithelium–mesenchymal-transition phenotype promoting cell migration *in vitro* and the formation of lung metastasis *in vivo*. Our results indicate that the Δ^{2-4} Merlin variant disrupts the normal function of Merlin and promotes tumour metastasis.

Biography

Zhong Li has completed his PhD from Shanghai Medical University and Post-doctoral studies from Shanghai Institute of Biochemistry, University of Rochester and Connecticut Health Center. He is the Vice President of Shanghai Institute of Cell Therapy, an immunotherapy research organization. He has published more than 31 papers in reputed journals and has been serving as a member of Precision Medicine Association affiliated to China Medicinal Biotech Association.

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