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Transforming growth factor-beta receptor interacting protein 1 negatively regulates Ezrin-mediated cancer cell migration

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The transforming growth factor-beta (TGF-beta) receptor interacting protein TRIP-1 is a WD40 repeat-containing protein that has the ability to bind to the cytoplasmic domain of the TGF-beta type II receptor in a kinase-dependent manner. Evidences have demonstrated that the transforming growth factor beta (TGF-beta) signal pathway plays an important role in metastasis promotion in the later stages of cancer progression, although it mediates growth inhibition in early stages. As a modulator of the TGF-beta response, the potential role of TRIP-1 in cancer invasion and metastasis through the TGF-beta signaling pathway has not been elucidated. In this study, we firstly examine the protein-protein interactions between TRIP-1 and Ezrin (a key component in tumor metastasis) through GST pull-down technology and found that TRIP-1 can bind with Ezrin. Co-immunoprecipitation experiments further confirmed that the 567th threonine residue of Ezrin and the last 20 amino acids of TRIP-1 are necessary for the binding interaction between Ezrin and TRIP-1. Phospho-mimicking mutant ezrinT567D, but not the nonphosphorylatable mutant ezrinT567A, stimulated formation of protein complexes. Immunofluorescent localization experiments revealed co-localization of proteins at a cell membrane. Importantly, we found that knock-down of TRIP-1 by RNA interference resulted in a blockade to Ezrin-induced hepatocellular carcinoma cell adhesion and migration by wound healing assay. Our findings suggest TRIP-1 may act as a negative regulator to reduce tumor metastasis by blocking TGF-β-mediated phosphorylation of ezrin.

Biography

Fei Yan has completed his Ph.D at the age of 28 years from Sichun University and postdoctoral studies from Tsinghua University Graduate School at Shenzhen, China. He is the associate professor of Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China. He has published more than 23 papers in reputed journals. His main research interests include the mechanisms of tumorigenesis and development, early-stage diagnosis and treatment of tumors. This work was supported by National Science Foundation Grants (Grant No. 30900749).

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