Role of Toca-1 In The invasion of Cancer Cells.

Harish Chander

Centre for Human Genetics and Molecular Medicine Central University of Punjab, Bathinda

Abstract—Metastatic adenocarcinomas equip themselves for signaling pathways that initiates the invasion of cancer cells. Toca-1 (transducer of Cdc42-dependent actin assembly-1) is expressed in highly invasive cancers. Toca-1 belongs to a CIP4 subfamily of F-BAR proteins. It has been shown that F-BAR (Fer/CIP4 homology-Bin/Amphiphysin/Rvs) proteins play an important role in cancer metastasis. Members of the one of the subfamily of F-BAR proteins have been shown to play a role in the invasion of lung cancer and breast cancer cells. These three family members are Toca-1 (Transducer of Cdc42-mediated actin assembly), FBP17 (formin binding protein1) and CIP4 (Cdc interacting protein 4). These proteins function as key scaffolds to recruit and activate major regulators (eg. Cdc42, formins, N-WASP, dynamin) of F-actin polymerization within invadopodia. Toca-1 localizes to the filamentous actin-rich invadopodia that are produced in response to stimulus for invasion. Stable knockdown (KD) of Toca-1 expression in MDA-MB-231 cells led to a significant defect in epidermal growth factor (EGF)induced cell migration and invasion. Toca-1 KD cells also showed significant defects in EGF- and Src-induced ECM digestion and formation of invadopodial membrane protrusions. Taken together, our results identify Toca-1 as a proinvasive protein in adenocarcinoma and a potential therapeutic target to limit tumor metastasis.