PTK7 promotes proliferation and invasion of esophageal squamous cell carcinoma cells

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A catalytically inactive receptor tyrosine kinase, protein tyrosine kinase 7 (PTK7), is frequently upregulated in several types of cancer, including esophageal squamous cell carcinoma (ESCC) and despite no catalytic activity, it displays oncogenic phenotypes in various cell lines. To understand the role of PTK7 in tumorigenesis, we have used the treatment of the extracellular domain of PTK7 (soluble PTK7; sPTK7) as a decoy receptor or knockdown of PTK7, to counteract PTK7 function. The sPTK7 treatment or PTK7 knockdown inhibits tyrosine phosphorylation of cellular proteins in ESCC cells, suggesting that PTK7 modulates the growth factor-induced activation of specific RPTKs. FGFR1 was one of the RPTKs that were highly upregulated at mRNA level in ESCC cell lines. PTK7 knockdown inhibited FGF-induced phosphorylation of FGFR1 and the activation of its downstream signaling pathways. PTK7 knockdown also reduced FGF-induced proliferation, anchorage-independent colony formation, wound healing, and invasion in ESCC cells. These data demonstrate that PTK7 increases the FGF-induced oncogenic functions of FGFR1 in ESCC cells. In addition, PTK7 knockdown reduced the degradation of gelatin and MMP-9 secretion, caused by the reduction of MMP9 mRNA level. PTK7 knockdown reduced the activation of NF- κ B and AP-1. These results indicate that PTK7 promotes tumorigenesis by activating FGFR1 and enhances MMP9 expression by activating AP-1 and NF- κ B, thereby increasing invasive properties of ESCC cells.