Annexin A2 is involved in activation of ERK upon endothelin-1 stimulation

Yuichi Mazaki, Tsunehito Higashi, Takahiro Horinouchi, Soichi Miwa

Dept. Cell. Pharmcol., Grad. Sch. Med., Hokkaido Univ.

Endothelin receptors (ETRs) is one of G protein coupled receptors, and consist of ET type A receptor (ET_AR) and ET type B receptor (ET_BR). The overexpression of endothelin (ET)-1 or ETRs is related to malignancy of human cancer, although ET-1 was originally identified as an endothelium-derived vasocontractile peptide. In cancer cells, ET-1 activates various signaling pathways, including mitogen-activated protein kinase, phosphatidylinositol 3-kinase, protein kinase C through ETRs, although the mechanisms by which ET-1 activates these signaling pathways remain uncertain. Here, we found that ETRs interacted with annexin A2, which is overexpressed in various cancers. Annexin A2 bound to ET_AR and ET_BR. Upon ET-1 stimulation, serine phosphorylation of annexin A2 increased, while there is no change in tyrosine phosphorylation of annexin A2. Furthermore, we found that annexin A2 silencing suppressed activation of ERK upon ET-1 stimulation. These results suggested that interaction of ETRs and annexin A2 may play important roles in activation of extracellular signal-regulated kinase upon ET-1 stimulation.