GRP78 promotes ERK activation through endothelin type B receptor

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Endothelin (ET)-1 is involved in various diseases, including cancer, hypertension, atherosclerosis, diabetes, and fibrotic diseases, although ET-1 is originally identified as endothelium-derived vasoconstrictive peptide. ET receptors belong to the class A of G protein-coupled receptor, and consist of ET type A receptor (ET_AR) and ET type B receptor (ET_BR). ET_AR and ET_BR generally exhibit the opposite responses, although many exceptions exist. Here, we attempted to identify ET_AR or ET_BR specific binding proteins to understand difference of ET_AR- and ET_BR-mediated responses upon ET-1 stimulation. We found that GRP78 exhibited a stronger binding affinity toward ET_BR than ET_AR. Overexpression of GRP78 promotes ET_BR-mediated ERK activation. In addition, the silencing of *GRP78* suppressed ET_BR-mediated ERK activation. On the other hand, ET_BR can localize GRP78 to cell periphery. Our results suggest that interaction of ET_BR with GRP78 affects the ERK activation and GRP78 localization.