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Transactivation of ETBR/MAPKs Involved in Endothelin-1-induced COX-2 Protein Expression and Cell Motility.

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Chondrosarcoma is a type of highly malignant tumor with a potent capacity to invade locally and cause distant metastasis. Endothelin-1 (ET-1) the most potent vasoconstrictor, plays a crucial role in migration and metastasis of human cancer cells. Cyclooxygenase-2 (COX-2) has been implicated in tumor metastasis. However, the effects of ET-1 in cell motility and COX-2 expression in chondrosarcoma cells are considerable unknown. The aim of this study was to investigate whether ET-1 is associated with the motility of human chondrosarcoma cell. We found that treatment of JJ012 human chondrosarcoma cells with ET-1 increased migration and expression of COX-2. Activations of MAPKs and activator protein-1 (AP-1) pathways after ET-1 treatment were demonstrated, and ET-1-induced expression of COX-2 and migration activity was inhibited by the specific inhibitor and mutant. Moreover, ET-1 increased the binding of c-Jun to the AP-1 element on the COX-2 promoter. Taken together, our results indicated that ET-1 enhances the migration of chondrosarcoma cells via increasing COX-2 expression and through activation ET-1/ETBR axis, MAPKs pathway, and AP-1 signal transduction pathway.

Key Word: Endothelin-1, Cyclooxygenase-2, MAPKs pathway, activator protein-1