Endothelin-1 drives epithelial to mesenchymal transition and metastatic progression in the human chondrosarcoma cell.

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Abstract:

Endothelin-1 (ET-1) induces epithelial-mesenchymal transition (EMT) accompanied by cellular differentiation and migration. Despite extensive transcriptomic profiling, identification of ET-1-inducible, EMT-specific protein during metastatic progression of chondrosarcoma remains elusive. Here, we functionally validate a previously described post-transcriptional pathway by which ET-1 modulates expression of EMT maker and migration. Stimulation of chondrosarcoma cells with ET-1 induced mRNA and protein expression of EMT marker such as N-cadherin and vimentin. Pretreatment of chondrosarcoma cells with endothelin-receptors, PLCg and AMP-activated protein kinase (AMPKa) inhibitors abolished ET-1-promoted migration and N-cadherin and vimentin expression. On the other hand, ET-1 treatment demonstrably activated PLCg, AMPKa, and TWIST signaling pathways. Furthermore, the expression levels of ET-1, vimentin, and TWIST were correlated in human chondrosarcoma specimens. Taken together, our results indicate that ET-1 enhances the EMT markers and migratory ability of human chondrosarcoma cells by increasing N-cadherin and vimentin expression via the PLCg and AMPKa, and TWIST pathways.

Key words: Endothelin-1(ET-1), chondrosarcoma, epithelial-mesenchymal transition, TWIST, migration