WISP-1 Increases Cell Migration and ICAM-1 Expression in Human Oral Squamous Cell Carcinomas

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Abstract

Oral squamous cell carcinomas (OSCC) have a striking tendency to migration and metastasis to cervical lymph nodes. Wnt-1 induced secreted protein 1 (WISP-1) belongs to the CCN family (CTGF/CYR61/NOV), which is secreted cysteine-rich proteins. However, the effects of WISP-1 on migration and Intercellular adhesion molecule-1 (ICAM-1) expression in human OSCC are largely unknown. First, we found that the expression of WISP-1 in human OSCC tissues was higher than in normal oral tissues. We also demonstrated that WISP-1 enhanced cell migration and ICAM-1 up-regulation in human OSCC. Transfection of cells with ICAM-1 siRNA reduced WISP-1-mediated cell migration. WISP-1 activated αvβ3 integrin, ASK1, JNK/p38, c-Jun, and AP-1 signal transduction pathway, and WISP-1-induced expression of ICAM-1 and migration activity was inhibited by the αvβ3 antibody or inhibitor of ASK1, p38, JNK, and c-Jun. In addition, human OSCC were infected with lentivirus containing human WISP-1 shRNA which reduced the migratory ability and ICAM-1 expression. Over all, we characterized an important role for WISP-1 which regulates cell migration by increasing ICAM-1 expression in human OSCC via the $\alpha v\beta 3$ integrin, ASK1, JNK/p38, c-Jun, and AP-1 signaling pathway.