The 24th Joint Annunal Conference of Biomedical Science
March 2009

Leptin Enhances Cell Migration in Human Chondrosacoma Cells through OBRl Leptin Receptor

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Abstract

Leptin, an adipocyte-derived cytokine that is closely associated with obesity, has recently been shown to be involved in carcinogenesis and cancer progression. Integrins are the major adhesive molecules in mammalian cells and have been associated with metastasis of cancer cells. In this study, we found that leptin increased the migration and the expression of alphavbeta3 integrin in human chondrosarcoma cells. We also found that human chondrosarcoma tissues and chondrosarcoma cell lines had significant expression of the long form (OBRl) leptin receptor, which was higher than that in normal cartilage and human primary chondrocyte. Leptin-mediated migration and integrin upregulation were attenuated by OBRl receptor antisense oligonucleotide. Activations of insulin receptor substrate (IRS)-1, phosphatidylinositol 3-kinase (PI3K), Akt and nuclear factor-kappaB (NF-kappaB) pathways after leptin treatment were demonstrated, and leptin-induced expression of integrin and migration activity was inhibited by the specific inhibitor, small-interfering RNA and mutant of IRS-1, PI3K, Akt and NF-kappaB cascades. Taken together, our results indicated that leptin enhances the migration of chondrosarcoma cells by increasing alphavbeta3 integrin expression through the OBR1/IRS-1/PI3K/Akt/NF-kappaB signal transduction pathway.