

Adiponectin promotes VEGF-dependent angiogenesis in human chondrosarcoma through PI3K, Akt, mTOR, and HIF- α pathway

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Abstract

Background:

Chondrosarcoma is a type of highly malignant tumor with a potent capacity to invade locally and cause distant metastasis. Adiponectin is a protein hormone secreted predominantly by differentiated adipocytes and has been reported to increase metastasis of human chondrosarcoma. On the other hand, angiogenesis is a critical step in tumor growth and metastasis. The aim of the present study was to examine the mechanism involved in adiponectin-mediated vascular endothelial growth factor (VEGF) expression and angiogenesis in human chondrosarcoma cells.

Questions/Purposes:

The effect of adiponectin on VEGF expression in human chondrosarcoma cells is mostly unknown. We first used qPCR, ELISA, and Western blotting analysis whether adiponectin increased VEGF expression in human chondrosarcoma cells. Second, how to increase VEGF expression by adiponectin stimulated. In addition, we further confirm chondrosarcoma cells secretes VEGF whether can induced endothelial progenitor cells (EPCs) migration and angiogenesis.

Methods:

Adiponectin and VEGF protein levels were determined by immunohistochemistry in patient specimens of human chondrosarcoma tissues. Adiponectin-mediated VEGF expression was assessed by qPCR, ELISA, and Western blotting. The xenograft tumor angiogenesis model was used to examine the role of adiponectin in tumor growth and tumor-associated angiogenesis.

Results:

In this study we first demonstrated that the expression of adiponectin was correlated with tumor stage according the immunohistochemistry analysis of human chondrosarcoma tissues. In addition, we also found that adiponectin increased VEGF expression in human chondrosarcoma cells and subsequently induced migration and tube formation in human EPCs. Adiponectin promoted VEGF expression through AdipoR, phosphoinositide 3 kinase (PI3K), Akt, mammalian target of rapamicin (mTOR), and hypoxia-inducible factor-1 α (HIF)-1 α signaling cascades.

Conclusions:

Our results showed that adiponectin promoted VEGF expression and angiogenesis in human chondrosarcoma. Therefore, adiponectin is crucial for tumor angiogenesis and growth, which may represent a novel target for anti-angiogenic therapy in human chondrosarcoma.