

論 文 要 旨

Hairy/enhancer-of-split related with YRPW motif protein 1 promotes osteosarcoma metastasis via matrix metalloproteinase 9 expression

鶴 亜里紗

Background: Activation of the Notch pathway has been reported in various types of cancers. However, the role of the hairy/enhancer-of-split related with YRPW motif protein 1 (HEY1), in osteosarcoma is unknown. We examined the function of HEY1 in osteosarcoma.

Methods: Expression of HEY1 was studied in human osteosarcoma. The effects of HEY1 in osteosarcoma were evaluated in vitro and in a xenograft model. Moreover, we examined the function of matrix metalloproteinase 9 (MMP9) as a downstream effector of HEY1.

Results: HEY1 was up-regulated in human osteosarcoma. Knockdown of HEY1 inhibited the invasion of osteosarcoma cell lines. In contrast, the forced expression of HEY1 increased invasion of mesenchymal stem cell. In addition, lung metastases were significantly inhibited by the knockdown of HEY1. We found that MMP9 was a downstream effector of HEY1 that promotes the invasion of osteosarcoma cells. Knockdown of HEY1 decreased the expression of MMP9. Addition of MMP9 rescued the invasion of osteosarcoma cells that had been rendered less invasive by knockdown of HEY1 expression.

Conclusions: Our findings suggested that HEY1 augmented the metastasis of osteosarcoma via up-regulation of MMP9 expression. Therefore, inhibition of HEY1 may be a novel therapeutic strategy for preventing osteosarcoma metastasis.