論 文 要 旨

Interleukin-1α Promotes Matrix Metalloproteinase-9 Expression, Cellular Motility, and Local Invasiveness of Ameloblastoma Cells

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Abstract

Aim: Although ameloblastoma is a benign tumor, its local invasiveness and recurrence rate are both high. Thus, regulation the invasiveness of ameloblastoma cells into surrounded tissue is required for understanding of its pathogenesis. Ameloblastoma cells also secrete several MMPs; however, the factors inducing their secretion remain unclear. We previously suggested that IL-1α derived from ameloblastoma cells triggers the production of inflammatory cytokines by stromal fibroblasts. In this study, we estimated whether IL-1α affect the behavior of ameloblastoma cells.

Methods: The gene expression of MMP-9 was assessed by Real-Time RT-PCR. The secretion of MMP-9 was assessed by ELISA. The motility of AM-3 ameloblastoma cells and Raw264.7 macrophage derived cells, and invasiveness of AM-3 cells were calculated by using Boyden chamber. Invasiveness of AM-3 cells toward HFF-2 fibroblasts were assessed using modified Double Layered Collagen Gel Hemisphere (DL-CGH).

Results: The mRNA expression and secretion of MMP-9 by AM-3 ameloblastoma cells were significantly increased by a stimulation with IL-1α. The motilities of AM-3 and RAW264.7 macrophage derived cells and the invasiveness of AM-3 cells were significantly enhanced by IL-1α and suppressed by an IL-1 receptor antagonist (IL-1Ra). The invasiveness of AM-3 cells towards HFF-2 fibroblasts in a Double-layered Collagen Gel Hemisphere model was suppressed by a treatment with IL-1Ra or an anti-IL-1α neutralizing antibody.

Conclusion: IL-1α itself or the IL-1α-dependent production of unidentified chemo attractants by stromal cells may be important for the local invasiveness of ameloblastoma cells and IL-1α might be a therapeutic target of the ameloblastoma.