論 文 要 旨

Regulation of IL-6 and IL-8 production by reciprocal cell-to-cell interactions between tumor cells and stromal fibroblasts through IL-1α in ameloblastoma.

エナメル上皮腫における IL-1α を介した 腫瘍細胞と間質線維芽細胞の相互作用による IL-6 および IL-8 産生制御

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Ameloblastoma is an odontogenic benign tumor that occurs in the jawbone, which invades bone and reoccurs locally. This tumor is treated by wide surgical excision and causes various problems, including changes in facial countenance and mastication disorders. Ameloblastomas have abundant tumor stroma, including fibroblasts and immune cells. Although cell-to-cell interactions are considered to be involved in the pathogenesis of many diseases, intercellular communications in ameloblastoma have not been fully investigated. In this study, we examined interactions between tumor cells and stromal fibroblasts via soluble factors in ameloblastoma.

We used a human ameloblastoma cell line (AM-3 ameloblastoma cells), human fibroblasts (HFF-2 fibroblasts), and primary-cultured fibroblasts from human ameloblastoma tissues, and analyzed the effect of ameloblastoma-associated cell-to-cell communications on gene expression, cytokine secretion, cellular motility and proliferation. AM-3 ameloblastoma cells secreted higher levels of interleukin (IL)-1α than HFF-2 fibroblasts. Treatment with conditioned medium from AM-3 ameloblastoma cells upregulated gene expression and secretion of IL-6 and IL-8 of HFF-2 fibroblasts and primary-cultured fibroblast cells from ameloblastoma tissues. The AM3-stimulated production of IL-6 and IL-8 in fibroblasts was neutralized by pretreatment of AM-3 cells with anti-IL-1α antibody and IL-1 receptor antagonist. Reciprocally, cellular motility of AM-3 ameloblastoma cells was stimulated by HFF-2 fibroblasts in IL-6 and IL-8 dependent manner. In conclusion, ameloblastoma cells and stromal fibroblasts behave interactively via these cytokines to create a microenvironment that leads to the extension of ameloblastomas.