

CD206+ tumor-associated macrophages promote proliferation and invasion in oral squamous cell carcinoma via EGF production

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<https://doi.org/10.15017/4060078>

出版情報：九州大学, 2019, 博士（歯学）, 課程博士

バージョン：

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(CD206陽性腫瘍随伴性マクロファージはEGF産生を介して口腔扁平上皮癌の増殖と浸潤に関与する)

区 分 : 甲

論 文 内 容 の 要 旨

Tumor-associated macrophages (TAMs) promote tumor progression and inhibit anti-tumor immune response by producing various mediators, such as IL-6, IL-8, IL-10, EGF and VEGF, and preferentially express CD163, CD204 and CD206. However, the role of these TAM subsets in oral squamous cell carcinoma (OSCC) remains unclear. Thus, we examined the expression and role of TAM subsets in OSCC, especially in cancer cell proliferation.

Forty-four patients with OSCC were analyzed for the expression of TAM markers and EGF, one of the proliferation potency cytokines by immunohistochemistry. EGF production of TAM subsets isolated from the OSCC patients was assessed by flow cytometry. Effects of conditioned medium from TAM subsets on the proliferation of OSCC cells were also examined.

CD163+ cells were detected diffusely all over the tumor and connective tissue area, while CD204+ and CD206+ cells were mainly detected in/around the tumors. Flow cytometric analysis revealed that CD206+ TAMs strongly produced EGF compared with CD163+ and/or CD204+ TAMs. Proliferation and invasion of OSCC cells cultured with conditioned medium of CD206+ TAMs were strongly enhanced and inhibited by anti-EGFR. The number of CD206+ TAMs positively correlated with the clinical stage and T classification. In addition, the ROC curve shows higher sensitivity and specificity of CD206+ expression for adverse prognosis.

Our results revealed differences in localization and EGF production among these TAM subsets. CD206+ TAM was suggested to play a key role in the proliferation and invasion of OSCC via EGF production.