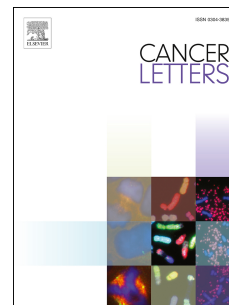


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PA28 γ acts as a dual regulator of IL-6 and CCL2 and contributes to tumor angiogenesis in oral squamous cell carcinoma

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Abstract

PA28 γ promotes tumor development and progression and is suggested to play a role in tumor angiogenesis, but the molecular mechanisms have not been investigated. Here, we found that PA28 γ enhanced the ability of OSCC cells to promote the migration, invasion, and tube formation of HUVECs and promoted tumor-induced angiogenesis in xenograft mice models *in vivo*. Then, a mechanism study revealed that the expression and secretion of IL-6 and CCL2 were dependent on PA28 γ expression. Furthermore, blocking IL-6 or CCL2 or the transcription factor NF- κ B induced the inhibition of tube formation in HUVECs co-cultured with PA28 γ -overexpression OSCC cell supernatants. Moreover, we revealed that p-STAT3 and p-AKT, which are downstream of the IL-6 and CCL2 signaling axis, were downregulated in HUVECs co-cultured with the PA28 γ -silenced supernatant and were upregulated with the PA28 γ -overexpressing supernatant. In addition, IL-6, CCL2 and PA28 γ expressions were correlated in a clinical OSCC cohort. Collectively, our study indicates that PA28 γ contributes to tumor angiogenesis by regulating IL-6 and CCL2. PA28 γ may be a novel therapeutic target as a dual regulator of IL-6 and CCL2 for treating PA28 γ -positive OSCC.

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