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学位論文の題名	<p>Regulatory T cells expressing abundant CTLA-4 on the cell surface with a proliferative gene profile are key features of human head and neck cancer (細胞表面に CTLA-4 を多く発現した制御性 T 細胞は増殖性の遺伝子プロファイルを持ち、ヒトの頭頸部癌における鍵となる特徴である)</p> <p>International Journal of Cancer. 2018 DOI: 10.1002/ijc.32024. In press.</p>
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Abstract

FOXP3⁺ regulatory T (Treg) cells control immunological self-tolerance and tumor immunity. Treg cells not only inhibit anti-tumor immunity in mice, but also expand in human cancer and attenuate the effect of immunotherapy in the cancer microenvironment. The suppression of Treg cells is regulated by cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4), whose expression on the cell surface is tightly regulated. Here we found that Treg cells expressing abundant CTLA-4 on the cell surface (surface-CTLA-4⁺ Treg) were expanded in human head and neck cancer tissues. RNA sequencing of surface-CTLA-4⁺ and surface-CTLA-4⁻ Treg cells infiltrating human head and neck cancer tissues revealed that surface-CTLA-4⁺ Treg cells have a previously undescribed gene expression profile correlating to cell cycle, cell proliferation, and DNA replication. Moreover, surface-CTLA-4⁺ Treg cells were PD-1⁺, actively proliferated and associated with CD45RA⁻ FOXP3^{high} Treg cells with strong suppressive function. Thus, surface-CTLA-4⁺ Treg cells with a proliferative gene expression signature and phenotype are key features of head and neck cancer. Targeting surface-CTLA-4⁺ Treg cells might be new strategies to evoke effective immune responses to head and neck cancer.