テネイシン C は口腔扁平上皮癌の免疫抑制性癌微小環境に関与する

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Cancer Immunol Res. **8**:1122-1138, 2020.

Tenascin-C Orchestrates an Immune-Suppressive Tumor Microenvironment in Oral Squamous Cell Carcinoma

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Abstract ： Inherent immune suppression represents a major challenge in the treatment of human cancer. The extracellular matrix molecule tenascin-C promotes cancer by multiple mechanisms, yet the roles of tenascin-C in tumor immunity are incompletely understood. Using a 4NQO-induced oral squamous cell carcinoma (OSCC) model with abundant and absent tenascin-C, we demonstrated that tenascin-C enforced an immune-suppressive lymphoid stroma via CCL21/CCR7 signaling, leading to increased metastatic tumors. Through TLR4, tenascin-C increased expression of CCR7 in CD11c+ myeloid cells. By inducing CCL21 in lymphatic endothelial cells via integrin α9β1 and binding to CCL21, tenascin-C immobilized CD11c+ cells in the stroma. Inversion of the lymph node-to-tumor CCL21 gradient, recruitment of T regulatory cells, high expression of anti-inflammatory cytokines, and matrisomal components were hallmarks of the tenascin-C-instructed lymphoid stroma. Ablation of tenascin-C or CCR7 blockade inhibited the lymphoid immune-suppressive stromal properties, reducing tumor growth, progression, and metastasis. Thus, targeting CCR7 could be relevant in human head and neck tumors, as high tenascin-C expression and an immune-suppressive stroma correlate to poor patient survival.

抄録　がん治療において免疫抑制作用は重要な問題となっている。テネイシン C は、がんの増悪化に関与する細胞外マトリックスであるが、本研究では tenascin-C やケモカイン受容体 CCR7 の機能抑制により免疫抑制性間質特製を抑制することができることを明らかにした

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