2-YIA-58 YIA

TP signaling in immune cells promotes lymphangiogenesis in the diaphragm during peritonitis

Seri Tsuru[1,2], Yoshiya Ito[2], Hiromi Matsuda[1,2], Kanako Hosono[2], Hirotsugu Okamoto[1], Masataka Majima[2]

[1](Department of Anesthesiology, Kitasato University School of Medicine, [2]Department of Pharmacology, Kitasato University School of Medicine

Lymphangiogenesis has functional consequences not only for lymphatic transport, but also for inflammation resolution. Thromboxane A_2 (TxA_2) has been suggested to involve not only in induction of inflammation, but also in resolution of inflammation. We investigated the functional role of TxA_2 receptor (TP) signaling in inflammation-associated formation of newly lymphatic vessels. Lymphangiogenesis in the diaphragm of TP knockout mice (TPKO) or their wild-type (WT) counterparts was induced by repeated intraperitoneal injection of LPS. Compared with WT, LPS-induced lymphangiogenesis in TPKO was suppressed, which was accompanied by reduced expression of vascular endothelial growth factor (VEGF)-C and VEGF-D in CD11b+ and CD4+ cells in diaphragm tissue. TP was expressed in CD11b+ and CD4+ cells, but not in LYVE-1+ cells (lymphatic vessels). U46619, an agonist for TxA_2, did not proliferate cultured lymphatic endothelial cells. As compared with controls, mice with macrophage TP receptor deletion showed attenuation of lymphangiogenesis with reduced expression of VEGF-C and VEGF-D. When fluorescein isothiocyanate (FITC)-dextran was injected into the peritoneal cavity, the amount of residual FITC-dextran in macrophage-specific deletion of TP receptor was greater than that in controls. The same was true for mice with T cell TP receptor deletion. The present results suggest that TP signaling in macrophages and T cells plays a critical role in inflammation-related lymphangiogenesis and drainage function of lymphatics in the diaphragm.