IL-1β induces the ectodomain shedding of LYVE-1 in cultured human lymphatic endothelial cells

Satoshi Hirakawa¹, Hidenori Okazaki², Koji Sayama³, Shigeki Higashiyama², Yoshiki Tokura¹

¹Dept. of Dermatology, Hamamatsu University School of Medicine
²Dept. of Dermatology, Ehime University Graduate School of Medicine
³Ehime Proteo-Medicine Research Center, Ehime University

Pathologic lymphangiogenesis requires a multistep process that involves the migration and proliferation of lymphatic endothelial cells (LECs). We previously demonstrated that the vascular endothelial growth factor-A promotes new lymphatic vessel growth in experimental mouse models. However, it remains unclear whether pathologic lymphangiogenesis may be initiated by inflammatory cytokines such as IL-1β. To answer this question, we initially subjected cultured human dermal LECs to adenoviral transduction inducing alkaline phosphatase-conjugated LYVE-1. IL-1β induced the ectodomain shedding of LYVE-1 in cultured LECs. This LYVE-1 shedding was mediated through the extracellular signal regulated kinase (ERK), and a disintegrin and metalloproteinase 17. Together, these results suggest that inflammatory cytokines may initiate pathologic lymphangiogenesis by decreasing cell-matrix contact through ECM receptors such as LYVE-1.