2-YIA-59 YIA

RAMP1 signaling facilitates angiogenesis and lymphangiogenesis in the endometriotic lesions in mice

Masako Honda[1,2], Yoshiya Ito[2], Kyoko Hattori[1,2], Kanako Hosono[2], Shuji Nakamoto[2], Fumisato Otaka[2], Seri Tsuru[2], Masataka Majima[2]

[1]Department of Obstetrics and Gynecology, Kitasato University School of Medicine, [2]Department of Pharmacology, Kitasato University School of Medicine

Newly formation of blood and lymphatic vessels is involved in the development of endometriosis. We have demonstrated that calcitonin gene-related peptide (CGRP) promotes wound healing and wound-associated formation of blood and lymphatic vessels via receptor activity-modifying protein 1 (RAMP1), a subunit of the CGRP receptor. In the present study, using wild-type (WT) mice and RAMP1 deficient ($RAMP1^{-/-}$) mice, we examined whether RAMP1 plays a role in the growth of endometriosis by angiogenic responses. Ectopic endometriosis model was created by transplantation of endometrial tissue fragments from donor mice into the peritoneal wall of host mice. The sizes and density of blood and lymphatic vessels in the $RAMP1^{-/-}$ implants from host $RAMP1^{-/-}$ mice ($RAMP1^{-/-}$ →$RAMP1^{-/-}$) were reduced as compared with the WT→WT. The mRNA levels of markers for blood and lymphatic vessels as well as growth factors for angiogenesis and lymphangiogenesis in the $RAMP1^{-/-}$→$RAMP1^{-/-}$ were lower than those in the WT→WT. Immunofluorescence demonstrated that RAMP1 was expressed in $CD11b^{+}$ and $S100A4^{+}$ cells, and these cells also co-localized with VEGF-A, VEGF-C, and VEGF-D. Cultured macrophages and fibroblasts increased the mRNA levels of VEGF-A, VEGF-C, and VEGF-D in a RAMP1 dependent manner. These results suggest that RAMP1 signaling in macrophages and fibroblasts is critical for the growth of endometriosis by promoting angiogenesis and lymphangiogenesis.