

33. IDENTIFICATION OF CHEMOKINES IMPORTANT FOR LEUKOCYTE RECRUITMENT TO THE HUMAN ENDOMETRIUM DURING EMBRYO IMPLANTATION

Rebecca Jones, Tu'uhevaha Kaitu'u, Natalie Hannan, Jin Zhang and Lois Salamonsen
Prince Henry's Institute of Medical Research, Clayton, Victoria

At the time of implantation the endometrium becomes a specialised immune environment to allow implantation of the semi-allogenic embryo. A large population of leukocytes, predominantly uterine NK cells and macrophages, infiltrate the endometrium and are believed to modulate trophoblast invasion and facilitate decidualisation. Despite their importance, the factors responsible for recruiting these cells to the endometrium and inducing their activation/differentiation to the 'uterine phenotype' are unknown. In this study, a gene array approach was utilised to identify which chemokines (family of chemotactic factors for leukocytes) are expressed by the endometrium at the time of embryo implantation. We identified eight chemokines that were expressed at this time: monocyte chemoattractant protein (MCP)-3, eotaxin, macrophage inflammatory protein (MIP)-1 β , fractalkine, 6Ckine, macrophage-derived chemokine (MDC), hemofiltrate CC chemokine (HCC)-1, and HCC-4. Real time RT-PCR was utilised to analyse their expression across the menstrual cycle and in early pregnancy. mRNA expression of MCP-3, 6Ckine, HCC-1, HCC-4, MDC and MIP-1 β was upregulated in the mid-secretory phase, with high expression maintained by MCP-3, 6Ckine, HCC-4 and MDC in early pregnancy. Immunohistochemistry was conducted to examine protein production and cellular source. All chemokines were predominantly localised to the glandular and luminal epithelial cells and decidualised stromal cells. HCC-1, MDC and 6Ckine were upregulated in the secretory phase and early pregnancy whilst MCP-3 and MIP-1 β were high throughout the cycle and early pregnancy. Immunostaining was also detected in infiltrating leukocytes for all chemokines, with maximal numbers of MDC-, HCC-1-, and MCP-3-positive leukocytes in early pregnancy. Furthermore staining for HCC-1, 6Ckine and MDC was prominent in vascular endothelium. All of the identified chemokines possess chemotactic activity for monocytes/macrophages (HCC-1 and -4, MCP-3, MIP-1 β) or NK cells (MCP-3, MDC, MIP-1 β), with the exception of 6Ckine which is a potent T cell chemoattractant. Chemokines expressed by the endothelium are likely to be involved in the initial recruitment of leukocytes from vessels, whilst chemokines produced by epithelial and stromal cells could be more important for the positioning and activation of leukocytes within the endometrium. This data supports a role for these chemokines in the establishment of pregnancy through the recruitment of pregnancy-associated leukocytes.