85. CO-EXPRESSION OF FRACTALKINE AND ITS RECEPTOR IN HUMAN ENDOMETRIUM SUPPORTS A ROLE FOR FRACTALKINE IN LEUKOCYTE RECRUITMENT AND ENDOMETRIAL REMODELLING

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Leukocytes are critical mediators of endometrial remodelling, particularly during embryo implantation and menstruation, through the production of inflammatory mediators, cytokines and enzymes. However, the mechanisms by which the different leukocyte subpopulations enter the uterus are unknown. The cyclical patterns are indicative of regulation by progesterone, but endometrial leukocytes do not posses progesterone receptors. We hypothesised that their migration is indirectly induced by progesterone-regulated chemokines. In another study (Jones *et al.* unpublished) we identified the most abundant chemokines in the endometrium at times of leukocyte recruitment. In the present study, fractalkine, one of the most abundant of these chemokines, and its receptor (CX_3CR1) were selected for detailed study. Fractalkine is a membrane-bound chemokine, which acts as an adhesion factor and chemoattractant for macrophages, T cells, neutrophils and natural killer (NK) cells. Fractalkine and CX_3CR1 protein production was assessed by immunohistochemistry in endometrial samples across the cycle, in early pregnancy and in women using progestin-only contraceptives. Fractalkine was localised predominantly to the glandular epithelial and decidualised stromal cells, with highest production in the secretory phase and in early pregnancy. Fractalkine production was also detected in subpopulations of endometrial leukocytes (identified as macrophages and uterine NK cells by serial immunostaining), with maximal numbers present in the proliferative phase and early pregnancy. CX_3CR1 was co-localised to the glandular epithelial and decidualised stromal cells, with highest expression in the secretory phase. However, leukocytes, identified as macrophages and neutrophils, possessing CX_3CR1 were in greatest abundance during the menstrual phase. Interestingly, in the presence of continuous progesterone, as in the endometrium of women using progestin-only contraceptives, immunoreactive fractalkine was markedly reduced in the glandular epithelium. In contrast increased immunostaining was observed in decidualised stroma and infiltrating leukocytes in these tissues. Such a pattern is suggestive of progesterone regulation. Co-localisation of ligand and receptor in the glands and decidua suggests a role for fractalkine in remodelling of the secretory glands and decidua. These findings support a role for fractalkine in the recruitment of leukocytes into the endometrium, especially in the secretory phase, in early pregnancy and in women using progestin-only contraceptives.

10.1071/SRB03Ab85