EXPRESSION OF CHEMOKINES AND THEIR RECEPTORS AT THE HUMAN MATERNAL-EMBRYONIC INTERFACE

***N. J. Hannan*[1,2], *R. L. Jones*[1], *L. A. Salamonsen*[1]**

[1]Prince Henry's Institute of Medical Research, Clayton, VIC, Australia; [2]Obstetrics and Gynecology, Monash University, Clayton, VIC, Australia

Human embryo implantation is a complex process involving attachment of the developing blastocyst to the receptive endometrial epithelium, and subsequent trophoblast invasion through decidua. This is regulated by crosstalk between the maternal and embryonic cells, however little is known about the factors involved in enabling and directing trophoblast invasion. Chemokines are cytokines that regulate leukocyte chemotaxis via stimulation of adhesion molecules and cell migration. We have previously shown that two chemokines, fractalkine and MCP-3, are produced by endometrial epithelial and decidual cells, maximally around the time of implantation and early pregnancy (1, 2). We hypothesized that endometrially derived fractalkine and MCP-3 are important for the attachment/invasion of fetal trophoblast cells during implantation. To investigate this, expression of fractalkine, MCP-3 and their receptors (CX3CR1, CCR1, CCR2, CCR3 and CCR5) were assessed in cell types present at the maternal-embryonic interface. RNA, extracted from three trophoblast cell lines (JEG-3 and two trophoblast-choriocarcinoma hybrids), a human epithelial cell line (HES), primary endometrial epithelial cells, mid-secretory endometrium and placental tissue, was subjected to RT-PCR for the chemokines and receptors. Both chemokines were produced by endometrial and placental cells. Chemokine receptor expression was more variable, CX3CR1, CCR1, 2 and 3 were expressed by one or more of the trophoblast cells lines while CX3CR1, CCR1, 2 and 5 were expressed by endometrial cells. Marked differences in expression patterns in the different cell lines highlight the importance of studies to select those cell lines of most physiological relevance: in this case, one that most closely resembles early invasive trophoblasts. These data confirm that chemokines are produced by maternal and embryonic cells during implantation and the strong expression of their receptors on trophoblast cells supports a role for chemokines in embryo implantation. Further, these studies have characterized a number of trophoblast cells for future trophoblast migration and attachment assays.

(1) Hannan, N., *et al*. *JCEM* (in press). (2) Jones, R., *et al*. *JCEM* (in press).

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