30. UTERINE EXTRACELLULAR MATRIX COMPONENTS ARE ALTERED DURING DEFECTIVE DECIDUALISATION IN INTERLEUKIN-11 RECEPTOR α DEFICIENT MICE

Christine White[1,2], *Lorraine Robb*[3] *and Lois Salamonsen*[1,2]

[1]Prince Henry's Institute of Medical Research, Clayton, 3168; [2]Dept of Obstetrics & Gynaecology, Monash University, Clayton, 3800; [3]Walter & Eliza Hall Institute of Medical Research, Parkville, 3050.

Implantation is dependent on the differentiation of endometrial stromal cells into decidual cells, and is facilitated by dramatic remodelling of the uterine extracellular matrix. Female interleukin-11 receptor α (IL-11Rα) deficient mice are infertile due to disrupted decidualisation, suggesting a critical role for IL-11 and its downstream target genes in implantation. The molecular targets of IL-11 in the uterus are unknown, but it is likely that IL-11 signalling modifies the expression of other genes important in decidualisation. This study aimed to identify genes regulated by IL-11 during decidualisation in mouse uterus and to examine their expression and localisation as an indication of functional significance during early pregnancy. Decidualisation was induced in pseudopregnant (plug = day 0) wildtype (*IL-11Ra*+/+) and IL-11Rα deficient (*IL-11Ra*-/-) littermates by oil injection into the uterine lumen on day 3. Test RNA extracted from whole uterus at 48 h after induction of decidualisation (n = 2/genotype) and reference RNA from wildtype unstimulated uterus (n = 16) were used to generate target cDNA for hybridisation of NIA 15K microarrays. Among 15,247 DNA probes, 14 showed increased and 4 decreased expression in *IL-11Ra*-/- uterus. These included 4 genes encoding extracellular matrix proteins – collagen III α1 (2.9-fold increase), secreted acidic cysteine-rich glycoprotein (SPARC, 2.3-fold increase), biglycan (1.8-fold increase) and nidogen 1/entactin (1.8-fold increase). Immunohistochemistry confirmed increased collagen III and biglycan protein expression in *IL-11Ra*-/- uterus at this time. In both *IL-11Ra*-/- and wildtype uterus, collagen III and biglycan were primarily localised to the outer connective tissue and smooth muscle cells of the myometrium, with diffuse staining in the cytoplasm of decidualised stromal cells. Interstitial compartments underlying luminal and glandular epithelium and surrounding blood vessels also showed strong immunoreactivity for both proteins. In the absence of IL-11Rα, stronger staining for collagen III was particularly evident underlying luminal epithelium and in the extracellular matrix supporting antimesometrial decidual cells. These data suggest that IL-11 may regulate changes in the uterine extracellular matrix that are necessary for decidualisation. By elucidating the role of IL-11 regulated genes in murine decidualisation, this study may identify novel targets for the manipulation of human fertility.

10.1071/SRB03Ab30