INTERLEUKIN-11 ENHANCES ENDOMETRIAL STROMAL CELL DECIDUALISATION VIA ACTIVATION AND INHIBITION OF TARGET GENES

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Differentiation of endometrial stromal cells into decidual cells is essential for successful embryo implantation. Interleukin (IL)-11 signalling is required for decidualisation in the mouse (1,2) and the expression pattern of IL-11 and its receptors during the menstrual cycle suggests a role for IL-11 in human decidualisation (3). Exogenous IL-11 has been shown to enhance hormone-induced decidualisation of human endometrial stromal cells in culture (4). This study aimed to determine the effects of IL-11 on downstream gene expression in endometrial stromal cells following 12 days of progesterone-induced decidualisation, and to examine the expression and functional significance of IL-11 target genes during this process. Stromal cells isolated from endometrial biopsies (n = 6) were decidualised with 17β-oestradiol and medroxyprogesterone acetate (EP) or EP with 100 ng/mL recombinant human IL-11. Medium was changed every 48 h, and total RNA extracted on Day 12 for gene expression analysis using custom-made 15K cDNA microarrays. Quantitative real-time RT-PCR was performed on the same samples to confirm gene expression levels. In subsequent experiments (n = 2), cells were cytocentrifuged onto glass slides for immunocytochemistry using specific antibodies. Microarray analysis revealed 16 upregulated and 11 downregulated cDNAs in EP + IL-11 compared to EP treated cells. Among these were IL-1β (6.1-fold upregulated) and insulin-like growth factor binding protein (IGFBP)-5 (3.6-fold downregulated). Using real-time RT-PCR, IL-11 was confirmed to increase IL-1β (fold change 1.3–107.1) and decrease IGFBP-5 (fold change 2.8–469.0) transcript abundance in 6 patients. Immunolocalisation of IL-1β in EP and EP + IL-11 treated cells revealed more intense vesicular cytoplasmic staining with IL-11 treatment, while staining intensity for IGFBP-5 was not affected. Interactions between IL-11 and its downstream targets IL-1β and IGFBP-5 are likely to have functional importance in early pregnancy, and may provide novel targets for the manipulation of human fertility.

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