EXPRESSION OF THE CHEMOKINE CXCL12 AND ITS RECEPTOR CXCR4 IN THE ACTIVATING MAMMALIAN OVARIAN FOLLICLE

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The mammalian ovary contains a finite number of oocytes that is determined during oogenesis in fetal life. As most of these oocytes are destined to undergo apoptosis, the initial primordial follicle population represents a valuable resource for the clinical manipulation of the female germ cell pool. However the events underlying the activation of the resting primordial follicle remain relatively poorly understood. A comparison was undertaken between whole 2-day and 7-day neonate mouse ovaries which represents ovaries with primordial follicles and primordial follicles / newly activated follicles respectively. The comparison took place at the level of gene expression utilizing cDNA microarray analysis. The mRNAs for the chemokine CXCL12 and its receptor CXCR4, were consistently shown to be up-regulated approximately 2-fold in 7-day tissue compared with 2-day tissue. Microarray results were confirmed for CXCL12 by real-time PCR analysis. CXCL12 and CXCR4 have been identified as essential for development of the haemopoietic, nervous and cardiovascular systems and have also been shown to be involved in the foetal migration of primordial germ cells to the gonads. These genes were selected for further analysis due to the known importance of other cytokine family members in primordial follicle activation. *In situ* hybridisation studies of CXCL12 revealed mRNA expression in oocytes of all stages, including primordial follicles, as well as epithelial, corpora luteal and stromal cells. In contrast CXCR4 mRNA expression appears to be restricted primarily to oocytes of all stages. This co-expression of ligand and receptor within the oocyte suggests an autocrine signaling mechanism. The age-dependent increase in CXCL12 and CXCR4 gene expression is likely to be a result of an increased oocyte cytoplasmic volume and/or the proportion of stromal cells present as follicles begin to activate in the neonate ovary. Examination of the timing of protein expression is currently underway to identify the role this chemokine signaling pathway plays in the initial activation of the mammalian primordial follicle.

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