EXTRACELLULAR MATRIX AND THE DEVELOPMENT AND ATRESIA OF BOVINE OVARIAN FOLLICLES

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Abstract

During reproductive life, adult mammalian ovaries contain a reserve of inactive oocytes surrounded by a layer of granulosa cells and separated from the surrounding stroma by the follicular basal lamina. Follicle activation is initially accompanied by growth of the oocyte and replication of granulosa cells. This is followed by differentiation of the adjacent stroma into the vascularised thecal layers, and formation of a fluid-filled antrum within the follicle. Loss of follicles by atresia is an important mechanism ensuring that only an appropriate number of oocytes reach the ovulatory stage. Following ovulation the ruptured follicles develop into corpora lutea.

Studies of the growth and atresia of follicles have primarily focussed on the roles of hormones, growth factors and cell death molecules in these processes. However, the extracellular matrix participates in the regulation of cellular growth both directly and indirectly through interaction with growth factors or their binding proteins. This thesis describes a body of research into changes in the composition of bovine ovarian extracellular matrix during follicular growth and atresia, at ovulation and in the corpus luteum.

The composition of the follicular basal lamina (including collagen type IV α1 to α6, laminin chains, nidogen-1 and -2, perlecan, and versican) was determined by immunohistochemical, biochemical, and gene expression analyses using bovine ovaries collected at an abattoir or in controlled herds, following *in vivo* monitoring of follicle growth by ultrasonography or by regulation with hormonal treatment.

The follicular basal lamina was observed to change in composition as a function of folliclular growth. Culture of granulosa cells showed production of basal lamina and induction by growth factors. A new basal lamina type of matrix (focimatrix) was identified within the membrana granulosa of large antral follicles. Focimatrix is developmentally regulated, although its function is still to be determined. At ovulation, some components of the follicular basal lamina and focimatrix are degraded, while granulosa cells express versican.

Degradation of the follicular basal lamina and focimatrix is completed during the early stages of formation of the corpus luteum, and luteal cells of the bovine and human are not surrounded by a basal lamina. Basal laminas within the bovine and human corpora lutea are only associated with the vasculature. In the bovine there is a reticular network of extracellular matrix throughout the corpus luteum and in the human, luteal parenchymal matrix and subendothelial basal laminas change in composition during development.

The follicular basal lamina is not degraded during the process of atresia. In the definitive characterisation of follicular atresia, a distinctive type of atresia was identified and named basal atresia. Features of basal atresia include precocious expression of cholesterol side-chain cleavage cytochrome P450 and 3β-hydroxysteroid dehydrogenase in granulosa cells, altered steroid concentrations, (increased progesterone and decreased testosterone and androstenedione) in follicular fluid, and increased cell death in the theca interna involving steroidogenic, endothelial and other cells.

The present studies have identified changes in matrix that are associated with folliculogenesis, its lack of change in atresia, destruction at ovulation and the development of new matrix in the corpora lutea.