

# Expression of Stat3 in germ cells of developing and adult mouse ovaries and testes

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## Abstract

The Signal transducers and activators of transcription (Stat) family of proteins plays diverse roles during differentiation in many tissues. Stat3 is an essential mammalian gene, critical during embryonic development. In mammals, Stat3 is differentially distributed in the cytoplasm of mature oocytes and in preimplantation embryos suggesting that Stat3 may be involved in determination of polarity. Here, we report that Stat3 protein is expressed in the cytoplasm of oocytes from primordial, primary and secondary follicles in the adult ovary and in developing acrosomes of round spermatids in the adult testis. Stat3 is also expressed in gonocytes, prospermatogonia, oogonia and oocytes of embryonic and neonatal gonads.

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## 1. Results and discussion

Shortly after their formation, female germ cells undergo a series of incomplete cell divisions resulting in clusters called cysts (Pepling and Spradling, 1998). The oogonia stop dividing and enter meiosis at approximately 13.5 dpc (days postcoitum), becoming oocytes, eventually arresting in prophase I. After birth, mouse germ cell cysts break down into individual oocytes that become surrounded by somatic pre-granulosa cells to form primordial follicles (Pepling and Spradling, 2001). During the process of cyst breakdown, a subset of oocytes in each cyst dies with only a third of the initial number of oocytes surviving (Pepling and Spradling, 2001). In the adult mouse, cohorts of primordial follicles are periodically recruited to enter a 3-week growth phase that ends in meiotic maturation and ovulation (Amleh and Dean, 2002). During this period, the oocyte grows and the surrounding granulosa cells proliferate. Only some follicles survive to maturity, the majority undergo atresia during which the oocyte and surrounding granulosa cells die by programmed cell death (Hsueh et al., 1994).

In the male, primordial germ cells aggregate with Sertoli cells to form seminiferous cords enclosed by peritubular cells (Mackay, 2000; Orth et al., 2000). Male germ cells divide until approximately 13.5 dpc when they exit the cell cycle and remain quiescent as gonocytes until a few days after birth (Monk and McLaren, 1981). The gonocytes are initially in a central position within the cords but in the neonate relocate to the basement membrane at the periphery of the tubules, become prospermatogonia and eventually develop into spermatogonial stem cells that produce spermatozoa (Brinster, 2002; Mackay, 2000; Orth et al., 2000). Differentiation of spermatogonia into spermatozoa takes about 5 weeks and begins when the germ cells enter meiosis and become spermatocytes. The result of meiosis is the formation of haploid spermatids that undergo spermiogenesis to form mature spermatozoa. During spermiogenesis, the acrosome, a secretory organelle important for sperm-egg penetration, begins to form (Ramalho-Santos et al., 2002).

The Signal transducers and activators of transcription (Stat) family of proteins is important during differentiation in many tissues (for reviews see (Ihle, 2001; Kisseleva et al., 2002)). Membrane receptors are activated by ligand binding, and in turn, activate Jak family protein kinases,

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which recruit and phosphorylate Stats. Phosphorylated Stat proteins homodimerize and translocate to the nucleus where they regulate transcription of target genes. This pathway can be activated by a large number of cytokines and growth factors in vertebrates (Hou et al., 2002). In mammals, there are seven known Stat proteins (Kisseleva et al., 2002).

In addition, the Stat family proteins are well conserved and homologous proteins have been found in *C. elegans*, *Dictyostelium*, *Drosophila* and zebrafish (Hou et al., 2002).

Stat3 is essential during mammalian development because mice with a targeted disruption of Stat3 die as embryos (Takeda et al., 1997). Studies of cultured cells and

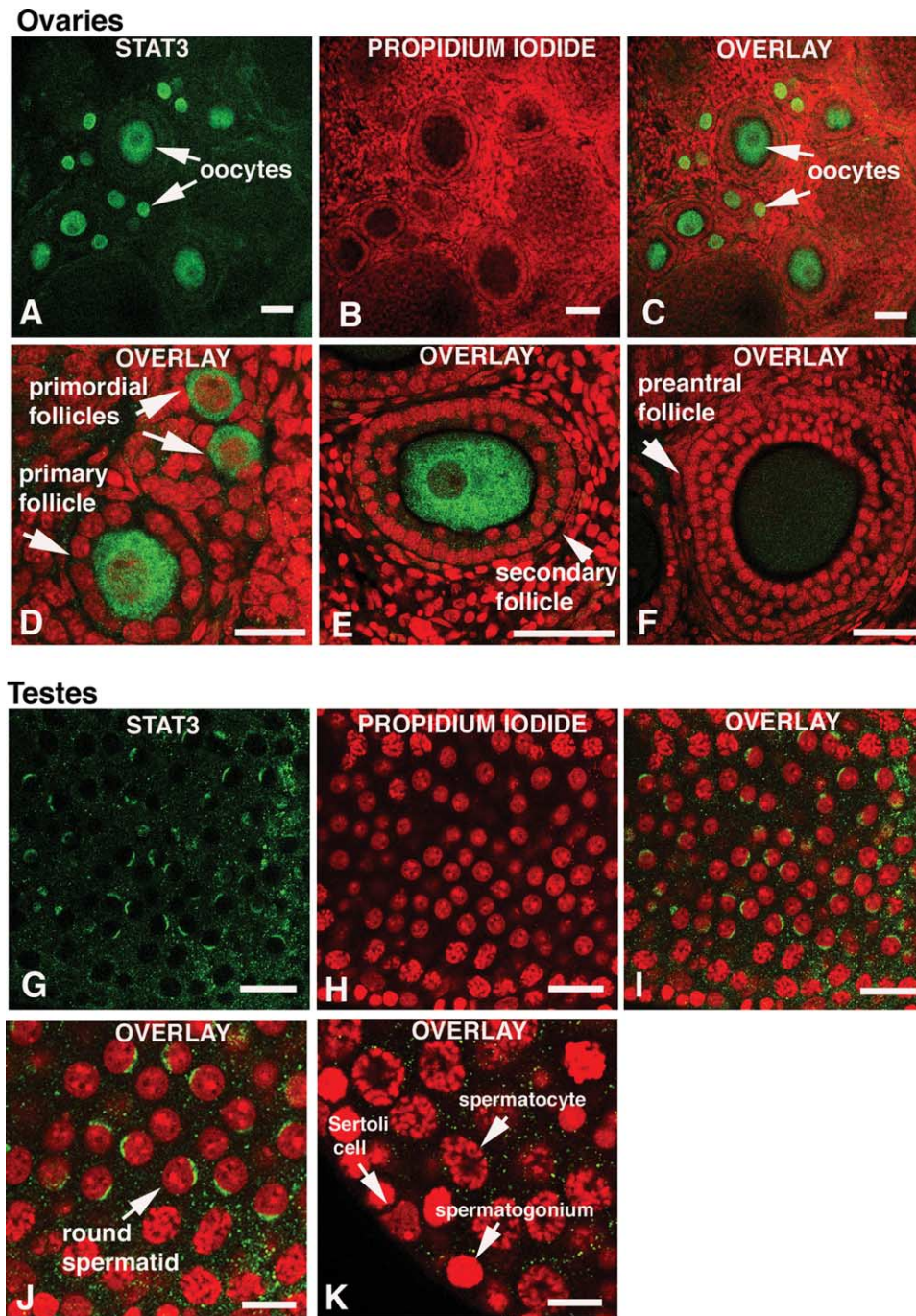


Fig. 1. Stat3 protein expression in adult mouse ovaries and testes. (A–C) low power confocal section of an adult ovary labeled with Stat3 antibody (A), propidium iodide (B) and overlay (C). Arrows in A and C indicate examples of labeled oocytes. High power view of Stat3 protein expression in oocytes of primordial and primary follicles (D), a secondary follicle (E), and a preantral follicle (F). (G–K) Confocal section of adult mouse testis labeled with Stat3 antibody (G), propidium iodide (H) and overlay (I) showing labeling of developing acrosomes in round spermatids. High power view of a confocal section from adult testis showing Stat3 antibody staining in (J) and lack of staining of spermatogonia, spermatocytes and Sertoli cells in (K). Stat3 (green), propidium iodide (red). Scale bar = 50  $\mu$ m A–C, E, F, = 20  $\mu$ m, D, G–I and = 10  $\mu$ m, J, K.

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