Introduction
Previous reports from this laboratory on a 24kDa protein isolated from rat testis by preparative gel electrophoresis showed that the protein was glycosylated (Shaha et al, 1991) and was a potent immunogen in rats and mice (Shaha et al, 1990a; Suri et al, 1993; and Shaha et al, 1990b). Antibodies against this protein, generated on active immunization of female rats by the intramuscular or the oral route, interfered with fertility (Shaha et al, 1990a; and Suri et al, 1993). Immunocytochemically this protein was localized on acrosome of rodent and primate sperm (Shaha et al, 1988). Mouse and hamster sperm-oocyte interactions were also inhibited by antibodies against this protein (Shaha et al, 1988; and Shaha et al, 1989). The entire gamut of studies implicated the 24kDa protein as playing a vital role in fertility.

Approaches to male fertility control via immunological means or by specific inhibition of relevant molecules logically involve the identification of novel physiologically active molecules that are specific to the male reproductive tract. Antibodies or other specific agents, that inhibit the functions of these biologically active molecules, may prove to be useful tools to disrupt specific stages in the germ cell development or the epididymal maturation of sperm, thereby offering a method for inhibition of fertility.

The mammalian testis consists of two compartments: the interstitium and the seminiferous tubules (Figure a). The composition of the interstitium is a little species-specific but generally, it contains Leydig cells, macrophages, lymph space and blood vessels. The seminiferous tubules are avascular and house different types of germ cells embedded
Introduction

Figure a: A diagrammatic representation of a cross-section of the testis showing the different testicular cell types and their interactions.
in Sertoli cells. The two compartments are separated by peritubular myoid cells and a basal lamina. The normal functioning of the testis depends on interactions between the different testicular cell types (Skinner, 1991), which are partially regulated by the pituitary hormones, luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

The fluid that bathes the interstitium is known as the interstitial fluid (IF) while the fluid contained in the seminiferous tubules is called, the tubular fluid (TF). The function of the interstitial Leydig cells is the production and secretion of androgens, mainly testosterone. Testosterone is an important regulator of Sertoli cell function and therefore of spermatogenesis. In most androgen target tissues, testosterone is converted to dihydrotestosterone by the enzyme, 5α-reductase. Dihydrotestosterone is known to bind to the androgen receptor with a higher affinity than testosterone, and is considered to be a more potent androgen. Both testosterone and dihydrotestosterone are involved in the manifestation of secondary sexual characteristics and play a vital role in regulating spermatogenesis.

Peritubular myoid cells form a layer of flattened cells between the interstitium and the seminiferous tubules. Together with Sertoli cells, they produce an extracellular matrix which provides structural support to the spermatogenic epithelium. Myoid cells seem to be involved in the contraction of the tubules, which may be necessary for the release and transport of the testicular spermatozoa. Peritubular cells appear to be important for the regulation of Sertoli cell function, since they secrete an androgen regulated factor-PModS, which influences many parameters of Sertoli cell function. It is hypothesized that PModS has an important role in the induction and maintenance of Sertoli cell differentiation.
Sertoli cells are the only somatic cell type of the spermatogenic epithelium. The cells proliferate rapidly during early fetal and early postnatal life, but do not divide after approximately 16 days of age in rats. After differentiation, adjacent Sertoli cells become interconnected by tight junctional complexes and together with endothelial cells (lining blood vessels and lymph space), peritubular cells and the basal lamina, form the blood-testis barrier. This barrier divides the tubules into a basal compartment containing the spermatogonia and the early spermatocytes and a luminal compartment, containing the more mature germ cells. The barrier prevents the passage of many substances and creates the unique microenvironment required for proper germ cell development. The impermeability of the barrier implies that Sertoli cells provide components necessary for germ cell survival at the luminal side of the barrier. The Sertoli cells also provide physical support for the developing germ cells. The formation of the blood-testis barrier is correlated with the onset of spermatogenesis and seminiferous tubular fluid production. The tubular fluid may serve as a vehicle for sperm transport and possibly play a role in further maturation of the testicular spermatozoa.

Spermatogenesis is the process by which immature germ cells develop to spermatozoa. Germ cell development takes place in the protected environment of the seminiferous tubules, as a defined series of developmental events, according to a tight schedule in time and place. The germ cells are arranged in specific cell associations, called the stages of the seminiferous epithelial cycle. For the rat, 14 different stages have been defined which make up one cycle, approximately of 13 days. For its complete development the germ cell traverses the different stages of the cycle 4 times, which takes 52 days in all.
Spermatogenesis does not seem to rely on direct control of the germ cells by the endocrine system, but rather is dependent on hormone action on Sertoli cells and cell-cell interactions between germ cells and Sertoli cells. In this respect the Sertoli cell is also referred to as the nursing and supporting cell of the germinal epithelium. Thus the main regulators of spermatogenesis, FSH and testosterone, have their effects via the Sertoli cell.

Once the spermatozoa leave the testis, they undergo a succession of changes in the male reproductive tract, associated with the cell surface leading to alterations in their functional capabilities. Mammalian spermatozoa acquire fertilizing ability during their epididymal transit, when molecules on the surface of sperm may be added, lost or modified as the sperm come in contact with the various fluids and cell types. In the female reproductive tract, the spermatozoa undergo capacitation and acrosome reaction which enables them to fertilize the egg (Yanagimachi et al, 1994).

A number of enzymatic and non-enzymatic sperm surface molecules are reported to be involved in sperm-oocyte interactions. Galactosyl transferase (Shur and Bennett, 1979), trypsin like enzyme (Saling, 1981), sialyltransferase (Shur and Bennett, 1979) and fucosyltransferase (Ram et al, 1989) are important for murine sperm-oocyte interaction. Lactate dehydrogenase-C4 a testis specific enzyme is known to be relevant to sperm function (Wheat and Goldberg, 1985a) and active immunization against this antigen causes a 50% reduction in fertility in female mice, rabbits and baboons (Wheat and Goldberg, 1985b). Human sperm surface proteins SP-10 (Herr et al, 1990) and FA-1 (Naz, 1993) are also reported to be important for fertilization. Glutathione
S-transferases have been reported to be present in the testis but a testis-specific role(s) for these molecules has not been reported so far.