

## Chapter 2

# The Sertoli Cell at a Glance

The testicles are compartmentalized organs whose functional units, the seminiferous tubules, are immersed in a web of loose connective tissue and interstitial cells (or Leydig cells). In the seminiferous tubules, the epithelium is compartmentalized due to the presence of unique somatic cells, named Sertoli cells (Fig. 2.1). These cells function as the structural elements of the seminiferous epithelium, physically supporting the ongoing of spermatogenesis and regulating the flow of nutrients, growth factors and other substances to male germ cells. In mammals, at the time of puberty, Sertoli cells suffer a profound alteration on their morphology and function, becoming morphologically and biochemically distinct from the undifferentiated cells.

### 2.1 Sertoli Cell Structure and Morphology

When fully differentiated, the Sertoli cell is a columnar shaped epithelial cell of large dimensions, which extends from the base of the seminiferous epithelium, the basement membrane, to the lumen of the tubules (Fig. 2.1) (Brooks 2007; Foley 2001; Rodriguez-Sosa and Dobrinski 2009). The basal portion of the Sertoli cells adhere to the basement membrane (or basal lamina), a fibrous structure composed of various extracellular matrix proteins (such as laminin, collagen and heparan sulfate) that maintains the structural integrity of the seminiferous tubules (Hadley et al. 1985).

In mammals, the size of the Sertoli cell shows a high variation, with the individual volume of the cell ranging from approximately 2000–7000  $\mu\text{m}^3$  (Russell and Peterson 1984; Russell et al. 1990). The volume density of these cells (expressed as a percentage of the entire seminiferous tubular epithelium) also varies within the several mammalian species, from approximately 15 % in mice to 40 % in humans (Russell et al. 1990).

Electron micrographs showed that the Sertoli cell possesses an expanded and clear cytoplasm with an irregular shape that varies from species to species (Russell and Brinster 1996; Russell et al. 1996). The majority of the Sertoli cell surface is in close association with the surface of germ cells (Fig. 2.1), illustrating the extent to which the Sertoli cell expands its cytoplasm to directly interact with the developing germ cells. In the cytoplasm, these cells exhibit several organelles, in particular great quantities of mitochondria, which indicate a high metabolic activity (Russell 1993a).

In most species, an irregular shaped nucleus can be found in the basal portion of the cytoplasm of the Sertoli cell. This nucleus is of large dimensions (up to 850  $\mu\text{m}^3$ ), with an irregular shape that depends on the stage of the seminiferous

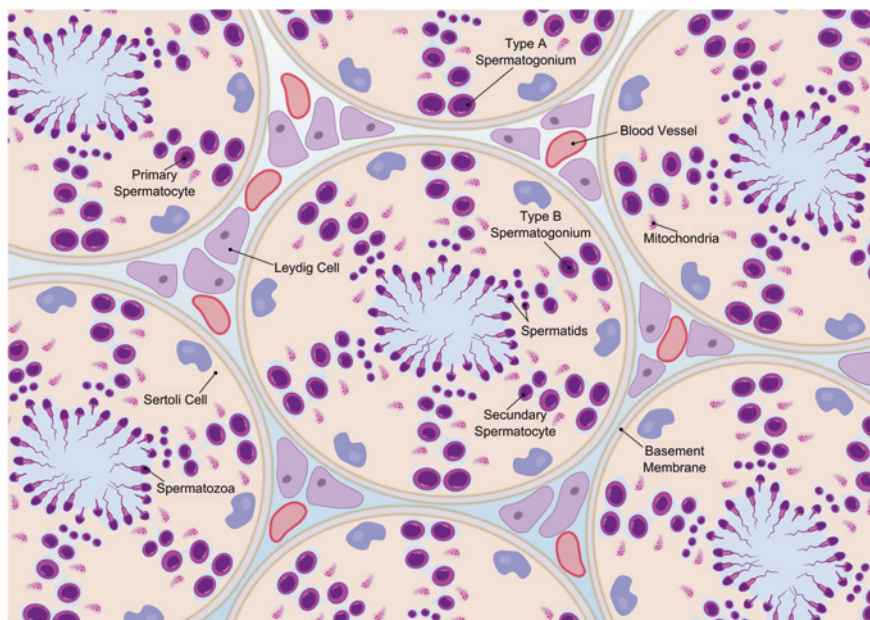


**Fig. 2.1** Schematic illustration of the seminiferous tubules. The seminiferous epithelium is formed by Sertoli cells and germ cells at different stages of development. Sertoli cell extends their cytoplasm from the basement membrane to the lumen of the seminiferous tubule. Leydig cells and blood vessels can be found in the interstitium, which is filled by the interstitial fluid. The majority of the surface of the Sertoli cell is in close association to several germ cells. In spermatogenesis, diploid spermatogonial stem cells origin male haploid germ cells from, through cellular division and differentiation

tubule cycle (Russell et al. 1990; Ye et al. 1993) and on the age of development of the individual (Heyn et al. 2001; Krzanowska and Bilinska 2000). The nuclear envelope is invested with deep invaginations (or indentations) that are associated with an accumulation of vimentin intermediate filaments. Moreover, multiple nuclear pores can be found in the nuclear envelope, whose density depends also on the stage of the spermatogenic cycle (Cavicchia et al. 1998). Another characteristic of the Sertoli cell nucleus is the large dimension nucleolus with a three-partite structure that can easily be recognized in the nucleoplasm, usually with two chromocenters associated at diametrically opposed sides in which the centromeric regions of the chromosomes are clustered (Guttenbach et al. 1996; Kushida et al. 1993).

An extensive network of continuous tubular structures with a few ribosomes attached to its surface, known as endoplasmic reticulum (ER), can also be found in the cytoplasm of the Sertoli cell. In the basal portion of these cells, the ER is associated with tight junctions (Brokelmann 1963; Dym and Fawcett 1970; Flickinger and Fawcett 1967) and ectoplasmic specializations (Russell 1977a; Russell and Clermont 1976), being part of the Sertoli—germ cell junctional complexes. While the rough ER is sparse and can be found in the basal region of the cell, the smooth ER is abundant in adult Sertoli cells and can be found near mitochondria, indicating that these cells are intensely involved in the metabolism of lipids or steroids (Russell 1993a). Mitochondria are quite numerous in Sertoli cells and dispersed among the other organelles. Their shape is very variable, with spherical or elongated mitochondria being more abundant, but they can also be cup- or donut-shaped (Bizarro et al. 2003). Tubular cristae are predominant, but the foliate forms are also present in mitochondria of Sertoli cells (Bizarro et al. 2003). These cells exhibit a small Golgi apparatus, being that this single network of stacked saccules is normally dispersed in the supranuclear region of the cell (Chen and Yates 1975; Hess and França 2005; Rambourg et al. 1974, 1979). Lysosomes and multivesicular bodies, resulting from the phagocytotic activity of Sertoli cells, are situated throughout the cytoplasm of the cell (Fig. 2.2), predominantly around the residual bodies and ectoplasmic specializations, with their abundance depending on the stage of spermatogenesis (Hess and França 2005).

The ectoplasmic specializations are cell junctional complexes that are established between two Sertoli cells (Russell 1993b) and between Sertoli cells and germ cells (Vogl et al. 2000), relying on cytoskeletal elements for structure and function, mainly actin filaments, but also microtubules and vimentin (Vogl et al. 1993). The adjacent Sertoli cells are also linked by tight junctions, creating a tight barrier known as the blood-testis barrier or Sertoli cell barrier. This junctional structure has a porosity of approximately 1000 daltons, ensuring that nothing with a higher molecular weight passes to the lumen of the seminiferous tubule (Dirami et al. 1991; Fawcett et al. 1973; Foley 2001). Besides being associated with elements of the cytoskeleton and with the smooth endoplasmic reticulum (McGinley et al. 1979; Russell and Clermont 1976; Russell 1977a, b, 1979a, 1993a), the ectoplasmic specializations and tight junctions have been linked with several other Sertoli cell proteins, including occludin, espin, sertolin and gelsolin (Li et al. 2014;

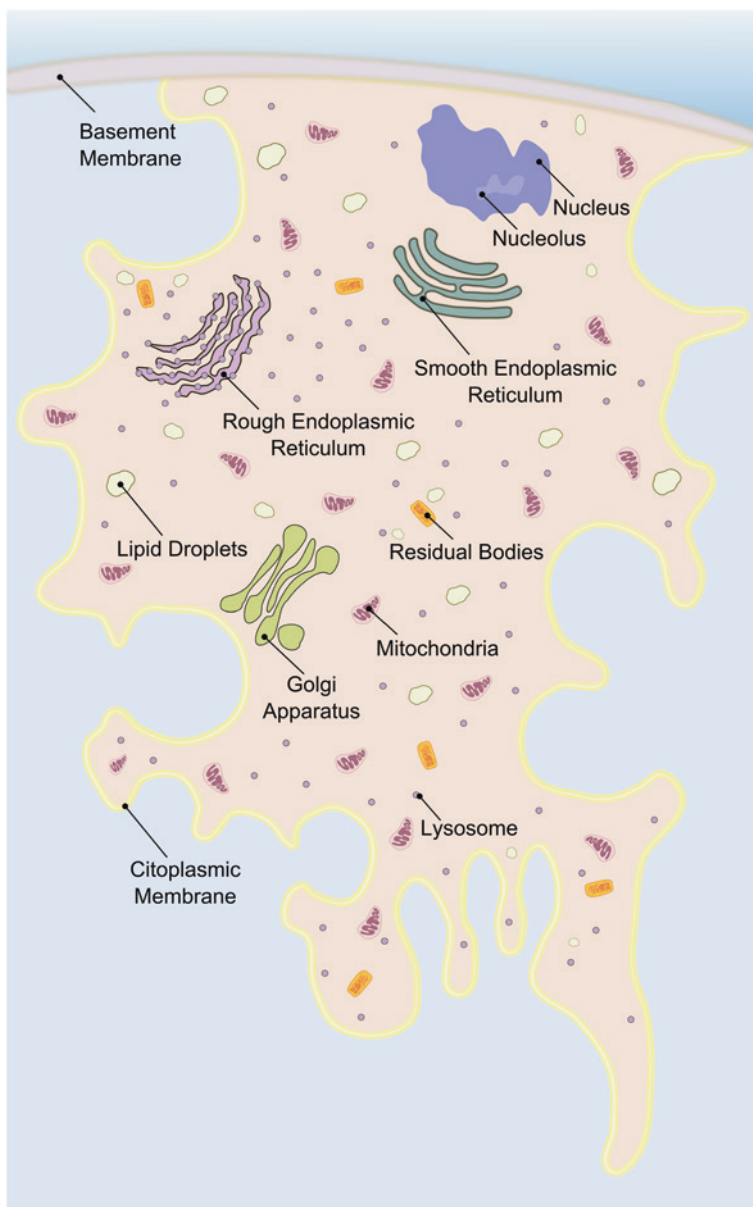


**Fig. 2.2** Diagram of a Sertoli cell. The Sertoli cell is a columnar shaped epithelial cell of large dimensions, where the basal portion of the cell adheres to the basement membrane. The mitochondria are abundant and disperse on the cytoplasm. The nucleus envelope presents deep invaginations and a large dimension nucleolus with a three-partite structure. The rough endoplasmic reticulum is sparse and can be found in the basal region, while the smooth endoplasmic reticulum can be found near mitochondria. The Golgi apparatus is normally dispersed in the supranuclear region of the cell. Lipid droplets and lysosomes are disperse throughout the cytoplasm of the cell. The lysosomes can be found around the residual bodies

Cheng and Mruk 2002). However, the organization of these junctional complexes is variable from species to species (Moroi et al. 1998; Parreira et al. 2002).

Several other components have been observed in the cytoplasm of Sertoli cell, among which lipid droplets and glycogen particles (Guo et al. 2003; Sertoli 1865; Slaughter and Means 1983), typically in the basal compartment, with their quantities varying between species and according to the spermatogenesis stage (Russell 1993a; Erkan and Sousa 2002; Fouquet 1968). The presence of lipid droplets has been associated with the ability of Sertoli cells to recycle lipids from the breakdown of germ cell degeneration and from residual body phagocytosis, although this hypothesis is not entirely consensual. Glycogen particles and glycogen metabolism-associated enzymes have also been described in Sertoli cells (Slaughter and Means 1983). The amount of glycogen present in these cells is stage and species dependent and an increase of glycogen storage has been reported in several pathological conditions (e.g. Sertoli cell only syndrome and Sertoli cell tumors) (Anniballo et al. 2000; Henley et al. 2002).

## 2.2 Sertoli Cell Physiology

The Sertoli cell is the key somatic element responsible for the regulation of spermatogenesis and for the establishment of the different rates of spermatozoa production (Orth et al. 1988; Walker and Cheng 2005). These cells, commonly known as “nurse cells”, have many important roles not only in the development of the testicles and its functions, but also in the expression of the male phenotype (Mruk and Cheng 2004; Sharpe et al. 2003). The central functions of the Sertoli cells are: (1) formation of the blood-testis barrier; (2) providing structural and nutritional support to the developing germ cells; (3) phagocytosis of residual bodies and degenerating germ cells; (4) production and release of regulatory factors; (5) establishment of a localized immune-privileged environment (Dym and Raj 1977; Feig et al. 1980; Alexander 1977; Johnson et al. 2008; Jutte et al. 1982; Setchell 1980; Silber 1978).

Among the most important functions of these cells is the creation of the special environment necessary for the development of germ cells and the regulation of the endocrine environment of the seminiferous tubules (Setchell 1980). The formation of the blood-testis barrier is responsible for excluding many of the substances that are present in the interstitial fluids from the tubular lumen (Setchell 1969). The blood-testis barrier tight junctions successfully avoid the movement of large molecules from the interstitial space to the lumen of the seminiferous tubules (Dym and Fawcett 1970; Aoki and Fawcett 1975).

Sertoli cells execute many of their functions by extending the cytoplasm in thin arm-like processes (in two dimensions) and cylindrical or sheet-like processes (in three dimensions), enclosing the multiple developing germ cells. Junctional interactions are established between Sertoli and developing germ cells, particularly ectoplasmic specializations (Russell 1977a; Russell and Clermont 1976), to help

connecting these cells. Desmosome-gap junctions are also present at the structural interface between Sertoli and germ cells, to help bind these cells together, being particularly abundant in spermatocytes (Russell et al. 1983).

The seminiferous tubule luminal fluid serves not only as a mean of transport for sperm, as, in addition, it allows the establishment of a favorable microenvironment for the occurrence of spermatogenesis. This fluid begins to be produced by Sertoli cells when they reach their mature state (Sharpe et al. 2003). Its composition is very stable due to the presence of the blood-testis barrier and is very different from the circulating plasma and testicular interstitial fluid. This fluid has been described as rich in  $\text{Na}^+$  and  $\text{Cl}^-$ , with a  $\text{K}^+$  concentration twofold higher than that of the other extracellular fluids (Clulow and Jones 2004). Another important feature of this luminal fluid is the control of its pH. This parameter is maintained by the action of intracellular buffers and also by the balance between the production and elimination of protons (Roos and Boron 1981). In fact, the Sertoli cell expresses several types of membrane ion transporters directly involved in the movement of acidic and basic particles through the membrane (Bernardino et al. 2013a). While the role of these membrane transporters is largely unknown, its operation and regulation is essential to determine the osmolarity and pH of the seminiferous tubule luminal fluid (Oliveira et al. 2009a, b). Various ion channels have also been identified in Sertoli cells (Rato et al. 2010). These channels serve as pores that allow the passive diffusion of ions through the membrane of these cells. Ion channels are typically selective for a particular ion species or a limited group of ion transport direction and depends on the electrochemical gradient that is established. These channels are regulated by multiple factors, such as  $\text{Ca}^{2+}$  concentration or pH (Hubner and Jentsch 2002) and have several functions, as for instance the transduction of electrical and chemical signals, the transepithelial transport, the regulation of cell volume and cytoplasmic or vesicular ion concentration. Furthermore, Sertoli cells must provide the nutritional supply during the development of germ cells (Griswold and McLean 2006). If in the early stages of development the germ cells use glucose as energy source, obtained from the systemic circulation (Riera et al. 2001; Brauchi et al. 2005), in later stages of development, germ cells lose the capacity to metabolize glucose (Boussouar and Benahmed 2004). So, spermatids and spermatocytes are dependent on lactate supplies provided by Sertoli cells (Bajpai et al. 1998b; Jutte et al. 1982; Nakamura et al. 1984a).

Paradoxically, despite being known as sustentacular cells, Sertoli cells are able to induce apoptosis of developing germ cells in an essential regulatory process, taking into account that one mature Sertoli cell can only support a limited number of developing germ cells. Thus, when the cell number exceeds this threshold, it is necessary to eliminate them to allow the spermatogenic process to adequately proceed (Xiong et al. 2009). In addition, the phagocytic activity of the germinal cells components is another important function of Sertoli cells (Griswold et al. 1988). The selective phagocytosis of germ cell residual bodies is a receptor-mediated activity that occurs in Sertoli cells (Morales et al. 1985, 1986). It results from the recognition of specific markers on plasmatic membrane of those residual bodies (Clermont et al. 1987), which have specific antigenic determinants distinct from

those present in the membranes of non-degenerating germ cells (Bellve and Moss 1983; Millette and Bellve 1980).

The secretions of the Sertoli cell, particularly growth factors and hormones, are also critical to the control of spermatogenesis and the reproductive function of males (Skinner 2005), since they strictly regulate the maturity of the male gonads and the safeguard of spermatogenesis (Levine et al. 2000; Clermont and Perey 1957). Several proteins and factors are secreted by these cells, such as the androgen binding protein (ABP) (Fritz et al. 1976b), transferrin (Skinner and Griswold 1980), glycoproteins (O'Brien et al. 1993), sulpho-proteins (Elkington and Fritz 1980) and myoinositol (Robinson and Fritz 1979). The Sertoli cell is also responsible for the secretion of several cytokines and other specific products for the development of germ cells (such as the c-Kit ligand, activin and inhibin) (Syed et al. 1988) that influence both germ cell development (Pollanen et al. 1989) and Sertoli cell function (Nehar et al. 1998; Huleihel and Lunenfeld 2002) and whose role will be discussed in the subsequent chapters.

### 2.3 Hormonal Control of Sertoli Cell Function

Hormones are key regulatory factors of the functioning of the Sertoli cell (Fig. 2.3). Among those, follicle-stimulating hormone (FSH), sex steroid hormones, thyroid hormones (TH) and insulin deserve a special emphasis. FSH is secreted by the pituitary in response to the secretion of gonadotropin releasing hormone (GnRH), which acts through G-protein coupled receptors, that, in the testicles, are exclusively located in the Sertoli cell (McLachlan et al. 2002). FSH has a central role on the male reproductive potential. Individuals with no functional receptors for FSH have smaller testicles. In fact, it has been reported that knockout mice for the receptor of this hormone have a very small number of Sertoli cells (Dierich et al. 1998), apart from presenting an altered spermatogenesis. Moreover they are diagnosed as azoospermic and/or teratozoospermic, although frequently classified as fertile (Tapanainen et al. 1997). This gonadotropin controls the proliferation of Sertoli cells during the perinatal period and the pubertal phase, determining the spermatogenic ability of male adults. The mechanism of action of FSH involves the cyclic AMP signaling pathway, through activation of G-proteins. FSH also increases the levels of phosphorylated protein kinase B (PKB-P) via a phosphatidylinositol 3-kinase (PI3K)-dependent mechanism (Meroni et al. 2002). The PI3K is an enzyme involved in the regulation of various biological processes, including mitogenesis, oxidative stress and glucose metabolism. FSH also stimulates the production and secretion of the hormone inhibin B by Sertoli cells. In fact, plasma levels of inhibin B are clinically used to evaluate the function of Sertoli cells during childhood. On the other hand, during adulthood, inhibin B levels are dependent on the presence of germ cells and therefore are reported to reflect the functional state of spermatogenesis (de Kretser et al. 2004). Of note, FSH also stimulates the production of other factors and substances, such as transferrin, lactate and androgen receptors.

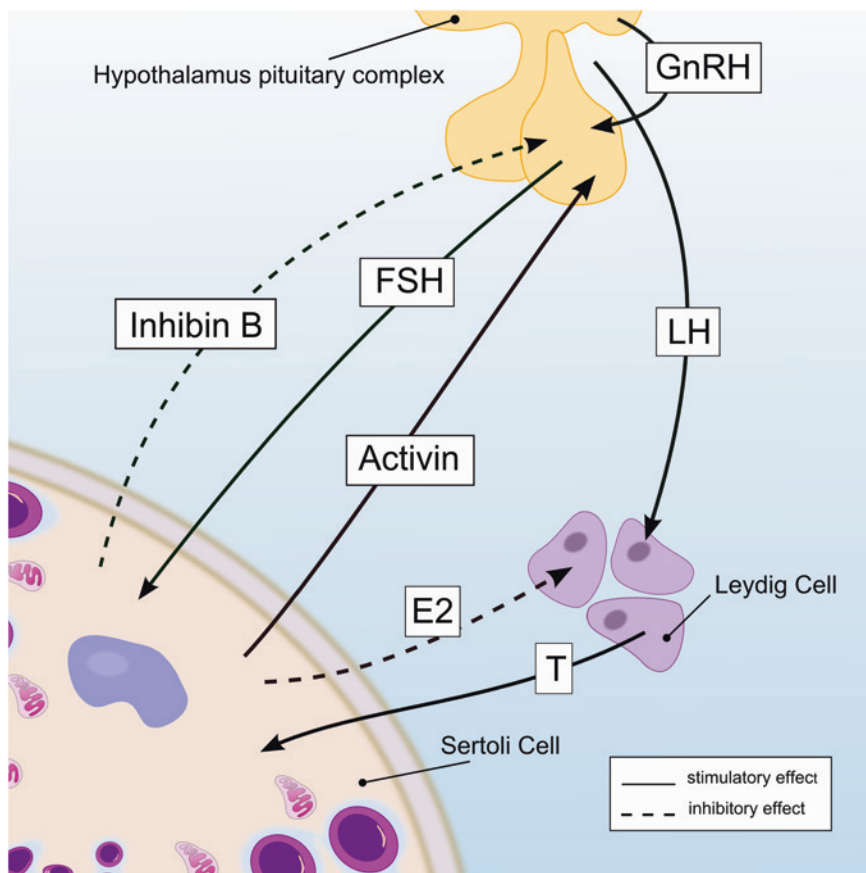


**Fig. 2.3** Hormonal regulation of hypothalamus pituitary gonad axis. The gonadotropin releasing hormone (*GnRH*) is synthesized by hypothalamus, which will stimulate the pituitary to produce the luteinizing hormone (*LH*) and the follicle-stimulating hormone (*FSH*). *LH* binds membrane receptors on Leydig cells and stimulates the testosterone (*T*) production. *FSH* binds membrane receptors on Sertoli cells, stimulating the production/secretion of 17β-estradiol (*E2*), activin and inhibin B. *E2* acts on Leydig cells inhibiting the production of testosterone. Activin and inhibin B produce a positive/negative feedback on pituitary, respectively. Abbreviations: *GnRH* gonadotropin releasing hormone; *LH* luteinizing hormone; *FSH* follicle-stimulating hormone; *T* testosterone; *E2* 17β-estradiol

The secretion of FSH is modulated by prolactin levels. While lower prolactin levels stimulate Sertoli cell growth, lactate production and synthesis of some proteins, elevated prolactin inhibits FSH secretion, which may compromise the male reproductive function (Scarabelli et al. 2003). However, the disruption of the secretion of this prolactin or its receptor in mice does not affect fertility, which illustrates that although this hormone serves as a controlling mechanism of Sertoli cell function, it is not vital for the reproductive function in males.

Spermatogenesis is dependent on the presence of a suitable intratesticular level of sex steroid hormones (androgens and estrogens). The Sertoli cells express androgen receptors, whereas germ cells lack these receptors (Lyon et al. 1975). Androgens are known as the male sex hormones and include various steroids, such as testosterone, androstenediol and 5- $\alpha$ -dihydrotestosterone (DHT). They have a central role on the masculinization of the reproductive tract and genitalia during the sexual differentiation process (Hughes 2001; Sultan et al. 2001) and are essential for initiation and maintenance of spermatogenesis (Roberts and Zirkin 1991). In fact, germ cell development is arrested at the spermatocytes stage (Chang et al. 2004) or early spermatid (De Gendt et al. 2004; Holdcraft and Braun 2004) when androgen receptors are ablated in Sertoli cells. The androgen receptor activity in Sertoli cells is regulated by testosterone (and its derivative DHT) (Lindzey et al. 1994), which is produced by Leydig cells in response to luteinizing hormone (LH). In fact, the physiology of the Sertoli cell is modulated by testosterone metabolites such as DHT, which has a biological activity two to three times higher than testosterone (Robaire and Viger 1995). Both androgens (testosterone and DHT) bind to and activate the same receptors, although DHT presents a much higher affinity (Deslypere et al. 1992). Androgen receptors are essential for normal spermatogenesis and when they are silenced on the Sertoli cell, the development of germ cells halts in the spermatocyte or primary spermatid stages (De Gendt et al. 2004; Holdcraft and Braun 2004), illustrating that the Sertoli cell is the preferred site of action for androgens in the control of spermatogenesis. Furthermore, it has been reported that increased expression of androgen receptor is directly related to the maturation of Sertoli cells (Buzek and Sanborn 1988). Indeed, androgens are necessary for the promotion of the integrity of the blood-testis barrier and assembly of junctional complexes (Meng et al. 2005; Wang et al. 2006).

The role of estrogens in male reproductive function has been under discussion in recent years. It is now accepted that these sex hormones also play an important role in the development and maintenance of the male reproductive function and, consequently, in male fertility (Carreau et al. 2008; Nilsson et al. 2001; O'Donnell et al. 2001). Estrogen biosynthesis is catalyzed by aromatase (O'Donnell et al. 2001). In the testicles, aromatase is expressed in immature Sertoli cells (Abney 1999; Fritz et al. 1976a), the major source of estrogens in prepubertal individuals, while in adults, the Leydig cells are the main responsible for the synthesis of estrogens (Carreau et al. 2009). A high concentration of estrogens has been reported in the testicular interstitial fluid (Rato et al. 2013) and in the *rete testis* (Free and Jaffe 1979). Moreover, estrogen concentration in the rat epididymis is approximately 25 times higher than in plasma (Kumari et al. 1980). These data suggest that estrogens play an active role in the control of spermatogenesis and male reproductive function. In fact, estrogens can modulate apoptotic signaling pathways in rat Sertoli cells (Simões et al. 2013), prevent the development of Leydig cells and inhibit the production of testosterone, stimulating spermatogenesis by decreasing apoptosis in post-meiotic spermatogenic cells and altering the proliferation and differentiation of spermatogonial cells (O'Donnell et al. 2001). Although the role of these hormones in the physiology of Sertoli cell is a controversial topic, their

action is mediated through the interaction with their specific receptors. All the subtypes of the membrane-bound (GPR30) and of the nuclear estrogen receptors (ER), ER $\alpha$  and ER $\beta$ , were identified in Sertoli cells (Oliveira et al. 2014a; Pelletier and El-Alfy 2000; Saunders et al. 2001, 2002; Taylor and Al-Azzawi 2000). Furthermore, Sertoli cell ER-knockout null mutations cause profound alterations in spermatogenesis and infertility (Chung et al. 1998).

The presence of insulin receptors has also been described in Sertoli cells (Oonk and Grootegeod 1987). Recently, it has been reported that insulin-deprived Sertoli cells present altered expression of metabolism-associated genes involved in the production and export of lactate, as well as altered secretion of lactate and consumption of glucose (Oliveira et al. 2012). The TH have been associated with an inhibition of the Sertoli cell cycle (Walker 2003). Neonatal administration of triiodothyronine (T3) to rats suppresses the proliferation of Sertoli cells (van Haaster et al. 1993). Of note, men with hyperthyroidism are frequently diagnosed with oligospermia and present a considerable lower sperm counts (Clyde et al. 1976). In addition, individuals with thyroid deregulation usually present symptoms of erectile dysfunction and decreased libido or impotence (Wagner et al. 2008). Hypothyroidism has been associated with a prolongation of the growth phase of the Sertoli cells, translating into a delay of the differentiation of these cells. This leads to an increase in the number of Sertoli cells and promotes the enlargement of the testicles and sperm production (van Haaster et al. 1992). Sertoli cells also possess receptors for the growth hormone (Gomez et al. 1998) and a deficiency on this hormone is associated with a smaller size of the testicles, illustrating a reduction in the number of Sertoli cells, although fertility is not compromised (Bartlett et al. 1990).

## 2.4 Pathophysiology of Sertoli Cells

The success of spermatogenesis is on the basis of male fertility. Taking into account that Sertoli cells support, protect and nourish the developing germ cells, the proper functioning of these somatic cells is essential for male reproductive function. Any failure in the process of maturation of the Sertoli cell means that these cells may no longer be able to support the development of germ cells. This is a dynamic process and the absence of germ cells, such as in cases of exposure to radiation, may lead to severe alterations in the function of the Sertoli cell, prompting the cell into a stage functionally identical to the immature state. Several pathologies are associated with de-differentiation of Sertoli cells. For instance, in seminiferous tubule constituted only by Sertoli cells, these cells exhibit one or more markers of an immature state (such as the anti-mullerian hormone or cytokeratin-18) and may even show a total absence of androgen receptors, which are known to be absent in immature Sertoli cells (Bar-Shira Maymon et al. 2000). Furthermore, Sertoli cells with immature phenotypes have been consistently associated with testicular germ cell cancer incidence, which has more than doubled in the last decades. Cryptorchidism, a condition in which the testicles did not descend properly from the abdominal cavity into

the scrotum, is one of the most important risk factor for developing testicular cancer and also a factor directly associated with low production of sperm. Testicles of individuals with cryptorchidism contain seminiferous tubules only with Sertoli cells and these cells have a number of characteristics associated with the immature state. In fact, cryptorchidism has been suggested to be more a consequence of an impaired differentiation of these cells than a cause for this phenomenon (Skakkebaek et al. 2001). In the last decade, a new concept associated with the male reproductive health has arisen: the testicular dysgenesis syndrome. This syndrome comprises several pathological manifestations as hypospadias (congenital malformation of the urethra), reduced sperm counts, testicular cancer, among others. Although these disorders may manifest at different stages of sexual development, they are thought to have a common origin in fetal life as the result (at least in part) of the abnormal functioning of Sertoli cells (Skakkebaek et al. 2001).

The Sertoli cell is also susceptible to the action of many toxic substances, pesticides and heavy metals. Many of these substances affect the cell cytoskeleton or induce chromatin condensation and vacuolization of the cytoplasm. The effect of endocrine disruptors and other environmental pollutants on the physiology and function of the Sertoli cell has received special attention from several researchers. Studies have consistently demonstrated that the administration of the synthetic estrogen diethylstilbestrol to rats reduces the number of Sertoli cells, disrupting the formation and maturation of the blood-testis barrier (Toyama et al. 2001). Recently, it has also been reported that a concentration of 2,4-dichlorophenoxyacetic acid in the range of values that can be found in the urine of men who directly work with this pesticide induces significant changes in the metabolism of Sertoli cells, with putative effects on spermatogenesis (Alves et al. 2013b).

As previously referred, one of the major functions of the Sertoli cell is to ensure the transport and metabolism of glucose to produce the metabolic precursors necessary for the developing germ cells (Robinson and Fritz 1981). Deregulation of the metabolic behavior of these somatic cells can compromise the energy supply to germ cells. Several metabolic diseases, which are currently major threats to public health (where we can highlight Diabetes Mellitus), have their genesis in insulin resistance and/or absence of insulin, as well as an inability of cells to respond efficiently to the stimulation by this hormone. In these circumstances, the metabolism of Sertoli cell undergoes important changes (Alves et al. 2012; Oliveira et al. 2012), causing impairment in the development of germ cells and, thus, in male fertility.

In fact, both the malfunction of Sertoli cells, as disturbances in their differentiation and/or maturation have been identified as crucial factors in the origin of the reproductive dysfunctions associated with various pathological conditions. It is essential to understand the physiology, structure and function of the Sertoli cell, as well as the mechanisms involved in its development and maturation, to better comprehend how all these processes can be influenced by our lifestyle and environment. It is likely that a more detailed knowledge of the functioning and maturation of the Sertoli cell will point toward specific molecular targets to counteract the deleterious effects of pathologies that affect the reproductive health of males.

Sertoli Cell Metabolism and Spermatogenesis

Oliveira, P.F.; Alves, M.G.

2015, VIII, 98 p. 14 illus., Softcover

ISBN: 978-3-319-19790-6