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Dynamics of Spermatogenesis

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Authors' contributions

This work was carried out in collaboration between all authors. Authors VD and VGK participated in designing, data analysis and drafted the manuscript. Author SN carried out manuscript writing and preparation. Author SGR participated review of the manuscript. All authors read and approved the final manuscript.

Review Article

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ABSTRACT

Spermatogenesis is the lengthy and chronological process. Spermatogenesis is characterized by three specific functional phases: spermatocytogenesis, meiosis, and spermiogenesis; and it involves spermatogonia, spermatocytes, and spermatids respectively. Various growth factors play important role in spermatogenesis and up to 178 genes and proteins are being reported which play important role in the process of self renewal and meiosis during spermatogenesis. The duration of spermatogenesis can only be approximated for any species and it has been considered to be about 4.5 times the cycle length of a given species. Various factors play important role in controlling the spermatogenesis like hormones, age, drugs, diet etc among which hormone testosterone elicits an action through hormone response elements, thus altering gene expression. Thus spermatogenesis is a dynamic process with well organized cellular and molecular events resulting in release of large number spermatozoa with ability to continue life on this planet earth.

Keywords: Spermatogenesis; dynamic; mechanisms; control; animals.

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1. INTRODUCTION

Spermatogenesis is the lengthy and chronological process. A few stem-cell spermatogonia, lining the base of seminiferous tubules divide by mitosis to maintain their own stem-cell numbers and to cyclically produce primary spermatocyte that in turn undergo meiosis to produce haploid spermatid which differentiate into spermatozoa released into the tubular lumen [1].

2. TESTICULAR HISTOLOGY

The testes of mammals are paired organs that essentially perform two functions, production of spermatozoa and synthesis of steroids. The testis is composed of numerous seminiferous tubules and the intervening interstitial space, all encased by a connective tissue capsule, the tunica albuginea Seminiferous tubules are coiled structures forming hairpin loops that empty at both ends into the rete testis [2], an anastomotic channel located at the vascular pole of the testis and lined by a cuboidal epithelium.

Seminiferous tubules are lined by an epithelium composed of germ cells and supporting Sertoli cells, with the latter being mitotically inactive in adults. Seminiferous tubules are enveloped by a tunica propria or limiting membrane comprised of contractile myoid (peritubular) cells interposed between connective tissue layers of collagen and elastic fibers, with myoid cells moving immature spermatozoa toward the rete testis. The interstitial space consists of androgen-producing Leydig cells, macrophages, blood, and lymphatic channels as well as nerves [3,4,5].

3. THREE PHASES OF SPERMATOGENESIS

3.1 Spermatocytogenesis

Spermatocytogenesis is the first phase of spermatogenesis and involves spermatogonia. It is a process of formation of spermatocyte from spermatogonia. Spermatogonia arise postnatally from gonocytes and are located at the base of seminiferous tubules in adults. Spermatocytogenesis functions to continue the lineage of stem cells by the production of uncommitted spermatogonia and produce committed spermatogonia, which result in production of spermatozoa after the end of duration of spermatogenesis for that species [1].
The three types of spermatogonia originally described include, the dust-like A spermatogonia, intermediate spermatogonia, and the crust-like or B spermatogonia. In the horse, five different sub- types of spermatogonia are characterized by either (a) small flattened nuclei (A_1); (b) large nuclei with apparently empty centers composed of euchromatin (A_2); (c) the largest nuclei with either one large nucleolus or large fragments of nucleoli (A_3); (d) large oval to spherical nuclei with large chromatin flakes (intermediate or B_1); or (e) small spherical nuclei with small chromatic flakes, as does the conventional B_2 spermatogonia, whose division yields preleptotene primary spermatocytes [1].

The spermatogonial number is dependent upon (a) the number of stem cells per testis; (b) the scheme of stem cell renewal; (c) the number of cell divisions from the stem cell to the primary spermatocyte and (d) the amount of degeneration of specific subtypes of spermatogonia.

3.1.1 Germ-cell degeneration during spermatogenesis

Germ-cell degeneration occurs throughout spermatogenesis. However, the greatest amount and impact occurs during spermatocytogenesis and meiosis and it may be due to chromosomal abnormalities, which may serve to limit the number of spermatogonial progeny or may be the result of a mechanism to eliminate cells containing abnormal chromosomes. However, simple selection to eliminate chromosomal abnormalities cannot explain the fact that, only certain types of spermatogonia usually undergo degeneration and the magnitude of degeneration is relatively constant for given types of A spermatogonia [6]. Though Germ cell degeneration plays pivotal role in quantitative and qualitative spermatogenesis, its mechanism and approaches to its prevention remains to be discovered [7].

3.2 Meiosis

Meiosis is the process by which genetic material is exchanged between homologous chromosomes and haploid spermatids are produced. Meiosis occurs only in germ cells. In males these cells are spermatocytes. Following the mitotic division of B_2 spermatogonia, preleptotene primary sprematocytes result. Following which primary spermatocytes undergo meiotic development to produce secondary spermatocyte [1].

During the first meiotic division, primary spermatocytes rapidly undergo nuclear-membrane dissolutions, metaphase (tetrada lignment), anaphase (separation of dyads of sister chromatids), telophase (complete separation of dyads). Secondary spermatocytes result from this division and contain a haploid number of duplicated chromosomes (i.e., XX or XY). These secondary spermatocytes undergo second meiotic division to form 4 Spermatids with 3 spermatids having X chromosome and 1 with Y chromosome [1].

Hence, one duplication of chromosomes followed by two divisions (one to separate paired homologous chromosomes and the second to separate sister chromatids) results in the production of haploid numbers of chromosomes in spermatids.

3.2.1 Intercellular bridges

Spermatocytes (like spermatogonia, spermatids, or residual bodies) are attached to one another by intercellular bridges. These bridges, between cells in the same developmental step, may function to facilitate: a) synchronous development or degeneration of similar germ cells, b) the production of committed spermatogonia, c) the differentiation of haploid spermatids, which now have only one sex chromosome and d) phagocytosis and digestion of residual bodies left behind at spermiation [6],

3.3 Spermiogenesis

Spermiogenesis is the morphologic differentiation of spermatids into spermatozoa. Spermatids, produced by the second meiotic division, differentiate from spherical cells with spherical nuclei to cells that have a streamlined head containing

penetrative enzymes and a condensed nucleus carrying the male genome and a tail necessary for cellular motility [1].

Development of spermatids has been divided into four phases: a) Golgi phase where in golgi complex produces membrane bound enzyme (acrosomal vesicles), b) Cap phase where acrosome forms cap over the nucleus, c) acrosomal phase where nucleus elongation and manchette (transient organelle found only in spermatid which gives rise to the tail region of the sperm) formation occurs and d) maturation phase where dissolution of manchette takes place and sperm is produced finally. These phases classification is based largely upon the development of the acrosome in the different spermatid types.

A recent development in the field of science has proposed that the sperms can be also developed from the pluripotent stem cells of the skin giving a hope to the infertile men to become a father [8].

3.3.1 Growth factors involved in spermatogenesis

SCF (Stem cell factor) is needed for mitosis and maintenance of differentiated type A spermatogonia, but not for proliferation of undifferentiated type A spermatogonia and it also acts as a factor involved in adhesion to Sertoli cells [9]. A Sertoli cell-derived growth factor, glial cell line derived neurotrophic factor (GDNF) [ID: T1-11], a member of the transforming growth factor-b superfamily appears to regulate proliferation and differentiation of uncommitted spermatogonia and SSCs in vitro and in vivo GDNF controls undifferentiated spermatogonia, with low levels causing depletion and high levels leading to increased numbers of spermatogonia [10]. The transcription factor Ets variant gene 5, ERM [ID: T1-32] is expressed in Sertoli cells and is required for SSC (spermatogonial stem cell) renewal [11]. The ectoplasmic specialization protein that is responsible for the development of the germ cells in the seminiferous tubules via the restructuring of adherens junctions that form between Sertoli cells and between Sertoli and germ cells can also be enlisted as a growth factor [12]. TNF α is known to have a role on the blood-testis barrier (BTB) via the effect on the extra cellular matrix [13]. Similarly other cytokines like IL 1, IL 6 (have role on spermatogenic cell differentiation and testicular steroidogenesis), leukaemia inhibitory factor, (transforming growth factor have role on testicular development), activin A, Nitric oxide etc. also appear to have a significant role in spermatogonia, spermatocytes and sertoli cells development. Since cytokines have a role in the spermatogenesis authors have also opined that the spermatogenesis process resembles chronic inflammatory process [14,15]. A recent discovery has also proposed that there is a dual role of CD147 where in it not only regulates the migration of spermatogonia via the induction MMP-2 production it also specifically regulates the survival/apoptosis of the spermatocytes but not the spermatogonia through p53 independent pathway [16].

3.3.2 Genes and proteins associated with spermatogonia and spermatocytes

Wide range of genes are reported to have a role in spermatogenesis which are conserved through evolution [17] and the study of this will help the future genetic investigators to focus on the infertility problems in a more rationalistic way [18,19] like cohension protein genes, synapsis and recombination genes, mismatch repair genes, post replication repair genes, DNA damage induced cell cycle check point genes and also proteins like heat shock and related proteins, cell cycle kinases,

protein important for chromatin organization which in turn is essential for the sperm production which is the recent target for the discovery of male contraceptives [20] and there are many other proteins whose exact function in the testis is yet to be discovered. Likewise there are up to 178 genes and proteins have been identified which has role in spermatogenesis directly or indirectly. They are involved in spermatogonial renewal and the meiotic process and shown to be essential for the spermatogenesis event [21]. Some of the important genes/proteins associated with spermatogonia and spermatocytes are presented in Table 1.

Table 1. Some of the important genes/proteins associated with spermatogonia and spermatocytes [21]

ID	Gene name	Exressed primarily by
T 1-1	Neurogenein 3 (NEURO 3)	Spermatogonia (undifferentiated)
T 1-2	v-kit Hardy-Zuckerman 4 feline sarcomaviral oncogenehomolog (receptor) (KIT)	Spermatogonia (differentiated type A)
T 1-4	Phosphoiositide-3-kinase,catalytic,alpha polypeptide (PIK3CA)	Spermatogonia
T 1-5	Phosphoiositide-3-kinase,catalytic,beta polypeptide (PIK3CB)	Spermatogonia
T 1-6	Phosphoiositide-3-kinase,catalytic,gamma polypeptide (PIK3CG)	Spermatogonia
T 1-7	Phosphoiositide-3-kinase,catalytic,delta polypeptide (PIK3CD)	Spermatogonia
T 1-8	Phosphoiositide-3-kinase, regulatory subunit 3 gamma (PIK3R3)	Spermatogonia
T 1-9	Phospholipase C, gamma 1 (PLCG 1)	Spermatogonia
T 1-10	V- src sarcoma (SRC)	Spermatogonia
T 1-12	v- Ha- ras Harvey rat sarcoma viral oncogene homolog (HRAS)	Spermatogonia
T 1-13	Mitogen activated protein kinase 3 (MAPK 3)	Spermatocytes
T 1-14	Mitogen activated protein kinase 1 (MAPK 1)	Spermatocytes
T 1-15	cAMP responsive element binding protein 1 (CREB 1)	Spermatogonia
T 1-16	Activating transcription factor (ATF 1)	Spermatogonia
T 1-17	cAMP responsive element modulator (CREM)	Spermatocytes and spermatids
T 1-19	Cyclin A1 (CCNA 1)	Spermatocytes
T 1-22	GDNF family receptor alpha (GFRA 1)	Spematocytes, Spermatids Sertoli and Leydig cells
T 1-23	Proliferating cell nuclear antigen (PCNA)	Spermatogonia Spermatocyte
T 1-37	Fibroblast growth factor 2 (FGF 2)	Spermatogonia Spermatocyte
T 1-42	Integrin alpha 6 (ITGA 6)	Spermatogonia
T 1-43	Integrin beta 1 (ITGB1)	Spermatogonia
T 1-44	CD 9 molecule (CD 9)	Spermatogonia

T 1-46	Epithelial cell adhesion molecule (EPCAM)	Spermatogonia
T 1-52	Deleted in azoospermia 4 (DAZ4)	Spermatogonia Spermatocyte
T 1-53	DAZ interactin protein 1 (DZIP 1)	Spermatogonia
T 1-68	Synaptonemal complex protein 2 (SYCP 2)	Spermatocytes
T 1-73	Testis expressed 12 (TEX 12)	Spermatocytes
T 1-75	Zinc finger protein 318 (ZNF318)	Spermatocytes
T 1-76	Structural maintenance of chromosomes 3 (SMC3)	Spermatocytes
T 1-82	RAD50 homolog (RAD50)	Spermatocytes
T 1-85	MRE 11 meiotic recombination 11 homolog (MRE11)	Spermatocytes
T 1-88	Topoisomerase (DNA) II alpha (TOP2A)	Spermatocytes
T 1-90	Tumor protein p53 (TP 53)	Spermatocytes
T 1-92	PSMC interactin protein (PSMC3IP)	Spermatocytes
T 1-94	Meiosis inhibitor 1 (MEI 1)	Spermatocytes
T 1-101	Replication protein A1 (RPA1)	Spermatocytes
T 1-109	Ubiquitin-conjugating enzyme E2A (UBE2A)	Spermatocytes
T 1-112	Polymerase eta (POLH)	Spermatocytes
T 1-116	Breast cancer 1,early onset (BRCA1)	Spermatocytes
T 1-119	Centromere protein E (CENPE)	Spermatocytes
T 1-126	Chromobox homolog 1 (CBX1)	Spermatocytes
T 1-132	Heat shock 70-k Da protein 2 (HSPA 2)	Spermatocytes
T 1-140	Solute carrier protein 2 (SLC2A1)	Spermatocytes
T 1-143	Aurora kinase B (AURKB)	Spermatocytes
T 1-155	Testis expressed gene 19.1 (FLJ 35767)	Spermatocytes
T 1-156	Transmembrane protein 30C (TMEM30C)	Spermatocytes
T 1-175	Protease,serine,21 (PRSS21)	Spermatocytes

3.3.3 Spermatogenic cycle

The spermatogenic cycle (cycle of the seminiferous tubular epithelium) is series of changes in a given region of seminiferous epithelium between two appearances of the same developmental stages. If we use spermiation as a refrence point, the cycle would be all the events that occur between two consecutive occasions of spermatozoan release from a given region of the seminiferous epithelium. To understand the cycle and development of germ cells throughout spermatogensis, it may be useful to compare spermatogenesis with a 4-year college model [1].

3.4 Comparison between College Model and Spermatogenesis

Using graduation as the reference point in the college model, the cycle would be all the events between two consecutive graduations. In both processes, the cycle length (time between two consecutive releases) is dictated by the frequency of cells or classes entering the process and is less than the duration of the entire process. While spermatozoa are released each 12.2 days in horses, the duration of spermatogenesis is 57 days. While graduation occurs yearly, college takes 4 years to complete .Hence, multiple generations of germ cells (spermatogonia, spermatocytes, and spermatids) or classes (freshmen, sophomores, juniors, and seniors) must occur simultaneously [22]. The amount of time between consecutive generations or classes is one cycle length. Furthermore, germ-cell degeneration in spermatogenesis and dropouts in college reduce the product yield (number of cells spermiated and number of students graduated, respectively).

In both cases, once the process starts, it continues at a defined rate such that cells (Golgi phase spermatids) or students (incoming freshmen) at a given developmental step are almost always associated with other cells (maturation-phase spermatids) or students (incoming sophomores, juniors, or seniors) at respective developmental steps. Differences between college model and spermatogenesis may help in further understanding of the dynamic process of spermatogenesis. Cell division magnifies the yield in spermatogenesis; however, no multiplying component occurs in college. Each committed spermatogonium entering spermatogenesis has a potential yield of 64 spermatozoa. In contrast, less than one student graduates for each student entering college [1].

In spermatogenesis, the frequency of product release is greater than in our college model. Resulting from college largely beginning only once a year in the fall, graduation for most students occurs only once a year, usually in late spring. In spermatogenesis, the production of newly committed spermatogonia is not synchronized among tubules and not simultaneous along the length of the same tubule. Therefore, somewhere in the testis, newly committed spermatogonia enter the process of spermatogenesis each second. This creates a continual release of spermatozoa into the lumen of seminiferous tubules. If college started each second instead of once in the fall, graduation would occur each second instead of once in the late spring. While this continual release seems wasteful, this assures that at least some male gametes are always available, even after exhaustive sexual activity, whenever female gametes are available for fertilization.

3.4.1 Cycle length of spermatogenesis

As mentioned earlier, the length of a cycle is the amount of time between consecutive releases of spermatozoa (spermiations) and is dictated by the frequency of newly committed spermatogonia entering the process.

The cycle lengths in days for various species are, 8.6 for the boar, 8.7 for the hamster, 8.9 for the mouse, 10.4 for the ram, 13.5 for the bull,13.6 for the beagle dog, 9.5 for the rhesus monkey, 12.2 for the horse12.9 for the rat. 16 for humans [23,24,25].

3.5 Duration of Spermatogenesis

The duration of spermatogenesis can only be approximated for any species due to the difficulty of determining the point at which committed A spermatogonia enter the process. In the absence of direct determination, it has been considered to be about 4.5 times the cycle length of a given species. This corresponds to four or five generations of germ cells found in each stage of the spermatogenic cycle [26]. Thus the duration of spermatogenesis can be approximated at 74 days in humans (16x4.5), 61 days in bulls and dogs (13.5x4.5), 60 days in rats(12.9x4.5).57 days in stallions.47 days in Ile de France rams, 39 days in boars (8.6x4.5) [16]. Recent studies have revealed that spermatogenic stages in the testis can be synchronized to three or four stages by the testicular injection of retinol in vitamin A-deficient rats. Syncronization apparently occurs by blocking the development of preleptotene primary spermatocytes by vitamin A deficiency and continuing their development when retinol is inject [27]. Recent studies have also shown that VAD (Vitamin A deficient diet) caused, in addition to an impairment of spermatogenesis at the

preleptotene spermatocyte step, a selective momentary arrest of surviving type A_1 spermatogonia at the G_2 phase of their cell cycle [28].

3.6 Stage of Spermatogenic Cycle

A stage in the cycle is defined as associations of four or five generations of germ cells formed in specific, chronological developmental steps, whose developmental age differs by a multiple of the cycle length plus a constant [7].

Stages of the cycle represent man-made divisions of naturally occurring and continuously changing cellular associations in a given region of the seminiferous tubules. Man-made divisions include: 14 stages in the rat, 8 stages in the bull, ram, boar, and horse, 6 stages in humans. Two types of classification of stages have been described and are based on the morphological changes of germ cells or the acrosomic development of spermatids in each stage [29].

3.7 Spermatogenic Wave

The spermatogenic wave is the spatial, sequential order of stages along the length of seminiferous tubules at any given time. The origin of the wave is unknown, but it results from synchronized but not simultaneous division of stem-cell spermatogonia in adjacent tubular segments along the length of the seminiferous tubule. The spermatogenic wave may function as a mechanism to assure a constant release of spermatozoa, reduce competition for hormones and metabolites used in a given stage, reduce tubular congestion that could be produced if spermiation occurred simultaneously along the entire length of the tubule, assure a constant flow of seminiferous tubular fluid to maintain the vehicle for spermatozoan transport and hormones needed by the epididymal epithelium, facilitate maturation of spermatozoa in the epididymis by a constant flow of spermatozoa and fluid from the testis. A constant release of spermatozoa is essential to maximize the opportunity for fertilization when female gametes only are available intermittently (cyclically). While changes in the spermatogenic cycle are seen over time in a given region of the tubule, the spermatogenic wave refers to the distribution of consecutive stages along the length of the seminiferous tubules at any given instance in time. The spermatogenic wave has been exploited to determine stage-specific changes in the seminiferous epithelium. Both FSH and androgens, essential hormones for spermatogenesis, seem to have different preferential stages in which they act. Also, there are stage-dependent differences in the production of androgen binding protein, maximal secretion of plasminogen activator, and of meiosis-inducing substance [30].

In the recent studies, BDADs (bis-[dichloroacetyl]-diamines) which are the compounds that can inhibit spermatogenesis via blocking the metabolism of vitamin A more specifically WIN 18,446 was used to manipulate the endogenous production of retinoic acid (RA) in the testis to further investigate the action of this compound on mammalian sperm production. The study resulted in blockage of spermatogonial differentiation and induced significant changes in the cycle of the seminiferous epithelium. WIN 18,446 treatments followed by injection of RA, had induced synchronous spermatogenesis in adulthood. The net result was pulsatile, rather than normal continuous, release of sperm from the seminiferous epithelium hence this

study described a novel technique that can enrich for specific germ cell populations within the testis, representing a valuable new tool for studying spermatogenesis [31].

3.7 Control of Spermatogenesis

3.7.1 Hormonal Influence

The two major cells involved in hormone production in the testis are the Leydig and Sertoli cells. These cells are stimulated by the gonadotrophins: Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) that are secreted by the anterior pituitary in response to Gonadotrophin Releasing Hormone (GnRH). Gonadotrophin releasing hormone is secreted by the hypothalamus and can be inhibited by increased concentrations of testosterone from the Leydig cells. The Leydig cells, in response to LH, convert cholesterol to the androgen testosterone. This conversion is initiated in the mitochondria by enzymatic cleavage of the cholesterol side chain to form pregnenolone. Pregnenolone is then transferred to the smooth endoplasmic reticulum where it is converted to testosterone through a series of intermediates steps [32].

In the male LH and testosterone are secreted in a pulsatile manner. The secretion of LH is followed by an increase in testosterone approximately an hour later. This release of LH is not only under hormonal control but also influenced by environmental stimuli. Visual and auditory sexual stimulation has been reported to cause an immediate release of a LH pulse in the bull [33]. Testosterone concentrations was reported in the bull at 0, 30 and 150 minutes following a GnRH challenge (100 µg im) to be of 7.26, 10.0 and 14.5 ng/ml, respectively [34] There is also reports of an increase in testosterone concentrations from 2 to 5 ng/ml before GnRH challenge (10 ng/kg of body weight IV) to 17 to 22 ng/ml after ~90 minutes [35].Also there has been use of deslorelin, an LH releasing hormone (LHRH) agonist, to induce an increase circulating testosterone from 2.4 to 11.8 ng/ml in the bull [36]. These studies prove the interaction of the hormones between the brain and the testis.

Testosterone and inhibin are transported to the brain and regulate the GnRH production from the hypothalamus and LH and FSH from the anterior pituitary by way of negative feedback [32]. Following bilateral castration, the negative feedback is eliminated resulting in a marked increase of both LH and FSH secretion [37]. These hormones all interact and regulate each other to keep the reproductive system functioning properly.

There are two major sources of cholesterol involved in the production of testicular steroids: cholesterol transported in the blood to the testis from elsewhere in the body; or from acetate, from the blood or formed from acetyl-coenzyme-A during glucose metabolism [38]. The main source of cholesterol utilized in steroid production is species specific as in the rat where ~40% of all cholesterol utilized in the testis originated from the plasma, but in the guinea pig only 13% is from plasma [38,39].

Testosterone is not stored within the Leydig cell; it is secreted into the interstitial fluid as it is synthesized. From here it is either i) taken up by the Sertoli cells and bound to androgen binding protein, which is then secreted by the Sertoli cell and transported through the seminiferous epithelium into the seminiferous tubule fluid and on into the epididymis ii) diffuses into the interstitial capillaries where it binds quickly to albumin for transport through the body, where it has wide ranging effects on all other tissues of the body. In target cells, this hormone passes through the plasma membranes by simple diffusion and bind to specific receptor proteins in the

nucleus. Hormone binding triggers changes in the conformation of the receptor proteins so that they become capable of interacting with specific regulatory sequences in DNA called hormone response elements (HREs), thus altering gene expression.

3.7.2 Other influences

Elevated temperature [40] or adversely cold [41] conditions are detrimental to sperrnatogenesis Radiation [42], drugs [43], vitamin A deficiency [44] limited diet [45], and toxic chemicals [46] are detrimental. Seasonal regression is seen in Rams and Stallions. Age also reduces number of germ cells ad daily sperm production in rabbits, rats, mice [1]. The recent study has shown the role of epigenetics in the control of spermatogenesis i.e., the obesity of the father is being discovered to induce hypomethylation of the insulin like growth factor (IGF 2) in the son [47].

3.7.3 Outlook

Spermiogenesis is a developmental process undergoing continuous differentiation to drive a diploid spermatogonium towards a haploid sperm cell [48]. The transformation from spermatogonium to spermatozoa is made possible by the stage-specific adaption of cytoskeleton and associated molecular motor proteins. KIFC1 is a C-terminal kinesin motor found to boast essential roles in acrosome biogenesis and nuclear reshaping during spermiogenesis in rat. KIFC1 works together with lamellar complex (LCx) and acroframosome (AFS) to drive acrosome formation and cellular transformation [48]. A combination of exogenous contractile forces generated by a stack of F-actin-containing hoops embracing the apical region of the elongating spermatid nucleus and an endogenous modulating mechanism dependent on the spermatid-containing acrosome-acroplaxome-manchette complex may play a cooperative role in the shaping of the spermatid head [49]. A tubulobulbar complex, formed by cytoplasmic processes protruding from the elongating spermatid head extending into the adjacent Sertoli cell, is located at the concave side of the spermatid head. The tubulobulbar complex might provide stabilizing conditions, together with the actin-afadin-nectin-2/nectin-3 adhesion unit, to enable sustained and balanced clutching exogenous forces applied during the elongation of the spermatid head [49]. Nuclear shaping is a critical event during sperm development as demonstrated by the incidence of male infertility associated with abnormal sperm head shaping [50]. Mouse and rat spermatids assemble in the subacrosomal space a cytoskeletal scaffold containing F-actin and Sak57, a keratin ortholog. The acroplaome nucleates an F-actin– keratin-containing assembly with the purpose of stabilizing and anchoring the developing acrosome during spermatid nuclear elongation. The acroplaxome may also provide a mechanical planar scaffold modulating external clutching forces generated by a stack of Sertoli cell F-actin–containing hoops encircling the elongating spermatid nucleus [50].

4. CONCLUSIONS

Spermatogenesis is a long process by which spermatozoa, found in the ejaculate are produced. Spermatogenesis involves mitosis to increase its yield, to reduce chromosome number and an unsurpassed example of cell differentiation in the production of the self propelled, penetrative enzyme-containing male-genome delivery system, namely, the spermatozoan / sperm. Thus a dynamic process with well organized cellular and molecular events results in release of large number spermatozoa with ability to continue life on this planet earth.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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