

Preface

This book, *Sertoli Cell Biology* vol. 2 is the third book in a series dedicated to understanding the Sertoli cells. Lonnie Russell and I edited the first book, entitled *The Sertoli Cell* and published by Cache River Press in 1993. This first book generated a lot of interest in our favorite cell, and we received very positive feedback on the utility of the information provided by many authors. After Lonnie's untimely death in 2001, the second book, entitled *Sertoli Cell Biology* and published in 2005 by Elsevier, was conceived and delivered. I co-edited this book along with Michael Skinner, and we dedicated it to Lonnie Russell. In *The Sertoli Cell*, Lonnie noted a linear increase in publications relating to Sertoli cells from the mid-1960s to the early 1990s. Hess and Franca, in *Sertoli Cell Biology*, continued this analysis and showed that publications relating to Sertoli cells rose from about 250 per year in 1990 to about 350 per year in 2003. A similar analysis shows that since 2003, the number of publications concerning Sertoli cells has risen to between 400 and 450 per year and has remained relatively constant through 2013. Thus, we can conclude that the scientific interest in these fascinating cells remains very strong.

In the preface to *The Sertoli Cell*, Lonnie and I mused over "dogmatic religious Sertologists" and the "germ cell worshipping cult." These two categorizations were an attempt to underscore the lack of information about how the Sertoli cells and the germ cells interacted and which one, if either, was most influential in directing the process. Working with Lonnie was a joy and a challenge. The joy came from his fun-loving yet warm embrace of science and life in general. The challenge for me was to keep up with his visionary approach to the biology of the testis.

In my opinion, the major advances in the field between 1993 and 2005 involved the ability to transplant spermatogonia in murine testes and establish long-term cultures of spermatogonia. These experiments revealed that much of germ cell development was cell autonomous and tipped the scale toward the germ cell worshipping cult. In addition, contributing to the disappointment of the dogmatic religious Sertologists was a list of important genes that had been genetically knocked out in Sertoli cells but still allowed germ cells to develop. Altogether, this information supported a notion that had been proposed in a review by Richard Sharpe in 1994 that the function of Sertoli cells was to allow the efficient but autonomous development of germ cells [1]. This idea was termed the "modified permissive view."

In an introductory chapter in *Sertoli Cell Biology*, I made two predictions about what would happen in the next 10 years: (i) *We would have nearly complete knowledge about genes expressed in Sertoli cells throughout development.* This first prediction was a safe one since the advent of array technologies was being applied to

the testis. We do have a lot more information about gene expression in the testis and in Sertoli cells than we had 10 years ago and even newer technologies such as RNAseq and RiboTag mice will complete this story. (ii) *We would have the capability to maintain most germ cells in culture and then transition them into haploid cells in vitro.* This second prediction seemed to be a safe one because of reports that some level of success had already been obtained. However, nearly 10 years later, the *in vitro* culture of stem cells and spermatogonia is well documented, but the progression through meiosis and the formation of spermatids has proven to be difficult. Thus far, the ultimate differentiation of cultured stem cells into functional gametes has not been demonstrated with any efficiency and reproducibility [2]. It appears that one of the barriers to spermatogenesis in culture is the requirement for Sertoli cells to provide both biochemical and structural components for this process. Score one for the dogmatic religious Sertologists.

Outside of any predictions, there were important advances in our understanding of Sertoli cells since 2005. Sertoli cell-specific deletion of the androgen receptor (SCARKO) by several groups showed that the initiation of meiosis in germ cells was independent of androgen action, but successful completion of meiosis and formation of round spermatids was dependent on functional androgen receptors in Sertoli cells (for review see Ref. [3]). It was also shown that a major defect in SCARKO mice involved components of the tight junctions. The role of microRNAs and noncoding RNAs in the testis and specifically in Sertoli cells became an area of interest for several research groups (for review see Refs. [4,5]). The role of the Sertoli cells in the initiation of meiosis via control of retinoic acid metabolism has become a research focus for other groups [6,7]. Prior to publication of the first book, *The Sertoli Cell*, Lonnie Russell published a model of a rat Sertoli cell that was assembled as a result of serial electron micrographs. This model at the time allowed the visualization of the complex structure of the Sertoli cell and was idolized by the dogmatic religious Sertologists [8–10]. In 2012, Smith and Braun, using more advanced technologies, described in detail how the tight junctions of the Sertoli cells open and close and allow the movement of the preleptotene spermatocytes from outside the blood–testis barrier to the interior [11]. This study underscored the complex structural interplay between the Sertoli cells and the germ cells.

I will not make any predictions for the next 10 years. It does appear that the differing views of the dogmatic religious Sertologists and the germ cell worshipping cult have been reconciled by what Lonnie Russell termed the “Presbyterian view.” This was a middle-of-the-road view that recognized the importance of the Sertoli cells in semiautonomous germ cell development. Much germ cell development does appear autonomous, but the completion of meiosis clearly requires something from Sertoli cells: Is it structural or a signaling event? As we approach 150 years since Enrico Sertoli described a new cell type and speculated that this cell was “linked to the production of spermatozoa,” we are still attempting to define this link.

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