Preface

Unwanted childlessness affects approximately one in six couples worldwide. Although the exact proportion of the predominant cause of the problem remains controversial, according to the World Health Organization (WHO), in nearly 40% of cases the cause can be attributed to the female, in 20% to the male, in 25% to both, and in 15% the cause remains unknown. Based on these figures, the incidence of male factor infertility in the general population is approximately 7%. The majority of these men, approximately 30%, experience irreversible idiopathic infertility and cannot father children without some form of medical intervention.

Male factor infertility, in addition, may be caused by testicular germ cell cancer, which is known to represent the most common cancer among young men, aged 15 to 35 years, in Western industrialized countries. The number of affected men has increased dramatically over the past 50 years. There is now growing evidence that human testicular germ cell cancer originates from fetal germ cells exhibiting an aberrant programme of gene expression, and tumour progression may be favoured by an aberrant Sertoli cell-germ cell communication.

Accepting the challenge of male factor infertility means having to improve our knowledge on the control mechanisms of testis-specific gene expression being involved in the regulation of Sertoli cell and germ cell differentiation. The Human Genome Project demonstrated the testis as one of the tissues of the body with the highest degree of tissue-specific gene expression, currently revealing approximately 23,000 testis expressed UniGenes in the human genome database. Although some of the transcripts represent tissue-specific alternatively spliced isoforms of somatic mRNAs, the majority are unique gene sequences.

Attention must be drawn to the Sertoli cell-germ cell communication, as it is already known that functional Sertoli cells are required for normal spermatogenic progression resulting in the continuous production of numerous fertile spermatozoa which, in turn, is necessary to maintain Sertoli cells in their functional differentiation state. Furthermore, the maturation of spermatogonial stem cells into fertile sperm requires stringent stage-specific sequential gene expression resulting in complete histone-to-protamine exchange followed by a stop of gene expression in haploid spermatids. As a consequence, haploid spermatids exhibit stage-specific but different expression of mRNAs and corresponding proteins due to temporal uncoupling of transcription and translation.

Unfortunately, in vitro, isolated male germ cells do not survive more than approximately 24 h. Co-culture systems with direct contact between germ cells and Sertoli cells, therefore, appear to be mandatory. To date, the most promising in vitro approach is the culture of whole seminiferous tubules displaying minimal disruption of the crucial Sertoli cell–germ cell contact. Targeted mutagenesis in the mouse, in addition, provides a powerful method for the study of control mechanisms that are involved in the regulation of gene expression in the testis and helps to gain new insights into the origins of male infertility. While knockout mice answer the question of what happens when a specific gene is absent, transgenic mice answer the question of which sequences are responsible for the manner in which genes are expressed. Recent developments in transplantation of spermatogonia, in addition, offer an exciting new technology for research in spermatogenesis. The combination of germ cell transplantation with culture and cryopreservation of spermatogonia opens new pathways for genetic engineering. Autologous transfer of spermatogonia might be used as an approach for fertility preservation in oncology patients.

The intention of the present monograph is to shed more light on the regulation of Sertoli cell and germ cell differentiation. Involving knockout and transgenic mouse models, we focus on (1) male factor infertility that might be related to altered maturation of Sertoli cells, (2) male factor infertility that might be due to incorrect histone-to-protamine exchange in haploid spermatids, and (3) progression of testicular germ cell cancer that might be favoured by an aberrant Sertoli cell–germ cell communication.

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