

The generation of spermatogonial stem cells and spermatogonia in mammals

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SUMMARY

Spermatogenesis is a complex series of cellular changes leading to the formation of haploid male gametes (spermatozoa) and includes mitotic, meiotic and post-meiotic phases. Spermatogonial stem cells (SSCs) are essential for the continuous lifelong production of spermatozoa. Spermatogenesis is initiated when SSC is triggered to undergo mitosis that gives rise to progenitors, which further differentiate into spermatogonia. In this review, we describe the origin of SSCs and other spermatogonia populations and summarize the knowledge concerning their markers. *Reproductive Biology 2012 12 1: 5-23.*

Key words: spermatogonial stem cell, spermatogonia, markers, seminiferous epithelium

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INTRODUCTION

Mammalian spermatogenesis is initiated by the conversion of gonocytes into spermatogonial stem cells (SSCs) that form the resident stem cells in the seminiferous epithelium. Spermatogenesis begins 5-7 days after birth in rodents and 10-13 years after birth in humans [21]. Spermatogonial stem cells provide the foundation for the continual production of spermatozoa throughout a male's lifetime [63] with millions of spermatozoa produced daily in adult testis.

ORIGIN OF THE SPERMATOGONIAL STEM CELL POOL

Progenitors of primordial germ cells (PGCs) are derived from the epiblast of blastocyst. Shortly before the epiblast separates into three germ layers: ectoderm, endoderm and mesoderm, the pluripotent cells of the epiblast differentiate into PGCs [15]. In mice, the first precursors of PGCs are morphologically identified on 6.0 to 6.5 days *post coitum* (dpc) in the proximal part of the epiblast. After that, the PGCs start to move, and approximately on 7.5-8.5 dpc they are observed at the base of allantois, which is located in the extraembryonic mesoderm [1, 15, 44, 65]. **Then, the PGCs are incorporated** into the epithelium of hindgut, and on 9.5 dpc they start to migrate into the dorsal mesentery which they reach on 10.5 dpc [15]. The mesoderm contributes to the development of the future aorta-gonads-mesonephros region (AGM region). Afterwards, PGCs migrate into the genital ridges lying on the dorsal body wall reaching them on 11.5 dpc [15, 44]. In humans, the migration of PGCs occurs between 5 to 8 week of gestation [1, 47].

PGCs can be distinguished by the expression of molecular markers. These early germ cells create small cluster of cells exhibiting high level of tissue non-specific alkaline phosphatase (TNAP) activity [44, 61]. The process of competence formation of these cells in murine epiblast depends on the expression of secreting bone morphogenetic proteins (BMPs: BMP4, BMP2 and BMP8b) that are released by the extraembryonic ectoderm [18, 35, 61, 62]. Recently, two new markers Fragilis (Ifitm3) and Stella (Dppa3 or

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