

Project Summary

Absence of spermatozoa in the seminal fluid is among the most common causes of male infertility. In many cases, the absence of sperm may be due to the inability of the testicles to provide the proper environment needed for its maturation. In such circumstances, the spermatogenesis process is interrupted and only immature germ cells can be located within the testicular tissue. An effective treatment for these patients is currently lacking. Maintaining immature germ cells *in vitro* in an environment, which is endowed with growth promoting factors may lead to enhancement of the maturation of these cells and to completion of spermatogenesis. The Sertoli cell is the only somatic cell in the testicular tissue that closely interacts with germ cells to create a favorable environment for spermatogenesis. It is considered as the nursing cell for the maturing spermatozoa as it secretes numerous proteins and other factors that influence germ cell division, differentiation and metabolism. On the other hand, follicle stimulating hormone and testosterone are needed to support germ cell differentiation through direct or indirect actions on Sertoli cells. They enhance Sertoli cell responses to insulin. Follicle stimulating hormone and insulin regulate the glucose metabolism and Sertoli cell lactate production, which is needed for normal spermiogenesis and spermatocyte RNA synthesis.

The objective of our study is to validate a new therapeutic modality using Sertoli-Germ cell co-cultures supplemented with recombinant follicle stimulating hormone (rFSH), testosterone (T) and insulin growth factor-I (IGF-I) in an attempt to bypass the interruption in the sperm maturation process. In order to achieve our aim, a sample from the testicular tissue will be taken from mutant mice characterized by maturation arrest. Immature germ cells (IGC) will be isolated from testicular tissue following mechanical shredding, and separated into homogenous populations using fluorescent activated cell sorting (FACS). IGC will be co-cultured with Sertoli cell media enriched with maturation promoting factors (rFSH, T, and IGF-I). The potential significance of our proposed study lies in the success of maturing sperm cells in an external environment. A co-culture system capable of completing spermiogenesis *in vitro* and the formation of mature sperm may constitute a therapeutic option for many patients currently considered infertile.

Key words: Male infertility, Maturation arrest, Sertoli cell, Germ cell, *in-vitro* culture