Fertility problems afflict millions men worldwide and this number is growing continuously. There are several reasons for male infertility ranging from anatomic defects, endocrinopathies and immunologic problems to exposures to environmental toxicants and stress factors. It became increasingly clear that spermatogenic dysfunctions play a significant role in the etiology of male infertility. However, still in many cases of infertility the underlying cause cannot be defined, due to not fully understanding a complicated process of spermatogenesis. Spermatogenesis (taking place in seminiferous epithelium of the testis) is a process in which germ cells undergo proliferation and differentiation to produce male gametes - spermatozoa. Key role in the control of spermatogenesis is assigned to testicular somatic cells, called Sertoli cells, which support germs cells structurally and functionally during the process of their differentiation. Sertoli cells communicate with adjacent germ cells i.e. by specialized cell-cell contacts. One type of such signaling in seminiferous epithelium is called juxtacrine communication. In juxtacrine interactions, protein from the inducing cell (ligand) interacts with the receptor of adjacent responding cell. It is well established that spermatogenesis is dependent upon the actions of hormones: testosterone produced in the testes and follitropin (FSH) secreted by the pituitary. The effects of both hormones are mediated by specific androgen and FSH receptors, which presence in seminiferous epithelium is restricted to Sertoli cells. Therefore, it is not surprising that Sertoli cells are considered as major mediators of hormone action in the control of spermatogenesis. However, to date the molecular pathways that link hormone-mediated signaling to juxtacrine communication in seminiferous epithelium are poorly understood.

Research hypothesis assumes that interplay between hormonal signaling and juxtacrine communication exists in seminiferous epithelium of the male gonad, and is important for the initiation and progress of spermatogenesis in rodents. The objective of the research project is to characterize the interactions between juxtacrine and hormonal (androgen and FSH) signaling in Sertoli cell, and their role in the regulation of spermatogenesis at the onset of puberty and in adult male.

To address this aim we will use animal models (pubertal and adult rats; adult bank vole males) as well as *in vitro* organ and cell cultures. First, we will check whether testosterone and FSH regulate juxtacrine communication in seminiferous epithelium. To that end production or action of these hormones will be blocked in pubertal and adult rats. Next, seasonally-breeding rodent, bank vole will be used as a natural model of FSH suppression. To gain insight into the intracellular mechanisms involved in the regulation of juxtacrine communication by the hormones, we will use *in vitro* organ and cell cultures. Finally, we will elucidate whether blockade of juxtacrine signaling may influence the ability of Sertoli cell to respond to hormonal signals.

The understanding of the mechanisms controlling spermatogenesis is still one of the main research challenges in the field of experimental andrology. The novelty of the project lies in searching for the links between hormone action and juxtacrine “dialogue” between the cells of seminiferous epithelium. In addition, the significance of these links for the initiation of spermatogenesis during puberty will be explored. The obtained results will be of general importance for the knowledge in the field of endocrinology and biology of reproduction. Any change in hormonal or direct signaling between the cells of the seminiferous tubule may result in impaired production of male gametes, leading to decreased fertility in males. Thus, the proposed studies may have a clinical relevance, potentially leading to improved andrology diagnostics.