



## AVAILABLE RESEARCH PROJECTS – MSc , PhD, PDF Laboratory of Jacques J. Tremblay

### Sertoli cells, Leydig cells, and male sex differentiation

Testicular development and function and male sex differentiation require the coordinated action of Sertoli and Leydig cells. Sertoli cells contribute to testicular development, the establishment of Leydig cells, and support germ cells during spermatogenesis. Leydig cells are the primary source of testosterone in men. There are two distinct populations of Leydig cells: the fetal population (FLC) and the adult population (ALC). FLCs are active during fetal life and produce androgens essential for fetal masculinization and male sexual differentiation. FLCs disappear after birth and are replaced by ALCs, which become active before puberty and remain functional throughout adult life. Testosterone produced by ALCs is essential for the onset of puberty, the initiation and maintenance of spermatogenesis, and the acquisition of male physical characteristics. Leydig cells, like Sertoli cells, are therefore essential for human health throughout life. Abnormal functioning of Sertoli or Leydig cells causes differences in sex development (DSD) and is also associated with numerous pathologies including undermasculinization, infertility, and hypogonadism. In addition, Leydig cells are particularly sensitive to many endocrine disruptors, but their mechanisms of action remain poorly understood.

Using a gene editing approach, we have recently generated novel transgenic mouse models that allow us to exclusively target either one of the Leydig cell populations constitutively or inducibly. Using these mouse models, it is now possible to specifically knock out a gene in FLCs and/or ALCs. These mice also allow us to selectively ablate functional ALCs in an adult testis while keeping Leydig stem cells intact, and to study the subsequent emergence of a new generation of ALCs.

Various projects are currently available including:

- Determine the role of various transcription factors (GATA4, GATA6, MEF2A/2C/2D, SF1, and others) in the differentiation and maintenance of Leydig cell identity and functions by gene knockout exclusively in FLC and/or ALC using our mouse models expressing iCre recombinase exclusively in Leydig cells;
- Determine the role of various transcription factors in testicular development, and in Sertoli cell differentiation and function by gene knockout using the Amh-Cre mouse line exclusively targeting Sertoli cells;
- Study the differentiation of a new generation of Leydig cells from resident Leydig stem cells in the adult testis;
- Determine the mechanism of action of endocrine disruptors in the regeneration of Leydig cells from resident stem cells.

These projects are available immediately for people wishing to complete a master's, doctorate, or postdoctoral degree.



In these projects, individuals will be required to work with mice (mandatory training is provided) and organ cultures. Under the supervision of a research professional, projects will involve mouse testis collection and preparation, thin sections, histology, direct fluorescence and immunofluorescence experiments. In addition, hormonal assays, gene expression (RNA-Seq and qRT -PCR), and fertility assays will be performed. Classical cell and molecular biology approaches (cell culture, protein-DNA interaction, promoter activity by luciferase assays, etc. ) will also be employed.

These projects are supported by research grants from the Canadian Institutes of Health Research (CIHR) and the Natural Sciences and Engineering Research Council of Canada (NSERC).

Interested candidates should have a background in biochemistry, microbiology, biology, biotechnology, or a related discipline. International applicants are welcome to apply, but priority will be given to Canadian citizens, permanent residents of Canada, and international students already in Canada. An affinity for working with laboratory animals is essential. Experience with current cell and molecular biology techniques is an asset. Demonstrate a strong motivation for biomedical research and have good communication skills (English, French).

To submit your application, please send a cover letter, a resume, and your transcripts by email to Jacques-J.Tremblay@crchudequebec.ulaval.ca.

