PhD Student position offer 2015-2018

Title: Deciphering the dynamics of proteins post-translational modifications during the epididymal maturation of spermatozoa

Supervisor: Charles Pineau, PhD
Co-supervisor: Mélanie Lagarrigue, PhD

Host Laboratory and team: Protim, Inserm Unit1085 – IRSET, Campus de Beaulieu CS2407, 35042 Rennes cedex France
www.protim.eu and www.irset.org

PhD Scholarship: Inserm-Brittany Council secured

PhD program context and objectives:
Male reproduction is a highly controlled process based on the coordinated expression of a set of regulated genes by testicular somatic and germ cells. Its purpose is the production of a functional gamete, the spermatozoon. Spermatozoa are not fertile or mobile upon their release by the testis. During sperm transit through the epididymis, most proteins on the surface of the cell will undergo numerous post-translational modifications (phosphorylation, S-nitrosylation, sumoylation, etc.). These ripening steps are not controlled exclusively by the gamete genome, but also rely on a set of spatial events, including the activity of epithelial cells in different areas of the epididymis and the presence of surrounding proteins in the seminal plasma. To date, there exist strong clinical data that establish a link between sperm quality and post-testicular maturation of the gamete. However, it is necessary to better understand the molecular basis underlying the steps in this maturation.

This project aims at understanding, in the context of male infertility, the biochemical mechanisms involved in the post-testicular maturation of sperm. Its primary objective is to identify in each region of the epididymis, specific mechanisms of gamete maturation whose alteration may be related to the fertilizing capacity of sperm and therefore with some male infertilities. Biological questions in this project are the following: (i) what are the major post-translational modifications altering sperm surface proteins during the gamete transit through the epididymis? (ii) what are the trade and processing of existing proteins between the epididymis, seminal plasma and sperm? (iii) is it possible to correlate the above events with specific regions of the epididymis and map their dynamics in situ? (iv) can we correlate the maturation defects of one or more proteins with the quality of the gamete?

Main steps of the PhD project:
The rat was chosen as the experimental model in the discovery phase. Targeted studies on candidate proteins will be conducted in both the rat and human. In a first step, post-translational modifications of sperm surface proteins at different regions of the epididymis will be characterized as exhaustively as possible by mass spectrometry. A priority focus will be given to phosphorylations. In a second step, the dynamic exchanges of proteins between cells of the endothelium epididymis, seminal plasma, and sperm will be mapped. This step is the very heart of the thesis project and is based on an original combination of approaches coupling large scale proteomics, integrative proteomics data mining and three-dimensional imaging by MALDI mass spectrometry. The final step of this work will be to correlate the maturation defect of one or more proteins of interest with an infertility phenotype (capacitation defects, impaired mobility).

Methodological and technical approaches considered:
This project will rely on the use of a combination of different approaches:
• Conventional techniques of cell biology and biochemistry;
• Advanced proteomics and peptidomics techniques;
• Integrative proteomics data mining;
• 3D MALDI imaging (a cutting-edge technology developed in the frame of the ‘3DMassomics’ European consortium);

The project is made possible through privileged access and training to state-of-the-art technologies available at the Protim Facility, a technological platform of the Biogenoest network.

Key words: Spermatogenesis, gamete maturation, post-translational modifications, epididymis, male infertility, proteomics, peptidomics, integrative proteomics, mass spectrometry, 3D MALDI imaging

Sought skills from the PhD applicant and acquired expertise during the PhD program:
A background in protein biochemistry and conceptual interest for proteomics and biological datamining, are desired. Showing an interest in reproductive biology and related diseases, particularly for male infertility, will be a plus. During the thesis, the candidate will be trained to acquire expertise in advanced proteomics, peptidomics, imaging mass spectrometry and knowledge on integrative proteomics concepts. She/he might also improve her/his skills in conventional techniques in cell biology and biochemistry. The applicant will also learn fundamental concepts on spermatogenesis, male infertilities and physiopathology of male reproduction.

A good level in English is mandatory. Knowledge of the French language is not required for working in the lab but will be useful for daily life. Free language courses in ‘French for Foreigners’ are offered at the University of Rennes 1.

Candidate selection:
Candidates with a master degree in Cellular biology or Biochemistry, obtained before September/October 2015, will be considered. Motivation, curiosity and desire to learn advanced techniques in proteomics and study male reproduction will be assessed for the selection of the candidate.

Candidates must postulate by e-mail to Charles Pineau (charles.pineau@inserm.fr) and send a cover letter, Curriculum vitae and two letters of recommendation before June 6, 2015. Selected candidates will be interviewed before the end of June 2015. The successful candidate will start in October 2015.
Recent publications of the host research team in the field of the PhD:


Reviews:


Supervisor biography:

Over the past thirty years, Charles Pineau has been working in the field of reproductive biology and is a renowned specialist of spermatogenesis. He has heavily invested in the development of proteomics, integrative genomics and bioinformatics technologies and his applying these to answer biological and clinically relevant problems in the field of testicular pathophysiology and reproductive toxicology. Dr Pineau currently serves as Research Director at IRSET (www.irset.org). He is also leading the Protim Facility (www.protim.eu). Dr Pineau’s team focuses on the deciphering of the testicular proteome in mammals with a priority given to the identification of novel germ cell proteins that play a key role in the normal and pathological spermatogenesis. His recent breakthrough work identifies novel testicular germ cell proteins using an approach that combines Shotgun proteomics and RNAseq analyses. Among other works, C. Pineau’s team presently uses germ cell-specific proteins markers identified by integrative proteomics for developing a diagnostic multiplex test of infertilities in men (FertichipTM).

Charles Pineau was President of the French Proteomics Society (SFEAP) from 2008 to 2011. He is also keenly interested in biotechnology and was the founder of Innova Proteomics, a Contract Research Organization (2003-2012). He serves as a recognized scientific expert in the field of male reproduction, proteomics and reproductive toxicology for national and international funding agencies. He is a scientific consultant for several pharmaceutical companies. Finally, among other activities, Charles Pineau is a council member of the Human Proteome Organization (HUPO) and vice-president of the Society for Reproductive Medicine (SMR).