Formulaire de stage (sur une page maximum)

Parcours M2 GGBS 2019-20

Laboratoire : CRTI/UMR1064 Intitulé/N° d’équipe : 2

Nom-Prénom de l’encadrant : JULLIEN Jerome

Courriel de l’encadrant : jj256@cam.ac.uk

Titre du stage : **Biochemical characterisation of postranslationally modified histone**  **retention in sperm.**

Résumé du projet proposé :

**Background**

The prime function of sperm is to deliver the paternal genome to the egg. However, the sperm also transmit to the embryos epigenetic informations regulating embryonic development. The precise nature, and mode of action, of such sperm derived epigenetic cues are not well defined. Elucidating the epigenetic mechanisms of sperm developmental programming is important because it will shed light on mechanisms involved in transgenerational transmission of acquired traits. Understanding how parental experience can influence development of the progeny has broad potential for improving human health.

To understand the epigenetic programming of sperm we focus on epigenetic marks associated with histones. In somatic cell, DNA is wrapped around histones containing multiple posttranslational modifications such as methylation, acetylation, ubiquitylation. These modifications are implicated in the regulation of transcription, replication, DNA repair etc…As such they have the potential to be the carrier of epigenetic informations transmitted by the sperm to the egg and could regulate these processes in embryos. During the formation of sperm, histones, and their associated modifications, are partially replaced by protamines and it is currently unclear how much histone based epigenetic information is retained by the sperm.

**Aims:**

The goal of this project is to provide a quantitative view of modified histone retention in the sperm of different animal species. This quantitation will be used to identify: (i) candidate histone mark for the developmental programming of sperm; (ii) the animal model exhibiting sperm epigenetic characteristics that are the most similar to that in human.

**Methods:**

A biochemical characterisation of sperm histones in five species will be carried out (human, bovine, equine, mouse, frog). Somatic cells will be used as a comparison. First, a large collection of antibodies against histones and modified histones will be used in quantitative Western Blot analysis (*i.e.* Li-coR). Second, the packaging of sperm chromatin with basic protein will be assessed by MNase digestion and capillary electrophoresis (*i.e.* TapeStation)

**Prospect**

Following up on this project we will obtain, by ChIP-seq analysis, a map of the distribution of the candidate programming histone marks in the genome of sperm in human and in the selected animal model. Functional involvement of this epigenetic marks in developmental programming will be tested in the animal model.