Formulaire de stage (sur une page maximum)

Parcours M2 GGBS 2019-20

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

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Titre du stage : **Epigenetic programming of the human male germ cell**

Résumé du projet proposé :

**Background**

We recently demonstrated that the sperm deliver to the eggs epigenetic informations necessary for embryos development. In frogs we have shown that such epigenetic programming of the sperm is in part based on the regulation of embryonic gene expression by sperm-derived modified histones. We now want to evaluate if such sperm modified histones could participate in gene expression regulation in human embryos. We hope that getting insight on sperm epigenetic programming in human could help elucidate the basis of some case of infertility.

**Aims**

The overall goal of this project is to carry out a correlative analysis between the epigenetic status of the sperm and the expression of genes in embryos derived from the same sperm. We specifically want to evaluate if genes with differential epigenetic marking between the sperm of different individuals are associated with differential gene expression in the corresponding embryos.

**Methods**

We will apply recently developed genome wide analysis protocols to pairs of sperm&embryos samples. First, we will carry out quantitative ChIP-seq analysis (Ice-ChIP, Grzybowski *et al.*, Mol Cell, 2015) of modified histones in sperm. This technique allows the identification of the genomic location where all sperm from one patient retain modified histones. The modified histones at these locations represent likely candidates for a role in epigenetic programming. We will aim to identify difference in these regions among the various patient analysed. Second, we will carry out single cell RNA-seq analysis in human embryos at the morula (when genes are first expressed) and blastocyst (when the first cell lineages have emerged) stages. In this analysis we will aim at distinguishing the expression of the genes from the maternal and paternal copy of the genome. In that way we can focus on potential regulation of the paternally derived gene by the paternally derived epigenetic features.

**Prospect**

The perspective of this work will be to extend our view of the epigenetic status of the sperm to additional features such as DNA methylation and small RNAs load. In that way we will get a comprehensive view of the sperm epigenome and its correlation with embryonic genes expression. We will then investigate if idiopathic case of male infertility are associated with defect in the epigenetic programming of sperm. Lastly we will evaluate whether paternal experience affect the epigenetic information retained in mature sperm.