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 : **Epigenome editing of a mature sperm**

Résumé du projet proposé :

**Background**

We and others have proposed that modified histones transmitted by the sperm to the egg are necessary for the regulation of genes in early embryos. However a formal demonstration that sperm derived modified histones are directly required for embryonic development is still missing. To fill that gap we have developed an assay in which an epigenetic mark, H2AK119ub, is fully erased from the chromatin of a mature sperm. We have shown that embryos derived from such epigenetically modified sperm developed abnormally and show defect in the expression of a small set of genes. These observations suggest that the presence of H2AK119ub in sperm chromatin is necessary for the regulation of the expression of a subset of gene in early embryogenesis.

**Aims**

To validate this model we will perform an experiment in which we will generate embryos from a mature sperm from which H2AK119ub was removed locally, from a subset of genes, rather than genome wide. In that way we will be able to directly test the requirement for H2AK119ub presence, at certain sperm genomic location, for the subsequent expression of gene in embryos.

**Methods**

We will use CRISPER dCas9 to target a chromatin modifier (USP21, able to remove H2AK119ub from chromatin) to certain genomic locations in mature sperm. Epigenome editing will be performed by incubating mature sperm in extract containing the epigenome editor. Various derivative of dcas9 mediated epigenome editing will be evaluated (direct fusion, suntag, or apatamer based). Epigenome editing will be assessed by ChIP-qPCR analysis of edited sperm chromatin.

**Prospect**

Embryos will be generated using H2AK119ub edited sperm. We will then score the embryonic development, as well as gene expression (RNA-seq), and transmission of sperm derived H2AK119ub (ChIP-seq) in early embryogenesis. This set of experiments will determine whether the presence of H2AK119ub around certain genes in sperm is necessary for subsequent embryonic development.