Formulaire de stage

Parcours M2 GGBS 2019-20

Laboratoire : **INSERM U1232 CRCINA**

Intitulé/N° d’équipe : **équipe 9 groupe « Apoptose, cancer & épigénétique »**

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Titre du stage :

**Study of cancer chemotherapy resistance by CRISPR/Cas9 genetic screening.**

Résumé du projet proposé :

Glioblastoma multiforme (GBM) is a very difficult tumor to treat and is a real clinical and scientific challenge. Following surgical excision when possible, most patients are treated by the Stupp protocol that combines radiotherapy and temozolomide (TMZ) therapy. Unfortunately, some patients do not respond to TMZ at first, or develop resistance several months later. The mechanisms involved in TMZ resistance include the activation of the MGMT gene by demethylation of its promoter. Once expressed, the MGMT protein is able to repair DNA damage caused by TMZ and thus allows GBM cells to survive. The epigenetic mechanisms allowing the emergence of resistance remain to this day a subject of exploration. Knowing its mechanisms could help to avoid its emergence, for example by proposing a co-treatment. We propose to use a powerful and innovative technology, high-throughput CRISPR Knock-Out screening (Shalem *et al.*, Science 2014, Wang *et al.*, Science 2014) and CRISPR-activation (Gilbert *et al.*, Cell 2014) to identify key actors in the emergence of TMZ resistance in cultured GBM cells. This approach will allow us to identify candidate genes that will be individually validated at a later stage *in vivo* and characterized functionally.

The Master student will be in charge of the CRISPR screen experiments and of the analysis of the sgRNA abundance from the Illumina sequencing data.