Internship proposition
One page max
M2 I3/0HNU 2024-25

Lab: CRCI2NA

team: Chromatin and Transcriptional Deregulation in Pediatric Bone Sarcoma (CHILD) – Team 9

Name and position of the supervisor: Steven GEORGES – Associate professor

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Candidate: Théo Bodet

Title of the internship: Epigenetic aspects of chemoresistance in alveolar rhabdomyosarcomas

Summary of the internship proposal:
Rhabdomyosarcoma (RMS) is a rare paediatric soft tissue cancer arising from striated muscle cells. There are various subtypes of RMS, including alveolar rhabdomyosarcoma (ARMS), which is often characterised by the presence of a PAX3/7-FOXO1 fusion protein. This protein acts as an oncogenic driver in these tumours. PAX3/7-FOXO1-positive ARMS have a poor prognosis, notably because of a very poor response to chemotherapy. It has recently been discovered that this protein is involved in the activation of super-enhancers (SE), genomic regulatory regions controlling key genes in cellular identity. This report suggests a link between expression of this protein, SE activity and resistance to treatment.

In this project, we hypothesise that the appearance of chemoresistance in rhabdomyosarcoma is due to the activation of super-enhancers that strongly regulate the expression of key genes. Identifying and then studying these genes would provide a better understanding of the resistance to treatment of these cancers and enable us to discover potential new therapeutic targets. Because of its role in the regulation of SEs, the PAX3-FOXO1 fusion protein could be essential in the adaptation of tumour cells to chemotherapy, thus explaining the poor response to treatment of PAX3/7-FOXO1-positive ARMS.

During this internship, involvement in chemoresistance of different genes regulated by SE (already identified by ChIP-seq) in our models will be investigated. The techniques used include cell biology (siRNA transfection, viability test, IC50 calculations), biochemistry (western blot), and *in ovo* model.

<u>Option(s) linked to the project:</u>

☐ Clinical Research Profile
☐ Data Analyst Profile
☐ Experimental Biology Profile