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

Lab: CRCI2NA

Team: 9 “CHILD”

Name and position of the supervisor: VERRECCHIA INSERM Research Director

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Candidate:

Title of the internship: Role of ionic channels in the development of Rhabdomyosarcoma

Summary of the internship proposal:

Scientific background: Rhabdomyosarcomas (RMS) are among the most common pediatric soft-tissue sarcomas. Despite advances in patient management, survival rates remain low, particularly for those with poor response to treatment or metastatic disease at diagnosis. Ion channels are structures that ensure the passage of ions across cell membranes. Aberrant expression of these channels has been shown in various tumor cell types, where their original functions are hijacked to promote tumor development. Our recent work has identified two ion channels whose expression is regulated by the RMS fusion protein PAX3FOXO1, playing a major role in the control of cell proliferation. In this context, we are continuing to investigate the role of these ion channels in the development of RMS.

Hypothesis and issues:

Our preliminary work has identified two ionic channels whose 1) expression is increased in RMS cells, 2) expression is associated with poor patient survival, and 3) whose expression regulates cell proliferation.

In this context, we investigate: 1) whether PAX3FOXO1 regulates the expression of these channels, 2) the role of these channels in controlling tumor cell proliferation in vitro or primary tumor growth in vivo, and 3) the role of these channels on the response to chemotherapy.

Main steps of the internship:

1) epigenetic and transcriptional regulation of these genes by PAX3FOXO1 (ChipSeq H3K27ac, CHIPSeqFli1, CHIPSeqPAX3...), 2) obtain stable clones of RMS cells expressing doxycycline-inducible shRNAs directed against the ionic conductances identified

-) effects of ionic conductance silencing on key functions in tumor development, such as cell proliferation, death and migration, and on response to chemotherapy in vitro and in vivo.

Option(s) linked to the project:

☐ Clinical Research Profile
☐ Data Analyst Profile
Experimental Biology Profile