UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Integrative Biology, Physiopathologies »

Proposal for a Master 2 internship – 2023-2024

Title: Characterization of immune infiltrate in PTEN$^{-/-}$ prostate cancers: role of LXR receptors in immune tumoral landscape.

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Summary:
The liver X receptors or LXR are nuclear receptors implicated in the regulation of genes involved in cholesterol synthesis, uptake and efflux. They are activated by oxysterols which are oxidized cholesterol derivates. Although their main functions rely to lipid metabolism, they also play a role in immune response. Indeed, it has been shown that mice deficient for LXRβ displayed splenomegaly due to proliferation of T cells. Although publications have reported that LXRs could exhibit an anti-tumoral role, there is no clear demonstration of their roles in prostate cancer. For that purpose, we have developed mouse models with local prostate cancers due to *Pten* loss, with and without LXR receptors. In these mice, we have shown that castration exacerbates immune cells infiltration in the tumours without LXR.
Based on that, we would like now to characterize the immune infiltrate and its modification according to each genotype and conditions. In a first part, the transcription modifications related to immune response will be studied *in silico* with available NGS data. In a second part, immunohistochemistry and immunofluorescence will be performed in tumours explants. In a third part, the findings will be assessed *in vitro* by functional studies on human tumour cell lines incubated with immune cells from mouse of different genotypes to characterize crosstalk between the immune and tumour cells.

Methodologies (key words) : bioinformatic analysis (R software, CibersortX, GSEA etc.), cell culture, molecular biology, *in vivo* experiments,, immunohistochemistry, immunofluorescence , flux cytometry.

Publications of the research group on the proposed topic (3 max.)

Bousset L, Septier A, Bunay J, Voisin A, Guiton R, Damon-Soubeyrant C, Renaud Y, De Haze A, Sapin V, Fogli A, Rambur A, De Joussineau C, Kocer A, Trousson A, Henry-Berger J, Höring M, Liebisch G, Matysik S, Lobaccaro JA, Morel L, Baron S. PLoS Biol. 2020 Dec 7;18(12):e3000948. doi: 10.1371/journal.pbio.3000948 Absence of nuclear receptors LXRs impairs immune response to androgen deprivation and leads to prostate neoplasia.
Bousset L, Rambur A, Fouache A, Bunay J, Morel L, Lobaccaro JA, Baron S, Trousson A, de Joussineau C. Int J Mol Sci. 2018 Aug 28;19(9):2545. doi: 10.3390/ijms19092545 New Insights in Prostate Cancer Development and Tumor Therapy: Modulation of Nuclear Receptors and the Specific Role of Liver X Receptors.