Sujet de stage de Master 2 - 2023

CARRIER Alice group: "Energetic metabolism and oxidative stress in cancer"
Host Lab: Cancer Research Center of Marseille (CRCM), team "Immunity & Cancer"

Project title: Impact of chemotherapeutic drugs on immunometabolism in pancreatic cancer
Type of rotation: M2 (6 months)
Supervisors: Alice Carrier and Scarlett Gallardo-Arriaga
email address: alice.carrier@inserm.fr

Pancreatic ductal adenocarcinoma (PDAC) is a deadly, late-diagnosing cancer that is resistant to current therapies, including immunotherapy (IT) [1]. This resistance is partly explained by tumor metabolic reprogramming and the presence of an immunosuppressive tumor microenvironment (TME) [2-4]. One mechanism of immunosuppression that remains to be explored is the metabolic reprogramming of immune cells (orienting their function and fate) in the TME [5,6]. Our laboratory has demonstrated that energy metabolism contributes to therapeutic resistance in PDAC [7,8], and is now exploring its role in immunosuppression to improve therapies. Our objectives are to evaluate the impact of chemotherapy and drugs targeting energy metabolism on immunometabolism and response to IT. The internship will involve analyzing immunometabolism in the tumor pancreas and spleen of treated and untreated PDAC (orthotopic syngeneic allograft model) mice, by flow cytometry using a combination of immune cell-specific antibodies and fluorescent metabolic probes.

References

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3. Reyes-Castellanos, G. *et al.* (2020) Mitochondrial Metabolism in PDAC: From Better Knowledge to New Targeting Strategies. *Biomedicines* 8, 270.
4. Falcomata, C. *et al.* (2023) Context-Specific Determinants of the Immunosuppressive Tumor Microenvironment in Pancreatic Cancer. *Cancer Discov* 13, 278-297.
5. Franco, F. *et al.* (2020) Metabolic and epigenetic regulation of T-cell exhaustion. *Nat Metab* 2, 1001-1012.
6. Leone, R.D. and Powell, J.D. (2020) Metabolism of immune cells in cancer. *Nat Rev Cancer* 20, 516-531.
7. Reyes-Castellanos, G. *et al.* (2023) Combining the antianginal drug perhexiline with chemotherapy induces complete pancreatic cancer regression in vivo. *iScience* 26, 106899.
8. Masoud, R. *et al.* (2020) Targeting Mitochondrial Complex I Overcomes Chemoresistance in High OXPHOS Pancreatic Cancer. *Cell Rep Med* 1, 100143.