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

Lab : CRCI^{2}NA
Team : TEAM 2 Nuclear Oncology Pr CHEREL Pr KRAEBER BODERE
Name and position of the supervisor : Edouard SAMARUT (MD), PH-U CHU de Nantes
Email of the supervisor : edouard.samarut@chu-nantes.fr
Candidate : M. LAFONT César
Title of the internship:
Validation of alpha therapy in meningiomas: preclinical evaluation of a radiolabeled somatostatin analogue with Actinium-225 (^{225}Ac) in a murine model of meningiomas (grades I or II) expressing somatostatin receptor type 2 (SSTR2).
Summary of the internship proposal:
Meningiomas represent 30% of intracranial tumors. The World Health Organization (WHO) classifies them into 3 grades which determines the therapeutic strategy. The standard treatment is surgical resection. External radiotherapy is indicated to treat remnants or recurrences inaccessible to surgery. Adjuvant chemotherapy and hormone therapy have not shown effectiveness so far. It turns out that some meningiomas, regardless of their grade, but more frequently in grades II or III, evade various therapeutic lines. The uncontrolled development of such tumors greatly impairs patients'quality of life and autonomy by progressively compressing adjacent neurological structures. Since the evolution is not explosive, the degradation in the patients'quality of life occurs over time. One of the main characteristics of meningiomas is the overexpression of SSTR2 which has allowed the application of a specific imaging technique using somatostatin analogs (PET-MR [68Ga]-DOTA-TOC).
In recent years, the treatment of refractory meningiomas has experienced a revival thanks to the advent of RIV. Indeed, based on the overexpression of SSTR2 by meningiomas therapy with beta-emitters (lutetium-177) coupled with somatostatin analogs has been considered. The use of RIV with beta emitters in meningiomas being recent, the results of ongoing clinical studies are not available, but it seems that achieving a tumor response is rare and most often we witness stabilization of the tumor disease. The use of alpha emitters is a promising approach to improve this targeted therapy. ^{225}Ac is primarily an alpha emitter.
Overall, current nuclear therapies using beta particles may not be optimal due to low linear energy transfer and a longer path in matter, which may affect healthy tissues. Conversely, alpha particles have a much higher linear energy transfer and a low penetration rate into adjacent tissues, potentially inducing more difficult-to-repair double-strand DNA lesions in tumor cells, while minimizing damage to healthy tissues. Preclinical studies have shown the advantage of alpha therapy in neuroendocrine tumors, and the goal would be to demonstrate it also for meningiomas.

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

Clinical Research Profile

Data Analyst Profile

Xxxxx<<>>à Experimental Biology Profile