Thesis project: "*Involvement of bystander and abscopal effects in targeted radionuclide therapy using alpha and Auger particles emitters*"

In Radioimmunotherapy (RIT), monoclonal antibodies directed cancer cells are labelled with radionuclides prior to their injection in patients for selective irradiation of tumour cells. It has been proposed that RIT acts through several mechanisms (1). The first class includes the direct effects of radiation that are related to the track through the cell of ionizing particles emitted by the targeted cell). The second class of effects concerns indirect effects including bystander and abscopal effects. Bystander effects correspond to release of signaling molecules (TNFα, IL33, IL6, TGFβ, IL8, ROS, RNS, DNA fragments) from irradiated cells towards neighboring non-irradiated cells or direct intercellular communication via gap junctions (e.g., *via* Ca^{2+} release). Abscopal effects correspond to biological effects measured at a distance from the irradiated tumor, and would be mediated by the immune system (2-6).
Objectives: The thesis project wants to investigate, at different scales (cells, tissues and whole organism), the ability of RIT using alpha, Auger particle emitters, to participate in the local tumour control through direct and indirect effects that involve tumour cells and their microenvironment.
Methodology will include secretome and multiplexe quantification analysis of secreted factors and anti-tumour immune response will be investigated by immunophenotyping the tumour microenvironment and lymphoid organs in two immunocompetent mice models. The final aim will be to optimise RIT by proposing efficient combinations (RIT/immunotherapy) or by determining the best therapeutic schedules (total dose, dose fractionation).

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