Subject 4**: Investigation of the anti-tumor efficacy of non-thermal plasma and ionizing Radiation in combination with a redox activatable theragnostic prodrug**

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Cancer is a leading cause of death worldwide and its incidence rate increases with the age of the population, the exposure to carcinogens and the modern lifestyle of the population. About two thirds of patients defeat their disease, and the combined action of surgery, radiotherapy and chemotherapy accounts for most cured cases. Alongside with these classical therapies, new therapies have emerged, such as anti-angiogenic therapy and immunotherapy. However, therapy resistance has been observed with every type of therapy that is available today, including poly-chemotherapy, radiotherapy, immunotherapy, and molecular targeted therapy. Accordingly, many new avenues have been explored in the last decades to battle this disease. One of them is the utilization of reactive oxygen species (ROS) as signalling and damaging agents [1]. ROS are not only generated as metabolic by-products but also in many physical therapies for medicine such as ionization radiation and photodynamic therapy [2, 3]. A recently emerging technology for ROS-based therapy is cold physical plasma (CAP) [4]. Electromagnetic radiation-triggered therapeutics are suffering from no translation into wide clinical applications for many years [5]. By the association of approaches from photoactivation and radiotherapy, G. Borg et coll. have recently developed theranostic prodrugs adapted for MRI imaging and activation into deep-tissues [6]. Gadolinium-modified azobenzene prodrugs (GdAzo) revealed efficient activation through cis-trans isomerization switch of the azobenzene moiety leading to an anti-tumor effect upon different types of ionizing radiations (photon, electron, proton). Mechanism investigations of this “radioswitch” activation pointed out the central role of the hydroxyl radicals (OH°) implying that multiple stimuli could be suitable for this activation concept as far as hydroxyl radicals are generated, which is the case during radiotherapy or CAP treatment [2, 7]. The project aims at investigating the anti-cancer efficacy of a combination of GdAzo prodrugs with either radiotherapy or plasma therapy. During the M2 internship, the candidate will essentially use human and mouse tumor cell lines in vitro, such as Panc-1, Capan-1, A549, HCT116, FaDu, SKOV-3, TC-1, and SV2 (pancreas, lung, colon, Head & Neck, ovarian) in order to establish the optimal conditions of the combined treatment to further use these conditions in vivo on xenograft mouse models. This project is interdisciplinary, involving researchers in biology (Institut Curie, UMR3347, UPSaclay), chemistry (Institut Curie, UMR9187, UPSaclay) and physic (LPGP, UMR8578, UPSaclay). The work will be performed at the Institut Curie (Orsay) and the LPGP (Orsay), the first one having various types of irradiators generating photons (XRad), protons, and electrons (ElectronFLASH 4000) and the second one a cold plasma device adapted for biomedical applications, essentially an He plasma jet [8].

Internship duration : 6 months
Your profile: M2 in Medical Physics, M2 SERP or any other M2 interfacing Physics/Chemistry/Biology/Medicine
Gratification : 591.51 €/month

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