université PARIS-SACLAY
FACULTÉ DE PHARMACIE

Graduate School: Health and Drug Research
Master 2 Pharmaceutical Technology and Biopharmacy

Company/laboratory/public institution: Sorbonne Université, laboratoire PHENIX

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Internship period: 20 January - 18 July 2025

Title of the project: Fusogenic liposomes encapsulating functionalized magnetic nanoparticles for a direct access to the cytosol.

1. *Description of the project*

Thanks to their interesting physicochemical properties, magnetic nanoparticles (MNP) are widely studied for biomedical applications[1]. Their ability to produce heat under an alternating magnetic field excitation, called magnetic hyperthermia, make them good candidates for cancer treatments[2]. They are also actively studied in cellular engineering, where they can remotely activate cellular processes[3]. However, these two applications of magnetic nanoparticles are limited by the way nanoparticles are internalized into cells. Indeed, this process called endocytosis, lead to the entrapment of the MNP inside small intracellular vesicles called endosomes. Because of their aggregation inside endosomes, the heat production from MNP is highly dampened[4], limiting their efficiency in killing cancer cells. It also prevents them from targeting and interacting with intracellular proteins or organelles.

In the PHENIX laboratory, we have been studying several strategies for MNP to avoid being trapped inside endosomes. The use of fusogenic liposomes, liposomes that are able to fuse with the cellular membrane to deliver its content directly inside the cytosol[5], is one of them. The goal of this M2 internship will be to study the encapsulation of core-shell γ-Fe_2O_3@SiO_2 nanoparticles inside fusogenic liposomes. The core-shell MNP will be synthesized so that they can diffuse in the cytosol (negatively charged, diameter smaller than 75 nm) and functionalized with peptides or antibodies in order to target intracellular mitochondria. Then the formation of fusogenic liposomes encapsulating these MNP will be thoroughly investigated, and the hybrid nano-objects will be fully characterized. The capacity of the liposomes to deliver the MNP into the cell cytosol will then be studied by fluorescence microscopy. Finally, their efficiency in killing cancer cells under an alternating magnetic field through magnetic hyperthermia will be determined.

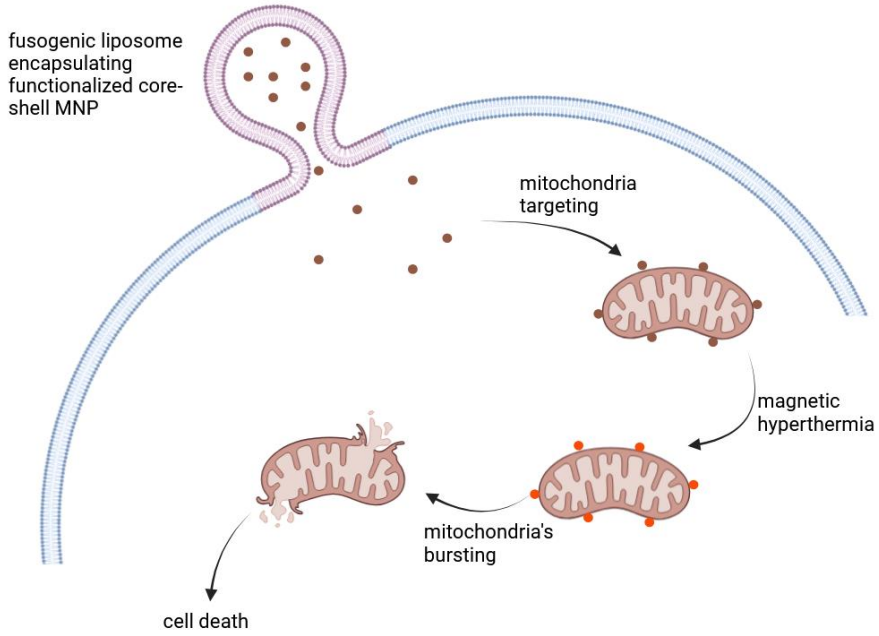

Figure 1. Scheme of the project

2. *Specific techniques or methods*

Liposomes synthesis by reverse phase evaporation.
Synthesis of magnetic nanoparticles made of an iron oxide core and a silica shell by sol-gel chemistry.
Bio-functionalization of MNP.
Dynamic light scattering, zetametry, transmission electron microscopy…
Cell culture, fluorescence and confocal microscopy.
Magnetic hyperthermia.

3. *References*

[1] Cardoso, V.F. et al., Adv. Healthc. Mater. 7, 1700845 (2018); [2] Beik, J. et al., J. Controlled Release 235, 205–221 (2016);[3] Monzel, C. et al., Chem. Sci. 8, 7330-7338 (2017) [4] Di Corato, R. et al., Biomaterials 35 (24), 6400–6411 (2014); [5] Chen, F. et al., RSC Adv. 2021, 11 (57), 35796-35805.