Sujet de stage M2 2023-24

Titre du projet : Magnetic controlled siRNA nanovectors by an alternating magnetic field for improved payload release

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Résumé du projet :
The research unit EA6295 "Nanomedicines and Nanoprobes" in Tours focuses on the development and the study of biocompatible nanosystems for therapeutic and/or diagnostic applications. The team has recently developed magnetic nanovectors of siRNA with the aim to deliver them via intravenous injection for targeted gene therapy in breast cancer. These targeted, stealth magnetic siRNA nanovectors are composed of a core of functionalized superparamagnetic iron oxide nanoparticles (SPION) loaded with siRNA and cationic polymers (NV-si) via electrostatic interactions.[1–3] The core of SPION is composed of magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3).[4] An external stimulus, such as an external magnetic field (MF), can allow to control these magnetic nanovectors. A static MF allows to target Triple Negative Breast Cancer (TNBC) cells and to favor NP accumulation in the tumor environment.[5,6] An alternating MF will induce magnetic particles oscillation that will lead to local heating and allow an accelerated payload release.[7,8] An accelerated payload release, once NV-si are delivered in the cell, allows to limit unwanted secondary effects and to potentiate their antitumor action. If the local heating attains temperatures above 42°C, cell death can also be induced due to a hyperthermia effect.[9] To investigate the influence of an external alternating magnetic field on the payload release of NV-si in TNBC cells, a novel equipment for generating alternating magnetic fields (magneTherm system from nanotherics) was acquired recently by the research team NMNS.
The master 2 project of 6 months consists in formulating NV-si, studying the responsiveness of NV-si to the alternating magnetic field and to optimize the MF parameters (magnetic field strength, frequency, exposure time) in order to control the payload release of NV-si in different conditions (NV-si in aqueous suspension, NV-si incubated in cell culture medium, NV-si incubated with cells). siRNA release will be analyzed using agarose gel electrophoresis or fluorescence spectroscopy, flow cytometry or confocal spectral imaging to follow fluorescent siRNA. The candidate will be integrated in a collaborative project entitled "Magnetic control for improved combination therapy in Triple Negative Breast Cancer (MAGCOT)", including three French teams and one Italian team, funded by the Institut National du Cancer (INCa, PLBIO22). A PhD and a post-doc student will help with the NV synthesis and cell culture experiments.

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