école doctorale **sciences pour l'ingénieur et microtechniques**

Thesis title: Development of microfluidic instrumented device to study and optimize interactions between nanoparticles and blood's proteins

Host Laboratory: FEMTO-ST institute, Micro-Nanosciences and systems (MN2S) department, 15B avenue des Montboucons 25000 Besançon and ICB institute, Nanosciences' Department, 9 avenue Alain Savary BP 47870, 21000 Dijon,.

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Speciality : Microsystems, microfluidics, nanoscience

Keywords: microfluidics, microdevices, nanoparticles, functionnalization

Job description:

Scientific context

Nanomedicine is a discipline, which has seen its interest growing during the last twenty years. Nanoparticles (NPs) with original physicochemical properties are interesting in medicine for therapy or diagnostic. However, unwanted protein adsorption happened on NPs once circulating in biological fluids decreasing their potential efficiency. This uncontrolled phenomenon is yet not well understood leading to a delay in the development and use of nanodrugs in medicine.

The main objective of this PhD will be to develop a device mimicking the blood stream to analyze, in flow NPs' physicochemical and biological behaviors and more specifically their interactions with plasmatic proteins.

This project will allow:

- To develop a microfluidic instrumented device to analyze in stream the behaviors of NPs in complex fluid like blood.
- To acquire knowledge and data about the role of the interactions between proteins and NPs
- To optimize synthesis parameters of NPs by functionalizing their surface with proteins of interest to obtain optimized nanodrugs for personalized nanomedical solutions.

This collaborative project will take place mainly at the MN2S department of FEMTO-ST with several months' missions at the ICB laboratory (Nanosciences department). Collaborations with University hospitals in Dijon and Besançon for blood analyses as well as with University of Geneva (Switzerland) for proteins analyses are planned during the PhD.

Description of the scientific project

Development of nanomedicine is slow down because of the lack of analyses mimicking living system. In fact, the vast majority of biological analyses is done in a static way and this approach does not allow a quick transposition of academic results to pharmaceutical industries. Furthermore, blood interactions of NPs irrevocably influence biological behaviors of nanohybrids developed for nanomedicine. Proteins/NPs interactions, called the protein corona, is a crucial parameter to understand and control in order to optimize NPs development.

At the beginning of the project, NPs functionalized with different chemistries will be synthesized. Iron oxide NPs could be chosen as their magnetic properties allowed their use in medical imaging (MRI) and for biological magnetic separation. Surface chemistries with different charges and molecules will be added to the iron oxide NPs. Then, these NPs will be tested in different fluids from the simplest (water) to the most complex (blood).

Developing an instrumented microfluidic device to analyze NPs in fluids' streams will allow obtaining better and more reliable understandings of the biological behaviors of these NPs. This microdevice will be link to different biochips in order to study the effect of different NPs' chemical surfaces on stability, agglomeration, proteins interactions and even hemostasis, inflammatory response and toxicity.

Thanks to the data and understanding obtained, NPs will then be functionalized with proteins of interest in order to obtain biomimetic nanohybrides with optimized biological behaviors (less toxicity, less hemostasis response…) also tested on the microdevice.

A forecast planning could be:

*1st year: D*evelopment of a prototype of microfluidic instrumented device.

2nd year: Study of NPs circulating in this microdevice in different fluids (from water to blood) and conditions (pH, temperature, velocity). Measurements of physicochemical parameters (dynamic size, agglomeration, proteins adsorbed) and optimization of the microfluidic prototype. Understanding of the role of these parameters on NPs biological behaviors.

3rd year: Measurements in stream of the NPs biological behaviors such as toxicity, inflammation and hemostasis. Functionalization of NPs with interesting proteins and characterizations of their new biological behaviors in the microfluidic device.

Bibliography:

Nanoscale Adv., 2021, 3, 1209–1229
Micromachines 2019, 8(10), 308

Applicant profil:

We are looking for a graduate student with a microtechnical background (microfluidics, microsystems) and with an interest in nanoscience. The candidate must have good communication skills to work collaboratively on a multidisciplinary subject between microsystems, nanoparticles, proteomics and medicine. Knowledge in chemistry and biology could be appreciated.
Applicants (for whom English is not the native language) should have a good level in English to read the scientific literature of the subjects, communicate at seminars and write publications.

Financing Institution: UBFC (EUR EIPHI (subject to financing))

Application deadline: 2023 September 30
Start of contract: 2023 December 1st

Applicants are invited to submit their application to the PhD supervisors.
Application must contain the following documents:

- CV
- Cover letter
- At least 1 reference letter
  Master's results (M1, M2)