Decoding intercellular communication mediated by extracellular vesicles in microreactor

Duration: 3 years; start date: October 1st 2017
Work place: FEMTO-ST Institute, Besançon, France
Skill area: Analytical Biochemistry
Deadline for applying: 27/09/2017

The PhD project

General context of the PhD. Thesis

Microparticles (MPs), small vesicles (50-1000 nm) from cell plasma membrane budding in response to different stimuli, play an important role in cell interactions, in physiological and pathological conditions. But, nowadays, the analysis of their composition, subpopulations and mode of action within the organism, is still a genuine challenge to which biologists and doctors are confronted. Communication between tumor cells and blood cells seems reciprocal, this is the cell inter-communication. Platelets seem to interact directly and indirectly with tumor and immune system, thus promoting the tumor progress. Numerous studies point out the role played by MPs on platelets in tumor inducible thrombosis. Investigate this flow of extracellular vesicles (EVs) by searching to better characterize/qualify/quantify the different MPs and their reciprocal effects will contribute to a better understanding of mechanisms involved in thrombosis and cancer.

It's of major interest to have investigation tools of these sub-micrometric biological objects that are very heterogeneous in size and covering 2 concentration decades, which make them difficult to analyze by conventional analytical instrumentations. Our recent development of a nanobioanalytical (NBA) platform combining different biophysical techniques (Surface Plasmon Resonance (SPR), Atomic Force Microscopy (AFM) and Mass Spectrometry (MS)), led us recently to a proof-of-concept of extracellular vesicles qualification; Obeid et al., 2017).

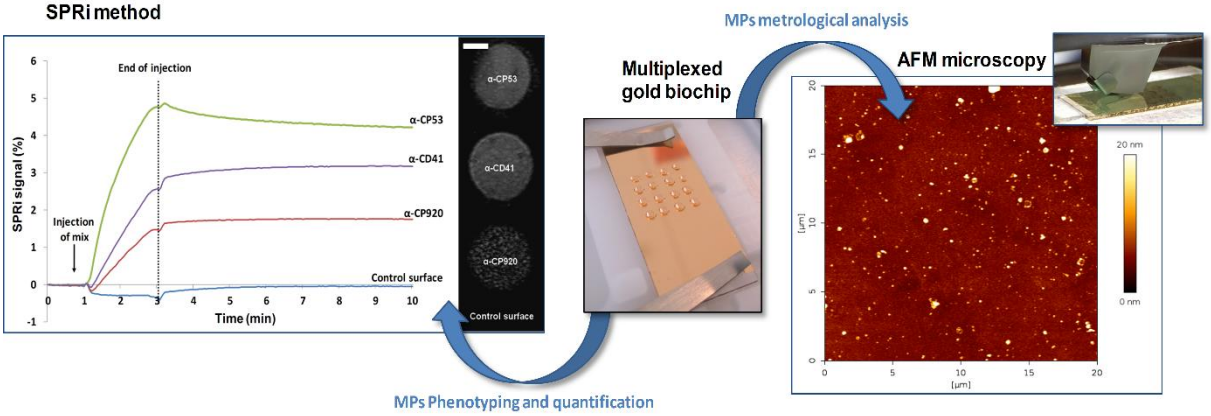

Figure Highlight: Multiplexed and label-free nanobioanalytical platform for phenotyping, sizing and counting blood microparticles (MPs) leading to potential discrimination of different extracellular vesicles in complex media.

Main objectives of the works

The present PhD project registers in a biological cancer context based on the analytical potential of the platform recently validated. This work consists in the exploration of EVs generated within a cell bioreactor involving tumor cell lines and platelets. This work will also support of an investigation program of a cell intercommunication mechanism for which our collaborator, Pr. T. Burnouf (Taipei Medical University, Taiwan), is an international expert.

The objectives is

1) to develop a micro-bioreactor for cell co-culture, notably of blood cells (platelets, lymphocytes) and a first model of tumor cells such as MCF-7 (breast cell line),

2) to qualify, by sampling, EVs sub-populations generated within the bioreactor with the nanobioanalytical platform.

3) to envision an interconnecting pathway between the bioreactor and the NBA platform in order to monitor, on line, the EVs' flow.

The overall project aims to provide dynamic information on EVs subpopulations generated during cell-cell crosstalk. Thus allowing a better understanding of induction mechanisms of their generation from activated cells and their role in dialog with tumor cells and their proliferation. This approach is unique at the international scale and results will bring data not available today to these complexity levels and nanometric dimensions of biological objects.

Surrounding of the PhD. thesis

The PhD thesis will be performed within the FEMTO-ST Institute in the research group BioMicroDevices of the Micro Nano Sciences and Systems department (MN2S), which works on the detection, characterization and quantification of biological objects in complex fluids for a better understanding of biological mechanisms related to patient pathologies. Activities are focused on: *i*) detection, quantification and possibly manipulation of biological targets of interest with the help of acoustic waves (study of acousto-fluidic interactions); *ii*) exploration of live cells, molecules and their interactions with environment: characterization platform by label-free technics; *iii*) integration of innovative and active materials in microdevices, development of specific biointerfaces; *iv*) microfluidic for microsystems development in liquid medium. In order to reach these objectives, the group relies on multidisciplinary skills: biochemistry, engineer sciences, nanobiosciences and on a unique technological potential.

Publications

- Obeid S, Ceroi A, Mourey G, Saas P, Elie-Caille C, Boireau W. Development of a NanoBioAnalytical platform for "on-chip" qualification and quantification of platelet-derived microparticles, 2017, Jul 15;93:250-259

- Remy-Martin F, El Osta M, Lucchi G, Zeggari R, Leblois T, Bellon S, Ducoroy P, Boireau W. Surface plasmon resonance imaging in arrays coupled with mass spectrometry (SUPRA-MS): proof of concept of on-chip characterization of a potential breast cancer marker in human plasma. Anal Bioanal Chem. 2012 Aug;404(2):423-32.

Applicant profile

We are seeking a candidate with a profile in analytical biochemistry. An experience in cellular biology would be a plus. Knowledge and interest in microtechnology and/or nanosciences are welcome.

Advisory team of the PhD

Dr Wilfrid BOIREAU: senior researcher, CNRS
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http://teams.femto-st.fr/BioMicroDevices/fr
http://www.femto-st.fr/fr/Departements-de-recherche/MN2S/Presentation/
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Application

Please send your application documents to the supervisors including a detailed CV, motivation letter dedicated to the proposed position, marks and ranks you obtained during your master degree or engineering school and at least one contact person (typically your supervisor for a training period, master thesis or responsible of your master diploma).