Université Lille Nord de France

Ecole doctorale régionale Sciences Pour l'Ingénieur
Lille Nord-de-France - 072

Titre Thèse	Biomarkers detection of neurodegenerative diseases by mass spectrometry		
(Co)-Directeur	Yannick Coffinier	E-mail : yannick.coffinier@univ-lille.fr	
(Co)-Directeur		E-mail :	
Laboratoire	IEMN	Web : Web : https://www.iemn.fr	
Equipe	Nanobiointerfaces	Web :	
	Contrat Doctoral Etablissement	Lille 1X UVHC ☐ ECL ☐ ISEN ☐	
Financement prévu	Président-Région ☐	Région – Autre x Préciser : ANR	
Acquis ☐	Président- Autre ☐ Préciser	DGA – Autre ☐ Préciser	
	Contrat de recherche ☐ Type ANR	Autre ☐	

Résumé du sujet :

Over the past decade, cell behavior on arrays of vertical nanostructures has been the focus of numerous studies aimed at evaluating these as tools for manipulating and probing single cells. Such arrays of high-aspect-ratio objects have proven to be largely compatible with mammalian cells and are currently being established as platforms for a wide variety of advanced applications. Among these nanoobjects, Nanoneedles (NNs) have rapidly emerged as a tool to interact with the intracellular environment of a large number of cells simultaneously, with limited perturbation of their physiological processes. This interaction provides characteristic advantages for minimally invasive cell and molecular biology investigations, as well as progression of biomedical translation of regenerative and precision medicine approaches. A quick string of several successful proofs of principles have established NNs' potential to efficiently deliver impermeant molecules, nanoparticles directly to the cell cytosol, and to sense the intracellular milieu across biological systems ranging from cells in culture to living organisms.

Nanoneedles are defined as nanomaterials presenting high aspect ratio object those belong to two main classes: single needles, externally manipulated to contact cells and tissues (near field microscope (AFM), Micromanipulator) or arrays of vertical high aspect ratio nanostructures supported on a substrate. This former encompasses a wide variety of nanostructures including nanowires, nanopillars, porous nanocones, nanotubes, and nanostraws. Variety of materials/dimension/shape make each type of NNs having different properties that befit specific sensing needs, that is to say various applications in mechanobiology, nanoelectrophysiology, optogenetic, nanophotonic and transfection/vectorization (drug delivery) as well.

Probing biomolecules from the intracellular compartment of living cells is one of the current challenge especially to detect specific biomarkers (metabolites, drugs, protein or peptide synthesis expression levels, ions, ...).

This project proposes the development of very innovative nanotool based on mass spectrometry detection to assess intracellular enzymatic activity and the detection of specific targets. Indeed, mass spectrometry (MS) is widely accepted as a 'gold-standard' method for identifying chemicals or biological products. To overcome inherent drawbacks of MALDI-MS (high background in the low molecular masses, non-uniform analytes deposition, and low sensitivity for small compounds...), micro- and nanostructured surfaces were developed and used as matrix-free LDI-MS methods (also called SALDI-MS). Based on this expertise, we aim at applying SALDI-MS nanoneedles based technology to perform very efficiently *in cellulo* biomarkers monitoring allowing to decipher *in situ* enzymatic activities.

Thus, we propose a new, minimally invasive nanoneedle based method for monitoring living cells by leveraging the ability of nanoneedle to access the cell cytoplasm and to get new insights in the understanding of biochemical processes occurring within cells. As a model study, we will mainly focus in this project on tauopathies biomarkers' detection (phosphopeptides and hyperphosphorylated Tau isoforms) and endogenous enzyme activity (kinase). Tau (tubulin-associated unit) is a neuronal protein regulated by phosphorylation/dephosphorylation events involved in the Alzheimer's disease propagation.

The project presented here is very interdisciplinary as it sits between system chemistry, biochemistry, nanotechnology and analytical sciences. We are thus looking for candidate with both strong academic records and a strong interest to work on such a challenging project. The candidate must have expertise in biochemistry/chemistry and an interest in micro-nanofabrication. A good level of English is also recommended.