PROPOSITION DE SUJET DE THESE DE DOCTORAT

Electrospray mass spectrometry for droplet-based microfluidics, application to redoxomics

Laboratory: Spectrométrie de Masse Biologique et Protéomique (SMBP USR CNRS 3149) - ESPCI ParisTech 75005 Paris

Direction : Dr Joelle VINH, joelle.vinh@espci.fr

Ecole doctorale: Chimie physique et chimie analytique de Paris Centre (ED 388)

Subject:

We have been working in quantitative proteomics and redoxomics. Redox-regulated proteins play fundamentally important roles not only during the defense of organisms against oxidative stress conditions but also as targets of cellular signaling events. Perturbations in redox homeostasis are associated with many different diseased conditions, including cancer, type2 diabetes, cardiovascular and neurodegenerative diseases, and aging. We want to enable confined sample processing with targeted MS analysis on oxidized proteins. We need to miniaturized our workflow in order to enable our strategy to succeed with very low amount of material such as clinical samples.

The goal of the present project is to interface droplet microfluidics with nanoESI MS with simple liquid/liquid interface using electrocoalescence with minimal diffusion of the compounds to enable automated MS screening in discovery (no a priori) or in targeted mode. The system will be sufficiently sensitive to allow analysis of the contents of single pL-nL droplets containing as little as 10-100 amol in targeted detection or 0.1-1 fmol in discovery untargeted analysis with a minimal throughput of 10Hz. The key feature of this system will be to design, test and fabricate a microfluidic device that can remove the oil phase using electrocoalescence and spacer droplets as close to the nano ESI nozzle as possible (0.8-1 cm for regular glass capillaries, but miniaturized nozzles have been connected within distances of a few mm). The system will be designed in order to minimize the Taylor-Aris dispersion and the dead volume to avoid unnecessary dilution of the droplet contents.

Several points will be studied:

- Optimization of the dimensions of the system
- Hydrophilic surface treatment of the aqueous channel
- Quasi planar solvent front by electroosmotic flow
- Spacer droplets to limit cross-contamination

Fellowship type: 3-years full time academic grant supported by the Labex Institut Pierre Gilles de Gennes (IPGG), to be started before the end of 2015

To apply: send by email CV + cover letter + recommendation letter **before 15/05/2015 to** Joelle VINH

Expected profile: Master M2 with a dominant in analytical chemistry, or analytical instrumentation. A (theoretical) knowledge in mass spectrometry and miniaturized separation techniques is expected. The candidates should be interested in analytical chemistry applied to biology since this doctoral project is at the interface of the two domains. He/she should have validated his/her first semester in M2 in chemistry or biochemistry, or his/her engineering degree (if possible with a final transcript >14/20) in April 2015, or a full M2 master degree in 2014.

Références

Majzoub K, et al. RACK1 controls IRES-mediated translation of viruses. Cell. 2014 Nov 20;159(5):1086-95.

Monet-Leprêtre M, et al A. Abnormal recruitment of extracellular matrix proteins by excess Notch3ECD : a new pathomechanism in CADASIL. *Brain*. 2013 ;136(Pt 6):1830-45..

Fukuyama H, et al. On-bead tryptic proteolysis : An attractive procedure for LC-MS/MS analysis of the Drosophila caspase 8 protein complex during immune response against bacteria. *J Proteomics*. 2012 ;75(15):4610-9.

Chiappetta, G et al. Proteome screens for Cys residues oxidation: the redoxome. *Methods Enzymol* 2010;473:199-216.