

## Proposition de sujet de thèse 2017

Marquage au sélénium et couplage électrophorèse capillaire/ICP-MS: une nouvelle alternative en pharmacologie.

Selenium labeling and hyphenated capillary electrophoresis/ICP-MS: a new alternative in pharmacology

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For several years, the recognition of the therapeutic activity of peptides has gained importance, offering new prospects in pharmaceutical development. Measurement of the affinity of the peptide for its target is a central step in the development of a drug. This is generally measured by radioactivity in competitive binding experiments between the peptide and a reference ligand, using labeled compounds. However, the use of radioactivity is not without constraints, handling and storage of these marked compounds in particular, which greatly limits the work at high throughput.

Within the framework of the ANR MTaQ, our objective is to develop an alternative method of detection and quantification by ICP / MS of molecules of therapeutic interest in cell cultures. To compete with radioactivity, this method must be fast, sensitive, selective, and allow to work with very small volumes of samples.

For this purpose, peptides have been chemically labeled by introducing selenium in order to improve detection and quantification thresholds. Preliminary results have shown that the coupling between capillary electrophoresis and ICP / MS makes it possible to separate the different compounds and to specifically detect selenium.

However, access to very low concentrations requires improvement of the detection limits by a preconcentration step. Different options will be considered. In particular, the benefits of an in-line preconcentration by solid phase extraction will be studied.

The candidate will be in charge of developing of rapid separative methods of complex mixtures leading to a quantitative detection of selenium labelled peptides in complex solutions containing many salts, organic compounds and proteins. For that purpose, he (she) will draw on the expertise of TECHSEP team that has developed for several years skills in designing, functionalizing and characterizing composite monolithic capillary columns enabling both enrichment of the samples and high resolution separations.

Once implemented, this CE / ICP-MS coupling will in particular be validated by the quantification of selenium derivatives of vasopressin and the determination of their affinity for the V1A receptor

*Mots-clés : Analyse de biomolécules – Développement de nouvelles méthodes analytiques*