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Chemical labeling associated to mass spectrometry as a powerful tool for peptide detection and quantification in biology

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Mass spectrometry represents a method of choice to identify and characterize peptides and proteins present in complex biological mixtures at low concentrations. In the attempt to develop potent MS methodologies, we work on the design and synthesis of chemical tags able to increase detection sensitivity and specificity through direct MS detection and/or directed fragmentation.

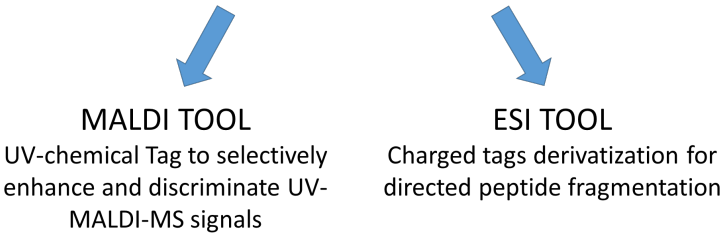

Figure 1

MALDI is well-known to provide very sensitive detection but not commonly used for quantitative measurements. On one hand, we aim at developing a novel approach that relies on the joint use of MALDI mass spectrometry and original labeling chemistries designed to specifically enhance the ionization of the tagged molecules. MALDI is well-known to provide very sensitive detection but not commonly used for quantitative measurements. Using MALDI for such purposes is challenging and has been successfully applied to track peptides at low concentrations in various media[1-3].

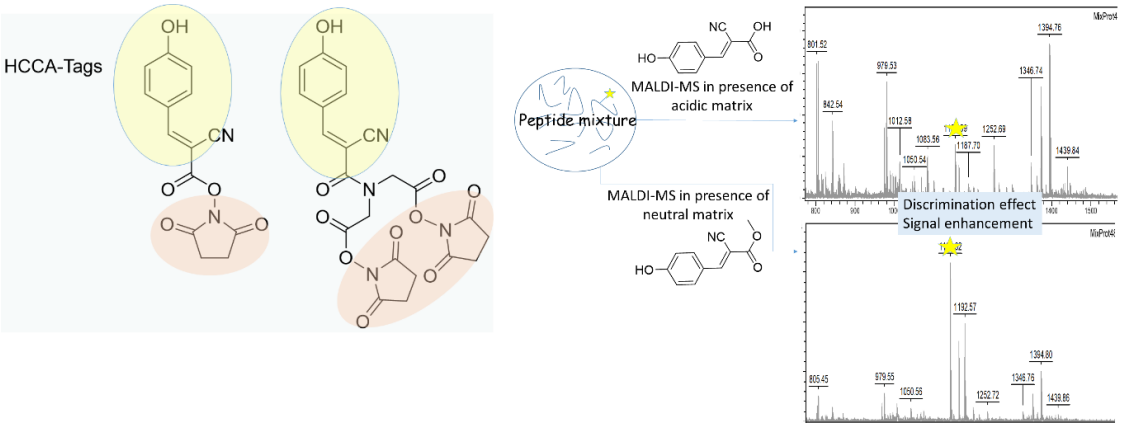

Figure 2

We developed a methodology associating HCCA (α-cyano-4-hydroxycinnamic acyl)-targeted peptide to be analyzed by MALDI-MS in a matrix such as HCCE (α-cyano-4-hydroxycinnamic methyl ester). This original approach allowed to selectively enhance and discriminate the MALDI-MS signals of targeted peptides. This concept was successfully applied to protein structure issues illustrated by the cross-linking of a model protein and peptide quantification for pharmacological studies of receptor/ligand systems[4,5].

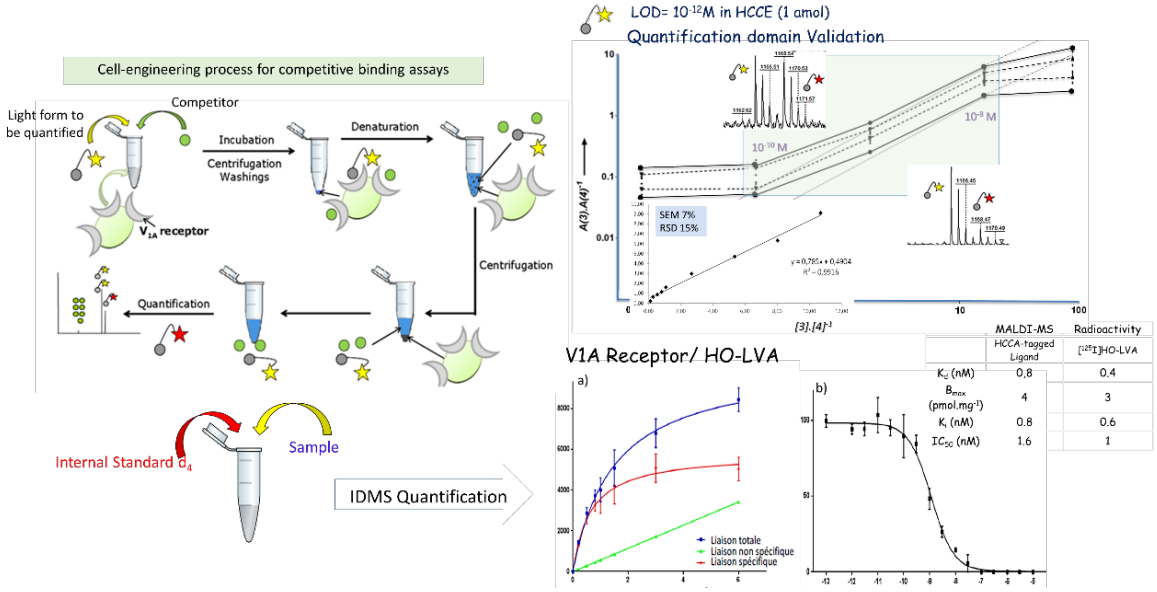

Figure 3

On the other hand, we focused on N-terminal positively charged peptide derivatization as efficient agents for directed ESI-MS fragmentation. We explored labeling by pyridinium-based molecules, well known in chemistry literature, generally for enantio-separation, pharmaceutical or biochemical analysis, showing a great tendency to meet some of the desired requirements to investigate the field of ESI-MS qualitative and quantitative analysis of biomolecules like proteins or peptides.

Two competing dissociation mechanisms can be suggested:

- Formation of α-ketene.
- Formation of an oxazolone. («a1 fragment analog »)

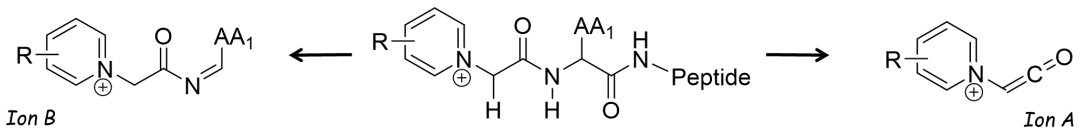

Figure 4

This technology should have a great impact in biosciences, in particular in research laboratories dealing with pharmacology. We will give you an account on the development of these methodologies.

References

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