DOCTORATS INDUSTRIALS

EL PLA DE DOCTORATS INDUSTRIALS

PROJECTE DE DOCTORAT INDUSTRIAL EXPEDIENT 2014 DI 033

DADES DE L'EMPRESA I DE L'ENTORN ACADÈMIC

Títol del projecte

Unknown structure elucidation. A Mass Spectrometry approach for small and peptide molecules

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BREU DESCRIPCIÓ DEL PROJECTE DE RECERCA

The structure elucidation of unknown substances is an open field that is relevant for the discovery not only of new drugs but also of potential biomarkers. This research project focus primary in a new algorithm for structure elucidation of small molecules based on high resolution mass spectrometry data in order to generate a set of potential solutions that later could be evaluate/ranked using nuclear magnetic resonance. The second part of the project is to extend this concept to the field of small peptides and new group of potential therapeutics.

The project will deal with new algorithms for the fragmentation and re-construction of the molecules comparing the extracted MS and MS2 or MSE data from targeted and non targeted mass spectrometry data. For the first part of the project the initial step in the process would be to perform an analysis a single molecule and the fragments derived from a single molecule (the fragment set to use contains the answer), them the analysis will be done with a set of fragments which contain for sure the ones from the molecule under consideration and the final step is the execution will consider a very large database (millions of fragments) and without adding the known ones. Finally, when the algorithm has been properly validated through these steps, it will be tested in different fields of application: metabolite identification of xenobiotics, chemical reaction by products, untargeted lipidomics and natural products structural elucidation. In order to perform this final application analysis a collaboration with Molecular Discovery Ltd, a UK based company and Perugia University in Italy has been already established.

For the second part of the project, several incubations of commercial cyclic and lineal peptides will be done in different media, for example in amidases. The previously developed algorithms will be used to determine the structure of the metabolites in each of the incubations and based on these peptide structures an analysis will be done on which are the peptide structure requirements for an amide bond to be cleavage by each of the amidades tested. This analysis will consider structure based modeling like docking or structure based virtual screening as well as the possibility to establish QSAR models with the characteristic of the aminoacid (natural or non-natural) that compose the metabolite. The outcome of the research will be a set of rules for each amidase used that will indicate the likelihood of a bond to be cleavage by that specific enzyme. Moreover, it should also consider the opposite predictive direction, if a certain bond is broken and identified by Mass Spectrometry data analysis in a specific media incubation, the system should be able to indicated which is the most likely enzyme to produce that reaction.