CEA, Institut de Génomique, Génoscope,
CNRS-UMR8030, Université d'Evry

Postdoctoral position (12 months)

Deadline for application: June 2021
Start date: from June-September 2021

Description

A postdoctoral position is now available in the Laboratory of Genomics and Biochemistry of Metabolism ("Laboratoire de Génomique et Biochimie du Métabolisme"), at Genoscope (Evry, France) in the framework of the collaborative ANR project Chiramics. The project's consortium includes Sorbonne University-l'IPCM Institut Parisien de Chime Moléculaire, CEA-Saclay SPI-LEMM and CEA-Evry Genoscope-LGBM. Chiramics project aims at developing a fast and sensitive chiral analysis method using mass spectrometry and its further application in metabolomics.

Indeed, the main challenge of metabolomics consists in characterizing the small size compounds (metabolites) that constitute the metabolome. At Genoscope, we have extensively worked on the identification of novel metabolites in uncharacterized bacterial metabolic pathways [1, 2]. Stereochemistry determination is considered as the highest level of molecular identification [3]. In the case of complex mixtures, mass spectrometry (MS) can be a method of choice instead of existing time-consuming techniques. MS-based approaches involve the non-covalent diastereomer species formation using a chiral reference displaying stereospecific gas phase behavior towards each studied enantiomer [4]. Chiral differentiation is obtained from the comparison of fragment ion abundance distribution of such diastereomeric ions involving each enantiomer of the compound of interest.

The aim of the proposed postdoctoral fellowship consists in developing and optimizing FTMS/MS methods using high resolution Orbitrap tandem for small molecule chiral discrimination within complex mixtures. Namely, it will focus on the systematic study of MS/MS fragmentation patterns of non-covalent diastereomer multimer ions, produced from various chiral metabolites and metabolite families. Probing an appropriate chiral reference (e.g. non-proteinogenic amino acid) as well as some transition metal cations (e.g. $Cu^{(II)}$, [5]) to improve chiral response will be performed for the different chiral metabolites and metabolite classes. In addition, the study of ion excitation conditions, e.g. using complementary collisional activation modes (as CID and HCD, [6]) and various excitation parameters (energy and duration) will be systematically conducted.

The postdoc candidate will be employed at Genoscope (Evry), and the communication with other partners of the consortium is anticipated.

Profile

The candidate should hold a PhD in chemistry, analytical chemistry, biological chemistry, organic chemistry or related fields with a strong background in mass spectrometry.

The candidate should have clear interest in and understanding of the fundamentals of mass spectrometry (ionization, gas phase interactions, fragmentation processes) and stereochemistry of small organic compounds.

The ability to use Orbitrap technique will represent a plus.

Funding

Gross salary is around 2 500 €/month.

Application

Interested applicants should send a cover letter exposing their skills set, previous achievements and research interests, a CV and the contact details (names) of two references.

Please, send the applications to edariy@genoscope.cns.fr and aperret@genoscope.cns.fr.

Keywords: high resolution mass spectrometry, stereochemistry of small biomolecules, gas phase dissociation.

[1] M. Thomas, L. Stuani, E. Darii et al. De novo structure determination of 3-((3-aminopropyl)amino)-4-hydroxybenzoic acid, a novel and abundant metabolite in Acinetobacter baylyi ADP1. *Metabolomics* (2019) 15: 45. DOI: 10.1007/s11306-019-1508-3 (PMID: 30874951).

[2] N. Perchat, PL. Saaidi, E. Darii et al. Elucidation of the trigonelline degradation pathway reveals previously undescribed enzymes and metabolites. *PNAS* (2018) 115(19) E4358-67. DOI: 10.1073/pnas.1722368115 (PMID: 29686076).[3] M.

[3] Chaleckis, I. Meister, P. Zhang et al. Challenges, progress and promises of metabolite annotation. *Curr Opin Biotechnol* (2019) 55:44–50. DOI: 10.1016/j.copbio.2018.07.010 (PMID: 30138778).

[4] JC. Tabet. Ion-molecule reactions in the gas phase. IX. Differentiation of enantiomeric menthols using a stereospecific SN_2 process induced by a chiral reagent. *Tetrahedron (*1987) 43(15), 3413-3420.

[5] C. Afonso, D. Lesage, F. Fournier et al. Origin of enantioselective reduction of quaternary copper D,L amino acid complexes under vibrational activation conditions. *Int. J. Mass Spectrom.* (2012) 312:185-94. DOI: 10.1016/j.ijms.2011.08.011 (hal-00708852).

[6] F. Ichou, A. Schwarzenberg, D. Lesage et al. Comparison of the activation time effects and the internal energy distributions for the CID, PQD and HCD excitation modes. *J Mass Spectrom* (2014) 49:498-508. DOI: 10.1002/jms.3365 (PMID: 24913402).