INSTITUT DES SCIENCES ANALYTIQUES

UNIVERSITÉ DE LYON

cnrs

Lyon 1

Revolutionizing blood stream infection diagnosis: multiplexed targeted assay by mass spectrometry to unveil bacterial antibiotic resistance profile and predict resistance level

Révolutionner le diagnostic des infections du système sanguin : dosage ciblé multiplexé par spectrométrie de masse pour dévoiler le profil de résistance aux antibiotiques bactériens et prédire le niveau de résistance

Directeur de thèse : Pr. Jérôme Lemoine - Institut des Sciences Analytiques - UMR5280 CNRS/Université Claude Bernard Lyon 1, 5 Rue de la Doua, 69100 Villeurbanne
Mail : jerome.lemoine@univ-lyon1.fr

Co-encadrement: Pr. François Vandenesch - Centre International de Recherche en Infectiologie/INSERM/Hospices Civils de Lyon

The increasing appearance of new antibiotic-resistant bacteria strains is seriously threatening human life, as recently underlined by the World Health Organization. As any delayed administration of active antimicrobial agents to patients in septic shock is tightly associated with a decrease in survival (7.5 % decrease per delayed hour), accurate and timely identification (ID), antibiotic resistance profiling and, ideally, antimicrobial susceptibility testing (AST) of the pathogen(s), are critical specifications to guide the choice of *ad hoc* therapy by the physicians.

We anticipate that the sensitivity and multiplexing capabilities of targeted mass spectrometry[1,2] (Multiple or Parallel Reaction Monitoring modes) is particularly relevant to tackle such a critical health concern and thus propose to develop a panel of proteomic assays covering the most prevalent resistance mechanisms associated with priority pathogens (according to the World Health Organization), thanks to a proprietary, patented, highly multiplexed targeted-MS approach (Scout-MRM). A special focus will be devoted to resistance mechanisms related to the class of betalactamine drugs, which show an extreme molecular diversity. Once developed from synthetic peptide libraries designed after mining the genomic databases and literature, each assay will be validated from strain collections in collaboration with the French Centres Nationaux de Référence de la Résistance aux Antibiotiques, before applying them to real clinical samples in blind conditions (collaboration with Croix Rousse Hospital). Beside the qualitative aspect of this first diagnosis level, i.e. presence of absence of any resistance mechanisms, a second objective lies in the building of predictive models of resistance level based on the quantitative measurements of proxy peptides. Ultimately, all these developments and assays could eventually be transferred in a clinical environment for effective use.

We are seeking a highly motivated and result-driven candidate to manage this research project, who ideally have a scientific background in analytical sciences, omics and/or (bio)informatics.

References

(1) Charretier, Y.; Dauwalder, O.; Franceschi, C.; et al. *Sci. Rep.* **2015**, *5*, 13944.
(2) Rougemont, B.; Bontemps Gallo, S.; Ayciriex, S.; et al. *Anal. Chem.* **2017**, *89* (3), 1421–1426.