<u>PhD project</u>: Development of innovative quantitative proteomics methods for the diagnosis/prognosis of fulminant multiple sclerosis

Context and Environment

Within the framework of the recently created Interdisciplinary Thematic Institutes (ITIs) of the University of Strasbourg, the **Strasbourg Drug Discovery and Development Institute** (IMS) is a space for novel and unique innovations with advanced skills and technology in the field of drug discovery and development. Thanks to a renowned basic research activity and well-established national and international networks, the IMS aims to develop finalized projects, ranging from *in silico* studies to setting up preclinical trials, creating intellectual property, forging industrial partnerships and launching companies.
The IMS (2021-2028) is based on the laboratory of excellence Medalis (2011-2020) which enabled its stakeholders to carry out fundamental research of high added value (more than 600 publications, 14 patents of which 4 are licensed), to generate a pipeline of potential drugs or advanced technologies for the treatment of cancer and inflammation. From now on, the IMS is based on 3 pillars federating research activities (Medalis), training (Euridis) and innovation / technology transfer (Inedis), all centered on the discovery and development of new drugs.

In this context, the Drug Discovery and Development (DDD) challenge grants every year two students with PhD fellowships to conduct an ambitious research project at the frontiers of two disciplines with an ultimate goal to solve a yearly identified medical need. To conduct the project selected this year, we are looking for a motivated candidate (with a background in analytical chemistry and/or proteomics) to create a duo with an already recruited PhD student, specialized in biology and multiple sclerosis.

Scientific Project

Fulminant multiple sclerosis (FMS) counts among the most severe forms of multiple sclerosis with no efficient and reliable early diagnostic methods today. Therefore, an urgent clinical need remains in identifying more precisely and rapidly different forms and stages of the disease (1). Searching for molecular biomarkers at the protein level using high performing mass spectrometry-based (MS) proteomics technologies promises to be a valuable route to reach this goal.

Major instrumental and bioinformatics developments have enabled MS-based proteomics to reach deep coverage of highly complex proteomes, such as whole cell lysates or biological fluids with a sensitivity down to the amol level and thousands of proteins identified in a couple hours (2,3).
Recently introduced Data Independent Acquisition (DIA) methods promise to further improve the potential of MS strategies, particularly in the context of clinical applications and searches of disease biomarkers. Indeed, the DIA acquisition mode offers increased depth of analysis compared to more classical Data Dependent Acquisition (DDA), while allowing precise, eventually absolute, quantification (4).

Main Objectives

The proposed PhD work should allow leveraging the intrinsic capabilities of DIA-MS.
Indeed, the first analytical challenge will be to setup and optimize new DIA methods on a last generation instrument to take advantage of an additional ion mobility separation capability of a TimsTOF Pro instrument from Bruker Daltonics. Setting up Parallel Accumulation Serial Fragmentation combined with DIA (DiaPASEF) methods should allow further deepening the coverage of the investigated proteomes (5).
The second goal will consist in using previously optimized methods to develop precise quantification assays on a predefined list of 25 biomarkers already known to be involved in multiple sclerosis in order to identify and validate a specific molecular signature of FMS. This should provide a first molecular diagnostic/prognostic for the early identification of FMS patients and molecular classification of multiple sclerosis forms.
Besides this targeted objective, the DiaPASEF methods will allow us to reach unprecedented coverage of the investigated proteomes and thus open an avenue of findings to detect new protein biomarkers involved in FMS.
All analytical developments will be conducted on well-calibrated standard samples before being applied on various animal models of multiple sclerosis, FMS, and relative controls. In addition, thanks to the clinical team involved in this project, we will anticipate the immediate transfer of the methods to human samples.

Hosting Laboratory

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Project partners

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