Master Thesis Project in Organic Chemistry

The gut microbiota and its metabolites in multiple sclerosis: new routes to predicting disability progression

Experimental Clinical Chemistry, Department of Medical Sciences, Uppsala University

Research group

Our research is carried out within the Experimental Clinical Chemistry group at the Department of Medical Sciences, Uppsala University, and its CARAMBA mass spectrometry laboratory led by Professor Kim Kultima. The group combines metabolomics, lipidomics and high-resolution mass spectrometry with machine learning and artificial intelligence to study multiple sclerosis (MS) and the role of environmental factors in disease development and severity. Alongside mass spectrometry, we use immune-based techniques for protein analysis, carry out register-based studies and take part in clinical trials.

Our work spans three main areas: developing new methods for the diagnosis and prognosis of neurological diseases; investigating the role of environmental pollutants, such as PFAS and PCBs, in the development and severity of diseases with an autoimmune component; and developing mass spectrometry-based methods to measure a broad range of small molecules (metabolomics and lipidomics), environmental pollutants and therapeutic drugs.

MS is a chronic autoimmune disease of the central nervous system and the most common cause of mobility impairment among young people in Sweden, where around a thousand people are diagnosed each year. A central goal of our MS research is to enable precision medicine: identifying, at an early stage, the patients at risk of faster progression or secondary progressive MS, so that exposure to ineffective treatments and their side effects can be limited. To do this we build predictive models trained on electronic health record data and new biomarkers, and apply conformal prediction to provide valid, individual-level measures of uncertainty.

We also use large cohort studies such as EIMS, together with ultra-high-performance liquid chromatography coupled to high-resolution mass spectrometry, to explore how genetics and the exposome, the totality of lifetime environmental exposures, shape the risk of autoimmune disease. Within this programme, our recent work on gut microbiota–modified bile acids has shown that these metabolites are altered in people with MS and associate with the risk of disability worsening, which forms the starting point for the project below.

Project description

This master project addresses one focused part of our wider MS research programme: expanding the set of reference standards available for studying gut microbiota–derived metabolites in MS. The gut microbiota produces and modifies a wide range of small molecules, including bile acids as well as other microbially derived metabolites, that signal to the host and may influence MS disease progression. Many of the metabolites that appear most relevant to MS are not available commercially as reference standards, which currently prevents us from confidently identifying and quantifying them in patient samples.

To remove this barrier, the project combines organic synthesis with analytical chemistry and translational research.

- Synthesise a selection of novel standards for gut microbiota–derived metabolites relevant to MS (for example bile acids or other microbial metabolites) that are not available commercially.
- Characterise the synthesised compounds by LC-MS, establishing chromatographic and mass-spectrometric properties such as retention behaviour and fragmentation patterns.
- Use the characterised standards to identify and confirm the corresponding metabolites in human samples, supported by our LC-HRMS method.
- Evaluate the role of the identified compounds in MS disease progression.

The project gives hands-on experience across the full workflow, from bench synthesis, through method development on modern high-resolution mass spectrometry instrumentation, to clinical relevance, within a translational research environment, and contributes directly to ongoing studies of MS disease progression.

Suitable student profile

We are looking for a motivated student who is curious about applying chemistry to questions in human health. The ideal candidate has:

- A strong background in chemistry, with a particular emphasis on organic chemistry and practical synthesis experience.
- Some familiarity with analytical chemistry, ideally including chromatography and/or mass spectrometry (training will be provided).
- An interest in metabolomics, the gut microbiota, and biomedical or translational research.
- The ability to work carefully and independently in the laboratory, while collaborating within a multidisciplinary team.

Practical information and how to apply

Extent / credits: 30 / 45 / 60 hp

Start date: After agreement

Location: Department of Medical Sciences, Uppsala University,

Supervisor / contact: Ida Erngren — ida.erngren@uu.se

To apply, please send a short letter of motivation together with your CV and a transcript of records to the contact above. We are happy to answer any questions about the project before you apply.