Within the European consortium Epic-XS (https://epic-xs.eu) three different 2-year post-doctoral positions are available at Utrecht University, placed within the Heck-lab (https://hecklab.com), Altelaar-lab (https://altelaarlabor.com/), and the Scheltema-lab (https://scheltemalab.com). The research emphasizes on the development of advanced mass spectrometry-based methods to address questions in proteomics and structural biology. The laboratory houses an excellent infrastructure, including a dozen state-of-the-art mass spectrometers, advanced separation technologies, bioinformatics, and laboratories for cell culture, biochemistry and molecular biology. The research group is vibrant and houses over 15 nationalities - Utrecht is a great place to be!

For all positions, the work is embedded in the European Proteomics program Epic-XS and participation in international meetings for this consortium is expected. The aim is to implement the developed technologies into the access sites, promoting collaborations.

Information

1. Position: PostDoc
2. Location: Utrecht University, Utrecht, Netherlands
3. Duration: 2 years (PostDoc)
4. Start date: After consultation, as soon as possible
5. Background: Experience with Proteomics Workflows, systems biology, high end proteomics is appreciated
6. Apply with motivation letter, CV and 2 references
7. Please state preference for 1 of the positions; potentially you will be considered for multiple
8. Deadline for application: 1st of June 2020
9. For information or application: c.c.heuzer@uu.nl
Position 1: Mass spectrometry driven structural investigations (https://scheltemalab.com)

The Scheltema laboratory focusses on the development and application of cross-linking mass spectrometry (XL-MS) to study protein-protein interactions. This technology utilizes small and agile reagents that covalently connect amino acids in close proximity. After proteolytic digestion, mass spectrometry can identify the connected amino acids. From these identifications distances constraints are derived that can be placed in in protein 3D structures, either known or directly predicted using this information. The structural details, at a resolution in the range of a few nanometers, allow resolving interaction interfaces between proteins. This can be done either in-vitro or in-situ in a close-to-native environment, making XL-MS an incredibly powerful approach for cell and structural biology.

For this position, you will join a team of dedicated researchers combining expertise in bioinformatics, biochemistry, mass spectrometry, and structural modeling on a variety of systems and organisms to answer cutting-edge questions in biological sciences. You are expected to apply size-exclusion chromatography and sucrose gradient ultracentrifugation to purify interesting protein assemblies, perform the cross-linking and mass spectrometry assays, perform data analysis and integrate the data into structural models. As part of the European Proteomics program Epic-XS you will interact and collaborate with international researchers and develop new methods for cross-linking mass spectrometry.

Recent illustrative work

1. P Albanese, S Tamara, G Saracco, C Pagliano, RA Scheltema (2020) How paired PSII-LHCII supercomplexes mediate the stacking of plant thylakoid membranes unveiled by integrative structural mass-spectrometry *Nature Communications* 11, 1361
Translational proteomics has made significant progress in recent years with improved protocols for the analysis of clinically important samples such as patient biopsy tissue material and different types of liquid biopsies. The analysis of patient tissue material allows the investigation of the disease state and the treatment response directly in the native in vivo environment and thereby provides valuable molecular disease information with high translational capacity. To make translational proteomics a main technology in clinical settings, several challenges need to be addressed. Here, we will focus on tissue biopsies, as the life in vivo setting, and extracellular vesicles (EVs), which potentially contain biomarkers for diagnosis and prognosis of disease conditions. Proteomics approaches will consist of high-end shotgun proteomics and targeted proteomics (e.g. DIA and SRM).

For this position, we seek a highly motivated biochemist or analytical chemist with proven expertise in mass spectrometry and clinical proteomics. You will join a team of dedicated researchers combining expertise in biochemistry, analytical chemistry, mass spectrometry and bioinformatics on a variety of systems to answer pressing clinical questions. As part of the European Proteomics program Epic-XS you will interact and collaborate with international researchers and develop new methods to translate proteomics results in clinically relevant information.

Recent illustrative work

Position 3: Native and top-down proteomics (https://hecklab.com)

In recent years we have been developing new mass analyzers and new fragmentation techniques targeted towards the direct analysis of intact proteins and protein complexes by native and top-down proteomics. Such analyses on the one hand allow us to directly probe stoichiometries and structures of large protein assemblies, like viruses and ribosome particles, on the other they make it possibly to identify and quantify distinct proteoforms of proteins highly modified by post-translational modifications such as phosphoproteins and (plasma) glycoproteins. Introducing charge detection single particle mass spectrometry and ECD and UVPD fragmentation on Orbitrap platforms has provided us with an unprecedented toolbox to discover so far little explored relevant parts of the proteome.

For this position, we seek a highly motivated biochemist or analytical chemist with proven expertise in biomolecular mass spectrometry. Having your own project, you will join a team of dedicated researchers combining expertise in bioinformatics, engineering and instrument development, biochemistry, analytical chemistry, and structural biology, and work on a variety of systems and organisms to answer cutting-edge questions in biological sciences. As part of the European Proteomics program Epic-XS you will interact and collaborate with international researchers and develop new methods for native mass spectrometry and top-down proteomics.

Recent illustrative work

2. JF Greisch, S Tamara, RA Scheltema, HWR Maxwell, RD Fagerlund, PC Fineran, S Tetter, D Hilvert, AJR Heck (2019) Expanding the mass range for UVPD-based native top-down mass spectrometry Chemical Science 10(30), 7163-7171