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Proteomics Experts Unite for EPIC-XS

BLOG (/proteomics/blog) Mar 22, 2019



Utrecht University EPIC-XS consortium members (from left to right): Richard Scheltema, Maarten Altelaar, Riccardo Zenezini Chiozzi and Franziska Völlmy

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Like many disciplines in systems biology, the proteomics research field is evolving at an astonishing rate. Recent advancements in the technologies available for proteomics research has leveraged a large number of research studies directed at exploring the role of proteins in biological processes.

The European Proteomics Infrastructure Consortium providing access (<https://epic-xs.eu/>) (EPIC-XS) consists of a network of experienced research groups that share one common goal: to facilitate the development and sustainability of proteomics explorations to researchers within the European Union. Co-ordinated by Albert Heck, the consortium aims to elevate the proteomics research field even higher. We spoke with Martina O'Flaherty from the EPIC-XS project office to learn more.

Molly Campbell (MC): Can you tell us about how the EPIC-XS Consortium came to be?

Martina O'Flaherty (MOF): EPIC-XS began as an extension of the PRIME-XS (<https://www.ncbi.nlm.nih.gov/pubmed/24958170>) project, a European Union Programme for research and technological development that started in 2011 and finished in 2015. The idea behind PRIME-XS was to bring the proteomics community together as a more coordinated scientific proteomic effort. While there were many institutions and facilities providing state of the art proteomics research, as a whole the European community wasn't very unified.

The idea was to form a platform where all scientists in the field of proteomics could further develop their skills and expertise in proteomics research and also have access to top of the range proteomics technologies.

The PRIME-XS programme finished in 2015 and while some projects developed further on their own merit, other projects did have the resources or finances to continue with further development. EPIC-XS takes over from PRIME-XS, and together with eleven of the twelve members which had previously been involved in the PRIME-XS project, there are an additional seven leading proteomics institutions participating in the EPIC-XS consortium.

MC: Why is it important to study proteomics and to ensure that proteomics technologies are available to all researchers across the life science fields?

MOF: Proteomics is important because proteins essentially represent the actual function of a cell. If you have mutation in DNA - it's the proteins that are ultimately affected.

If we can understand how proteins express themselves, how they function, how they interact, their structural orientation, then we gain insight into potential disease biomarkers that can be used for detection, treatment and in some cases, prevention of diseases. Take for example the cancer research field; in recent years, proteomic technologies have led to enormous advances in the basic research of medicine because it's become possible to identify cancer cells in biopsies.

In order to develop novel methodologies and technologies to combat and understand proteins and their link to diseases, you need to have high end state of the art equipment and in-house expertise.

Mass spectrometry is key to proteomic research and allows us to study proteins on a large scale in living cells and organisms. However, top of the range MS equipment can be very costly, not only to purchase but also to maintain and run.

This is where EPIC-XS can help researchers, by making, not only high-end MS technology accessible, but also by facilitating access to expert scientists across the diverse proteomics field.

MC: There are four joint research activities (JRAs) within EPIC-XS, can you describe what these research activities are and their aims?

MOF: JRA 1 - *Computational Proteomics and Cross-Omics Integration* is led by Professor Lennart Martens (<http://www.vib.be/en/research/scientists/Pages/Lennart-Martens-Lab.aspx>) from the Vlaams Instituut voor Biotechnologie (VIB) in Ghent, Belgium. This project involves many research partners from within the EPIC-XS platform. This project will develop algorithms and software standards for data handling, providing support across the consortium, for managing processes and data manipulation. This software development technology will form a robust, scalable, integrated, quality-controlled data analysis pipeline, with fully reproducible and traceable data analysis. The datasets generated by JRA's 2, 3 and 4 will be supported by these bioinformatics tools.

JRA 2 - *Future and Emerging Proteomics Technologies* is lead by Dr. Julia Chamot-Rooke (<https://research.pasteur.fr/en/team/mass-spectrometry-for-biology/>) from the Pasteur Institute (IP) Paris, France. This joint research activity also involves a significant number of research partners from the consortium. With this JRA project, investigation into the development of ground-breaking novel proteomics technologies that will improve sample throughput, PTM analysis, sensitivity towards single cell analysis, reproducibility, dynamic range, multiplexing capabilities and proteome coverage will be investigated. The aim is to go beyond state of the art, to bring proteomics into the future, taking research one step further. As with all JRA's these technologies will be made directly available to the scientific community through their implementation in the EPIC-XS access sites.

JRA 3 - *Translational Proteomics* is lead by Professor Matthias Mann (<https://www.biochem.mpg.de/en/rd/mann>) from the University of Copenhagen, Denmark. This is a project focused on making translational proteome profiling a more mainstream technology in a clinical setting. The aim is to address some of the most recent bottlenecks in clinical proteomics, by developing robust, reproducible high throughput proteomics workflows to analyze large sample cohorts from patient samples. Tackling the dynamic range in the plasma proteome and investigation of PTM's and epigenetics as biomarkers for disease states will also form part of this project. These technologies will be made directly available to the scientific community through their implementation in the EPIC-XS access sites.

JRA 4: *Proteome Organization, Structural and Spatial Proteomics* is lead by Professor Paola Picotti (<http://www.imsb.ethz.ch/research/picotti/PeoplePicotti/paola-picotti.html>), Institute of Molecular Systems Biology, ETH, Zurich, Switzerland. JRA will focus on the higher order areas of proteome organization, such as the development, and the integration of different mass spectrometry (MS) based proteomic technologies. It will be used to characterise the subcellular organization of the proteome and the higher order structure of proteins. Again, the bioinformatic tools needed for these technologies will be co-developed with the Joint Research Activity 1. These technologies will be made directly available to the scientific community through their implementation in the

EPIC-XS access sites.

MC: The initiative is coordinated by Albert Heck - what other world-renowned researchers from the proteomics field are involved in the consortium? Can you give examples of their laboratories research interests?

MOF: There are several world-renowned scientific researchers within the consortium who have made pioneering advancements in the field of proteomics.

Professor Matthias Mann (<https://www.biochem.mpg.de/en/rd/mann>) from the University of Copenhagen.

The first protocols to perform in-gel digestion of proteins and handling of small amounts of biological samples and the ability to rapidly identify peptides by matching their MS fragmentation spectra to sequence databases were developed by Matthias Mann. The Mann research group in clinical proteomics (<https://www.cpr.ku.dk/research/proteomics/mann-group/>) are investigating biological markers for early detection of metabolic disorders such as diabetes and cancer. Another area of focus is the interpretation of "multi-omics" data, which is still a challenge. Often, a single "omics" dimension is not sufficient to capture the full complexity of a disease. To overcome these challenges, the Matthias group is developing the Clinical Knowledge Graph where multi-omics data, together with vast amounts of meta-data, is collected and harmonized – enabling analyses and providing an excellent ecosystem for machine learning.

Professor Bernard Küster (<http://www.professoren.tum.de/en/kuester-bernhard/>) is the chair of Proteomics and Bioanalytics (<https://proteomics.wzw.tum.de/index.php?id=2>) at the Technical University of Munich.

The research interests of Bernard Küster focuses on a range of questions relating to how proteins interact with each other and with active pharmaceutical ingredients, which molecular mechanisms play a role in cancer, and how these can be used for individual approaches to clinical treatment. He uses chemical and biochemical methods as well as spectroscopic and bioinformatic high throughput technologies. Together with other consortium members, he has conducted pioneering research relating to the higher-order organization of protein complexes and structural proteomics, and even whole proteome; paving the way for groundbreaking new insights into biological systems.

Professor Mathias Uhlén (<https://www.kth.se/pro/sysbio/uhlen-group/researchers/mathias-uhlen-1.67763>) from the KTH Institute, Royal Institute of Technology, Stockholm.

The research of Professor Uhlén is focused on protein science, antibody engineering and precision medicine and studies range from basic research in human and microbial biology to more applied research, including clinical applications in cancer, infectious diseases, cardiovascular diseases, autoimmune diseases and neurobiology.

Since 2003 he has been the head of an international effort to map the human proteome with antibodies. He created an open source knowledge base resource, the Human Protein Atlas (<https://www.proteinatlas.org/>), using antibodies and various omics technologies.

MC: What challenges currently exist in the proteomics research field and how do EPIC-XS hope to overcome them?

MOF: Despite significant advancements in the field of proteomics, the challenges faced by proteomic researchers are still quite high. Unlike DNA and RNA, proteins are more difficult to work with. Protein expression spans many more orders of dynamic range and cannot be amplified like DNA or RNA, so less abundant species are more difficult to detect. Hence improving sensitivity and dynamic range of proteomics analysis is essential. Added to this challenge is the fact that there may be more than several million distinct protein molecules in a cell, potentially each having their own distinct properties and functions. This makes comprehensive analysis of proteome digests extremely challenging. The activity of proteins in vivo means that they can be regulated by localization, binding to other molecules (proteins, DNA, RNA, metabolites, drugs etc) and other structural alterations.

The application of proteomics to clinical research poses further important challenges, notably the massive biological variability between individual organisms/humans. The technical challenges faced involve robustness, efficiency reproducibility, high throughput, standardization of methodologies as well as costs related to analysis. Overcoming these challenges is one of the main goals of the EU Future Enabling Technologies (FET) project MSMed (<https://www.cpr.ku.dk/research/proteomics/olsen/msmed/>) (including Matthias Mann, Jesper Olsen and Albert Heck) which is closely connected to EPIC-XS and the major commercial industrial developers.

Equipment cost is also a precluding factor for the widespread use of proteomics in clinical laboratory and for many institutions engaged in life science research. Most proteomics technologies use complex instrumentation, critical computing power, and expensive consumables. Taken together with the need to acquire, train and retain highly qualified research staff, long-term sustainability of mass spectrometry equipment can be a challenge. As a result, the major contributors to progressive advancements in the field of proteomics are largely made by a small group of pioneers in the field, many located in Europe and are partners in EPIC-XS.

Logistical hurdles presented by the significant number of datasets that can be generated by proteomics methodologies, will also be addressed within EPIC-XS. There is a very strong link on proteomics bioinformatics with the ELIXIR ESFRI project, where the proteomics community is led by EPIC-XS partners (Oliver Kohlbacher, Lennart Martens, Juan Antonio Vizcaino). Also, developments in this context will be aligned within the European Open Science Cloud (EoSC), where partner EBI is involved in the current project EoSCPilot.

Providing the broader proteomics community optimal access to experts in the field, and enabling them to utilize high-end mass spectrometry technology, hardware and bioinformatics tools, will help overcome many of these challenges. EPIC-XS will facilitate this access and will also provide hands-on training for researchers, helping to develop best practice workflow, and will also aid the dissemination of proteomics data into publicly available databases and broaden the expertise of experienced scientists and those new to the field of proteomics.

MC: What support can scientists wanting to conduct proteomics research expect from EPIC-XS?

MOF: Support for scientists is provided by allowing researchers open access to the research facilities within the EPIC-XS platform. They will gain expert advice with respect to execution of their proteomics experiments and will be provided with the technical support necessary to perform their experiments. There is ample expertise within the consortium to guide life science research projects throughout Europe, both through their prior involvement in PRIME-XS and their strong involvement in national proteomics initiatives and facilities.

EPIC-XS also provides a supportive role in summer schools, training courses, and workshops such as the MaxQuant Summer School, the European Summer School in Advanced Proteomics, Advanced Biomolecular Mass Spectrometry course and many more. The first workshop on Chromatin Proteomics (<https://chromatinproteomics2019.febsevents.org/>) will be held in September 2019, in Greece.

Martina O'Flaherty was speaking to Molly Campbell, Science Writer, Technology Networks.

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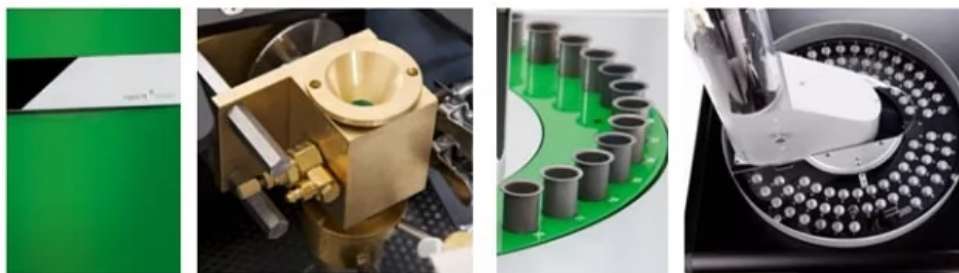
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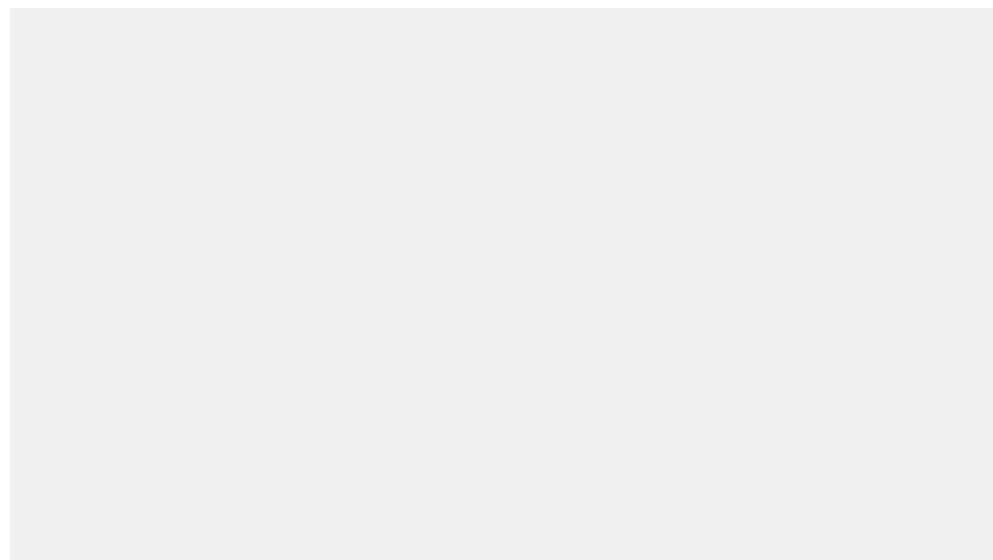
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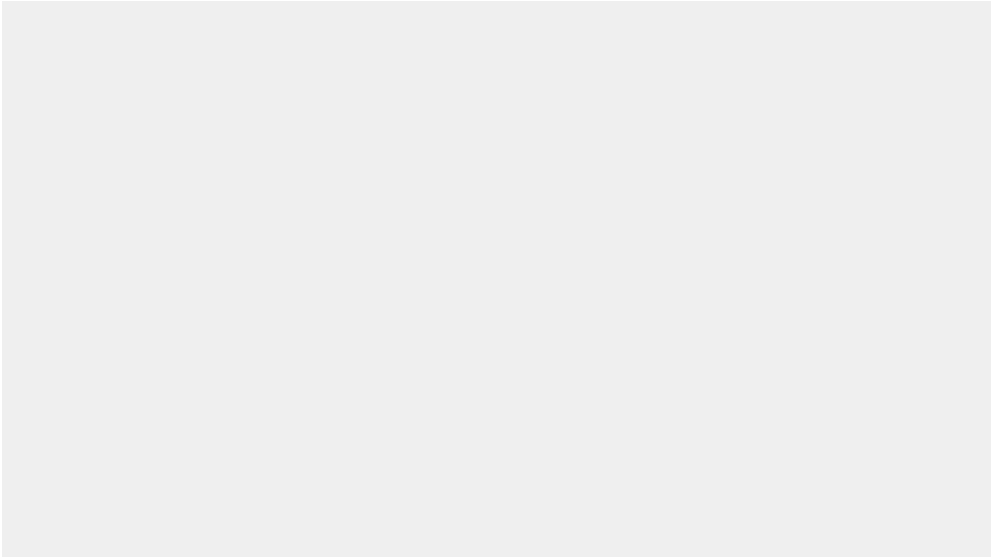
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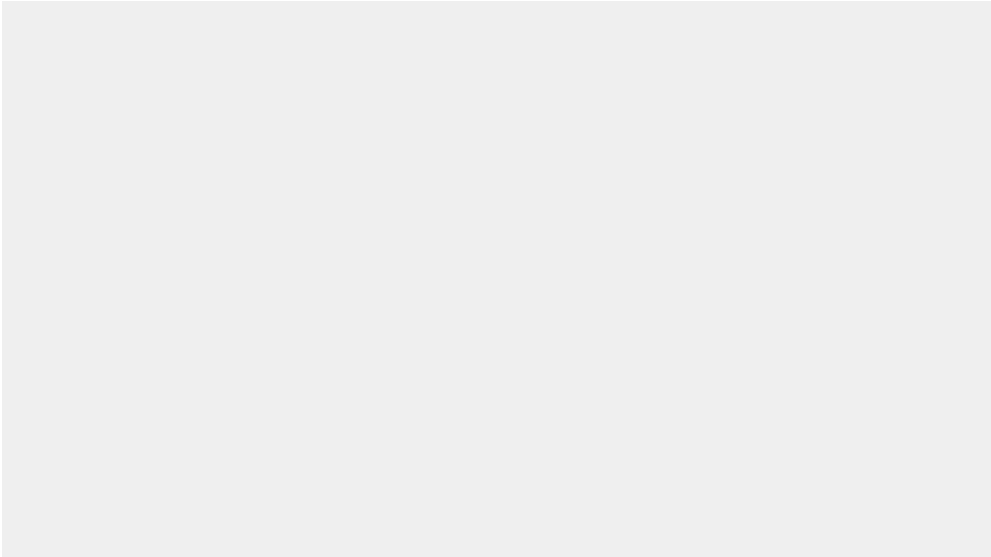
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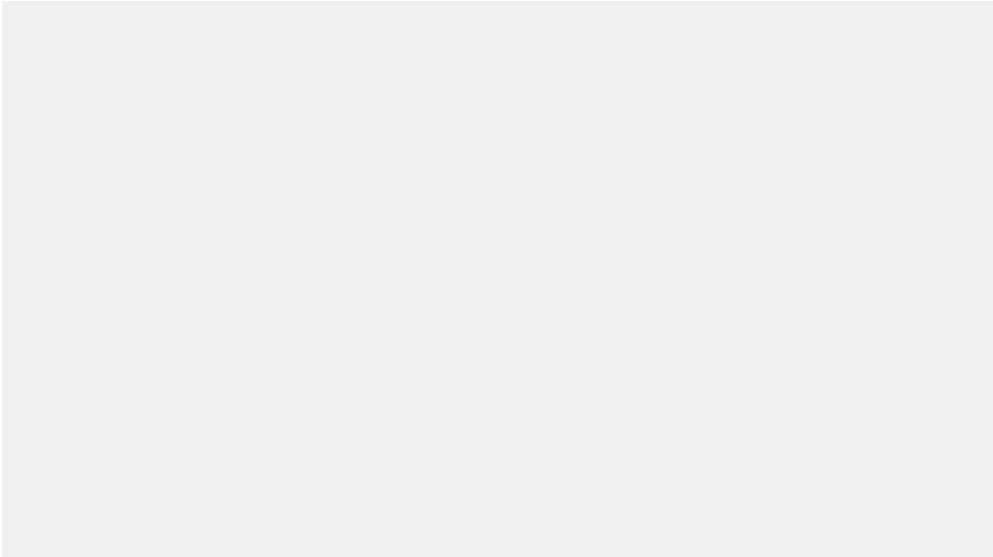
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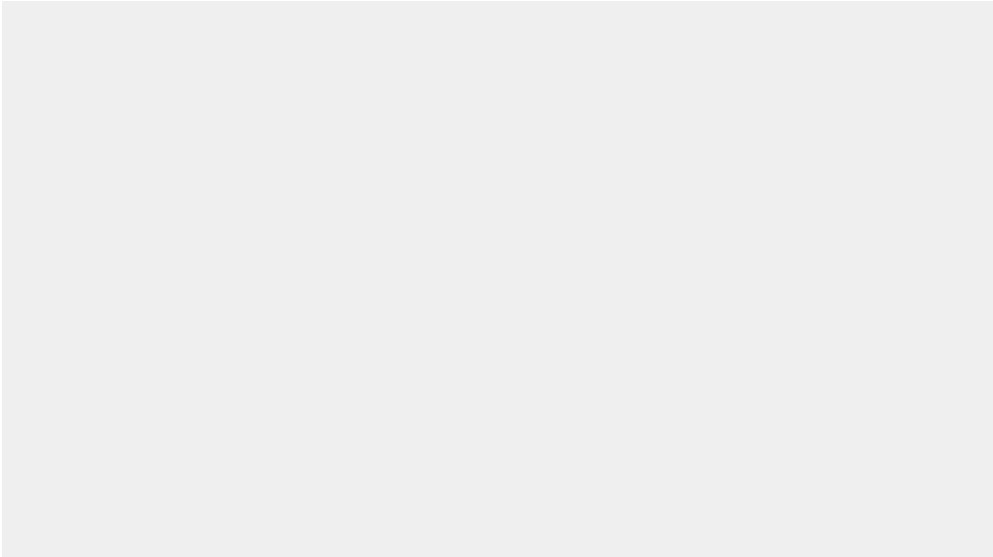
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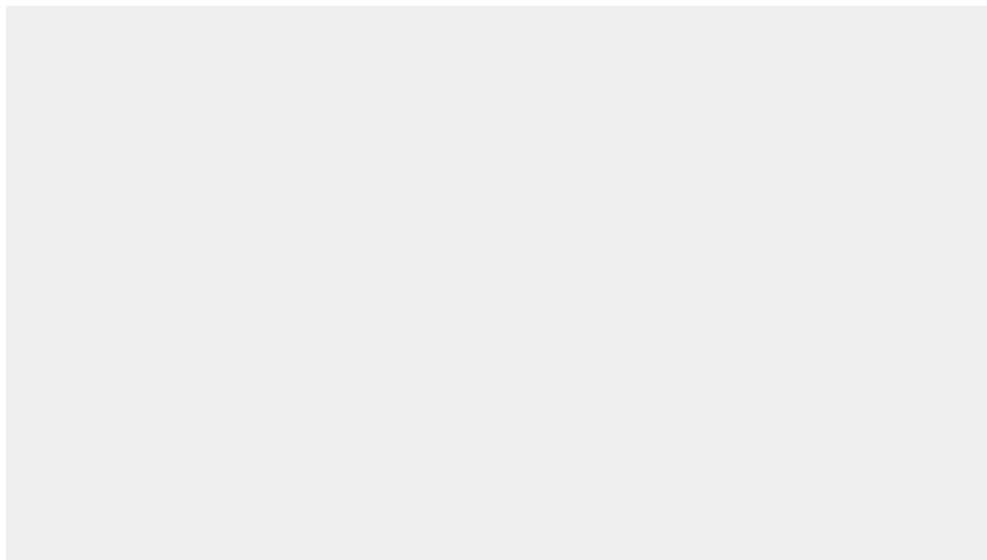
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