The FEBS Journal

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EDITOR PROFILE

Editor Profile: Albert Heck

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doi:10.1111/febs.15888

In this special interview series, we profile members of *The FEBS Journal* editorial board to highlight their research and perspectives on the journal and more. Albert Heck is Professor of Chemistry and Pharmaceutical Sciences at Utrecht University, Scientific Director of the Netherlands Proteomics Center, and Head of the Biomolecular Mass Spectrometry and Proteomics group in Utrecht University since September 1998. He has served as Editorial Board Member of *The FEBS Journal* since 2020.

Can you give an overview of your research group's major focus and goals?

My research focuses on the development and applications of mass spectrometry-based proteomics. We introduced several technologies for phospho-enrichment and the use of alternative proteases and hybrid peptide fragmentation techniques. In addition, we pioneered native mass spectrometry and cross-linking mass spectrometry for addressing questions in structural biology. Our primary goal is to address the question: What makes a gene product a functional protein? Therefore, a detailed knowledge about a protein's proteoforms (e.g., the post-translational modifications it harbors) and interactions is crucial.

From a broad point of view, why is it important to delve into these research questions?

Each gene translates into a functional entity at the protein level. However, for each gene product, nature can represent a plethora of different proteoforms that all exhibit different functions. The histones are core examples of such proteins, but nearly every protein undergoes modifications to regulate its activity and interactions. If we truly want to understand molecular biology, we need to study these modifications and their functional consequences. I often say that it is through these modifications that proteins can communicate with each other.

What's been your favorite personal breakthrough, to date?

Having always been technology-driven, there are quite a few technological milestones I could mention. Our first work on phosphopeptide enrichment was a real impetus for my career in proteomics. Additionally, our first work on using native mass spectrometry to analyze intact viruses started a lot of collaborations in structural biology, now complemented by our cross-linking technologies.

What research thread in your laboratory are you currently most excited about?

Making such a choice is nearly impossible. Currently, we dedicate a lot of our efforts to the vital questions: 'Which antibodies make up our personal repertoire in serum and other body fluids?' and 'How do these protect us against pathogens?'. Characterizing antibodies by mass spectrometry-based sequencing is a key technical challenge that we face.

Mass spectrometry is continuously developing, and that is really exciting for a technology that originated now more than 120 years ago. I always like to see what biological questions are not yet addressed by mass spectrometry and see whether we can also open up that field. Some of the challenges in mass spectrometry always remain the same: increased sensitivity (now for single-cell analysis), specificity (to see all proteoforms), and speed.

Have you always been interested in science and was it inevitable that you would end up in this career?

My career in science has not been unidirectional. I started with a great interest in theoretical and physical chemistry and performed postdoctoral research in chemical reaction dynamics. I turned to molecular biology and biochemistry only later in my career and approached these fields with a technology-driven perspective. At some point in my career, I was asked to lead a program in which I was allowed to work with (supposedly) the most powerful mass spectrometer in the world, let us say the Ferrari of mass spectrometry. At that point, I decided that the work should focus on biomolecules, an area I did not know much about, which was actually the start of my fascination for the main question of my career: How do proteins work?

How do you balance management of your research group with your other academic and professional commitments?

Research is teamwork, wherein everyone should take and be given responsibilities and credits. If the spirit in the team is good, managing your team is easy.

What advice can you offer an early-career researcher who is hoping to forge a successful career in academia?

Follow your heart, but also be open to unexpected directions in your career. I often feel that the true breakthroughs in certain areas of science are not made by the experts in that field, but by 'outsiders' who enter that field and use their unique expertise to solve some of the long-lasting key questions. Thus, it also helps to read papers outside your own niche, as well as to attend conferences outside your niche.

How were you persuaded to join the editorial board of *The FEBS Journal*? In what ways do you think that the journal stands out from other journals in the Biochemistry & Molecular Biology sector?

Seamus Martin played an important role in inducing me to join the board, but I also feel strongly that we should support scientific societies such as FEBS and the journals that they develop, as compared to

commercial publishers/scientific organizations. While I like other journals such as JBC and MCP as well as *The FEBS Journal*, I appreciate that not all scientific societies should be coordinated from the United States, so the Europe-focused history of FEBS appealed to me.

Do you have a favorite *The FEBS Journal* paper?

If allowed, I will pick our own minireview 'Proteomics beyond Trypsin', which also happens to be a very well-cited paper (Tsiatsiani, L. and Heck, A.J.R. (2015) https://doi.org/10.1111/febs.13287). What I liked the most in this piece of work is that we proposed a virtual protease, called idealase, that would cleave nonsequence specifically, but exactly after 100 amino acids, making long peptides that are ideal for mass spectrometry-based sequencing. This protease does not yet exist, but maybe with advances in protein nanopores, resembling proteasome particles, it may be on the horizon. Since this paper, I dare to propose more tools we need, instead of describing those we already have.

What long-lasting impact will the COVID-19 pandemic have on science and the public's perception of it, in your view?

That is still very hard to predict. It has been great to see how science responded to this global threat and seemingly 'solved' it, but it is also scary to see how we all overreacted, with more than 30 000 papers on SARS-CoV-2 in 9 months. In the years before COVID-19, funding for viruses and infection was very restricted. I just hope that we now make wise decisions

and fund fundamental research not only on SARS-CoV-2, but also on other viruses, bacterial infections, and immunology-related diseases. We can only respond to these threats if we have fundamental knowledge about how they work.

Tell us something about yourself that we might be surprised to hear...

I am equally proud of some of my scientific achievements as I am of the fact that I ran a dozen marathons in many of the most beautiful places of the world, such as Paris, Berlin, Madrid, Chicago, and Amsterdam. In fact, my running medals have a prominent place in my office at the university. Running marathons teaches you how to deal with ups and downs and provides you with the stamina to endure, whatever happens, as you know that the rewards come at the finish line, even if you are, by then, exhausted. That mindset helps me also in science.