FcRn-Targeted Therapies for Autoimmune Disorders

SPEAKER INTERVIEW

AN EXCLUSIVE SPEAKER INTERVIEW

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Jan Terje Andersen is a professor in biomedical innovation at the Department of Pharmacology, the Faculty of Medicine at University of Oslo, and a research group leader at Department of Immunology, Oslo University Hospital. He is heading the Laboratory of Adaptive Immunity and Homeostasis, which is studying the cellular processes and molecular interplay underlying the functions of the two most abundant proteins in blood, albumin and IgG.

Jan has also obtained the Fridtjof Nansen Prize for Early Career Achievements, Oslo University Hospital Early Career Award and is a member of The Young Academy of Norway.

What led you to this field of research, and what is exciting you most within the space of FcRn-based research and autoimmune therapeutics?

The beauty of complexity! As a student, I was intrigued about how extremely well our immune system is coordinated via networks of interactions taking place between molecules and cells. This immune orchestration is of utmost importance to keep us healthy, but if not properly controlled it may lead to the development of serious diseases. It was obvious that an in-depth understanding of this multi-complexity could lead to new and specific treatment options.

Therefore, I started to study molecular immunology. I was lucky to join the research group of Professor Inger Sandlie, who had a keen interest in dissecting the antibody architecture with an eye on innovation. This was early 2000 and my master thesis was about recombinant production of human FcRn. During this time, I visited the lab of Professor Søren Buus at the University of Copenhagen, who just had established a bacterial production system for soluble MHC class I molecules. We adopted the protocol to FcRn, and this early work evolved into an FcRn reagent platform that today is part of Immunitrack ApS. The plan was that the bacterial-derived FcRn was to be used by a Norwegian biotech in their phage display selection strategy. This never happened as the company was acquired and ended up in Russia.

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It has been a very exciting journey so far. I am amazed at how FcRn has evolved as a broadly expressed cellular receptor that controls the plasma half-life of two completely unrelated plasma proteins, IgG and albumin, via a remarkably similar pH-dependent manner. Hence, how FcRn operates at very distinct body sites is fundamental for their versatile functions, spanning both immunological and non-immunological processes. Understanding this biology has tremendous implications for the development of novel IgG and albumin-based therapeutic formats. Therefore, FcRn is at the top of its game, as knowledge about its biology and how it can be manipulated can guide molecular design.

There has been a lot of activity in the field over the past 12 months, from some innovative biotechs raising a lot of investment to advance their pipeline to even large pharma companies acquiring smaller businesses – what do you think has driven all of this recent activity?

Evidence is rising that FcRn may be a spot-on target that can rapidly accelerate the removal of pathogenic IgG from the blood of patients having severe autoimmune diseases. While the preclinical data supporting such approaches have been around for a long time, it is not until recently that robust clinical results have been revealed from independent players, each having their preferred FcRn-targeting strategy. This causes optimism that new treatment modalities will reach the market for patients in need.

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The antibody market is also growing rapidly, and both small and large companies are expanding their antibody pipelines. Even companies that traditionally have had their focus on small molecular drugs are establishing their antibody pipeline. There is a willingness to invest early on, as the approval rate is rather high for antibodies compared with small molecular modalities.

Generating antibodies is no longer a challenge as a range of different selection platforms is available. However, to design innovative candidates, specifically tailored for a fine-tuned mode of action, an adequate understanding of the biology that drives the diseases is essential. As such, the lack of mechanistic insights at a molecular level is lacking for many challenging diseases. I think this has become very clear to the antibody community, which is also the reason why the industry is joining forces with academic labs having unique knowledge.

In this regard, bioavailability is a commercially competitive differentiator, which may greatly affect the dosing, frequency of administration, and patient compliance, especially for those on long-term treatments of chronic diseases. As such, it is extremely relevant to consider how designed IgG-based molecules engage FcRn. We also experience that there is increasing interest in re-visiting the possibility to explore albumin as a drug carrier by harvesting from recent insights into the FcRn-albumin relationship.

We've also come to learn that the field of FcRn-based research is a little fragmented – is this something you would agree with, and why is it important for you to bring all experts currently working in this field together?

As an immunologist, I was not sure whether I should jump on the albumin train back during my PhD. However, the more I read up on the role of albumin as a molecular taxi that transports a plethora of cargo, I got convinced that I had to consider both ligands to get a better understanding of how FcRn operates. I found it striking that two proteins with very distinct biophysical properties and the ability to bind distinct receptors, also share a common feature, a long plasma half-life due to pH-dependent binding to FcRn.

I strongly believe that bridging expertise from different disciplines is the way to go to develop new innovative concepts. This includes close collaboration between academia, biotechs, and the pharma sector. When we join forces, we can make a difference by translating research results into inventions and the commercialization of products that can change people's life. That is also a driving force for my lab.

What are you looking forward to most at the FcRn-Targeted Therapies for Autoimmune Disorders Summit, and what can attendees expect to take away from your presentation?

I'm looking forward to hearing the talks and views from colleagues that I highly admire as well as those that I have not yet had the opportunity to meet in person. My perspective will be to give a glimpse into how my lab is harvesting from our molecular and cellular understanding of FcRn in design of both novel IgG- and albumin- based molecules with tailored binding and transport properties. I will also discuss the possibility to target FcRn expressed at mucosal surfaces for non-invasive delivery of protein-based drug as well as subunit vaccine candidates.

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