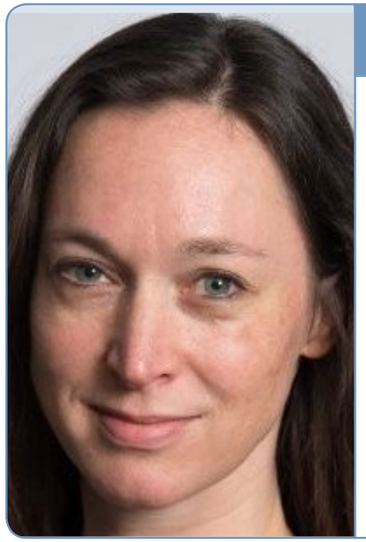
MONOCLONAL ANTIBODIES AND BIOASSAYS WITHIN BIOLOGICS



BARBARA HEBEIS, Associate Director Bioassay Development, Biopharmaceutical Development, **AstraZeneca**

Barbara has over 15 years' experience in the pharmaceutical industry, spanning Drug Discovery and Drug Development. After a Post Doc in B cell signalling at the Babraham Institute, Cambridge, she held positions in Drug Discovery at GSK, Stevenage and Boehringer Ingelheim, Vienna. She was working on small molecules and biologics from target validation to candidate selection covering Virology, Autoimmunity and Inflammation and later Oncology. She then moved into CMC Services at Envigo, Huntingdon (formerly NDA Analytics at Huntingdon Life Sciences), leading a team of Bioassay Scientists developing a wide range of potency release and characterisation methods for products from monoclonal antibodies to a seven-peptide allergy vaccine, as well as cell therapy products. She currently heads up the Bioassay Development Group at AstraZeneca, Cambridge, supporting large molecule clinical products with Bioassays for process and formulation development, characterisation as well as clinical release.

Where are we now in terms of monoclonal antibody research?

I think monoclonal antibodies have gone from being the new kid on the block in terms of therapeutics to being quite common now, and maybe a third, or even half the drugs being approved in the recent years. It's basically routine for us in the pharmaceutical industry, and it breeds a bit of complacency. When you've got an exceptional situation with potentially post-translational modifications, we don't initially recognise that it's a more complex project than all the others.

Why is it important to talk about the bioassay strategies?

What arose from this maturity of the technology is that for most functions in developing monoclonal antibodies, the process development, formulation development, and even the development of physicochemical analytical methods, have become platform. Methods are already developed, and they only need to be tweaked a little bit to fit the new product. In the case of the bioassay, or the potency assay, that's different, because we are dependent on whatever the mode of action of the drug is. So, we really have to adapt to every new drug, and we have to come up with something from scratch. The challenge is, if you are living in a world of platforms, the timelines that are expected are getting shorter and shorter, but our job is still the same.

What are the current challenges you come up against?

You get squeezed into the timelines, with something that is very unpredictable.

What are the next steps for research?

What we're seeing is that the number of straight monoclonal antibodies in our portfolio is diminishing and will either have antibodies with something conjugated onto them, or completely different molecules, or even cell and gene therapy. I think most of our work is currently focused on adapting to that change and supporting those other products.

What would you say are the top three takeaways you're hoping people get from your presentation?

As I mentioned before, when you see an antibody that doesn't just look like your standard monoclonal antibody, be careful; there are implications for many different functions in that process. That's not only affecting analytics, but also process development, so if you have another candidate, go for another candidate.

What do you think are the most important technologies that are impacting the biologics field?

It's gene editing, and gene and cell therapy. It's a natural progression of what we've seen. There was the worldwide age of chemistry, where we tried to generate mainly chemical drugs. Then we came across the age of biology and we generated those biologic drugs. Now we're in a situation to provide the patient with the means of making them in their own bodies.

What do you think of the current innovations in the biologics market, and what trends do you think will impact the industry the most?

I think some of the trends are delivery. We've never been as good as small molecules in that most of our drugs were injectables or infusibles, which is even worse and it's not convenient for the patient. The focus is shifting to what is right for the patient and new delivery technologies, e.g. AI technologies that can be controlled or read off remotely, will probably grow.

Have there been any big biologics stories in 2019 so far that really stood out for you?

What just recently occurred to me hearing quite a lot about gene therapy is that, evidently, you might want to treat patients that are very young and very fragile, and that there have been reports in the news about patients being potentially affected by the therapy. These diseases are life threatening diseases, and often there's no survival past a certain age. They are life changing. I think the public probably needs to be more educated about how to respond to these things. When there are these kinds of events, where you think gene therapy will be shown in a negative light, it has to be taken with a pinch of salt, considering the types of patients that are being treated and also the types of successes that can be seen.

Where do you think the biologics industry is heading?

I think it's diversifying. It's been very focused on antibodies. Now we've got a lot of different new modalities, peptides, peptide fusions, wild and wonderful molecules and cell and gene therapy, and that diversification expands to the types of treatment options patients will have.