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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Ben Schumann

Benjamin Schumann is a Group Leader at the Francis Crick Institute and a Senior Lecturer in Chemical Biology at Imperial College London, UK. His research focuses on developing precision tools to advance the field of glycobiology and study of the roles of sugars in human health and disease. After completing his undergraduate and doctoral studies in Germany in biochemistry and synthetic chemistry, he moved to Stanford University in California, USA. There, he used bioorthogonal 'click chemistry' techniques to understand some of the intricacies of glycobiology. In 2018, he established his independent lab in the UK, where he leads an interdisciplinary group combining organic synthesis methods with cutting-edge quantitative biology to study glycans in various model systems. We spoke with Ben to learn more about how he found the 'sweet spot' for his career, his approaches to scientific mentorship and why more biologists should pay attention to glycans.

Ben Schumann

What inspired you to become a scientist?

Early on, I was always good at maths and languages, but I didn't really know what I wanted to do until the last few years of school. My science curriculum included organic chemistry on the chemistry side and metabolism on the biology side, and I had great teachers who conveyed these. Collectively, all this made me consider biochemistry, because it sounded super interesting and fun. I applied to a couple of universities and decided to study biochemistry at the University of Tübingen in Germany. I didn't really know what to expect, but I happened to really like it.

After your undergraduate training in biochemistry, you moved into synthetic chemistry of glycans and then molecular and cellular glycobiology – what in particular made glycobiology 'click' for you?

When I was an undergraduate student, my biochemistry curriculum was quite heavy on the chemistry side. I realized that basics in organic chemistry are indispensable to make a good biochemist; you need to have a structural understanding of what molecules look like to be able to manipulate them. Within that curriculum, I had the opportunity to do internships abroad. One such placement was with Ten Feizi at Imperial College London, incidentally where I am now. I got into the organic chemistry aspects of manipulating glycans, functionalizing them for microarray chips to study binding interactions. There was something fascinating about how challenging it is to work with glycans, because they are unlike other biomolecules; you cannot clone a glycan, for example. I think that's what inspired me to go into that field and maybe make a difference.

Afterwards, I applied for a PhD with Peter Seeberger at the Freie Universität Berlin/Max Planck Institute in Potsdam, Germany. In his lab, I really wanted to learn organic synthesis, which, as a biochemist, is a bit daunting. With Peter's fantastic support and the help of great lab mates, I was taught from the bottom up how to synthesize my own glycans. I was able to work on the whole pipeline of chemical glycobiology, from making complex glycans to using them *in vivo*. I came out of the lab well-rounded in chemical biology, looking forward to the next adventure.

In 2016, you undertook a postdoc with Prof. Caroyln Bertozzi at Stanford who shared the 2022 Nobel Prize in Chemistry for the development of bioorthogonal 'click chemistry' techniques. What was the most important thing you learned from having her as a scientific mentor?

Carolyn brings out the best in people, empowering them to shine. One thing that all lab members and alumni will point out is that she leads by example – by being a good person. For instance, my partner and I had moved from Europe to the US with a newborn baby at the time, and Carolyn could not have been more accommodating. You want to emulate not only the scientific force of nature that she is, but also her compassion and the way she interacts with people. I think that's equally as important as being a superb scientist.

You then started your own lab in 2018 at Imperial College London and the Francis Crick Institute, UK. What did you feel was the biggest challenge to overcome as a new PI?

The one thing that you underestimate is being responsible for people and their careers, successes and failures. Thankfully, there are training courses on how to lead and manage a lab, but it's still a bit different from the real experience. At the same time, imposter

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The Chemical Glycobiology Lab led by Ben Schumann. From left to right: front row, David Sharp, Anna Cioce, Ganka Bineva-Todd, Sophie Schmidt, Zhen Li, Lucia Di Vagno, Yu Liu, Beatriz Calle; back row, Mia Zol-Hanlon, William Browne, Ben Schumann, Edgar Gonzalez-Rodriguez, Abdul Zafar.

syndrome is telling you, 'Am I really the right person for this job? Am I really good enough?' For me, the approach to dealing with all this was to ask for help and find access to mentors who can give you advice.

Another challenge was to build up a lab that has a coherent, positive atmosphere that people feel comfortable in; one that makes it enjoyable to deal with the 'people' aspects and to do the work. You will worry less if your team support each other, and you can focus your time on how best to empower them. Once you have that, scientific progress is kind of a corollary.

Normally, when you start your own lab, you still do some lab work or data analysis yourself, but that gradually decreases. At some point, I realized that it is not really viable for me to work at the bench anymore without other people missing out on my advice. My lab members are amazing, so there is nothing that I would bring to the table that they cannot do. I also have other types of commitments now, especially meetings and teaching, that I have to factor in.

I am not sure if I am particularly lucky, but I really like the way that my lab works together. We have a great diversity of people, with different working styles that come together and somehow create a coherent atmosphere where everyone plays their part to do cool science.

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What are the main questions your lab is currently trying to answer?

The 2022 Nobel Prize in Chemistry was awarded in part for the ability to adorn sugars with chemical tags to profile them in biological settings, by using so-called 'bioorthogonal' chemistry. This is important because, as mentioned above, glycans cannot be cloned or easily manipulated by traditional molecular biology methods. Bioorthogonally tagged sugars have been amazing for, say, visualizing cell surface glycoproteins. The chemistry side of that field has experienced a tremendous boost in the past decades, and a lot has happened to make the bioorthogonal reactions faster, more selective and viable in living organisms. What we are focused on now is the expansion of biological specificity. Modern quantitative biology has great instrumentation to measure how things work physiologically, but that needs really specific readouts; if the reagent that you are using is not specific enough, then your assay probably won't be very good. A few years ago, we did not have a lot of specificity in reading out the activities of individual glycosyltransferase enzymes or individual glycan subtypes in cells, or the glycans derived from particular cell types. We had a limited arsenal of tools to make these compounds enzymatically, or techniques such as really sensitive mass spectrometry or CRISPR. Now, having all these at our disposal enables us to ask questions that we could not ask before. Having access to both chemistry and biomedicine further catalyses progress: I can work with the chemists to make new molecules, which can be quite complicated and intricate from a synthetic point, and we can also work with preeminent biologists who can use our tools.

Your work combines synthetic chemistry approaches with cell biology; what are the benefits and/or challenges of managing an interdisciplinary lab?

It's not as hard as I thought it would be. The first generations of students and postdocs that I recruited were mostly chemists who were excited about learning molecular and cell biology. This approach was not necessarily planned, but as mentioned above, there is something about chemistry education that makes you understand structurally how proteins work, and that is something that I am quite particular about. When someone is engineering an enzyme, I want them to really know what they are doing to a protein chemically. It was also important to establish a critical knowledge base – for instance, to understand how different click reactions work and how they are compatible with each other.

We then needed to branch out and increase our biological knowledge, so I recruited people with different backgrounds from all aspects of biology. That is amazing to have, but only possible because we have a solid core expertise in chemical glycobiology.

We also draw a lot from collaborations. Fortunately, our field is not that small anymore and there are experts in all types of model systems in glycobiology. There is a vast amount of literature about glycans and how they work. As a toolmaker, my work is inherently collaborative, anyway. It is not too hard to reach out to people who know more about certain types of glycans in other organisms than we do.

Is being a 'toolmaker' an important part of what drives you as a scientist?

Yes, I think so. When you start your lab, you think about what kind of scientist you want to be. Do you want to single out a particular biological problem and focus on it? Or do you want to work with other people, developing tools for them to push the field forward? Both are fine, but I always found immense joy in figuring out what people need. I like to ask colleagues: 'what would you like to be able to do?'. Can we make it come true for them? Often the answer is no, but sometimes it is doable. When you develop a tool and others use it, they can push forward in new directions that you have never thought about.

Despite a rich history of research, glycans are notoriously difficult to study. What are the most important obstacles you've faced during your work?

Every glycobiologist has felt like an evangelist at some point in time, trying to convince people that what they are studying is important. There is an inherent bias as to why we do not look into glycans. One reason is because they are difficult to handle, but another is that you don't find a lot of glycans in published protein structures. This is not because they are not there, but because we have to chop them off to crystallize a protein. Slowly, people are

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getting used to the idea that you cannot understand the whole nature of your protein if you are disregarding the glycans. Colleagues will approach me and ask, "I think my protein is glycosylated, what do I do?" My answers, to be honest, are often limited, because there are very few straightforward approaches and solving a glycobiology problem can take quite a bit of effort. Mass spectrometry of glycans or glycopeptides is a whole different art from mass spectrometry of proteins, but glycobiologists inherently like a challenge, so I think people are keen on trying new methods and characterizing very complicated systems.

Working on glycoproteins is also a great opportunity – there are so many glycobiologists out there that can make a big difference. Once you have embraced that glycans might have an impact and be relevant to the biological problem you are interested in, then half the work is already done. Mostly, we have used reductionist approaches to understand how biomolecules work, but we are at a stage where we do not have to be quite that reductionist anymore to get a complete picture. Glycans are part of that, and in the future, scientists won't have a choice anymore but to look into glycobiology. It is a relatively small field, but rapidly growing in relevance.

The glycosciences community in the UK is absolutely fantastic. It is really supportive – people are just genuinely happy to help each other out.

Over the course of your career, you've had experience in labs in Germany, China, the USA and the UK. How have your international experiences shaped your research and your scientific outlook?

I took a lot from each of these experiences. Understanding cultural differences and taking yourself out of your own silo are really important facets of doing science. I am still in touch with collaboration partners I have had in all these different places. If you make new connections, you understand where people are coming from and why they are doing a certain type of work. As a German, it was helpful to go to California and get a healthy dose of enthusiasm, which is something that you cannot avoid when you are in the Bay Area. I can only recommend to people to experience a different ecosystem, and to do it early in their career if they can. We should not make this a prerequisite, but it is certainly enriching.

Being closer to family was a major reason why we came back to Europe from the US, and working in outstanding chemistry and biomedical environments was a great opportunity. The glycosciences community in the UK is absolutely fantastic. It is really supportive – people are just genuinely happy to help each other out.

What is the best science-related advice you have ever received? Is there any other advice you would give to young scientists?

Something that has stuck with me was a piece of advice that was not related to science at all. I had a fantastic primary school teacher who taught us simple Latin proverbs. The most memorable for me was: *Quidquid agis prudenter agas et respice finem.* Roughly translated: whatever you do, do it wisely and consider the outcome. I really like the phrase and tell it to my kids now. It just fits with everything in lab work and in daily life.

Also, another point I that think young scientists should be mindful of is that having imposter syndrome is absolutely normal. You don't always see it, but pretty much everyone has it. At conferences and in papers, you see the cool stuff other people are doing, but you never see the failures. You are constantly exposed to just a positive excerpt of other people's work. I think it is really important to point this out, to take away a little bit of that fear of failure.

You mentioned that you and your wife had a newborn around the time you started your postdoc. Do you have any advice on how to balance raising a family with developing your career?

My PhD advisor recommended that we should not hold out if we wanted to start a family. I can only agree with that. In both of my previous labs, making time for family was absolutely normal, and I think it is important to choose an environment that is accommodating. You have to find your own way to make work be as fulfilling as it can be, while still spending quality time with your family.

Finally, could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?

I used to play the trumpet in a reggae and ska band. When I was an undergraduate, we travelled through Germany and played gigs, which was a lot of fun. I picked it up again during the COVID-19 lockdown, but I hadn't played in a while. It is a very involved instrument, and you have to practice a lot; daily, ideally, in order to be able to play a concert. I also used to play the piano when I was younger, although never really well. Both of my daughters are learning to play now, and so I recently picked it up again.

Benjamin Schumann was interviewed by Amelia Glazier, Features & Reviews Editor for Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.