

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Philip Zegerman

Philip Zegerman earned his undergraduate degree from the University of Cambridge, where he later also pursued a PhD in the lab of Tony Kouzarides at the Gurdon Institute. For his postdoctoral work, he switched fields from chromatin modifications to DNA replication, and joined John Diffley's lab at Cancer Research UK, at Clare Hall in London. In 2009, Philip moved back to Cambridge to start his own group at the Gurdon Institute. He is an EMBO Young Investigator, and his lab is interested in how the initiation of DNA replication is regulated.

What first motivated you to become a scientist?

I have strong memories of doing experiments at school, which I think greatly influenced me. I remember one experiment very clearly, when I was probably about nine or ten. We went on a field trip and trapped and counted mice in a field. Doing experiments was really lots of fun and I was good at it. I originally thought I was going to be an entomologist studying beetles because I loved insects, but when I went to university I started studying medical sciences and ended up in biochemistry and molecular biology.

Your current research focuses on the regulation of DNA replication initiation. What are the particular questions your group is pursuing at the moment?

It's vitally important for all cells to make a perfect copy of the genome once and only once in every cell cycle. We're studying initiation as the key regulatory event that must be strictly controlled within the cell cycle. This process has really interesting implications for how proliferation and differentiation are coordinated in large organisms. It also has important implications for diseases like cancer, where failures in replication lead to genome instability, which causes cancers, but also where DNA replication is targeted by most chemotherapies.

Which organisms do you use to answer these questions?

We use a wide range of organisms. That's the beauty of working with replication; it's essential for all organisms. We work on eukaryotic replication, and we study mostly budding yeast, but given our interest in whole organisms, and being at the Gurdon Institute as well, we have started to diversify and look into metazoans. We have somebody working in worms, and I've been doing some studies in frogs. It's very exciting.

Is it hard to work with different model systems?

It is challenging; there are some major advantages, for example funding. If you can show funders that your process is important across organisms, that's very good; it particularly helps if it's in an organism that they like to fund, with relevance to disease models. There are, of course, challenges. There's always a certain amount of



time it takes to get up and running in a different system. But we're very lucky here at the Gurdon Institute – we have lots of organisms within the building, and we have a very collaborative environment, so there's never been any 'activation energy' required for moving systems and everyone's been very helpful. It's really the perfect environment for us to test different ideas in different systems.

Are there any new techniques that you're adapting for your research right now?

We're setting up a live-cell assay for replication initiation in worms. By taking advantage of the beautiful microscopy you can do in worms, with our knowledge of the molecular biology of replication initiation that we take mostly from yeast, we're trying to set up a system in which we can visualise individual initiation events on DNA, in individual cells. If it works, then we could have the first system in which we can really study replication initiation live in a whole organism.

How have your collaborations influenced your research and do you have any advice on collaborating?

I continue to see collaborators to be really important in our work, particularly as we're moving into different systems. Of course, collaborations aren't without difficulties, like any project. I think the important advice that I would give to somebody is: don't collaborate for the sake of it. You have to have a goal at the end of it and that goal has to be mutually agreed. Collaborations often lead you in exciting new ways and it's a great way of meeting new people and networking and learning new areas of science, which I think is very important.

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Phil as a child in his school uniform outside his father's shop.

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Many early career scientists often find that the advice given by senior scientists on how to establish a successful academic career can be outdated in the current funding climate. As someone who has established their lab relatively recently, what advice would you give?

Funding has changed so significantly since the banking crash, so young scientists have to be really aware of the pitfalls. I think my major piece of advice is that most grants are time limited. You can apply for most starting grants only in a certain window after your PhD, and if that window is approaching and you’re still a postdoc, then apply for it anyway, because that window is going to close. Even if you don’t have a firm job in place, apply for the money first and then get the job. The funders are really clear that they want people who are fresh out of their PhDs. That creates extra pressure, of course. I think when I was a postdoc I was sufficiently naïve and if I were to do it again, I would probably have applied a year earlier for most funding.

You changed fields from DNA and chromatin modification after your PhD. How did that influence your career later on?

I think that changing fields is a really undervalued part of a person’s career trajectory. When I finished my PhD, I was certain that I wanted to discover a new field. That’s why I moved into DNA replication. I really think that was an important part of my career. I enjoy the field and the questions that we have, and, of course, because I have an understanding of the chromatin field, if our questions do (and they frequently do) have implications for nucleosome remodelling or

chromatin assembly, I have that experience of my PhD that allows me to understand different fields, and gives me a new angle. But having said that, because most grants are time limited, there is an expectation that postdocs will get papers out really quickly and if you change fields you can be at a disadvantage. I think that’s a real shame, because it’s important for people to cross fields and even do more than one postdoc. I think that’s a positive thing.

“... changing fields is a really undervalued part of a person’s career trajectory.”

What are your views on the feasibility of being both a good parent and a good scientist?

Being a parent is difficult full stop! I don’t think the challenges that scientists face are different to any professional or that there’s anything particularly special about science that makes it difficult to be a parent. That’s not to say that it isn’t challenging. Of course, it’s much harder for women, because being away from the bench or the lab can be difficult if it’s for long periods of time. But that shouldn’t discourage people from having children; I had both my kids when I was a postdoc, so if you’re organised then it shouldn’t be a problem – it can be managed. Lots of people do it, so it’s obviously possible.

Are universities providing enough support for scientists with families?

There’s always more support that could be given. I think that one of the major challenges in the southeast of England is the extreme pressure on nursery places that are very expensive. Universities are increasingly encouraged to provide their own childcare – the University of Cambridge has a very small number of such places. Childcare is very expensive, so any kind of incentive that can allow parents to pay their nursery fees out of their gross salary should be encouraged.

I asked you before why you became a scientist. What motivates you now?

Science is inspiring. I think that’s what motivates me – doing science that can transcend the normal desk jobs of this world, to really be inspired by something new, interesting and exciting. I also often get very inspired by going and hearing other people talk. Last week Professor Johannes Walter came from Harvard, and he gave such an excellent, exciting and interesting talk about replication regulation that not only was I impressed by his work, but it encouraged me to go back to the lab and find out something that could be as good as that, and I find that very motivating.

Could you share with us an interesting fact about yourself that people wouldn’t know just by looking at your CV?

I do a lot of gardening, and I grow lots of fruit and vegetables. We had a very big garden when I was a child, and I was in charge of mowing the lawn and doing the gardening, and it stayed with me. I had an allotment even when I lived in London. I’m still fascinated by plants and insects, and growing things, and my kids are quite into it now. It’s becoming a family hobby. They like eating the food more than growing it though.

Video interview

An additional, short video interview with Philip Zegerman is also available, and can be viewed directly here: <http://jcs.biologists.org/lookup/suppl/doi:10.1242/jcs.178145/-DC1> or on the JCS Interviews page: <http://jcs.biologists.org/site/collection/interviews.xhtml>.

Philip Zegerman was interviewed by Anna Bobrowska, Editorial Intern at *Journal of Cell Science*. This piece has been edited and condensed with approval from the interviewee.