Hooke Medal 2014
BSCB Science Writing Prize winner
Meeting reports
When did you first decide to pursue a career in science?
It’s difficult to say exactly but as a child, although I didn’t know what career I wanted to pursue, I knew that I wanted to wake up in the morning and be thrilled about going to work. I had a small microscope as a child and was fascinated by snowflakes: evanescent and so beautiful! I would spend winter afternoons looking down the microscope! My aim in life is not to be bored and science is wonderful for this. Each day you go into the lab not knowing what you will discover and you get to do things that people have never done before.

How and when did you first become interested in protein misfolding?
I went to New York to do a Postdoc with David Ron. This was a very exciting time in my career because we knew that mammalian cells had an Unfolded Protein Response (UPR) but we didn’t know anything about it. So it was a really fun time to discover how cells deal with misfolded proteins in the endoplasmic reticulum. After this, I wanted to move on to look at how misfolded proteins were associated with disease. Although I had worked on the UPR, I had never seen a misfolded protein in a cell; therefore I wanted to look at protein aggregation in cells and how this is involved in disease.

What are the big questions your lab currently focuses on?
The big question we are working on is how can we rescue cells from a failure in protein quality control. As we age, protein quality control starts to decline, leading to an accumulation of misfolded proteins and disease. Therefore, what we are trying to do is to tweak protein quality control in cells to try and boost the cell’s ability to cope during ageing. The way we are doing this is to look for approaches that promote cell survival in the presence of disrupted protein quality control. Cells with disrupted protein quality control die and we are trying to find mechanisms that will keep these cells alive. This is very exciting for two reasons: 1. we are finding novel basic cellular pathways that have not been described before, and 2. we are discovering pathways that in the future could help in the treatment of human disease.

Another big question we are addressing is how do aggregated proteins get into cells? People were initially sceptical about our results in this area but now several other labs are using the assays we have developed and
have made similar observations so it is really rewarding. I am confident that with technical advances we will really crack this question one day.

**What has been your most exciting discovery to date?**

The work we are doing at the moment keeps me awake at night. We have found ways to rescue cells from the lethal accumulation of misfolded proteins. In the future, once we understand the mechanisms involved, this work will be immensely useful for designing new therapeutic strategies to treat disease. So not only is it exciting work, it is also very rewarding.

**You've worked in France, the US and the UK – what are the main differences in the way labs are run? Science is carried out between these three countries?**

From the very start of my career, during my PhD in Pierre Chambon's lab, I realised that science has to be international and that your work has to be internationally competitive to be significant. Because science is international, Strasbourg, New York and Cambridge are all very similar. It is the institution that makes the difference and not the country. The LMB in Cambridge operates in a manner that is similar to how Pierre ran his Institute in Strasbourg. The lab runs on a very communal basis – sharing resources and equipment. This means that we can rapidly evolve from one technique to another to try and find the best way to answer our questions. We use a full spectrum of techniques – from biophysics through to animal models. We will use whatever it takes to answer important questions.

**Did you ever think you wouldn't make it to be a Team Leader and, if so, why?**

I always wanted to lead my own research – that was really my drive throughout my career and being a Team Leader is the way to do that. I still have doubts even now but in science we have to doubt. We have to constantly challenge our judgements and ourselves. I was even talking to a Nobel Prize winner recently; he still had enormous doubts over his competence and his abilities and was still insecure about submitting papers! It's reassuring that everyone has doubts.

**What were the biggest obstacles you've had to overcome during your progression to Team Leader?**

There were definitely bumps on the road. Some bumps bigger than others. But science is always the drive. Pierre Chambon advised me to “Focus on the science”. This has really helped me to forget about the obstacles and difficulties.

**How did you find the transition from being a Postdoc to being a Team Leader?**

Very slow – but for the right reasons. First, I had two maternity leave periods, which obviously slowed things down. I also wanted to define a new research area and develop my niche. I had to spend a lot of time thinking about the direction I wanted my research to take and find important problems worth tackling. So although the transition was slow, it was definitely worth it.

**Who has been your most inspiring mentor and how have they helped you?**

I've always been extremely fortunate to work with very bright people. I have already mentioned Pierre Chambon who has been influential and inspiring. My Postdoc supervisor, David Ron, was also an extremely clever scientist who shaped the way I think and plan my research today. My time in his lab was very inspiring.

**What do you enjoy most about being a Team Leader?**

Everything! We're having a fantastic time in the lab right now. I have a fantastic group who are doing fantastic work and it's very exciting. The lab are generating lots of data and we're having lots of interesting discussions. I also enjoy getting CVs from talented individuals – it makes me feel very honoured that they have applied to my lab. I also find guiding research a lot of fun. I still like to do experiments – when I have the chance. I think it's important not to get too detached from the bench.

**....and the least?**

Paperwork.

**What advice do you have for PhD students when looking for a Postdoc position?**

Follow your gut feeling – don't try to be too strategic. Go where your passion takes you. You have to be driven by passion in science to be successful. On a more practical note, go to a well-funded lab so that you can do the best research. Make sure you will have a mentor who is available and not always travelling, and that the lab are as dynamic as you because this will also drive your science forward. It's also a good idea to have two projects – one more risky and one "safer" project but you have to be careful not to get too distracted.

**What advice do you have for Postdocs who are looking to become independent?**

Get yourself known. Don't be shy about going out and talking to people in your field about your work and what you are doing. You want people to know you and your work. Lots of people are very happy to give advice so if there is no one in your institute who can help then look outside for advice. It's also good to get advice from people at different stages of their careers.

**How do you spend your time outside the lab?**

I have two children and so I balance my work with family time. Sometimes the balance isn't always right and I have to reset it. I also try to spare some quality time for friends, rare but precious. I also love cooking. I think it's important to balance an active, demanding job with physical activity so I also like to kayak and go to the gym.

**Any other advice for young scientists?**

I always feel rather flattered when I'm invited to graduate student symposia. It means that our work has gone from the bench to PubMed and back out to students. It's very exciting. What I've found is that many PhD students worry about the future, about the uncertainty in science and how their career will progress. I say be fearless! There is no reason to be afraid. You shouldn't be afraid to move. Go where your science takes you and follow your gut feeling. You have to be willing to invest yourself in the things you believe to be important and then I think you can't fail. Being a Team Leader is such a nice career – we can do what we want! It's a very exciting job.