

CELL SCIENTISTS TO WATCH

Cell Scientist to Watch – Jeremy Carlton

Jeremy Carlton received his Bachelor's degree in Natural Sciences from Queens' College, Cambridge, and moved to the University of Bristol for a PhD in Biochemistry with Pete Cullen, working on endosomal trafficking in mammalian cells. He then joined the laboratory of Juan Martin-Serrano at King's College, London, for postdoctoral work studying the role of ESCRT proteins in HIV-1 release. He was awarded a Wellcome Trust Research Career Development Fellowship and moved to the Division of Cancer Studies at King's in 2012 to establish his independent research group. In 2017, he became a Wellcome Trust Senior Research Fellow and EMBO Young Investigator and moved his laboratory on secondment from King's to the Francis Crick Institute, London. His research is focused on organelle dynamics during mammalian cell division.

What inspired you to become a scientist?

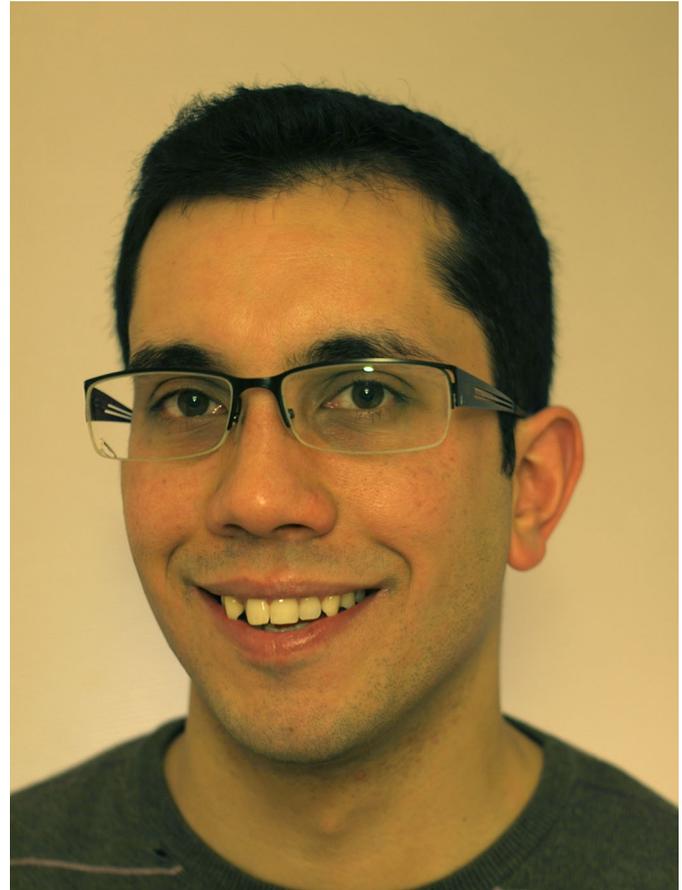
My mum was an immunologist who worked at the Chester Beatty labs in London and my dad was an aeronautical engineer. I grew up in an environment where we loved finding out how and why things work and becoming a scientist felt like a very natural progression. However, for a long time, I was determined to be a physicist or a chemist, and I only moved into biology when I realised I couldn't understand the physics or the maths [laughs]. At this time at university, I remember thinking back to when we were at school and how much I loved dissecting things like the heart or the lungs and learning about how these organs functioned inside our own bodies – this pushed me back to biology.

Rather than organs or tissue organisation, you're interested in subcellular processes such as cytokinesis or intracellular trafficking. How did this curiosity evolve?

During my pharmacology lectures, Michael Edwardson (University of Cambridge) gave a lecture that included a discussion of endosomes as sorting organelles, and that concept really clicked for me. I thought it was fascinating that cells had this internal sorting machinery, but I also loved membranes and at the time was toying with undertaking a PhD with Robin Irvine (University of Cambridge) who was working on phosphoinositides. Just as my degree finished, one of Robin's ex-postdocs, Pete Cullen, posted a flyer to recruit a PhD student in Bristol and I thought this would be a really fun thing to do. I was lucky enough to get an offer and it was when I got to Bristol that we started working on endosomes and everything came together.

And did your PhD work lead you automatically towards the endosomal sorting complex required for transport (ESCRT) machinery?

Pete was a great advisor and one of the things he did at the end of my PhD was to give me a bit of time to really think about what area I wanted to move into. While I was studying the role of sorting nexins during my PhD, the ESCRT machinery, which does a really



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important bit of endosomal sorting, was discovered by Scott Emr's lab, then at UCSD. ESCRT biology was something I found fascinating and I was also hooked by the fact that virologists had discovered that HIV hijacked ESCRTs in order to bud out of cells. At the time, I was absolutely desperate to be an HIV biologist and focussed my postdoc search in this area. I managed to get a great postdoc with Juan Martin-Serrano in London and although we did a bit of work on viral budding, we went on to discover that ESCRTs were also needed for cytokinesis, the final stage of cell division.

What questions are your lab trying to answer just now?

When I set up my lab, I began thinking about other cellular events that ESCRTs might be involved in and we actually stumbled upon the role of ESCRTs in nuclear envelope regeneration. This is a really important aspect of rebuilding the nucleus during mitotic exit that makes sure that this organelle is properly sealed and compartmentalised. In my lab now, we're still looking at ESCRT-dependent nuclear envelope regeneration and repair, and are trying to understand how ESCRTs are switched on at the right time and in the right place to regenerate this organelle. We are trying to unpick some of the signalling pathways that may control ESCRT assembly and explain why assembly is confined only to the nuclear envelope and does not occur in the peripheral ER. We are also looking to

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Members of the Carlton lab at the ASCB-EMBO conference 2019. It's important to attend all of the sessions, even the party ones in the Smithsonian Museum of Natural History!

understand how ESCRT proteins can bind to membranes and we want to generate some structural information on how that ESCRT–membrane interaction occurs. Furthermore, related to cell division, we are interested in how other organelles are properly distributed during the division process and reassembled in daughter cells. I think a lot of cell division research has been focused on the cytoskeleton; in the future, perhaps more emphasis will be on how cells deal with organelles during this process.

You mentioned that you stumbled upon the role of ESCRTs in nuclear envelope reformation – was that serendipity?

When I started my lab, we were working on something completely different – whether ESCRT proteins protected against cellular transformation. Unfortunately, that project wasn't going very well. I had always hoped that ESCRTs were involved in nuclear envelope reformation, but could never see it – it turns out that nuclear envelope assembly persists for about 3 min over the whole cell cycle. Then, in a lab meeting, my postdoc put up a picture of a field of view of cells and there was one cell that was just in the right phase of the cell cycle and we could see a few dots of ESCRTs around the nucleus. It wasn't what we were focusing on at the time, but it was there. From then we knew exactly the cell cycle phase to target and when to start the movies. Maybe 'stumbled upon it' is the wrong word; it was a hypothesis we had generated and hoped would happen, but we struggled to visualise it for quite some time.

It's still a good example of how it's always worth looking at all of your generated data and in an unbiased way, right?

Yes, it's a very important point. We do a lot of microscopy and I really want my trainees to look at all of their cells and get a real feeling of how their cells and their labelled proteins actually behave. Hopefully they will then be able to pick up differences, spurious

localisations or things that they can't understand. Oftentimes it is that strange or odd localisation that leads to really exciting discoveries. It was the same in Juan's lab when we found a role for ESCRTs in cytokinesis: it was an 'oh my word, what are ESCRTs doing at the mid-body and why are there so many nuclei in my knockdown cells?' moment!

What has been the most influential publication or work in your field recently?

Recently, we have been influenced in our thinking by the work of Adam Frost (UCSF) and Patrick Lusk (Yale) who identified interactions between ESCRT proteins and a family of inner-membrane proteins. This has led to a lot of new and exciting biology that we don't really understand and has opened up a new avenue in our research and caused us to think about these ESCRT proteins as much more than just cytoplasmic regulators, but also regulators of nuclear biology.

What challenges did you face when starting your own lab that you didn't expect?

I remember being, well, a little bit terrified. There was nobody to go to, whether you had a problem or an amazing blot; you only had yourself to tell about it. A real challenge was learning how to manage people and how to get the best out of them. I suspect this true for many, but learning that everybody is different and you need to work out different ways to get the best out of different people is a big challenge of the role.

How are the challenges that you're facing now different?

They have changed a bit in that the lab has grown, so it's harder for me to be as hands-on with projects and I need to try and take a step back and think more strategically about what people are doing. In this phase, it's about balancing the workload and trying to manage all of the different responsibilities at King's and at Crick.

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Are you still doing experiments yourself?

Yes, I try to be at the bench most days! Maybe my time management issues would be solved if I did a little less lab work, but I really love bench work and I'll happily nip in to do some cloning, PCR or microscopy. Nowadays I can't really run any projects myself but I can jump in and help students who are struggling with aspects of their experiments, or prepare tools that might be useful for the lab.

What is the best science-related advice you ever received?

Both Pete and Juan were amazing mentors; they created an environment where science was fun and exciting and where you could break down discipline boundaries – I would love to replicate that in the work that we do. As for advice, Simon Bullock (MRC LMB, Cambridge) told me once that in order to be successful, you just have to “find something that no-one else is doing; do that and do it well” - a good strategy that sounds easier than it actually is. However, the advice I found most useful was not science related: it was an interview in the business pages of the Evening Standard. I normally skip straight over these pages, but there was a quote in big letters that said: ‘The main thing is to keep the main thing the main thing.’ It sounds really trite, but that phrase stuck in my mind and

when I get distracted by other calls on my time, I find it really useful to keep going back to that mantra!

“...find something that no-one else is doing; do that and do it well...”

When asked in a recent interview who you look up to, you mentioned your wife, a lecturer in ancient history at Royal Holloway. Could you tell us more about her?

In the life sciences, you are very rarely exposed to how the humanities side of universities are run. This is a system with lots of PhD students, but with few opportunities for postdocs, few open faculty positions, and without the degree of research support and funding that is enjoyed in the sciences. It's been an amazing journey to see her move from PhD student to hourly-paid teaching fellow on short-term contract after short-term contract in different universities,

to eking out an independent line of enquiry for herself that she managed to turn into a research grant, and now a monograph and a faculty position off the back of that! Her persistence, perseverance and ability are really inspiring.

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

Related to the above: my wife and I spend many of our holidays on archaeological digs because that's the 'research' part for her. She needs to go to these ancient Roman sites and explore them, so I have a very good knowledge of the street layout of Pompeii and Herculaneum [laughs]. It's an amazing break from my own research – I can switch off completely and just concentrate on taking photos and measurements on a different scale.

Jeremy Carlton was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.