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CELL SCIENTISTS TO WATCH

Cell scientist to watch–David Bryant

David Bryant studied music composition and biological science at the University of Queensland, Brisbane, Australia, and graduated with a BSc in biochemistry. He pursued his PhD in the laboratory of Jennifer Stow at the Institute for Molecular Bioscience with a focus on cellular trafficking mechanisms for E-cadherin. David then moved to San Francisco for his postdoctoral work on apical polarity establishment in a three-dimensional context in the laboratory of Keith Mostov. After an NIH Pathway to Independence (PI) award in 2012, David moved to the University of Glasgow, where he established his own research group in 2014 at the Cancer Research UK Beatson Institute. His work focuses on collective cell polarity in 3D tumours, and how the gain and loss of polarity influences development, as well as cancer invasion and progression.

David Bryant

What inspired you to become a scientist?

My interest is in problem solving. At university I studied science and music composition. Although they might seem disconnected, they're really different sides of the same coin. You try to compose something from scratch and there's no manual how to do it. Problem solving is trial, error and a lot of patience. Slowly, the parts that make up the whole unravel and you put them back together into something that is more than the sum of its parts – whether that's music or biology, to me, that's always been endlessly fascinating.

Moving from Australia to San Francisco in 2006 to work with Keith Mostov – do you feel like you hit the right note at the right time?

Yes, I wanted to know how cells work in the context of an organism and, at that time, among others, Keith was pioneering 3D cell culture to understand cell polarity. We jokingly say that Hans Clevers' (Utrecht) work has made a flat world turn round – 3D-culture studies have really exploded in number since his seminal work on intestinal organoids. For someone like myself and others, who were in the labs of Keith or Joan Brugge (Harvard), toiling away on 3D cultures, it was satisfying when everyone started to see the light.

What questions are your lab trying to answer just now?

We want to understand how cells behave collectively and how this is important for tissue development and also for dysregulation of polarity in cancer. Despite the popularity of 3D cell culture, there are still a number of challenges, such as the added complexity of having many cells instead of having one, that change and grow over time. It's important to understand the dynamics of how multiple cells are behaving all at once. In addition to this, there is extreme heterogeneity in the way that 3D cultures work. These might seem like problems on the surface but I actually think they're clues to the biology. In my lab, we've developed tools for image analysis, 3D culture and data mining that allow us to manipulate, film and analyse 3D cultures in massive parallel numbers. With good tools and large sample numbers we begin to unravel how the complexity and the dynamics of the way cells change over time work, and how this might contribute to development or cancer.

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Which aspects of your work have you found particularly challenging?

When you're trying to do something new, the onus is on you to make other people understand why it is important. A lot of the time in biology, we want a simple answer: is the average of one population different to the average of another population? We're obsessed with the mean or the median but maybe there are lots of different sub-populations, each doing interesting things. Therefore, the hardest challenge for us has been – because it is more difficult – getting people to believe that we shouldn't just take the average as a representation of everything. Instead, we need to look a little deeper: is there heterogeneity and, if so, is it important?

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Dave out with his dog Lucy, enjoying a sunny day and the lovely Scottish scenery.

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

For me, the most influential work recently has been coming from advances in single-cell technologies and applying it to multicellularity. I'm straddling a couple of new fields and I'm learning so much from what has been published in single-cell sequencing, flow or mass cytometry and immunology. If we treat each spheroid or organoid as a single object, there are a lot of parallels in the technology that has been developed to deconvolve heterogeneity in other fields.

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

I was quite young when I finished my PhD and I decided I wanted to do a long postdoc to feel ready to be responsible not just for my own career, but for the careers of other people. At UCSF, there were a lot of opportunities to develop non-bench, soft skills in science. I spent some time trying to develop these skills and in combination with a long postdoc, I felt that I had a little bit of a head start in what I thought being a group leader would be like. But the theory and actually doing it are two very different things. I'd say that the biggest challenge initially – despite having fantastic support at the Beatson – was that it's very daunting and hard to accept that you have to make choices without being sure about most of them. But with time you realise that you can only make the best decision you can with the time and information that you have and, with experience, you begin to accept that. Also, at the very beginning of your career, it's difficult to assess how long different tasks take and how quickly you can work on several things. Therefore, you can't be realistic about saying yes and no to things until you've got that rhythm but, I guess, the point is it comes eventually, you just have to keep going.

Are you still doing experiments yourself?

I don't do a lot of wet lab bench work anymore; instead I help with computational work, such as image and data analysis and programming. This is really just to be an extra pair of hands to the projects in the lab whilst maintaining my other commitments and work schedule. I try those things we're not really sure are working, because it frees up people in the lab and allows them to do the experimental part. Once I've figured out the computational stuff, then I hand it over to the lab and they can use it.

How do you deal with experimental roadblocks or mistakes being made in the lab?

This is an interesting point you bring up because another big challenge that you face as a new group leader is that you think your students and postdocs are just a logical extension of how you would do things, but it is not necessarily the same for somebody else. The upside of this is of course that you'll form synergies but, initially, you must have a lot of patience as other people grow and learn. I have a fairly easy temperament about it – the point of working together is to work together, not in a vertical hierarchy. So I often giggle and laugh when people make mistakes, because it breaks the ice and you learn from those mistakes. I encourage people to make mistakes – not too often and not too expensive – but in ways that allow them to learn.

> "…it's instrumental to find somebody who will mentor you and look after you during the transition to independence."

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

Before I had my own lab, I spoke to as many people as possible at different career stages to try to find out what the commonalities between their advice was. I think that the best advice came from Lucy O'Brien at Stanford, who was in Keith's lab before me. Although we didn't overlap, she was really instrumental in helping me transition from postdoc to group leader. The point that really stuck with me was that, if you want to do science as a career, you're going to have to network, to market your research. Make sure your passion for what you're doing is shared with others. My advice I'd put forward to people about to start their lab: it's instrumental to find somebody who will mentor you and look after you during the transition to independence. This may not be your postdoctoral advisor or your PhD advisor, it might be someone who was a postdoc a couple of years before you – just like Lucy in my case. Someone that you can bounce ideas off and you're not afraid of telling 'I don't know what I'm doing, can you help me?', is really absolutely crucial in making the jump.

What is your advice on establishing good collaborations?

It's a fragile thing to transition encounters at conferences and exchange of ideas to a productive collaboration; one has to make very sure that the objectives of both people involved are on the same track. It isn't always the case, and that's just normal and natural. I think you have to choose collaborations where you almost get an emergent feature, where each part separately will only be better by combining them. Of course, as a junior group leader, that's a tricky

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balancing act because you need to be generally the senior author, and you need to not dilute the efforts of your people and their careers. I don't have the magic formula for how to do this well. Here at the Beatson, we're a highly collaborative institute and it's set up in such a way to foster collaborations, so I'm very lucky that it's very easy to do in-house.

How do you get the most out of the meetings you attend, particularly in the early stages of your career?

Many of us suffer from imposter syndrome where we think, 'oh, I'm not really sure how I got here'. And the untruth to imposter syndrome is assuming that everybody else doesn't feel the same way. Once you accept that we're all the same people in the same boat, just trying to work out science as best as we can, it breaks down some of this barrier. It's then much easier to chat to people and say, 'hey, this is where my research is at, this is where I'm going and these are my ideas, what do you think?', rather than having to show up and present yourself as the most polished person with all the answers. I give a talk here at the Beatson every year to postdocs about the transition to independence and most people are surprised when I tell them that I'm actually painfully introverted and very, very shy. Because I want to share my passion for science I force myself – and it gets easier every single time – to be as interactive as I can and to become more extroverted. It's absolutely surmountable and that's what I try to tell the postdocs: be open and honest and that will become infectious, even if you feel like being quiet and shy.

How do you achieve a work–life balance when you're trying to establish yourself as an independent investigator?

That's definitely a work in progress. I have a wonderful, patient, supportive and accommodating partner who helps me right the boat when it starts to rock too far one way or the other. This is inevitably the case for work; as said earlier, in the beginning you don't really know how long things will take and you want to say yes to as many things as you can. To me it's like walking under Niagara Falls – if you keep walking, eventually the waterfall will stop. I personally try to work no more than 9 hours a day, 5 days a week. Whereas that's not always possible, to completely switch off from work is really important in recharging. I play the piano and go to the gym a lot and I try to take my dog for walks at the weekend, just out in the country to get away. I'm very regimented now about having uninterrupted non-work time and that way, I find that I work smarter, not longer.

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

I'm fascinated by languages – ever since I was a little kid I wanted to be a diplomat at the UN, speaking as many languages as possible. That didn't quite work out because it turns out I'm not so great at languages! But science might be a way to get back to my original dream career; by trying to take sabbaticals in countries where I can speak the languages, I could brush up on new science and improve old language skills. Another funny thing about my career choices: when I was at a juncture point between choosing music and science, I chose science over music – because I didn't think I had the resilience to face the rejection of being in the music industry. I guess when I took that decision I did not quite have a realistic picture of what science would be! [laughs]

David Bryant 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.