

Talented emerging scientist.. John Grainger

1. How did you become interested in research relating to your area?

The area that my group is currently most interested in is defining key mechanisms by which different bodily organs communicate to develop an appropriate immune response – what you might call inter-organ immunology. This is an area that I've been interested in for the past few years since starting my group but it's been a stepwise evolution throughout my PhD and postdoc to get to this point. My initial



training was in immunoparasitology at the University of Edinburgh with Prof. Rick Maizels and was focussed on understanding how gastrointestinal worms manipulate the host immune response. Although, I grew to love worms I also became fascinated in immunology and, given that worms live in the gut, the gut immune system. So for my postdoc I moved to Dr. Yasmine Belkaid's lab at the National Institutes of Health (NIH) in the US to work on more basic mucosal immunology questions and specifically to understand the factors that control innate cell function during gut infection. It was during this time that one of my studies led me to understand that many of the features that are typically attributed to factors the immune cells experience in the gut are in fact due to previously unappreciated signals they experience while they're developing in the blood and bone marrow. It's this novel concept of long-range signals sent out to the blood and bone marrow from the inflamed organ, such as the gut, that the group is now largely focussed on.

2. Describe your research & the program/lab that you are in?

The research in my group aims to utilise experimental parasite infections in mice along with patient samples to understand inter-organ communication following immune activation. We use a variety of approaches to do this including flow-cytometry, immune cell sorting, in vitro primary cell culture and genomewide transcriptional analysis. At this time we're particularly interested in one-type of immune cell – the monocyte. It develops in the bone marrow but ultimately is recruited to almost all sites of inflammation and injury and we've found, for example, that very early after your gut is infected long-range signals from the gut can go back to the bone marrow to instruct the function of developing monocytes. This wasn't previously understood. There are lots of different signals that we're now actively working on. Obviously, those that are coming from the immune system but also nervous system signals and also those derived from the commensal bacteria in the gut that become altered during parasite infection.

3. What makes you unique – why, of all applicants, do you think YOU got funded?

I think that part of what makes me unique is my initial training in immunoparasitology. As I've started to move into different disease areas, particularly inflammatory diseases, I think my parasite history gives me a different viewpoint to those coming from a more traditional immunology or autoimmune disease background. Because parasites have co-evolved with their host my first exposure to the immune system was not in thinking about how it can go wrong but how it works in

an appropriate way – it seems to me that far more peoples' training begins at the opposite starting point, in terms of thinking about what happens in negative disease states. One thing that's also clear about parasites is that the immune response towards them is highly contextual depending on the parasite and the organ it infects. I think in the era of personalised medicine having a strong understanding of heterogeneity of immune responses has really held me in good stead.

4. Obviously it depends on the project, but in addition to this how much do you think is dependent on the presentation you did and the place in which you are doing the project?

I think that the presentation and place matter hugely. Given the current highly competitive funding environment the interviewing panel will probably have several excellent candidates. The presentation is, therefore, key in providing another opportunity for you to get across the importance of your research and show the panel that you're a dynamic individual who has the focus and enthusiasm to deliver it. However, I think no matter how exceptional your presentation and project is the interview panel is also aiming to understand whether you can achieve the goals of the study in the place you're located. From this perspective, at least for my work, being based within the Division of Infection, Immunity and Respiratory Medicine at the University of Manchester has been ideal. The decades long excellence in parasite immunology at the University of Manchester along with the unique opportunities for furthering inflammation research provided by the Manchester Collaborative Centre for Inflammation Research (MCCIR) has meant that the environment has always been perceived by reviewers as exceptional.

5. Describe your unforgettable (proudest) moment in science, and the most challenging situation that you have had to overcome (lessons learnt) so far?

If I'm allowed, I think I have three moments that I'm equally proud of. The first was publishing the results of my PhD. In my studies, I found that worms secrete a mimic of a host cytokine, TGF-beta, which modulates the immune response. It had been hypothesised for many years that parasites may do this but it felt like such a privilege to be able to be the individual to finally demonstrate this. The other moments I'm particularly proud of are being awarded independent fellowships from the Wellcome Trust and Royal Society and then The Kennedy Trust. The time and effort in terms of writing and preparing for interview for these fellowships is huge and when you get them it's just so exciting to think that you'll be able to carry on doing the research that you think is so critical for at least the next few years. In terms of challenging situations, I think one of the most challenging has been balancing career decisions with my wife, Joanne Konkel (another group leader at the University of Manchester) to ensure that we both have the opportunity to pursue our personal career goals. To some degree this is all about finding a compromise that suits both parties but obviously in the competitive world of science this can be difficult. Getting suitable postdocs for both of us was probably the hardest example of this. We decided up front that there was no way we wouldn't be living in the same city and so restricted our applications to large institutions where we were likely to both find positions we were happy with. Ultimately, this led to us moving to the National Institutes of Health (one of the largest research institutions in the world). I think the lesson I learnt from this is that forward planning is sometimes absolutely critical, we had to figure out postdocs almost a year in advance and I just don't think we could have come up with such an optimal situation if we hadn't have been so focused for such a long time getting two excellent positions. Unfortunately, I haven't necessarily learnt to apply this lesson to all areas of my scientific career – as my lab well know!

6. Where is your biggest stress at this stage of your career?

I think the biggest stress is managing the transition from running a solo research project to managing a group. As a postdoc you don't really get a lot of management experience and then suddenly you're thrown in at the deep end managing several individuals. Not only have you got to rapidly figure out how to keep on top of several distinct topics but you've also got to figure out the best way to support each individual. When you've got enthusiastic and motivated staff and students what you want to do is ensure that you're doing the best you can for their future careers and this feels like a huge responsibility. Finding additional grant funding and maintaining your publication output are pretty big stresses too.

7. What area(s) do you wish to specialise in in the future?

Obviously there are a lot of different areas that my group could investigate based around the concept of organ communication during an immune response but we're currently focused on pushing forward with a few main themes. We're particularly interested in the ways in which organ communication can become aberrant in disease states. This has led to exciting grants being awarded with the Division of Neuroscience and Experimental Psychology investigating altered immune function in stroke and most recently I was awarded a Senior Fellowship by The Kennedy Trust for Rheumatology Research to work with the Division of Musculoskeletal and Dermatological Sciences establishing the importance of organ communication in rheumatoid arthritis. In general, I think that one of the great things about the University of Manchester is how keen people are within the Faculty to interact on inter-disciplinary projects and I'm sure this will mean in the future we'll be developing a lot of unexpected new projects.

8. What would be your advice for talented emerging scientists?

I think that if you're a talented scientist who wants to pursue a successful career in science you need to figure out quickly what your main exceptional skills are and how you can use them to ensure you have the opportunity to study the research topic you're enthusiastic about. Science is not done in a bubble and there are lots of different types of individuals that run brilliant labs with very different personality types and management styles. For me, I find that my thinking is very influenced by the people who are around me and one thing that has been critical is identifying scientists that I can learn from and who can be advocates for me in supporting my future career. Many of whom are now based here at the University of Manchester.