

Cellular Microbiology Interview – Dr Duncan Wilson

Duncan Wilson

Introduction

Duncan did his PhD with Dr Lubomira Stateva at the University of Manchester on the role of phosphodiesterases in *Candida albicans* physiology, and then continued his Post-Doctoral research at the Hans Knoell Institute, Jena, Germany with Professor Bernhard Hube. Duncan moved to Aberdeen in 2014 and is a Henry Dale fellow there. He is interested in how pathogenic fungi compete with their hosts for essential micronutrients and is using a combination of molecular and cellular biology, together with models of host-pathogen interactions, to dissect the mechanisms of micronutrient assimilation by the major human fungal pathogen, *Candida albicans*.

1. What is your research background - what did you first start working on at the beginning of your academic career?

I studied Microbiology at Glasgow. Although this was mainly bacteria, I managed to land an Honours project with Julia Douglas - one of the legends in *Candida* biology - and do some cool experiments on *Candida albicans* biofilm formation; and a summer placement in fungal clinical diagnostics with Gillian Shankland. After that it was straight down to Manchester for my PhD with Lubomira Stateva on cyclic AMP signalling in *C. albicans*. This was an industrially sponsored PhD and I spent half a year even further down in Pfizer, Kent, with Tim Young.

It was then off to Jena, Germany, to post-doc with Bernie Hube. When I was writing my thesis, his name was popping up on so many good papers. I thought it was pronounced Hube. Turned out it's pronounced Hube. Moving away to Germany was obviously a big decision, but one of the best I've made. Landing a great mentor, wherever that may be is a *huge* plus. I'd say that a stint in another country is a great part of developing your career.

2. Have you always wanted to work in academia?

I had no idea what I was going to do with my life. So, I went to University. Thankfully ended up doing Microbiology which I liked a lot. I was also pretty lucky to get academic, clinical and industrial experience in mycology early on in my career. So, by then, I knew I wanted to become an academic researcher.

3. How has your early work brought you to what you are working on now?

I've been working on the human fungal pathogen *Candida albicans* since day one. So that's an obvious one. But the reason for studying micronutrients? My post-doc advisor, Bernie Hube, said - work on this protein Pra1, because it's got potential zinc-binding motifs. I thought, that sounds like the most boring thing in the world - but then I started reading about micronutrients and nutritional immunity, which turned out to be really interesting with lots of implications in fungal virulence.

Then I discovered a novel system that *Candida* uses to scavenge zinc. Basically, the fungus releases a zinc binding protein which sequesters the metal, supplying it back to the cell for assimilation and growth. I called this the zincophore system and, based on evolutionary studies, it looks like many more fungi might employ it.

For me, this was a turning point because it was when I realized exactly what I wanted to focus on. Before that I felt like a bit of a Jack of all trades, master of none (in the field of *Candida* pathogenicity mechanisms anyway).

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If I could offer any advice it would therefore be to find your own niche within your field; something you really like, and that you can develop. I decided to base my independent career on micronutrient uptake. I probably spent at least half a year planning out, with notebook, pen and pint, where I thought this field should be going before I put fingers to keyboard and wrote my Fellowship application. I landed a Wellcome Trust Sir Henry Dale Fellowship and moved to Aberdeen to start my own group. That's been four years now, and it's turned out well: I've built my team, found out lots of interesting stuff about fungal micronutrient homeostasis and published a good few papers on my discoveries.

4. What first attracted you to your field?

As I was saying, my Honours degree was almost all about the world of bacteria. But there were a couple of lectures on medical mycology that fascinated me. The first time I saw *Candida albicans* hyphae, I thought - that's for me.

5. What do you think the most interesting questions are at the moment in fungal micronutrient assimilation?

There are many. There's been a lot of great work done on iron (by Daniel Kornitzer and Hubertus Haas for example), but apart from Jose Calera's work in *Aspergillus*, not much was known about zinc in other fungi. Zinc is really important for eukaryotes like fungi, and ourselves. This is because almost 10% of their proteins need zinc to function. You name a cellular process, there's a very high chance zinc is involved.

When it comes to cellular assimilation, it's all about the pH (acidity) of the environment; but, with fungi being eukaryotes, probably the most important thing is intracellular storage and mobilization; and that's what my group are working on now. I've found that *Candida* can store really high levels of zinc within intracellular organelles and use these reservoirs to grow when zinc becomes limited.

This is extremely important because it means these pathogens may be completely immune to nutritional immunity; bringing a packed lunch to the infection.

6. Where do you think fungal microbiology is headed in the future? What do we need to be thinking about?

Fungal pathogens are either environmentally acquired, or are commensal colonisers. I think that understanding how these species have evolved in their natural (non-pathogenic) habitats will be key in recognizing, and exploiting, their strengths and weaknesses.

Aside from that, probably the most important thing is getting more people to appreciate their true medical importance - it is underappreciated that fungi kill more people than malaria (by a long way), and about the same as TB; yet this is not even known by many microbiologists.

7. What do you enjoy the most about your work? And what about the least?

Everything, apart from... admin. I really like scientific debate, coming up with new ideas. And there are few things as satisfying as making an observation for the first time.

8. Academia is known for being challenging in terms of high workloads and long hours - how do you strive to achieve a work-life balance?

I'm pretty lucky at the moment as I'm a Research Fellow, so I can focus on that. I enjoy having the time to develop my field.

9. What has been the most surprising result you've had in your career so far?

Two things. The first is our discovery of candidalysin. I really thought that invasive *C. albicans* filaments would inherently damage host cells. Not so. It's the toxin. We published that two years ago in Nature.

The other was based on careful observation, and a bit of luck: the first observation I made in my PhD was that a *C. albicans* cyclic AMP signalling defective mutant exhibited a weird colony

morphology on agar media. I called it the “popcorn morphology”. Over ten years later, my Honours student showed me the exact same colony morphology with a zinc homeostatic mutant we’d made. Maybe this is a coincidence, but it turns out we’ve been able to start mapping the regulatory pathway governing intracellular zinc homeostasis pretty accurately, based on these two apparently pretty random observations. Keep your eyes open!

10. What advice would you give to other early career researchers starting out in their career given your experiences?

Do what you want to do, but frame your question within a field which is a current hot topic. Collaborate - both ways - it will either make your project better or will get you an easy co-authorship.

When it comes to the transition from postdoc to academic independence (if that’s what you want), go for that next stage when you’re ready for it - most funding agencies have lifted the eligibility cap thing. So don’t rush it.

11. What has been your most rewarding experience so far? Why?

After becoming a PI - building a group. I’ve been really lucky to recruit an excellent team of PhD and Masters students that’re a pleasure to work with. Having fun with fungi and zinc.

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