

## Interview with the Guest Editor – Derek Walsh

Derek Walsh obtained his PhD in cell biology at Dublin City University (DCU), Ireland, in 2000. After a brief stint as a postdoc at Columbia University, he then joined Ian Mohr's lab for a postdoc at New York University (NYU) School of Medicine to study translational regulation in herpesviruses and poxviruses. He received a Science Foundation Ireland (SFI) Investigator Award to move back to Ireland and establish his own research group in 2006. However, the financial crisis and withdrawal of support systems from SFI forced him to close his lab in 2011. He returned to New York where his former mentor, Ian Mohr, took him back under his wing and helped him rebuild his career over the next 3 years. Despite Hurricane Sandy devastating the lab at NYU in 2012, just like the herpesviruses he studies, Derek is not that easy to get rid of. In 2014, he was recruited to Northwestern University, Chicago, where he reestablished his own research program and became Professor in 2019. His research has revealed mechanisms by which poxviruses regulate translation, taking control of the ribosomes and signalling pathways of the host. Another line of research in his lab has shown how herpesviruses use microtubules to control cellular architecture.

### What are your research interests?

We are broadly interested in how large DNA viruses take control of host cell functions to replicate, and our projects break down into two main areas. In the first, we are interested in how poxviruses take control of host ribosomes to regulate protein synthesis, both by directly targeting ribosomes and through regulation of upstream signalling pathways such as mammalian/mechanistic target of rapamycin (mTOR). In the other, we are interested in how herpesviruses use microtubules to regulate both intracellular virion trafficking and, more recently, how they control nuclear polarity. During this process, we observed that the herpesvirus cytomegalovirus causes a strange phenomenon whereby the nucleus rotates, and this subsequently got us interested in how cytoplasmic microtubules control events inside the nucleus.

### What attracted you to the field of DNA viruses?

Growing up in Ireland I read about Ebola outbreaks that were happening in Africa in the 1990s, which prompted me to read the book 'The Hot Zone' and sparked my interest in viruses. There weren't any real opportunities to study virology in Ireland and I was interested in living in another country anyway, so after doing my PhD in cell biology I moved to New York to work on viruses. During my PhD, I worked on mRNA translation and realized that aspects of translation were widely studied for RNA viruses, but there were interesting gaps in knowledge in the DNA virus field. I noticed that Ian Mohr at NYU School of Medicine was doing some really interesting work on herpesviruses in that general area, so I reached out to him and ended up joining his lab. Ian is a truly amazing mentor, super smart and open to new



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projects, so we explored several herpesviruses and he helped me to branch out into poxviruses as I transitioned to setting up my own lab. Not only did Ian save my career after the fiasco of Ireland, I learned a lot in his lab that really shaped me as a scientist and ultimately as a mentor. Working with him also solidified my path to focusing on DNA viruses even though we now do quite different things.

### Viruses can hijack and control cells in many ways; is there a particular mechanism you find most fascinating or would like to investigate in the future?

Absolutely, too many to count and many of them are fascinating, well beyond our own specific research interests. There are lots of things I wish we could dig into, but we focus on viral control of ribosomes, mTOR signaling and nuclear architecture. The things that viruses do to cells to replicate are pretty astonishing at times and they teach us so much about cell biology; I'm not sure if I'm a virologist or a cell biologist who just lets viruses teach me how specific cellular functions work. While we know where we want to take our current research, I'm not sure what other areas we'd like to investigate in the future. I tend to be quite open to new postdocs or students bringing a new idea or technique into the lab, with my job being an advisory 'devil's advocate' (and financier, of course), so that can change our directions quite unexpectedly. But that keeps us on our toes, it's fun and keeps our research fresh.

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Derek and his wife getting some sun along the riverfront in Chicago, near their apartment building, during the pandemic.

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**Recent work from your lab applied automated cell imaging and AI-based image analysis to reveal how viruses can control the nucleus. How do you see artificial intelligence shaping cell biology research in the future?**

Oh, boy, I’m not sure where to even start on that one. From DeepMind’s recent progress in predicting protein structures down to the simpler (relative to DeepMind) applications we used to analyze complex imaging data sets, there is so much that AI can do in both a predictive and analytical sense. And I’m sure there’ll be lots of other things it can do, too. Although, to me at least, it won’t replace the need to scientifically validate what it predicts or outputs from analysis, but it will be a very powerful addition to our scientific toolkit.

**Why did you accept the invitation to become a Guest Editor for Journal of Cell Science?**

Michael Way [Editor-in-Chief of Journal of Cell Science] is the simple answer. I’ve never acted as an editor before and it seemed like an interesting challenge. Michael is a great guy and I’ve always been a fan of his work. We met at a poxvirus meeting in Taiwan and an ASCB meeting in San Diego and after that, when he asked if I’d do this, of course I said yes.

**Do you feel you learned something with regards to the relationship between editors and authors in your Guest Editor role?**

A lot, yes. From the editor’s perspective, I realized how hard it can be at times to find reviewers and get reviews back in a reasonable timeframe. I know many of us, as authors, get really frustrated at long review times, which is a real problem when you are anxious to

get your story out there and the submission-to-publication process, even on good papers, is incredibly long. We often blame the journal or editor, but I realize it’s not as straightforward as that. From the author side of things, I think it’s really important that editors listen to authors as well as reviewers, and for reviewers to start considering what is truly needed for a paper to be scientifically sound and acceptable for publication. All too often editors listen to that one very vocal negative reviewer and simply hit the ‘reject’ button on what is in reality a good paper at its core. And all too often reviewers feel they have to ask for experiments, even if the paper is already a solid story. Often the experiments asked are of specific interest to the reviewer but not the authors, and not essential to the validity of the findings. In our journal clubs we talk about the figures ‘the reviewer asked for’ as they are often glaringly obvious sidetracks. I really think reviewers need to be able to detach from this thinking and accept that sometimes a paper is just good as is. I’ve seen this once or twice and it is so refreshing. I also think the pandemic, with limited lab access, has introduced these ideas more broadly, which is great and hopefully it sticks.

**The past year has obviously been defined by the pandemic. Do you feel that a silver lining has been that the public’s understanding about viruses – and their appreciation for virologists – has grown?**

Yes and no. Funnily enough, I live in a very large high-rise in downtown Chicago and I’ve been helping our condo board to consider safety procedures in common areas such as lifts (or elevators as I now have to call them), and that’s definitely triggered some “huh, now I’m glad people do research on viruses”-type responses. In many cases, I think there is a greater appreciation of what virologists actually do, and hopefully that will also trickle up to open-minded policy makers so that they increase funding for research into a broad range of viruses to increase preparedness. Without getting political, it is a major relief that we now have a science-driven administration back in power that will take this pandemic, and the others that will undoubtedly happen, seriously.

But on the flip-side, the spread of disinformation about the virus and vaccines – not to mention general hatred – on social media is gut-wrenchingly disappointing to see. That’s the main reason I don’t have a social media presence on any of the platforms.

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**Can you mention a few broad themes that emerge from this Special Issue?**

That’s hard to say, as the Special Issue has been quite diverse, which is actually great to see and is a reflection of the broad ways in which pathogens manipulate cells. Without picking any favorites but to highlight the diversity, reports range from  $\text{Ca}^{2+}$  signaling and hypermigration during toxoplasma infection to pyroptosis in leishmania systems, to miRNA functions during viral infection and a humanized zebrafish model of staphylococcal infection.

**When you're not a Guest Editor or doing research, what are the things you do for fun?**

Making cocktails and cooking. It's something I got into while living in New York City, and it's become very handy given that restaurants and bars are closed during the pandemic, although we order in quite a bit to try to help local restaurants survive. I also

like music, so my wife and I usually combine all three over the weekend. I also like traveling, but obviously that's on the back-burner for now, too.

Derek Walsh was interviewed by Máté Pálffy, Features & Reviews Editor at Journal of Cell Science.