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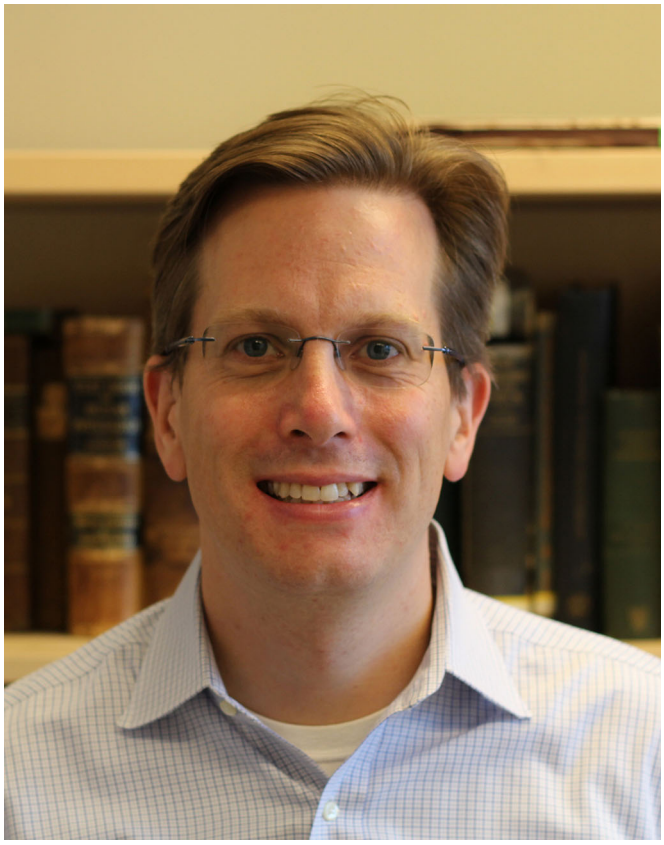
CELL SCIENTISTS TO WATCH

Interview with the Guest Editor – Andrew Ewald

Andrew Ewald is an Associate Professor of Cell Biology, Oncology and Biomedical Engineering at the Johns Hopkins University School of Medicine, Baltimore, MD. He joined the Johns Hopkins faculty in 2008, after postdoctoral work with Zena Werb in mammary biology and cancer at the University of California, San Francisco. Andrew earned his PhD in 2003 in biochemistry and molecular biophysics from the California Institute of Technology, studying with Scott Fraser. Andrew studies how organs form and how breast cancer progresses to metastasis. His laboratory recently identified a unique class of breast cancer cells that lead the process of invasion into surrounding tissues – a first step in cancer metastasis. Andrew is the Guest Editor for this Special Issue (Issue 1, 2017) on 3D cell biology for Journal of Cell Science, and is now a permanent Editor for the journal.



What are your research interests?

We're interested in how cells cooperate to build epithelial tissues during normal development and how genes alter cell behaviours to drive cancer progression. Our particular interest lies in how cell–cell interactions – between cells of both the same and different types – are driving this process. Our experimental model system is the mammary gland; there we're interested in the process of branching morphogenesis that generates the extensive ductal network that will be used to carry milk during pregnancy and lactation. Importantly, these same epithelial ducts can give rise to breast tumours, and we're interested in how they acquire the ability to proliferate without limit, to separate from the primary tumour, and then travel to and colonise distant organs in the body.

Which model system do you use to address these questions?

We use genetically engineered mouse models as our main hypothesis-generating system to try to figure out how things work at the cellular and molecular levels. Then, in our cancer studies, we actually test these hypotheses in human breast tumours, both from primary and metastatic sites. We've studied about a hundred breast tumours in the past 24 months: patients' tumour tissue is sent from surgery to pathology to our laboratory, and then we're able to culture it live, image it and study in molecular detail how that tumour is able to drive proliferative, invasive and metastatic cell behaviours.

What attracted you to this field?

My undergraduate training was actually in physics, but I was very interested in biochemistry and was heading towards structural biology. My graduate advisor, Scott Fraser, pioneered efforts to image cell behaviours in intact tissues to watch how tissues and organs form during early development. I thought this was a fantastic example of 4D structural biology; it was just at a different scale of size and complexity. So I switched my focus from thinking about molecular structure to thinking about how molecular activities regulate cell, tissue and organ structure. During my PhD studies, I became interested specifically in parallels between single-cell and collective cell migration. I was then looking for an interesting model system to study collective migrations and which would benefit from my imaging approaches. When I met Zena Werb at a conference, I was fascinated by the rich complexity of the biological signalling that she had elucidated in her lab, so I moved there and studied branching morphogenesis and breast cancer. While at UCSF, I had the great fortune to learn first-hand about 3D culture from pioneers in the field, such as Mina Bissell, Keith Mostov and Zena herself.

What recent findings do you find most exciting?

There are several exciting areas that I follow in the literature, such as the use of induced pluripotent stem cells to generate complex tissues and organs. I am specifically interested in how recent papers might change our point of view of the potential unit of regenerative medicine. Several recent papers introduced the idea that you could deliver patient-derived organoids to a site of injury and allow these new cells to repair the organ in place, instead of building a whole new organ for transplantation. It's not working perfectly yet, but I'm very excited by the idea. Also, the degree to which high-resolution 4D imaging is becoming integrated broadly across many labs and

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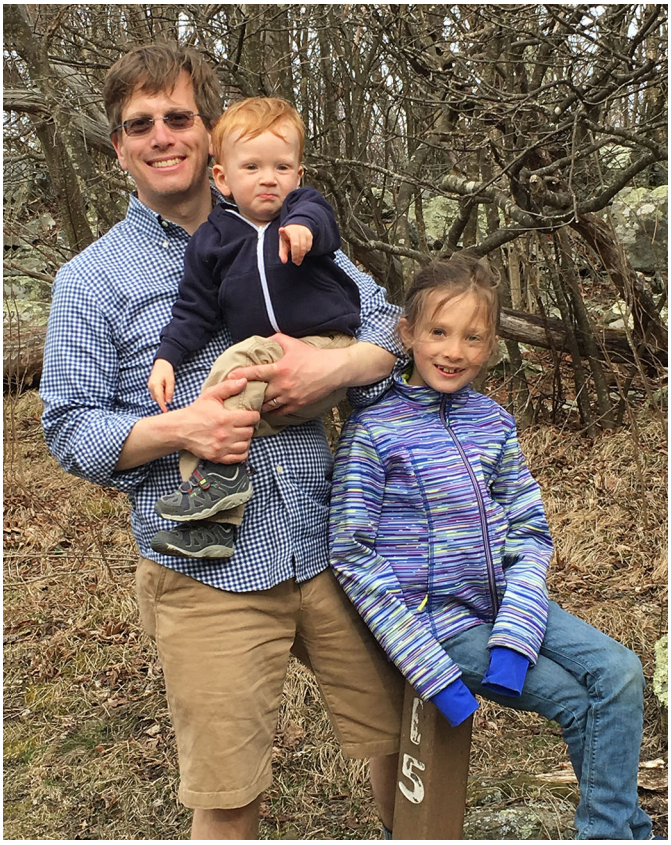

When he isn't in the lab, Andrew enjoys spending time outdoors with his family, both hiking and mountain biking. This picture was taken just after they reached the summit of Stony Man Mountain in Shenandoah National Park with his son, Michael, and daughter, Eleanor.

questions is great. It's becoming another technique, like genetics or biochemistry, that a lab is expected to be able to utilise, so we're getting a much richer understanding of how cellular processes work in the context of tissues and organs. I think the most exciting papers are always when you're bringing together different techniques to develop a multidimensional understanding of the process.

Where do you think the field of cell biology is heading?

At present there is a gap between our rich understanding of subcellular structure and molecular function in isolated cells and our anatomic, genetic, and physiological understanding of tissues and organs. I think the future lies in bridging these gaps and achieving a mechanistic understanding of how molecularly regulated changes in cell behaviour drive alterations in organ function and organismal health. Achieving this goal will require the integration of diverse experimental and computational techniques to understand cooperative and competitive dynamics among hundreds and thousands of interacting cells in the normal milieu of their 3D microenvironment. I anticipate that recent technical advances in CRISPR and light-sheet microscopy will be very useful in achieving these goals.

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

The first part of my answer is service. All of the opportunities I have had and discoveries I have made have been built on the contributions of many people. It takes a lot of people to run a university, to award grants from the NIH, to review and edit papers so we can all publish them, and I feel there's a responsibility to contribute to these institutions. I said 'yes' to JCS in particular because I really like The Company of Biologists' publications; I've published in three of them, JCS, Development and Disease Models and Mechanisms. And I feel like I have had a very fair review process each time, whatever the ultimate decision. We publish in a wide range of journals and it's clear from the review process at JCS that the editors are scientists, that the reviewers are scientists, and it's got a very serious mission and it works very hard to identify high-quality papers and to publish them in a way that lets the researchers get back to their research.

What did you hope to get out of this role?

I was very interested to see behind the curtains of how the review process works. It has been fun to learn more about emerging themes in cell biology and to gain more insight into what others view as the key advances and the key model systems and technologies in 3D cell biology. It has also given me a much deeper understanding of the manuscript review process. I pay much more attention to my cover letters and to my suggestions for reviewers than I did before. It really is in your interest as an author to make it as easy as possible for the editor to understand why this is not only a strong paper, but an appropriate paper for the journal. I think it has been a real education to serve as an editor and it has already made me better at my job.

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What was your role in handling manuscripts for Journal of Cell Science?

Guest Editorship at JCS is time-limited, but while you are a Guest Editor you are fully an editor of the journal, manuscripts are assigned to you and you have the authority to determine which are most suitable for publication. This is actually quite different from other journals, where you might be 'Guest Editor', but not have authority over the papers. I sit down, I read the whole paper and then I decide whether it's a good fit for the journal and whether it's likely to fare well in peer review. If I decide it's not appropriate for JCS, I write an individualised letter to explain why not; if it is appropriate, I send it out for review as quickly as possible. The goal is to have that whole process, from receiving the assignment to having the decision to go to review, made within 48 h. I think I've hit the mark for most manuscripts. At JCS, it's the editor who decides whether it goes in, it's not a voting process among the referees; they're advising, but the editor decides. At JCS, people are very responsive, so it's very easy for the editors to seek opinions from each other, and the format for the reviewer comments recently changed to a more structured feedback request, helping the editor to focus on the most important points. It is about identifying the things that are necessary to do in order for the paper to be publishable in JCS, rather than giving the reviewers an open-ended platform for requesting more experiments.

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And how were you involved with the Special Issue on 3D cell biology?

I have been the editor for all of the papers submitted for the special issue. We received very interesting papers that were responding to the idea of 3D cell biology in very different ways. We had several papers using light and electron microscopy to reconstruct the 3D structure of specific subcellular organelles, papers that determined the molecular differences in signalling between cells in 2D and 3D environments, and submissions covering fundamental cell biology within a 3D environment, such as a developing embryo or a 3D epithelial cyst. It has been exciting, across the spectrum, to have witnessed what the field is excited by.

Andy Ewald was interviewed by Anna Bobrowska, Editorial Intern at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.