Received: 27 November 2023 | Accepted: 28 November 2023

DOI: 10.1002/cm.21817

PERSPECTIVE

CYTOSKELETON WILEY

An interview with Douglas N. Robinson—Johns Hopkins School of Medicine, Baltimore, Maryland, USA

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KEYWORDS: interview

1 | WOULD YOU BRIEFLY EXPLAIN WHAT YOUR RESEARCH GROUP IS STUDYING?

Our research interest at its core pertains to the fundamentals of cell shape control and cell shape change. The idea behind that, for instance, is, if our cells did not have the ability to take on and assume very specific shapes for each of their functions, then biology could not happen the way we all enjoy it. We would just be blobs of cells if our cells could not form different structures. But then, they have to be able to dynamically change those structures, their shapes, and so forth, in order to be able to do things like cell division and morphogenesis, where they transition from one cell type to another and then eventually give rise to things like tissues, organs, and organ systems.

The other angle that I would like to point out is: who has been better at diagnosing disease for the past 100 plus years? A pathologist! Someone who goes in and looks at tissue and goes:

> "Oh, those cells don't look right. They're not shaped normally."

And so, the idea was, by understanding these fundamental principles, not only would we get insights into how normal healthy cells function, but also how processes go awry during diseases. Then, we like to take our concepts and apply them to different disease states, two of which are cancer, focusing first on pancreatic cancer, and COPD.

2 | WHY DID YOU CHOOSE A CAREER IN THE CYTOSKELETON RESEARCH?

My dad was a veterinarian. When you are the son of a vet, that means you are his automatic go-to person, my sister as well was one of his go-to people, when somebody could not show up or they needed extra help in the practice. As it is veterinary medicine, you can get a lot of hands on experience at a very early age. I got exposed, I think, to the medical profession through that means. Medical physicians might disagree, but there is actually a lot more similarity than one might imagine. Veterinarians also do not get to learn just one species, they have to know all species, and they never know what they are going to have to treat and what issues they might have to address, and sometimes they have to do so on very short notice. Therefore, I got a close up view of what the medical profession could look like, again, from the perspective of a veterinarian. My dad ran a private practice, and I got to appreciate the breadth of organisms across evolution. He dealt with everything from dogs, cats, horses, cows, pigs, sheep, and so forth. Then, there were the other species like iguanas, fish, and even a lion in one case! Exposed to this, you get to appreciate that range. The other side of this is that I grew up on a farm where we bred livestock, including cattle and sheep. The way I like to describe it is—it was my dad's hobby, but my job!

Our cattle and sheep became examples of selective breeding. I was constantly looking for the ram that would best complement the ewes that I had on the farm at the time. Since my dad was a veterinarian, he said we can do this on our own and order cattle semen from a catalogue. We considered each cow's features and picked the bull that we thought best complemented that cow. What we did really was a hybrid vigor study over several years. That got me interested in genetics. I also became interested in the genetic basis of disease along the way.

Over the course of my time raising the sheep, we had about three lambs that had spider lamb syndrome; it is devastating to watch because the lambs grow faster than their bones can keep up. Eventually, they collapse under their weight. You have to put them down because you do not want them to suffer. Through this, I got a close up view of what a genetic disease looked like. Actually, the genetic cause of this syndrome was finally identified in the field when

I was in grad school. But, it was the combination of our lambs with spider lamb syndrome and our selective breeding project with our cattle and sheep that got me interested in developmental genetics and the genetics of disease. When you put it all together, you get focused on trying to uncover the basic fundamental molecular mechanisms that give rise to disease. Okay, long winded answer, but that was the path!

3 | OF ALL OF YOUR RESEARCH PROJECTS WHICH WAS YOUR FAVORITE AND WHY?

Oh, gosh, that is like picking which of your kids do you prefer, and I love them all. I think going back to the notion of fundamental principles of cell-shape change, and trying to ask that from a very basic fundamental point of view, like how does it work?

I started with cell division—cytokinesis—as a model shape process using *Dictyostelium discoideum* as a model organism, which is super quantitative and quantitatively stereotypical. For example, each cell does cytokinesis with the same kind of kinetics if they are of the same genotype. From these studies emerged principles about how the machinery in-play drives this process.

Another question that spun out of our work was that I felt that, regarding the cytoskeleton, we were taking a lot of concepts and principles from muscle and applying them to non-muscle cells. There is a lot of rationale for that, but a muscle does not turn over as dynamically and as fast as a non-muscle cell does. So, I got worried that we were maybe a little bit too heavily dependent upon that model. The critical experiment that has driven muscle biology impeccably, has been the ability to isolate the muscle or the components within it and apply mechanical force or resistance, and then look and see how the muscle would respond. Therefore, we asked, can we do the same thing on a non-muscle cell? We started using micropipette aspiration; I like to describe this as "sending the dividing cell to the gym"—we would make the cell "work out." With this approach, we uncovered many principles of how a cell senses and responds to this mechanical disturbance and is then able to correct it.

Well, guess what? It turns out that through this whole process (and I'm summarizing many 10s of papers here), this ended up leading us to a molecular program (a mechanoresponsive program) for how the cells sense and respond to mechanical disturbances that turns out to be elevated in cancer. As a field, we always are very excited about the primary tumor, but actually by the time we identify the primary tumor, cells have already started metastasizing. Those metastatic cells are going through this process of experiencing an ever-changing mechanical landscape—everything from the stiffness of the local environment to having to squeeze between cells as they invade tissue, to experiencing and surviving shear stresses in the circulatory system. This mechanoresponsive machinery turns out to be really crucial for how the cells respond and adapt to that ever-changing mechanical landscape.

All of this came from trying to ask that fundamental question, and then go:

> "Oh, gosh, this is exactly what cancer cells are leveraging to become metastatic and become those killers which end up taking out the patient in the long run."

4 | WHAT ARE YOUR FAVORITE PASTIMES OUTSIDE OF RESEARCH?

Before I get into that, I have to tell you a little sidebar, which is not really such a sidebar anymore. 15 years ago, my lab and I had the opportunity to create an outreach program for young people from socioeconomically under-resourced backgrounds. This year was our 15th year. The program, which we call the Johns Hopkins Initiative for Careers in Science and Medicine (CSM), has evolved to where it has fifth grade, high school, undergrad, and postgrad sub-programs, and we have had 635 scholars to date across all components. They all are from the low income and educationally under-resourced backgrounds. Our scholars are crushing it in every way. When you look and see all the amazing things that our scholars have done and are doing, it is truly amazing. The CSM has now grown beyond being just a hobby for me, it is really a passion, or to be bolder, maybe even a moral obligation.

On top of that, we have two Border Collies, when you have two borders you border on insanity! They are high energy. You probably know the F-bomb. We spell it FRIS-BEE! As soon as you say the word frisbee, they are "Yeah, it's time!!" We try to spend as much time as possible boating, and we belong to a boat club. So, it is a collection of all the above that we spend a fair bit of time doing.

5 | WHAT WAS THE FIRST THING YOU DO WHEN YOU WAKE UP?

Check my email and clear out the email from the night before. I try to have at least one work project that I get done, you know, something that can be done fairly quickly before anybody else gets up.

6 | WHAT OBJECT IS MOST IMPORTANT?

Does family count? So, my mom, my wife, and my daughters. They are not objects; however, they are most important to me.

7 | WHAT IS IN YOUR POCKETS RIGHT NOW? WHAT HAVE YOU GOT IN YOUR POCKETS?

Literally? Usually, my car and office keys.

For more information, check out these websites:

1. Lab URL: http://robinsonlab.cellbio.jhmi.edu/
2. SARE URL: http://sare.cellbio.jhmi.edu/
3. CSM URL: http://csm.cellbio.jhmi.edu/

AUTHOR BIOGRAPHY

Douglas N. Robinson is a Professor of Cell Biology at Johns Hopkins School of Medicine. He also holds appointments in Pharmacology and Molecular Sciences, Medicine (Pulmonary Division), Oncology (GI Division), and Chemical and Biomolecular Engineering. In his research, he investigates how cells control their shapes for normal human health. In particular, his lab initially uses a model organism *Dictyostelium* to discover fundamental concepts and then applies these insights to human diseases, including cancer and lung disease. His lab has also built an outreach initiative for high school students from low-income and educationally under-resourced backgrounds. Now, Doug and his colleagues have expanded the effort by creating a pathway program called the Johns Hopkins Initiative for Careers in Science and Medicine (CSM). The CSM has now served over 635 scholars from 5th grade to high school to undergraduate to post-baccalaureate levels. He completed his B.S. degree at Purdue University (1991), his doctoral degree with Lynn Cooley at Yale University School of Medicine (1997), and his postdoctoral training with Jim Spudich at Stanford University School of Medicine (1997–2001). He was a Damon Runyon Fellow, a Burroughs Wellcome Career Award in the Biomedical Sciences recipient, a Beckman Young Investigator, and an American Cancer Society Research Scholar. He is the 2015 recipient of the Johns Hopkins University Professors' Award for Excellence in Teaching in Biomedical Sciences and the 2016 recipient of the Biophysical Society's Emily M. Gray Award for "Significant Contributions to Education in Biophysics." He also received the American Society for Biochemistry and Molecular Biology's 2017 Ruth Kirschstein Diversity in Science Award for "the encouragement of underrepresented minorities to enter the scientific enterprise and/or to the effective mentorship of those within it." In 2018, he received the Provost's Prize for Faculty Excellence in Diversity, and in 2020, he became a Fellow of the American Society for Cell Biology. In 2022, he became a Fellow of the American Association for the Advancement of Science.

How to cite this article: Trevorrow, P., & Robinson, D. N. (2023). An interview with Douglas N. Robinson—Johns Hopkins School of Medicine, Baltimore, Maryland, USA. *Cytoskeleton*, 1–3. https://doi.org/10.1002/cm.21817