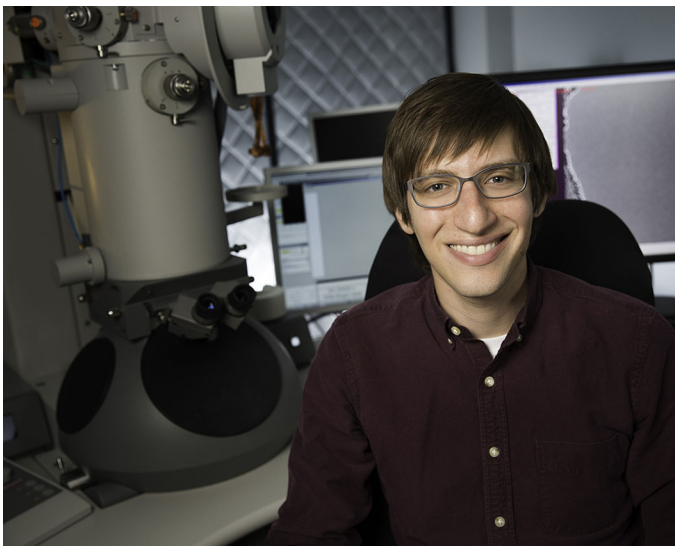
© 2017. Published by The Company of Biologists Ltd | Journal of Cell Science (2017) 130, 3607-3609 doi:10.1242/jcs.210658

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Gregory Alushin

Gregory Alushin received his bachelor degree in biochemistry from Columbia University in 2006. He then joined the laboratory of Eva Nogales to work on structural aspects of microtubules and kinetochores for his PhD in biophysics, and graduated from the University of California, Berkeley in 2012. Greg then moved to the National Heart, Lung and Blood Institute, NIH, Bethesda, as a postdoctoral fellow with Clare Waterman. In 2013, he received an Early Independence Award from the NIH, enabling him to establish his own laboratory. Greg has been an Assistant Professor at Rockefeller University, New York, since 2017. He has received the Norton B. Gilula Award from the American Society for Cell Biology, the Presidential Early Career Award for Scientists and Engineers, and was named one of *Forbes*' '30 under 30 in science and healthcare' in 2014. Research in his laboratory focuses on understanding how actin responds to mechanical forces and how this response affects cellular signalling.



Gregory Alushin

What inspired you to become a scientist?

I actually came to science a little bit later in my personal development than some people do. I was much more interested in writing and literature, and before going to college I thought I was going to be a journalist. At college, I ended up taking a few science classes, and I took a great organic chemistry course with Ronald Breslow at Columbia, which I loved and I wanted to know more. After that, I took further science classes and worked in labs and I got curious about how biology works. I guess I never looked back.

You then did your PhD in Berkeley with Eva Nogales. How did this come about?

I got tuned into Eva's research during an undergraduate research experience, which actually doesn't appear on my CV. I worked with Steven Almo at Albert Einstein College of Medicine for a summer and stayed on for a year. Ironically, he's the only person I've worked with who I haven't published a paper with, although it was a very formative intellectual experience. There, I got interested in protein–protein interactions and how they can create a network topology of function in the cell. I learned a little about cryo-electron microscopy (cryo-EM) as it was popping up at the time as a great method to study macromolecular complexes. When I then got into Berkeley, Eva was one of the group leaders I was most interested in working with, and it turned out pretty well.

A PhD in biophysics, cryo-EM – did you do a lot of engineering and experimental optimization?

Certainly. In biophysical research in general, and in cryo-EM in the earlier days – to say that makes me feel old – before it became as mainstream as it is today, there was definitely a huge element of tinkering. I feel it's different from cell biology research, where you're working with cells and imaging them many times and under different conditions during the course of a study. With cryo-EM, you don't necessarily do tons and tons of experiments – you have to think very carefully about each one. Also – especially before all of the automation and digital cameras we have now – when you got time on the instrument, you would have to stay up for almost 24 hours straight collecting data on film and developing everything in the same day. You collect some data once, then you write a little bit of software to analyse it. A program doesn't work and you tinker with it, run it again… I do really enjoy that side of biophysics and structural biology – the fiddling and optimization.

What questions are your lab trying to answer just now?

The big problem we're working on is how do cells sense mechanics and forces. In particular, how do forces – either external or generated by the cell itself – modify the conformation of macromolecules in a way that allows these molecules to participate in signal transduction cascades? We're really getting to the nitty-gritty of how a force would elicit a conformational change in a molecule that would, for instance, enable a binding interaction that would then speak to a kinase. We're focused on how the actin cytoskeleton and actin filaments themselves are remodelled in response to force. Furthermore, we are currently doing a lot of technology development; we're trying to make substrates where we can put actin filaments under either tension or compression and then directly visualize, with cryo-EM, the conformational changes that are elicited. We'll use that technology to dissect how those forces and the corresponding conformational changes regulate the binding interactions of actin. There's also our more traditional structural biology projects, where we're looking at the interactions of actin with binding partners. We've been trying to get some high-resolution structures of unconventional myosin bound to actin in multiple states. Finally, we're imaging cells to look at actin-associated proteins and actin in the parts of the cell where they're experiencing a large amount of force. The protein zyxin is a LIM domain protein that localises to actin when it's experiencing extreme forces, and zyxin actually brings in a cellular machinery to

Gregory Alushin's contact details: Laboratory of Structural Biophysics and Mechanobiology, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA.
E-mail: galushin@rockefeller.edu

Journal of Cell Science

Journal of Cell Science (2017) 130, 3607-3609 doi:10.1242/jcs.210658

Greg in a rowing boat in Central Park

repair these filaments. We're aiming to find other proteins that use that LIM domain module to localize to actin to exert other functions, for instance cellular signalling.

What inspired you to work on mechanical forces in cell biology?

I went to my post-doc interview with Clare Waterman (NIH), and I had proposed to work on microtubule–actin interactions, but I followed her advice not to work on it because this field is such a black box. When I eventually got to her lab, I started working on actin and mechanotransduction, as I just got really interested in that problem. I can't point to a specific publication or moment of inspiration – it was more being in that environment and her lab for about nine months. It's a very exciting area and still mostly in the realm of phenomenology, where people are seeing that cells react in certain ways, to certain types of physical perturbations or different mechanical environments. They're starting to know which molecules are involved, but they really don't understand how the molecules execute the processes that make the phenomenon work. So it's a great area for structural biology to come in and try to answer some of those questions. After I had started working with Clare, the NIH asked me if I wanted to apply for this early independence award, which is the grant that I got that allowed me to start my own lab without completing a traditional postdoc. Clare very generously let me take with me what was essentially the project I was working on in her lab, with a bit of re-factoring towards structural biology.

How does such a transition to group leader go? Did you tell everyone "Bye, I have the grant, I'll be down the hall"?

That's kind of how it worked. Actually, on the day the grant came through, I was getting to the lab very late and I got a call on my cell phone from Clare. I just thought to myself 'oh man, I'm in trouble'! But Clare had found out before I did that I gotten the grant and that's why she called. A little celebration later, I converted from being her postdoc into being in her department. I guess it's correct, I did essentially move down the hall and start a small group on the spot.

What challenges did you face when starting your own lab that you didn't expect?

It was pretty challenging – a lot of fun but also tough. I didn't get a traditional start-up grant from the NIH and I therefore had to furnish my lab completely from scratch. I ended up salvaging a lot of equipment from storage at the NIH, trying to piece together a lab from stuff other people had thrown away. It was good fun though, and of course I got new things as well. Together with hiring people, it was a challenge of logistics; putting together all the parts to have a functioning group.

Are you still doing experiments yourself?

Since I've arrived at Rockefeller, my group has expanded pretty quickly, so I don't do a ton of bench work. But that was even true at the NIH. I'd say my role – in terms of original research – is computational. I still do a lot of image analysis and putting together software for it for both cell and cryo-EM data. I'm the computer guy in the lab, I do all the IT stuff and systems administration of our Linux workstations. It's the thing that I enjoy the most in the lab, so it's nice that I get to do my favourite type of work.

How do you achieve a work–life balance when you're trying to establish yourself as an independent investigator?

Earlier on in my career I didn't have a routine at all. I would just go work all the time, or whenever it was convenient. Now I try to set a schedule for myself, and try to keep to it. You always have to make exceptions of course, but that strategy has helped me become more efficient with my time. I do think that in science, especially academic science, there tends to be a culture of presenteeism: if you're in the lab 16 hours a day, you must be doing something awesome. But that's not necessarily true and sometimes you can just be spinning your wheels and not be very efficient. Being goal-oriented, rather than time-oriented, can make one more efficient.

"Being goal-oriented, rather than time-oriented, can make one more efficient."

Does this include setting aside time purely for writing and switching your emails off etc., as some investigators do?

I don't turn off my email – I like to know what's going on, but I won't respond. I do set aside chunks of focus time to write, that is true. It is one the hardest things: to really focus on writing and not get bothered while you're doing it. Sometimes, I like to shift my hours to be slightly later in the day and that tends to give me time to focus on writing in the evening when other people aren't around.

What is the best science-related advice you ever received?

It's advice I've been given about how you spend your time: in terms of the amount of blood and sweat it will take to complete a project, it is just as time consuming to do something less interesting as it is to do something interesting. Try to pick the best problems to work on. I think that's absolutely true, and in my own lab prioritizing what to

Journal of Cell Science

Journal of Cell Science (2017) 130, 3607-3609 doi:10.1242/jcs.210658

focus on has become all the more important. I believe everyone should try to develop the ability to pick good problems, and that's something I try to impart to the people who work with me. You just have to really focus on what you're most excited about and what is most exciting for science.

What is your advice on establishing good collaborations?
A great litmus test for a collaboration is whether or not it is a two-way street, or am I providing simply a service for someone else? I like collaborating with people where the project makes sense for both labs in terms of our scientific interests and moving forward with the core projects in both labs. Also, the recipe for a good collaboration is people who I find simulating to talk to and can bounce ideas off of, maybe even outside of the specific problem we're working on together. Find someone you find simulating to interact with, beyond just the idea of getting a nice publication together.

"…it is just as time consuming to do something less interesting as it is to do something interesting. Try to pick the best problems to work on."

How do you get the most out of the meetings you attend, particularly in the early stages of your career?
I should say that I'm a pretty shy person, so meetings aren't necessarily intrinsically enjoyable for me, but I do think they're really important and I get a lot out of them. I like finding opportunities for structured interactions with people at conferences, because that's a good way to get around shyness. Going to posters is a really great way to meet people at meetings, especially junior people, and it gives you a way to really talk to them about science. As for the big meetings, don't try to see everything, it's impossible. I've become a real believer in picking a session and sticking with it, trying to get a sense of where a field is, and that's also the chance to get to know that community a little better.

Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?
I wrote and edited for the Berkeley Science Review when I was in graduate school, and eventually I became Editor-in-Chief and ran that operation for a year. It was a really good experience. I learned how to communicate very different types of science, and I think it helped me a lot in writing papers and grants. It was also an opportunity to learn how to manage people to some extent. I also like exercise in general, such as rock climbing, and I've done a lot of martial arts in my life, but not lately. I have a black belt in Taekwondo. I used to be a competitive fighter in college, and I was the captain of the Columbia Taekwondo team, but I've actually got a lot more into Tai Chi later in life.

Gregory Alushin was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.