People & Ideas

Jim Bear: Delineating the mechanics of cell migration

Bear studies the role of actin and its regulation in cell motility.

Jim Bear started focusing on biological sciences in high school, thanks to an outstanding biology teacher. Under the mentorship of Karl Saxe in graduate school at Emory University and Frank Gertler during his postdoctoral training at MIT, Bear grew interested in understanding the fundamental cytoskeletal dynamics of cell migration—in particular with regards to the contribution of actin and its regulators. In his PhD dissertation, Bear characterized a suppressor mutation of the G protein–coupled receptor cAR2 in *Dictyostelium,* which he named SCAR for Suppressor of CAR. The same protein was shortly after called WAVE in other organisms and is now known to activate the Arp2/3 complex to nucleate actin filaments. Throughout his time in Frank Gertler's lab, Bear turned his attention to different actin-modulating proteins—Ena/VASP—and how they affect the cytoskeleton as cells move and migrate. Now a tenured professor at the UNC School of Medicine, Bear combines genetics, biochemistry, and high-resolution live cell microscopy approaches to dissect the mechanisms of actin-based motility. We contacted him to learn more.

What interested you about actin dynamics and their contribution to cell motility?

From my graduate and postdoctoral work, I developed a deep curiosity about the actin cytoskeleton. I also learned that I loved microscopes and making movies of cells crawling around. Naturally, in my own lab we spend lots of time looking at the actin inside of cells crawling around. We started out studying the Coronin family of actin regulators, and we're still pushing ahead with cells derived from Coronin knockout mice. We're now also looking at other factors that regulate actin dynamics during migration such as GMFβ.

What are you currently working on? What is up next for you?

A few years ago, two things came together in the lab that have led us in an exciting new direction. First, we discovered that some mammalian cells could actually survive without the Arp2/3 complex. Second, we finally got a microfluidic system working that allowed us to do directional migration experiments on slow moving cells like fibroblasts. We focused on migration towards soluble cues (chemotaxis) and migration towards substrate-bound cues (haptotaxis). We assumed that cells without the Arp2/3 complex would be a good control group for the chemotaxis experiments since Arp2/3 was clearly thought to be essential for this process. To our utter surprise, the cells without Arp2/3 moved slowly but could still chemotax! However, these same cells could not respond to haptotactic cues such as substrate-bound ECM proteins (1). These results have spurred us to dig more deeply into both chemotaxis and haptotaxis. We are now looking carefully at some of the signaling events during these processes with collaborators such as Jason Haugh at NC State, and we are beginning to incorporate quantitative/modeling approaches into our repertoire.

> "To our utter surprise, the cells... moved slowly but could still chemotax!"

What's your approach to research?

I have always "followed my nose" when it comes to science. I figure if an idea is interesting and exciting to me, then perhaps other people will think so as well. Intuition is an underrated concept in science. However, this approach must be paired with very careful and quantitative experiments. Nice images and pretty movies are great, but at the end of the day, I want numbers.

What did you learn during your PhD and postdoc that helped prepare you for being a group leader? What were you unprepared for?

PHOTO COURTESY OF JIM BEAR

Jim Bear

I think being a student and a postdoc in fairly small labs that were just starting out was very helpful since we were expected to do a bit of everything. The people trained in big labs take a lot of things for granted. I think the one thing that took me by surprise was how different people require very different management styles to maximize their productivity. Some people need much more hand-holding, and some require the occasional kick in the behind. Figuring out which approach to use was and remains a challenge.

What has been the biggest accomplishment in your career so far?

The work on Ena/VASP proteins from my postdoc days in Frank Gertler's lab at MIT has probably had the biggest impact. These are certainly my highest cited papers (2, 3). We discovered that these proteins could extend barbed ends, in part by antagonizing capping protein, and leading to long, unbranched filaments. At the time, this was a very novel concept, but is now fairly well accepted in the field. I am very excited about our recent studies on different kinds of directed migration (4). I think this work has the potential to really change the field. Time will tell.

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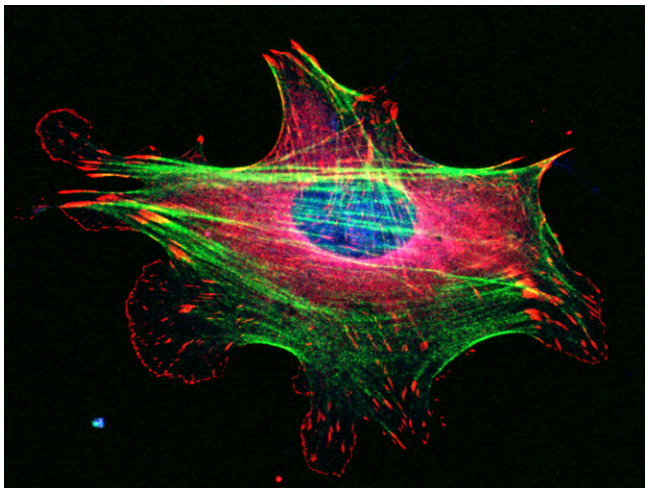

IMAGE COURTESY OF JIM BEAR

Mouse fibroblast expressing Myosin Light Chain-GFP (green), stained for vinculin (red) and DNA (blue). This MLC-GFP construct has been a key reagent for dissecting fibroblast chemotaxis.

What has been the biggest challenge in your career so far?
I had a really tough stretch a couple of years ago with several negative funding decisions that were deeply disappointing. I got so stressed that I came down with a case of shingles, which is just as painful as everyone says. At times like that, you just have to put your head down and focus on the science. It all worked out in the end.

Who were your key influences early in your career?
My graduate and postdoctoral mentors had a huge impact on my professional and personal development. I've tried to blend the best of two very different styles of mentorship when it comes to managing my own group. I also had tremendous mentors at UNC during my junior faculty days, such as Mike Schaller, Keith Burridge, and Pat Brennwald.

What is the best advice you have been given?
Never, ever hit "send" on an email when you are angry. I've done this a couple of times and regretted it every time.

What hobbies do you have?
I love tinkering and building things. Replying to emails does not really satisfy this urge. What I have been doing for the last few years is building 3D printers. The maker movement is really cool and empowering. Occasionally, I print something for the lab or a protein model for teaching, but mostly I amuse myself or make toys for the kids.

What do you think you would be if not a scientist?
I have a cousin who owns a company that builds church organs by hand. Really big instruments, like for cathedrals. They are one of a handful of such companies in the world. Each one takes about five years to build. Not that I am particularly musical, but I am fascinated by this level of craftsmanship and commitment to doing something really well. I think this kind of work would be interesting and rewarding.

What has been your biggest accomplishment outside of the lab?
Raising two kids with my wife, although, honestly, she deserves most of the credit. Also, "helping" to build several killer pinewood derby race cars while the boys were in cub scouts.

Any tips for a successful research career?
Work on something that really fascinates you—something that you can't stop thinking about, even when you are on vacation. I think all successful researchers are a little bit obsessed with their topic. This can get you through some difficult times in a research career like losing a grant or getting scooped.

"Intuition is an underrated concept in science."

1. Wu, C., et al. 2012. *Cell.* 148:973–987.
2. Bear, J.E., et al. 2000. *Cell.* 101:717–728.
3. Bear, J.E., et al. 2002. *Cell.* 109:509–521.
4. Asokan, S.B. et al. 2014. *Dev. Cell.* 31:747–760.

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