

Rebecca Worthylake: The flooding of science

Starting up a brand new lab is difficult enough. But when a hurricane soon forces you thousands of miles from your new research home, a whole new layer of complications arises, as Rebecca Worthylake recently found.

Blood cells aren't pigeonholed by their name. Although they circulate in the blood, white blood cells such as leukocytes often fight their way out of the vessels to fight infection. The decision to leave is not theirs alone; endothelial cells send signals that cause blood cells to attach to the vessel wall and migrate to the inflammation site (1). The blood cell then uses signaling pathways coordinated by the Rho GTPase family to loosen the endothelial barrier (2) and make its own cytoskeletal changes (3) that allow it to migrate through the vessel, a process called extravasation. The signals must be precise, as inappropriate leakage can cause inflammatory disorders (4).

Like the leukocytes she studies, Becky Worthylake knows when to go with the flow and when to fight for staying power. Not long after she moved to New Orleans as an assistant professor at Louisiana State University Health Science Center, Katrina forced Worthylake to relocate. But even while the city still recovers from the devastation, she has found that returning to New Orleans is worth the effort.

BEFORE THE STORM

How were you first drawn into biology?

I was actually a math major at first, but after taking some psychology courses, I got really interested in science. I switched my major to chemistry with the idea of going on to graduate school, but I first wanted to get a little bit of lab experience. So I went to work as a technician in a lab that was differentiating muscle cells from myoblasts into myofibers.

I thought that was really exciting, that you could get cells to change their behavior in a culture setting. I wanted to know how cells understood where they were in

the body and how they would know what to do based on their environment.

Did you get to follow up on that interest?

Yes, in graduate school (at the University of Utah), I worked with breast tumor cells. We would culture them on matrigel, where they could form these little acini structures. At that point, I decided that I was really interested in the mechanisms that regulated the changes in cell shape and cell movement that would allow the cells to form those sorts of structures.

Then I went to the University of North Carolina to work with Keith Burrige on Rho signaling and the regulation of the cytoskeleton and cell migration. A lot of their work was with fibroblasts and epithelial cells at the time. I decided to look at the migration of leukocytes because leukocytes are normally highly migratory cells, even in adults, whereas fibroblasts aren't as motile. In particular, I was interested in their migration during inflammation, when they interact with the lining of the blood vessel wall, penetrate, and invade across the endothelium.

You are still working on this subject area now in your own lab?

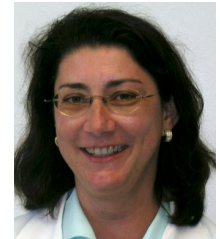
I am. We're also expanding on it to understand how the same sort of mechanisms regulate tumor cell migration during metastasis. This would be during the late stages of metastasis, when the tumor cell is circulating in the bloodstream.

There are a lot of molecular parallels between tumor cell and leukocyte extravasation. Some of the adhesion molecules that mediate the interaction with the endothelial cells are the same. A few years ago, it also became clear that some tumor cells overexpress chemokine receptors that are normally found on leukocytes.

RIDING THE WAVES

You moved to New Orleans not long before Katrina hit the city.

Less than a year before, yes. My husband is also a faculty member here in the biochemistry department. We were here for about nine months, and then the storm hit.



Becky Worthylake

What happened to you when the storm hit?

We had evacuated beforehand. We were in Houston when it hit, and then from what we saw on TV, we knew we weren't going to be going back anytime soon. My husband and I drove across the country to Oregon because that's home to both of us. We just got in the car and kept going.

What did scientists who had left New Orleans do while they were away?

I would say most scientists who were displaced found labs to go and stay in. Many times, people went back to places where you already knew people, like the lab they had been in before, or a university where you had a collaborator. And there were a lot of offers of help within the scientific community to help house people temporarily.

What did you and the rest of your lab do?

I was contacted by several people asking if I wanted to come and have space. But we actually declined for personal reasons. So my husband and I stayed with his parents for three months before we could go back to New Orleans. We both wrote grants, sitting at my in-laws' dining room table. Also, our house had flooded, so there were really a lot of issues to deal with outside of work.

At that point I only had one research associate, and she stayed with family in Baton Rouge. Then she started working at a lab in Baton Rouge, where she had worked as an undergraduate.

How about others in your department?

For instance, Andy Catling had previously worked in Michael Weber's lab at the University of Virginia. He went back there, and they made space for him. He took his whole lab and continued on with his own research there.

Then there was Suresh Alahari. He did some collaborative work at different labs, where he was able to learn some techniques that he didn't know before. So for him it worked out almost like a sabbatical.

What were some of the logistics of getting your lab back on its feet?

The main thing was having to replace all your reagent stocks. We remade some, and then called up collaborators to get some, so we didn't have to make them all from scratch.

We also had to move to new lab space. When we first came back to New Orleans, LSU was not open. So we were put up at Children's Hospital uptown in New Orleans, which is an area that did not flood. They opened space for several LSU researchers there.

In June last year, the LSU Medical School reopened, and then I moved in here. That was initially also a temporary space, and since then we've moved again. So we've actually had our lab in three different places since the storm—all in New Orleans, but still it's disruptive.

Was there any special financial support?

There was support in the form of supplements to grants so that you could replace all of the materials and time that you had lost. I had an American Heart Association grant, so I got a supplement from them. People who had NIH grants got supplements from NIH. These were basically special funding mechanisms to help you restore lost reagents.

What sort of delay do you think the storm cost your research?

I would say it took until the beginning of this year to feel like we were hitting stride again. It took that long to feel like experiments were going as smoothly as they should be. We got tired of replacing everything, and then we started just replacing the things that we needed to do certain key experiments. We built up slowly.

The other thing that slowed us down was personnel. I had hired a post-doc, but then that was canceled because of the storm. He went someplace else. Before I even felt comfortable to try to recruit after the storm, I needed to feel sure that the situation in New Orleans was stable. I finally hired a post-doc last October, but that was essentially a year delay.

RESTORATION

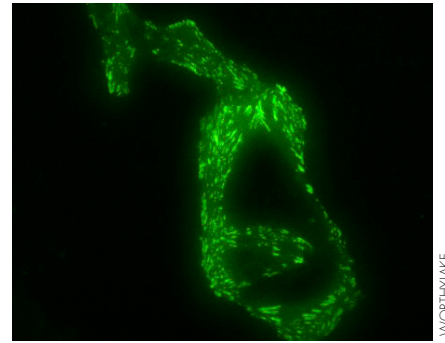
Now that you're back to full strength, you are part a small group at LSU that is interested in cell adhesion and migration.

There are four of us right now. Andy Catling is working on MAP kinase signaling and scaffolding molecules and how that's involved in adhesion and migration. Suresh Alahari works on PAK kinase and on a protein that he discovered called Nischarin, which is down-regulated in advanced breast cancers. He's working on how those signaling proteins regulate adhesion and migration. My husband David uses x-ray crystallography to study the structures of proteins involved in Rho family signaling.

We all get together every other week and have a group lab meeting. We borrow reagents, and we talk about experiments in the hallway all the time. We have some collaborative studies, but right now it's more that we're sharing ideas, as we've each got our own individual take on things. For me that makes the whole environment here good.

How is the New Orleans campus of LSU faring now, post-storm?

All the recovery plans for the city call for developing health care industry and biomedical research as a driver of the econo-



Worthylake is interested in how this breast cell's environment instructs its shape.

my in New Orleans. It adds to the traditional tourism industry. There's actually been a lot of support from the state to improve the facilities here.

We've had the opportunity to purchase state-of-the-art equipment recently for imaging and proteomics facilities, to increase our technical capabilities. There's also a large recruiting effort, which we hope will add to our group. We've had several very talented people come through for interviews.

"The people here are tough and optimistic about the future."

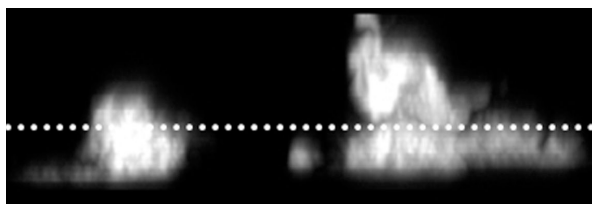
How is the morale of the faculty?

I think there was some natural selection. The people who have remained here are tough and optimistic about the future. In general the attitudes that people have here are, I guess you could say, cautiously optimistic.

Is that how you feel as well?

Yes. I'm hoping that we're going to continue to recruit more people, because we did lose some faculty. I'm hopeful that we're going to keep building up on our cell adhesion and migration group as well, because it's a really great environment. I think we managed to convince our families that we weren't completely insane by staying in New Orleans! **JCB**

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2. Wittchen, E.S., et al. 2005. *J. Biol. Chem.* 280:11675–11682.
3. Worthylake, R.A., et al. 2001. *J. Cell Biol.* 154:147–160.
4. Libby, P. 2002. *Nature.* 420:868–874.



White blood cells use Rho family GTPases to work their way through the vessel barrier (dashed line).