Gilbert Weidinger: Regeneration researcher

Weidinger wants to grow new limbs and organs.

Some vertebrates, such as fish, amphibians, and lizards, have the ability to replace lost limbs and regenerate organs. Regeneration requires the reactivation of signaling molecules that were used during embryonic development. Weidinger has spent his career so far studying aspects of zebrafish embryogenesis, including the role of Wnt signaling molecules (1, 2), and has more recently been investigating how these Wnt pathways are used to rebuild zebrafish fins and hearts (3–5).

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The regenerative capacity of mammals is extremely limited, yet mammals possess many of the developmental signaling molecules that other vertebrates reactivate for regeneration, such as the Wnts. Why is it then that regeneration pathways no longer function in mammals, Weidinger wonders. By learning more about what controls Wnt signaling and its involvement in regeneration in zebrafish, he hopes to find clues.

After completing his postdoc with Randall Moon at the University of Washington in Seattle in 2006, Weidinger moved to the University of Dresden where he now leads his own research group.

STARTING OUT

Did you always want to be a scientist?

I don't think so, no. Actually, in high school I was leaning toward politics. Then I was going back and forth deciding whether to study science or politics. In the end, when I went to university (in Salzburg, Austria), I thought, "Okay, I'll go try out both." In Austria, you can sign up for courses and you don't have to decide immediately what you want to do. I was so excited by my first biology courses, however, that I decided I was not going to do any more politics.

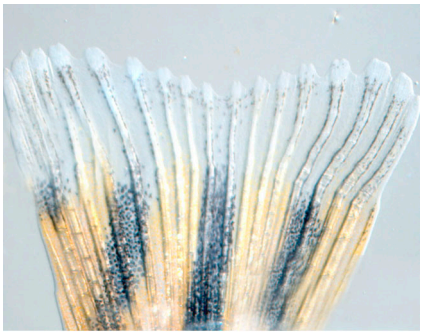
After university you did a Ph.D. with Erez Raz in Germany. What made you choose his lab?

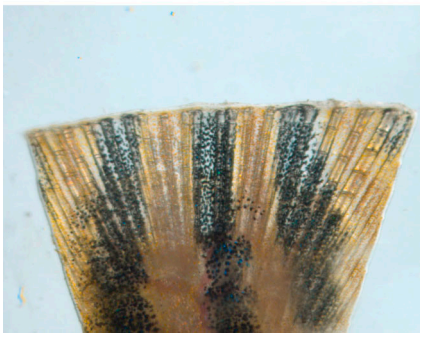
I really wanted to work with zebrafish. In my undergraduate studies, I did a diploma thesis project on *Xenopus* frogs. We thought back then that this was an old-fashioned model, and it would die out—of course, that hasn't happened. But I thought, like a lot of people, that zebrafish might be more versatile than frog, because you can easily do genetic screens.

I actually applied for a Ph.D. position with Wolfgang Driever, who was quite famous for his genetic screens in zebrafish. He didn't have a position available, but luckily Erez had just started his own little group in the same department.

What was your project?

I started a project on germ cell development. Back then, germ cells had been studied mainly in invertebrates. Very little was known about vertebrates, except for the mouse.





Mutant zebrafish (bottom) that fail to grow back their chopped off tails help Weidinger to understand how regeneration works.

Gilbert Weidinger

Most invertebrates specify germ cells very, very early in embryogenesis, but mice and other mammals induce germ cells much later (during gastrulation). At the time, the indications were that germ cell development in nonmammalian vertebrates might happen in a way more similar to invertebrates than to mammals. And it turns out that it does.

What's the benefit of studying nonmammalian vertebrates, such as fish, if their germ cell development is so different from mammals?

Actually, it turns out that a lot of the molecules that are involved are conserved, and probably have similar functions, it's just that they are needed at a different stage of development.

I think that it's important to study these differences in developmental biology. For a long time, people have looked for the similarities between species and have been excited to see that a lot of things are conserved. And now it's time to try to figure out what are the differences. Because, of course, there are differences—the organisms look different, they have to develop differently at some point.

Text and Interview by Ruth Williams
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MOVING STATESIDE

After your Ph.D., you did a postdoc with Randall Moon in Seattle. What made you choose that lab?

I wanted to continue studying the early events of zebrafish embryo development, and Randy had been doing great work showing that Wnt signaling is very important for those kind of things.

I also really wanted to go to the U.S., so I only applied for postdocs there. I felt it could be a great experience to live abroad and to see how science and life work there.

Would you recommend a stint in the U.S. to non-U.S. scientists who are thinking about doing a postdoc?

Yes. The breadth of choice for joining a great lab is bigger in the U.S. There's more great science in the U.S., more world-class science, because the funding is better and it's a bigger country. There's very good science in Europe too, but it's more limited.

It was a great experience for me, and I think it's very useful to see how science is structured, and how the universities are organized. You gain a slightly different perspective.

When and why did you move to Dresden?

I just started here a year ago. It is really a great place in Germany for cell biology. I'm at the Institute for Biotechnology. Dresden also has the Max Planck Institute for Cell Biology and Genetics, which is a great place. And there's a new research center for regenerative therapies, which has received a lot of investment. There's a lot going on there: new groups are being hired, new professorships, the funding is very good.

There are also a lot of interactions among the institutes, which is great. We share talks and have a common graduate school.

TINY FISH, BIG QUESTIONS

How have you found the first year, setting up your own lab?

It went pretty smoothly, so I'm happy. Of course, it's a big change from the way you work as a postdoc. I now have the responsibility of hiring people, dealing with the administration, the budget, and all those things. It's a steep learning curve, but it was okay.

I was very lucky that I could share the fish facility with Michael Brand's lab (the director of this institute). Building a fish facility is a lot of work and can take a lot of time. But all I had to do was move my fish from the U.S.

Did you take them on the plane? Did you give them the window seat?

[*Laughs.*] No, you send them in the post as live embryos. You send them when they're one day old, they arrive a couple days later, and when they're five days old, you need to start feeding them. So, there's a convenient window of five days in which to post them.

What are you currently studying in these fish?

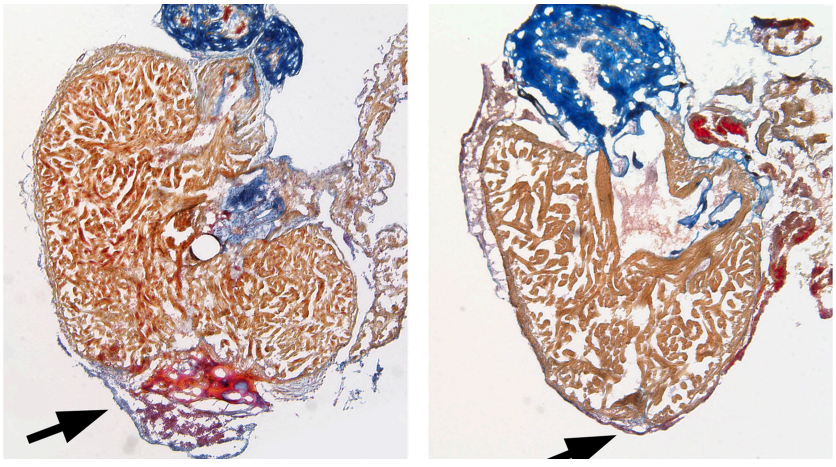
The big question for me now is regeneration. How does it work, what are the molecular mechanisms that regulate it? I'm mainly interested in epimorphic regeneration, which is the regeneration of complex organs and limbs—in our case, the fins or the heart of the fish.

"Maybe mammalian cells are competent for regeneration, but they're not receiving the right signals in response to injury."

We're trying to figure out how these things work, how they're regulated, and why lower vertebrates are much better than mammals at regenerating. In mammals, the liver regenerates well, but all the other organs essentially don't. In lower vertebrates—fish and amphibia—the heart can regenerate, so can the spinal cord, the brain, the retina, the lens, the kidney.

Maybe some of the signaling mechanisms that the lower vertebrates use are just not being activated in mammals. Maybe mammalian cells are competent for regeneration, but they're not receiving the right signals in response to injury. If we find out what the signals are in lower vertebrates, maybe one of the next steps would be to test those signals in mammals.

If one knows more about the mechanisms, one can actually think about therapies that might activate mechanisms that are dormant in mammals. JCB



A heart injury (arrow, left panel) repairs without a trace (right panel) in zebrafish. Mammals lack the regeneration process responsible for such scar-less repair.

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