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FIRST PERSON

First person – Michael Bachmann

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Michael Bachmann is first author on 'Induction of ligand promiscuity of αVβ3 integrin by mechanical force', published in JCS. Michael conducted the research described in this article while a PhD student in Prof. Martin Bastmeyer's lab at the Karlsruhe Institute of Technology, Germany. He is now a postdoc in the lab of Prof. Bernhard Wehrle-Haller at the Université de Genève, Switzerland, investigating how integrin αVβ3 is able to tune its ligand selectivity based on mechanical pull causing changes in integrin conformation.

Michael Bachmann

How would you explain the main findings of your paper in lay terms?

Integrins are proteins helping cells to attach to their environment [the extracellular matrix (ECM)], and to sense its composition and stiffness. You might expect that integrins should be able to 'see' and to recognize differences in this environment. But surprisingly, a large group of integrins and of ECM proteins seem to bind to each other without caring so much for their binding partner (known as ligand promiscuity). We offered one integrin, αVβ3 integrin, a choice of two different binding partners – fibronectin and vitronectin – on a molecular length scale. Surprisingly, we found that αVβ3 integrins not only prefer vitronectin, but that this preference can be tuned by pulling on αVβ3 integrins; with increasing mechanical force fibronectin suddenly becomes a possible binding partner for αVβ3 integrin as well. Thus, a cell can choose how promiscuous its αVβ3 integrins are. From there we went on and tried to understand how this is achieved on a molecular level. It seems that two different shapes (conformations) of αVβ3 integrin decide whether only vitronectin or both vitronectin and fibronectin are binding partners. Mechanical pull appears to be the critical mediator for changing between these shapes/conformations.

Were there any specific challenges associated with this project? If so, how did you overcome them?

This work relied heavily on development of new techniques. Since 2009, we have used a prototype of a Zeiss Elyra PS.1 and tried establishing live-cell imaging on that machine. That was challenging but it was also extremely exciting to be involved in super-resolution microscopy from the beginning. And the improved resolution was really helpful to (literally) see what's going on better. At the same time, we developed new surface-patterning techniques. Luckily, we could rely on a lot of expertise that was already present in the lab of Prof. Martin Bastmeyer. Eventually we were able to combine both fields, microscopy and patterning, which was clearly the cornerstone that allowed us to go on with this project.

When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

When I started reading the literature about integrins I got the impression that αVβ3 integrin is, together with α5β1 integrin, a very relevant fibronectin receptor. Having had this mindset, I was really excited when I saw for the first time that αVβ3 integrin avoids fibronectin so much.

Why did you choose Journal of Cell Science for your paper?

We published recently another manuscript about integrins in JCS (Soto-Ribeiro et al., 2019, doi: 10.1242/jcs.224493) and were very pleased with the whole process of reviewing, editing, and finally publishing our work. Also, many other excellent integrin-related manuscripts appeared in the last months in JCS, and we hope to join this club.

"Integrins are super exciting but also super complicated (at least to me)."

Have you had any significant mentors who have helped you beyond supervision in the lab?

Integrins are super exciting but also super complicated (at least to me). Fortunately, we had Prof. Berni (Bernhard) Wehrle-Haller helping us make sense of our data. I guess we would have shied away from integrins without him. His help was clearly essential for this project but eventually also convinced me to continue with a career in science and to continue studying integrins.

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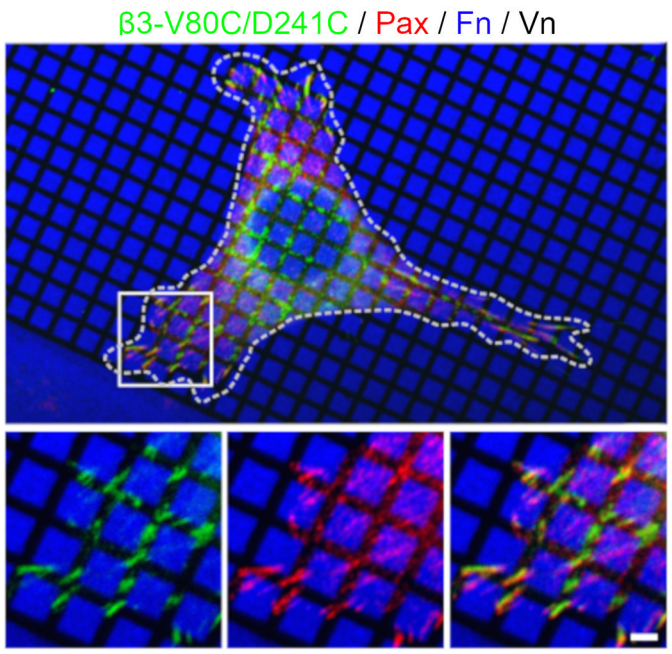

Cell expressing an αVβ3 integrin with a mutation that prevents transition to the extended-open conformation of the integrin. The cell is cultured on a fibronectin (Fn) and vitronectin (Vn) (Fn, blue; Vn, black) binary choice substrate and stained for paxillin (red). The integrin with the mutation (green) is able to bind Vn but not Fn.

What's next for you?

I joined Berni Wehrle-Haller's lab a bit more than a year ago as a postdoc. I guess it's the perfect place to stay super excited about integrins while becoming able to deal with the complexity of integrins. Between my PhD and my first postdoc, I worked as a high school teacher for biology and physics. It was nice but I missed working in science, and now I hope that I will be able to stay in science and to study integrins in more detail in the next years.

Tell us something interesting about yourself that wouldn't be on your CV

My parents are farmers and I worked on our farm every weekend during my PhD. That was always good to get my head free from the lab work. It also taught me acquiescence: no matter how hard you work, if it doesn't rain you lose your harvest. That kind of 'farmer zen' can be quite helpful in the lab. No matter how hard you work, some experiments just won't work. Luckily, in this manuscript we had more experiments that worked than those that didn't.

Reference

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