

Christine Jacobs-Wagner: Drawing the bacterial organizational chart

Jacobs-Wagner has been at the forefront of a revolution in bacterial cell biology.

Given their small size, you might think that bacteria don't need to be particularly organized: every protein would never be too far away from where it was needed. In fact, it's become increasingly clear in recent years that bacterial cells are highly ordered, coordinating their components in time and space to ensure the cells' rapid and efficient proliferation.

Christine Jacobs-Wagner's studies on the polarized bacterium *Caulobacter crescentus* have been central to this sea change in the way bacteria are viewed, adapting techniques used in eukaryotic cell biology to investigate proteins involved in cell cycle control, fate determination, and cell morphology. Jacobs-Wagner's interest in bacteria began as an undergraduate at the University of Liège in her native Belgium, and continued as a globe-trotting PhD student. Working in several laboratories around the world, Jacobs-Wagner demonstrated that expression of the β -lactam antibiotic resistance gene is induced by the cytoplasmic breakdown products that accumulate when cell wall synthesis is inhibited by antibiotics (1).

Jacobs-Wagner was introduced to *Caulobacter* as a postdoc in Lucy Shapiro's laboratory at Stanford University, where she discovered that a regulatory kinase changed its cellular localization over the course of the cell cycle (2). Jacobs-Wagner began her own lab at Yale in 2001, where she has continued to study how *Caulobacter* polarize (3) and how the polar localization of regulatory proteins directs the cell cycle and daughter cell fate (4, 5). She is also interested in the bacterial cytoskeleton, having identified the prokaryotic equivalent of intermediate filaments (6) and determined how they generate the curved shape of *Caulobacter* cells (7). In a recent interview, Jacobs-Wagner explained why studying bacteria fits her personality, and how the perception of these organisms has changed over the last decade.

LE TOUR

Did you always want to be a scientist?

Absolutely not. I grew up in Belgium, in a town near Liège, and when I was young I wanted to be a cyclist like Eddy Merckx! In high school, I couldn't decide what I wanted to do but ultimately, I chose to study biochemistry at university. But even then I didn't know I was going to be a researcher. It wasn't until the third year of my PhD that I really got hooked and knew I wanted an academic career.

How did you end up studying bacteria?

The last year of my undergraduate degree was dedicated to research. I wanted to improve my English, so I carried out my undergraduate work abroad. Staffan Normark welcomed me into his lab at Washington University in St. Louis, and that's where I started with bacteria. There are so many interesting things in science that if

I'd started with something else, I probably would have continued with that instead, but bacteria turned out to be the perfect choice for me. Because they grow fast, you can do a lot of experiments quickly. It fits my personality as I'm a little impatient! I also like the level of complexity in a single cell.

Where did you do your PhD?

In five years, I went to five different labs in four different countries. I stayed in the lab at Wash U. for the first year and then I went back to Liège where my supervisor was Jean-Marie Frère. Next I spent six months in Ted Park's lab at Tufts University in Boston and a few weeks in Jean van Heijenoort's lab in Paris-Orsay before returning to Staffan Normark's lab, which by that time had relocated to the Karolinska Institute in Stockholm.

My philosophy was that, rather than continually reinventing the wheel, I'd go to the labs that had the right methodologies to address the question I was interested in.



Christine Jacobs-Wagner

I went there with my samples because I felt it would be more productive and I'd learn much more. They were some of the best years of my life—I loved moving to different places and learning new cultures—but it was a little disruptive. I wouldn't want my students to travel as much, although I encourage them to spend a few months in a different lab when possible.

A SCIENTIFICALLY FERTILE CRESCENT

Why did you join Lucy Shapiro's lab for your postdoc?

By the end of my PhD I was in love with bacteria and wanted to stay in the field. There were so many questions that I thought needed answering. I contacted five different people and Lucy's was the first lab I interviewed in. I thought that what she was doing was so fabulous, and the model system—*Caulobacter crescentus*—offered so many opportunities, that I canceled my other four interviews and signed up with Lucy.

Why is Caulobacter a good model system?

I'm interested in temporal and spatial questions, and *Caulobacter* is really good for addressing both. We actually know very little about the bacterial cell cycle, and *Caulobacter* can be synchronized using a simple centrifugation technique. Then you can monitor the process you're

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interested in as the bacteria go through the cell cycle. You can synchronize other bacteria, but the methods aren't as easy.

Then there's *Caulobacter's* asymmetry. We're realizing that all bacteria are polarized, but typically only at the molecular level, whereas *Caulobacter* has entire appendages—such as the flagellum and stalk—that form at specific cell poles. In addition, it divides asymmetrically to produce two daughter cells of unequal size that have different fates. Symmetry-breaking mechanisms are a fundamental question in biology, but because this is at a single-cell level, it's highly tractable.

But I don't feel loyalty to *Caulobacter*. We have used other bacterial models on several occasions in the past. And right now, we're thinking about some experiments that would make more sense for us to do in *E. coli*. I try to use the best system to address whatever I find interesting.

How has bacterial cell biology changed in the last decade?

Bacteria were thought of as amorphous bags of molecules, floating around with no organization. Now we know that they exhibit extensive spatial organization that is important for many cellular functions. There are many processes that we didn't fully understand because we weren't aware of the cell's organization.

My perception of bacteria changed during my postdoc when I was studying a kinase called CckA that regulates the cell cycle. I fused it to GFP and went to Rich Losick's lab to use his fluorescence microscope—back to my old habit of going wherever I needed to. I found that this kinase localized to the cell poles, and that its organization changed during the cell cycle. The spatial regulation really opened our eyes and we realized that we had to start looking at proteins in cells to really understand their function. Once we and others started to do this, it really revolutionized the field.

SHARED APPROACHES

You're in the Molecular, Cellular and Developmental Biology department at

Yale. Does it benefit your research to work with non-bacteriologists?

Absolutely—our questions and approaches are similar, so it's been a tremendous help to be surrounded by some fantastic eukaryotic cell biologists and microscopists. We're also collaborating with a computational biologist—Thierry Emonet—as our work is becoming more and more quantitative.

One of your first achievements at Yale was the discovery of crescentin—the bacterial version of intermediate filaments. How did that come about?

It was an accident really. My postdoc at the time, Nora Ausmees, was doing a visual genetic screen for mutants that failed to localize proteins to the cell poles. She found *Caulobacter* cells that had lost their crescent shape, which we found really intriguing. In science, it's important to keep an open mind. If you see something interesting, it can be worth pursuing even if it's not what you were originally looking for.

Caulobacter grows by adding cell wall material along its length. The osmotic pressure exerted by the cytoplasm stretches the cell wall which, in turn, facilitates further growth, presumably because you need to break cell wall bonds to incorporate new material. Crescentin forms a filamentous structure on one side of the cell, and we

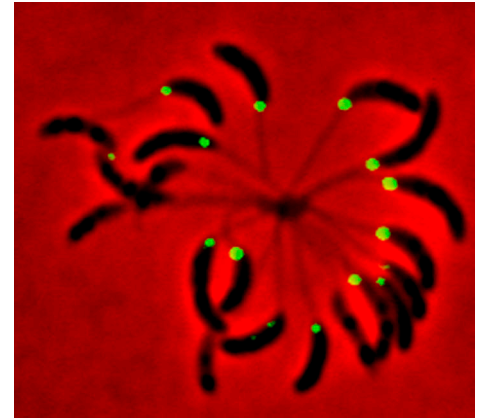
think it provides mechanical resistance to these stretching forces, so that growth is favored on the other side. Over time, this leads to the cells becoming curved.

What's your favorite paper of all the ones you've published?

The next one is always my favorite! Once a paper is in press, I'm already more fascinated by what's coming next. My students and postdocs are fantastic—they always come up with something more exciting than the work we've already done.

What is your lab working on now?

The doubling time of most bacteria is remarkably fast, and in that time they have to do a lot of important things such as



A rosette of *Caulobacter crescentus* cells expressing a fluorescent version of the asymmetrically localized cell cycle kinase DivJ.

growing, replicating, and segregating their DNA, and finally dividing. The reason they proliferate so well is that they can coordinate all these processes so that they occur at the right time and place. We want to understand this temporal and spatial organization. In this context, we are also interested in cytoskeletal elements that are involved in chromosome segregation, cell division, and cell morphogenesis. We need to understand how they affect these processes and how their assembly is regulated.

I read that you used to be an accomplished badminton player...

Only by Belgian standards! But yes, I was on the international team and was very dedicated to the sport, but I ruined my shoulder when I was 22 and had to stop playing. That was probably a good thing for my scientific career because I could focus on it more. But I still play sports now. I love soccer, running, hiking, and—when we're on vacation—I do kiteboarding.

What do you think you'd be if you weren't a scientist?

I don't know... I became a scientist a little bit by chance, but I still think that if I had another life, I'd probably be a scientist again because it's perfect for me. I really love it—it's the absolute best!

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