

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Ana Garcia-Saez

Ana Garcia-Saez graduated with a master's degree in biochemistry from the University of Valencia, Spain, before completing a PhD in the laboratory of Jesus Salgado in 2005. Afterwards Ana joined the research group of Petra Schwille at the Dresden University of Technology, Germany. In 2010, she started her own group at BioQuant, the Center for Quantitative Analysis of Molecular and Cellular Biosystems, at Heidelberg University with funding from the Max Planck Institute for Intelligent Systems and the German Cancer Research Centre (DKFZ). Since 2013, Ana has been a full Professor at the University of Tübingen. Her work focuses on membrane dynamics of mitochondria and the interaction of proteins with membrane lipids in the context of cell death programs, where she uses biophysical models and single-molecule high-resolution microscopy.

What inspired you to become a scientist?

I always wanted to be a scientist. As a kid, I wanted to be like Leonardo da Vinci, like Marie Curie or go to the moon. It was based on a very romantic idea – dedicating one's life to understanding how the universe or life works. In school, I was then really fascinated to learn about DNA and how all this information is encoded in the genome by simply a combination of four bases.

What motivates you now?

I shifted from DNA to proteins, because they have so many functions and they are like little machines. Then, I came across membrane proteins; they seemed like a very challenging subject, because it was so difficult to do biochemistry with them, that I thought it an interesting path to go. And that's how I got into membrane proteins and apoptosis.

What are the questions your lab is trying to answer just now?

We are working on the regulation of cell death and we focus on a key step, which is the permeabilisation of the outer mitochondrial membrane. This step really decides whether the cell is going to commit to die or not. We'd like to understand how the Bcl-2 family of proteins make holes in the outer membrane, because membranes usually do not have holes; it's a very interesting process from a physical and chemical point of view. We now suspect that it's not just one protein that is making a hole in the membrane, but that it includes deep structural reorganisations of the mitochondria. Furthermore, in recent years the field has realised that other pathways that regulate cell death, apart from apoptosis, also feature membrane permeabilisation. We therefore try to understand the biophysical mechanisms and common features regulating membrane permeabilisation during the different forms of cell death.

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What fascinates you so much about membrane biology?

Membranes are very dynamic and they are constantly undergoing transformation, and we still know very little of how this works. There's a cell biologist's approach to it, wanting to identify the components and how they work, but there are also physical forces at play to control how the membrane behaves. This is also true for mechanical forces at the cortex or even cell division, where you clearly see the relevance of the physical properties of the system in order to make the biological process work. I want to get to the intrinsic properties of membranes and what it means for their function.

Would you call yourself a biophysicist, a biochemist or a cell biologist?

I sometimes ask myself the same question, what am I? To the cell biologists, I'm a biophysicist and vice versa. But I'm a cell biologist at heart. My background is in biochemistry, and I simply am very much interested in having a quantitative approach to biology; I think that biophysical methods offer this possibility as a tool to understand how biology works.

What challenges did you face when starting your own lab that you didn't expect?

I really loved starting my own lab; I thought this is my thing, I did the right move. But the most challenging thing was to suddenly be 'on the dark side of the force'. Becoming a group leader changed my relationships with other scientists; not that I changed as a person, but somehow I was perceived differently from the PhD students and postdocs I used to interact with as peers before. It took me a bit



Ana enjoys playing ultimate (frisbee).

longer to find colleagues that were group leaders that I could identify with – many were older professors, had families and were simply not in the same age group. There was a loneliness as a group leader in the beginning that I had to get used to. Other challenges were the responsibilities that come with leading a research group, namely, managing people, funding and publishing.

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How are the challenges that you’re facing now different?

Now this workload has simply multiplied. There are more people to supervise, more grants and papers to write, and I still only have the same 24 hours available – or even less, because now I have children at home! I thus always had the impression that I didn’t manage to finish what I wanted to do during the day, but at a certain point, I accepted it and now I just do my best. If I do this, I am fine with what I achieve during my day in the office and the lab. I mean, one can always come up with more work that needs to be done...

How do you achieve a work–life balance when you’re trying to establish yourself as an independent investigator?

When I started my group, I didn’t have kids and I decided I would work as much as possible before having them, in order to get things

going in the right direction for my research career. I think I worked too much then, more than you’re supposed to. When I had my kids I reduced my working hours quite a bit, and I have to say it was not easy. It is now very important to me to take some time off for myself to maintain my mental health – to do sports, to go dancing, to meet friends. But after all, I have to say I’m a nerd; for me, science is a passion and I never really dissociate life from work. Even now, when I’m playing with my kids, I have scientific thoughts – I think of projects or I have ideas for experiments. Actually, when I’m working I also think about my kids, so I am not a very good example of organisation!

What does being a nerd look like? Your kid pokes a hole in his football, and you think about a perforated mitochondrial membrane?

Exactly! *laughs* Well, I have a two-year-old boy and he doesn’t sleep well at all during the night. He keeps me up quite often, and these hours in the dark are a very good time to think about experiments, collaborations and publications.

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What is the most important advice you would give to someone about to start their own lab?

An important piece of advice that has been with me ever since and that is true both for life and work is ‘where there’s a will there’s a way’, and this is certainly true for everyone. I believe when you start your lab you usually have the passion that is needed to succeed; make sure you keep it. Being pragmatic is also important: it’s key that you focus on a few projects and that you manage to publish something during your first funding period, because these initial years of your career are what is going to define you for whatever comes next.

What is your advice on establishing good collaborations?

The most important things are a common interest in the research and that the teams involved really want to solve a problem. You also need to trust your collaborators and have a positive attitude. When we want to work on something in our lab but we don’t have the expertise, I often contact a lab with the knowledge needed and I try to establish a collaboration. This might be risky sometimes, but I’m an optimist; I am in this business because I love science and I have a romantic idea about it. Therefore I think it should be open and we should all share knowledge in order to progress.

Could you tell us an interesting fact about yourself that people wouldn’t know by looking at your CV?

I like to be physically active. I play ultimate (frisbee), which is one of my free-time activity highlights at the moment. At my age it’s complicated to be able to play in a team and ultimate offers this possibility. I also love dancing, this is my second passion – I could dance all night long.

Ana Garcia-Saez was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.