

## EDITOR PROFILE

**Editor Profile: Ana García Sáez**

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In this special interview series, we profile members of *The FEBS Journal* editorial board to highlight their research focus, perspectives on the journal and future directions in their field. Ana García-Sáez is Professor at the CECAD Research Center, Institute for Genetics, University of Cologne (Germany). She has served as an Editorial Board Member of *The FEBS Journal* since 2021.

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**Can you give an overview of your research group's major focus and goals?**

In my lab, we are interested in understanding dynamic processes in biological membranes, and more specifically how molecular mechanisms and physical principles are coordinated to give rise to function. We study cell death signalling pathways, with a focus on the membrane changes that take place during the execution phase, ranging from mitochondrial alterations in apoptosis to plasma membrane permeabilization in regulated necrosis. For this, we use advanced microscopy methods including single-molecule imaging and super-resolution microscopy approaches in combination with membrane model systems and cultured cells.

**From a broad point of view, why is it important to delve into these research questions?**

Biological membranes are basic constituents of living organisms and understanding their dynamic organization and functional mechanisms is a fundamental question in biology. Besides this, the modulation of cell death pathways offers therapeutic opportunities for a range of diseases, from cancer to neurodegenerative and immune disorders. Detailed knowledge of the molecular mechanisms involved in the different pathways and their

functional consequences is critical for the development of effective drugs. In our case, we try to understand how cell death executioners alter the permeability barrier of the cellular membranes where they act. Based on this new knowledge, new modulators of death effectors can be identified, which have the potential to control membrane permeabilization for the induction or inhibition of cell death and thereby alter disease outcomes.

**What has been your favourite (personal) breakthrough, to date? How did you feel when you made this discovery and realized the wider implications?**

My favourite discovery is probably the direct visualization of apoptotic pores in the mitochondria of dying cells. It is true when people say "seeing is believing", as this finding finally revealed how mitochondrial permeabilization is mediated by BAX and BAK in apoptosis. Being able to image the pores was a very exciting moment. At the same time, we were surprised by the broad distribution of structures formed by these proteins, in contrast to other well-defined pores in the cell, like the nuclear pore. This has shaped our research directions and led us to discover how BAK and BAX determine the growth rate of the apoptotic pore based on their distinct oligomerization kinetics and their ability to regulate each other.



### **What research thread in your lab are you currently most excited about?**

I am very excited about the new perspectives opened by the quantitative analysis of the apoptotic pore growth over time. Besides revealing unexpected mechanistic and functional differences between apoptosis executors that would not have been evident otherwise, this gives us a tool to evaluate how other factors may regulate mitochondrial permeabilization in apoptosis. Additionally, we are very interested in extending this type of study to other “death pores” so that we learn about the molecular mechanisms involved.

### **What are the key ongoing challenges in your field, and can you discuss ways that these might be addressed?**

I find that understanding the general principles, as well as the key differences, in the mechanisms of “death pores” will be key to grasp the role of membrane permeabilization in the execution of cell death. Moreover, we are only starting to understand the non-death-related functions of cell death pathway components, specifically for paracrine signalling and during cell fate decisions. I find the sublethal consequences of “death pore” formation particularly interesting. Obviously, I am biased, but I think that investigating these questions with advanced microscopy and quantitative methods will bring new insights from a different perspective.

### **Have you always been interested in science and was it inevitable that you would end up in this career? Were there any particular events, influences or mentors that shaped your research direction?**

I have to admit that I have always been romantically interested in science and in knowledge about the world around us. Therefore, this was always my first choice as a career and I worked hard, focused and found joy in this career direction. That said, I have always known that I would also be happy if I had other jobs because there are many, many alternative paths that I find professionally interesting. It was during my post-doc that I decided to give all I had to try to make a career in academia. And with dedication, perseverance and taking the opportunities I was offered, I managed to progress through the system to where I am now. I was lucky to have great mentors during my PhD, post-doc and group leader stages that gave me great advice and from whom I learned different aspects of how to be a researcher.

### **How do you balance management of your research group with your other academic and professional commitments?**

It's tight. I am learning to say “no” to requests that I consider unnecessary. But since the research of my group is the most interesting part of my work, I make sure that I book the time in my calendar to do science and to interact with my group members. I have to admit that being able to travel again to conferences and so on in the past year has made it more challenging!

### **What advice can you offer an early career researcher who is hoping to forge a successful career in academia?**

Important is the path, not the aim. If you are an early career researcher, you are already having a career in academia, so enjoy and make the most of every part of the trip. The definition of a successful career is subjective, but giving your best will always give you peace of mind, no matter where you end up. Then, there is strategic planning, identifying emerging fields and acquiring demanded skills that make you unique; that

is also important to increase the chances of professional success.

**What long-lasting impact will the COVID-19 pandemic have on science and the public's perception of it, in your view?**

I want to believe that it has become a bit clearer for society, and especially for the broader public, that investment in research can have a very strong impact in fighting current and potential future challenges for humanity.

**How were you persuaded to join the Editorial Board of *The FEBS Journal*? In what ways do you think that the journal stands out from other journals in the Biochemistry & Molecular Biology sector?**

I have always held *The FEBS Journal* in high regard. I find of particularly importance the fact that it is

European and that it is associated with a scientific society whose purpose is non-profit. So, I was happy to participate in this project, and also curious to learn how the journal works from the inside.

**Do you have a favourite *The FEBS Journal* paper?**

My favourite paper is “MAVS polymers smaller than 80 nm induce mitochondrial membrane remodeling and interferon signaling” by Modis and colleagues. They used super-resolution microscopy to visualize MAVS assemblies in cells and identified mitochondrial remodelling associated with MAVS activation, which improved our understanding of how this protein functions in the sensing of double-stranded DNA.

**Tell us something about yourself that we might be surprised to hear!**

I am trying to improve my rice cooking skills, going beyond “paella” to other types of traditional Valencian rice recipes typical of my homeland.