Pilar Alcaide: “Motivation is key for a satisfying, enjoyable career in research”

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Pilar Alcaide is Professor of Immunology at Tufts University. She completed her doctorate in biology at the Autonomous University of Madrid and moved to the USA to continue her scientific career. Her laboratory researches the cell and molecular mechanisms of the traffic of leukocytes in acute and chronic inflammatory settings, with a particular focus on T cells and their role in chronic inflammatory diseases and heart failure. During her doctoral studies, she researched immunosuppression during acute T. cruzi infection, and as an independent researcher, she was a pioneer in the emerging field of T-cell mediated inflammation in heart failure. Her group has made important discoveries in cardio-immunology, particularly related to adaptive immunity in heart failure with a reduced ejection fraction. She also makes significant efforts in mentorship of students and junior professors.

- **How did you decide to become a scientist?**

I was really interested in biology during my teens. But I was also interested in many other things, including sports science and football. So it wouldn't be true to say that I always wanted to be a scientist. At university, I specialized in biology and, in my last two years, in molecular biology. From my first cell biology class, I was fascinated by immune cells and my interest grew when I had my first immunology class and worked on a scientific literature project about the benefits and side effects of nonsteroidal anti-inflammatory drugs. When someone suffers an autoimmune disease, the immune system seemed fascinating to me and that's why I chose immunology for my doctoral research. However, I deliberately avoided studying my autoimmune disease because I didn't want to be thinking about it all the time. When the time came to think about what to do next after finishing the doctorate, I knew I had to do an academic post-doc. It was difficult to decide if I wanted to broaden my training in immunology or apply it to other fields. As immune cells need vasculature to circulate between organs and exercise their effector functions, I felt that the cardiovascular system was the next logical step for my scientific growth. I made the right decision. I love what I have learned and continue to learn about cardiovascular diseases. The integration of immunology and cardiovascular biology has substantially contributed to our understanding of many aetiologies of cardiovascular diseases. Several scientists, me included, have gone from identifying immune cells in unexpected cardiovascular organs to learning that stromal cells are also an important component of our immune response. There is an immense potential to make discoveries at the cardiovascular-immune system intersection that will almost certainly lead to new therapies.

- **You have just received the Excellence in Science Award for leadership, mentorship and research…**

It is awarded by the American Professional Society Federation, which includes over 30 scientific associations from immunology to oncology or the cardiovascular field. It was a pleasant surprise. They give three prizes: one to the most senior people, another to younger researchers who have been in the field of research for less than 8 years and finally, the one they awarded me, which is for consolidated research. They considered that I had impact in the field of immunology in cardiovascular research.

- **I was the first person to discover that there were immune system cells in the heart.**

It had been discovered in people who had had myocardial infarction or with autoimmunity, when there is direct damage to the heart. However, we didn't know whether they were present in patients with heart failure caused by other aetiologies, who had not had damage in the heart. So we were the first.

- **And why was that discovery important?**

It is important because we assume that T cells, the cells of the immune system, have evolved to

combat infection or to promote wound healing. That's why it was not surprising that there should be cells in the heart if there was a viral infection that reached the heart or if you have a heart attack, which is also a wound that needs to heal. But there were a group of patients with heart failure that had not been caused either by infection or by myocardial infarction. In the laboratory, we saw that these patients, when they are waiting to receive a transplant and have an unknown aetiology, also have T cells, which made us think: they are there and since they haven't gone to do any good, they must be doing something bad. Really, they are doing what they have been trained to do: cause fibrosis, which is necessary if you have a wound or a myocardial infarction. But they do it when there has been no lesion, causing a type of pathological fibrosis, which means that the heart neither contracts nor relaxes correctly. And that causes heart failure.

I had that idea, but before doing it all experimentally, we decided to obtain samples from patients with non-ischaemic heart failure, i.e. who have never had a heart attack or a known viral infection involving the heart. In that group of patients, we saw that there were T cells. The next step, in the laboratory, was to study whether those cells were good or bad. We studied these T cells in animals in the laboratory.

- **What percentage of patients have this type of heart failure?**

It depends on how you categorise heart failure. If your definition depends on reduced or preserved ejection fraction, it would be 50%. There are 50% of patients whose ejection fraction is not compromised, but they suffer heart failure because their heart does not relax and enlarges. Of the other 50%, who have a compromised ejection fraction, meaning their heart does not contract properly, half are due to heart attacks and the other half due to unknown causes, which may be heart valve disease, congenital disease, high blood pressure, the toxicity of chemotherapy agents (anthracyclines)…

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Do you think the position of women in science has changed since the beginning of your career?

For me, the greatest change has been awareness. Awareness about the importance of a better representation of women, of micro-aggression and the importance of speaking out when things are not right. Awareness is the first step towards a positive change and communication is key. I have spent more time in the USA than in my home country, where I began my career, which means I can comment more on the differences in the USA than in Spain. In the USA, the representation of women has increased in comparison to what it was when I began my career in science. Being seen, listened to and the centre of attention as a female scientist can leave a lasting mark on the next generation of women in science, who now have more models to follow than we did.

When I look back to my first years in science in Spain and the USA, I also see improvements in other aspects from the creation of facilities for breastfeeding at work, or even changing the system to allow for maternity leave in the 'post-doctoral period' in terms, for instance, of grant applications. However, there is still room for improvement, and we still need to advance a great deal. Achieving these advances will not only benefit female scientists but the whole research community.

At institutional level we are seeing things change. My university has felt a breath of fresh air with the appointment of a female Chancellor. But she is almost the only one. Representation is important, but I believe that representation has to be done properly.

- **What are you most proud of in your career?**

There are so many things I'm proud of. I think we should be proud of each step; however small it may seem. I am very proud of having completed my doctorate at the same time as I was a footballer

with Real Madrid, following both of my passions. I am also very happy to have left my comfort zone of Madrid and come to the USA as a person and a scientist. And I am excessively proud that, while I did it, I managed to have three wonderful children who appreciate what I do and are proud of me. Finally, I'm proud that my discoveries in research have attained recognition within the cardiovascular community and of having become part of a network of colleagues and friends with whom I love working and interacting. Remembering when I knew only a few people in my field and felt intimidated when making a presentation or showing my scientific knowledge and comparing that to where I am now is a fantastic feeling.

- **What advice would you give people who are setting out on their research careers now?**

Take heart, follow your passion and enjoy what you do. Motivation is key for a satisfying, enjoyable career in research. Find the thing that keeps you motivated, projects or experiments that enthuse you, and work hard to finish them because it is fun and satisfying. If you don't have motivation, then follow your passion elsewhere. No other job in the world allows you to be creative and attempt experiments with so many possibilities of failure. But, when the experiment "works" and you make a new discovery, it is published and you see it take life as other scientists improve and develop findings, the feeling of being part of something bigger is stimulating. Finally, my advice is to not be afraid to present or discuss your science and meet other scientists who you may only know through their work but not in person, regardless of how "big" their names are. I recommend taking advantage of every opportunity to do just that. Peer review always leads to professional growth, helps build a network and, often, along the way, you meet incredible people you can learn and have fun with.

- **What do you think of the CNIC?**

Internationally, and in the cardiovascular world, it is well known, and its researchers publish well. I sometimes collaborate with Pilar [Martín], although we haven't had any joint projects yet. For two years I was director of the American Heart Association (AHA) Basic Cardiovascular Science Congress and later, for another two years, I was head of Basic Cardiovascular Science during the AHA Scientific Sessions. I always try to give visibility to Spanish scientists

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