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## • A Portuguese research in Sweden.

I went to <u>Karolinska Institute</u> in the late '90s as a medical student, just to try doing research in a different place because I had already done some research in Lisbon. I really liked the atmosphere—it was very international and high-tech.

I had the opportunity to conduct research while continuing my clinical education. I'm a doctor from Lisbon, and when I first went to Stockholm, I was already in the final years of medical school. I returned to Portugal because I wanted to be a clinician, but in Sweden, they told me, "Here, you can combine clinical work with research." The opportunity to integrate both fields really captivated me. Sweden had excellent infrastructure, funding, and a very diverse international environment. That's why I stayed. I went back and forth for many years, and then finally, I settled there. In the meantime, my husband also received a job offer in Sweden. We moved together, thinking, "We'll just do our PhDs and then go back home." But after the PhD, we thought, "We'll just complete our residencies and then return." Then it became, "Let's do a short postdoc, and then we'll go back." And then, "I'll just finish this grant..." And suddenly, 23 years later, I'm still here. It felt like a never-ending postdoc, but now I'm a full professor leading a very international research team of 17 people from about 10 different nationalities.

• You mentioned that your lab consists of 176 people from 10 different nationalities. Do you think this diversity benefits research?

Oh, absolutely. Diversity is essential. Different cultures bring different approaches to problem-solving, different inspirations. It's incredibly enriching. We need both men and women, all working toward the same goal. More perspectives mean more brainpower. If everyone thought the same way, it would be very boring—and possibly ineffective. I love the diversity. It is one of the things that motivates me to get up in the morning.

 Since your studies and your move to Sweden, have you always focused on cardiovascular disease and atherosclerotic plaques, or have you changed direction over the years?

No, I was always focused on the cardiovascular system. I started collecting my first samples in Portugal as a medical student because I noticed that surgeons were discarding them. Initially, I wanted to be a surgeon, so I assisted in surgeries in my free time. I saw them throwing away this incredibly important material—the very substance that causes fatal diseases—and thought, "We should study this." That is how it all started.

I had a strong curiosity about these deadly plaques that we were removing from patients to help them become better. I felt an urgent need to understand them: What are they? Why are they formed? That curiosity drove me. I had already done some basic research in Portugal, but in Sweden, I saw the potential of even more advanced technology that could help me study these plaques in greater depth. At the time, those high-tech machines were not often available in Portugal. So I decided to take my samples there to learn also from the brilliant minds in Sweden.

Portugal also needed more clinicians, so I felt I could return home to treat patients. But research became my passion. Throughout my career, I balanced my time—50% research, 50% clinical practice. It was like a hobby that became an integral part of my life. Of course, sometimes it felt like I was working 100% in both fields! But I loved it. Eventually, the professor who welcomed me in

Stockholm moved to Lund University, so when I returned from Portugal, I went to Lund instead. I also had clinical experiences in Germany, which was another enriching cultural and professional experience. Learning Swedish was tough—I had to take evening classes—but it was worth it.

 Now that you are a full professor, do you still have time to see patients and conduct research?

Yes. Since becoming a full professor—well, I was 39 at the time —I reduced my clinical time. Before that, I divided my time equally: 50% with patients, 50% with my research group. Now, I spend about 30% in the clinic and 70% in research. So I still balance my "hobby" with patient care.

• How important is it to do both? Some people focus solely on research or clinical practice, but you have maintained both.

For me, it is essential. Seeing patients inspires my research. When I treat someone, I see a problem that needs solving. Clinical work provides immediate fulfillment—you help rapidly one patient at a time. But research has the potential to help many people, though it takes years to see the results. This combination is a luxury! I love having both immediate and long-term impacts.

Some of the research questions I investigate actually come from my patients. They ask questions I don't always have the answers to, so I take those questions back to the lab. Years later, after countless experiments, I can get closer to giving them answers. That is an incredible feeling. It makes my research meaningful because I remember the faces of the people who inspired it.

• Atherosclerotic plaques are a leading cause of death worldwide. Can early detection make a significant difference?

Absolutely. These plaques cause heart attacks and strokes. If we detect them early, we can treat them before they become dangerous. In my research, we use two main strategies. One approach is to study plaque mechanisms—how they form and rupture—so we can develop targeted treatments to prevent them. The other approach involves blood markers or imaging techniques to detect plaques before they cause harm.

 Biomarkers seem like an easier solution for clinical practice compared to imaging, which requires specialized equipment. How early can biomarkers detect plaques?

Biomarkers are easier to implement because they only require a blood test for instance. But the challenge is identifying the right molecules—there are many substances in the blood, so we need to find the most relevant markers. Imaging is also crucial, especially non-invasive techniques like ultrasound, which doesn't use radiation and can be done with portable devices. This makes it accessible even in low-resource settings. Both approaches are promising for the future.

• Can we detect the plaques early, or even before they appear??

That's a \$1 million question, right? But of course, there are many ways to approach it. My research group is working on two main strategies. One involves studying plaques to understand the mechanisms behind their formation or rupture, which can lead to strokes. By understanding these mechanisms, we can potentially find new ways to "calm" the plaques down or prevent them from forming altogether. So, this is one branch of my research.

The second branch focuses on understanding what happens inside the plaque—how some molecules leak out and enter the bloodstream. These molecules could eventually serve as biomarkers, which could be detected through a blood test. It is a simpler way to get valuable information compared to imaging.

Now, about imaging techniques: we are exploring ways to take images of the blood vessels to identify when plaques are forming or whether an existing plaque is dangerous. These two approaches—biomarkers in the blood and imaging—are the main focus of my lab in Sweden at the moment.

 You mentioned biomarkers earlier, and this might sound like a silly question, but would the first approach (biomarkers) be easier to implement in clinical practice than the imaging one? Imaging requires specific machines, and it is more expensive, right? How early can we detect these markers in the blood?

Yes, biomarkers are easier to transfer into clinical practice. With blood tests, you only need a small drop of blood, and from that, you can get a lot of information. The challenge is that there are so many substances circulating in the blood, so identifying the right molecules can be tricky. You would likely need a combination of several key molecules to get accurate results. That is one challenge with biomarkers. On the other hand, I really enjoy the non-invasive imaging techniques, like ultrasound and computed tomography. Ultrasound, in particular, doesn't require radiation, and it is an exciting tool because it's easy to use, portable, and relatively inexpensive. You could even use it in low-resource settings, where there is no access to advanced equipment. Imagine using a handheld ultrasound device to screen large populations or help differentiate high-risk from low risk subjects, which is something I think might have a lot of potential for the future. The goal is to create simple, portable, and affordable methods that can help people, especially in places where more expensive and high-tech equipment is not available. I really believe in bringing simple solutions to the people who need them most.

 Do you think these simple methods could change the cardiovascular landscape in the next few years?

Absolutely. It is happening gradually. For example, cholesterol levels are already a well-known biomarker, and in recent years, markers like CRP (C-reactive protein, indicating inflammation) have gained traction. As we continue to discover more specific biomarkers, the outlook is promising. When it comes to imaging, we're already using ultrasound widely, especially for pregnant women, but also in cardiovascular disease. The work we're doing—developing new algorithms and techniques to enhance imaging—isn't too far from being implemented. We're already using the machines, so it is just a matter of refining them to help identify plaques more clearly. Of course, there are challenges, and things always take longer than we'd like. Researchers tend to be optimistic! One of the hurdles in technology development is the new regulations in Europe (MDR), which are more demanding. The regulatory aspect requires a lot of work, but we're already making progress there. So, I don't think it will take too long before we get to where we want to be.

• At CNIC, we have a large study with Nordic countries called REACT. Does this align with your work?

That sounds exciting! It is similar to studies we're conducting in Sweden. Collaboration is essential, and proving results across multiple cohorts strengthens our findings. I'd love to work together.

What advice would you give future cardiologists and researchers?

I think the most important thing for future cardiologists is that despite all the technology that's emerging, they should always remember the human aspect of their work. I came across a quote by Sir Osler that I really like: "They may sometimes cure, often treat, but always comfort." I find this really meaningful, and I think it's an essential aspect of being a cardiologist.

For me, mentoring is one of my life's missions. Helping the new generation is one of the keys to making a positive impact. I feel a responsibility to pass on what I have learned, no matter how little

that may seem. It's something I take deeply to heart. In a way, it's similar to how I approach working with patients: you help them improve their health, and with research, you help them make better progress in science. For the researchers, I always encourage them to learn from their mistakes. My son, who is a teenager, often talks about the concept of "journey before destination," which he reads about in his fantasy books. It's not just about the outcome, but about the process. Mistakes are fantastic learning opportunities, so I tell them to be positive, embrace their errors, and pursue their passion.

What I try to do is help them find their goals. And when the time comes for me to leave this world, I hope people will say that I was a little crazy, but that I contributed to helping patients and supporting my younger colleagues. They may be students today, but they will be my colleagues tomorrow. I feel a responsibility to help them become not just excellent professionals, but also amazing human beings.

 That reminds me of something we did recently. We created an article about former students who were here 15 or 20 years ago. Now, they're leading departments and making an impact in their respective countries. We interviewed four or five of them to hear their reflections on their time here and the journey they've taken to reach leadership roles.

I think this ties into what Osler said—"comforting people." Research is a long-term way of helping people, advancing knowledge that ultimately improves their lives. Another principle I always tell them—and one I try to live by myself—is: treat others the way you would like to be treated. These are my guiding values: passion, kindness, and empathy. If you can't cure someone or provide the perfect treatment, at least you can offer them comfort because at the end of the day, we are all human. That's my approach.

• Do you remember when you were a teenager? Did you always know you wanted to be a doctor?

Yes, since I was three years old. I was frequently sick as a child and spent a lot of time in hospitals. Back then, parents weren't allowed to stay overnight with their children, so I would be alone in the hospital. I cried a lot, of course, but I also developed this sense that hospitals were places where healing happens, where you can help people. That sense of wanting to help stuck with me. I always knew I wanted to be a doctor. Over time, I considered different specialties, but I always knew I wanted to help others through medicine. It's funny—and again my son recently taught me the concept of "journey before destination," which is something I now truly appreciate. It feels like I've always been on that journey.

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