

INTERVIEW

Disease-specific therapeutic interventions in Type 1 diabetes



Pere Santamaria*: Pere Santamaria is a professor in the Department of Microbiology, Immunology and Infectious Diseases and director of the Julia McFarlane Diabetes Research Centre in the Faculty of Medicine at the University of Calgary (AB, Canada). He is also a group leader at the Institut d'Investigacions Biomediques August Pi i Sunyer in Barcelona, Spain, and Scientific Founder of Parvus Therapeutics, Inc. He earned an MD and PhD degree from the University of Barcelona (Barcelona, Spain) in 1983 and 1987, respectively, and completed his medical speciality training in clinical immunology in 1987, also in Barcelona.

From 1988 to 1992, he pursued postdoctoral research training in the Department of Medicine and Institute of Human Genetics at the University of Minnesota (MN, USA). He joined the Faculty of Medicine at the University of Calgary in 1992 as an assistant professor. In 2009, he was the founder of Parvus Therapeutics Inc., a biopharmaceutical company that specializes in the development of nanovaccines for the treatment of autoimmune diseases. Santamaria has been the recipient of several honors and awards, including the Alberta Heritage Foundation for Medical Research Senior Scholar, Scientist and Senior Scientist awards, the Canadian Diabetes Association Young Investigator award and the Juvenile Diabetes Research Foundation Scholar award, among others. Over the years, Santamaria has served on numerous national and international grant review committees, serves on the editorial boards of several scientific journals, and is a regular reviewer for many others. Santamaria's research focuses on the pathogenesis, immunogenetics and treatment of autoimmune Type 1 diabetes. He currently holds major research grants from several national and international granting agencies, holds several patents and patent applications, speaks regularly at national and international scientific meetings, research institutions and universities and has written more than 150 publications.

Q How did your career lead you to working in diabetes?

When I was growing up, I became interested in medical research; however, I had no idea how to get into it. I thought that medicine was the best route to it and, therefore, I pursued a medical degree. I was particularly intrigued by immunology, and therefore did my residency in clinical immunology. While doing this, I realized that I needed to learn how to ask scientific questions or test hypotheses in

a laboratory setting. Consequently, I did a PhD in immunology and cellular biology. I have always been fascinated by the inner workings of the immune system and autoimmunity was something that particularly intrigued me, but my focus on Type 1 diabetes was determined by fate. As I was completing my PhD, I met a professor in Barcelona (Spain), who had carried out diabetes research abroad, who graciously offered to help me follow his path. I secured a postdoctoral position in the



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USA, focusing on the immunogenetics of Type 1 diabetes. Type 1 diabetes has been the focus of most of my work ever since.

Q Were there any colleagues in particular that you worked with who really influenced the path that your research has taken?

It was professor Alberto de Leiva from Barcelona who had a lasting influence on my career and helped me with the choices that led me to where I am today. I met him at a time when I had no idea how to get into medical research. My parents could not advise me as to what academic path I should take because they never had the opportunity to study. In Spain at that time, biomedical research was not particularly well funded. I knew that I wanted to go abroad and not only continue my education but also help generate new knowledge through research. However, I needed guidance on how to achieve this. I had met Professor De Leiva at a meeting and he went out of his way to help me, despite not knowing me personally. I will never forget his helping hand. He played a pivotal role in my career at a stage when I really needed it, and I am very grateful for this. My mentors during my postdoctoral training (José Barbosa, Stephen Rich and Tony Faras) also played an important role in my career; they nurtured my scientific curiosity and, importantly, gave me the freedom to follow my instincts.

Q What do you consider to be the biggest achievement in your career so far?

Through both slow progressing, curiosity-driven research and a healthy dose of serendipity, I was fortunate to stumble upon a new immunotherapeutic approach based on nanotechnology for the treatment of Type 1 diabetes and other autoimmune disorders. Our nanomedicines reset autoimmune responses without compromising the ability of the immune system to fight off infections and cancer by triggering a new immunological pathway. I believe strongly in the potential of this technology and, thus, consider this to be my biggest achievement. We are currently working hard to try to bring this therapy to the door of the clinic.

Q Do you think it will take a long time to get this research to clinical trials?

I founded a therapeutics company to lead this process. It is one thing to raise operating funds from research funding agencies to test scientific hypotheses in the academic setting, but it is quite another to raise the capital required to manufacture and develop a drug for use in humans. Research is an extremely important enterprise for society because it generates new knowledge and, in the long run, creates products. However, the amount of capital required to advance a new compound to the clinic is several orders of magnitude greater than that needed to run experiments in an academic laboratory. It will take us approximately 12–18 months to reach Phase I clinical trials once we are appropriately funded.

Q What do you think has been the biggest breakthrough in diabetes management research in recent years?

This is a hard one to answer. In my opinion, it is not appropriate to equate all important discoveries with breakthroughs; a breakthrough either changes the way we treat a particular disease or revolutionizes a field of research. There have been paradigm shifts in diabetes research in the last couple of decades, but I would hesitate to call any of these a real breakthrough. At the end of the day, insulin remains the only therapeutic option for Type 1 diabetic patients. However, please note that I am not trivializing important advances in, for example, islet transplantation, as a therapeutic approach for patients with brittle diabetes, or the enormous progress in our understanding of the disease process, including the identification of genetic determinants and their contribution to disease susceptibility or resistance.

Q Could you tell me a bit more about the research you are working on at the moment?

We have discovered that autoimmune diseases create what we call ‘memory’ against themselves. In the case of Type 1 diabetes, for example, the autoimmune process leads to the destruction of the cells that make insulin in the pancreas but also generates a

type of white blood cell that tries to put the brakes on the disease. This process – ‘the brake’ – is based on immunological ‘memory’. We believe that during natural evolution, the immune system has evolved to be able to sense and react to autoimmune attacks by mounting counter-regulatory (antiautoimmune) responses that aim to blunt the attacks. This process is either inefficient in patients with autoimmune diseases or is overwhelmed by the disease-causing autoimmune attacks. Our nanomedicines are based on the discovery of this type of counter-regulatory immune circuitry; they dramatically potentiate these counter-regulatory responses and reset the immune system to its normal state. In other words, our nanomedicines boost the immunological memory that the disease process generates against itself and, thus, operate by boosting a naturally occurring phenomenon.

Q Do you think this research could ever lead to a cure for diabetes?

I believe so, but we have to be cautious because we have not yet tested our nanomedicines in humans. All I can tell you is that in mice these nanomedicines effectively reset the autoimmune response to its normal state and can render diabetic mice insulin independent for life.

Q Do you think the media focuses too much on Type 2 diabetes?

Yes, there is much of focus on Type 2 diabetes but this is understandable because the prevalence of Type 2 diabetes in industrialized societies is much greater than that of Type 1 diabetes, and the gap is increasing owing to the obesity epidemic. The healthcare costs associated with Type 2 diabetes are significantly greater than those caused by Type 1 diabetes. At personal and family levels, however, the impact of Type 1 diabetes is more significant because the disease typically manifests itself in young children or adolescents and, therefore, affects

the quality of life of the family as a whole and for a much longer period of time than Type 2 diabetes.

However, it should be noted that Type 2 diabetes has an immunological component that had not been appreciated until a few years ago. In a way, Type 2 diabetes can be considered to be an inflammatory disease with some autoimmune components. The differences between Type 1 and Type 2 diabetes are not as great as originally thought.

Q Where do you see the field of research going in the next 5–10 years?

Funding bodies, governments and societies are pushing for more efforts in translation as there is an increased need to bring treatments to the bedside. Society expects scientists to develop new drugs and treatments, and to accelerate the translation of these into clinical practice. I support these efforts; however, I also firmly believe that it is essential that we continue to support basic, fundamental, curiosity-driven research. Curiosity-driven research has been at the root of all the breakthroughs made in science; it unleashes the power of instinctive thinking and brings the curious mind to places it didn’t foresee, hence real discoveries and breakthroughs.

Disclaimer

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P Santamaria is the scientific founder of Parvus Therapeutics, Inc. P Santamaria has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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