Investigator Spotlight: The JDRF-nPOD Scientists Who Seek the Cure for

Each month, we highlight one of the nPOD investigators. Thanks to the fundraising of all the JDRF chapters, these scientists are able to have access to nPOD samples for their work. We'll let them introduce themselves, tell you about their research, and their lives.

Decio Eizirik, M.D., D.Med., Ph.D. (Universitet Libre de Bruxelles, Brussels, Belgium)

1. Tell us about your education and background. Where are you from, and where did you go to school? I was born in Porto Alegre, Brazil; I attended medical school and did my training in internal medicine/endocrinology/diabetes there. After this, I did a D.Med. at the University of Sao Paulo (USP), working half-time in endocrinology/diabetes and half-time in basic research. Part of my thesis was done at the University of British Columbia, in Canada. After defending my thesis, I got a position as Assistant Professor of Internal Medicine at USP, and decided to do a one-year post-doctoral fellowship at the Uppsala University in Sweden. The goal was to learn techniques for long-term pancreatic islet culture, a method largely developed in Sweden. This one-year fellowship turned into ten years of work in Sweden! While there, I did a second Ph.D. in cell/molecular biology and decided to focus on basic research, and to pursue a career in diabetes. At this time I received great help from JDRF, which provided me with a post-doctoral fellowship and a Career Development Award—both were crucial for continuing my research activities.

2. Where do you currently work and what is your position? What does "a day in the life" look like for you?

I am presently full Professor and Director of the Laboratory for Experimental Medicine and Center for Diabetes at the Universitet Libre de Bruxelles (ULB) in Brussels, Belgium. I've been at ULB since 2002; our laboratory has grown from a small group of 12 colleagues to more than 30 people with four groups working on different aspects of pancreatic beta cell research. My main focus is on type 1 diabetes. Most of my time is devoted to research: discussing projects; interpreting data; having meetings with my post-



My typical day of work starts at 7:15 am and goes until 7:00 pm. A couple of days per week I escape at lunch time to go to the gym. I usually work on Saturday mornings, but do my best to keep Sundays free.

3. Why diabetes? How did you get involved in diabetes and/or what made you want to work in diabetes research?

My interest in diabetes started during my fifth year of medical school, when I got a position as Student Research Assistant to Professor Jorge Gross, at the Hospital de Clinics de Porto Alegre. Jorge was just returning from his training in Sao Paulo, and was establishing the endocrine/diabetes unit at the hospital. His special research interest was the long-term complications of diabetes. Since his group was very small, I was suddenly involved in outpatient clinics—under his supervision—and in clinical research on diabetes nephropathy (kidney damage) and neuropathy (nerve damage). I loved it! Diabetes complications then, in the early 1980's, were much more prevalent than today. I closely followed many patients who were suffering with terminal kidney disease. (At that time in Brazil, diabetic patients were not yet candidates for kidney transplantation, so they were treated with peritoneal dialysis.) It was very sad to see these patients—many of them young—suffering and dying. This made me realize that the best research focus would be on disease prevention, to avoid these devastating complications. This started a journey that continues today.

4. Tell us about your research.

Our key question is to understand why and how pancreatic beta cells are killed in type 1 diabetes. Then, based on this knowledge, develop novel approaches to protect them—and hopefully, prevent disease.

It is fair to say that our work has introduced a paradigm shift in the field, indicating that the "battle" leading to beta cell loss in diabetes is fought, to a large extent, inside the beta cells themselves. Signaling coming from the beta cells leads to a "dialogue" with the invading immune cells that amplify the immune assault. We have recently shown that this dialogue is regulated, at least in part, by candidate genes for diabetes acting at the beta cell level. Most of the research effort in type 1 diabetes pathogenesis has focused on the immune system, and it is, to a good extent, our own work that indicated the important role for the pancreatic beta cells in the disease.

5. What are your thoughts on the progress being made in T1D as a whole?

There has been major progress in recent years in the understanding on how the immune system attacks and kills pancreatic beta cells, but this has not yet led to translation into novel clinical approaches. The big problem is that we still don't understand what leads the immune system to recognize beta cells as "foreign" and start attacking them. Until this is clarified, it will be difficult to re-educate the immune system, and convince it to "forget" the beta cells.

If I look back at my time as a young doctor treating patients with T1D, the major advances in therapeutic are technology-related, such as better and easier ways to inject insulin; better insulins; and, of crucial importance, the possibility to easily measure glucose several times a day. This has had a major impact in improving glycemic control and consequently decreasing complications, improving both life expectancy and the quality of life for patients.



6. Why is diabetes research so important?

Because type 1 diabetes remains a chronic incurable disease that affects millions of children, teenagers, and adults all over the world. The disease can be treated, but not cured. Until we have understood what causes it, and are able to prevent diabetes, research must go on.

7. Do you have anything else you would like to share? Is there anyone to thank or acknowledge? Can you comment on the need for funds from sources such as JDRF?

In recent years, it has become clear that human type 1 diabetes has major differences compared to the available mouse and rat models. Thus, it is critical to study the human disease from human specimens. Since pancreatic biopsy is not, in my view, an ethically acceptable option, the only way ahead is to collaborate and share all available pancreatic materials, such as from organ donors, as proposed by nPOD. This is "Priority One." The efforts of nPOD should be supported both by researchers in the field and by funding agencies.

Regarding thanks, I have had wonderful mentors that made a difference in my career. Jorge Gross and Renato Migliorini in Brazil, and Claes Hellerstom in Sweden, were decisive for my development. And, as mentioned above, JDRF helped me a lot in the transition from post-doc to Assistant/Associate Professor. They have been supporting my research since then. I really appreciate working with funding agencies driven by patients—this reminds me why we are doing research, and helps us focus on the most relevant issues.

We and other colleagues in the field are working really hard to better understand diabetes and to improve its treatment. Unfortunately, as with other autoimmune diseases, we are dealing with a terribly complicated problem. It may eventually need individualized therapies. I would love to see this solved while I am still around!

8. When you're not working, what do you like to do for fun?

Reading: I read a lot of literature in my spare moments. Since I learned a few languages by working in different countries, I can read some books in their original language, which I really enjoy. I also like cycling, walking, and going to movies and concerts with my wife. She is a diabetologist and diabetes researcher—which makes it easier for both of us to understand why the other spends so many hours in the lab. A couple of weeks per year, we either travel to Brazil—particularly to a beach in the south of the country—or, in more recent years, to east Asia. We have a weak spot for Cambodia, Burma, and Thailand.







For more information about nPOD, please visit our website: <u>www.jdrfnpod.org</u>

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