INTERVIEW

Diabetes Management

Is stem cell research the future for Type 1 diabetes?

Robert R Henry* speaks to Daphne Boulicault, Commissioning Editor: Robert R Henry is professor of medicine in the Division of Endocrinology and Metabolism at the University of California, San Diego. He is also chief of both the Section of Endocrinology, Metabolism and Diabetes and the Center for Metabolic Research at the VA Medical Center in San Diego. Dr Henry received his medical degree from the University of Manitoba Medical School, Manitoba, Canada, where he also completed his residency in internal medicine and fellowship in endocrinology. He is past president of the American Diabetes Association, Medicine and Science (2011) and is a member of the American Association of Clinical Endocrinology, the European Association for the Study of Diabetes, the Obesity Society, the Endocrine Society, Western Society for Clinical Investigation, Western Association of Physicians, the American Federation for Clinical Research and the Royal College of Physicians Edinburgh. His research is funded by the National Institutes of Health-NIDDK, the Department of Veterans Affairs and numerous pharmaceutical grants. Recent awards include the Distinguished Clinical Scientist Award from the American Diabetes Association, the Mary Jane Kugal Award of the Juvenile Diabetes Research Foundation International, the Robert H Williams-Rachmiel Levine Award from the Western Metabolism Club, Frontiers in Science Award from American Association of Clinical Endocrinology and the Banting Medal for Public Service from the American Diabetes Association. Dr Henry has published more than 400 journal articles and chapters. His current clinical research interests involve the study of new therapies for Type 1 and 2 diabetes and obesity. Basic science interests include study of the metabolic and cardiovascular regulation of human skeletal muscle and adipose tissue secretory products including adiponectin, signal interactions between skeletal muscle and adipose tissue and defects of insulin signal transduction in these tissues of obese and diabetic patients.

KEYWORDS
• stell cells • therapy
• Type 1 diabetes

Q Could you give us an overview on your career to date?

I graduated from the University of Manitoba Medical School (Canada) in 1975 before going on to complete a fellowship in internal medicine. During this time I also completed a fellowship in endocrinology in 1981. After spending a year on staff at the University of Manitoba Health Sciences Centre I moved to the USA and enrolled in a postdoctoral degree with a focus on specialist techniques in diabetes research at the University of Colorado (USA) Health Sciences Center.

In January 1984 I moved to San Diego and for the last 31 years I have been on faculty at the University of California, San Diego (UCSD) and attending staff at the VA Medical Center (USA). I have established a significant research focus at the VA Medical Center, in

*University of California, San Diego, CA, USA; and Section of Endocrinology, Metabolism & Diabetes, Veterans Affairs Healthcare System, San Diego, CA, USA; rrhenry@ucsd.edu

Future Medicine part of fsg

collaboration with the university, at the Center for Metabolic Research. The research center comprises eight beds for metabolic research through which we have conducted studies into Type 1 and 2 diabetes, primarily, for over 25 years. Future plans include establishment of a research group at the UC San Diego Clinical and Translational Research Institute that focuses primarily on research of Type 1 diabetes.

I also have a basic research laboratory in which we conduct studies on human tissues (mainly muscle and adipose tissues) and the use of stem cells from these tissues.

Q What inspired you to work in the field of diabetes?

When I was a student in the early 1970s, diabetes was widely known as a poorly treated, very common (up to 50% among adult indigent populations) disease. The complications associated with the disease really piqued my interest and I wanted to learn more about the pathophysiology of diabetes and methods to improve the therapeutics.

Q Have any colleagues, past or present, particularly influenced you and your work?

Dr Charles Faiman played a major role in recruiting me into endocrinology. After my stint in internal medicine at the University of Manitoba, he convinced me to join the endocrinology team as a fellow. Once he and the hospital recognized my focus and interest in diabetes, they funded my initial postdoctoral period in diabetes research at the University of Colorado.

Colorado was where I met my next colleague of major significance in my career, Dr Jerrold Olefsky. It was he who invited me to continue my diabetes research in San Diego at UCSD. I had planned on staying in San Diego for just a year or two but became intensely involved in diabetes research. At UCSD, I found a stimulating, academic environment where I have worked happily for over 25 years.

Q What would you describe as the biggest achievement of your career?

The act of improving peoples' lives, even if in a small way, will continue to be my greatest professional achievement. I think that some of the small discoveries I have made or contributed to have helped patients and I hope that the therapeutics I hope to develop will help many more people in the future. I honestly believe that my purpose, through my work, is improving the quality and duration of the lives of people with diabetes.

Q Have there been any recent advances in therapies for Type 2 diabetes that excited you?

Many of the new therapeutics for both Type 1 and 2 diabetes has been a major area of excitement for me. I am currently conducting numerous clinical trials which I believe hold great promise for those affected with or by diabetes.

Q Recently, you have become involved in some fascinating work around stem cell therapy for Type 1 diabetes. How did this change in focus come about?

I have been involved in Type 1 diabetes for a long time, mainly in therapeutics, but my major focus has tended toward Type 2 diabetes. About 5 years ago, this tide started to change due to the great strides that were being made in understanding Type 1 diabetes, and both diagnostics and therapeutics in the area improved as a result. The insulins became much more effective alongside our ability to monitor the changes that affected blood glucose. These advances made the field of Type 1 diabetes fascinating to me and I could not stay away, particularly as I already had the facilities to study most aspects of clinical diabetes at my fingertips. Five years later I would estimate that close to 50% of my research concerns Type 1 diabetes. In fact, I recently appointed a new junior faculty member within my group, Dr Jeremy Pettis, who I hope will expand the stem cell research of our work even further.

Q Do you believe a cure for Type 1 diabetes is possible?

My personal view is that stem cells will be the major advance here, in terms of addressing and effectively curbing the underlying pathophysiology of Type 1 diabetes. It will definitely take some time to perfect the science but I believe positive results are forthcoming in the foreseeable future. It is inevitable that such an approach will be effective to some degree though I would not yet predict a cure per say. Nonetheless, the research is moving so quickly that we will soon see results.

I think it is well within our grasp to obtain substantial β-cell insulin secretory function using stem cells. Our laboratory is employing the approach of a device (containing the embryonic stem cells) that prevents the immune cells from entering the device and destroying the

β cells while allowing normal cell growth and metabolism to take place. At the moment we are concerned with finding the optimal site in the body where the growth of these stem cells is best.

Another line of therapy which holds great promise is that directed toward modulating or blocking the autoimmune response that essentially destroys β cells. My laboratory is also involved in this work through looking at monoclonal antibodies that alter the T-cell response involved in the destruction of the B cells.

It is important to remember that medicine is a process in which small improvements add up to better outcomes. Type 1 diabetes is a lifelong disease often starting in childhood and the advances I have seen since I began my career in 1980 are astounding. I would predict that the same kind of developments and frame shift will occur in the next 10–15 years.

In all, I believe a total cure is not something we in the diabetes community should be solely focusing on right now in Type 1 diabetes. The first goal is to achieve some kind of sustainable insulin secretion, and I believe we are heading in the right direction. Eventually, perhaps in the next decade or so, a true cure is a real possibility.

Q Where do you see your field progressing in the next 5–10 years?

The two components that I focus on in diabetes include the pathophysiology of the disease and the complications that arise from it. I believe the future in terms of understanding the basic pathophysiology is extremely bright, and for Type 1 diabetes will be mainly concerned with targeting the body's autoimmune response.

Outcomes in complications have improved dramatically and retinopathy has seen some amazing advances, but there is still further to go. A lot of work remains to be done for neuropathy and nephropathy, and I believe the development of targeted approaches for these complications will be the key. Overall, the future for those with diabetes will be significantly improved by the therapeutics in development.

Disclaimer

The opinions expressed in this article are those of the interviewee and do not necessarily reflect the views of Future Medicine Ltd.

Financial & competing interests disclosure

RR Henry is funded to do the stem cell research implants by ViaCyte Pharmaceutical and UCSD Sanford Stem Cell Clinical Center. The author 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.

No writing assistance was utilized in the production of this manuscript.