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Islet cell research brings hope for a diabetes cure: Meeting report from the 6th annual islet society meeting in Stellenbosch, South Africa

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The International Diabetes Federation predicts that, over the next twenty years, the largest increase in the prevalence of diabetes will be in the Africa region. Recognizing an unmet need for more focus on Africa and engagement with African scholars, the Islet Society held its 6th annual meeting July 20–21, 2014 in Stellenbosch, South Africa. Here, we present a report that covers the presentations and discussion points from that meeting. Work was presented on a variety of topics and included presentations by a significant proportion of Africa diabetes researchers. Overall, it was an excellent conference, with many new international collaborations initiated. We hope that other groups will also respond to the need for more conferences in Africa and focused on Africa.

Introduction

The International Diabetes Federation has recently reported that the highest increase in the prevalence of diabetes among world regions will be in Africa over the next 20 years, with the numbers expected to more than double by 2035. This led to the theme of the Second African Diabetes Congress held in Yaoundé on the 25th–28th February 2014 titled "Diabetes: Challenges and opportunities in Africa". There is a clear need for more conferences within Africa and focused on Africa.

The Islet Society held its 6th annual meeting in the Western Cape of South Africa in July 2014. Delegates from 12 countries representing 6 continents gathered to present and discuss their latest islet research. African representatives were from Cameroon, Malawi, Nigeria and South Africa. At this Annual Meeting of the Islet Society, a wide range of fundamental research was presented, and this work fell into the 4 broad focus areas: novel therapeutic target molecules and pathways, programming effects of diet and exercise on glucose homeostasis, plant extracts with antidiabetic properties, and models and technologies for diabetes research.

The Epigenetic Effects of Diet and Exercise on Glucose Homeostasis

The potential epigenetic programming effects of glucose homeostasis by exercise or diet was presented by 2 speakers. Dr. Marlin Cerf, a senior research scientist from the Medical Research Council in South Africa, addressed the potential programming of animals exposed to high fat diets in development and/or early life, and showed that, depending on when parent animals were fed a high fat diet, various outcomes including low birth weight, altered glycaemic control, and increased islet number and size were observed in the offspring. Mr. Jose Maria Costa Junior form the State University of Campinas in Brazil reported on a study carried out to investigate the effects of exercise training in male mice on the modulation of glucose homeostasis and pancreatic islet function in the offspring. Contrary to the hypothesized outcome, exercise training in fathers did not ameliorate the deleterious effects of a high fat diet in offspring; however, when compared to offspring of sedentary fathers, offspring of trained fathers exhibited better insulin responses when fed a standard chow diet.

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Potential Therapeutic Targets

Prof. Anjan Kowluru from the Wayne State University in the USA presented extensive research findings on various potential therapeutic diabetes targets. Rac1, a GTP-binding protein of the Rho subfamily, is known to play a modulatory role in glucose-stimulated insulin secretion. Vav2, a nucleotide exchange factor required for Rac1 activation, was presented as a novel regulator of insulin secretion by β cells based on the results of research on Vav2 knockdown and inhibitor studies. NADPH oxidase (Nox), which generates ROS, plays a vital role in β cell function; however, constitutive expression of Nox resulted in oxidative stress, mitochondrial damage and thus dysfunction in pancreatic islets. Nox, therefore, also represents a potential diabetes drug target; however, because of the importance of the enzyme in β cell function, a fine balance of modulation needs to be achieved for this to be a successful therapeutic option. Nox has also been investigated in the context of diabetic retinopathy by Prof. Renu Kowluru of the same University. When Nox was activated by high glucose levels, consequently retinal ROS levels were increased in the context of glucolipotoxicity. She demonstrated that inhibition of Nox prevents mitochondrial ROS and cell apoptosis, indicating Nox as a novel therapeutic target for retinopathy.

A further novel therapeutic target for type 2 diabetes was presented by Dr. Roshni Singaraja from the National University of Singapore. HIP14, a palmitoyl transferase critical for neurotransmission via palmitoylation of various neuronal proteins, is widely expressed and in particular is highly expressed in brain and islet tissues. In addition to causing neurological dysfunction resembling Huntington's disease, knockout of HIP14 was shown by Dr. Singaraja to result in improved glucose tolerance in high fat-fed mice, suggesting HIP14 to be a target for improved insulin sensitivity and resistance to type 2 diabetes.

Antidiabetic Plant Extracts

Traditional medicine has been and continues to be valued in many African cultures, and it is thus not surprising that research on plant extracts with potential antidiabetic properties was presented by several African delegates of the Islet meeting. Mrs. Nirishni Chellan from the Medical Research Council in South Africa showed the extract of Cyclopia maculata, a plant native to South Africa, has a number of favorable effects, including attenuation of palmitic acid-induced apoptosis and reduction of ROS levels, on pancreatic islets isolated from streptozotocin-treated rats. Extracts of Sphenocentrum jollynum and Momordica charantia, plants native to Nigeria, were also demonstrated by Dr Omobola Komolafe from the Obafemi Awolowo University, Nigeria, to ameliorate the adverse effects of streptozotocin-induced diabetes on β cell microanatomy and blood cell counts, respectively.

Models and Technologies for Diabetes Research

Another theme at this year's Islet Society meeting was techniques and models with which to undertake diabetes research. Prof. Erdal Karaoz from the Kocaeli University in Turkey presented an experimental in vitro model of type 1 diabetes developed by his research group. The model, in which T-cells are activated by β cell apoptotic body antigen-presenting dendritic cells to recognize and attack islet cells, may allow for elucidation of autoimmune mechanisms of type 1 diabetes and in particular novel in vitro high-throughput screening approaches.

Prof. James Johnson from the University of British Columbia in Canada presented data on β cell death mechanisms obtained by powerful imaging techniques. This research on "kinetic, multiparameter imaging of β cell death" revealed that β cell death proceeds via multiple mechanisms. In response to various stressors or inducers of cell death, β cell death was rarely observed to occur via the "classical" apoptosis events. In fact, the majority of primary β-cells died from forms of partial apoptosis. This is in contrast to the observations in the transformed MIN6 cell line. These findings have implications for how islet research, specifically measurement of β cell death, should be conducted.

Further modern research technologies were presented by Prof. Anandwardhan Hardikar from the University of Sydney in Australia in the context of the RAPID (RNA-based analysis / prediction of Islet Death) study. The RAPID study is an extensive assessment of non-coding RNAs, specifically miRNAs, as potential biomarkers of islet death and thus as predictors of diabetes. His presentation included information on various powerful high-throughput PCR platforms and the advantages and disadvantages associated with such technologies, especially in the context of diabetes research.

Data presented by Mr. Juziel Manda, a researcher from Dr. Venant Tchokonte-Nana's Islet Research Laboratory from Stellenbosch University, showed that unlike in the protocol of mesenchymal cell isolation in bone marrow, the mesenchymal cell isolation in pancreatic tissues needs to be modified with the use of blood plasma to ease sticking of the cells on the culture rack. Furthermore, Dr. Yuliya Krivova from the Human Morphology RAMS in Russia demonstrated that the transcriptional factor NeuroD1 was critical for endocrine cell differentiation and that the majority of the pancreatic duct cells in the second trimester of pregnancy are directed into an endocrine cell fate. Meanwhile, Patricia Clara Kotze of the Islet Research Laboratory at the Stellenbosch University reported Ngn3 positive expressing cells in peripancreatic fat tissues following pancreatic duct ligation.

Conclusion

The 2014 Islet Society Annual Meeting, the first to be held on African soil, was a great success. The relatively small number of delegates allowed for useful discussions to take place, facilitating the formation of important connections and collaborative agreements. The importance of networking was highlighted by MD Shahidul Islam of the Karolinska Institutet, Sweden, and president of the Islet Society. In its presentation, he emphasized the need for researchers not only to expand their research networks, but also to enrich them by making not only self-similar connections, but including experts from distant fields. The society president ended his presentation by encouraging us as researchers to "facilitate networking between distant fields in a thoughtful way".