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EDITORIAL

Insulin Therapy Inactivation is connected to NAFLD and Diabetes Severity Index

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Discoveries in genomic medicine and nutrition sciences have become important to maintain insulin dosing and timing in diabetic individuals to prevent the natural progression of hyperglycemia induced severity of diabetic complications [1-3]. Medical devices that promote diabetes technology assist with continuous subcutaneous insulin infusion that play an important role in the treatment of diabetes [3]. Preventing the micro and macrovascular consequences of prolonged hyperglycemia and delaying the progressive loss of β-cell function are the key goals of anti-diabetes therapies [4]. In key milestones of diabetes technology development include the artificial pancreas that may be one of the most promising treatments of diabetes [3]. In diabetes complications the severity index with the global chronic disease epidemic [5] may involve uncontrolled progression that may override basic insulin therapy with costs expected to reach 250 billion dollars [6-8].

The gene environment interaction now identify the nuclear receptor gene Sirtuin 1 (Sirt 1) that regulates appetite and neuron proliferation to be involved in the induction of Type 3 diabetes and insulin resistance [9-11]. Sirt 1 is a nicotinamide adenine dinucleotide (NAD+) dependent class III histone deacetylase (HDAC) that targets transcription factors to adapt gene expression to metabolic activity and the deacetylation of other nuclear receptors indicate its critical involvement in insulin resistance [9-11]. The interest in glucose metabolism has accelerated with the role of Sirt 1 and its role in the transcriptional regulation of p53 linked to p53 transcriptional regulation of caveolin 1 expression associated with insulin receptor transport and activity [12]. In situ hybridization analysis has localized the human Sirt 1 gene to chromosome 10q21.3 and linked to various diseases [13] with deletions, inversions and aberrations in chromosome 10q21.3 [11]. Sirt 1 is involved in the release of insulin from beta cells in the pancreas with Sirt 1 deficiency involved in beta cell dysfunction in rodents [14,15]. Sirt 1 function is critical to maintain insulin therapy and a Sirt 1 inhibitor such as bacterial lipopolysaccharides [12] should be assessed to prevent interference in emerging insulin technologies [1-4].

The use of various anti-hyperglycemic drugs are important to type 2 diabetes therapy with effects on beta cell and neuron function relevant to Alzheimer's disease [16]. The nature of drug treatment and combination therapy are critical to maintain pancreatic beta cell function with connections between drug treatment and insulin therapy essential to prevent various organ diseases **(Figure 1)**. Heat therapy has been used to maintain anti- hyperglycemic drug treatment with heat shock response important to treatment of insulin resistance [17,18] and linked to new alternative diabetic therapy [1-4]. The discovery of the heat shock gene Sirt 1 [19] has raised concerns with relevance to heat therapy (sauna/hot tub) and needs careful evaluation to prevent suprachiasmatic nucleus Sirt 1 inactivation [20] involved in the metabolism of glucose and heat shock protein 70 with relevance to core body temperature and defective immune system [20,21].

Nutritional therapy has become essential to maintain insulin and anti-hyperglycemic drug therapy in diabetics. Non alcoholic fatty liver disease (NAFLD) is associated with the complications of Type 2/Type 3 diabetes [5,22] with the amount/nature of food intake important to the progression of uncontrolled hyperglycemia. Dietary phosphatidylinositol (gm/day) may stabilize NAFLD and prevent hyperglycemia [23,24]. Use of Sirt 1 activators [25] are essential to prevent the long term side effects of Sirt 1 inhibitors (suramin/sirtinol) [23]

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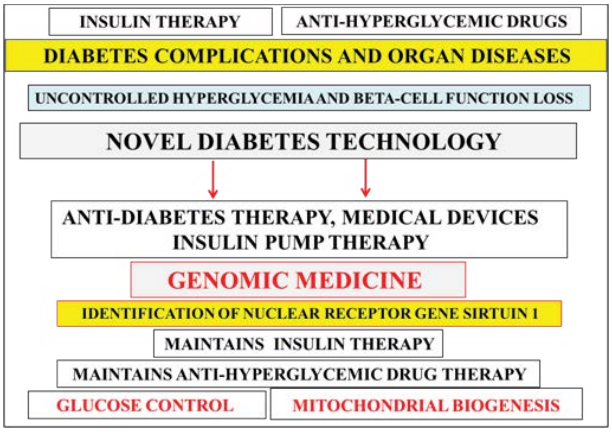

Figure 1: In diabetes severe complications are now associated with the global chronic disease epidemic and override basic insulin therapy and anti-hyperglycemic drug therapy. The estimated cost to diabetes is expected to be 250 billion dollars with ineffective diabetes technology. The discovery of Sirt 1 will allow interventions to reverse NAFLD that is connected to ineffective insulin and anti-hyperglycemic drug therapy with Sirt 1 activation associated with the successful milestones in diabetes technology.

with their use critical to maintain novel diabetes technology [1-4]. The use of functional foods [26] and Sirt 1 activators such as magnesium [27] are essential to prevent mitophagy that is a major cellular defect related to organ diseases in diabetes [5].

Insulin and anti-hyperglycemic drug therapy have been used to maintain glucose homeostasis but mitophagy persists and is a major concern to programmed cell death in diabetes **(Figure 1**). The discovery of caffeine as a Sirt 1 modulator [28] has raised concerns with relevance to the global NAFLD epidemic [28]. Defective caffeine metabolism [25,28] in NAFLD and Type 3 diabetes may overide insulin/drug therapy and various key diabetic technologies underdevelopment (**Figure 1**). Diabetes and appetite control are critical to insulin/drug therapy [29,30] with Sirt 1 involved in food regulation, mitochondrial biogenesis and connected to glucose metabolism (**Figure 1**) in man.

Conclusion

In the global chronic disease epidemic complications of diabetes has raised concerns with relevance to Type 3 diabetes. Suprachiasmatic neurons that regulate peripheral glucose levels are at increased risk for apoptosis with mitophagy a major concern in neurodegenerative disease and diabetes. Nutritional therapy that involve functional foods and Sirt 1 activators regulate suprachiasmatic nucleus function, appetite control, beta cell function and reverse NAFLD essential for insulin resistance control and important to the milestones in diabetes technology development.

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References

1. Cahn A, Akirov A, Raz I (2017) Digital health technology and diabetes management. J Diabetes. [Epub ahead of print]. [View Article]
2. Ginsberg BH (1994) The role of technology in diabetes therapy. Diabetes Care Suppl 1:50-5. [View Article]
3. Kovatchev BP (2012) Diabetes Technology: Markers, Monitoring, Assessment, and Control of Blood Glucose Fluctuations in Diabetes. Scientifica Volume 2012: Article ID 283821, 14 pages. [View Article]
4. Brunton SA, Kruger DF, Funnell MM (2016) Role of Emerging Insulin Technologies in the Initiation and Intensification of Insulin Therapy for Diabetes in Primary Care. Clin Diabetes 34: 34-43. [View Article]
5. Vigersky RA (2015) The Benefits, Limitations, and Cost-Effectiveness of Advanced Technologies in the Management of Patients With Diabetes Mellitus. J Diabetes Sci Technol 9: 320-330. [View Article]
6. Martins IJ (2015) Diabetes and Organ Dysfunction in the Developing and Developed. Global Journal of Medical Research: F Diseases 15: 15-21. [View Article]
7. American Diabetes Association (2013) Economic Costs of Diabetes in the U.S. in 2012. Diabetes Care 36: 1033–1046. [View Article]
8. Young BA, Lin E, Von Korff M, Simon G, Ciechanowski P, et al (2008) Diabetes complications severity index and risk of mortality, hospitalization, and healthcare utilization. Am J Manag Care 14: 15-23. [View Article]
9. Martins IJ (2016) Diet and Nutrition reverse Type 3 Diabetes and Accelerated Aging linked to Global chronic diseases. J Diab Res Ther 2: 1-6. [View Article]
10. Martins IJ (2016) Type 3 diabetes with links to NAFLD and Other Chronic Diseases in the Western World. Int J Diab 1: 1-5. [View Article]
11. Martins IJ (2016) Early diagnosis of neuron mitochondrial dysfunction may reverse global metabolic and neurodegenerative disease. Global Journal of Medical Research 2: 1-8. [View Article]
12. Martins IJ (2017) The Future of Genomic Medicine Involves the Maintenance of Sirtuin 1 in Global Populations. Int J Mol Biol 2: 00013. [View Article]
13. Martins IJ (2017) Genomic Medicine and Management of Genetic Disorders. J Genet Disord 1: 1. [View Article]
14. Martins IJ (2017) Single Gene Inactivation with Implications to Diabetes and Multiple Organ Dysfunction Syndrome. J Clin Epigenet 3: 1-8. [View Article]
15. Pinho AV, Bensellam M, Wauters E, Rees M, Giry-Laterriere M, et al (2015) Pancreas-Specific Sirt1-Deficiency in Mice Compromises Beta-Cell Function without Development of Hyperglycemia. PLoS One 10:e0128012. [View Article]
16. Raz I (2013) Guideline Approach to Therapy in Patients With Newly Diagnosed Type 2 Diabetes. Diabetes Care 36: S139-S144. [View Article]
17. Krause M, Ludwig MS, Heck TG, Takahashi HK (2015) Heat shock proteins and heat therapy for type 2 diabetes: pros and cons. Curr Opin Clin Nutr Metab Care 18: 374-80. [View Article]

18. Kondo T, Motoshima H, Igata M, Kawashima J, Matsumura T et al. (2014) The Role of Heat Shock Response in Insulin Resistance and Diabetes. Diabetes Metab J 38: 100-106. [View Article]

19. Martins IJ (2016) Heat shock gene Sirtuin 1 regulates post-prandial lipid metabolism with relevance to nutrition and appetite regulation in diabetes. International Journal of Diabetes and Clinical Diagnosis. Int J Diab Clin Diagn 3: 1-3. [View Article]

20. Martins IJ (2017) Regulation of Core Body Temperature and the Immune System Determines Species Longevity. Curr Updates Gerontol 1: 1-6. [View Article]

21. Martins IJ (2017) Heat Therapy With Relevance to the Reversal of NAFLD and Diabetes. J Diabetes Metab Disord 4: 1-3. [View Article]

22. Martins, IJ (2014) Induction of NAFLD with Increased Risk of Obesity and Chronic Diseases in Developed Countries. Open Journal of Endocrine and Metabolic Diseases 4: 90-110. [View Article]

23. Martins, IJ (2015) Overnutrition Determines LPS Regulation of Mycotoxin Induced Neurotoxicity in Neurodegenerative Diseases. Int J Mol Sci 16: 29554-29573. [View Article]

24. Shirouchi B, Nagao K, Inoue N, Furuya K, Koga S, et al (2008) Dietary phosphatidylinositol prevents the development of nonalcoholic fatty liver disease in Zucker (fa/fa) rats. J Agric Food Chem 56: 2375-9. [View Article]

25. Martins IJ (2017) Nutrition Therapy Regulates Caffeine Metabolism with Relevance to NAFLD and Induction of Type 3 Diabetes. J Diabetes Metab Disord 4: 1-10. [View Article]

26. Martins IJ (2017) Functional Foods and Active molecules with relevance to Health and Chronic disease. Functional Foods in Health and Disease 7: 833-836. [View Article]

27. Martins IJ (2016) Magnesium Therapy Prevents Senescence with the Reversal of Diabetes and Alzheimer's Disease. Health 8: 694-710. [View Article]

28. Martins IJ (2017) Caffeine with Links to NAFLD and Accelerated Brain Aging. Chapter: Non-Alcoholic Fatty Liver Disease - Molecular Bases, Prevention and Treatment. InTech - Open Science Open Minds | InTechOpen. [View Article]

29. Martins IJ (2013) Appetite dysregulation and obesity in Western Countries Ian J Martins · First edited by Emma Jones, LAP LAMBERT Academic Publishing. [View Article]

30. Martins IJ (2016) Appetite Control with Relevance to Mitochondrial Biogenesis and Activation of Post- Prandial Lipid Metabolism in Obesity Linked Diabetes. Ann Obes Disord 1: 1-3. [View Article]

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