**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 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 linked to new alternative diabetic therapy [1-4].

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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Insulin and anti-hyperglycemic drug therapy have been used to maintain glucose homeostasis but mitophagy persists and is a major cellular defect related to organ diseases in diabetes [5].

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.

**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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