Advances in Biomarkers and Insulin Therapy with Relevance to Reversal of Diabetes

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The projected cost of diabetes and biomarker analysis is expected to cost billions of dollars with the diabetes epidemic to escalate to a pandemic by the year 2050 [1]. In Type 2 diabetes major efforts with biomarker research has identified various biomarkers [2-4] to assess the progression and severity of insulin resistance and to delay accelerated aging and the multiple organ disease syndrome. Concerns with the use of biomarkers from clinical studies have escalated with relevance to onset, progression and drug therapy related to the clinical outcomes in diabetes [5]. Biomarkers may include markers that determine the severity of hyperglycemia such as hemoglobin A1c (HbA1c) and advanced glycation end products [6]. Genomic markers in diabetes indicate measurement of microRNA and other potential biomarkers such as C-reactive protein, 2-aminoadipic acid and betatrophin [7]. Early detection of Type 2 diabetes now includes biomarkers such as 10- and 12-(Z,E)-hydroxyoctadecadienoic acids, insulin, leptin, and adiponectin [8].

Major concern with relevance to the diabetes pandemic has now reassessed the relevance of hyperglycemia and mitophagy connected to neurodegenerative diseases [9]. In diabetes mitophagy has been associated with the severity of the disease but diabetes biomarker studies [2-8] may not predict the severity of mitophagy in Type 2 diabetes. Biomarker tests for mitochondrial disorders [10-14] are now the focus and research of many
laboratories with specific biomarkers identified to determine the detection of mitochondrial disorders. The interest mitochondrial function has accelerated with recent research that highlights the role of mitochondrial dysfunction in the induction of insulin resistance and Type 2 diabetes [15-18]. In the pancreas, mitochondrial activation is essential for insulin secretion and the action of insulin in various tissues [16-17]. Major interventions to improve mitochondrial dysfunction are now central to the immune system connected to metabolic and cardiovascular abnormalities in Type 2 diabetes [19].

Major advances in medical research now identify an anti-aging gene that is connected to mitochondrial biogenesis, insulin resistance and organ disease [19]. The anti-aging gene Sirtuin 1 (Sirt 1) is nicotinamide adenine dinucleotide (NAD +) dependent class III histone deacetylase (HDAC) and its regulation of the immune system is critical to the prevention of mitophagy with connections of Sirt 1 that target transcription factors such as p53 to adapt gene expression to the immune system [20], metabolic activity with deacetylation of nuclear receptors associated with insulin resistance. Sirt 1 expression can be altered by micro RNA (mi-34a, mi-132 and mi-122) that determine p53 effects on Sirt 1 expression with relevance to Type 3 diabetes, cardiovascular disease and metabolic disease [19]. Advances in biomarkers in diabetes should now include plasma Sirt1 levels [21-22] with relevance to its severity in diabetes [23-25] and its connection to neurodegenerative diseases. Insulin therapy may not improve biomarkers that have been identified to assess the severity of insulin resistance but measurement of plasma Sirt 1 levels may assist with intensive insulin therapy with relevance mitochondrial function and insulin secretion [26-27].

Recent discoveries identify the heat shock gene Sirt 1 [28] to be defective in Type 3 diabetes with the defective suprachiasmatic regulation responsible for the inactivation of the adipose tissue and liver interaction [29] and relevant tomitophagy and pancreas dysfunction (Figure 1) in Type 2 diabetes [29-30]. The heat shock gene Sirt 1 [28] is now associated with heat shock protein (HSP) disorders connected to mitophagy in diseases such as obesity, diabetes and neurodegenerative diseases [31-34]. The suprachiasmatic nucleus is critical to the regulation of the circadian rhythm [30] and involved in the regulation of various protein biomarkers such as HSP, fibroblast growth factors, brain derived growth factor and adiponectin [35-39]. Biomarkers such as Sirt 1, heat shock proteins, adiponectin, fibroblast growth factors, insulin, glucagon, apelin and brain derived growth factors (Figure 1) need to be determined early in a diabetic’s life to avoid Sirt 1 repression connected tomitophagy and defective insulin secretion in obesity, diabetes and neurodegenerative diseases.

Reversal of diabetes may require specific dietary interventions [28-29, 40-41] to maintain plasma Sirt 1 levels with temperature dysregulation [28, 42] and appetite control [30, 39] associated with insulin therapy [43-44] relevant to mitochondrial biogenesis, insulin secretion and autoimmune disease [45]. Insulin treatment, intensification of insulin regimens and adjustment of insulin doses [46] will require measurement of plasma Sirt 1 levels (acute phase proteins) in future clinical trials in diabetes relevant to insulin treatment (hyperglycemia) connected to the maintenance of the immune system [19].
Figure 1. The suprachiasmatic nucleus is important to the activation of the adipose tissue-liver interaction that is critical to mitochondria function and pancreas insulin release in Type 2 diabetes (Panel A). The suprachiasmatic nucleus is linked to circadian regulation of various biomarkers associated with mitochondrial apoptosis in Type 3 diabetes and various chronic diseases (Panel B).

Conclusion
Identification of biomarker tests in diabetes to assess Sirt 1 repression linked to autoimmune disease and mitophagy has become of critical importance to the expected diabetes pandemic connected to various organ diseases. Plasma Sirt 1 analysis with other biomarkers are essential to determine autoimmune disease connected to mitophagy and the reversal of Type 2/Type 3 diabetes. Insulin therapy to prevent hyperglycemia now requires Sirt 1 expression to determine mitochondrial function and insulin secretion with relevance to programmed cell death in obesity, diabetes and neurodegenerative diseases. Diet, temperature regulation and insulin therapy may improve Sirt 1 levels connected to the prevention of primary autoimmune disease in the pancreas (insulin secretion), adipose tissue, liver and brain.

Conflicts of Interest
The author(s) report(s) no conflict(s) of interest(s). The author along are responsible for content and writing of the paper.

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