Genomic Medicine and Endocrine Autoimmunity as Key to Mitochondrial Disease

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Editorial

The diabetes epidemic and the induction of various chronic diseases are expected to affect approx. 592 people by the year 2035. Diabetes and its connections to endocrine autoimmunity [1-3] has become important to metabolic disease with relevance to the non alcoholic fatty liver disease (NAFLD) epidemic and neurodegenerative diseases [4]. The urgency to prevent the largest diabetes epidemic in history has now assessed multiple risk factors involved with induction of Type 3 diabetes connected to various chronic diseases [4]. Interest in Type 3 diabetes has accelerated in the past 15 years with the critical importance of anti-aging genes [5,6] with relevance to autoimmune disease and mitophagy [7] and the global diabetes epidemic. The regulation of these genes is controlled by the heat shock gene Sirtuin 1 (Sirt 1) that is connected to appetite, immune and core body temperature regulation with relevance tomitophagy in NAFLD and metabolic disease.

Figure 1: Genomic medicine and regulation of the heat shock gene Sirtuin 1 (Sirt 1) is connected to Type 3 diabetes, endocrine autoimmunity and mitochondrial disease. Unhealthy diets and lifestyle changes determine defective suprachiasmatic nucleus regulation (SCN) relevant to Type 3 diabetes/endocrine autoimmunity and the predicted diabetes pandemic by the year 2035.
Diabetes as an endocrine disease now indicates stress [8] as a major factor in the induction of brain aging and Type 3 diabetes connected to endocrine autoimmunity [9]. The increased global susceptibility to insulin resistance associated with brain aging and neurodegenerative diseases now indicate neuron vulnerability to mitophagy critical to the reversal of the diabetes pandemic. Interests in Sirt 1 in Type 3 diabetes with relevance to insulin resistance and autoimmune disease has accelerated to prevent accelerated mitochondrial apoptosis (Figure 1) and brain aging [7]. Sirt 1 is a nicotinamide adenine dinucleotide (NAD +) dependent class III histone deacetylase (HDAC) and as a heat shock gene [5,10] is involved in the deacetylation of heat shock factor 1 (HSF 1), regulation of heat shock proteins (HSP) and nitric oxide metabolism connected to natural killer cell activity, mitophagy and autoimmune disease in neuro degeneration and various chronic diseases.

Type 3 diabetes and endocrine autoimmunity now involves attack by the immune system and implicates the major histocompatibility complex (MHC) to be relevant to diabetes and endocrine autoimmunity. MHC molecules are cell-surface glycoproteins that regulate adaptive immune responses and interference with MHC gene expression at the level of transcription is involved with autoimmune disease [11,12]. Recent advances in genetics now reveal Sirt 1 to be involved with immune and endocrine disturbances (Figure 1) in these diseases [7,10]. Sirt 1 as a deacetylase targets transcription factors to adapt gene expression to immune regulation, metabolic activity and insulin resistance. Sirt 1 regulates the major histocompatibility complex class II (MHC-II) genes at the level of transcription important to the immune recognition and autoimmune disease in various species [13-16]. Sirt 1 deacetylates the master regulator CIITA (adaptive immune response) that determines the expression of MHC-II genes and autoimmune disease [14, 16-18].

The connections between diabetes, endocrine dysfunction and mitochondrial disease involve Sirt 1 and various hormones involved with endocrine autoimmunity and mitochondrial disease [19-22]. Sirt 1 is involved in mitochondrial biogenesis [23] and its regulation of the suprachiasmatic nucleus (SCN) is connected to various brain hormones and immunological diseases [7]. Sirt 1 regulation of hormones such as apelin, brain derived neurotrophic factor, growth hormone, neuropeptide Y, adiponectin and fibroblast growth factor 21 are connected to prevention of autoimmune disease [7,24-26]. The accelerated brain aging in the current global diabetes pandemic may now be relevant to endocrine autoimmune disease, mitophagy and cancer [19-22]. Endocrine treatment of mitochondrial disease [27-32] may be completely inhibited by Sirt1 transcriptional dysregulation and relevant to mitochondrial HSP-antigen presentation [33-35].

Genomic medicine and maintenance of the SCN is critical for prevention of endocrine autoimmunity with relevance to mitochondrial disease (Figure 1). Core body temperature [36], unhealthy diets [37] and lifestyle changes/stress [8] in diabetes can inactivate the SCN with accelerated Type 3 diabetes and neuro degeneration. The connections between endocrinology and autoimmune disease are determined by Sirt 1 repression of MHC genes that may involve the induction of antigenic and immunogenic proteins [38] and lipids [7] with relevance to mitochondrial apoptosis. Specific diets with Sirt 1 activators/Sirt 1 inhibitors [4,38] in the developing world are required to reverse Sirt 1 repression and maintain immune recognition essential for human survival and prevention of diabetes and various chronic diseases. Sirt 1 as the anti-aging gene now determines longevity [39] in various species with its repression connected to the induction of endocrine autoimmunity and hyperglycemic mitochondrial apoptosis in the global diabetes epidemic [2,3].

Conclusion

Genomic medicine treatment of diabetes is critical in the current global diabetes epidemic to prevent the expected diabetes pandemic predicted to occur by the year 2035. The major concern with Type 3 diabetes in the global population is related to a defective SCN with relevance to uncontrolled peripheral glucose levels and endocrine autoimmune disease. Appetite regulation and genomic medicine are critical to Sirt 1’s regulation of the MHC genes with relevance to maintenance of immune recognition and endocrine hormone treatment of mitophagy. In the developing world the major concern for a diabetes pandemic is mitophagy and will require diets with Sirt 1 activators to prevent Type 3 diabetes, endocrine autoimmune and mitochondrial disease.

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