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Type 3 diabetes with links to NAFLD and Other Chronic Diseases in the Western World

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Short Communication

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Type 3 diabetes with links to NAFLD and Other Chronic Diseases in the Western World

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Abstract

In the year 2015 it is now estimated that 30% of the Western World will now progress to non alcoholic fatty liver disease (NAFLD) and by the year 2050 if NAFLD remains untreated in the Western world the prevalence of the disease may rise to 40% of the global population. Type 3 diabetes and circadian rhythm disturbances may be involved in the induction of NAFLD that may promote insulin resistance and various chronic diseases such as cardiovascular disease, pancreatic disease, kidney disease and neurodegenerative disease. Multiple risk factors that induce Type 3 diabetes and NAFLD include stress, magnesium deficiency, bacterial lipopolysaccharide contamination, drug induced toxicity, xenobiotic levels, unhealthy diet/lifestyle factors and defective thermoregulation. Early diagnosis of Type 3 diabetes by multiple assessment techniques such as proteomics, genomics and lipidomics may allow reversal or stabilization of NAFLD that may progress slowly from simple non-alcoholic steatosis to non-alcoholic steatohepatitis and to hepatic fibrosis/cirrhosis of liver and hepatoma. Analysis of plasma constituents such as heat shock proteins (60,70, 90), amyloid beta, adiponectin, fibroblast growth factor 21, ceramide, sphingosine-1-phosphate, vasoactive intestinal peptide, thrombospondin 1, acute phase reactants may indicate progression of Type 3 diabetes and NAFLD and these results may not be consistent with normal plasma glucose and cholesterol levels. Early nutritional interventions with temperature regulation are required to reverse premature brain disease in diabetes (Type 3/Type2) that is connected to the rapid metabolism of heat shock proteins and amyloid beta oligomers that determine the severity of insulin resistance and NAFLD in individuals in the Western World.

Short Communication

Type 3 diabetes and circadian rhythm disturbances may be involved in the induction of non alcoholic fatty liver disease (NAFLD) that may promote insulin resistance and various chronic diseases such as cardiovascular disease, pancreatic disease, kidney disease, obesity and neurodegenerative disease [1,2]. The aging process involves the loss of neurons from the brain with relevance to Type 3 diabetes and NAFLD. After the age of 25 years neurons start to decrease in the brain [3] and may be associated with toxic adipokine release from adipocytes or liver dysfunction [1] that is linked to the increased concentration of drugs and xenobiotics that accumulate in the brain that become toxic to mitochondria and lead to the death of neurons [4-6].

Interests in the genetic regulation of diabetes has accelerated and now involves the nuclear receptor Sirtuin 1 (Sirt 1) that is associated with insulin resistance and involvesneuron senescence in the brain with hepatic steatosis linked to the induction of NAFLD [7]. Hypothalamic neurons involve Sirt 1 regulation of the suprachiasmatic nucleus (SCN) with the maintenance of brain and whole body glucose homeostasis in various species and man [8-10]. In the year 2015 it is now estimated that 30% of the Western World will now progress to NAFLD [11-13] and interests in brain Sirt 1 and its transcriptional dysregulation involves circadian disturbances relevant to Type 2 or Type 3 diabetes and now identify combined Type 3 and Type 2 diabetes as individuals that are extremely sensitive to accelerated NAFLD [5,7]. Multiple risk factors that involve Sirt 1 dysregulationin combined Type 3 and Type 2 diabetes that inducevarious chronic diseasesand include stress [14], magnesium deficiency [15], bacterial lipopolysaccharides [16,17], drug induced toxicity, xenobiotic levels [5], unhealthy diet/lifestyle factors and defective thermoregulation (Figure 1).

Stress as a factor for the induction of Type 3 diabetes and NAFLD has become of major concern with alterations in the autonomic

nervous system [18] and hypothalamic pituitary axis in Western communities. In recent years the apelinergic pathway [14] has been connectedto insulin resistance and NAFLD with apelin regulated stress pathways associated with defective autonomic pathways in neuroendocrine and various chronic diseases. Interests in apelingeric defective pathways with relevance to Type 3 diabetes [14] have escalated and thermoregulation dysfunction in Type 2 diabetes [19,20] involved in the early induction of NAFLD in these individuals. Furthermore thermoregulation dysfunction, apelinergic defective pathways and diabetes has rapidly become an important factor in the induction of metabolic and cardiovascular disease with interests in temperature regulation and circadian rhythm disturbances [21,22] involved in the induction of the combined the effects of Type 3 diabetes and Type 2 diabetes in various chronic diseases (Figure 1).

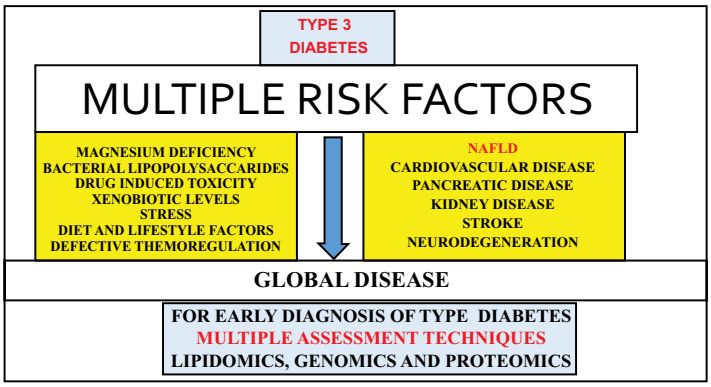

Figure 1: Prevention of Type 3 diabetes involves the consideration of many risk factors that include stress, diet, lifestyle, thermoregulation, neuron xenobiotic toxicity and bacterial contamination. The risk factors associated with Type 3 diabetes may induce various chronic diseases and with the global Type 2 diabetes accelerate the early induction of NAFLD in these individuals. Multiple tests are required to diagnose Type 3 diabetes and with diet and lifestyle changes [2] the severity of global Type 2 diabetes and NAFLD may be reduced.

Thermoregulation dysfunction now identifies the anti-aging gene Sirt 1 as the temperature sensitive gene that is linked to defective apelinergic pathways, NAFLD and various chronic diseases. Research in Sirt 1 and its involvement in temperature regulation [23-29] has escalated to prevent the induction of chronic diseases such as NAFLD with Sirt 1 dysregulation observed in both individuals with Type 3 and Type 2 diabetes [5,7,14,30,31]. Temperature regulation of Sirt 1 (NAD+ dependent class III histone deacetylase) has become important to the deacetylation of heat shock factor 1 (HSF1) [26,28,29] that protectneurons from protein-damaging stress associated with misfolded proteins such as heat shock protein 70 (HSP70) [32-37] and the Alzheimer's disease amyloid beta involved with the regulation of the insulin-receptorspathways [38,39].

Sirt 1 is involved with the circadian regulation of cellular heat shock protein (HSP) 60, 70 and 90 with temperature regulation closely associated with Sirt 1 activity/HSP levels in cells [23-29,32-37,40-42] and may be relevant to the heat shock response in Type 2 diabetes [43-45]. Interests in peripheral HSP 70 and amyloid beta metabolism (Figure 2) have escalated with thermoregulation important to the peripheral sink amyloid beta model [7] with relevance to HSP 70 in neuron amyloid beta metabolism and insulin receptor interactions. Temperature regulation of Sirt 1 is now relevant to abnormal transcriptional regulation of the transcription factor p53 with heat shock protein associated with p53 accumulation [46] with relevance to mitochondrial apoptosis, cholesterol/amyloid beta metabolism and NAFLD [7,45,47]. LPS has been shown to induce HSPs in various cells [48-50] and LPS in various species has been shown induce thermoregulatory dysfunction [51,52]. The role of LPS in thermodysregulation involves Sirt 1 dysregulation [53] and neuron apoptosis determined by interactions between HSPs and amyloid beta with relevance to magnesium levels in the brain and periphery [54-57].

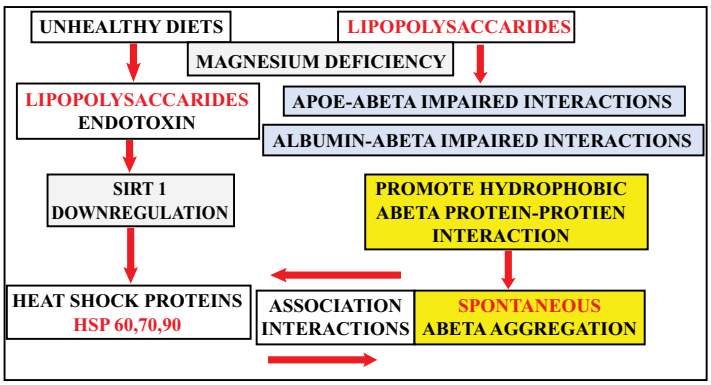

Figure 2: The nuclear receptor Sirt 1 is responsible for the metabolism of HSP (60,70,90) and amyloid beta oligomers. Sirt 1 dysregulation has been linked with Type 3 and Type 2 patients with relevance to plasma and brain HSP and amyloid beta metabolism. LPS reduces magnesium levels with relevance to the metabolism of HSPs and amyloid beta oligomers in the blood plasma and brain. Magnesium deficiency may be relevant to abnormal membrane interactions that involve HSP and amyloid beta interactions with the insulin receptor in the brain and the periphery.

Diets that are low in calories (low fat/sugar diets) and without inhibitors activate Sirt 1 with relevance to prevention of neuron senescence and Type 3 diabetes/NAFLD [58]. Brain temperature dysregulation connected to liver dysfunction may markedly delay the metabolism of saturated fats versus monounsaturated oils such as olive oil and associated with the development of insulin resistance in man [59,60]. Consumption of fats such as palm oil (palmitic acid rich) and virgin coconut oil (saturated fatty acids) that are solid (20-24C) versus the consumption of olive oil (monounsaturated) that is liquid to temperature (4C) may be sensitive to abnormal body temperature dysregulation with the induction of NAFLD. Diets that contain alcohol and fat promote the absorption of LPS with relevance to neuron membrane fluidity and body temperature dysregulationinvolve the abnormal metabolism of HSPs/amyloid beta oligomers [35-37,61-66] (Figure 2). In individuals with early neuron senescence in Western communities early diagnosis of Type 3 diabetes by multiple assessment techniques such as proteomics, genomics and lipidomics may allow reversal or stabilization of NAFLD that may progress slowly from simple non-alcoholic

steatosis to non-alcoholic steatohepatitis and to hepatic fibrosis/cirrhosis of liver and hepatoma. Analysis of plasma constituents such as LPS, HSP 60, HSP 70,adiponectin, fibroblast growth factor 21, ceramide, sphingosine-1-phosphate, vasoactive intestinal peptide, thrombospondin 1, acute phase reactants may indicate the progression of Type 3 diabetes tothe severity to NAFLD (Figure 1) and these results may not be consistent with normal plasma glucose and cholesterol levels [67-72]. Furthermore, early nutritional interventions and brain temperature regulation to reverse premature neuron senescence and Type 3/Type 2 diabetes may delay the stages and progression to NAFLD that may be connected to irreversible hepatic fibrosis, brain insulin resistance and severity of chronic diseases in individuals in the Western World.

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