Heat Shock Gene Sirtuin 1 Regulates Post-Prandial Lipid Metabolism with Relevance to Nutrition and Appetite Regulation in Diabetes

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Publication History:
Received: September 15, 2016
Accepted: November 01, 2016
Published: November 03, 2016

Keywords:
Amyloid beta, Anti-aging genes, diet, Heat shock gene, Heat shock proteins, NAFLD, Ontogeny, Post-prandial, Sirtuin 1, Transcription factors

New discoveries in medicine are required to understand the importance of appetite regulation that is associated with the overconsumption of food in Type 2 and Type 3 diabetes. Food restriction in diabetes is essential to maintain the hepatic metabolism of dietary fat with relevance to defective post-prandial lipid metabolism and to the global non-alcoholic fatty liver disease (NAFLD) epidemic [1,2]. Premature brain aging has become important with the development of Type 3 diabetes and Alzheimer's disease [3] that is associated with repression of the anti-aging gene Sirtuin 1 (Sirt 1) relevant to post-prandial lipid metabolism, amyloid beta metabolism (peptide involved in amyloid beta plaques) and circadian rhythm abnormalities in the brain biological clock associated with the development of NAFLD. Nutritional interventions such as very low carbohydrate diets have become important to diabetes (Figure 1) to reverse defective post-prandial lipid and amyloid beta metabolism without atherogenic lipoprotein formation [4,5] with the prevention of accelerated atherosclerosis in various communities. Western diets that are high in fat and glucose are linked to diabetes and NAFLD with anti-aging gene Sirt 1 transcriptional dysregulation [6] in cell and tissues associated with hyperglycemia, mitochondrial apoptosis and delayed hepatic fat and amyloid beta metabolism (Figure 1).

![Image](https://example.com/image1.png)

Figure 1: In diabetes and neurodegenerative diseases nutritional interventions are required to activate the anti-aging gene Sirt 1 and prevent defective liver lipid metabolism (NAFLD) and amyloid beta metabolism. Diets that are low in fat such as very low carbohydrate diets activate the calorie sensitive gene Sirt 1 with glucose metabolism connected to accelerated hepatic lipid/amyloid beta metabolism in diabetes and neurodegenerative diseases.

Accelerated aging that disturbs the brain to liver crosstalk [6,7] involves the calorie sensitive gene Sirtuin 1 (Sirt 1) that is a nicotinamide adenine dinucleotide class III histone deacetylase involved in the prevention of defective post-prandial metabolism and NAFLD [8-10]. The intake of fat is sensitive to the regulation of the heat shock gene Sirt 1 that is responsible for the metabolism of heat shock proteins (HSP) [3] that are produced by living cells in response to temperature regulation above physiological levels [11, 12]. Heat shock proteins facilitate the rapid metabolism by the liver of amyloid beta by preventing its misfolding and aggregation in the brain [3,13,14]. Sirt 1 is also sensitive to α-synuclein metabolism [15] and relevant to temperature alterations in α-synuclein oligomer and amyloid beta formation [16, 17].

Down regulation of Sirt 1 expression and activity disturbs the nuclear and mitochondria interactions with effects on the metabolism of fatty acids, glucose and amyloid beta metabolism in diabetes [16, 17]. Heat shock protein (HSP) induces endoplasmic reticulum stress (ER) stress with delayed metabolism of amyloid beta/α-synuclein oligomers associated with liver disease linked to NAFLD and neurodegenerative diseases. ER stress is associated with programmed cell death with relevance to mitochondrial apoptosis, defective post-prandial lipid metabolism and NAFLD [18-22] with Sirt 1 regulation of PGC1α associated with mitochondrial biogenesis after ingestion of various fat diets. Sirt 1 regulates HSP by deactylation of heat shock factor (HSF) via peroxisome proliferator-activated receptor gamma co-activator 1-alpha (PGC1α) as a critical repressor of HSF1-mediated transcriptional programs [23,24]. Sirt 1 is involved in body temperature regulation of the mammalian target of rapamycin (mTOR) signaling through the tumor suppressor tuberous sclerosis complex 1 with relevance to the expression of hepatic PGC-1α and fibroblast growth factor 21 (FGF21) [25-29].

Sirt 1 regulation of cell senescence in diabetes involves cell ontogeny with transcriptional ontogeny defective via the transcriptional factor p53 involved in the regulation of various other anti-aging genes [30-35] such as klotho, p66shc, FOXO3a, micro RNA 34a [18] and transcription factors involved post-prandial lipid metabolism, metabolic activity, insulin resistance, cellular ontogeny, inflammation and source are credited.
and xenobiotic metabolism [18, 36] (Figure 2). In the developing and developed world, diabetic treatment has become important with defective SirT1 gene expression determined by miR-34a [18, 36] related to defective cell proliferation in the brain and the liver (Figure 2). Defective thermoregulation may be relevant to ingestion of food (Sirt1 defective) with inappropriate post-prandial lipid and amyloid beta metabolism that inactivate magnesium therapy that may now be relevant to HSP and amyloid beta metabolism with relevance to myocardial infarction [3, 37].

Food restriction and fasting regulate Sirt1 and FGF21 involved in the prevention of the metabolic syndrome and maintenance of high density lipoprotein levels [39-41]. FGF21 therapy [42, 43] in Type 2 and Type 3 diabetes may be ineffective with the development of cardiac aging with relevance to core body temperature regulation that is determined by miR-34a/Sirt1 gene expression with low adiponectin levels [36, 44] (Figure 2). Healthy diets that maintain Sirt1 activity in the brain and liver have become important to many diabetics in developed and developing world with relevance to food technology and hepatic lipid metabolism. The repression of the anti-aging gene Sirt1 that maintain the heat shock gene Sirtuin 1 expression but also careful cell transcriptional ontogeny and membrane transformations in the brain and liver during prolonged fasting. Diabetes 63: 4064-4075.

Figure 2: Appetite regulation in diabetes involve the maintenance of the heat shock gene Sirtuin 1 that is essential for thermo regulation function and hepatic lipid metabolism. The repression of the anti-aging gene Sirt1 involves p53/mTOR dysregulation of the other anti-aging genes (klotho, p66shc, FOXO3a) associated with hepatic lipid, heat shock protein, and amyloid beta metabolism. FGF21 treatment in diabetes has become important to NAFLD [38] and myocardial infarction treatment [39, 40] but defective cell transcriptional ontology in the liver and brain related to miR-34a inhibition of Sirtuin 1/transcription factors interactions inactivates hepatic lipid metabolism with the induction of NAFLD, defective amyloid beta metabolism, and neurodegenerative disease.

Conclusion

Dyslipidemia is one of the key risk factors for cardiovascular disease in diabetes. The management of dyslipidemia in diabetes continues to remain controversial and improvements in the characteristic diabetic dyslipidemia of high triglyceride and low HDL may not indicate that defective cell ontology is underway early in life. Diabetes and defective hepatic cell transcriptional programs induce delayed post-prandial lipid metabolism associated with Western diets rich in fat and glucose. The clinical management of diabetes in the young and elderly now not only involves appetite regulation with calorie restricted diets that maintain the heat shock gene Sirt1 expression but also careful core body temperature (37°C) to activate hepatic and brain Sirt1. The biological active release of FGF21 is connected to Sirt1 activation and glucose homeostasis with relevance to treatment of dyslipidemia, NAFLD, cardiovascular disease and neurodegenerative diseases. Consumption of Sirt1 inhibitors such as alcohol, suramin and palmitic acid should be avoided to prevent defective liver and brain cell ontology in the young and the elderly to prevent hyperglycemia induced oxidative stress and myocardial infarction.

Funding

This work was supported by grants from Edith Cowan University, the McCusker Alzheimer's Research Foundation and the National Health and Medical Research Council.

References


