Sirtuin 1, a Diagnostic Protein Marker and its Relevance to Chronic Disease and Therapeutic Drug Interventions

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Abstract

Critical interpretations and analysis in diagnostic proteomics have accelerated with relevance to various biomarker tests that involve proteomics, lipidomics and genomics that assist with drug therapy to prevent programmed cell death with relevance to severity of global chronic disease progression. Reversal of global non-alcoholic fatty liver disease (NAFLD) is essential with analysis of various plasma components that may override diagnostic proteomics with relevance to defective nuclear-mitochondria interactions and therapeutic drug efficacy. Therapeutic drug effectiveness and the measurement of multiple proteins/peptides for patient care requirements now require anti-aging gene Sirtuin 1 (Sirt 1) analysis that is related to toxic amyloid beta-protein interactions and relevant to therapeutic drug metabolism in diabetes and neurodegenerative diseases.

Keywords: Sirtuin 1; Diagnosis; Global; Disease; Drug; Proteomics; Amyloid Beta; Non-Alcoholic Fatty Liver Disease; Diabetes; Neurodegeneration

Proteomics has been the systematic study of many proteins to provide structure, function and control of biological systems in health and disease. Advances in methods and technologies designed for peptide/protein complex analysis has advanced rapidly with mass accuracy and sensitivity [1-3]. Proteomics with proteomic pattern diagnostics is now an expanding field of research. The plasma proteome is now in an important position to interpret the intersection between prevent programmed cell death with relevance to severity of global chronic disease progression. Proteomic-based approaches for biomarker investigation may allow elucidation of pathways and identification of individuals who are most likely to respond to specific drug therapeutic interventions [4,5] with possible prediction of patients side effects to various drugs [6]. The majority of current drug targets are proteins, such as G protein-coupled receptors, ion channels, enzymes and components of hormone signaling pathways [7]. The progress and challenges in the translational application of proteomic technologies are to interpret post-translational modifications and protein-protein interactions in disease.

Prevalent global chronic diseases such as cardiovascular disease, non-alcoholic fatty liver disease (NAFLD), diabetes and neurodegenerative diseases have raised major concern. Factors that regulate chronic disease progression have been explored with major changes in proteomic profiles involved in the acceleration of chronic diseases. The proteomic profiles [1-3] may not be relevant to drug therapy/metabolism or stabilize insulin resistance relevant to disease progression [8,9]. The need to assess proteomic profiles with relevance to biomarker tests [10-14] in chronic disease may not be relevant and may not optimize drug therapy or improve therapeutic outcomes with possible drug-drug interactions [15] or drug-protein interactions [16-18] relevant to mitophagy in the global chronic disease epidemic. Interest in applying proteomics to gain a better understanding of disease progression requires identification of novel proteins and their interactions for early detection of disease associated with acceleration of drug therapeutics [4-6]. The importance of diagnostic proteomics is now connected to nutrition, neurodegeneration with its important role in the primary regulation of the amyloid clearance pathway [19-22] connected to drug/xenobiotic metabolism [23].

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Diagnostic proteomics and its relevance to early diagnosis of neuron apoptosis has accelerated with the plasma proteome analysis that may be relevant to neuron mitochondrial apoptosis [24]. Proteins such as apelin, angiotensin II, adiponectin, transforming growth factor beta, Tumour necrosis factor alpha, GDF11, heat shock proteins (HSP 70, HSP 60), gelsolin, insulin like growth factor 1, fibroblast growth factor 21, hepatocyte growth factor, nerve growth factor and thrombospondin 1 are now relevant to the transcription factor p53 [23] and its post-transcriptional regulation of the nuclear receptor Sirtuin 1 (Sirt 1). Sirt 1 is a nicotinamide adenine dinucleotide (NAD+) dependent class III histone deacetylase (HDAC) that targets transcription factors such as p53 to adapt gene expression to metabolic activity and the deacetylation of nuclear receptors indicate their critical involvement in insulin resistance [23]. Sirt 1 is now important to mitochondrial biogenesis and its regulation of protein/amyloid beta [21,22] and drug metabolism is connected to mitochondrial apoptosis and neurodegenerative disease [24].

Dietary regulation of nuclear receptors involves the calorie sensitive gene Sirt 1 involved in the metabolism of glucose, fatty acids, cholesterol and xenobiotics [25,26]. Sirt 1 activation of pregnane X receptor (PXR) is responsible for cytochrome p450 expression and the hepatic metabolism of drugs [25]. Therapeutic drug interventions involve activation of Sirt 1 by healthy diets that contain Sirt 1 activators connected to the reversal of NAFLD [9,27,28]. Sirt 1 is critical to pharmacological management with relevance to antibiotic resistance, epilepsy induced stroke, insulin therapy and antimicrobial activation [29-33].

To avoid inadvertent errors in proteomics and the systematic study of many proteins, Sirt 1 (plasma, cytoplasmic and nuclear analysis) should be conducted to interpret proteomic pattern diagnostics in biological systems in health and disease [34-40]. Sirt 1’s analysis in the nucleus and cytoplasm may assist with defects in nuclear-mitochondria interactions and may override misinterpretations in proteomic pattern diagnostics (Figure 1). Sirt 1 plasma analysis is important to the regulation of toxic amyloid beta oligomers with its direct interaction with specific acute phase proteins (serum amyloid protein P, serum amyloid protein A, adiponectin/alpha 2 macroglobulin, adiponectin/TSP-1, gelsolin, complement components, transthyretin and clusterin) [19,21,41-44] that may override important proteomic technologies [1-3,45,46]. Sirt 1 regulation of toxic amyloid beta-protein interactions (Figure 1) are critical to drug metabolism [4,5,22] with decreased plasma Sirt 1 levels [34-40] associated with increased drug-protein interactions [16-18] or drug-xenobiotic interactions [47-49].

**Figure 1:** Plasma proteome profiles require Sirt 1 analysis important to toxic amyloid beta: protein interactions and drug:protein interactions with relevance to drug metabolism and connected to mitochondrial apoptosis and global chronic disease. Sirt 1 regulation of adiponectin levels is related to adiponectin interactions with alpha 2 macroglobulin and thrombospondin 1 with relevance to toxic amyloid beta metabolism. Acute phase proteins such as Sirt 1 that regulate hepatic toxic amyloid beta metabolism determine amyloid beta interactions with other plasma proteins such as transthyretin, clusterin and gelsolin. Sirt 1 (plasma, cytoplasmic and nuclear analysis) should be conducted to interpret defects in nuclear-mitochondria interactions in health and disease to avoid inadvertent errors with proteomic pattern diagnostics in advanced proteomic technologies with relevance to accelerated neuron death.
Plasma Sirt 1 and its regulation of heat shock protein 70 (HSP 70) and antimicrobial proteins metabolism are connected to the immune system [31,51] with repression of Sirt 1 related to HSP 70 induced programmed cell death with relevance to inactivation of drug therapy [52]. Dietary regulation of Sirt 1 is important to chronic disease with bacterial lipopolysaccharides (LPS) and patulin relevant to defective posttranslational/post transcriptional alterations [53-56]. The progress and challenges in the translational application of proteomic technologies are to interpret post-translational modifications and protein-protein interactions [57] in disease but LPS and mycotoxin have now become important and may override proteomic interpretations in health and disease. Interest in plasma Sirt 1 analysis has become important to amyloid beta-acute phase proteins interactions with LPS critical to hepatic Sirt 1 repression and membrane transformation with relevance to drug metabolism [58-60]. LPS regulates Sirt 1 levels [58-60] and Sirt 1 is now referred to as an inflammatory target protein in vivo [61]. LPS inactivates toxic amyloid beta metabolism by interference with apolipoprotein E-phospholipid transfer protein, apolipoprotein A1, albumin, transferrin, and lactoferrin [62-64].

Nutritional proteomics [65,66] has become important to prevent programmed cell death with relevance to severity of global chronic disease progression. The links between diet and genomics [23] are now important to Sirt 1 regulation with connections to nutritional proteomics and nutritional lipidomics [67,68]. Sirt 1 is now an important nutritional biomarker [69,70] that is connected to the nuclear-mitochondria interaction and plasma Sirt 1 levels are important to proteomics and drug metabolism. Sirt 1 activators and their consumption determine Sirt 1 levels important to proteomic technologies (protein profiles) to gain a better understanding of drug therapy in chronic disease progression.

Conclusion

Proteomic-based approaches for biomarker investigation is now important to interpret the intersection between proteomic pattern diagnostics and programmed cell death with relevance to severity of global chronic disease progression. Proteomic profiles that include plasma Sirt 1 and protein analysis are critical to determine defects in the nuclear-mitochondria interaction relevant to the severity of cardiovascular disease, NAFLD, diabetes and neurodegenerative diseases. Sirt 1’s control of biological systems in health and disease involve toxic amyloid beta and protein interactions with Sirt 1 repression associated with inactivation of drug/xenobiotic metabolism with acceleration of chronic disease progression. Interest in applying proteomics to disease progression requires early plasma Sirt 1 analysis for detection of disease protein biomarkers associated with inactivation rapid toxic amyloid beta and therapeutic drug metabolism.

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