

# Updates in Nutritional Disorders and Therapy

Editorial

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## Defective Interplay between Adipose Tissue and Immune System Induces Non Alcoholic Fatty Liver Disease

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### Original Submission

**Received:** January 10, 2017

**Accepted:** January 24, 2017

**Published:** February 08, 2017

**Open Peer Review Status:** Editorials, news items, analysis articles, and features do not undergo external peer review.

**How to cite this article:** Martins IJ. Defective Interplay between Adipose Tissue and Immune System Induces Non Alcoholic Fatty Liver Disease. Updates Nutr Disorders Ther. (2017) 1: 3.1

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## Keywords

Adipose Tissue; Non Alcoholic Fatty Liver Disease; Sirtuin 1; Immunometabolism; Immune; Nutrition; Heat Shock Proteins; Thermoregulation; Autoimmune Disease; Natural Killer Cells

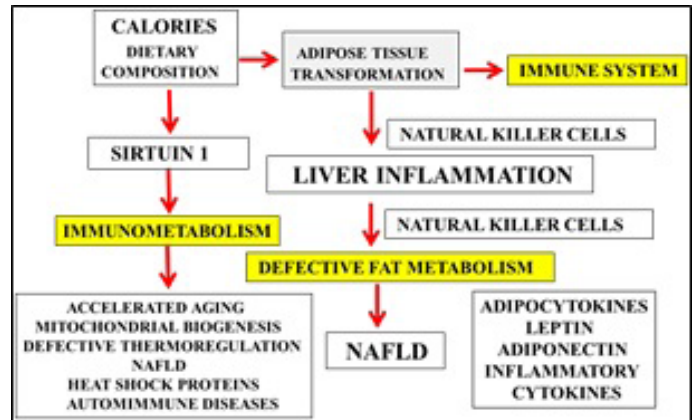
## Editorial

Multiple theories of aging have been proposed and the immune theory of aging may involve adipose tissue transformation with activation of immune responses that involve macrophages and immune cells that lead to liver inflammation [1] and the induction of non alcoholic fatty liver disease (NAFLD). The importance of ingested dietary fat and adipose tissue as the organ most susceptible to programmed cell death pathways and transformation has become important to determine the release of adipocyte inflammatory cytokines, hormones and heat shock proteins (HSP) that trigger liver inflammation and NAFLD in global communities [2-8]. Diet and the immune system are closely linked with dietary fatty acid composition [9] such as the saturated fatty acid palmitic acid (toxicity) versus beneficial unsaturated fatty acids that play a central role in immune reactivity in the liver [10-12]. Furthermore, food consumption that prevent programmed cell death pathways in mouse and man may be relevant to gene expression [12-17] that regulate the adipose tissue to release factors such as adiponectin, leptin, heat shock proteins [6-8,10,11,18-20] that regulate inflammatory cytokines to maintain liver function and to prevent NAFLD in man.

Immunometabolism and accelerated aging is now connected to the adipose tissue and liver crosstalk with the mitochondria theory of aging important to both immune function [21,22] and metabolism of fats in the adipose tissue and liver. The ingestion of the amount of fat is critical to the adipose tissue-liver cross with immune reactivity connected to mitophagy and induction of NAFLD. The nutrient sensing gene Sirtuin 1 (Sirt 1) is now important to the nuclear-mitochondria interaction [12] with deacetylation of transcription factor p53 important to the adipose tissue and liver fat metabolism. The p53 is involved in immune responses, metabolism and mitochondrial apoptosis [23-31] with diet, drugs and environment [32] critical to the regulation of Sirt 1/p53 immunometabolism and induction of NAFLD in the developed world.

Thermoregulation defects in geriatric populations [33] indicate immune response alterations [34] that accelerate various chronic diseases in these individuals. Autoimmune disorders in the geriatric populations have been described and the heat shock gene Sirt 1 defective in these populations [35,36] may indicate connections between defective thermoregulation and autoimmune diseases [37-40]. Nutrition and the immune system may be the primary therapy for prevention of NAFLD in global populations with dietary fat intake and the immune response critical to survival of various individuals in the developed world. Dietary fat composition and the immune system

[41-44] are associated with adipose tissue immune responses with natural killer cell activity relevant to liver inflammation and the induction of NAFLD [45-52].



**Figure 1:** The adipose tissue-liver crosstalk is defective in NAFLD individuals in the developed world. Dietary calories and composition determine adipose tissue transformation that induce liver inflammation with the induction of NAFLD. The gene Sirtuin 1 regulates immunometabolism and is primarily involved with immune defects (increased inflammatory cytokines, natural killer cells) with secondary effects on hepatic fat metabolism. Immunometabolism defects are connected to defective thermoregulation that induce mitochondrial apoptosis and autoimmune diseases.

In the developing world increased plasma bacterial lipopolysaccharides (LPS) levels are now relevant to immune response alterations, autoimmune diseases and NAFLD [32,53]. LPS and repression of Sirt 1 has been indicated [54] with LPS linked to p53 alterations [12] with altered immunometabolism now important as an inducing agent in immune responses, cholesterol metabolism and NAFLD [55]. Diets that activate Sirt 1 such as calorie restricted diets and dietary composition that contain activators (leucine, alpha lipoic acid, pyruvic acid, resveratrol) of Sirt 1 have become important to immunometabolism and maintenance of the adipose tissue-liver crosstalk. Inhibitors of the adipose tissue-liver interplay and regulation of immunometabolism (Sirt1/p53) in the developed world may include alcohol, palmitic acid and drugs such as Suramin and Sirtinol in individuals in the developed world. Individuals involved with physical exercise regimes may deplete magnesium (Sirt 1 activator) reserves essential for immune function and liver cholesterol metabolism [56-58] in the developed world. LPS may induce magnesium deficiency [58] with relevance to adipose tissue-liver immunometabolism defects in the developing world.

## Conclusion

In the developed world nutritional interventions have become critical to prevent the NAFLD epidemic that may afflict between 30-40 % of global population by the year 2050. Primary mode of diet therapy should regulate the immune response to prevent liver inflammation that affects the hepatic metabo-

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lism of dietary fat with the induction of NAFLD. Diet, drugs and lifestyles changes are important to body magnesium balance and therapy with relevance to immunometabolism to prevent mitochondrial apoptosis involved in the defective adipose tissue-liver interplay associated with autoimmune diseases in geriatric individuals in the developed world.

## Acknowledgements

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

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