Some novel modulators of obesity and atherogenic factors

Metabolic syndrome is a complex disease that encompasses obesity, type 2 diabetes, hypertension and hyperlipidemia. Poor dietary habits and sedentary life style lead to impaired adipose tissue fuel handling and ectopic lipid deposition in vital organs such as liver, pancreas, muscle and heart. Transcriptional coactivators peroxisome proliferator receptor coactivator 1 alpha and beta (PGC1α, PGC1β) as well as sterol regulatory element-binding proteins (SREBPs) play vital roles in regulating the lipid oxidizing and lipogenic genes and thereby control the progression of obesity and metabolic syndrome. AMP-activated protein kinase (AMPK) and Sirtuins (SIRT) are two metabolic fuel sensors that directly affect PGCs and SREBPs through phosphorylation and deacetylation, respectively. A number of natural modulators have a direct impact on the intracellular status of AMPK and SIRTs, and thereby may play vital roles in maintaining lipid homeostasis. We show that low ω3-polyunsaturated fatty acids (low-ω3FA) and soy proteins effectively attenuate high-fat diet-induced hyperlipidemia and hepatosteatosis. They also prevent the downregulation of hepatic SIRT1 and PGC1α and their target fatty acid oxidation pathway genes and attenuate the upregulation of hepatic PGC1α and SREBP1c and their target lipogenic pathway genes via the phosphorylation of AMPK. Similarly, dietary curcumin protects against high-ω3FA-induced hepatosteatosis. Simultaneously, polyphenol, quercetin upregulates paraoxonase 1 (PON1) mRNA and causes significant increase in serum PON1 and homocysteine thiolactonase (HCT), the key anti-atherogenic enzymes. Moreover, quercetin protects against high-ω3FA-induced oxidative stress by increasing the antioxidant glutathione and decreasing the toxic lipid peroxidation product 4-hydroxynonenal. He will discuss the status of the relative roles of these transcriptional coactivators, and the central roles of AMPK and SIRT in the maintenance of lipid homeostasis with special emphasis on how novel dietary supplements such as low-ω3FA, soy proteins, and curcumin may serve adjunct therapeutic agents in the treatment of obesity, metabolic syndrome and cardiovascular risks in conjunction with traditional drug therapy.

Recent Publications


Biography

M Raj Lakshman is currently working as the Director of Research Laboratories and the Chief of Lipid Research at the VA Medical Center, Washington DC. He also has joint appointments as a Professor in the Departments of Biochemistry and Molecular Medicine as well as in the Department of Medicine at the George Washington University, Washington DC. He directs studies in the areas of Alcoholism, Alcoholic Liver Disease, Oxidative Stress, Coronary Artery Disease, Lipids & Lipoproteins, Metabolic and Genetic Obesity, Hepatotoxins, Gene Regulation and Expression. He joined the National Institute of Health, to work on Alcoholic Hyperlipidemia under the able guidance of Professors Richard Veech, Nobel Laureate and Hans Krebs. In 1979, he received the prestigious VA Research Career Scientist Award working in the field of Alcohol and Alcoholism at the VA Medical Center, Washington DC. He was honored with Washington Heart Ball Research Award in 1990 in the field of Hyperlipidemia.

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