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Hepatoprotective role of thymosin β4 (Tβ4) in alcoholic liver disease

Thymosin beta4 (Tβ4), an actin sequestering protein, is involved in tissue development and regeneration. It prevents inflammation and fibrosis in several tissues. We investigated the Hepatoprotective role of Tβ4 in chronic ethanol (EtOH) and lipopolysaccharide (LPS)-induced liver injury as well as in liver regeneration after partial hepatectomy in chronic EtOH fed mice. We demonstrated that Tβ4 treatment prevented EtOH and LPS-mediated oxidative stress by decreasing ROS and lipid peroxidation; and increasing the antioxidants, glutathione and manganese-dependent superoxide dismutase. It also prevented the activation of nuclear factor KappaB by blocking the phosphorylation of IκB, thereby prevented pro-inflammatory cytokine production. Moreover, Tβ4 prevented fibrogenesis by suppressing the epigenetic repressor, methyl-CpG binding protein2 that coordinately reversed the expression of peroxisome proliferator-activated receptor-γ and down-regulated fibrogenic genes, platelet derived growth factor β-receptor, α-smooth muscle actin, collagen1, and fibronectin, resulting in reduced fibrosis. Tβ4 also promoted liver regeneration after partial hepatectomy in EtOH-fed mice by increasing hepatocyte regeneration markers, hepatocyte growth factor and its receptor (c-Met) and α-fetoprotein, as well as proliferation markers, proliferating cell nuclear antigen and Ki-67. Our data suggest that Tβ4 has antioxidant, anti-inflammatory, anti-fibrotic and regenerative potential during alcoholic liver injury.

Speaker Biography

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

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