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Synergy between ASH and NASH

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Fatty liver (hepatosteatosis) is the earliest abnormality in the pathogenesis of alcoholic steatohepatitis (ASH) and non-alcoholic steatohepatitis (NASH) and either due to metabolic risk factors associated with chronic alcohol abuse or with insulin resistance and/or metabolic syndrome in the absence of alcohol consumption. When unchecked, both ASH and NASH lead to liver fibrosis, cirrhosis, hepatocellular carcinoma (HCC) and eventual death. A number of common mechanisms contribute to the above various stages of hepatocyte injury including lipotoxicity, endotoxin release, oxidative and ER stress leading to increased pro-inflammatory cytokines that stimulate hepatic fibrogenesis and cirrhosis by activating the quiescent hepatic stellate cells (HSC) into myofibroblasts. Significantly, patients with either ASH or NASH respond favorably to early treatment modalities to reduce hepatic fat accumulation and consequently increased inflammatory signaling and activation of hepatic stellate cells. Although the pathogenic pathways associated with ASH and NASH is seemingly similar, differentiation of the molecular mechanisms of the pathogenesis of these liver diseases is critical in identifying the unique molecular signatures especially in the early diagnosis of ASH and NASH. Current clinical practice requires the invasive biopsy procedure for the conclusive diagnosis of ASH and NASH. Micro RNAs (miRNAs) are ~22 nucleotide non-coding sequences that bind to the 3'-untranslated region of target transcripts and regulate gene expression by degradation of target mRNAs or inhibition of translation. Emerging studies may prove to establish miRNAs as excellent non-invasive tools for the early diagnosis of various stages of liver diseases.

Biography

M 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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