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Serum microRNA-122 and miR-155 as biomarkers of liver injury and inflammation in models of acute and chronic liver disease

Shashi Bala
University of Massachusetts Medical School

Et al.

SERUM MICRORNA-122 AND MIR-155 AS BIOMARKERS OF LIVER INJURY AND INFLAMMATION IN MODELS OF ACUTE AND CHRONIC LIVER DISEASE

Shashi Bala, Jan Petrasek, Shiv Mundkur, Donna Catalano, Jeanine Ward, Ivan Levin, Hawau Alao, Karen Kodys and Gyongyi Szabo

University of Massachusetts Medical School, Worcester, MA-01605

Contact: Shashi.bala@umassmed.edu

Background: MicroRNAs (miRs) are small non-coding molecules that regulate gene expression. MiRs expression levels change not only in diseased tissues but also in circulation. Further, miRs are stable in frozen samples that make them attractive for biomarker discovery. Recent reports suggest altered expression of circulating miRNAs in various diseases. MiR-122 is highly abundant in hepatocytes where it regulates different metabolic pathways while miR-155 is a central regulator of inflammation. The aim of this study was to evaluate circulating miRNAs as potential markers of hepatocyte damage and inflammation in liver diseases.

Methods: Serum/plasma and liver samples were collected from C57/BL6 mice after: 1. Chronic alcohol feeding with Lieber-deCarli diet containing alcohol or pair-fed diet for 5 weeks 2. Acetaminophen (APAP) administration. 3. TLR9/4 administration. 4. CCL4 administration. Serum/plasma ALT was evaluated and total RNA was analyzed for miRNAs expression with TaqMan MicroRNA assay. Non-parametric Mann-Whitney test was used for statistics.

Results: The alcohol, APAP, TLR9/TLR4 and CCL4, -induced liver injury models all resulted in ALT increase and more important, in increased serum/plasma miR-122 levels compared to control mice. There was a linear correlation between miR-122 and ALT levels. After CCL4 treatment, serum miR-122 was upregulated as early as one week over controls and it remained elevated. No increase in serum miR-122 in Toll like receptor 4 or NADPH oxidase–deficient mice was found after alcohol feeding as these KO mice were protected from alcohol-induced liver injury and inflammation. Alcohol-, APAP, TLR9/TLR4 and CCL4-induced liver damage all involve in activation of the inflammatory cascade. Consistent with this, we found increased serum miR-155 levels.

Conclusion: Our novel results show that serum/plasma miR-122 up-regulation correlates with ALT, thus, miR-122 could be a useful biomarker in acute and chronic liver injury. We also report that serum miR-155 is increased in liver disease with inflammation.