Oxidative stress and altered gene expression occurs in a metabolic liver disease model

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A team of researchers under the direction of Dr. Jeffrey Teckman in the Department of Pediatrics at St. Louis University, have demonstrated that oxidative stress occurs in a genetic model of alpha-1-antitrypsin deficiency. This is the most common genetic liver disorder in children and can lead to cirrhosis and hepatocellular carcinoma in adults. Some cases may require liver transplantation. The report, published in the October 2012 issue of *Experimental Biology and Medicine*, suggests that treatment with antioxidants might be of therapeutic benefit for some individuals.

"We have evidence of oxidative stress in livers from an animal model that expresses the classical Z variant form of alpha-1-antitrypsin. The animal model recapitulates the human liver disease, in which the livers accumulate polymers of alpha-1-antitrypsin mutant Z protein, developing fibrosis and hepatocellular carcinoma with age", says Dr. Marcus. Potentially, non-invasive treatment involving long-term regulation of antioxidant levels could ameliorate the oxidative stress and retard the advancement of disease.

"This is an exciting new report which may help us understand the extreme variability between different patients with this same, single gene, metabolic liver disease. These findings may inform the pathophysiology of other liver diseases as well", says Dr. Teckman. In clinical studies, liver disease from alpha-1-antitrypsin mutant Z protein has shown considerable variability in severity and progression, suggesting that as yet undescribed genetic modifiers may influence

disease development. Based on this study, certain antioxidant enzymes involved in oxidative stress defense could be useful targets for further examination. Using microarray technology, the investigators have identified a number of potential alterations in gene expression pathways that could modify the development of liver pathologies. This information could be useful in defining genetic variants that may influence individual susceptibility and in facilitating the design of appropriate treatments.

Steven R. Goodman, PhD, Editor-in-Chief of Experimental Biology and Medicine said, "Teckman and colleagues have demonstrated that oxidative stress occurs in an animal model of Alpha-1-antitrypsin deficiency. This suggests that antioxidant treatment may be beneficial in this most common genetic liver disorder in children."

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