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Contact: Aimee Frank

AFrank@gastro.org

301-941-2620

[American Gastroenterological Association](#)

New techniques redefine assessment of liver disease

WASHINGTON, D.C. (May 20, 2007) · Research presented today at Digestive Disease Week 2007 (DDW 2007) introduces unique methods for evaluating patients with non-alcoholic fatty liver disease (NAFLD). NAFLD is the most common liver disease in the world and the development of novel procedures for definitively diagnosing the disease and assessing its prognosis is extremely important for tailoring effective treatments. DDW is the largest international gathering of physicians and researchers in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery.

"Defeating the most common liver disease means continuing research in a field that is progressively transforming," said Jacquelyn J. Maher, M.D., University of California, San Francisco. "The methods highlighted in these studies will permit doctors to accurately identify NAFLD and potentially predict treatment outcomes, using less invasive approaches than the current standards."

Noninvasive Assessment of Hepatocyte Apoptosis in Nonalcoholic Fatty Liver Disease: A Multicenter Validation Study (Abstract #3)

While a liver biopsy is the standard method of diagnosis and disease progression for non-alcoholic steatohepatitis (NASH), the most extreme form of nonalcoholic fatty liver disease (NAFLD), researchers previously demonstrated that a less invasive blood test to determine caspase three-generated cytokeratin 18 fragment levels (a noninvasive biomarker test, CK-18) can predict the incidence and magnitude of NASH. A study conducted by researchers at the Cleveland Clinic in Ohio validates the utility of this novel biomarker for NASH diagnosis and assessment of disease severity in a large NAFLD population.

As an ancillary study of the NASH National Institute of Health Clinical Research Network (CRN), 178 patients with well-characterized biopsy-proven NAFLD participated in this study. Another 150 age-matched health controls were analyzed to validate the biomarker methodology. The team tested the NAFLD patients' blood levels for CK-18 fragments, ranging from 68 to 3000 U/L,

which were significantly higher than those observed in the 150 healthy controls (average of 45 U/L blood level).

Results reveal that accurately determining CK-18 fragment levels in the blood differentiates NASH from simple steatosis in patients with NAFLD, supporting the potential of this test in clinical practice as a noninvasive NASH biomarker. In addition to finding that CK-18 could work as a marker of NASH, the study showed that for every 50 U/L increase, the likelihood of having definitive NASH (as opposed to simple steatosis) increased by 74 percent.

"Noninvasive tools are urgently needed for the diagnosis and assessment of NASH in patients with NAFLD," says Ariel Feldstein, M.D., of Cleveland Clinic Foundation, and co-author of this study. "This method of measuring CK-18 fragment levels in the blood may prove to be an effective noninvasive biomarker for the disease that will assist in diagnosis and prompt treatment."

Dr. Feldstein will present this study on Sunday, May 20, at 9:00 a.m. in Room 207.

Can Phosphoproteomic Analysis of White Adipose Tissue (WAT) Predict Presence of Insulin Resistance (IR) and Resolution of Diabetes Mellitus (DM) in Non-Alcoholic Fatty Liver Disease (NAFLD)" (Abstract #T1105)

Diabetic patients with NAFLD are at risk for progressive liver disease. In this study, researchers examined connections between white adipose tissue (WAT, white fat) in the abdomen and medical disorders including insulin resistance (IR, inadequate response to insulin) and diabetes mellitus (DM, a metabolic disorder characterized by high blood sugar) in patients with obesity and NAFLD to evaluate whether cell signaling pathway profiles within WAT are associated with the presence of IR and whether they can predict the resolution of DM after weight loss. It is important to note that some obese diabetics can completely resolve DM after weight loss.

This study, conducted by researchers at George Mason University in Fairfax, Va., included 144 patients undergoing bariatric surgery. Prior to surgery, 41 percent of these patients had evidence of IR measured by a blood test. Twenty-five percent of the 144 patients had clinically overt DM prior to surgery. At the time of surgery, WAT was collected for protein profiling. The results were analyzed to determine whether this technique could (a) accurately predict IR in obese individuals and (b) identify which diabetic patients were destined to resolve their DM postoperatively.

Comparing patients with IR to those without IR, the phosphorylation levels of 10 proteins were significantly different between these two groups. When comparing 15 diabetics who resolved their DM after weight loss to 10 who did not, 20 proteins were marked as significantly different between the two groups. Nearly all of these proteins are associated with insulin signaling, which leads to abnormal blood glucose levels and diabetes, leading researchers to the conclusion that "prognostic biomarkers" can be developed that can potentially predict resolution of important complications of obesity such as DM.

"Recognition of specific cell signaling pathways using Reverse Phase Protein Microarrays of WAT appears to help differentiate patients with insulin resistance from those without insulin resistance," according to Zobair Younossi, M.D., of Inova Health System's Translational Research Centers in Fairfax, Va., and senior author of the study. "With further confirmatory studies, this type of analysis may be effective at predicting resolution of clinically overt DM after weight-loss surgery."

Dr. Younossi will present this study on Tuesday, May 22, at 8:00 a.m. in Hall E.

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Digestive Disease Week 3 (DDW 3) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW takes place May 19-24, 2007 in Washington, D.C. The meeting showcases more than 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology.
