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IL28B gene predicts treatment outcome for liver transplantation patients

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German researchers have found a significant association of IL28B genotypes to interferon-based antiviral treatment outcome, and to graft inflammation caused by hepatitis C virus (HCV). The study determined that the presence of G-allele serves as a marker for severe HCV-induced graft inflammation, as well as a predictor for unsuccessful treatment. Study findings -- the largest to report on the role IL28B variants in a transplant cohort with recurrent HCV -- are published in the March issue of *Liver Transplantation*, a journal of the American Association for the Study of Liver Diseases.

The IL28B gene encodes interferons (IFNs), which are proteins made by lymphocytes to motivate the immune system in the presence of pathogens. IFN-α proteins are produced by leukocytes and are prevalent in the presence of a viral infection such as HCV. Researchers determined the prevalence of IL28B genotypes (GG, GT, TT) in 183 liver transplant patients, analyzing 605 protocol liver biopsies performed six months to ten or more years after transplantation.

The authors determined that the presence of G-allele was a marker for more severe graft inflammation and was observed to have a strong association to antiviral treatment failure in 103 of 159 patients. T-allele was more frequent among patients with lower inflammation grades, concluding a definite association between IL28B G-allele and HCV-induced graft inflammation, and the G-allele as a predictor of unsuccessful antiviral treatment. The team also found that IL28B genotypes did not seem to affect median fibrosis.

"Successful liver transplantation creates a unique population of quasi-normal individuals relying on a harmonic interaction of two different genetic backgrounds," said Dennis Eurich, MD, from the Department of General, Visceral and Transplant Surgery at Charité, Campus Virchow in Berlin and lead author of the current study. "IL28B polymorphisms may help to identify patients at risk for developing more severe graft hepatitis . These genetic variants might help to individually predict potential response to antiviral therapy, enabling medical professionals to appropriately adapt treatment."

A related editorial also published in *Liver Transplantation* this month acknowledges the association between IL28B polymorphisms and HCV-induced graft inflammation, and the prediction of treatment outcomes. Geoffrey McCaughan from the Centenary Institute in Australia said, "The exact mechanisms of how this association results in higher sustained virologic response rates remain unclear, however the data has invigorated research into both prediction of treatment outcomes and the mechanisms of control of HCV replication and clearance."

Infection with HCV is the primary cause of cirrhosis of the liver and liver cancer worldwide. Up to 30% of liver transplants will develop graft cirrhosis within five years after liver transplantation due to recurrent HCV-infection. HCV-induced graft fibrosis is the main determinant of morbidity and mortality of liver transplant patients.

More information: "Relationship between IL-28b Gene Polymorphism and Histological Severity of HCV-Induced Graft Inflammation and Response to Antiviral Therapy after Liver Transplantation." Dennis Eurich, Sabine Boas-Knoop, Martin Ruehl, M. Schulz, Esperanza Carrillo, Thomas Berg, Ruth Neuhaus, Peter Neuhaus, Ulf Neumann, and Marcus Bahra. Liver Transplantation; Published Online: December 6, 2011 (DOI: 10.1002/lt.22235) Print Issue Date: March 2011.