

# New Biomarker Predicts Response to Hepatitis C Treatment

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(PhysOrg.com) -- Researchers have identified the first genetic marker that predicts response to hepatitis C treatments, and a single letter of DNA code appears to make a huge difference. Duke University Medical Center scientists says the biomarker not only predicts who is most likely to respond to treatment and who isn't, but also may explain why there are such different rates of response among racial and ethnic groups, a phenomenon that has puzzled physicians for years.

"For geneticists, understanding response to treatment for [hepatitis C infection](#) has been almost like a Holy Grail," says David Goldstein, Ph.D., director of the Center for Human Genome Variation in Duke's Institute for Genome Sciences & Policy and the senior author of the study. "The side effects of hepatitis treatment can be brutal, and about half the time, the treatment fails to eradicate the virus. This discovery enables us to give patients valuable information that will help them and their doctors decide what is best for them. This is what personalized medicine is all about."

The discovery is reported online in the journal *Nature*.

[Hepatitis C](#) is one of the most common infections in the world, affecting an estimated 170 million people. Many can live with the disease for years without any serious complications. About a quarter of the time, however, the infection leads to cirrhosis of the liver, which, in turn, can lead to liver cancer or death or the need for a transplant. Hepatitis C is the leading cause for liver transplants in the U.S.

Treatment typically involves 48 weeks of interferon plus the antiviral drug ribavirin. Some patients develop such taxing side effects that they stop treatment. Physicians have long observed that African-Americans are less likely to respond to treatments than Caucasians, while East Asian patients seem to respond the best. But until now, no one has known why.

"This discovery appears to explain a large part of it. It is most certainly a triumph of translational medicine," says John McHutchison, M.D., associate director of the Duke Clinical Research Institute, a member of the Division of Gastroenterology in the School of Medicine at Duke and study co-author. "This is a perfect example of bedside to bench and back to bedside investigation."

The new marker is a single letter change - a C instead of a T - in a tiny segment of DNA near the IL28B gene. Researchers found it by studying 1671 individuals who participated in the IDEAL study, a multi-center clinical trial that compared the two most widely used therapies among patients with the most common form of the disease in the U.S. and Europe. McHutchison was the lead investigator of the recently published IDEAL study, which found no clinically meaningful differences in overall viral response among the regimens.

In conducting the current study, Goldstein and his colleagues found that the patients who had the single-letter change in their DNA were significantly more likely to respond to treatment than those who did not have it. "Eighty percent of those with the favorable response genotype eradicated the virus, while only about 30 percent with the less favorable response genotype did so. With differences of that magnitude, patients considering therapy may want to know what their genotype is before they start treatment," says Goldstein.

Goldstein says they were struck by the finding that the "good" genotype proved beneficial to patients in all population subgroups. "But because it

appears significantly more often among Caucasian populations than it does among African populations, we feel it explains much of the difference in response rates we see between African Americans and those of European ancestry," says Goldstein. "This tells us that individual genetic makeup is much more important determinant of response to treatment than is race or ethnicity."

Researchers found that African Americans with the favorable (CC) genotype had a significantly higher rate of response to treatment (53.3 percent) than did individuals of European ancestry who had the less favorable (TT) genotype (33.3 percent).

The researchers also ran tests to see if the presence of the [biomarker](#) was related in any way to viral load, a measure of how much virus was circulating in the patient before treatment started. They found a significant association in all groups. "Interestingly, we found that the C allele, although associated with better treatment response, was associated with a higher viral load at baseline - something we have traditionally viewed as a negative prognostic marker when it comes to treatment response," says McHutchison.

That finding, along with other evidence gleaned in the research, suggests that patients who have the beneficial [genetic marker](#) might be especially adept at spontaneously clearing the virus through some as yet unknown mechanism, says McHutchison. "It was thrilling to discover such an important biological marker related to response to hepatitis C treatments, but at the same time, the findings tell us there is a lot more work to do before we can fully understand how patients' immune systems protect them from the virus."

"This stunning finding supports the integration of research efforts that previously were not connected," says Robert Califf, M.D., vice chancellor for clinical research and director of the Duke Translational

Medicine Institute. "Drs. Goldstein, McHutchison and colleagues have combined world class genotyping and clinical trials management in an academic medical center with an industry sponsored clinical trial to produce a set of findings that are likely to change practice. Their focus on modification of clinical outcomes is especially important to note as we design future studies."

Some members of the research team are interested in finding a way to routinely test for the new marker, but McHutchison says important work still needs to be done. "This study only pertains to patients with genotype 1 infection. We still need to evaluate the polymorphism among patients with less common genotypes of hepatitis C."

Source: Duke University Medical Center ([news](#) : [web](#))

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