

Finding strengths—and weaknesses—in hepatitis C's armor

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Using a specially selected library of different hepatitis C viruses, a team of researchers led by Johns Hopkins scientists has identified tiny differences in the pathogens' outer shell proteins that underpin their resistance to antibodies. The findings, reported in the January 2015 issue of the *Journal of Clinical Investigation*, suggest a reason why some patients' immune systems can't fend off hepatitis C infections, and they reveal distinct challenges for those trying to craft a successful vaccine to prevent them. Due to concerns about the rising costs of newly available hepatitis C drugs, researchers are looking to a vaccine as a more viable and less costly option.

The systems of some people who become infected with the liver-ravaging [hepatitis C](#) virus launch a robust immune attack, producing [antibodies](#) that attach to a broad array of the germs with different genetic makeups. About one-third of these individuals successfully clear the pathogen from their bodies. However, says Justin Bailey, M.D., Ph.D., assistant professor of medicine in the Division of Infectious Diseases in the Johns Hopkins University School of Medicine, no single antibody has been found that can neutralize all strains of hepatitis C virus.

To better understand how hepatitis C viruses avoid even the most [broadly neutralizing antibodies](#), Bailey; Stuart C. Ray, M.D., professor of medicine in the Division of Infectious Diseases in the Johns Hopkins University School of Medicine; and colleagues tested the power of 18 antibodies known to broadly attack the virus against a library of 19 viral

strains that make up about 94 percent of the genetic variability of hepatitis C viruses in the most common genetic group, called genotype 1.

The researchers found that these antibodies clustered into just three groups, with members of a group able to attach to the same subsets of [viral strains](#). Searching for the mechanism behind this clustering, the researchers analyzed the components of the proteins that make up the viral envelopes, the viruses' outer shells. Their investigation identified tiny but potent differences in these proteins among the strains, making each vulnerable to certain clusters of antibodies but resistant to others.

In a surprising twist, says Bailey, many of the protein variations aren't located where antibodies are known to attach.

The team then tested blood plasma samples from 18 chronically infected hepatitis C patients. Without exception, the researchers found that the same viral variations leading to antibody resistance in the laboratory also led to antibody resistance in the patients' plasma, giving real-world confirmation of their lab findings.

Because the protein differences prevent any one antibody from battling all hepatitis C strains, says Bailey, an effective vaccine to prevent the disease may need to stimulate many different antibodies to account for the virus' genetic diversity. Future research efforts in his lab and others, he adds, will build on these findings by identifying which antibody combinations will be essential for such a vaccine.

"We can now start to identify antibodies from different clusters that are likely to be complementary to each other in their neutralizing ability, rather than using antibodies from just a single cluster," Bailey says.

More information: *Journal of Clinical Investigation*,
www.jci.org/articles/view/78794

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