

Genetic hint for ridding the body of hepatitis C

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More than seventy percent of people who contract Hepatitis C will live with the virus that causes it for the rest of their lives and some will develop serious liver disease including cancer. However, 30 to 40 percent of those infected somehow defeat the infection and get rid of the virus with no treatment. In this week's Advanced Online Publication at *Nature*, Johns Hopkins researchers working as part of an international team report the discovery of the strongest genetic alteration associated with the ability to get rid of the infection.

"If we knew why some people got rid of the disease on their own, then maybe we could figure out ways to help other people who didn't," says David Thomas, M.D., professor of medicine and director of <u>infectious</u> <u>diseases</u> at Johns Hopkins. "Or maybe even help prevent infections entirely."

A previous study led by David Goldstein at Duke University had found a variation in a single chemical of DNA, known as a single-nucleotide polymorphism, or SNP, near the IL28B gene, which while poorly understood, is thought to help the immune response to Hepatitis C viral infection. People infected with Hepatitis C, who carried the C/C variation SNP near their IL28B gene, were found more likely to respond to hepatitis C treatment, which can rid some patients of the <u>virus</u>.

So the Hopkins-and-National-Institutes-of-Health-led team wondered if the C/C variation—as opposed to the C/T or T/T alternatives—also played a role in some peoples' ability to get rid of the virus without the



help of medication. To do this, they assembled information from six different studies that had over many years collected DNA and Hepatitis C infection information from people all over the world. The team then analyzed DNA at the IL28B gene from a total of 1008 patients: 620 persistently infected and 388 who had been infected but no longer carried any virus. DNA analysis revealed that of the 388 patients who no longer carried virus, 264 have the C/C variation.

"This is the strongest clue to date to understanding what would constitute a successful immune response," says Thomas. "We don't yet know the significance of this C variant, but we know we need to do more work to find out what it means and whether it might be helpful to halting the disease."

In addition to confirming that the C/C variant correlates with the ability to get rid of the virus once infected, the researchers also noticed an intriguing trend: the C/C variant does not appear equally in all populations.

To investigate further, they analyzed DNA from more than 2300 people worldwide in order to further examine distribution of the C/C variant in different populations. Of the 428 samples from Africa, only 148 carried the C/C genotype. In contrast, of the European samples 520 out of 761 carried the C/C variant. The most striking were the DNA samples from Asia, where 738 of 824 samples carried C/C.

"We wonder if this SNP also explains some of the genetic basis for the population difference of <u>Hepatitis C</u> clearance," says Chloe Thio, M.D., associate professor of medicine. "It's been reported that African-Americans are less likely to clear the disease than Caucasians."

The team plans to pursue this research further to better understand why some populations become chronically infected. Says Thio, "This is an



exciting step towards better understanding of what the <u>immune response</u> is against the virus so we can improve our therapies."

Source: Johns Hopkins Medical Institutions

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