New hope for hep C vaccine

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Hopes for an effective vaccine and treatment against the potentially fatal hepatitis C infection have received a major boost following the discovery of two 'Achilles' heels' within the virus.

A team of medical researchers from the University of New South Wales (UNSW) studied individuals at high risk of hepatitis C (HCV) infection, including a number identified within a few weeks of the onset of infection.

Using a new technique called next generation deep sequencing and sophisticated computer analytics the team, led by Professor Andrew Lloyd and Associate Professor Peter White, were able to identify the 'founder' virus responsible for the initial infection and then track changes within the virus as it was targeted by the immune system.

"We discovered that hepatitis C has not one but two 'Achilles' heels' that provide opportunities for vaccine development," said Dr Fabio Luciani, from UNSW's Inflammation and Infection Research Centre and the research team's biostatistician.

"If we can help the immune system to attack the virus at these weak points early on, then we could eliminate the infection in the body completely," he said.

A paper describing the breakthrough appears in the leading scientific journal in the field of virology, *PLoS Pathogens*.

Hepatitis C virus infection is a global pandemic with more than 120 million people infected worldwide, including some 200,000 Australians. The virus causes progressive liver disease leading to cirrhosis, liver failure and cancer. Current antiviral treatments are arduous, costly, and only partially effective.

Team member and virologist Dr Rowena Bull said the discovery of the weakest links meant vaccine researchers could now focus their attentions on the most likely avenues for success.

“The first weak point was identified at transmission, when the virus has to survive the transfer from one individual to another,” Dr Bull said.

“The second weakness, and surprise finding, was the significant drop in the diversity of the viral variants in each individual studied, occurring about three months after transmission, around the time where the immune system is starting to combat the virus. A lower number of variants means the virus is easier to target.”

Study leader Professor Lloyd said the discoveries were significant because of their potential to overcome longstanding barriers to hepatitis C vaccine development.

“To date hepatitis C has been difficult to target with single interventions because there are many different strains of the virus,” he said. “In addition, like HIV, the hepatitis C virus mutates very rapidly and exists as a complex family of mutated viruses within every infected individual, meaning the virus can avoid efforts by the immune system to keep it under control,” Professor Lloyd said.

“What’s more, a third of infected people can have an effective immune response that eliminates the virus early on. This means key initial immune responses were difficult to identify and study because early

infection and elimination can go unrecognised."

Professor Lloyd said work is now underway to identify the key immunological features of the founder viruses in order to guide new vaccines.

"Further research will test the extent of the immune response against these founder viruses in a cohort of very early infected individuals," he said.

More information: Bull RA, Luciani F, McElroy K, Gaudieri S, Pham ST, et al. (2011) Sequential Bottlenecks Drive Viral Evolution in Early Acute Hepatitis C Virus Infection. *PLoS Pathog* 7(9): e1002243. doi:10.1371/journal.ppat.1002243