Canine hepatitis C virus discovery opens up new doors for research

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In a study to be published online this week in the *Proceedings of the National Academy of Sciences*, researchers report the discovery of a novel hepatitis C-like virus in dogs. The identification and characterization of this virus gives scientists new insights into how hepatitis C in humans may have evolved and provides scientists renewed hope to develop a model system to study how it causes disease.

The research was conducted at the Center for Infection and Immunity (CII) at Columbia University's Mailman School of Public Health, the University of Edinburgh, the Center for the Study of Hepatitis C and Pfizer Veterinary Medicine.

Human hepatitis C virus (HCV) affects approximately 200 million people worldwide. According to the Centers for Disease Control and Prevention (CDC), 3.2 million people in the United States are chronically infected. The majority of these patients do not know they are carrying the virus, thus serving as a source of infection for others. HCV, which can cause liver disease and liver cancer, is most often transmitted following large or repeated exposure to infected blood. Persons who use injection drugs; are HIV-positive; or are children of infected mothers have the highest risk of infection.

The discovery of canine hepatitis C virus (CHV) marks the first known instance of hepatitis-like infection in non-human primates and suggests that the virus may have been introduced into human populations through contact with dogs or some other related species more than 500 years ago,

long after the domestication of dogs.

CHV belongs to a group of viruses known as hepaciviruses, which also includes GBV-B, a virus that causes hepatitis in tamarins, small monkeys from Central and South America. Among these viruses, HCV is most closely related to its canine counterpart, a finding that surprised first author Dr. Amit Kapoor, an investigator in the Center for Infection and Immunity and Assistant Professor of Pathology..

"Considering the origin of HIV," Dr. Kapoor explains, "we expected to find the closest homologs, or genetic relatives, of HCV in non-human primates. However, while we were analyzing samples from dogs involved in outbreaks of respiratory disease, we came upon a virus that was more similar to HCV than other viruses of the same family. So far, we have only detected CHV in sick animals, a few of which had died of unknown causes. Because of its close genetic similarity to HCV, we suggested the name of canine hepacivirus."

According to Dr. Charles Rice, Scientific and Executive Director of the Center for the Study of Hepatitis C at The Rockefeller University and one of the collaborators involved in the study, "the origins of HCV remain a mystery. These findings underscore the need to look beyond primates for clues to the origins of HCV."

Viral zoonoses, infections that are transmitted from animals to humans, account for about 70% of human emerging infectious diseases. Although transmission between species is uncommon, sustained contact over time can increase the likelihood that a virus adapted to infect humans will evolve. Since their domestication about 10,000 years ago, dogs have been close human companions. Whether humans and dogs were independently infected with an ancestral virus by another species or whether dogs infected humans (or vice versa) cannot be determined from this study. There is NO current risk that dogs can infect humans

with either HCV or CHV.

Using a sequencing platform provided by Roche 454 Life Sciences and state-of-the-art-molecular techniques, Dr. Kapoor, together with scientists at the University of Edinburg, The Rockefeller University and Pfizer, determined that like HCV, CHV's genome contained RNA secondary structures called GORS that allow viruses to chronically infect their natural hosts. Moreover, the sequence of genes that encode proteins involved in virus infection and replication were very similar between HCV and CHV.

Until recently, studies into how hepatitis C causes disease in humans have been limited by the lack of animal and cell culture models. According to CII Director Dr. Ian Lipkin, "The identification and characterization of CHV signals the advent of a new tractable animal model for hepatitis C. This discovery provides new tools for understanding how this virus causes disease, and will facilitate drug and vaccine research and development."

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