Combination of direct antivirals may be key to curing hepatitis C

May 5 2010

A combination of antiviral drugs may be needed to combat the drug resistance that rapidly develops in potentially deadly hepatitis C infections, a new study using sophisticated computer and mathematical modeling has shown.

Using probabilistic and viral dynamic models, researchers at the University of Illinois at Chicago, Oakland University and Los Alamos National Laboratory predict why rapid resistance emerges in hepatitis C virus and show that a combination of drugs that can fight three or more mutated strains may be needed to eradicate the virus from the body. They compared their model with data from a clinical trial of the new direct-acting antiviral medication telaprevir.

The findings are published in *Science Translational Medicine*.

Hepatitis C is a progressive liver disease that can lead to cirrhosis and liver cancer. Current standard treatment is a combination of the antiviral drugs interferon and ribavirin for a period of 24 to 48 weeks -- a regimen that is long and expensive, carries side effects, and is successful only in about half of patients.

Intensive effort has focused on developing direct antiviral drugs. But the virus is genetically diverse, and so may be particularly prone to develop resistance, said Harel Dahari, research assistant professor of hepatology in the UIC College of Medicine and one of the paper's co-authors.

One way to combat resistance would be to administer multiple drugs, each with a different mechanism of inhibiting the virus.

"We found that rapid emergence of resistance to these types of drugs is due to a population of viruses already present, allowing the resistant virus to become the dominant strain," said Dahari.

The researchers suggest that a combination of new antiviral drugs will be needed to fight all of the resistant virus strains and achieve better cure rates for the disease.

"We are moving to a new era where we can treat these patients with direct-acting agents against the virus, in which we specifically target the life-cycle of the virus," Dahari said.

To replace the standard treatment, four or more different types of direct drugs may be needed, Dahari said. However, some patients may need fewer drugs. It depends on the level of the virus in their blood, among other factors.

It is frustrating for patients to go through a long, difficult treatment and know that they might not be cured, said Dr. Scott Cotler, associate professor of medicine at UIC and a hepatologist who treats patients at the University of Illinois Medical Center's Walter Payton Liver Center.

"Patients are looking forward to a day when they don't have to take interferon and ribavirin," said Cotler. "But as we are learning with this study, if we are going to need four different direct drugs, it is going to be awhile before we get there. Now at least we know where the goal line is."

Dahari suggests that future treatment that includes the standard treatment and direct antivirals, such as telaprevir or boceprevir, will be

tailored to each patient and that using direct antivirals may also shorten the duration of treatment.

Provided by University of Illinois at Chicago