Natural compound blocks hepatitis C infection

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Researchers have identified two cellular proteins that are important factors in hepatitis C virus infection, a finding that may result in the approval of new and less toxic treatments for the disease, which can lead to liver cancer and cirrhosis.

An estimated 270 to 300 million people worldwide are infected with hepatitis C and the conventional treatments - interferon and ribavirin - can have significant side effects. A new drug targeting cellular proteins rather than viral proteins would be a valuable addition to the treatment arsenal, said Samuel French, an assistant professor of pathology and senior author of the study.

French and his team set out to identify the cellular factors involved in hepatitis C replication and, using mass spectrometry, found that heat shock proteins (HSPs) 40 and 70 were important for viral infection. HSP 70 was previously known to be involved, but HSP 40 was linked for the first time to hepatitis C infection, French said. They further showed that the natural compound Quercetin, which inhibits the synthesis of these proteins, significantly inhibits viral infection in tissue culture.

"This is an important finding because we can block these proteins with the idea of
reducing the level of the virus in people and, ideally, completely eliminate it," said French, who also is a researcher at UCLA's Jonsson Comprehensive Cancer Center.

The study appeared in the most recent issue of the journal *Hepatology*.

Since Quercetin has been shown to inhibit hepatitis C infection, French said, a Phase I clinical trial will be launched at UCLA to determine if the compound is safe and effective.

Quercetin is a plant-derived bioflavonoid, and is used by some people as a nutritional supplement. Laboratory studies show it may have anti-inflammatory and antioxidant properties, and it is being investigated for a wide range of potential health benefits. Currently, there are early-stage clinical trials testing quercetin for safety and efficacy against sarcoidosis, asthma and glucose absorption in obesity and diabetes.

"Because Quercetin targets cellular proteins rather than viral proteins, there is less likelihood of developing viral resistance," French said. "Cellular proteins cannot change like viral proteins can."

Many patients in the United States have a type of hepatitis C virus that does not respond to the standard treatments. In these cases, if the virus can't be blocked, end-stage liver disease and, ultimately, death may occur. Once HSP 40 and 70 were identified, French and his team used Quercetin in an attempt to block the proteins and found that the compound "reduced infectious particle production at non-toxic concentrations," according to the study.

"Quercetin may allow for the dissection of the viral life cycle and has potential therapeutic use to reduce virus production with low associated toxicity," the study states.

The UCLA clinical trial will most likely target those with type 1 hepatitis C, which is the non-responsive type prevalent in this country. Only about 50 percent of those with type 1 hepatitis C respond to treatment, French said.

Volunteers with type 1 hepatitis C who opt not to undergo conventional therapies would be recruited for the study. In other studies in other diseases, Quercetin has resulted in no significant side effects, French said.

"A non-toxic treatment for chronic hepatitis C would be great because our current therapies have significant side effects and only a certain percentage of the patient population responds," French said.

Provided by University of California - Los Angeles