

Grapefruit compound may help combat hepatitis C infection

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A compound that naturally occurs in grapefruit and other citrus fruits may be able to block the secretion of hepatitis C virus (HCV) from infected cells, a process required to maintain chronic infection. A team of researchers from the Massachusetts General Hospital Center for Engineering in Medicine (MGH-CEM) report that HCV is bound to very low-density lipoprotein (vLDL, a so-called “bad” cholesterol) when it is secreted from liver cells and that the viral secretion required to pass infection to other cells may be blocked by the common flavonoid naringenin.

If the results of this study extend to human patients, a combination of naringenin and antiviral medication might allow patient to clear the virus from their livers. The report will appear in an upcoming issue of the journal *Hepatology*.

“By finding that HCV is secreted from infected cells by latching onto vLDL, we have identified a key pathway in the viral lifecycle,” says Yaakov Nahmias, PhD, of the MGH-CEM, the paper’s lead author. “These results suggest that lipid-lowering drugs, as well as supplements, such as naringenin, may be combined with traditional antiviral therapies to reduce or even eliminate HCV from infected patients”

HCV is the leading cause of chronic viral liver disease in the United States and infects about 3 percent of the world population. Current antiviral medications are effective in only half of infected patients, 70 percent of whom develop chronic infection that can lead to cirrhosis or

liver cancer. Since the virus does not integrate its genetic material into the DNA of infected cells the way HIV does, totally clearing the virus could be possible if new cells were not being infected by secreted virus.

“Identifying the route by which HCV is released from cells introduces a new therapeutic target,” says Martin Yarmush, MD, PhD, director of the MGH-CEM and the paper’s senior author. “That pathway’s dependence on cholesterol metabolism could allow us to interfere with viral propagation to other cells and tissues, using tools already developed for atherosclerosis treatment.” Yarmush is the Helen Andrus Benedict Professor of Surgery and Bioengineering at Harvard Medical School (HMS).

Grapefruit’s bitter taste is caused the presence of the flavonoid naringin, which is metabolized into naringenin, an antioxidant previously reported to help lower cholesterol levels. Considerable research has suggested that HCV infects liver cells by, in essence, “hitching a ride” onto the natural lipoprotein-cholesterol metabolic pathway. Since earlier evidence has shown that naringenin can reduce secretion of vLDL from liver cells, the researchers examined whether the compound might also lower HCV secretion from infected cells. Their experiments confirmed that naringenin does reduce the secretion of HCV from infected cell lines and showed that the compound inhibits the mechanism for secreting a specific lipoprotein that binds HCV.

“This work presents the possibility that non-toxic levels of a dietary supplement, such as naringenin, could effectively block HCV secretion,” says Raymond Chung, MD, MGH director of Hepatology and one of the study authors, “This approach might eventually be used to treat patients who do not respond to or cannot take traditional interferon-based treatment or be used in combination with other agents to boost success rates.”

Source: Massachusetts General Hospital

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