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HEPATITIS

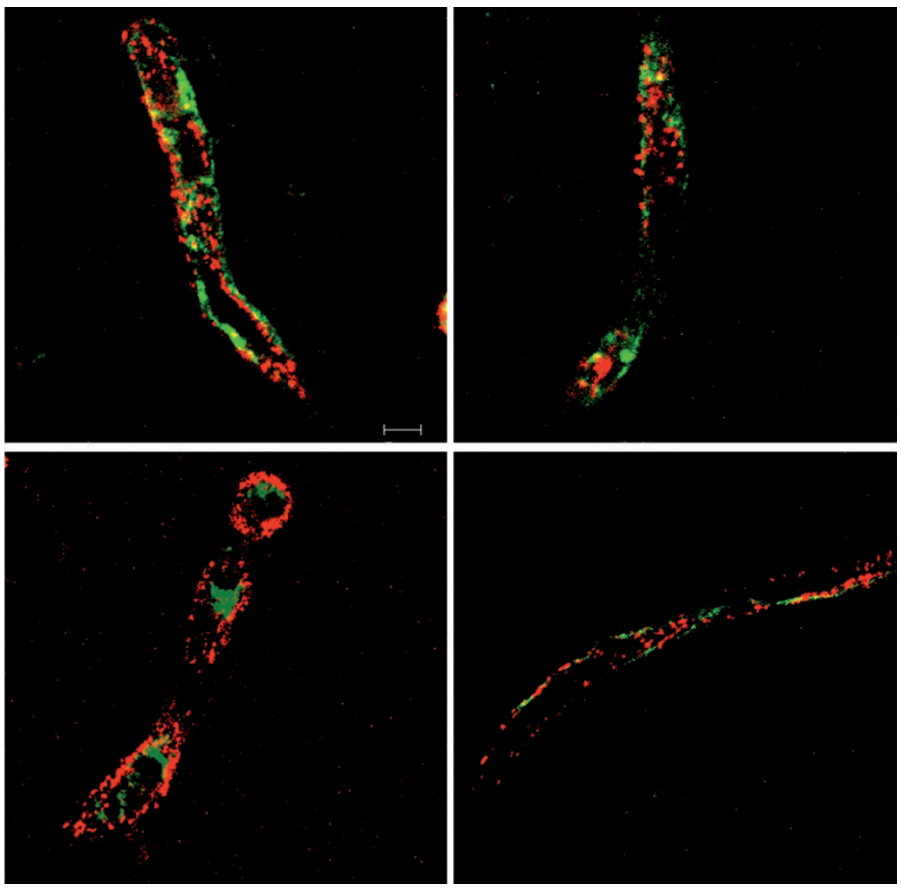
Brain endothelial cells support HCV entry and replication

Nicola Fletcher, Jane McKeating and colleagues have demonstrated that human brain endothelial cells express all the main receptors required for HCV entry. "This is the first report that cells of the central nervous system (CNS) support HCV entry and replication *in vitro*," says McKeating.

Chronic HCV infection causes progressive liver disease and can also be associated with various CNS abnormalities. To date, however, few studies have investigated the mechanisms by which these abnormalities arise, that is, whether they are a result of impaired hepatic function or virus replication in the CNS. Thus, the researchers quantified HCV RNA levels in the brain and liver of 10 individuals infected with HCV. They also investigated the expression of HCV entry receptors in the brain, and conducted *in vitro* studies to ascertain whether two brain-derived endothelial cell lines could support HCV infection.

HCV RNA was detected in multiple brain samples from four of the patients (although at much lower levels than in the liver samples), and microvascular endothelia expressed all of the essential HCV entry receptors. The two cell lines supported HCV entry and replication; infection was inhibited by receptor-specific antibodies, interferon and antiviral agents. Furthermore, infection caused endothelial cell apoptosis, potentially providing a mechanism for the mild neurocognitive impairment observed in patients with chronic hepatitis C.

"We have now demonstrated that HCV can infect brain endothelial cells, providing the first model to study HCV neuropathology," concludes McKeating. The researchers also suspect that brain endothelial cells might provide a viral reservoir during antiviral treatment.



HCV receptor expression in human brain tissue. Courtesy of J. McKeating.

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Original article Fletcher, N. F. *et al.* Hepatitis C virus infects the endothelial cells of the blood–brain barrier. *Gastroenterology* doi:10.1053/j.gastro.2011.11.028