**Trends in Microbiology** | Microbe of the Month

Special Issue: Antimicrobial Resistance and Novel Therapeutics

# Hepatitis C Virus

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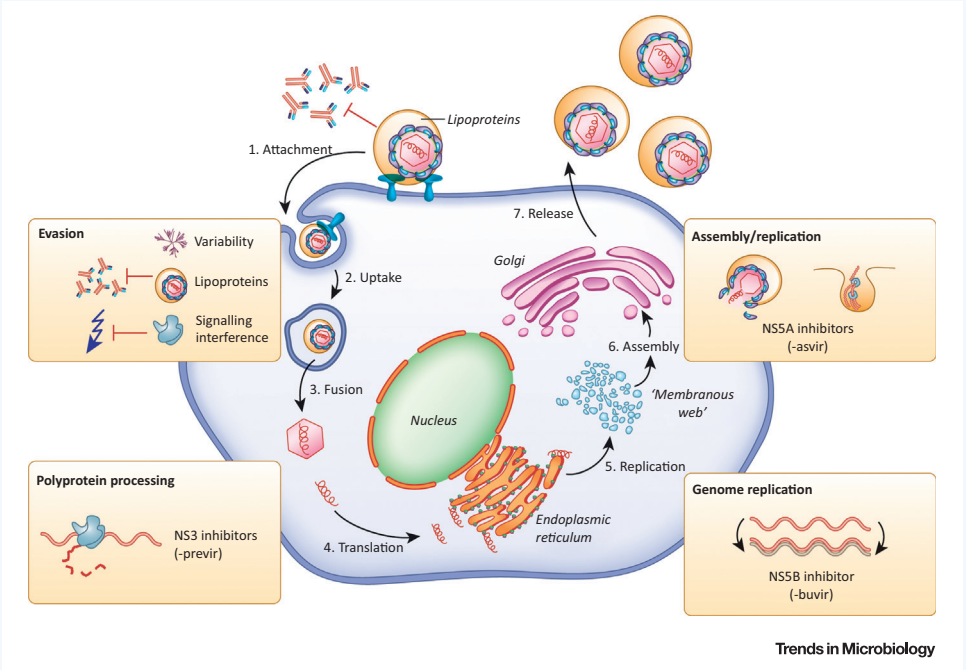
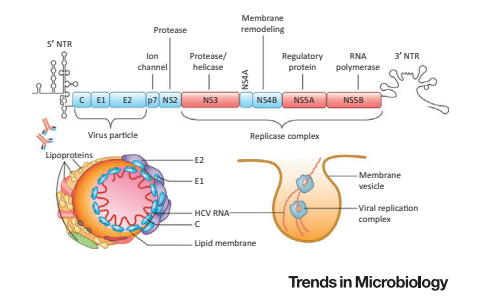



Hepatitis C virus (HCV) is an enveloped, RNA virus transmitted through blood-to-blood contact. It infects humans only and primarily targets liver cells. HCV evades innate and adaptive immunity and establishes chronic infections in 70% of cases. If untreated, 20% of patients develop liver cirrhosis, and a fraction of these progress to hepatocellular carcinoma. Annually, 400 000 patients die globally due to HCV infection. Direct-acting antivirals (DAAs) are licensed and target three viral proteins: the NS3-4A protease needed for processing the viral polyprotein, the NS5A phosphoprotein that regulates RNA replication and virus assembly, and the viral RNA-dependent RNA polymerase (NS5B) that catalyzes genome replication. Combination therapies cure more than 95% of treated patients. Approximately 71 million people are chronically infected and 1.7 million new infections occur annually. Treatment-induced cure does not protect from viral reinfection. A prophylactic vaccine is under development.




**TAXONOMY AND CLASSIFICATION:**
**GENOME:** Single-stranded positive-sense RNA
**FAMILY:** Flaviviridae
**GENUS:** *Hepacivirus*
**GENOTYPES:** Seven

**KEY FACTS:**
The HCV genome is 9.6 kb and encodes a single polyprotein, which is cleaved by cellular and viral enzymes into ten mature proteins.

The three structural proteins comprise the viral particle while the nonstructural proteins are involved in viral replication.

Viral strains differ by up to 30% at the nucleotide level and are classified into seven genotypes.

The viral NS3-4A protease targets innate immune signaling molecules, facilitating immune evasion.

Incorporation of host lipoproteins into virions contributes to antibody escape and facilitates binding to liver cells.

HCV evolves as a quasispecies within infected patients.

**DISEASE FACTS:**
HCV is parenterally transmitted. Unsafe use of needles and high-risk sexual behavior are risk factors for transmission. Screening of blood products has reduced transmission rates.

Chronic infection causes fibrosis, cirrhosis, and hepatocellular carcinoma. Two thirds of patients develop extrahepatic manifestations like cryoglobulinemia vasculitis.

Virus replication dysregulates metabolic processes, facilitating liver steatosis and inflammation.

Combination DAA therapies achieve cure rates greater than 95%.

In patients failing therapy, viruses develop drug resistance. However, salvage therapies with modified drug combinations currently cure most patients upon retreatment.

Viral reinfection is possible and occurs frequently in populations at high risk of HCV exposure.

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