COMMENTARY

Antiviral targets for hepatitis C and molecular virology

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ABSTRACT

Approximately 170 million people worldwide have the Hepatitis C Virus (HCV). Antiviral therapy with pegylated interferon alfa and ribavirin as a combination is the foundation for preventing HCV infection sequelae. To identify infection, direct treatment choices, and gauge the virological response to antiviral therapy, the use of serological and virological assays has grown to be crucial in the management of HCV infection. For the diagnosis of acute and chronic hepatitis C, anti-HCV antibody and HCV RNA tests are employed. Since the HCV genotype affects the indication, the course of treatment, the dosage of ribavirin, and the method of virological surveillance, it is important to systematically determine the genotype before starting treatment. Hepatocellular carcinoma and liver cirrhosis are primarily brought on by chronic hepatitis C globally. Although there are few treatment options available right now, research into the molecular virology of hepatitis C has helped identify new antiviral targets. In addition, model systems for testing new therapeutic approaches in vivo and in vitro have been developed. HCV RNA monitoring during therapy is used to adjust the length of treatment for HCV genotype 1 infections, and molecular assays are used to evaluate the end of treatment and, most significantly, the sustained virological response, or the therapy's endpoint. Both acute and persistent infections are brought on by the Hepatitis C Virus (HCV). The majority of acute HCV infections do not develop into life-threatening conditions and are typically asymptomatic. Within 6 months of infection without receiving any therapy, 30% (15%–45%) of infected individuals naturally eliminate the virus.

Key Words: *Hepatitis C; Molecular virology*

INTRODUCTION

A chronic HCV infection will affect the remaining 70% (55%–85%) of people. Within 20 years, cirrhosis can develop in 15% to 30% of people with chronic HCV infection. A blood-borne virus, the hepatitis C virus. The most frequent methods of transmission are sharing of injection equipment, sharing of unscreened blood and blood products, and the reusing or improper sterilizing of medical equipment, particularly syringes and needles in healthcare settings. HCV can be transmitted by sexual activities that expose people to blood, such as having many partners or having intercourse with men, as well as from an infected mother to her unborn child; however, these mechanisms of transmission are less prevalent. Breast milk, food, water, or casual physical contact with an infected individual (such as a hug, kiss, or sharing of food or drinks) do not spread hepatitis C.

Hepatitis C can take between two weeks and six months to develop. About 80% of persons after an initial infection show no symptoms. Fever, lethargy, loss of appetite, nausea, vomiting, abdominal discomfort, dark urine, pale feces, joint pain, and jaundice are some of the acute symptoms that can be seen in affected individuals (yellowing of the skin and the whites of the eyes).

Few persons are diagnosed when the infection is new because new HCV infections are frequently asymptomatic. Asymptomatic for decades before symptoms appear as a result of severe liver damage, chronic HCV infection is frequently undetected in those who go on to develop it.

Two procedures are used to diagnose HCV infection:

- One way to determine whether someone has been infected with the virus is to perform a serological test for anti-HCV antibodies.
- If the anti-HCV antibody test is positive, a nucleic acid test for HCV Ribonucleic Acid (RNA) is necessary to confirm the chronic infection and the requirement for treatment. This test is crucial since 30% of HCV infection sufferers spontaneously recover from the illness without the need for medication due to a potent immune response. They will test positive for anti-HCV antibodies despite no longer being infected. You can either perform this nucleic acid for HCV RNA in a lab or a clinic with a straightforward point-of-care device.

In rare cases, the immune system can successfully fight off a new HCV infection without the need for medication. But therapy is required if HCV infection progresses to the chronic stage. Curing hepatitis C is the main objective of treatment. For all adults, teenagers, and children under the age of three who have a chronic hepatitis C infection, the World Health Organization advises therapy with pan-genotypic Direct-Acting Antivirals (DAAs). Depending on the presence or absence of cirrhosis, DAAs can cure the majority of people with HCV infection, and treatment duration is brief (often 12 weeks to 24 weeks). WHO updated its guidelines in 2022 to encourage utilizing the same pan-genotypic therapies for treating adolescents and young children as they do for treating adults.

Because there is no effective treatment or vaccination for hepatitis C, prevention relies on lowering the risk of infection in hospitals and among other high-risk groups. This includes those who inject drugs and males who have intercourse with men, especially those who have HIV or are on pre-exposure prophylaxis for HIV. WHO's primary prevention recommendations include the following: safe and appropriate use of medical injections; safe handling and disposal of sharps and waste; provision of thorough harm-reduction services to people who inject drugs; testing of donated blood for HBV and HCV (as well as HIV and syphilis); training of health personnel; and prevention of exposure to blood during sex.

The combination of interferon-alpha and ribavirin has enhanced sustained response rates, according to recent research. Even with these advancements, more potent treatments are still required. Clinical trials are now being conducted to assess several substitute medications. The viral NS3 serine protease, the RNA helicase, and the RNA-dependent RNA polymerase have all been identified as particular antiviral targets thanks to recent developments in the molecular virology of hepatitis C. In addition, several experimental systems are being used to investigate gene therapy approaches intended to block HCV gene expression and replication as well as immunotherapeutic ideas intended to strengthen the cellular immune response against HCV. These and other cutting-edge antiviral techniques might eventually supplement the current therapeutic approaches.

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