Editorial

Found in Translation

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Since the identification of the hepatitis C virus (HCV) and subsequent cloning of its genome in 1989, only relatively modest progress had been made in the treatment of its chronic infection until recently. Interferon-alfa was approved in 1991 for the treatment of HCV infection, and provided a sustained virological response (SVR) of 9% for genotype 1, and 20–30% for genotypes 2 and 3. With the addition of ribavirin in 1998, the SVR of interferon-ribavirin combination therapy increased to 29% for genotype 1, and 62% for genotypes 2 and 3. The development of long-acting pegylated (PEG)-interferons plus ribavirin in 2001–2002 increased SVR incrementally to 41% for genotype 1, and 82% for genotypes 2 and 3. After this advance, the situation remained static for almost 10 years without significant breakthroughs, until the advent of the protease inhibitors telaprevir and boceprevir in 2011. These agents represent the vanguard of a new class of HCV drugs, the direct-acting antiviral agents, and a new era in the treatment of HCV. With the triple therapy regimen of PEG-interferon, ribavirin, and either telaprevir or boceprevir, the SVR for genotype 1 HCV ranges from 70 to 80%. Now, for the first time, persons infected with genotype 1 HCV can expect a higher than 50% chance of achieving an SVR to antiviral therapy.

The development of current protease inhibitors exemplifies translational research at its best. Fundamental structural crystallographic data on HCV proteases led to an understanding of the dimensions and chemical environment of the catalytic area. Based on these details, molecules were synthesized with peptide-like backbones containing several non-natural side chains arranged to optimally interact with catalytic domains of the HCV protease. Binding assays permitted screening of molecules capable of tight interactions with the protease. This, coupled with advances in the development of cell culture systems, allowed identification of agents that effectively inhibited HCV replication. Use of model human serine proteases permitted large-scale screening, and exclusion of molecules with the potential for causing side effects through the unintended interactions with host serine proteases. Development of these agents represents the translation of research on molecules at the bench to highly effective drugs at the bedside, and US FDA approval has made these new powerful agents available to the public as the first true ''designer'' drugs for the treatment of hepatitis C.

Perhaps even more exciting than these advances in the understanding of the virus, and development of hepatitis therapeutics is evidence that research activity is continuing at a feverish pace, in both academic and commercial laboratories, with large financial commitments. Breakthroughs are continuing to be made on many fronts contributing to anti-HCV drug development. Having achieved this first quantum leap forward, the main goal of future research will be to develop new agents that will have fewer side effects, especially those attributed to interferon-like immune modulators, and broader specificity in terms of HCV genotypes, decreased drug-drug interactions, and especially decreased likelihood of the development of drug resistance.

The objective of the *Journal of Clinical and Translational Hepatology* is to identify and publish articles that represent similar translations of fundamental research to contributions of direct practical value. Therefore, we believe that it is entirely fitting that we devote the theme of the inaugural issue of the *Journal of Clinical and Translational Hepatology* to drug development in hepatology.

In the coming months, we intend to apply the same approach to the selection of articles of translational importance to other areas of hepatology. In particular, the increased understanding of the mechanisms of development of autoimmune liver and biliary diseases, and powerful agents for their treatment will be addressed. Infectious and inflammatory, as well as nutritional and neoplastic conditions of the liver will be areas of thematic emphasis for future issues.

These are exciting times for clinicians and investigators who are interested in the liver and its diseases. We are thrilled to share the excitement by bringing to your attention the latest advances in translational research in hepatology through the pages of this new journal!

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Conflict of interest

None

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