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Extremely potent, pan-genotypic Hepatitis C virus NS5A inhibitors based on novel core structures

Hepatitis C virus (HCV) infection often leads to serious liver diseases such as cirrhosis followed eventually by hepatocellular carcinoma. Several HCV RNA gene products (NS2, NS3, NS4A, NS4B, NS5A and NS5B) involved in the reproduction of HCV have been instensively studied for new therapeutic target identification. Recently, combinations of direct acting antivirals (DAA) including HCV NS3/4A protease inhibitors such as boceprevir, telaprevir, paritaprevir, and grazoprevir, polymerase inhibitors such as sofosbuvir and dasabuvir, and NS5A inhibitors such as daclatasvir, ledipasvir, ombitasvir, elbasvir and velpatasvir have shown successful arrest of the infection. However, even with the new DAA's, resistance to the drugs in patients infected with various strains of HCV has emerged. Therefore development of effective anti-HCV drug candidates possessing pan-genotype activities is still needed. Herein we report the discovery of a series of extremely potent HCV NS5A inhibitors based on a few new core skeletons. From these efforts, we have identified a series of NS5A inhibitors that exhibit highly potent anti-HCV activities particularly against several genetic variants and some mutant strains. Several interesting compounds were further evaluated with other studies and are shown to be nontoxic and anticipated to be effective HCV drug candidates.

Biography

B Moon Kim has completed his PhD and postdoctoral studies at M.I.T. After 5 year experience at Merck Research Laboratories in USA, he took a faculty position at the Chemistry Department of Seoul Naitonal University Korea. He was Chemistry Department Chair and Director of the BK21 Chemistry & Molecular Engineering Division at SNU. He has published more than 120 papers and 25 patents and has been serving as an editorial board member of Bioorganic Medicinal Chemistry and Bioorgnaic & Medicinal Chemistry Letters and an editor-in-chief of Bulletin of the Korean Chemical Society.

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