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Ciclopirox Inhibits Hepatitis B Virus Secretion by Blocking Capsid Assembly

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Chronic hepatitis B virus (HBV) infection can cause cirrhosis and hepatocellular carcinoma and is therefore a serious public health problem. Infected patients are currently treated with nucleoside/nucleotide analogs and interferon α, but this approach is not curative. Here, we screen 978 FDA-approved compounds for their ability to inhibit HBV replication in HBV-expressing HepG2.2.15 cells. We find that ciclopirox, a synthetic antifungal agent, strongly inhibits HBV replication in cells and in mice by blocking HBV capsid assembly. The crystal structure of the HBV core protein and ciclopirox complex reveals a unique binding mode at dimer-dimer interfaces. Ciclopirox synergizes with nucleoside/nucleotide analogs to prevent HBV replication in cells and in a humanized liver mouse model. Therefore, orally-administered ciclopirox may provide a novel opportunity to combat chronic HBV infection by blocking HBV capsid assembly.

Biography:

Dr. Yoon-Jun Kim MD, PhD has been Professor of Internal Medicine at Seoul National University College of Medicine since 2013. While doing so, he remains active in the medical community through taking on leading roles in various professional societies such as Chair of the Academic Committee of The Korean Radio-Embolization Association, a position he has held since 2013, and from 2013 to 2014, he functioned as Chair of Academic Committee of The Korean Liver Cancer Study Group. Also, he served as secretary general of The Korean Liver Cancer Study Group from 2014 to 2015. Concurrently, he has been Editor-in-Chief of Clinical and Molecular Hepatology, a medical journal that publishes clinical and basic research on liver diseases, since 2015. His educational background began in the same college that he is now professor at, where he graduated from Seoul National University College of Medicine in 1992 and later went on to attain his Ph.D. there in 2001. Since graduating, his research interests in his particular field have included clinical studies of HBV infection and HCC, host genomics in HBV-related liver disease, clinical studies of NASH, cancer genomics of HCC, and basic studies of HCC pathogenesis.