World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:18, No:12, 2024

Human Par14 and Par17 Isomerases Bind Hepatitis B Virus Components Inside and Out

Authors : Umar Saeed

Abstract : Peptidyl-prolyl cis/trans isomerases Par14 and Par17 in humans play crucial roles in diverse cellular processes, including protein folding, chromatin remodeling, DNA binding, ribosome biogenesis, and cell cycle progression. However, the effects of Par14 and Par17 on viral replication have been explored to a limited extent. We first time discovered their influential roles in promoting Hepatitis B Virus replication. In this study, we observed that in the presence of HBx, either Par14 or Par17 could upregulate HBV replication. However, in the absence of HBx, neither Par14 nor Par17 had any effect on replication. Their mechanism of action involves binding to specific motifs within HBc and HBx proteins. Notably, they target the conserved 133Arg-Pro134 (RP) motif of HBc and the 19RP20-28RP29 motifs of HBx. This interaction is fundamental for the stability of HBx, core particles, and HBc. Par14 and Par17 exhibit versatility by binding both outside and inside core particles, thereby facilitating core particle assembly through their participation in HBc dimer-dimer interactions. NAGE and immunoblotting analyses unveiled the binding of Par14/Par17 to core particles. Co-immunoprecipitation experiments further demonstrated the interaction of Par14/Par17 with core particle assembly-defective and dimer-positive HBc-Y132A. It's essential to emphasize that R133 is the key residue in the HBc RP motif that governs their interaction with Par14/Par17. Chromatin immunoprecipitation conducted on HBV-infected cells elucidated the participation of residues S19 and E46/D74 in Par14 and S44 and E71/D99 in Par17 in the recruitment of 133RP134 motif-containing HBc into cccDNA. Depleting PIN4 in liver cell lines results in a significant reduction in cccDNA levels, pgRNA, sgRNAs, HBc, core particle assembly, and HBV DNA synthesis. Notably, parvulin inhibitors like juglone and PiB have proven to be effective in substantially reducing HBV replication. These inhibitors weaken the interaction between HBV core particles and Par14/Par17, underscoring the dynamic nature of this interaction. It's also worth noting that specific Par14/Par17 inhibitors hold promise as potential therapeutic options for chronic hepatitis B.

Keywords : Par14Par17, HBx, HBc, cccDNA, HBV
Conference Title : ICVH 2024 : International Conference on Viral Hepatitis
Conference Location : Dubai, United Arab Emirates
Conference Dates : December 23-24, 2024

Open Science Index, Biomedical and Biological Engineering Vol:18, No:12, 2024 publications.waset.org/abstracts/183303.pdf