Reply to correspondence

Reply to correspondence regarding “Class II Transactivator Restricts Viral Replication, Extending its Effect to HBV”

Cho-Rong Lee and Sung-Gyoo Park*

College of Pharmacy and Research Institute of Pharmaceutical Science, Seoul National University, Seoul 08826, Republic of Korea

*Corresponding author: Sung-Gyoo Park, PhD, College of Pharmacy and Research Institute of Pharmaceutical Science, Seoul National University, Seoul 08826, Republic of Korea. E-mail address: riceo2@snu.ac.kr. https://orcid.org/0000-0003-3702-5765
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We are grateful to Mehrangiz Dezhbord and Professor Kyun-Hwan Kim for their Correspondence\(^1\) in response to our editorial entitled 'Class II Transactivator Restricts Viral Replication, Extending its Effect to HBV.'\(^2\) As they mentioned previously, Class II Transactivator (CIITA) increases the expression of MHC class II molecules, which are mainly expressed in antigen-presenting cells (APCs) and also in hepatocytes under certain conditions. In addition to CIITA's role in APCs, the recent study on its non-canonical function in relation to HBV inhibition in hepatocytes presents highly intriguing finding.\(^3\)

In our editorial, we highlighted instances where CIITA is involved in immune evasion mechanisms or contributes to antiviral mechanisms against various viruses.\(^2\) As the authors pointed out, CIITA is involved in the inhibition of HBV replication and, conversely, acts as a target for the suppression of antiviral activity by HBx. CIITA's ambivalence regarding HBV appears highly valuable for developing potential therapeutic strategies to combat HBV infection. We also agree with their opinion that follow-up research is needed on the exact mechanism by which HBx inhibits CIITA activity, as this remains elusive.

Dezhbord et al. demonstrated that the interaction between HBx and CIITA increases the protein stability of CIITA but leads to functional impairment. The mechanism by which HBx interferes with the antiviral activity of CIITA is still unknown. Research on the domains of CIITA may provide additional insights into the mechanisms of its translocation and post-translational modifications.\(^3\) CIITA consists of several functional domains typically associated with transcription factors or coactivators, including an activation domain, an acetyltransferase domain, a proline/serine/threonine domain, a GTP-binding domain (GBD), and a leucine-rich repeat region domain. CIITA activity is modulated by its cellular localization, with the GBD regulating its shuttling between the nucleus and cytoplasm.\(^4\) A defect in the nuclear translocation of CIITA can lead to immunodeficiency diseases such as bare lymphocyte syndrome. The ability of CIITA to effectively enter and exit the nucleus is crucial for regulating its capacity to transactivate target MHC class II genes.\(^5\) Its activity is known to be modulated by several
post-translational modifications, including phosphorylation, ubiquitination, acetylation, and deacetylation. Therefore, through further research on these issues, we hope to accumulate knowledge about the detailed mechanism and role of CIITA in chronic hepatitis B and apply it to treatment.

**Author contributions**

CR Lee drafted the manuscript. SG Park edited and finalized the manuscript.

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**Conflicts of interest**

The authors have no conflicts of interest to declare.
References


2. Lee CR, Park SG. Class II Transactivator Restricts Viral Replication, Extending its Effect to HBV. Clin Mol Hepatol 2024.


