Reviewer's report

**Title:** Molecular analysis of hepatitis B virus (HBV) in an HIV co-infected patient with reactivation of occult HBV infection following discontinuation of lamivudine-including antiretroviral therapy.

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**Reviewer:** Stephen Kwok-Wing Tsui

**Reviewer's report:**

Costantini et al. has reported a case with HIV and HBV co-infection. HBV evolution was observed at a 9-year interval and resumption of ART allowed control of plasma HBV DNA levels.

1. A lot of single amino acid substitution have been recently reported in HBV occult infection, e.g. Utsumi et al. (Utsumi T, Yano Y, Truong BX, Kawabata M, Hayashi Y. Characteristics of occult hepatitis B virus infection in the Solomon Islands. Int J Mol Med. 2011 Jun;27(6):829-34.) or Yuan et al. (Yuan Q, Ou SH, Chen CR, Ge SX, Pei B, Chen QR, Yan Q, Lin YC, Ni HY, Huang CH, Yeo AE, Shih JW, Zhang J, Xia NS. Molecular characteristics of occult hepatitis B virus from blood donors in southeast China. J Clin Microbiol. 2010 Feb;48(2):357-62). So, the novelty of the mutations reported in this article is very limited.

2. When the mutations in the HBV genomes in 2001 and 2010 were compared. The variant V224AV in 2001 genome was disappeared in 2010 genome. Assuming that back mutations are rare, it is possible that there were quasi species in 2001. During the course of treatment, the species with D144E became more dominant and the species with V224A decreased in proportion. The existent of quasi species was supported by the V224AV in the 2001 genome. This possibility cannot be completely ruled out using the PCR and direct sequencing. Cloning or other methods for quasi species differentiation should be used in order to claim the genome evolution.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.