



ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8385

Title: Immunopathogenesis of chronic hepatitis B

Reviewer code: 02521807

Science editor: Gou, Su-Xin

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Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, RECOMMENDATION, CONCLUSION. It lists various grades (A-E) and corresponding actions like 'Accept', 'High priority for publication', 'Rejection', 'Minor revision', and 'Major revision'.

COMMENTS TO AUTHORS

This is a thorough and valuable review of the HBV pathogenesis. This reviewer only suggest to include some topics: (i) The role of intrahepatic antibodies to HBc in the pathogenesis of acute liver failure (Farci et al., PNAS 2010); (ii) Consider to include the study performed by Lang et al (PNAS 2012; 109:1210-5) who described an additional NK cell role in HBV-induced immunopathogenesis. (iii) Typing error should be amended. On page 13 line 3 (actively) and line 6 (double negative NKT). (iv) Two abbreviations (FoxP3 and PD-1) appear extensively explained after their first inclusion on the text. Please relocate. Likewise, the abbreviation "Stat1" needs an explanation (page 16, line 9). (v) The expression "anti-inflammatory cytokines (IFNg)" could be misinterpreted and needs a brief explanation (page 16, line 3).



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Title: Immunopathogenesis of chronic hepatitis B

Reviewer code: 02527808

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Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, RECOMMENDATION, CONCLUSION. It lists various grades from A to E and corresponding actions like 'Accept', 'High priority for publication', 'Rejection', 'Minor revision', and 'Major revision'.

COMMENTS TO AUTHORS

The review is well written comprehensive but missing some clinical aspects& recent data: -The recent discovery that alpha-taxilin plays an essential role for release of HBV-DNA containing particles. Needs to be discussed. (Hoffmann et al - Journal of Hepatology , Pages 934-941, November 2013) - Acute-on-chronic liver failure (ACLF) is a relatively common complication in CHB patients following certain precipitating events. Previous reports have indicated that certain immune cells such as myeloid DCs (mDCs), plasmacytoid DCs (pDCs) and T cell subsets, are enriched into the livers of ACLF patients; (this must be clarified) 33 Zhang et al J. Hepatol. 2008; 49: 396-406. -The issue of using immune markers as indices to guide clinicians in formulating prognosis and treatment decisions ex: * when CHB patients receive entecavir therapy, the restored cytokine production of NK cells participates in viral clearance. Tjwaet al . J. Hepatol. 2011; 54: 209-18. *During IFN-a treatment, the dampened Z39Ig (a novelinhibitor of the B7 superfamily) signals from macrophages are also found to be associated with IFN-a responsiveness in CHB Patients Guo et al Clin. Immunol. 2010; 136: 282-91.) *Restoration of peripheral mDCs was observed during the course of adefovir treatment and may represent a prognostic marker for favorable responses. Similarly, the recovery of functional pDCs during IFN-a therapy may also have the same predictive value. * A recent study further reported that lamivudine therapy is able to reduce HBV DNA to an undetectable level, but the patients may only exhibit a transient restoration of circulating DC (Zhang et al ,Journal of Gastroenterology and Hepatology 27 (2012) 223-230). - The role of immune molecules such as micro RNAs & The proposed immunotherapeutic strategies for HBV disease include blockade of PD-1/PD-L1 interaction, an anti-apoptotic drug9 and a monoclonal antibody that specifically



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Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road, Wan Chai, Hong Kong, China

recognizes peptide/MHC class I complex (HBc18-27: HLA-A2) on the HBV-infected cell surface or adoptive TCR-redirected T cells need to be more clarified & discussed. - The number of references is in need to be reduced (delete the old one).