

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4742

Title: IDENTIFICATION AND CHARACTERIZATION OF A NOVEL BIPARTITE NLS IN THE HBV POLYMERASE

Reviewer code: 00503935

Science editor: Wen, Ling-Ling

Date sent for review: 2013-07-22 19:33

Date reviewed: 2013-08-27 17:38

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

General comments: The paper (identification and characterization of a novel bipartite NLS in the HBV polymerase) done by Luperger et al. has been reviewed. In this work, they identified a novel NLS located in the terminal protein domain of HBV polymerase and defined a CKII phosphorylation site (threonine) which is adjacent to the NLS. In the early infection of HBV, this threonine residue is phosphorylated by CKII which leads to karyopherin- β 2 and HBV polymerase interacting and subsequently allowing the HBV genome and polymerase complex entering the nucleus to initiate the HBV DNA gap-filling and transcription. By using mutagenesis, they altered NLS amino acid sequences or substituted the threonine residue of putative CKII phosphorylation site into isoleucine or glutamine, they observed loss of HBV replication in the former two constructs and increase HBV replication in the last construct. This observation has never been reported and merited for publication. Nevertheless, this threonine residue is conserved in all mammalian HBV (including various subtypes of human HBV and woodchuck HBV and ground squirrel HBV) but not in avian HBV. This difference may reflect a new control has been evolved to interact with host factor, karyopherin, to facilitate HBV complex importation into the nucleus along the pathway of hepadnaviruses evolution.

Minor comments: 1. Inconsistence of hepatoma cell line nomenclature in different places, please follow the original designation shown in ref.22. 2. In consistence of using P and Pol in various places. 3. In the introduction, the statement of "100-fold increased risk of developing primary HCC" should double check many other epidemiological studies. Suggest to add a reference showing a thrombin cutting site located in the TP domain. It leads to a discussion whether whole Pol protein or only TP forms a complex with HBV genome when the complex is imported into the nucleus. 4. It is better to



Baishideng Publishing Group Co., Limited

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

provide a scheme of HBV domains above the fig. 1a and to indicate the location of novel finding sites of NLS and CKII and label the amino acid sequence number for the stretch of sequence in the original fib 1a for clarity.