

## **Response to Reviewers**

**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 24984

**Manuscript Type:** Basic Study

**Title:** Screening the Potential Role of Killer Immunoglobulin Receptors Genes among Individuals Vaccinated against Hepatitis B Virus in Lebanon

*Nada M Melhem et al.*

**Response to Reviewer 1: Code 00068637**

**Comments to authors:** The major point is that there is no significant association between the frequency of KIR genes and anti-HBs antibodies. Although it is a negative result, it could be an indicant for understanding the role of KIR loci in response to HB vaccine.

**Comment 1:** The manuscript is not well organized and its terms and expressions about HB vaccination, immune response to HB vaccine not specialized in HBV research related fields or not clear. Such as HBV vaccinated and non-vaccinated participants.

**Response:** The author went over the entire manuscript and checked the terms related to hepatitis B vaccination as well as immune responses and modified as needed as per the reviewer's suggestion. The changes are in track changes in the attached 24984-Review document.

**Comment 2:** In the results section, in the part of "Characteristics of study participants", information of participants are not specified, "diluted" important messages related to anti-HBs antibodies and vaccine. The paragraph should be reorganized as well as table

1 by deleting not related information. The non-related information could be put into the Materials and Methods.

**Response:** The author addressed the reviewer's concern by deleting the non-related information as suggested above; this is reflected by deleting the information in Table 1 on history related to injury by contaminated syringe as well as data on contact with HBV or HCV patient or carrier. Moreover, the paragraph on characteristics of study participants was reorganized and nomenclatures/terms related to vaccination status as well as immune responses were changed as shown in track change. This is done to clarify the classification of participants as suggested by the reviewer.

**Comment 3:** There are some information not related with anti-HBs antibodies responses. Such as KIR genotypes and genes frequencies including Table 2; Linkage disequilibrium analysis; Table 5

**Response:** While we concur with the reviewer that Table 2 does not have information related to the levels of anti-HBs antibodies; however, this study was performed originally to determine whether the expression of KIR genes is associated with levels of protection following vaccination against hepatitis B. As for table 7 on Linkage disequilibrium, the author agrees with the reviewer and accordingly deleted it along with its corresponding data from the materials and methods and the results section. As for Table 5, the author kept it since it addresses the relationship between the AA, AB and BB genotypes and the expressed KIR genes among study participants, even though the immune response component of this study is not included in this part. This is a natural description of the relationship since A and B genotypes are associated with the

expression of a number of KIR genes as described in the results section under KIR genotypes and genes frequencies.

**Comment 4:** In the manuscript, it is not clear about how to deciding participants vaccinated or not vaccinated in KIR genes frequencies among vaccinated and non-vaccinated participants.

**Response:** The author clarified this part regarding the classification of participants into vaccinated and non-vaccinated against hepatitis B in the results section under characteristics of study participants and in the rest of the manuscript as needed.

**Comment 5:** The impression about the manuscript was not well written. It needs authors to spend much more time to reorganize and write the manuscript.

**Response:** The author reorganized the manuscript to become clearer to the reader as per the reviewer's comment. The changes are in track changes across the manuscript.

**Comment 6:** To improve this manuscript (revision), author needs some help from someone familiar with HB vaccination and immune response to HB vaccine.

**Response:** In order to address this concern, the author revised the manuscript and the terminology related to vaccination and immune responses. Kindly not that the PI is a viral immunologist by training and adhered to the terminology used in the literature on HBV as suggested by the reviewer.

**Response to Reviewer 2: Code 03538036**

**Comments to authors:** A good manuscript on an interesting subject: Please consider the followings:

**Comment 1:** The abstract is insufficient; it needs some details and need a clear conclusion.

**Response:** The abstract was modified to address the reviewer's concern. The methods, results and conclusion were elaborated to address this comment.

**Comment 2:** The English of the manuscript needs revision. There are numerous grammatical and syntax errors in the manuscript; e.g., This study aims to explore the role of killer immunoglobulin/ the A haplotypes was detected...

**Response:** The author addressed the reviewer's concern and made the necessary corrections across the manuscript.

**Comment 3:** Abbreviations list is needed.

**Response:** While an abbreviation list is not required by the journal, the author made sure to define the acronyms when used for the first time across the manuscript as per the comment inserted within the manuscript.

**Comment 4:** The aim of the study is not clear; more details are needed about the rationale of the study.

**Response:** The aim of the study was elaborated as per the reviewer's comment in the last part of the introduction (pages 8-9). The author added the recent literature linking

immune responses following vaccination with genetic factors and linked the rationale of the study to existing evidence.

**Comment 5:** The sample size is too small to suggest generalizable results

**Response:** We concur with the reviewer regarding the sample size of our study. The limitations and its impact on the results are discussed accordingly at the end of the discussion (page 20).

**Comment 6:** The results and tables are good.

**Response:** Nothing to address here as per the reviewer's comment.

**Comment 7:** The Discussion is short and it lacks focus. The authors should concentrate on interpretation of their findings and their relevance to the field of study. The discussion should be used for the interpretation of data and for pointing out the significance of the findings.

**Response:** We modified the discussion to reflect the interpretation of the findings as per this comment (the newly added interpretation as well as the significance of the findings are underlined in the discussion).

**Comment 8:** The conclusion must be added separately

**Response:** The author added concluding remarks on page 20.