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## Letter to the Editor

# Comment on "A New Immunogenic Structure of Polyepitopic Fusion against *Leishmania major*: In Silico Study"

***Hamidreza Majidiani [1,2], Seyyed Amir Hosseini [3]**

1. *Healthy Aging Research Centre, Neyshabur University of Medical Sciences, Neyshabur, Iran*
2. *Department of Basic Medical Sciences, Faculty of Medicine, Neyshabur University of Medical Sciences, Neyshabur, Iran*
3. *Department of Internal Medicine, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran*

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*Correspondence Emails:
Hamidreza.majidiani@gmail.com,
majidianih1@nums.ac.ir

## Dear Editor-in-Chief

A recent article entitled "A new immunogenic structure of Polyepitopic fusion against *Leishmania major*: *In silico* study" (1) caught our attention and read it with interest. In our point of view, there were several huge scientific and technical gaps in the present manuscript. At the first glance, the English writing of the article is extremely weak and seriously demands major revision in terms of grammar and phrasing. Also, there was no scientific background regarding the biological functions and importance of each selected protein.

We are wondering why the bacterial B-type flagellin protein belonged to *Pseudomonas aeruginosa* (accession: P72151.2) has been selected and mentioned as *L. major* protein! If it has been chosen as an adjuvant to enhance immunogenicity, why MHC-binders have been predicted for this protein? Although most parts of the *Leishmania* genome has been well conserved throughout its species (2), but it was better to select *L. major*-specific sequences, whereas KMP11 and LPG63 accession numbers mentioned in Methods belonged to *L. infantum*. Also, as far as we know, LPG is a lipophosphoglycan protein, while the accession number for LPG3 protein is named as "putative glucose-regulated protein 94". There were no details on the type of HLA alleles, peptide lengths, prediction thresholds, epitope repeats, adjuvants, etc. in epitope prediction and vaccine design sections, which decrease the reproducibility of the research. Inverse

linker utilization was observed which compromises the function of the designed vaccine, so that CTLs were connected using GPGPG, HTLs were linked using AAY, B-cell epitopes were adjoined by EAAAK (3).

Further in Methods section, the authors sought to validate the modeled and refined 3D structure of the MEV using PROCHECK and Prosa-Web tools. Validation is only beneficial when we want to compare the 3D structure before and after refinement, that was not performed here.

In this study, the predicted epitopes were only screened in terms of antigenicity and allergenicity, while there exist lack of cytokine induction screening step (*e.g.*, IL-4, IFN-γ) for CTL and HTL binders, which decreases the value of the paper to a great extent. Not all T $CD_8^+$ cell populations are protective in leishmaniasis. The cytolytic T $CD_8^+$ cells are implicated in pathology during disease, because of perforin activity, while those lacking perforin produce IFN-γ and are implicated in protection (4). In addition, due to the dual role of T $CD_4^+$ cells in eliciting Th1 and Th2 responses, the authors should have screened the respective epitopes in terms of IFN-γ induction capacity. Moreover, humoral immune responses are not implicated in immunity against leishmaniasis and even may indicate to parasite persistence (5).

In conclusion, we believe that that, this study dealing with MEV vaccine design against *L. major* does not qualify the required minimum standards for reverse vaccinology studies.

## Conflict of interest

The authors declare none.

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