

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62999

Title: The ORF3 protein of Hepatitis E virus: Multi-function protein with endless potential

Reviewer's code: 00051373

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: China

Manuscript submission date: 2021-01-27

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-27 09:34

Reviewer performed review: 2021-01-28 15:18

Review time: 1 Day and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Thank you very much to let me have an opportunity to read this comprehensive review on the multiple pathogenic roles of HEV-ORF3. Manuscript is well written and preparation.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62999

Title: The ORF3 protein of Hepatitis E virus: Multi-function protein with endless potential

Reviewer's code: 00183463

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Croatia

Author's Country/Territory: China

Manuscript submission date: 2021-01-27

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-31 20:17

Reviewer performed review: 2021-01-31 20:36

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This paper represents an excellent overview of current knowledge about the role of different HEV proteins in transmission, pathogenesis, and immune response to infection. Review especially refers to role of HEV-ORF3 proteins. Authors indicate the directions for further research and possible role of HEV-ORF3 in vaccine development. The review represents very good quality and I have no major objections.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62999

Title: The ORF3 protein of Hepatitis E virus: Multi-function protein with endless potential

Reviewer's code: 00506601

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-01-27

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-29 20:31

Reviewer performed review: 2021-02-08 17:11

Review time: 9 Days and 20 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No



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SPECIFIC COMMENTS TO AUTHORS

World Journal of Gastroenterology Manuscript Review-Manuscript NO: 62999: The ORF3 protein of Hepatitis E virus: Multi-function protein with endless potential This is a well written overview of the genetic structure of HEV and how the three well define ORFs effect cross species tropism and potential markers for vaccine development. My only comment is on page 3 second paragraph the author talks about the high seroprevalence of HIV in the general population that may be due to undetected HEV circulation. The author references only a Dutch paper though there are many other countries including the USA. Decline in Hepatitis E Virus Antibody Prevalence in the United States From 1988–1994 to 2009–2010 Eyasu H. Teshale, Maxine M. Denniston, Jan Drobeniuc, Saleem Kamili, Chong-Gee Teo, and Scott D. Holmberg Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, Georgia The Journal of Infectious Diseases® 2015;211:366–73 A few more epidemiological papers from other countries would be helpful to this review.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62999

Title: The ORF3 protein of Hepatitis E virus: Multi-function protein with endless potential

Reviewer's code: 02528622

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Research Scientist, Senior Research Fellow

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-01-27

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-01-28 21:09

Reviewer performed review: 2021-02-14 17:49

Review time: 16 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

In this paper by Yan and Nan., the authors present a comprehensive review of our current understanding on HEV ORF3 protein. This is a well written review paper summarizing the most up-to-date information on this issue. I only have one minor comment; perhaps the authors could supplement their document with a figure summarizing what is known about the role of HEV ORF3 in the regulation of the host immune response. I also believe that sections 2, 3.1, 3.2 and 3.4 can be reduced significantly and moved to the introduction section. The afore mentioned sections, while interesting, are lengthy and deviate the attention from the main subject, the ORF3 protein.