

PEER-REVIEW REPORT

Name of journal: *World Journal of Experimental Medicine*

Manuscript NO: 75660

Title: Complement-mediated microvascular injury and thrombosis in the pathogenesis of severe COVID-19: A review

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05395205

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor, Postdoc

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-02-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-09 02:52

Reviewer performed review: 2022-02-09 05:55

Review time: 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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 Grade E: Do not publish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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

**Peer-reviewer
statements**

Peer-Review: ☒ Anonymous ☐ Onymous

Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

In this review manuscript (Manuscript NO: 75660), the authors discussed the role of complement in the development of thrombotic microangiopathy and summarized the current data on complement inhibitors as COVID-19 therapeutics. The topic is interesting. Some suggestions are listed as below: 1. Only a small proportion of patients develop aggressive disease but reliable clinical indicators to identify these patients early in disease progression are lacking. The time window for optimal intervention and the patient populations that could benefit from therapeutic complement inhibition have yet to be established. This point should be discussed. 2. There are 3 distinct pathways of complement activation, the classical complement pathway, the alternative complement pathway, and the lectin pathway. In the context of thromboinflammation, the three complement pathways are capable of activating the coagulation cascade causing thrombotic microangiopathy and end-organ damage, mostly manifesting as lung, kidney, and cutaneous disease. Which pathway can be specifically targeted for severe COVID-19? 3. How many people have been vaccinated in mentioned studies? The role of COVID-19 vaccinations in complement activation and preventing severe COVID-19 should be discussed. 4. Potential side effects of complement inhibitors should be discussed. 5. Dynamic changes of complement levels in the conditions of severe and non-severe COVID-19 should be shown. 6. Some similar reviews have already been published.

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Peer-review model: Single blind

Reviewer's code: 05229914

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chairman, Chief Doctor, Director

Reviewer's Country/Territory: Thailand

Author's Country/Territory: United States

Manuscript submission date: 2022-02-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-09 05:19

Reviewer performed review: 2022-02-11 05:17

Review time: 1 Day and 23 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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (High priority) <input 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



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

Peer-reviewer statements	Peer-Review: [] Anonymous [Y] Onymous Conflicts-of-Interest: [] Yes [Y] No
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SPECIFIC COMMENTS TO AUTHORS

Absolutely no need for me to change anything in the flow of the review. A parenthesis deleted and an acronym added. Recommend to publish.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Experimental Medicine*

Manuscript NO: 75660

Title: Complement-mediated microvascular injury and thrombosis in the pathogenesis of severe COVID-19: A review

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05395205

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor, Postdoc

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-02-09

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2022-05-12 11:45

Reviewer performed review: 2022-05-12 11:51

Review time: 1 Hour

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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have addressed my concerns.