

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Nephrology

**ESPS manuscript NO:** 23164

**Title:** C5b-9 does not mediate tubulointerstitial injury in experimental acute glomerular disease characterized by selective proteinuria

**Reviewer's code:** 00503255

**Reviewer's country:** Japan

**Science editor:** Shui Qiu

**Date sent for review:** 2015-11-03 09:08

**Date reviewed:** 2015-11-04 10:12

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

The authors experimentally studied C6 + and C6- rats with acute protein overload nephropathy (AON) to clarify whether C5b-9 mediate early tubulointerstitial injury in acute PON and concluded C5b-9 did not mediate tubulointerstitial injury in acute glomerular diseases characterized by selective proteinuria. The paper is well designed and written, but several minor errors were found. 1. page 10, line 17: "Table 2" should be changed to "Table 1" 2. page 10, line 20: "Table 3" should be changed to "Table 2" 3. page 10, line 22: "Table 4" should be changed to "Table 3" 4. Table 4, PON Day 4, C6-, Interstitial ED-1: The authors described "21.0 1.8+" here. What is "+"? No explanation was found in the table. 5. Table 4, PON Day 8, C6+, Protein cast: The authors described "1.1 0.3#" here. The authors defined that "#" represented  $P < 0.05$  when compared to PON Day 2, C6+. However, data of protein cast of PON Day 2, C6+ was absent in Table 4.

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**ESPS manuscript NO:** 23164

**Title:** C5b-9 does not mediate tubulointerstitial injury in experimental acute glomerular disease characterized by selective proteinuria

**Reviewer's code:** 00503014

**Reviewer's country:** China

**Science editor:** Shui Qiu

**Date sent for review:** 2015-11-03 09:08

**Date reviewed:** 2015-11-10 14:56

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" 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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Dr. Rangan GK et al. studied whether C5b-9 has a pathogenic role in tubulointerstitial injury in a renal disease model characterized by acute highly selective proteinuria. They concluded that C5b-9 does not mediate tubulointerstitial injury in acute glomerular diseases characterized by selective proteinuria. Major comments 1. The authors should furthermore explain the findings that in C6+ rats with PON, the tubulointerstitial expression of C5b-9 was increased and localized predominantly to the basolateral surface of tubular epithelial cells, whereas it was undetectable in C6- animals. Could the C6- animals model be a null-immunogenicity animal? 2. Except minimal change diseases, most GN-related proteinuria is non-selective proteinuria. Is the conclusion limited to pathophysiology of MCD only? The author should clarify the point. 3. Many GNs are accompanied "intrinsic factors" and leading to proteinuria, in contrast to overflow proteinuria. I doubt that the protein-overload nephropathy (PON) is appropriate for the nephropathy work-up.

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**ESPS manuscript NO:** 23164

**Title:** C5b-9 does not mediate tubulointerstitial injury in experimental acute glomerular disease characterized by selective proteinuria

**Reviewer's code:** 00503182

**Reviewer's country:** Egypt

**Science editor:** Shui Qiu

**Date sent for review:** 2015-11-03 09:08

**Date reviewed:** 2015-11-10 17:27

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The article overall is first priority publication. There are minimal grammar mistakes. I wonder that although the data are non-parameteric and authors used Kruskal wallis test for test of difference, yet they express central values as means. Median in these situation is of utmost importance.

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**Name of journal:** World Journal of Nephrology

**ESPS manuscript NO:** 23164

**Title:** C5b-9 does not mediate tubulointerstitial injury in experimental acute glomerular disease characterized by selective proteinuria

**Reviewer's code:** 00503339

**Reviewer's country:** United States

**Science editor:** Shui Qiu

**Date sent for review:** 2015-11-03 09:08

**Date reviewed:** 2015-11-11 00:26

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

A reasonable approach to testing the importance of C5b-9 in human kidney disorders characterized by proteinuria and associated renal injury. One issue that must be raised and discussed is: Concern in accepting the finding as applicable to patients with proteinuria as the Discussion did not include either validation of the role of C5b-9 in rodent kidney disease nor was there evidence that rat exposure to bovine serum albumin - injected into study rats to simulate protein release in human kidney disease - reproduces the environment present in human proteinuria. Indeed, there are numerous examples of satisfactory treatments of induced renal diseases in rodents that are ineffective when tested in patients with kidney disorders so that this issue should be raised and discussed in the present report. Overall, an interesting and potentially important study that requires addition of discussion of the probability that its findings in rodents may transplate into a therapy for proteinuric patients.

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**Name of journal:** World Journal of Nephrology

**ESPS manuscript NO:** 23164

**Title:** C5b-9 does not mediate tubulointerstitial injury in experimental acute glomerular disease characterized by selective proteinuria

**Reviewer's code:** 00503043

**Reviewer's country:** Canada

**Science editor:** Shui Qiu

**Date sent for review:** 2015-11-03 09:08

**Date reviewed:** 2015-11-12 09:51

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

In the study, it was aimed to investigate whether C5b-9 has a pathogenic role in tubulointerstitial injury in a renal disease model characterized by acute highly selective proteinuria. The author found that C5b-9 does not mediate tubulointerstitial injury in acute glomerular diseases characterized by selective proteinuria. The subject is interesting and has certain clinical significance. However, the paper has some important limits stated as follows: 1. Title : The author eventually result showed that C5b-9 does not mediate tubulointerstitial injury in acute glomerular diseases characterized by selective proteinuria. We suggest that author revised the title. 2. Material and method: I am not certain whether are there congenital kidney disease in (PVG) rats and C6 deficiency rats? Please provide proper data. For example, urinary protein test 3. The description of results is very poor, which is one of the main weaknesses of the manuscript. 4. In this paper, most of the references of partial old, you have better take references in recent five years. conclusion In conclusion, This manuscript should be subjected to revision to be deemed for publication.