Reviewer Assessment

Adrienne Sulistyo, Abidur Rahman, George Biouss, Lina Antounians and Augusto Zani*

Animal models of necrotizing enterocolitis: review of the literature and state of the art

https://doi.org/10.1515/iss-2017-0050
Received December 20, 2017; accepted February 19, 2018

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Reviewers' Comments to Original Submission

Reviewer 1: anonymous

Jan 09, 2018

Reviewer Recommendation Term:	Accept with Minor Revision
Overall Reviewer Manuscript Rating:	N/A

Custom Review Questions	**Response**
Is the subject area appropriate for you?	4
Does the title clearly reflect the paper's content?	4
Does the abstract clearly reflect the paper's content?	4
Do the keywords clearly reflect the paper's content?	4
Does the introduction present the problem clearly?	4
Are the results/conclusions justified?	4
How comprehensive and up-to-date is the subject matter presented?	4
How adequate is the data presentation?	4
Are units and terminology used correctly?	4
Is the number of cases adequate?	4
Are the experimental methods/clinical studies adequate?	4
Is the length appropriate in relation to the content?	4
Does the reader get new insights from the article?	4
Please rate the practical significance.	4
Please rate the accuracy of methods.	4
Please rate the statistical evaluation and quality control.	4
Please rate the appropriateness of the figures and tables.	4
Please rate the appropriateness of the references.	4
Please evaluate the writing style and use of language.	4
Please judge the overall scientific quality of the manuscript.	4
Are you willing to review the revision of this manuscript?	Yes

Comments to Authors:
In this study different animal models of NEC are introduced. Their advantages and disadvantages are discussed. Overall, this review gives a good overview of methods and models to induce NEC.
Minor revision:

Page 3: "...Dvorak et al proposed the following histology based scoring system...". The cited publi-cation is from 2002, but this scoring system has been introduced earlier.
Page 6: The authors state, that Paneth cells were identified as key players in NEC pathogenesis. In contrast to rats and mice, which develop Paneth cells after around two weeks after birth, humans develop these cells during the first trimester of gestation. So in humans NEC occurs in the pres-ence of Paneth cells. This difference should be addressed.

Reviewer 2: anonymous

Jan 02, 2018

Reviewer Recommendation Term:	Accept
Overall Reviewer Manuscript Rating:	N/A

Custom Review Questions	**Response**
Is the subject area appropriate for you?	5 - High/Yes
Does the title clearly reflect the paper's content?	5 - High/Yes
Does the abstract clearly reflect the paper's content?	5 - High/Yes
Do the keywords clearly reflect the paper's content?	5 - High/Yes
Does the introduction present the problem clearly?	5 - High/Yes
Are the results/conclusions justified?	5 - High/Yes
How comprehensive and up-to-date is the subject matter presented?	5 - High/Yes
How adequate is the data presentation?	N/A
Are units and terminology used correctly?	5 - High/Yes
Is the number of cases adequate?	N/A
Are the experimental methods/clinical studies adequate?	N/A
Is the length appropriate in relation to the content?	5 - High/Yes
Does the reader get new insights from the article?	4
Please rate the practical significance.	4
Please rate the accuracy of methods.	N/A
Please rate the statistical evaluation and quality control.	N/A
Please rate the appropriateness of the figures and tables.	5 - High/Yes
Please rate the appropriateness of the references.	5 - High/Yes
Please evaluate the writing style and use of language.	5 - High/Yes
Please judge the overall scientific quality of the manuscript.	5 - High/Yes
Are you willing to review the revision of this manuscript?	Yes

Comments to Authors:
Animal models of Necrotizing Enterocolitis: Review of the literature and State of the Art for Innovative Surgical Sciences.
The author described all established animal models for Necrotizing Enterocolitis (NEC). He discussed specific details of each model and their implication for NEC in humans. Particularly, the summarizing table makes clear the advantages and disadvantages of the models of different animals including their impact for specific scientific problems.

Authors' Response to Reviewer Comments

Feb 15, 2018

Dear Editor,

Re: Ms. No. ISS-2017-0050

Many thanks for giving us the opportunity to revise our manuscript entitled: "Animal Models of Necrotizing Enterocolitis: Review of the Literature and State of the Art". We have condiered the Reviewers' comments, implemented the suggested changes (highlighted in yellow in the text), and provided a point-by-point response as indicated below.

Thank you in advance for further consideration,

Reviewer #1: Minor revision:
Page 3: "…Dvorak et al proposed the following histology based scoring system…". The cited publi-cation is from 2002, but this scoring system has been introduced earlier.
We have added a reference of an earlier publication from the same research group (Nadler et al 2000), where the authors had qualitatively described the histological differences that were then quantified by Dvorak et al in 2002.
Page 6: The authors state, that Paneth cells were identified as key players in NEC pathogenesis. In contrast to rats and mice, which develop Paneth cells after around two weeks after birth, humans develop these cells during the first trimester of gestation. So in humans NEC occurs in the presence of Paneth cells. This difference should be addressed.
We are grateful to the Reviewer's comment as it gave us the opportunity to expand on this topic. A sentence explaining the late development of Paneth cells in rodents has been added to the text (page 6).
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Reviewer #2: The author described all established animal models for Necrotizing Enterocolitis (NEC). He discussed specific details of each model and their implication for NEC in humans. Particularly, the summarizing table makes clear the advantages and disadvantages of the models of different animals including their impact for specific scientific problems. I have no further comments and suggest accepting the manuscript for publication.

We are thankful for the comments made.

Reviewers' Comments to Revision

Reviewer 1: anonymous

Feb 17, 2018

Reviewer Recommendation Term:	Accept
Overall Reviewer Manuscript Rating:	N/A

Custom Review Questions	**Response**
Is the subject area appropriate for you?	5 - High/Yes
Does the title clearly reflect the paper's content?	5 - High/Yes
Does the abstract clearly reflect the paper's content?	5 - High/Yes
Do the keywords clearly reflect the paper's content?	5 - High/Yes
Does the introduction present the problem clearly?	5 - High/Yes
Are the results/conclusions justified?	5 - High/Yes
How comprehensive and up-to-date is the subject matter presented?	5 - High/Yes
How adequate is the data presentation?	5 - High/Yes
Are units and terminology used correctly?	5 - High/Yes
Is the number of cases adequate?	5 - High/Yes
Are the experimental methods/clinical studies adequate?	5 - High/Yes
Is the length appropriate in relation to the content?	5 - High/Yes
Does the reader get new insights from the article?	5 - High/Yes
Please rate the practical significance.	5 - High/Yes
Please rate the accuracy of methods.	5 - High/Yes
Please rate the statistical evaluation and quality control.	5 - High/Yes
Please rate the appropriateness of the figures and tables.	5 - High/Yes
Please rate the appropriateness of the references.	5 - High/Yes
Please evaluate the writing style and use of language.	5 - High/Yes
Please judge the overall scientific quality of the manuscript.	5 - High/Yes
Are you willing to review the revision of this manuscript?	No: done

Comments to Authors:
It's ok