

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 56606

Title: Lactobacillus bulgaricus inhibits colitis-associated cancer via a negative regulation of intestinal inflammation in azoxymethane/dextran sodium sulfate model

Reviewer's code: 02527569

Position: Editorial Board

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Brazil

Manuscript submission date: 2020-05-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-05-07 03:25

Reviewer performed review: 2020-05-07 05:34

Review time: 2 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 Grade E: Do not publish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 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 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 checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dr. Silveira describes in this manuscript following points: 1) Lactobacillus inhibits tumorigenesis in AOM/DSS model 2) Lactobacillus attenuates intestinal inflammation 3) Lactobacillus attenuates inflammatory cytokine production in non-tumorous lesions 4) Lactobacillus attenuates inflammatory cytokine levels in tumor lesions The study is straightforward in the point of the inhibitory role of Lactobacillus on inflammation in AOM/DSS model. The phenotype observed is interesting and may be important in the IBD field to prevent inflammation-associated tumorigenesis. The major point which should be determined before further consideration is the molecular mechanisms how Lactobacillus inhibits intestinal inflammation in this model. The authors should provide some evidence about the possible molecular mechanisms how Lactobacillus inhibited intestinal inflammation. Otherwise, the study is too phenotypical. Minor points 1. Please provide results that Lactobacillus is actually colonized in large intestine in these experiments. 2. Please provide histological findings during the course of the experiments. 3. It is better to add some experimental results without AOM treatment.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 56606

Title: Lactobacillus bulgaricus inhibits colitis-associated cancer via a negative regulation of intestinal inflammation in azoxymethane/dextran sodium sulfate model

Reviewer's code: 03805206

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Brazil

Manuscript submission date: 2020-05-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-05-07 03:38

Reviewer performed review: 2020-05-07 09:41

Review time: 6 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 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: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In the manuscript entitled “Lactobacillus bulgaricus inhibits colitis-associated cancer via a negative regulation of intestinal inflammation” the authors present the possibility of prevention of colitis-associated cancer using probiotics (Lactobacillus bulgaricus). I read your document with interest. There are a few comments. Major points 1. You showed that the tumor volume and size in Lb treated group were lower. I am interested in these results. Does the tumor develop earlier in the control group? This is a question about the timing of tumor development. 2. In early human CAC, the tumor has usually flat shape. What is the shape of the tumor in this study? Please consider the shape of the tumor. 3. Was there a relationship between the size/volume of the tumor and cytokine production? 4. CAC is caused by long-term inflammation usually over 10 years. Do you think there is any difference between the acute phase or the chronic phase? Furthermore, based on your research results, what kind of protocol can you consider for clinical application in humans? (probiotics admission period etc.) 5. Looking at the title, it feels like a paper targeted human CAC. Minor points 6. In this manuscript, you did not show the incidence of tumors in detail. I think you had better describe the range of tumor numbers. Because we would like to know if there are variations in the tumor numbers in each case. 7. I think you wrote the LAB incorrectly in the background of the abstract section.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 56606

Title: Lactobacillus bulgaricus inhibits colitis-associated cancer via a negative regulation of intestinal inflammation in azoxymethane/dextran sodium sulfate model

Reviewer's code: 02527569

Position: Editorial Board

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Brazil

Manuscript submission date: 2020-05-07

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-07-20 00:13

Reviewer performed review: 2020-07-20 00:28

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 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 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 statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors responded to most of my concerns.