

Reviewer #1:

1)The abstract section fails to provide a comprehensive summary of the review's content.

Authors: Many thanks for the suggestion. The abstract was revised in order to better recapitulate the manuscript content (see Abstract line 9 and lines 17-19).

2)The key terms do not accurately reflect the main focus, and it is recommended to revise them.

Authors: Key words were changed/implemented as suggested by the reviewer.

3)The references do not adequately represent the current state of research; therefore, it is suggested to remove them and instead cite articles from the past 3-5 years.

Authors: nine references were replaced with more recent publications or removed (5,8,9,20,21,23,24,25,33,40). We were not able to further update references since the majority of them represented seminal and/or historical publications. However, more than 50% of citations fail in the last decade in the current version. New references tracked in yellow.

4)The discussion section does not address the core issues raised in the review, thus requiring further elaboration on the main points.

Authors: Many thanks for your observation. We better clarified these aspects and the aims of our manuscript, in the conclusion section (see page 12, lines 5-11 from the bottom).

Reviewer #2:

1) The manuscript mentions that "Escherichia coli and aromatic phenolic bacteria are associated with PBC" (Page 5, line 6). However, there is a lack of further explanation regarding the mechanisms underlying this association.

Authors: Many thanks for your suggestion. Data linking gut microbioma to PBC progression were included (see page 6, lines 17-25).

2) When this manuscript refers to the impairment of bile duct epithelial secretion on page 6, it may be better to review the impact of the bile metabolic microenvironment on its secretion.

Authors: Thanks for the suggestion. The role of ductal microenvironment, on cholangiocyte secretion, has been mentioned and a review focusing on this issue is now included in the reference (see page 8, lines 11-14 from the bottom and reference 33)

3)Page 4 of the manuscript, it is mentions that anti-mitochondrial antibody (AMA) initiates PBC. It is recommended to further review the mechanisms by which AMA causes PBC.

Authors: Many thanks for your observation. We better clarified the relationship between AMA appearance in blood and PBC onset, that mainly derives from clinical observation (see page 6, last two lines and page 7, first two lines).

Reviewer #3:

1) ... it would be beneficial if the authors briefly described their method of selecting the literature reviewed.

Authors: Thanks for the suggestion to improve the manuscript. The indication on literature review was included (see page 4, last six lines).

2)..... in the conclusion, emphasizing the novelty of the paper and how it contributes to advancing our standard knowledge about PBC would be beneficial.

Authors: We underscore the novel aspects of our manuscript in the conclusions section (see page 12, lines 5-11 from the bottom).

Reviewer #4:

This mini-review is excellent on discussing the molecular and cellular mechanism on the genesis and development of the primary biliary cholangitis, and the authors gave us a totally different view if this.

Authors: Many thanks for appreciating our manuscript