nutrients-2787894

Response to reviewers' and Academic Editor comments

We thank the referees and the editor for the helpful comments on the manuscript. We have addressed the issues according to the reviewer's comments/suggestions. We believe that these modifications have improved the paper. Changes are highlighted in the revised version of the manuscript.

Comments from the reviewers:

Reviewer #1 (Round 1):

The authors focus on the impact of food-derived, thus exogenous miRNAs as regulators of biological functions on human health and the development of diseases. They also discuss target miRNAs of different nutrients.
The topic is interesting and well-delivered. There are three figures and one table for a better understanding. The manuscript is clear, relevant to the field and presented in a well-structured manner. Most of the references are from the last five years. Self-citation or plagiarism is not detected. Many reviews discuss cross-kingdom regulation by miRNAs, but this manuscript is novel in its present structure.
The strength of the manuscript is to raise the attention to diet-related miRNA-based regulation.

We thank the Reviewer for the helpful comments. The revision has been performed according to Reviewer' requests. The suggestions have undoubtedly contributed to strengthen the manuscript (revision marked in yellow).

The main weakness may be the pronunciation of confounders. Namely, if there is no supplementary intake of natural or synthetic miRNAs, many phytochemicals or ingredients of animal-based food may modify the risk of diseases. The confounder-related limitations should be discussed better.

Reply: According to Reviewer suggestion, the confounder-related limitations have been better discussed in the "*5. Questions opening on the potential impact of dietary miRNAs on health and disease*" section.
"The evaluation of food-derived xenomiRNA effects cannot refrain from considering the co-existence of a great variety of dietary bioactive compounds. In absence of supplementary intake of dietary exogenous miRNAs, many phytochemicals or animal-based food derivatives may modify the risk of diseases, targeting the reported biological effects [29, 165]. Indeed, several food-derived compounds exert their regulatory effects on different diseases either by upregulating or down-regulating different signaling pathways, as well as acting on many epigenetic patterns [166]. Dietary constituents are able to affect other epigenetic mechanisms, including DNA status modulation, histone methylation, and acetylation, by aiming key epigenetic modulators such as DNA methyltransferases and histone deacetylases, thus resulting in local or global changes in epigenetics and subsequent gene transcription and expression levels [29, 165-166]."
Please, see lines 549-559.