Response Letter

**Manuscript ID:** 90603, Basic Study

**Manuscript Title:** Changes in bacterial composition and metabolic pathways associated with ornithine aspartate intake in a rat model of metabolic dysfunction-associated steatotic liver disease

We received the reviewers’ comments on the manuscript entitled "Changes in bacterial composition and metabolic pathways associated with ornithine aspartate intake in a rat model of metabolic dysfunction-associated steatotic liver disease" (90603, Basic Study). We are grateful for their valuable time and useful contributions. We have addressed each of their concerns as outlined below:

**Reviewer’s Comments** - This study examined the effect of ornithine aspartate (LOLA) on metabolic-associated liver disease (MASLD) in rats. This study is an extension of authors efforts in the field (PMID 32982365, 35070008, 36551202), focusing on gut microbiota. In general, the experiments were logically designed and well conducted, and the comprehensive bioinformatics including R packages were used to analyze the data. The results obtained are sound and could add to our understanding of pharmacological effects of LOLA against MASLD. Listed below are specific comments:

**Reviewer’s Comments 1:** General characteristics (Table S1) should be used as Table 1, as these basic data are essential for understanding the effects of LOLA on MASLD. Two comments on the Table: (1) “0,001” should be 0.001; (2) “20,5222” could be “20.52”, “2921,3080” could be “2921” per “4 effective number rule”.

**Answer:** As requested by the reviewer, Table S1 was renamed as Table 1. Appropriate punctuation adjustments have been made to the table 1, and the “4 effective number rule” was respected.

**Reviewer’s Comments - 2:** The important information from their prior work (PMID 36551202, Ref 11) on LOLA on MASLD should be adequately referenced to give readers a big picture of the study.

**Answer:** As suggested by the reviewer, a paragraph has been added to the discussion, encompassing important information from our previous works.
Reviewer's Comments - 3: Others

a. Line 49 “Ornithine Aspartate” could be “ornithine aspartate” to be consistent with their prior publication (e.g., Ref 11) and the text (e.g., line 85).

b. Line 240, 301, 317, 326: “l-ornithine, l-aspartate” should be “L-ornithine, L-aspartate” to be consistent throughout the manuscript.

c. Line 54, 109, 119, 122: Add a space between number and units as “200 mg, 10 µg” throughout the manuscript.

Answer: The corrections to nomenclature and spacing between number and units have been made as requested in comments 3.a, 3.b, and 3.c.