Thank you very much for your good suggestions and questions. We have revised our manuscript as your suggestion and give some explanation as followings.

Reviewer #1:

Question 1： Major concern: In this day and age, MASLD is the correct term, and not NAFLD. Please, review the paper and correct this (https://www.aasld. org/new-masld-nomenclature).

Answer: We learned about MASLD on the website recommended by the reviewers. According to the reviewer's comments, we replaced NAFLD with MASLD and give a new explanatory paragraph. The new paragraph: In 2023, the global hepatology community renamed nonalcoholic fatty liver disease (NAFLD) as metabolic dysfunction-associated steatotic liver disease (MASLD). MASLD is the most common chronic liver disease worldwide. Patients presenting hepatic steatosis and at least one of five cardiometabolic risk factors are diagnosed with MASLD.

Question 2： Some minor suggestions: The sentence "Although AMP-activated protein kinase (AMPK) activation induces autophagy, aging is associated with decreased AMPK activation..." could be clarified by mentioning that AMPK activation is a regulator of autophagy and aging-related changes in AMPK activation may impact autophagic processes.

Answer: We have revised our manuscript as your suggestion: AMPK activation is a regulator of autophagy and aging-related changes in AMPK activation may impact autophagic processes, which results in decreased formation of autophagosomes and further hastening of the aging process.

Question 3： The sentence "Mitochondrial homeostasis is closely related to the occurrence and development of NAFLD" is a broad statement. It might be helpful to briefly mention specific aspects of mitochondrial homeostasis that are crucial for NAFLD development.

Answer: We have revised our manuscript as your suggestion: The mitochondrial homeostasis is closely related associated with hepatic lipid metabolism and exacerbates the development of MASLD.

Question 4: The section discussing TLR5-deficient mice could be nuanced by highlighting the complexity of the relationship between TLR5 and metabolic syndrome, as it seems to have dual effects according to the presented studies.

Answer: We have revised our manuscript as your suggestion: However, another study revealed that TLR5-deficient mice exhibited characteristics of metabolic syndrome, such as obesity, insulin resistance, and hepatic steatosis. Furthermore, transplanting the GM from TLR5-deficient mice into healthy mice exhibited the performance of metabolic syndrome in healthy mice.

Question 5: The sentence "Additionally, the transplantation of GM from younger mice to older mice could reverse age-related changes in the gut, eyes, and brain" is factually accurate, but for a more comprehensive understanding, specifying the key findings related to gut health from the study or studies would be beneficial.

Answer: We have revised our manuscript as your suggestion: Additionally, the transplantation of GM from younger mice to older mice could reverse age-related changes in the gut, eyes, and brain. Aged mice receiving young donor microbiota had reduced cortical and callosal microglia, reduced expression of inflammatory complement protein C3 in the retina, and reduced circulating concentrations of lipopolysaccharide (LPS)-binding protein (LBP), to levels comparable to young mice[39].

Reviewer #2:

Question 1: In the section of Mitochondrial homeostasis, the authors indicate that fragmented mitochondrial DND accumulates in nuclear. Any reference for this? How could this occur and the pertinent mechanism?

Answer: We have revised our manuscript as your suggestion: It has been shown that the absence of the gene encoding the nonhomologous end-joining enzyme known as DNA ligase IV (DNL4) exacerbates linear mitochondrial DNA (mtDNA) aggregation in the nucleus. Cheng et al. proposed that linear nuclear mtDNA fragments accelerate aging in yme1-1 mutant cells by affecting nuclear DNA replication, recombination, repair, and transcription.

Question 2: Fructose intake or consumption is a major cause of NAFLD, the contribution of this sugar to NAFLD in aged cohorts, should be elaborated.

Answer: We have revised our manuscript as your suggestion: High fructose intake induces de novo lipid biosynthesis in the liver. This process does not depend on ATP citrate lyase (ACLY) but rather on the intestinal microflora which metabolizes fructose to acetate and converts the latter to acetyl coenzyme A (acetyl-CoA). Altered intestinal permeability, gut dysbiosis, and increased fructose intake exacerbate hepatic lipid accumulation and contribute to the development of MASLD in elderly patients.