Reviewer's report

Title: Differential hepatotoxicity of dietary and DNL-derived palmitate in the methionine-choline-deficient model of steatohepatitis

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Reviewer: ALEXANDER WREE

Reviewer's report:

The manuscript by Pierce et al. describes the results of a comparative feeding project focusing on hepatotoxicity and lipotoxicity in mice fed with different MCD formulas. They compare the effect of custom MCD diets with four different macronutrient combinations. Results are presented in a clear manner and the manuscript is well written and easily understandable. I just have some additional comments.

The MCD model is, despite its know drawbacks, used and established to study the development of NAFLD and NASH. In the manuscript authors use “custom MCD formulas” (page 2, line 8). How do the custom formulas differ from the “standard” MCD diet?

One major problem in studying the development of NAFLD and NASH in mice is the lack of development of insulin resistance when compared to the course of disease in human. Do any of the custom MCD diets used in this manuscript overcome this issues?

A major hallmark in the progression of liver disease is the activation and trans-differentiation of hepatic stellate cells to collagen producing myofibroblast. This effect has been demonstrated over and over in the “standard” MCD diet. Do the different “custom MCD formulas” show similar effects?

Minor comments and errata

The list of abbreviation is missing some items, e.g. SCD-1, DNL.

The indication of significant differences using a mix of numbers and asterisks is not easily understandable.

With the suggested minor, but in my opinion essential changes, the manuscript by Pierce et al. may be re-submitted for publication in BMC Gastroenterology.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests