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: Julia Kälsch

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Review of BMC Gastroenterology Article titled “Differential hepatotoxicity of dietary and DNL-derived palmitate in the methionine-choline-deficient model of steatohepatitis” by Andrew A. Pierce, Michael K. Pickens, Kevin Siao, James P. Grenert and Jacquelyn J. Maher

The manuscript by Andrew A. Pierce et al. performed an analysis of liver injury induced by custom methionine-choline-deficient (MCD) diet with 4 different macronutrient combinations in mice. The objective of the study was to determine whether dietary palmitate exerts the same toxicity as carbohydrate-derived palmitate.

Adult male mice were fed for 21 days with one of different custom methionine-choline-sufficient (MCS) or MCD diet formulas. The custom-made formulas contained different components of carbohydrates and fats (e.g. starch or sucrose, oleate or palmitate). After the mice were killed, serum alanine aminotransferase (ALT) was measured, triglyceride and fatty acid analysis was performed by extracting lipids from fresh liver tissue, furthermore, gene expression was evaluated by extraction of total RNA from liver tissue. Results were compared by analysis of variance with Tukey post-hoc testing.

The manuscript is well written and the study design was appropriate for the given aims. The authors managed to sum up interesting and important results mainly indicating that dietary and DNL palmitate have different effects on liver cells in mice. They also managed the challenge to visualize their results, clearly giving the reader an impression of the most important findings.

Major comments:
- No major comments

Minor comments:
- The authors should also measure aspartate amino transferase (AST), not only ALT, as well as gamma-glutamyl transferase (GGT), to determine the whole spectrum of liver damage.
- Performance of M-30 and M-65 cell death assay would be another tool to evaluate the difference in liver injury.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.