Reviewer's report

Title: Risk Interaction of Obesity, Insulin Resistance and Hormone-Sensitive Lipase Promoter Polymorphisms in the Development of Fatty Liver

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Reviewer: Dominique Langin

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The paper by Hsiao et al. investigates the interactions between hormone-sensitive lipase genetic polymorphisms, obesity and fatty liver.

1. The power of the study and the lack of replication are of concern. For analyses of surrogate parameters of insulin resistance such as HOMA-IR and other clinical parameters, the number of individuals is limited compared to published studies. The impact of the hormone-sensitive lipase promoter -60 C>G polymorphism on triglyceride levels in the glucose intolerant group (n=299) seems marginal especially as the glucose intolerance group is a heterogeneous mix of conditions as it encompasses all individuals with fasting glucose > 100mg/dl. Classification according to the presence and absence of the metabolic syndrome was of interest in the context of the study. However, waist circumference is not reported.

2. Interpretation of the impact of the hormone-sensitive lipase promoter -60 C>G polymorphism focuses on the action of the enzyme in the liver. However, the lipase is expressed at much higher levels in adipose tissue where it controls the release of fatty acids into the bloodstream and hence liver exposure to fatty acids. Therefore, it is likely that the impact on lipid metabolism of variations in hormone-sensitive lipase activity will be influenced by its level of expression in adipose tissue.

Level of interest: An article of limited interest

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'