Reviewer's report

Title: Obesogen, BDE-47, impairs insulin sensitivity in mice with liver-specific Pten deficiency

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Reviewer: Ouliana Ziouzenkova

Reviewer's report:

Manuscript 'Obesogen, BDE-47, impairs insulin sensitivity in mice with liver-specific Pten deficiency' by McIntyre et al. describes interesting findings of effect of the environmental pollutant BDE-47 on metabolic effects, such as obesity and glucose tolerance in mice. Although this paper is very important for understanding the role of environment in obesity and related metabolic disorders, few important issues need to be addressed prior to publication. Do mice accumulate BDE-47 in blood, liver, or adipose? Rodents have much more potent peroxisomal oxidation of xenobiotic compounds in the liver than humans. This may lead to fast catabolism of BDE-47 and decrease their metabolic impact. On the other hand, an increase in peroxisomal proliferation may increase mice susceptibility to liver cancer. Was PPARα expression increased in the liver of BDE-47-treated mice compared to controls?

The addition of new experimental data (BDE-47 analysis in blood and/or tissues) and PPARα and/or peroxisomal proliferation assessment will make authors' finding more relevant for assessment of potential deleterious effects of BDE-47 for humans.

There are no indications in literature or in this paper that BDE-47 is an obesogen, the current structure and descriptions/discussions in this paper is misleading. Finally, in humans BDE-47 is present in pg/g body weight, thus current treatment ug/g body weight should not be discussed as a treatment with low doses.

Major comments:

#1. Fig 2.

The data presentation is unclear. Fig A is missing standard deviation. Insulin sensitivity should be compared between DMSO and BDE-47 groups within same (one or two) genotype. The analysis of differences between genotypes is important but less relevant for this paper.

#2. Were insulin levels in plasma influenced by BDE-47?

Minor comments:

The effects could be more pronounce on high-fat diets.

1. Is the question posed by the authors well defined?
Yes

2. Are the methods appropriate and well described?
   partially

3. Are the data sound?
   Yes but the data are insufficient

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Partially (see comments)

6. Are limitations of the work clearly stated?
   Not sufficiently. The difference between rodents and humans was not addressed

7. Do the authors clearly acknowledge any work upon which they are building both published and unpublished?
   yes

8. Do the title and abstract accurately convey what has been found?
   No, BDE is not an 'obesogen'

9. Is the writing acceptable?
   Yes