

**Author's response to reviews**

**Title:** Differential Susceptibility to Obesity Between Male, Female and Ovariectomized Female Mice

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Dear Nutrition Journal Editorial Team:

Response to reviewer's comments

Please consider the enclosed revised manuscript (MS: 1166553548223041) entitled "**Differential Susceptibility to Obesity Between Male and Female Mice**" by Jina Hong, et al. for publication in The Nutrition Journal. We found the reviewer's comments very helpful in strengthening the paper as detailed below:

### Reviewer's report

**Title:** Differential Susceptibility to Obesity Between Male and Female Mice

**Reviewer:** Melinda Wilson

### Reviewer's report:

Major Revisions:

1. One-way ANOVA is not the appropriate statistical test to make conclusions between the gender groups. A two-way ANOVA (gender group x diet) at each time-point should be analyzed. Additionally, a repeated-measure analysis of weight over time or a two-way ANOVA (time x diet) within each group could also be included. Additionally, there is no indication of the statistical differences presented in Figure 1.

This section has been revised—also the figure legend has been revised to show the statistical differences.

2. While feeding paradigms (calorie restricted, low fat and high fat) are interesting, the overall finding that ovariectomy increases body weight in female mice has been described numerous times in the literature. Therefore, the statement "a direct comparison in the susceptibility to body weight gain between males, females, and ovariectomized females has not been made" is too strong. This is an overstatement of the novelty of this study. The authors should focus the discussion on the addressing the effects of the different feeding paradigms as this is the most novel part of the study.

We agree with the reviewer—that the effects of ovariectomy on body weight have been previously reported; also, the differential susceptibility to obesity between males and females has also been reported—however, the question that we have answer by comparing—males—vs.—females—vs.—OVX females—in the same experiments is whether removal of the ovaries makes females gain body weight like males—this comparison has not been make and is therefore novel. We reviewed the literature and found that this comparison has not been made (e.g., PubMed/MEDLINE and TOXLINE). However, we have also revised the discussion as suggested by the reviewer.

Minor Revisions:

1. More details about the body composition assessment should be provided in the methods section.

This section has been revised.

### Reviewer's report

**Title:** Differential Susceptibility to Obesity Between Male and Female Mice

**Reviewer:** Blanka Zelezna

Major points:

1. Only total fat weight is given, not fat distribution and comparison of the ratio between subcutaneous and visceral fat in groups fed with HF diet.

The reviewer is correct we did not differentiate between subcutaneous and visceral fat, the discussion has been modified to indicate this. However, in future experiments we will measure the different types of body fat.

2. Neither metabolic (blood glucose, triglycerides, free fatty acids, insulin, leptin...) nor inflammatory parameters (blood leptin, CRP...) are given. 3. Hypothesis on obesity as chronic inflammatory state is not mentioned. 4. All these items mentioned are necessary if a link between obesity and cancer is to be discussed.

Measuring such factors would require a more extensive study, which will be carried out in the future. The discussion section has been modified to fit our data---the hypothesis regarding inflammation was not discussed because we have not measured markers associated with inflammation in our animals---however, we will measure them in future experiments.

Minor points:

How old were the mice when ovariectomized? They were 4-5 weeks of age.