

Thank you for your careful reading of our manuscript. We have added the additional information as noted below, and included in the revised manuscript (verbatim text in **red**).

For example, in the Abstract- stains were not specified – Lines 18-19, Diversity Outbred was now specified: “840 genetically unique Diversity Outbred mice”

number of female and male were not specified – Line 19, number of male and female mice now specified: “mice of both sexes (n=417 male and 423 female)”

percent of fat (and cholesterol) in high fat diet was not specified

Now present on lines 20-22, composition of the diets is now noted in the abstract: “on both a control chow (% kcals in diet: Protein 22%, Carbohydrate 62%, Fat 16%, no cholesterol) and high fat high sucrose (% kcals in diet: Protein 15%, Carbohydrate 41%, Fat 45%, 0.05% cholesterol).”

p values were not specified

Line 25, p-values for DO and BXD mice calcium associations are now included: “in both diversity outbred ($p=3.0 \times 10^{-43}$) and BXD ($p=0.005$) mice”

Fig 1B- where is the BW marked?

BW was included in a previous analysis before the addition of more data. Once that data was included and we re-analyzed the data it was no longer included in the pruned regression trees. Thank you for catching that error, this has now been removed.

Which strain?

For 1b, strain is indicated on line 83. This analysis was done in the 840 DO mice.

Additionally, were the mice monitored for food consumption?

There is no measure of food consumption included and therefore no analysis was done for that measure.

This manuscript lacks many details that should be added (referencing to ref 9 in not enough). –

Lines 59-70 more details were added from reference [9] regarding the DO mice: “Animals were first received at wean age (3 weeks old) and then distributed into cages of five same-sex animals per cage. Animals were housed in pressurized, individually ventilated cages (Thoren Caging Systems, Hazelton, PA) with pine bedding (Crobb Box, Ellsworth, ME) and had ad libitum access to food. Blood from mice was obtained from the retro-orbital sinus after administration of tetracaine HCl (a topical anesthetic) using a heparin-coated microcapillary tube and collected into a 1.5-ml Eppendorf tube. For collection of blood plasma, approximately 150µl of whole blood was collected into a tube and plasma was separated by centrifugation at 10,000 rpm for 10 min at 4° Celsius and removed into a clean Eppendorf tube”

More detailed discussion should be written regarding the relationship between diet and cholesterol and calcium levels

Lines 150-156 offer more discussion between diet, cholesterol, and calcium levels: “We were not surprised that HFHS feeding raised cholesterol, as this has been widely observed in mice, rats and humans. This is likely due to a combination of increased dietary cholesterol, triglycerides and body fat in these mice. The calcium relationship with cholesterol that was identified here is a unique observation in mice. As the magnitude of elevations of cholesterol and calcium from HFHS diet were similar, and that diet did not alter calcium levels, it is possible that calcium and diet are independent predictors of cholesterol homeostasis.”