The current manuscript shows an interesting metabolic comparison between lean and fatty pigs focus on insulin sensitivity and glucose metabolism. These results increase available data of Iberian breed to improve its characterization. This knowledge could be useful both for Iberian pig production and biomedical studies using the Iberian breed as a biomedical model. In general, the manuscript is well written and has a good explanation of insulin index calculations. These indexes are not common in animal production and with their explanation are easy to understand. However, some main points need to be reviewed to considerer the quality of this manuscript.

First, the **number of pigs** of both breeds is low, and metabolite measures usually have high variability. This could be one of reason to draw reliable conclusions because CIs have to be wide. It is only commented in a sentence (L236), and I think this situation could be more discussed at the beginning of Discussion or further studies proposed later to reinforce these results.

Second, I missed finding **main data about pigs**. As their age, measures about fat tissues and weight averages separated by breed found in other studies cited below in the Discussion. They are breeds with different growth speeds, so it is difficult to think that they had similar age and weight. These data could be useful to compare their results to other studies. On the other hand, although these breeds are classified as lean and fatty, some variable about their condition, such as subcutaneous backfat, abdominal circumference or BMI (body mass index) could be useful in this metabolism study to improve its interpretation.

Regarding **statistical analysis and result presentation**, I am not sure about some points. About the fixed effect of time sampling, time is directly considered in analyses with repeated measures. Then, I think it is not necessary to include it as a fixed factor in their explanation because this might be misleading. It seems that authors did more analysis not well explained using time with categories. I would also like to know why to use pooled SEM for both groups and not separated by groups. I prefer the second option (more informative), so review it in F1-3, I do not know whether SEMs are the same in both data or different. This should also be considered in F4-6, there is no variability measure.

On the other hand, in F1-3, their captions say that 'Comparisons versus basal or control treatment' were made (it is not described in M&M). I suppose that is a contrast of each time point vs basal point (first time) by breed because it is a default analysis that SAS includes when repeated measures are used. These contrasts are made default vs. the last point. I suppose that authors changed it, but then, why the basal point is compared with itself? And how a comparison with the same values is significantly different? Maybe I misunderstood it, but if this is the situation, they should improve the statistical explanation. Alternatively, these p-values could be the result of the comparison between breeds in each point. I do not know, they must clarify it. I also think there is a mistake in HOMAB results, please review it. Last questions, why is there a common basal mean of all metabolites if some of them are different by breed? Or is there a reason to give that data in common? After these questions, I would like to know which basal levels were used to correct AUC, joint or separated? There are more requests about this section below as minor reviews.

Related to some doubts described above, I think that some points could be improved in Discussion. The last part of the Discussion is well conducted and is easy to understand and follow. However, I do not have the same feeling reading other parts. I recommend a general review to focus on the main idea, but I propose some specific points. At the beginning (L214-227), some sentences mislead to interpret results and are not clear (such as lower insulin concentrations that are not a result here). I think that the age data would be essential to interpret information from cited papers. Regarding lactate, I think that high basal lactate levels might indicate a higher risk of insulin resistant, but it is not considered a fact. Indeed, there is

evidence of greater changes in lactate release in control individuals than in obese individual after insulin doses. So, the role of this metabolite is not clear, although it is important to consider it.

At last, the **conclusion** of this study seems to be that these growing Iberian pigs showed differences that may indicate an early stage of insulin resistance (abstract). However, this idea was not possible to find at the end of the Discussion because there was no conclusion or summary paragraph. Thus, the end looks like unfinished. On the other hand, the Implications section states the insulin resistance without doubts. I think it is important to unify the study conclusion.

Moreover, <u>some details</u> should also be considered to improve the quality of the manuscript or its understanding.

First, I recommend changing the two last **keywords**. Maybe using fatty and lean swine breeds could be easier to find.

Second, I suggest reviewing possible **misspelling** and some expression in English. I suppose there is one in some p-values (ex. 0.01 < P < 0.001; L25-26, 28, 30, 167-69,). I think '> P <' or '0.001 < P < 0.01' are correct. There are also some sentences in parentheses without closing. Regarding English, I propose to change 'associated to' to 'associated with', 'animals cared' to 'animals were cared' and 'over a 1 min' to 'over one min' and do a general revision. Another point is the use of Iberian alone (without pigs, breed…) because sometimes makes readability difficult.

Regarding **Material and Methods**, I would like to know the intra- and inter-assay CVs rest of molecules, even if they are common (manuscript or annexe). I also think units of fasting insulin and glucose should be indicated the first time they are named, in HOMA index calculations or previously. At last, I would like to know if the standard diet and the energy level of maintenance after surgery were the same for both breeds or if different diets and calculation were used for the Iberian breed.

Regarding **Results**, I think that the interaction of time and breed is the most interesting difference and would be indicated after fasting values and not to give all the priority to breed differences. I would also like to know whether there are differences by breed in the fasting values of the rest of metabolites. They gave some common basal levels that have different between both breeds. At last, naming in figure captions the variability measure used in figures would improve their understanding.

Finally, there are some points in the **Discussion**. In L239, a common pattern in many models of obesity is commented, please one citation at least. No significant interaction of breed and time in lactate concentrations were found, so its levels were always higher, please rewrite the sentence (L263-6). Cholesterol concentrations in dyslipidemia may be increased. This was not discussed only its HDL and LDL fractions, although their values are not available.

I hope this manuscript can be improved. Reading this paper was a pleasant experience allowing me to learn more about insulin sensitivity and other physiological processes in a fatty pig breed, so I encourage authors to do it.