Author’s response to reviews

Title: The association of circulating irisin with metabolic risk factors in Chinese adults: a crosssectional community-based study

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Author’s response to reviews:

Dear editor,

We have changed our manuscript according to your comments, please find our enclosed clean PDF, please don’t hesitate to contact me if there is problem. Thank you for your time and effort.

1. Please move the "Availability of data and materials" section to beneath the "Declarations" header.

We have moved the "Availability of data and materials" section to beneath the "Declarations"

2. We note that the current submission contains some textual overlap with other previously published works, in particular:

Page 3 lines 20-22 and 29-31, page 4 lines 25-28, page 5 lines 1-2, page 9 lines 5-9, lines 5-7 of the Conclusions:

While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work.

If there is overlap in the Methods section, please ensure to summarize the methods and cite the source.

Please re-phrase these sections to minimise overlap.

We have rephrased these sections to minimize the overlap:

1. Page 3 lines 20-22, Exercise can induce expression of peroxisome proliferator-activated receptor gamma coactivator-1α (PGC-1α) of skeletal muscle, which promotes the expression of FNDC5, therefore stimulates the secretion of irisin.

   Expression of peroxisome proliferator-activated receptor gamma coactivator-1α (PGC-1α) of skeletal muscle can be induced by exercise which can stimulate the irisin secretion by endorsing the expression of FNDC5.

2. Page 3 lines 29-31, Most studies showed a positive correlation between circulating irisin levels at baseline or FNDC5 mRNA expression and body mass index (BMI)

   Positive association between circulating irisin levels at baseline or FNDC5 mRNA expression and body mass index (BMI) was demonstrated in most of the studies.

3. Page 4 lines 25-28, Blood samples were collected from all participants after a 12-h overnight fasting and immediately centrifuged. Serum and plasma were taken for analysis of the biochemical markers.

   Blood samples were collected after a 12-h overnight fasting, instantly centrifuged; serum and plasma were used for biochemical marker analysis.

4. Page 5 lines 1-2, All variables were checked for normality by using Shapiro-Wilk test. Continuous variables were expressed as mean±SD. Student’s t test was used for normally distributed variables.

   Shapiro-Wilk test was used for checking normality of all variables. Continuous variables were expressed as mean±SD. Student’s t test was used for normally distributed variables.

5. Page 9 lines 5-9, Shanaki M et al. also found that irisin was negatively correlated with HOMA-IR and insulin in patients with nonalcoholic fatty liver disease (NAFLD). A recent
study showed a negative correlation of HOMA-IR with circulating irisin levels in young girls suggesting that irisin secretion at an early age might delay the onset of obesity, insulin resistance and T2DM.

The negative association of irisin with HOMA-IR and insulin in patients with nonalcoholic fatty liver disease (NAFLD) was also demonstrated by Shanaki M et al. A negative association of HOMA-IR and circulating irisin levels in young girls demonstrated in a recent study indicate that the onset of obesity, insulin resistance and T2DM might be delayed by the irisin secretion at an early age.

6. lines 5-7 of the Conclusions, However, further studies are needed to deepen in several aspects of irisin secretion and metabolism in order to clarify its full potential as a meaningful drug target in human disease states.

However, in order to elucidate the potential of irisin as a valuable drug target in human disease conditions, additional studies on the aspects of secretion and metabolism of irisin are required.

3. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

We have uploaded the clean version of our manuscript.