

## **ANSWERS TO REVIEWERS**

**Q1. The introduction, materials and methods in the paper work very well, especially Western blot analysis, Proteomic analysis, Fluxomic analysis and Metabolomic analysis.**

A1. We appreciate your kind good impressions about introduction and material and methods, and hope that, after this revision, also the rest of the manuscript has reached the same quality. We have included corrections suggested by the reviewer and by the scientific editor.

**Q2. Results are good, and the figures are clear but the results got in the experiments should be described objectively, not conclusions were made; In addition, the part of discussion is not well discussed combined with results and references and should make some modifications.**

A2. Conclusions have been removed from the results section, in order to be more objective. The discussion has been improved referring to the results and the references, as suggested by the reviewer.

**Q3. The references are not up-to-date, references of the last 10 years should be cited.**

A3. Old references have been removed and substituted with more recent ones, in most cases. In cases where a newer reference has not been found to replace the previous one, the previous reference has been maintained but complemented with an up to date one.

**Q4. The language is not fluent, suggesting that the paper should be language-edited by native english-speaker editors.**

A4. English language has been completely reviewed and corrected by an independent native English-speaker to improve grammar and readability. Particularly, the English revision has been performed by Dr. Serena Rosner, M.D.