Dear Reviewer,

We would like to thank Reviewer 2 for acknowledging the efforts made to improve the manuscript, particularly in clarifying that the proposed NRF2/ETS1 axis is presented as an associative rather than a causal mechanism. However, we note that despite these revisions, the reviewer still raise concerns regarding the lack of direct causal evidence, without suggesting specific additional experiments that would address this point. At this stage, we are confident that we have made all the possible efforts throughout the manuscript to carefully frame our conclusions as associative and to avoid overinterpretation of the data. Further mechanistic dissection of the NRF2/ETS1 relationship would require extensive additional experimentation, which goes beyond the scope of the current study and cannot reasonably be completed within the 10 days of revision timeframe.
Similarly, with respect to the conditioned-medium experiments, we revised the text in the second revision to avoid overinterpretation and now explicitly acknowledge the limitations of these experiments. The discussion has been adjusted to clarify that our findings suggest, but do not conclusively demonstrate, a metabolite-driven effect.

Regarding the presentation of replicates of the western blot data, we are somewhat surprised by the reviewer's comment. As shown in the submitted file, all protein analyses are supported by western blots performed in three biological replicates, as requested. Thus, we sincerely do not understand the specific expectations of the reviewer to meet the journal's standards for data transparency.
Overall, we believe that across the previous two rounds of revision we have carefully addressed the reviewers' comments and significantly improved the manuscript. While additional experiments could certainly further expand on the mechanistic aspects, we respectfully suggest that these would be more appropriate for future studies rather than a requirement for the current submission.
In light of the points outlined above, we hope that we have adequately addressed the reviewer's comments in our previous revisions. We thank you for your understanding and remain at your disposal for any further clarification.

On behalf of all the Authors,
Sincerely,



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