201204_INS_RG_1_REV3

Response to editorial comments/items:

RE: Placental transcriptomes differ in human pregnancies complicated by severe fetal left heart obstruction (our reference 201204-INS-RG-RV-2)

Your manuscript must also address the following items:

1. Ensure that the manuscript title conforms to the strictly enforced 15-word limit.

Checked. Current: 13 words.

2. Confirm that all author names are correct and complete. The published author list will appear as presented in your submitted Word document.

Confirmed.

3. Ensure that protein and gene symbols are formatted correctly and are consistent with NCBI Gene nomenclature. See Gene Nomenclature and Style for details: https://insight.jci.org/kiosks/publish/genestyle.

Formatted and checked.

4. JCI style does not permit claims of novelty unless they are qualified (e.g., what we believe to be novel). Please remove or qualify novelty statements in the abstract and text. Synonyms for novel (new, previously unknown, for the first time, etc.) must also be qualified or removed.

We have carefully reviewed the abstract and main text and have removed or appropriately used qualified statement (e.g. to our knowledge) implying novelty.

5. Per JCI style, statements of significance are limited specifically to statistical significance. Revise other instances to 'substantial', 'marked', or a similar synonym.

We have made these changes accordingly throughout the revised manuscript.

6. For any individuals providing gifts of materials, specify the affiliation and location (including city) in Methods where appropriate.

Not applicable.

7. The provided database for your large data sets, Texas Data Repository, is not sufficient. You must use an MINSEQE-compliant public database as appropriate and provide the accession number in the Data Availability section of Methods in the main text of the manuscript. Please note, the data must be deposited and made public as a condition of acceptance.

We have released the study with dbGaP for individual-level sequencing data under accession number phs004957.v1.p1 and added to the Data Availability section. We have also deposited the de-identified raw and normalized count data in the NCBI Gene Expression Omnibus (GEO), and a GEO accession number has been included (GSE345721). The following secure token has been created to allow review of record GSE345721.

8. For all antibodies used, ensure that the source and catalog/clone number (in the case of commercial antibodies) or a description/reference to a description of the generation of custom antibodies is provided.

The details of the antibodies used, including the source and catalog/clone numbers are provided in Supplemental Table 10

9. Ensure that the source of all cell lines/animals used is indicated.

Not applicable.

10. If this work is funded partially or in full by the NIH, ensure that you have included a statement per the NIH Public Access Policy (https://insight.jci.org/kiosks/nih-access-policy) at the beginning of the Funding support section.

The following statement has been included as per the NIH Public Access Policy. 'This work is the result of NIH funding, in whole or in part, and is subject to the NIH Public Access Policy. Through acceptance of this federal funding, the NIH has been given a right to make the work publicly available in PubMed Central'.

11. Remove all funding sources from the Acknowledgments and create a Funding support section that states sources of support in the form of grants as a list, providing all necessary information; for example, name of the funder(s), grant number(s), and recipient author(s) as appropriate. Include an NIH public access statement, if applicable.

Created a new funding support section.

12. Ensure that all references are present, there are no duplicates, and the reference list is formatted according to journal style (https://insight.jci.org/kiosks/publish/examples). We strongly encourage use of EndNote in Microsoft Word to ensure that the format is correct. Furthermore, limit the use of URLs within the main text to citation of online databases and similar websites; if a URL refers to a publication, convert it to a numbered reference with complete bibliographic details.

References were formatted using EndNote, and the list has been checked.

13. Confirm that you have provided supporting data values associated with the main manuscript and supplement material — including values for all data points shown in graphs and values behind any reported means — in a single Excel (XLS) file (distinct from any other supplemental material) using separate tabs for each applicable figure panel, with clear labeling for each tab. Ensure that the "Supporting data values" file is called out in the "Data availability" section in Methods.

Supporting data values associated with the main manuscript and supplement material are provided in a single XLS file and called out in the data availability section.

14. Please review the final version of the supplement that was included in your submission. The supplemental material will be published exactly as presented.

Reviewed

15. Ensure that all figures are prepared according to journal style (https://insight.jci.org/kiosks/publish/figures); in particular, use 8 pt Helvetica or Arial font for labels, and avoid bold type. More detailed figure information is below:

All Figures:
-Confirm that all of the figures are presented on portrait-oriented pages.
-Remove all bold text from the images, including the labelling text.
-Ensure that the figure legends indicate the statistical test for each applicable panel. For representative experiments, the figure legends should indicate the number of times the experiment was conducted.

Figures are presented on portrait-orientation, removed all bold texts from images, and statistical test indicated for each applicable panel.