We thank the reviewers for their careful consideration, comments and time. Please find our point-by-point response below.

- First, such serial connection of microfluidic system do not only change the oxygen level in the medium, but also the quantity of glucose, serum factors, waste products, etc etc. Therefore, the biological effect observed (albumin production and localization of HF1A) could not be linked only to an oxygen gradient. Two control experiments could be run : one with different oxygen tension in the incubator, or re-using the medium obtained at the outlet of the 8 chambers in a second experiment (and so subjecting the 1st chamber to a normal level of oxygen but lower amount of glucose and different mix of factors).

  We added measurements for glucose and ammonia in the medium flowthrough (outlet) and added these results as a figure in supplementary information. We also performed experiments using hypoxia mimicking chemicals and measured the oxygen levels in the medium (inlet and outlets of different numbers of interconnected MCs).

- Better caracterization of the oxygen gradient would be necessary. In particular, what is the oxygen decrease for a chain of 1MC, 2MC, 3MC, 4MC ? Is there any contribution of the tubing length ?

  We have added the measurements of oxygen in the medium in the outlet after the suggested numbers of MCs. To minimize the influence we used the shortest possible length of tubing for connecting MCs.

- In the introduction, a description of the liver geometry and that hepatocyte zonation is necessary, for example with an illustration, to understand the link between oxygen gradient and the in-vivo situation.

  We prepared and added a graphical abstract and improved the introduction to make this point more clear.

- As the manuscript deals with oxygen control in microfluidic system, a state of the art of the solutions already proposed seems necessary.

  As stated above we improved the introduction and added additional references, both for introduction and discussion.

- Description of the microfluidic chips used has to be completed : material (O2 permeability ?), dimensions of the chambers, material of the tubings (O2 permeability ?).

  We have added information on the material of the MCs used.

  To get more information the company has performed OTR studies, however with different dedicated geometries. The OTR from these experiments was 660.6 ± 15.6 g/m^2 . We did, however, not add this information, since these measurements were not obtained with the MCs used in our experiments.

Minor points:

- In the introduction, the retention of the CDH1 mRNA is not clear and do not bring anything to the manuscript, except an extra self-citation for the authors.

  We removed this citation.

- Better citations could be found for the first concept of culturing cells in microfluidic systems (l.69)

  We added other citations.

- What are the inlets/outlets 1 and 4 ? (l.88)

  We changed/improved the description in the text.

- A short description of the principle of the O2 sensors would be useful !

  We added a schematic diagram from the manufacturer Presens of the O_2 sensor used with some minor adjustments for our experimental setup.