

Response to reviewers' and editorial comments

Editorial comments:

* Some minor edits were made to your manuscript to comply with JoVE format. Specifically, many steps in the protocol were re-written in the imperative tense (do this, mix that, etc.) Please download the updated version of the manuscript from the "file inventory" and use this version for revisions. Please maintain these formatting and content changes throughout all subsequent manuscript revisions.

We have checked these editorial changes and we do approve them.

* Additionally your table of materials was edited to remove all copyright and trademark symbols, which cannot be published anywhere in a JoVE manuscript.

* Your video file could not be properly opened. Please check the file and upload the video in a JoVE supported format (see the instructions for authors).

From the instructions, we do not understand why the video was not functioning. We used what we thought was a supported format. We are providing 3 new formats and hope one of them will be suitable.

* Please take this opportunity to thoroughly proofread your manuscript to ensure that there are no spelling or grammar issues. Your JoVE editor will not copy-edit your manuscript and any errors in your submitted revision may be present in the published version.

We have carefully checked our manuscript again.

Reviewers' comments:

Reviewer #1:

This is a well described technical manuscript that follows a recent publication by the same group now in press in Development (Ref 28 of the present MS).

This new technical manuscript perfectly illustrates and complements the one just published and is important for the scientific community.

I do not have major concerns but only very minor ones:

-1- introduction, line 4: please replace acinar by exocrine as it is mainly duct-like cell lines that have been generated

We replaced acinar by exocrine.

-2- introduction, line 5: islets can in fact be maintained in some cases few weeks in culture without cell proliferation. The authors could change their sentence

We changed the sentence to indicate a culture of weeks instead of days.

-3- Table on organoid medium and other component: the table is a bit difficult to read as the lines are not perfectly aligned. Moreover, the term "EFG" should be replaced by "EGF"

We tried to realign the lines and changed the formatting.

Reviewer #2:

Manuscript Summary:

This is an interesting, accurate and important manuscript that describes for the first time a method to expand mouse embryonic pancreas early progenitors and follow organogenesis in vitro.

The methods are extremely well detailed and documented.

Major Concerns:

N/A

Minor Concerns:

N/A

Additional Comments to Authors:

N/A

Reviewer #3:

Manuscript Summary:

This is a clear and detailed description of 3D culture conditions to grow and manipulate embryonic pancreas in vitro. The study provides good evidence of the advantages and disadvantages of the described system and will be useful to those in the pancreas differentiation field as well as those with different areas of expertise.

Major Concerns:

None

Minor Concerns:

In 1.3.1 of the protocol, it would be useful to precisely indicate which inner organs.

We did indicate which inner organs.

Additional Comments to Authors:

N/A