Dear reviewers,

I would like to thank you all the kind comments about our article. Your suggestions have greatly improved the manuscript.

English grammar and style of the paper has been corrected by a proofreading and editing service (we have attached the non-native certificate along with the rest of the documents).

We also answered point-by-point all the queries raised by the reviewers.

1) We have replaced the "tumorgraft" with "tumour xenograft" through the manuscript
2) We also changed "There were no statistical differences..." for "There were no significant differences…" (pages 4, 13, 14, 16).
3) In the "Abstract" section, the results have been clarified and the conclusion has been re-written in an appropriate way.
4) The explanation/legend for Table 4 was expanded. The procedure for the measurement of cell proliferation (Ki67), cell death (TUNEL), angiogenesis (CD31) and fibrogenesis (α-smooth muscle actin, or alpha-SMA) has been indicated in the table and legend.
5) Statistics have been reviewed by an biostatistician (Bioestatistic Statement has been attached)
6) The information and bibliography regarding the use of CD31 as a marker of angiogenesis and alpha-SMA as a marker of fibrogenesis in pancreatic cancer has been included.

   Page 18: "…Regarding tumour angiogenesis, the evaluation of tumour vascularisation is important in the investigation of pancreatic cancer. The extension of the vascular network is fundamental to assess the response to the treatment of antitumor drugs. Multiple authors use a microvessel density analysis system by CD31 expression in pancreatic PDX similar to ours. [5, 33, 34]"

   Page 17: "…The election in our study of alpha SMA as a marker for fibrogenesis is based on the intense desmoplasia presented by pancreatic tumours. The pancreatic stellate cells involved in tumour desmoplasia are characterised by expressing α-SMA and by the synthesis of procollagen a-1T which are the main components of the extracellular matrix that constitute desmoplasia.[31, 32]"

7) We have included images of tissue H&E and Masson staining, and immunohistochemistry analysis (Ki67, CD31, TUNEL and alpha-SMA) from the three PDX experimental through F1, F2 and F3 stages. We have also included an image of the skin tumour area from subcutaneous xenografts.
8) We have corrected the drawback observed within the "Discussion" section:

Page 15: "...The apparent lack of correlation between any of these parameters, together with the rate of engraftment, may reflect a biological phenomenon, or it may be simply being due to an insufficient number of human tumours in some groups. However, similar results have been obtained in other studies [25]. This could be one of the limitations of this study. For this reason, new studies with higher numbers of participants are required. In addition, a genetic assessment of the samples could have enriched the study and might have explained this phenomenon".

Page 16: "…The practical utility of tumour xenografts needs to be addressed in terms of engraftment speed and reproducibility. In fact, tumour xenografts show a rather limited engraftment rate and slow tumour growth. However, those models are readily applicable for drug experiment because, once a xenograft has been successfully engrafted, it can be used after several freeze-thaw cycles and several passages[5].

9) A sentence referring to the aggressiveness of the tumour itself as a reason by which the pancreatic and intraperitoneal models grows better that the subcutaneous model has been added in the "Discussion" section

Page 16: "…Pancreatic and intraperitoneal models are more invasive and thus might include more suffering/physiological burden in a mouse. That might be one of reasons why the tumour xenograft grows better subcutaneously".

Page 19: "…Intraperitoneal and pancreatic PDX models presented a greater morbidity and mortality than subcutaneous model"

Yours faithfully

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