3rd June 2016
Dear Editor,

Title: Therapeutic potential of targeting acinar cell reprogramming in pancreatic cancer ESPS Manuscript NO: 26444

Thanks for revising the manuscript. Improvements have been made based on the suggestions of reviewers.

Responses to the Reviewer #2

Comment 1&2) Several grammatical mistakes and misspellings are present in whole the text. There are several redundant descriptions in whole the text.
Response: We are sorry for the substandard English used and the misspellings made in the manuscript. We have carefully revised the manuscript and have improved the language.

Comment 3) In addition to KRAS mutation, p53 mutation is detectable around 75% of pancreatic cancer. However, the authors did not mention this issue.
Response: Thanks for the suggestion of including p53 mutation that is important in PDAC in the manuscript. Since some studies suggested that p53 may not be involved in ADM but in the development of higher grades PanINs and PDAC, more studies are needed to confirm the role of p53 in ADM. However, one p53-related pathway: PI3K/Akt signaling which is involved in ADM is now added in the review.

Comment 4) Among various molecular targets for the inhibition of ADM, which target(s) the authors recommend as the most promising one?
Response: Thanks for the reviewer's suggestion. Among those potential methods in PDAC reprogramming, more studies are needed to confirm the success in reprogramming. For example, since mRNA level of acinar markers such as amylase is only tested for DKK3 knockdown in PDAC cell line, the changes in protein level of acinar markers is needed to be studied. Also, for PD325901 which is only tested in PanIN, in vitro and in vivo studies using PDAC are also needed.

Comment 5)"Therapeutic targets in PDAC Reprogramming" should be shortened. Too long.
Response: Thanks for the reviewer's suggestion. We have revised the title as "Targeting PDAC Reprogramming"

Sincerely,

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