

Dear Editors and Reviewers:

Thank you very much for your letter and for the reviewers' comments concerning our manuscript entitled "MiR-29a up-regulation in AR42J cells contributes to apoptosis via targeting TNFRSF1A gene". Those comments are all valuable and helpful for revising and improving our paper. We have studied the comments and suggestions carefully and made corrections which we hope meet with approval. Here, we provide the detailed answers to each question and suggestion.

Reviewer 1

The manuscript demonstrated that miR-29a, which has been demonstrated to play an important role in apoptosis, is elevated significantly in acute edematous pancreatitis. The data are interesting and the experiments are well-organized. Those findings give novel information on the pathogenesis of acute pancreatitis. However, the differences and similarities between chemically-induced acute pancreatitis and acute pancreatitis in humans, which is mostly caused by gallstones or alcohol, are unclear. The authors should discuss on that point.

Our response

Thank you for your comment.

In this research, we focused on apoptosis in acute pancreatitis. Apoptosis is an important pattern of pancreatic acinar cell death in acute pancreatitis. We established AEP model by injecting rats with L-arginine and the result of TUNEL assays confirmed that apoptosis occurred in pancreatic acinar cells. We also induced the AR42J cells to apoptosis by using recombinant rat TNF- α . Apoptosis happened in our chemically-induced acute pancreatitis model and in the acute pancreatitis caused by other reasons such as gallstones and alcohol in humans. In the Discussion section, we added the suitability of the L-arginine model to AEP human disease.

Reviewer 2

It is necessary to clarified the sample size of the experimental study. And clarified the suitability of the L-arginine model to AEP human disease. In the Results section there are many phases that corresponds to Methods section.

Our response

Thank you for your comment.

In the Materials and methods section, the sample size of the experimental study has been added (We added n=6).

In accordance with your suggestion, we added the the suitability of the L-arginine model to AEP human disease in the Discussion section.

We adjusted the order of the Results section and now Result section corresponds to Methods section.

Thank you and best regards.

Yours sincerely

Qiang Fu