Dear Dr. Ying Dou:

Thank you for your decision letter on our submitted manuscript (ID:46809) entitled "c.753_754delAG, a novel CFTR mutation found in a Chinese patient with cystic fibrosis: A case report and review of literature". We would like to thank the reviewers for their constructive and positive comments and suggestions for revision of the manuscript.

We have revised the manuscript accordingly and it is attached to this letter for your consideration. All amendments are highlighted in red text in the revised manuscript. In addition, point-by-point responses to the reviewers' individual comments are listed below.

We hope that the revision is now acceptable for the publication in your journal and look forward to hearing from you soon.

Yours sincerely,

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Responses to Reviewer's comments

1. p. 1: in the title, maybe, it is better to replace "review of literature" with "review of published CF patients in China", if it is not too long

Response: Thank you for this comment. Corrections of title have been made in the revised manuscript.

2. p. 6, physical examination: you should add the girl's height and percentiles, and calculate also body mass index and percentiles

Response: Thank you for this comment. Height and body mass index have been added in the revised manuscript to address this.

3. p. 6, laboratory examination: did you perform any test for pancreatic insufficiency e.g. stool elastase or faecal fat excretion test?

Response: Thank you for this comment. We didn't perform the test for pancreatic insufficiency e.g. stool elastase or faecal fat excretion test due to the limitations of laboratory conditions

4 . p. 7, imaging: can you explain a bit more this focal liver lesion, as it is not typical for CF. Did you perform liver biopsy?

Response: Thank you for this comment. We didn't perform the liver biopsy. In patients with cystic fibrosis, the liver is also the organ affected by the dense secretion of digestive juice. Bile secreted by the liver can clog bile ducts and damage the liver. Liver CT scan revealed a low-density lesion in the left lobe of the liver. Explainations has been added in the revised manuscript to address this.

5. p. 7, imaging: instead of “Echocardiography of pancreas …” you probably meant “Ultrasonography … “ or “Echography of …”.

Response: Thank you for this comment. It refers to Ultrasonography of pancreas.Corrections have been made in the revised manuscript.

6. p. 8, Fig. 3: You show 3 different DNA sequences and wrote that the mutation of CF patient and mother is seen. But the pattern is similar but not exactly the same between patient and father. Is the figure right? Can you explain?

Response: Thank you for this comment. The figure is right, which shows the forward sequence of the locus. Because of the frameshift mutation exists the monther’s positive sequence, the forward graph is not available and can be represented by the reverse sequence graph. The graph of reverse sequence has been shown in the revised manuscript. CFTR genomic sequencing results for exon 7 show a heterozygous mutation of c.753_754delAG chr7-117176607-1171766 08 p.R251Sfs*6 in the CF patient and her mother. Exon 7 of CFTR was normal in her father.

7. p. 9, treatment: which antibiotic did you prescribe and for how long?

Response: Thank you for this comment. We give the antibiotic treatment with ceftazidime for 3 weeks.

8. p. 9, nutritional support: can you describe “nutritional support” more in detail. Which kind of food and advice was given?

Response: Thank you for this comment. nutritional support treatment

including fat-soluble vitamins, powdered milk with high calorie.

9. p. 10, follow-up: what was nutritional status (body weight, height, and BMI)? Did you manage to eradicate P. aeruginosa infection? How did you check for pulmonary disease regression/progression? Did you introduce any regular physiotherapy or some treatment for pulmonary disease?

Response: Thank you for this comment. After being discharged from our hospital , the children was followed up monthly in the outpatient clinic. She had one time of pulmonary infection .The general situation remained well up to date. she weighed 13 kg, height was 95 cm, body mass index was 14.4. We give the low dose azithromycin anti-inflammatory treatment to eradicate P. aeruginosa infection. We do regular examinations of respiratory rate,oxygen saturation and high resolution CT of chest to evaluate the pulmonary disease regression/progression. We introduce regular atomized bronchodilators such as terbutaline and oral secretion expellant including acetylcysteine to help remove respiratory secretions. These treatments have been added in the revised manuscript to address this.

10. p. 16, discussion: you have to adapt the last two sentences. As it is not clear from your case if the patient had pancreatic sufficiency or insufficiency you cannot conclude like this. Elevated serum lipase, which has not been mentioned before, is not a sign of severe mutation, more of possible pancreatitis which is more commonly seen in heterozygous CF carriers or in those with milder mutations and pancreatic sufficiency. Please,

discuss and/or adapt.

Response: Thank you for this comment. Discussion has been added in the revised manuscript to address this.

11. p. 18 and p. 24; references: references no. 5 and 41 are the same.

Response: Thank you for this comment. Corrections have been made in the revised manuscript.