I appreciate the review of my manuscript and I am very pleased with the valuable comments.

I would like to resolve all issues raised in the peer review report and make a point-by-point response.

1. *However, the editorial mainly descripts the metabolome results on HCV related liver fibrosis, lacking the in-depth comparison between the recent study (Ref.19) and the previous results (Ref. 13-18).*

   Thank you for your comments. I made in-depth comparison between the recent study (Ref.19) and the previous results (Ref. 13-18) and clarify in the documents.

   I have added the following sentences.

(Page 6) Consistent with the findings by Cano *et al*. (15), detection of sterols, such as 18:0 and 20:5 cholesteryl esters, among patients with F1 fibrosis revealed downregulation of cholesteryl esters in rapid "fibrosers." Furthermore, the detection of diacylglycerols among patients with F1 fibrosis supported previous results that diacylglycerols were downregulated in patients with severe fibrosis (16). Conversely, the significant upregulation of acylcarnitines among patients with F4 fibrosis mirrored the hyper-carcinogenic state observed in HCC patients (13). These studies have provided useful information regarding detection of the

fibrosis grade and underlying pathways in HCV infection.

2. Furthermore, the innovative explanation of the current research (Ref.19) and the potential values of these metabolome techniques are needed to be expounded.

I agree with your comments and clarify the advantage of the current research (Ref.19) and advantage of metabolome study.

I have added the following sentences.

(Page 5) ESI is a soft-ionization technique that limits ion excitation, resulting in minimal or no analyte fragmentation (20). This ionization technique has revolutionized the analysis of large biomolecules, such as the detection of coenzyme A in the present study.

(Page 4) Metabolomics offers a unique advantage because it represents the current physiological "state" of an individual, allowing exploration of factors that influence the human phenotype.