Reviewer’s report

Title: Infection with HIV and HCV enhances the release of Fatty Acid Synthase into circulation: Evidence for a novel indicator of viral co-infection

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Reviewer: Munechika Enjoji

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This paper reports the findings that HIV-infected patients show significant elevation of serum FASN levels compared with uninfected individuals and the increase is greater in HCV co-infected patients. Authors are exploring the new clinical possibility of measuring serum FASN concentrations in HIV-infected patients, I think. However, in some points, I cannot understand authors' explanation well.

Major comments

1. As is generally accepted, host lipid metabolism is frequently altered by antiviral therapies. To get fundamental evidence, patients under antiviral treatments should be excluded at first and authors should simply compare treatment-naïve patients with control.

2. Circulating FASN may be from hepatocytes in HCV-infected patients. Where is FASN mainly originated from, T cells, adipocytes, hepatocytes, muscle...? Is the correlation between FASN and CD4 count meaning that T cells are the FASN provider?

3. Authors think of estrogen as a stimulator of FASN expression. Why are FASN levels in females (HIV+, HCV-) lower compared with males or control? Do you mean that estrogen expression is suppressed by HIV infection? Fig 1B and C: in female patients, HCV (infection to the liver) appears predominant effector for FASN up-regulation.

4. Authors mentioned the association between the FASN levels and insulin resistance many times. However, insulin resistance is not found in HOMA-IR in patients (Table 2, 3). Please explain it.

5. “Hypercholesterolemia and low HDL-cholesterol levels were more prominent in HCV co-infected patients and in those under PI treatment”, authors wrote. But no evidences are found in the data (Table 2, 3).

6. Authors wrote, “FASN release is an active and controlled process through the activation of AMPK” and “upon AMPK activation, the release of excess FASN may provide a rapid mechanism to prevent further energy consumption”. In my knowledge as a general notion, AMPK activation induces the suppression of FASN and ACC which are enzymes for fatty acid synthesis. This appears contrary to your explanation.
7. FASN and ALT levels show strong correlation and their concentration is much higher in HCV+ patients (ALT levels are within the normal range in HCV-negative patients). This means that their elevation results from cell death (mainly by liver damage) and leakage?

8. As demonstrated in many studies, HCV infection directly induces FASN expression in hepatocytes. Are there some similar pathways for FASN induction in HIV-infected cells?

Minor comments
1. “Evidence for a novel indicator of viral co-infection” in the title means that serum FASN concentration is clinically meaningful for HCV+HIV co-infection but not for HIV infection?

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests