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

Version: 1 Date: 1 February 2010

Reviewer: Qiang Liu

Reviewer’s report:

Gerard Aragonès et al. evaluated the use of the level of circulating fatty acid synthase (FASN) as an indicator for HIV and HCV co-infection. The major finding of this work is that, in comparison to healthy individuals, the levels of FASN are significantly higher in HIV-infected individuals and co-infection with HCV further and significantly increases FASN. Since infections of both HIV and HCV have been associated with metabolic abnormalities, characterization of FASN, a key player in the host lipogenic pathway, is important for understanding pathogenic mechanisms by these two viruses. As such, this article investigated an important question. The experimental design, interpretation of the data, and discussion are sound in general. However, the following points need to be addressed prior to its acceptance for publication.

1. The impact of viral load on FASN levels? FASN levels are significantly higher in HIV patients than healthy individuals (Figure 1A). Does this include subjects with undetectable and detectable HIV viral loads? If so, it would be interesting to further compare the FASN levels between these two groups. As well, co-infection with HCV further increases FASN with statistical significance (by the way, this should be stated clearly in the second paragraph of the Results session). It would be critical to include the information of HCV infections, such as viral loads and genotypes because different HCV genotypes may play different roles in modulating lipid metabolism.

2. The authors were not able to correlate the increased FASN levels with expected changes in non-esterified fatty acids in HIV patients. Is this also the case for HCV co-infections? The authors should perform this experiment which will provide evidence supporting their hypothesis where they believe FASN expression is regulated by a unique mechanism in HIV infection and not in HCV infection (in the middle of the first paragraph in the Discussion).

3. In an effort to correlate FASN levels with inflammation, the authors measured a number of markers such as IL-8 and MCP-1. HCV co-infection increases IL-8 levels but does not reach statistic significance (Fig. 2C). This seems at odd with previous findings where the IL-8 levels are significantly higher in HCV infected patients than healthy controls (e.g., Polyak, et al., JVI, 2001). Reasons for this discrepancy should be discussed.

4. The authors have found increased MCP-1 levels which showed a good correlation with FASN levels. While this seems to fit with the role of MCP-1 in modulating lipogenesis, the lack of an effect of HCV infection on MCP-1
expression is somewhat puzzling (Fig. 2A). Once again, do the MCP-1 levels correlate with HIV and/or HCV viral loads?

Minor point:
Please number the pages and lines.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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.