Reviewer's report

Title: Detection of allele specific difference of IL28B mRNA expression

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Reviewer: Tai-Chung Tseng

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General Comments:
Variants of the interleukin-28B (IL28B) gene have been associated with both spontaneous and treatment-induced clearance of HCV infection. Attempts to link polymorphisms of the IL28B gene with variation in the level of IL28B expression have been inconclusive.

In this paper, Knapp et al developed an assay, which allows the relative quantification of the two IL28B transcripts in cells heterozygous for IL28B.rs4803217 in the 3'UTR of the IL28B gene and in strong linkage disequilibrium (LD) with the predictive marker rs12979860. The authors claimed that he could differentiate mRNA from different alleles of rs12979860.

Although this assay is interesting, the results are not convincing. In addition, I could not see clinical significance of this assay in the study. Finally, the PBMC data did not support that his assay could be linked to clinical samples. The details are listed in the major comments.

Major Comments:

1. The authors used figure 3 of “relationship between dCt and varying ratios of allele 1 (allele A) and 2 (allele C)” to show their assay is robust. However, I can not understand the figure well. For example, what does HET HH23 mean? In addition, such the presentation is not convincing either.

2. If the author would like to address that IL28B mRNA expression level is different between C allele and T allele of rs12979860, the author should first show the mRNA level in liver is different between patients with CC genotype and those with TT genotype in rs12979860. Obviously, I did not see the data. Even if it was true, the authors should show that C allele-specific mRNA level is higher that T-specific mRNA level in patients with heterozygous. The data from patients’ PBMC did not support it.

3. The authors showed that the correlation between rs12979860 and rs8099917 is not strong, which is obviously against the current knowledge. I doubt whether their genotyping assay is correct or not.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

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