Reviewer’s report

Title: Hepatic inflammation mediated by hepatitis C virus core protein is ameliorated by blocking complement activation

Version: 1 Date: 26 September 2008

Reviewer: Jefferson Chan

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BMS-Medical Genomics Manuscript-Chang, Bissell et al.

In this manuscript, Chang et. al. examined the pathogenesis of inflammation and fibrosis associated with chronic hepatitis C infection. A Tet-inducible model was used in which HCV core protein is expressed in adult mouse hepatocytes to mimic more closely the situation in human HCV infection. The main findings in this paper are: 1) expression of HCV core at intermediate levels leads to liver damage, oxidative stress and steatohepatitis; 2) expression at high or low levels leads to steatosis only; 3) degree of steatosis correlated with level of core expression; 4) complement pathway genes (and other genes) were found to be altered by Microarray analysis; 5) treatment with CD55 (decay accelerating factor for complement) protects against liver damage in transgenics.

Major points

1) Inflammation was minimal to none (at least histologically) in transgenics expressing high levels of core protein. Yet gene expression analysis showed changes in complement pathway genes as in transgenics expressing intermediate levels of core. Is the complement pathway activated only in intermediate core-expressor but not in high expressors? Could pathology in this model mediated by another (or more than one) pathway?

2) Genes identified in the Microarray studies should be shown instead of just listing the categories.

3. Show qPCR results in a table or graph for each of reading.

Minor points

4) Organ names should be used in labeling of figure 1G, H, I, instead of numbers.

5) Label for Y-axis is missing in Figure 1J.

6) Upper labels are in Table 1 are not separated.

7) Errors, missing words, etc

-page 8, line 12…”total 30 genes..” should be “a total of 30 genes…”
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.