Reviewer's report

Title: Experimental infection of Balb/c nude mice with Hepatitis E virus

Version: 3 Date: 16 January 2009

Reviewer: Saleem Kamili

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The data presented in this paper show that swine isolate of HEV can be transmitted to Balb/c nude mice. Development of a mouse model for hepatitis E virus infection will certainly help in addressing many outstanding issues in the pathogenesis and replication strategy of HEV.

Although, the language of the paper has been improved from the first version, it still needs a major revision and editing by an English editor.

I have following specific comments for the authors:

Background:
The Background is written incoherently with extensive redundancies and all stressing on the zoonosis of HEV infection. Till date the only conclusive molecular evidence that HEV infection is transmitted from animals to humans has been published from Japan; viral genomic sequences of amplicons from the deer or boar meat were identical from the patients who had developed HEV infection after ingesting this meat. The authors create an impression in the readers’ mind as if HEV is frequently transmitted from animals to humans “Hepatitis E has become a widespread zoonosis”. This is simply not true. Similarly, statements like “Rodents are considered to be a potential reservoir for human transmission…” is not correct. Till date, to the best of my knowledge, HEV RNA has not been detected in rats anywhere. The Introduction of the manuscript starts with an incorrect statement like “Hepatitis E (HE) is an acute fulminant hepatitis in adults”. Hepatitis E is an acute self-limiting disease in adults!

Please rewrite the Background and make a case why there is a need to develop a small animal model for HEV infection.

Methods

ELISA determination:
Please delete “serum was prepared from blood……20 min”. This is too commonplace to be included in the methods.

RT-PCR detection
Please replace the text “A reverse transcription analysis was conducted……” with a simple statement like “reverse transcription was performed using……”

The oC is missing from all the temperatures shown in the RT-PCR protocol.

Results:

Please describe what were the criteria of “apparent clinical disease” in mice.
Why was not the PCR for negative strand of HEV RNA performed on the tissues harvested from the infected mice?

The activities of liver enzymes: Please delete the first sentence.

Discussion:

The authors need to clearly what they mean by clinical signs of infection in mice. Viral antigen and HEV RNA detection in various tissues are not “typical symptoms” but are evidences of infection and viral replication.

References #11 and #34 are the same references. Please make necessary corrections in the citation and the bibliography.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**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