Hypothesis for the turnover of HCV to mouse mammary tumor virus like: a novel ultrastructure prospective

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Abstract
Hepatitis C virus (HCV) is a rising cause of morbidity and mortality worldwide. The present work gives emphasis on the ultrastructural study of the infected liver cells and the virus–hepatocyte interactions. Increased knowledge concerning this issue may be the keystone for better management and new regimen of treatment for this disease. The material of this study consisted of 65 needle liver biopsies taken from patients proved positive for HCV-RNA by polymerase chain reaction. The liver biopsies were processed for light and electron microscopic examination. Ultrastructural findings of this work supported a new hypothesis for the turnover of HCV to mouse mammary tumor virus like. The study postulates that HCV has the capability to progress, assemble, and replicate into retrovirus depending on the host hepatocellular structure. This hypothesis may pave the way for deeper studies that can lead to the production of HCV vaccine and to understand the relation between the high incidence of hepatocellular carcinoma and HCV infection.

Introduction
Hepatitis C virus is a rising cause of chronic liver disease and hepatocellular carcinoma worldwide [1, 2]. Its prevalence among the Egyptian population ranges from 6% to more than 14% [3]. Understanding of the pathological liver changes accompanying the infection still need more investigation specially it was proved extremely difficult to visualize virus particles from infected serum and tissues directly [4].

Material & Methods
The material of this study consisted of 65 needle liver biopsies. They were collected from patients having positive serum HCV RNA, of genotype 4 and not suffering from any other associating liver diseases. Informed consent was obtained from all patients according to the rules of Declaration of Helsinki. Liver biopsies were processed for light and electron microscopic study. The stage of fibrosis and grade of activity were evaluated according to the METAVIR scoring system. Electron microscopic examination was done using Philips EM 208S.

Results
Four main morphological cellular changes were disclosed in the examined ultrathin liver sections: Mitochondrial alteration, intracellular fat deposition, cytoplasmic membranotubular structures, and excessive electron-dense proteinaceous materials in the cytoplasm or distending the endoplasmic reticulum. HCV virion particles of about 40 to 55nm in diameter with fine surface projections were depicted in one of the examined cases. Also rough endoplasmic reticulum with ruffled end studded with regularly arranged spike like proteinous material taken the picture of racquet-shape appearance was often seen in the examined sections. They were of moderately variable size ranging between 100 to 300 nm and mimic the mouse mammary tumor virus [5] (Fig.1a). In consequence, the authors of the present work proposed an ultrastructural scenario for the potential capacity of the detected HCV virion to transfer into mammary tumor virus like. This scenario starts by viral invagination into mitochondria. This is followed by the formation of electron-dense lamellar structures or paracrystalline filaments in their matrix.
and integration of the latter with the cytoplasmic rough endoplasmic reticulum. The integrated endoplasmic reticulum with the lamellar structures, presumed to be of viral origin, encircle the mitochondrial liberated matrix and constituting the viral core with tail or lamellar extension. The end result is the formation of structure that mimics the mouse mammary tumor virus [Fig.2a – 2b].

Our hypothesis is supported by the results of the cell culture infection model for hepatitis C virus done by Gastaminza et al. [6]. They reported that the infectious HCV particles are assembled intracellular and the biochemical composition of the intracellular infectious particles differ from that of the infectious particles in the supernatant. Also, this hypothesis can clarify the cause of the difficulty that faced researchers to produce culture system supporting virus production and the difficulty to visualize virus particles from infected serum and tissues directly [4].

**In conclusion** this study may be step forward to understand the intracellular behaviour of HCV virion and open new prospect for the production of curative treatment and vaccine production. Also, it may point to the cause of the increase incidence of hepatocellular carcinoma in HCV infected liver.

**Reference**


