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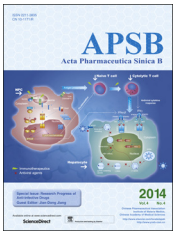

ORIGINAL ARTICLE

Replication priority of hepatitis C virus genotype 2a in a Chinese cohort

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Abstract HCV genotypes have been documented in clinical practice. The aim of this study was to determine the replication priority of different HCV genotypes in a Chinese HCV positive cohort. Serum samples from 491 apparently healthy Chinese blood donors testing positive for HCV antibodies and naive to antiviral drug therapy were tested. Genotyping analysis showed that genotypes 1b and 2a were predominant and accounted for 77.6% of the HCV infections. Among the genotype groups, individuals infected with genotype 2a had an HCV RNA viral load (10^8 copies/mL) about 200-fold (lg, 2.3) greater than those infected with other genotypes (10^4–10^5 copies/mL) indicating a replication priority of genotype 2a. However, there was no correlation between HCV genotype and antibody response suggesting that the amplification advantage of genotype 2a results from a favorable interaction with the host cellular environment. In conclusion, HCV genotypes 1b and 2a are the predominant genotypes in China and genotype 2a possesses a significant replication priority compared

Abbreviations: EDTA, ethylenediaminetetraacetic acid; GPT, glutamate-pyruvate transaminase; HCV, hepatitis C virus; NS3, NS4 and NS5, non-structure protein 3, 4 and 5; RdRp, RNA dependent RNA polymerase; SVR, sustained virological response

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with the other genotypes. This suggests the existence of host cellular factors that may act as drug-targets for entirely clearing HCV infection in the future.

1. Introduction

Hepatitis C virus (HCV) belongs to the family *Flaviviridae* and is a single-stranded RNA virus with genetic variability. The genetic diversity extends to seven major genotypes with 30–35% difference at the nucleotide level[1]. In relation to the response to antiviral therapy, HCV genotypes 2 and 3 show a greater therapeutic response to interferon/ribavirin regimen than the other genotypes especially in the initial stages of treatment[2,3]. Epidemiologically, genotype 1 is the most widespread globally and is the most prevalent of the seven; genotypes 2 and 3 are common in the far East; genotype 4 has been documented in the Middle East and North Africa, genotype 5a in South Africa and genotype 6 in Southeast Asia[4–6]. HCV genotypes are also associated with disease progression; for instance, Japan-specific HCV genotype 1b (J subtype) shows a low pathogenicity[7]. To further understand the biological significance of HCV genotypes, we investigated the prevalence, viral replication priority and characteristics of the antibody response for each of the genotypes in blood samples from an HCV positive Chinese cohort of blood donors not previously treated with any antiviral agent. The results provide an opportunity to examine the HCV replication capacity of the different genotypes in an infection course free of drug intervention.

2. Materials and methods

2.1. Serum samples

Serum samples from 491 seemingly healthy blood donors (297 male, 194 female; age range 18–60; average age 36.8) collected at the Langfang Blood Center (about 200 miles South of Beijing, China) were selected based on a positive test for HCV antibodies and no history of antiviral drug therapy (*i.e.* this was the first time HCV antibodies were detected). Of the 491 individuals, 166 showed an elevated liver transaminase indicating an abnormality in their liver function. Blood was collected into EDTA tubes followed by serum isolation by centrifugation at 1000 rpm for 10 min at room temperature. Serum samples were stored at −80 °C prior to testing. The study was approved by the Research Committees of the Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, and the National Institutes for Food and Drug Control.

2.2. HCV testing

Serum HCV antibodies were detected using the Abbott HCV antibody detection kit (Axsym System HCV version 3.0). Quantitation of HCV RNA was done using the Cobas HCV RNA kit (Roche, New Jersey). HCV genotyping was carried out using a kit from Ningbo Ruixin Biotech Inc. (Ningbo, China) and a Boao-5800 microarray reader (Beijing, China). To explore the antibody response characteristics of each HCV genotype, the antibody reaction to the HCV epitope antigens Core, NS3, NS4 and NS5 was examined using an HCV antibody detection kit from Jin-Wei-Kai Biotech Inc. (Beijing, China). All tests were performed in triplicate according to the manufacturers' instructions. The antibody response was taken as positive when the average S/C value >1. The antibody positive rate to HCV epitopes of serum was calculated as positive number detected/total number detected × 100%.

2.3. Statistical methods

Differences in mean viral load among study groups were tested using the Student's t-test for equal or unequal variances depending on a preliminary F test for homogeneity of variance.

Table 1 Blood viral RNA load in individuals infected with different HCV genotypes.

Genotype	Group size[a] (female/male)	HCV RNA viral load (copy/mL)		P[c]
		Mean	SE[b]	
1a	33(13/20)	1.63×10^4	3.67×10^3	
1b	204(80/124)	6.17×10^5	3.70×10^5	0.006
2a	177(77/100)	1.12×10^8	4.89×10^7	
2b	33(11/22)	2.91×10^4	1.15×10^3	
3a	13(3/10)	1.67×10^4	6.66×10^3	
3b	9(3/6)	1.78×10^4	3.67×10^3	
6	12(2/10)	4.31×10^5	3.64×10^3	
Unidentified	10(5/5)	3.31×10^5	5.03×10^4	

[a]Number of subjects.
[b]Standard error.
[c]1b *vs* 2a, using unpaired Student's t-test.