Molecular epidemiology of HBV and HCV infection in Greece

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VIRAL HEPATITIS PREVENTION BOARD MEETING
Molecular epidemiology studies implementing modern tools (phylogenetics and phylodynamics) can provide answers about:

- The “type” of the circulating viral strains.
- The dispersal of viral epidemics.
- The origin of viral infections.
- The date of the first introduction of an epidemic.
- The temporal trends (growth rate) of an epidemic.
Molecular epidemiology of HBV infection
HBV has been isolated from humans, apes and new world monkeys (woolly monkeys).
HBV sequences from humans have been classified into eight genotypes (A-H) differing by at least 8%.
Additionally, three clades of HBV isolates from apes (chimps, gibbons and orangutans) appear to be additional genotypes of HBV.
Numerous subgenotypes of HBV have been described.
HBV genotypes and subgenotypes show a distinct geographic distribution.
Phylogeny of HBV from humans and apes

Woolly monkeys

F
H
G
D
E
B
A
C

Humans
Chimps
Gibbons
Orangutans
Gorilla
Origin of HBV
HBV genotypes and subgenotypes

Schaefer 2007
Geographic distribution of HBV genotypes

Schaefer 2007
Prevalent HBV genotypes in Europe

Schaefer 2007
Distribution of HBV genotypes in Europe

Schaefer 2007
• Genotypes H and F are outliers to the HBV sequences from humans and apes.
• The distribution of HBV genotypes differs greatly according to the geographic region.
• Genotype A prevails in Central and Northern Europe.
• Genotype D circulates at a high frequency in Southern Eastern Europe.
• Additionally, almost all HBV genotypes were detected at a low prevalence.
HBV genotypes in Africa

Kramvis et al., 2007
Molecular epidemiology of HBV infection in Greece
• HBV genotypes were determined in 64 patients as part of drug resistance testing.
• 58 of the patients were receiving antiviral treatment and 6 were treatment naïve.
• Phylogenetic analysis of HBV sequences in partial pol (aa 118-356) from 64 patients in Greece revealed:
  • 56 (87.5%) clustered as genotype D
  • 6 (9.4%) and 2 (3.1%) fell within genotypes A and G, respectively.

Magiorkinis et al, 2007
HBV genotype D is the most frequent (88%) clade in Greece. Genotypes A and G were also detected. A detected at a higher prevalence than G. 23 out of 56 genotype D sequences (41%) isolated from patients in Greece fell within a monophyletic cluster. Therefore, HBV infection spreads within Greece. Previous findings are in accordance with epidemiological information. Our findings are in accordance with a previous study (Dimou et al, AASLD 2003).
Molecular epidemiology of HCV
Previous classification of HCV
Current classification of HCV

Timm and Roggendorf 2007
African origin of HCV

Western countries

Sub-Saharan Africa
Southeastern Asia

Simmonds 2001
Global distribution of HCV genotypes

Available at http://hcv.lanl.gov
HCV genotypes in Europe

Available at http://hcv.lanl.gov
Molecular epidemiology of HCV infection in Greece
Blood samples were retrieved from 1686 HCV-chronically infected patients during 1987-2002.

HCV genotypes were determined in 1585 patients by using Inno-Lipa method on the 5’-noncoding region of HCV.

41 samples typed as genotype 4 were further analyzed by DNA sequencing and phylogenetic analysis in partial NS5B.
Prevalence of HCV genotypes in Greece

Katsoulidou et al., 2006
HCV genotypes in Greece

Katsoulidou et al, 2006
HCV genotypes in Europe
Putative origin of genotype 4
HCV genotypes in Africa
Analysis of HCV genotype 4

Katsoulidou et al, 2006
Estimated incidence of HCV infection

Katsoulidou et al., 2006
### Results of molecular clock analysis

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Magiorkinis et al, 2006
Several different HCV genotypes were detected in Greece.
HCV infection, in contrast to HBV, isn’t similar to other Mediterranean countries.
Most of the patients infected with genotype 3 were IDUs.
Most of the HCV 4 sequences were classified as 4a.
The estimated incidence of genotype 3 increased dramatically in the late 1970s.
Dating of the HCV 3a revealed that the epidemic originated in early eighties in Greece.