HBV safety subgroup

Brief report
Main areas of new research

• Mechanisms of OBI
• OBI and cellular immunity
• Infectivity of OBI
Mechanisms of OBI

- The main advance is the change of concept that the defect in production, excretion and detection of S protein/HBsAg is a major cause of OBIs.
- The mutations leading to changes in RNA folding interfered with S mRNA splicing that plays a role in HBsAg production.
- The amino acid substitutions accumulated in the S protein MHR and extra MHR domains interfere with:
  - Viral replication
  - S protein production and export
  - HBsAg detection
Potential mechanisms of OBI

(El Chaar, Hepatology, 2010; Svicher, Antiviral Research, 2012; Martin, J Vir Hep, 2012; Huang, J Hepatol, 2012)

CCC DNA → OBI-specific mutations

Nucleotide level

Affects S RNA splicing

Spliced proteins
A453G
G458A
G463A

HBsAg production?

HBsAg detection
Y100S
R122P
C124R/Y
C137W/Y
C139R
T140I
K141E
D144A

Amino acid level

In MHR

Affects

HBsAg replication
S136P
C139R
D144A

Outside MHR

Affects

HBsAg excretion
D119R
Q129R
G145R

HBsAg excretion
M75T
P178R
OBI cellular immunity

• An article was published by S Sauleda’s group:
  Results suggest that most OBIs whether or not with detectable anti-HBs are recovered infections.

• A similar study is ongoing in collaboration with Drs P Manzini and P Ghiazza from Turin, Italy; Dr I Gonzalez-Fraile, Valladolid, Spain; Dr JM Garcia, Oviedo, Spain and Dr CK Lin, Hong Kong
  This study includes B-cell, particularly memory B-cells in addition to T-cell studies.
Infectivity of OBIs

- A European collaborative study including groups from Croatia, Denmark, Germany, Poland and Spain assembled 104 patients receiving products from 24 donors (19 look back, 5 trace back)
- Overall infectivity is estimated at 28%
- Infectivity is dependent on:
  - Presence of anti-HBs in product or patient (vaccinated) $P=0.013$
  - Volume of plasma in product ($P<0.001$ RCC vs FFP)
  - Minimum Infectious Dose 1050 copies
  - But not on immune status of recipients (NS)
- Manuscript submitted for publication
Japanese Red Cross Study on OBI transmission according to anti-HBc level

- Lookback by Satake, Tadokoro et al. presented later in this session
NAT yield samples received for confirmation and sequencing in 2011-12

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<tr>
<th>Country</th>
<th>Samples</th>
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<td>Poland</td>
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<td>P Grabarczyk, Warsaw</td>
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Total: 60
Training on HBV methods for HBV safety group collaborators

• Dr Ye Xiangjin, Shenzhen Blood Centre, China
• Dr Wang Wenjing, Southern Medical College, Guangzhou, China
• Dr Li Tingting, Southern Medical College, Guangzhou, China
• Dr Patricia Araujo, ABCS, Sao Paulo, Brazil