Infectious Diseases

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The Challenge of Infectious Disease

Infectious disease represents the greatest challenge to mankind

- From 2007, more than 50% of the world’s population now lives in cities
- Deforestation together with climate change is altering human–animal reservoir relationships
- Rapid development of new viral and bacterial strains
- Rapid air travel
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**A new pathogen is now emerging at a rate of approximately one per year**
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Chronic infections such as Hepatitis B (HBV), Hepatitis C (HCV) and HIV are threats to public health
The Problem of Hepatitis B

• A major viral infection of the liver acquired
  – By children borne to carrier mothers
  – As a result of drug abuse
  – Through blood transfusion or use of contaminated instruments and needles
• In Asia over 10% of the adult population are carriers of hepatitis B virus (HBV) and at risk of developing cirrhosis and liver cancer
• China has very effective childhood immunisation programmes to prevent new infections
• There remain >50 million adult carriers at risk of serious liver disease
• Antivirals are not the answer
Hepatitis B Therapeutic Vaccines

- Global vaccine market estimated at $5.5b with expected growth of 13.5% p.a. to in excess of $10bn by 2010
- The market share for therapeutic vaccines will rise progressively over the next 3-5 yrs
- Cost of treating chronic hepatitis B is $700m p.a. in the USA alone, $10,000 per patient
- Globally over 1.2 million new HBV infections per year, 200,000 in the USA
- By 2010, 5 million people worldwide will require treatment
- Estimated cost per dose of a therapeutic vaccine $500
Developing an effective post exposure vaccine for treating chronic hepatitis B

• Collaborative project between Professors Wen YuMei, Yuan ZhengHong at the Shanghai Medical College of Fudan University and myself at RVC

• Wen and colleagues have developed an immune complex immunogen combining viral envelope protein and specific antibodies – technology licensed to Yudan Biotechnology in Pudong

• We have developed new technologies for vaccine delivery with promise for post-exposure prophylaxis

• Aim is to capture the complementary expertise and technology to develop a novel post-exposure therapeutic vaccine
The World’s Population

[Map of the world showing population distribution with countries labeled, including China, India, Japan, Indonesia, USA, Canada, UK, Mexico, Brazil, France, Italy, Spain, CIS, Nigeria, Portugal, Germany, Pakistan, Bangladesh, Philippines, and Indonesia.]
Global Prevalence of Hepatitis B Carriage

- China
- India
- Japan
- Indonesia
- Australia
- New Zealand
- Philippines
- USA
- Canada
- UK
- Mexico
- Brazil
- France
- Italy
- Spain
- CIS
- Nigeria
- Portugal
- Pakistan
- Bangladesh
- Scandinavia

Legend:
- Grey: <2%
- Yellow: 2 - 8%
- Red: >8%

10^7 people
The Concept of Post-Exposure Immunisation for Chronic Hepatitis B

Debilitating long term disease

Treatment with antiviral drugs

Sustained Clinical improvement

Immexis
Development of novel therapeutic vaccines

Post-exposure therapeutic vaccination

Transaminases to baseline
Eliminate inflammation
Reduce / eliminate levels of cccDNA
Minimise fibrosis
Immune Complex Immunogen
(Professor Wen YuMei, Shanghai)

• Take existing licensed hepatitis B vaccine used for preventative immunisation of children in China
• Complex this with human antibodies to the surface protein (HBsAg) of the virus
• Inject into adult virus carriers
• … expected result is the stimulation of cells required for eliminating virus from the liver
• Phase 1 trials conducted; phase 2a in progress
• Issues relate to quality and specificity of antibody and delivery of the immune complex (“YIC”)
Post-exposure prophylaxis of chronic hepatitis B

**HLA-II**

- YIC: 700,000
- HBsAg: 500,000
- Anti-HBs: 300,000
- Blank: 200,000

\[ p = 0.015 \]

**CD86**

- YIC: 300,000
- HBsAg: 200,000
- Anti-HBs: 150,000
- Blank: 50,000

\[ p = 0.015 \]

**CD80**

- YIC: 70,000
- HBsAg: 30,000
- Anti-HBs: 20,000
- Blank: 10,000

\[ p = 0.009 \]

**CD40**

- YIC: 200,000
- HBsAg: 150,000
- Anti-HBs: 100,000
- Blank: 50,000

\[ p = 0.034 \]
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Conclusions

- Post-exposure prophylaxis expected to result in new therapeutic approaches to chronic infectious diseases
- Utilises the skills and experience of two groups that has collaborated since 1980
- Further development is required regarding
  - (a) internationally accepted source of anti-HBV antibodies
  - (b) standardisation of methods and potential scale-up
  - (c) incorporation into a delivery vehicle
- Extension possible to other infectious diseases of importance to China e.g. hepatitis C
Inoculation practiced since circa 1100AD

“…. this foreign art of vaccination may be carried out in all provinces, for it will truly prolong life.”

Yuen Yuen, Governor-General, Liang Kwang Provinces, 1817
谢谢!