Freeze-dried influenza vaccines for non-parenteral administration

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Vaccine stabilisation by sugar-glass technology

Inulin 

Amorphous matrix = glass

Spray drying freeze drying

Inulin-stabilized whole virus influenza vaccine is stable at high temperature

Storage stability: 3 M; 30°C

unprocessed WIV

WIV spray freeze-dried with inulin

Problems of current vaccines

Vaccines in suspension require cold chain for storage and transport

Needle-based administration requires trained personnel and causes dangerous waste

Harshad Patil, Senthil Murugappan

Murugappan/Patil et al 2013
Administration forms for (spray) freeze-dried vaccines

- sublingual tablet
- inhalable powder

Sublingual immunization primes for serum and mucosal antibody responses

- Serum HI
- Serum IgG
- Mucosal IgA

- vaccine: NIBRG14 (H5N1)
- WIV w/o adjuvant

Sublingual immunization primes for heterologous i.m. boost

- Serum HI
- Serum IgG
- Mucosal IgA

- NIBRG14
- NIBRG23

Intranasal vs pulmonary vaccination

- Nose spray
  - surface 0.018 m²

- Inhalation
  - surface 70 m²

sublingual tablets ideal vaccine for stock-piling!
Set-up of mouse studies

A/California/7/2009 (H1N1)  
SFD WIV +/- adjuvant  
Day 0  
Day 5  
Day 21  
Day 31  
Day 34  
challenge  
sacrifice  

A/PR/8/34 (H1N1)  
SFD WIV +/- adjuvant  

Pulmonary immunization does not induce inflammation

Data: day 1 after 2. immunization

Pulmonary administered vaccines induce high serum antibody titers

Pulmonary vaccines induce mucosal IgA responses

Patil et al, manuscript in preparation
GPI-0100-adjuvanted WIV induces partial protection against heterologous infection

Conclusions

• Sugar-glass technique is suitable for generating highly stable vaccines
• Sublingual tablets:
  — prime systemic and mucosal antibody responses for homologous and heterologous i.m. boost
  — possible stand-alone vaccine if properly adjuvanted
• Pulmonary administered dry powder vaccine:
  — induces systemic and mucosal immune responses
  — capable of providing heterologous protection if vaccine is properly adjuvanted (GPI-0100)

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