Plenary Session 2: Landscape
Mucosal Vaccine Delivery

Next-Generation Vaccine Delivery Technology Meeting
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“Most pathogens access the body through the mucosal membranes. Therefore, effective vaccines that protect at these sites are much needed”.

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Mucosal Delivery: Oral, rectal, nasal, vaginal, sublingual

Live versus subunit:

- **Live organisms**: mucosal portal of *infection*
  - **Success**: polio, rota [oral]
    - LAIV, (measles) [airways]
  - **Moderate**: Salmonella, cholera, (shigella [oral])
    - Multivalent live disappointing
  - **Attenuation<>immunity**
    - viruses more established?
- **Subunit / killed**: route of *immunisation*
  - Non-immunogenic or weak
    - Multiple doses, short lived (oral cholera, ETEC)
  - Adjuvants: toxicity / ineffective (Ivag)
Mucosal IgA: Necessary and effective? (in humans)

Overview:

- Dogma that mucosal delivery will induce protective SIgA whereas IM will not:
  - Alum adjuvanted Gardasil high protection against cervical basal cell (openly exposed) HPV infection
    - IgG can protect mucosal surfaces – no IgA
  - eIPV can prevent mucosal polio transmission via IgG
  - IM Shigella/Salmonella conjugates
  - Confusing story over HIV STEP trial correlation with serum IgA, impact of gut adeno CMI?
- Series of failed Phase 1 trials of mucosal prime- parenteral boost
Correlates: Models don’t predict mucosal responses

Description:

• Small animals do not always predict
  • Rabbit noses / vaginas respond to anything. Anatomy different
  • Primates (human & non-human) needed ?? Especially reactogenicity?
• Industrialized country citizens do not predict globally

Status:

• Correlates of protection / reactogenicity may differ when localised mucosal immunity / reactions in place
  • LAIV – serum HAI??
  • How to measure and model ??
Mucosal vaccines: Benefits and Challenges

Benefits:
- Needle-free: HIV/HBV/HCV
- *Maybe* SIgA induced??????

Challenges:
- Tropical Barriers
- Weak, short lived responses
  - failure to mucosal prime
- Mucosal adjuvants / toxicity / attenuation / high antigen doses
- Clean Water Supply
- Delivery devices / buffers / 2-stage immunisations / days→ EPI
Mucosal vaccines: Opportunities + Way Forward

Global Public Health Challenge:

• Most infections via mucosal surface
  • HIV / TB / STDs / pneumonia / gastroenteritis / meningitis

Technology Availability:

• Live viral vaccines – available and potentially adaptable to mucosal delivery
• Cheap, reliable devices to convert existing syringe/needle combination for mucosal delivery, integrate into EPI
• Better understanding of mucosal immunity – antigens – mIgG – adjuvants – duration – magnitude – targeting
• Multivalent parenteral subunit vaccines, adjuvanted, conjugates? GMMAs? – safe injection devices?
• Expectations management for what mucosal delivery offers