Pan-sarbecovirus booster vaccination

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Can we succeed in making Pan-XX vaccine?!

- Pan-flu vaccine
- Pan-dengue vaccine
- Pan-CoV vaccine
- Pan-sarbeCoV vaccine
- Pan-henipavirus vaccine
A One Health Hendra virus vaccine

Hendra-Australia
60-80% mortality

Nipah-Philippines

Nipah-Malaysia+Singapore
40% mortality

Nipah-Bangladesh+India
70% mortality
Equivac® HeV

Breakthrough Hendra virus vaccine released for horses

By John Tillary; Anna Cnossen and staff

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A recombinant subunit vaccine formulation protects against lethal Nipah virus challenge in cats

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CEPI-funded Nipah virus vaccine candidate first to reach Phase I clinical trial

The HeV-sG-V Nipah vaccine candidate
Amino acid sequence identity

78% between Hendra and Nipah receptor binding proteins (G)
76% between SARS-CoV-1 and SARS-CoV-2 receptor binding protein (S)
97.7% between SARS-CoV-2 ancestral and Omicron receptor binding protein (S)
Coronavirus protective immunity (especially NAb-mediated immunity) is much more virus/strain-specific

Mixing of virus-specific NAbs (cocktail)

Induction of cross-NAbs (sequential, cross-clade)
Proposed mechanism

- SARS-specific NAb epitopes
- COVID-specific NAb epitopes
- Cross-virus NAb epitopes

1. SARS exposure or vaccine
2. COVID exposure or vaccine
3. SARS exposure → COVID vaccine
NAbs against 10 sarbecoviruses

Tan et al. NEJM (2021)
A pan-sarbecovirus booster vaccine candidate

• Designed a “consensus” Spike protein (C1.25) from all known Clade-1 SARS-like CoVs (mainly from bats)
• “Priming” mice with two doses of BNT162b2
• Cross-clade boosting with two “formulations”:
  • In-house trimeric S (25 ug) + experimental adjuvant
  • GMP cell bank-derived trimeric S (1 ug) + approved human adjuvant
• All groups produced pan-sarbecovirus NAbs
• NAbs assayed using our multiplex surrogate VNT (10 → 16 → 21 plex!)
16-plex sVNT

Clade 2

Clade 1

PPP
PPC-1ug
PPC-25ug
PPC-ddj
PBS

SARS-CoV-2
Delta
Gamma
Lambda
Omicron
GX-P5L
Rs2018B
RsSHCo14
SARS-CoV-1
The cross-clade boosting produced broad NAbs for all known ACE2-binding sarbecoviruses.

The P-P-C1.25 boosting is better than the P-P-P for all (21) viruses except for ancestral and VOC alpha.

The C1.25 boosting has significantly increased the NAb breadth, but there is still room for optimization to increase the absolute NAb titer.
Future/ongoing projects

• C1.25 mRNA boosting vaccine
• Other protein delivery systems (VLP, nanoparticle, etc)
• Dose optimization and comparison of different adjuvants