World Health Organization

Meeting summary

Philip Krause
Chair, WHO COVID Vaccines Research Expert Group

Advancing the development of pan-sarbecovirus vaccines

March 25, 2022

R&DBlueprint
Powering research to prevent epidemics

Conclusions

There is substantial genetic diversity among beta coronaviruses. Variants can evade vaccine neutralizing responses. Pan sarbecovirus vaccines will protect against future variants and future crossovers to humans.

Challenges include virologic (breadth, drift, identification of conserved epitopes & assay development [panels]), models (small/large animals, ARDS, VAERD, human challenge), immune (pre-immune status, kinetics, CoP), Product development plan. Strategies include conserved epitopes, chimeric vaccines, multiplex vaccines, nanoparticle RBD-focused vaccines. Considerations: full length vs RBD, epitopes, domain-specific targeting across viruses, heterologous immunogens & regimens, adjuvants, role of T cells

Viruses emerge due to mutation & due to changes in contact between humans & infected vector or host (weather, animal exposures). Animal reservoirs present challenges and opportunities for control.

Evolution continues with uncertain direction. Variant origin hypotheses: undersampled humans, animals(e.g., mink, deer, unknown), immunocompromised. Immune escape, virus transmissibility, virulence. Broader vaccine thinking may benefit SARS-CoV-2 response

Conclusions (2)

Increasing numbers of coronaviruses have been identified. Most have bat hosts. Climate change may alter diversity and likelihood of crossover.

SARS, MERS, COVID can cause severe pulmonary disease, comorbidities and age increase risk, diarrhea and fecal shedding. COVID infects upper respiratory tract, has lower mortality (though similar to SARS in severe disease). Long COVID seen with SARS-CoV-2.

CoV-specific Nabs are often very strain-specific, suggesting importance of inducing cross-neutralizing antibodies. Mosaics, epitope-focusing, chimeric, heterologous prime/boost. T cell immunogens & Ab immunogens important, focusing on conserved epitopes. Boosting with trimeric consensus spike (PPC) gave better neut response vs. variants than PPP. Nanoparticles are a useful scaffold for presenting antigens. Anti CD40 approach may improve durability & T cell responses. Overall, mosaic vaccines showed promise for inducing neutralizing responses to variants. Class 4 anti-RBD (at base) are most conserved region. Higher immune responses can provide broader protection.

Conclusions (3)

Immunobridging approaches proposed for use with SARS-CoV-2 vaccines may also have utility in evaluating more broadly protective vaccines. In-deployment studies and CHIM may play a role where immunobridging is not supported.

Janssen: favors immunogens that induce broad cellular responses.

SII: favors more antigens than just RBD. Is interested in preventing viral spread with vaccines. Intranasal codon-deoptimized vaccines in prime boost strategy.

Osivax: N based T cell component

Challenges: TPP. Clinical trial considerations in seropositive populations, Standardizing T cell assays as possible measures of protection

SARS-CoV-1 and SARS-CoV-2 use ACE-2. Other sarbecoviruses do not, so goal of ACE2 binding sarbecovirus vaccine may be a more achievable goal (otherwise need more research). Needed: better understanding of cross-protection & immunity in humans, reagents & animal models

Conclusions (4)

It is critically important to proceed with development of vaccines with broader specificity. Some of these approaches will address current needs with SARS-CoV-2. Long COVID and severe disease are both important outcomes. Value of single dose, oral/nasal administration. Need standardized approaches to evaluation, standardized assays. Panels of viruses. Need more data on non-neutralizing CoPs against severe disease. How will this perform in people with preexisting seropositivity.

Concerns seem manageable: biosafety. Could CHIM be associated with long COVID? Questions about relative importance of humoral vs. cellular immunity in preventing severe disease.

Challenge of breadth vs high efficacy can be met and it is considered feasible to use criteria for SARS-CoV-2 vaccines to make these vaccines available initially.

NIAID, INSERM, France, CEPI are investing in new vaccine approaches and supportive science.

Conclusions (5)

WHO is offering a forum for follow-up discussions to facilitate exchange of ideas and to help with research coordination.

What we learn about increasing breadth of protection against SARS-CoV-2 will doubtless have additional future implications