CLIPPINGS

Theme: Immunization

Vero-cell derived inactivated vaccine candidate for SARS-Cov-2 *(Science. 2020; eabc1932)*

Researchers from Sinovac Biotech, China developed a pilot-scale production of a purified inactivated SARS-CoV-2 virus vaccine candidate (PiCoVacc), which induced SARS-CoV-2-specific neutralizing antibodies in mice, rats, and non-human primates. These antibodies neutralized 10 representative SARS-CoV-2 strains, suggesting a possible broader neutralizing ability. Three immunizations provided protection in macaques against SARS-CoV-2 challenge, without observable antibody-dependent enhancement of infection. The vaccinated monkeys tolerated well a SARS-CoV-2 virus challenge after 3 weeks of vaccination and none developed a full-blown infection. The monkeys given the highest dose of vaccine had the best response. In contrast, four control animals developed high levels of viral RNA in several body parts and severe pneumonia.

The old-fashioned inactivation methodology used can be developed easily by many vaccine developers in low- and middle-income countries, and the absence of lung damage in vaccinated animals with relatively low levels of antibodies lessens the concern about vaccine enhancement. However, the number of animals was too small and the fact that monkeys do not develop the most severe symptoms that SARS-CoV-2 causes in humans.

Oxford Group's vaccine prevents severe Covid-19 pneumonia in rhesus macaques (*bioRxiv. 2020.05.13.093195*)

The Oxford group researchers show that the adenovirus-vectored vaccine ChAdOx1 nCoV-19, encoding the spike protein of SARS-CoV-2, is immunogenic in mice. A single vaccination with ChAdOx1 nCoV-19 induced a humoral and cellular immune response in rhesus macaques. They observed a significantly reduced viral load in bronchoalveolar lavage fluid and respiratory tract tissue of vaccinated animals, and no pneumonia was observed in vaccinated rhesus macaques. At 7 days post inoculation, all animals were euthanized, and tissues were collected. Viral genomic (gRNA) was detected in nose swabs from all animals and no difference in viral load in nose swabs was found on any days between vaccinated and control animals. None of the vaccinated monkeys developed pulmonary pathology after inoculation with SARS-CoV-2. Importantly, no evidence of immune-enhanced disease following viral challenge in vaccinated animals was observed.

These observations are marked contrast to the results reported from Sinovac trial, as the vaccine did not protect the animals from infection; though, it prevented severe disease. Thus, the vaccine did not provide sterilizing immunity to the virus challenge, the gold standard for any vaccine, but it may provide partial protection. The moot question is that will partial protection be enough to control the COVID-19 pandemic?

SARS-Cov-2 infection protects against re-challenge in rhesus macaques *(Science 2020; science.abc4776)*

An understanding of protective immunity to SARS-CoV-2 is critical for strategies aimed at ending the pandemic. A key unanswered question is whether infection with SARS-CoV-2 results in protective immunity against re-exposure. Chandrashekar, *et al.,* developed a rhesus macaque model of SARS-CoV-2 infection and observed that macaques had high viral loads in the respiratory tract, humoral and cellular immune responses, and pathologic evidence of viral pneumonia. Following initial viral clearance, animals were re-challenged with SARS-CoV-2 and showed 5 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa compared with primary infection. Anamnestic immune responses following re-challenge suggested that protection was mediated by immunologic control. These data show that SARS-CoV-2 infection induced protective immunity against re-exposure in nonhuman primates. However, it should be emphasized that there are important differences between SARS-CoV-2 infection in monkeys and humans, with many parameters still yet to be defined in both species.

DNA vaccine protection against SARS-CoV-2 in rhesus macaques *(Science.2020; eabc6284)*

In this study, researchers developed a series of DNA vaccine candidates expressing different forms of the SARS-CoV-2 Spike (S) protein and evaluated them in 35 rhesus macaques. Vaccinated animals developed humoral and cellular immune responses, including neutralizing antibody titers comparable to those found in convalescent humans and macaques infected with SARS-CoV-2. Following vaccination, all animals were challenged with SARS-CoV-2, and the vaccine encoding the full-length S protein resulted in >3.1 and >3.7 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa, respectively, as compared with sham controls. Vaccine-elicited neutralizing antibody titers correlated with protective efficacy, suggesting an immune correlate of protection. These data demonstrate vaccine protection against SARS-CoV-2 in nonhuman primates.

Truly little is known about immune correlates of protection and protective efficacy of candidate SARS-CoV-2 vaccines in animal models. In this study, the researchers demonstrate vaccine protection with substantial reductions in median viral loads in BAL and nasal swabs, in immunized animals compared with controls.

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