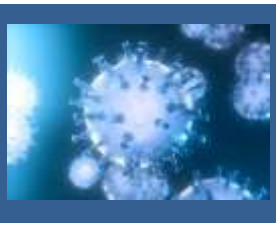
# COVID-19

***Sep 09-15, 2021***



# RESEARCH PUBLICATIONS

**Publication Date: Sep 15, 2021**

## Safety and immunogenicity of an inactivated COVID-19 vaccine, BBIBP-CorV, in people younger than 18 years: A randomised, double-blind, controlled, phase 1/2 trial


### Abstract

*Background*: Although SARS-CoV-2 infection often causes milder symptoms in children and adolescents, young people might still play a key part in SARS-CoV-2 transmission. An efficacious vaccine for children and adolescents could therefore assist pandemic control. For further evaluation of the inactivated COVID-19 vaccine candidate BBIBP-CorV, we assessed the safety and immunogenicity of BBIBP-CorV in participants aged 3–17 years.

*Methods*: A randomised, double-blind, controlled, phase 1/2 trial was done at Shangqiu City Liangyuan District Center for Disease Control and Prevention in Henan, China. In phases 1 and 2, healthy participants were stratified according to age (3–5 years, 6–12 years, or 13–17 years) and dose group. Individuals with a history of SARS-CoV-2 or SARS-CoV infection were excluded. All participants were randomly assigned, using stratified block randomisation (block size eight), to receive three doses of 2 μg, 4 μg, or 8 μg of vaccine or control (1:1:1:1) 28 days apart. The primary outcome, safety, was analysed in the safety set, which consisted of participants who had received at least one vaccination after being randomly assigned, and had any safety evaluation information. The secondary outcomes were geometric meant titre (GMT) of the neutralising antibody against infectious SARS-CoV-2 and were analysed based on the full analysis set. This study is registered with www.chictr.org.cn, ChiCTR2000032459, and is ongoing.

*Findings*: Between Aug 14, 2020, and Sept 24, 2020, 445 participants were screened, and 288 eligible participants were randomly assigned to vaccine (n=216, 24 for each dose level [2/4/8 μg] in each of three age cohorts [3–5, 6–12, and 13–17 years]) or control (n=72, 24 for each age cohort [3–5, 6–12, and 13–17 years]) in phase 1. In phase 2, 810 participants were screened and 720 eligible participants were randomly assigned and allocated to vaccine (n=540, 60 for each dose level [2/4/8 μg] in each of three age cohorts [3–5, 6–12, and 13–17 years]) or control (n=180, 60 for each age cohort [3–5, 6–12, and 13–17 years]). The most common injection site adverse reaction was pain (ten [4%] 251 participants in all vaccination groups of the 3–5 years cohort; 23 [9·1%] of 252 participants in all vaccination groups and one [1·2%] of 84 in the control group of the 6–12 years cohort; 20 [7·9%] of 252 participants in all vaccination groups of the 13–17 years cohort). The most common systematic adverse reaction was fever (32 [12·7%] of 251 participants in all vaccination groups and six [7·1%] of 84 participants in the control group of the 3–5 years cohort; 13 [5·2%] of 252 participants in the vaccination groups and one [1·2%] of 84 in the control group of the 6–12 years cohort; 26 [10·3%] of 252 participants in all vaccination groups and eight [9·5%] of 84 in the control group of the 13–17 years cohort). Adverse reactions were mostly mild to moderate in severity. The neutralising antibody GMT against the SARS-CoV-2 virus ranged from 105·3 to 180·2 in the 3–5 years cohort, 84·1 to 168·6 in the 6–12 years cohort, and 88·0 to 155·7 in the 13–17 years cohort on day 28 after the second vaccination; and ranged from 143·5 to 224·4 in the 3–5 years cohort, 127 to 184·8 in the 6–12 years cohort, and 150·7 to 199 in the 13–17 years cohort on day 28 after the third vaccination.

*Interpretation*: The inactivated COVID-19 vaccine BBIBP-CorV is safe and well tolerated at all tested dose levels in participants aged 3–17 years. BBIBP-CorV also elicited robust humoral responses against SARS-CoV-2 infection after two doses. Our findings support the use of a 4 μg dose and two-shot regimen BBIBP-CorV in phase 3 trials in the population younger than 18 years to further ascertain its safety and protection efficacy against COVID-19.

**Reference**

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00462-X/fulltext

## A single dose of SARS-CoV-2 FINLAY-FR-1A vaccine enhances neutralization response in COVID-19 convalescents, with a very good safety profile: An open-label phase 1 clinical trial


### Abstract

*Background*: As a first step towards a vaccine protecting COVID-19 convalescents from reinfection, we evaluated FINLAY-FR-1A vaccine in a clinical trial.

*Methods*: Thirty COVID-19 convalescents aged 22-57 years were studied: convalescents of mild COVID-19, asymptomatic convalescents, both with PCR-positive at the moment of diagnosis; and individuals with subclinical infection detected by viral-specific IgG. They received a single intramuscular injection of the FINLAY-FR-1A vaccine (50 μg of the recombinant dimeric receptor binding domain). The primary outcomes were safety and reactogenicity, assessed over 28 days after vaccination. The secondary outcome was vaccine immunogenicity. Humoral response at baseline and following vaccination was evaluated by ELISA and live-virus neutralization test. The effector T cellular response was also assessed. Cuban Public Registry of Clinical Trials, WHO-ICTRP: https://rpcec.sld.cu/en/trials/RPCEC00000349-En.

*Findings*: No serious adverse events were reported. Minor adverse events were found, the most common, local pain: 3 (10%) and redness: 2 (6·7%). The vaccine elicited a >21 fold increase in IgG anti-RBD antibodies 28 days after vaccination. The median of inhibitory antibody titres (94·0%) was three times greater than that of the COVID-19 convalescent panel. Virus neutralization titres higher than 1:160 were found in 24 (80%) participants. There was also an increase in RBD-specific T cells producing IFN-γ and TNF-α.

*Interpretation*: A single dose of the FINLAY-FR-1A vaccine against SARS-CoV-2 was an efficient booster of pre-existing natural immunity, with excellent safety profile.


### Reference


https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00075-2/fulltext

## Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): A phase 3, randomised, controlled, open-label trial


### Abstract

*Background*: The antiviral efficacy of remdesivir against SARS-CoV-2 is still controversial. We aimed to evaluate the clinical efficacy of remdesivir plus standard of care compared with standard of care alone in patients admitted to hospital with COVID-19, with indication of oxygen or ventilator support.

*Methods*: DisCoVeRy was a phase 3, open-label, adaptive, multicentre, randomised, controlled trial conducted in 48 sites in Europe (France, Belgium, Austria, Portugal, Luxembourg). Adult patients (aged ≥18 years) admitted to hospital with laboratory-confirmed SARS-CoV-2 infection and illness of any duration were eligible if they had clinical evidence of hypoxaemic pneumonia, or required oxygen supplementation. Exclusion criteria included elevated liver enzymes, severe chronic kidney disease, any contraindication to one of the studied treatments or their use in the 29 days before random assignment, or use of ribavirin, as well as pregnancy or breastfeeding. Participants were randomly assigned (1:1:1:1:1) to receive standard of care alone or in combination with remdesivir, lopinavir–ritonavir, lopinavir–ritonavir and interferon beta-1a, or hydroxychloroquine. Randomisation used computer-generated blocks of various sizes; it was stratified on severity of disease at inclusion and on European administrative region. Remdesivir was administered as 200 mg intravenous infusion on day 1, followed by once daily, 1-h infusions of 100 mg up to 9 days, for a total duration of 10 days. It could be stopped after 5 days if the participant was discharged. The primary outcome was the clinical status at day 15 measured by the WHO seven-point ordinal scale, assessed in the intention-to-treat population. Safety was assessed in the modified intention-to-treat population and was one of the secondary outcomes. This trial is registered with the European Clinical Trials Database, EudraCT2020-000936-23, and ClinicalTrials.gov, NCT04315948.

*Findings*: Between March 22, 2020, and Jan 21, 2021, 857 participants were enrolled and randomly assigned to remdesivir plus standard of care (n=429) or standard of care

only (n=428). 15 participants were excluded from analysis in the remdesivir group, and ten in the control group. At day 15, the distribution of the WHO ordinal scale was: (1) not hospitalised, no limitations on activities (61 [15%] of 414 in the remdesivir group vs 73 [17%] of 418 in the control group); (2) not hospitalised, limitation on activities (129 [31%] vs 132 [32%]); (3) hospitalised, not requiring supplemental oxygen (50 [12%] vs 29 [7%]); (4) hospitalised, requiring supplemental oxygen (76 [18%] vs 67 [16%]); (5) hospitalised, on non-invasive ventilation or high flow oxygen devices (15 [4%] vs 14 [3%]); (6) hospitalised, on invasive mechanical ventilation or extracorporeal membrane oxygenation (62 [15%] vs 79 [19%]); (7) death (21 [5%] vs 24 [6%]). The difference between treatment groups was not significant (odds ratio 0·98 [95% CI 0·77–1·25]; p=0·85). There was no significant difference in the occurrence of serious adverse events between treatment groups (remdesivir, 135 [33%] of 406 vs control, 130 [31%] of 418; p=0·48). Three deaths (acute respiratory distress syndrome, bacterial infection, and hepatorenal syndrome) were considered related to remdesivir by the investigators, but only one by the sponsor's safety team (hepatorenal syndrome).

*Interpretation*: No clinical benefit was observed from the use of remdesivir in patients who were admitted to hospital for COVID-19, were symptomatic for more than 7 days, and required oxygen support.

**Reference**

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00485-0/fulltext

## Low-dose mRNA-1273 COVID-19 vaccine generates durable memory enhanced by cross-reactive T cells

**Abstract**

*Introduction*: Understanding human immune responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA vaccines is of interest for a panoply of reasons. mRNA vaccines have demonstrated impressive protection against COVID-19, but the durability of immunity has been a major unknown. Moreover, a better understanding of age-associated differences and mRNA vaccine dose response curves for dose sparing considerations is needed. Additionally, the impact of preexisting cross-reactive memory on immune responses to SARS-CoV-2 proteins remains an open question. Cross-reactive memory CD4+ T cells recognizing SARS-CoV-2 have been

found in ~50% of individuals. A vaccine trial is a controlled context for testing the relevance of such cross-reactive T cells. Each of these topics was addressed in this study using blood samples from a National Institutes of Health clinical trial of 25-µg mRNA-1273 COVID-19 vaccinees as well as from 100-µg mRNA-1273 COVID-19 vaccinees and SARS-CoV-2–infected individuals.

*Rationale*: Vaccination and infection are two different paths to immunity. Comparison of vaccine-generated and infection-generated immune memory is of value. Given evidence that antibodies, CD4+ T cells, and CD8+ T cells can each participate in protective immunity against COVID-19, we measured acute and memory SARS-CoV-2 spike–specific antibodies, CD4+ T cells, and CD8+ T cells in the blood of subjects who received a low-dose (25 µg) or standard-dose (100 µg) mRNA-1273 COVID-19 vaccine. Immunological measurements were used to address the four issues described above: namely, the durability of immune memory over 7 months after vaccination, mRNA vaccine dose responses, age differences, and the impact of preexisting cross-reactive T cells.

*Results*: Longitudinal samples from 35 volunteers immunized with 25 µg of mRNA-1273 on days 1 and 29 were used to measure SARS-CoV-2 spike–binding antibodies, receptor binding domain (RBD)–binding antibodies, SARS-CoV-2 pseudovirus (PSV) neutralizing antibodies, spike-specific CD4+ T cells, and spike-specific CD8+ T cells. Overall, substantial anti-spike, anti-RBD, and PSV neutralizing antibodies were induced in response to two 25-µg mRNA-1273 vaccinations, were maintained in 88 to 100% of vaccinees for at least 6 months after the second immunization, and were comparable in magnitude and quality to those observed 6 to 7 months after infection with SARS-CoV-2.

Spike-specific CD4+ T cells were generated by low-dose mRNA-1273 and were maintained as memory CD4+ T cells. We observed strong T follicular helper (TFH) and type 1 T helper cell polarization of these cells, which is advantageous for antiviral immunity. Spike-specific CD8+ T cells were detectable in 88% of vaccinees and maintained for at least 6 months in 67% of vaccinees. Spike-specific CD4+ or CD8+ T cell frequencies were not lower in older vaccinee groups than in 18- to 55-year-olds, either in the acute or memory phase. Thus, 25-µg mRNA-1273 vaccination induced

spike antibody levels and memory T cell frequencies at 7 months after vaccination similar to those observed for COVID-19 cases 7 months after symptom onset.

Next, to assess the impact of mRNA dosing, we compared immune responses between 25-µg and 100-µg doses of mRNA-1273 vaccine. Peak anti-spike, anti-RBD, and PSV neutralizing antibody levels were about twofold higher in 100-µg vaccinees than in 25-µg vaccinees. Spike-specific CD4+ T cells responses were ~1.4-to-2.0-fold higher in 100-µg vaccinees, whereas peak CD8+ T cell responses were comparable between 25-µg and 100-µg dose regimens.

Finally, to address potential positive or negative effects of preexisting cross-reactive memory T cells, we compared 25-µg mRNA-1273 COVID-19 vaccine responses between subjects with or without measurable preexisting SARS-CoV-2 spike–reactive memory CD4+ T cells. Preexisting immunity enhanced vaccine antibody responses after a single vaccine dose, which was associated with higher spike-specific TFH cells and total spike-specific CD4+ T cell responses. Individuals with preexisting cross-reactive memory T cells also sustained higher SARS-CoV-2–neutralizing antibodies 6 months after vaccination.

*Conclusion*: The 25-µg dose of mRNA-1273 vaccine induces durable and functional T cell and antibody memory at comparable magnitude to natural infection. This work expands our understanding of immune memory to mRNA vaccine in humans, vaccine dose sparing, and possible timing of boosters. Finally, these data provide evidence that cross-reactive memory CD4+ T cells are biologically relevant and can exert a considerable positive influence on immunity generated by vaccination, with potential implications for vaccines and SARS-CoV-2 infections.

**Reference**

https://www.science.org/doi/10.1126/science.abj9853

## Bispecific antibodies targeting distinct regions of the spike protein potently neutralize SARS-CoV-2 variants of concern

**Abstract**

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern threatens the efficacy of existing vaccines and therapeutic

antibodies and underscores the need for additional antibody-based tools that potently neutralize variants by targeting multiple sites of the spike protein. We isolated 216 monoclonal antibodies targeting SARS-CoV-2 from plasmablasts and memory B cells collected from patients with coronavirus disease 2019. The three most potent antibodies targeted distinct regions of the receptor binding domain (RBD), and all three neutralized the SARS-CoV-2 Alpha and Beta variants. The crystal structure of the most potent antibody, CV503, revealed that it binds to the ridge region of SARS-CoV-2 RBD, competes with the angiotensin-converting enzyme 2 receptor, and has limited contact with key variant residues K417, E484, and N501. We designed bispecific antibodies by combining nonoverlapping specificities and identified five bispecific antibodies that inhibit SARS-CoV-2 infection at concentrations of less than 1 ng/ml. Through a distinct mode of action, three bispecific antibodies cross-linked adjacent spike proteins using dual N-terminal domain–RBD specificities. One bispecific antibody was greater than 100-fold more potent than a cocktail of its parent monoclonals in vitro and prevented clinical disease in a hamster model at a dose of 2.5 mg/kg. Two bispecific antibodies in our panel comparably neutralized the Alpha, Beta, Gamma, and Delta variants and wild-type virus. Furthermore, a bispecific antibody that neutralized the Beta variant protected hamsters against SARS-CoV-2 expressing the E484K mutation. Thus, bispecific antibodies represent a promising next-generation countermeasure against SARS-CoV-2 variants of concern.

**Reference**

https://www.science.org/doi/10.1126/scitranslmed.abj5413

**Publication Date: Sep 12, 2021**

## Transmission, viral kinetics and clinical characteristics of the emergent SARS-CoV-2 Delta VOC in Guangzhou, China

**Abstract**

*Background*: A novel variant of SARS-CoV-2, the Delta variant of concern (VOC, also known as lineage B.1.617.2), is fast becoming the dominant strain globally. We reported the epidemiological, viral, and clinical characteristics of hospitalized patients infected with the Delta VOC during the local outbreak in Guangzhou, China.

*Methods*: The epidemiological and clinical information were extracted pertaining to the 159 cases infected with the Delta VOC across seven transmission generations between May 21 and June 18, 2021. The whole chain of the Delta VOC transmission was described. Kinetics of viral load and clinical characteristics were compared with a cohort of wild-type infection in 2020 admitted to the Guangzhou Eighth People's Hospital.

*Findings*: There were four transmission generations within the first ten days. The Delta VOC yielded a significantly shorter incubation period (4.0 vs. 6.0 days), higher viral load (20.6 vs. 34.0, cycle threshold of the ORF1a/b gene), and a longer duration of viral shedding in pharyngeal swab samples (14.0 vs. 8.0 days) compared with the wild-type strain. In cases with critical illness, the proportion of patients over the age of 60 was higher in the Delta VOC group than in the wild-type strain (100.0% vs. 69.2%, p = 0.03). The Delta VOC had a higher risk than wild-type infection in deterioration to critical status (hazards ratio 2.98 [95%CI 1.29-6.86]; p = 0.01).

*Interpretation*: Infection with the Delta VOC is characterized by markedly increased transmissibility, viral loads and risk of disease progression compared with the wild-type strain, calling for more intensive prevention and control measures to contain future outbreaks.

**Reference**

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00409-0/fulltext

## Effectiveness of the first component of Gam-COVID-Vac (Sputnik V) on reduction of SARS-CoV-2 confirmed infections, hospitalisations and mortality in patients aged 60-79: A retrospective cohort study in Argentina

**Abstract**

*Background*: A first-dose of various vaccines provides acceptable protection against infections by SARS-CoV-2 and evolution to the most severe forms of COVID-19. The recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), was proven efficacious but information about effectiveness in the real-world setting is lacking. The aim of our study was to investigate the association between the rollout of the first component (rAd26) of Gam-COVID-Vac and PCR-positive tests, hospitalisations and deaths.

*Methods*: A retrospective cohort study was conducted which analyzed individuals aged 60-79 who self-registered in the online vaccination system of the Province of Buenos Aires, Argentina, from December 29, 2020 to March 21, 2021. Exclusion criteria were having a previous positive RT-PCR or antigen tests for SARS-CoV-2, having received other vaccines, or two doses of any vaccine.

Proportions of new laboratory-confirmed SARS-CoV-2 infections, hospitalisations and deaths until 83 days of vaccination were compared between vaccinated and unvaccinated subjects. Vaccine effectiveness for the three outcomes was calculated as (1–OR) × 100. Kaplan-Meier cumulative incidence curves were constructed.

*Findings*: During the study period 415995 registered subjects received the first component of Gam-COVID-Vac; 40387 belonged to the 60-79 age group, and were compared to 38978 unvaccinated. Vaccine effectiveness for preventing laboratory-confirmed infections was 78•6% [CI95% 74·8 - 81·7]; and for reducing hospitalizations and deaths was, respectively, 87·6% [CI95% 80·3 - 92·2] and 84·8% [CI95% 75·0 - 90·7]. Effectiveness was high across all subgroups.

*Interpretation*: Similarly to other vaccines, the administration of one dose of Gam-COVID-Vac was effective for a wide range of COVID-19–related outcomes.

**Reference**

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00406-5/fulltext

**Publication Date: Sep 09, 2021**

## Dynamic IgG seropositivity after rollout of CoronaVac and BNT162b2 COVID-19 vaccines in Chile: A sentinel surveillance study

**Abstract**

*Background*: By July 14, 2021, 81·3 % of adults (aged ≥18 years) in Chile had received a first SARS-CoV-2 vaccine and 72·3% had received a second SARS-CoV-2 vaccine, with the majority of people given Sinovac's inactivated CoronaVac vaccine (75·3% of vaccines dispensed) or Pfizer–BioNTech's mRNA BNT162b2 vaccine (20·9% of vaccines dispensed). Due to the absence of simultaneous real-world data for these

vaccines, it wass aimed to compare SARS-CoV-2 IgG positivity between vaccines using a dynamic national monitoring strategy.

*Methods*: From March 12, 2021, 28 testing stations for SARS-CoV-2 IgG detection were installed in hotspots based on cellular-phone mobility tracking within the most populated cities in Chile. Individuals voluntarily approaching the testing stations were invited to do a lateral flow test by finger prick and respond to a questionnaire on sociodemographic characteristics, vaccination status (including type of vaccine if one was received), variables associated with SARS-CoV-2 exposure, and comorbidities. The proportion of individuals testing positive for anti-SARS-CoV-2 IgG across sites by week were compared since vaccination between recipients of CoronaVac and BNT162b2. Unvaccinated participants served as a control population and were matched to vaccinated individuals on the basis of date of presentation to the testing station, gender, and age group. Individuals were excluded from the analysis if they were younger than 18 years, had no declared gender, had an invalid IgG test result, had previously tested positive for SARS-CoV-2 infection on PCR, could not recall their vaccination status, or had been immunised against COVID-19 with vaccines other than CoronaVac or BNT162b2. Here, we report data collected up to July 2, 2021.

*Findings*: Of 64 813 individuals enrolled, 56 261 were included in the final analysis, of whom 33 533 (59·6%) had received at least one dose of the CoronaVac vaccine, 8947 (15·9%) had received at least one dose of the BNT162b2 vaccine, and 13 781 (24·5%) had not received a vaccine. SARS-CoV-2 IgG positivity during week 4 after the first dose of CoronaVac was 28·1% (95% CI 25·0–31·2; 220 of 783 individuals), reaching a peak of 77·4% (75·5–79·3; 1473 of 1902 individuals) during week 3 after the second dose. SARS-CoV-2 IgG positivity during week 4 after the first dose of the BNT162b2 vaccine was 79·4% (75·7–83·1; 367 of 462 individuals), increasing to 96·5% (94·9–98·1; 497 of 515 individuals) during week 3 after the second dose and remaining above 92% until the end of the study. For unvaccinated individuals, IgG seropositivity ranged from 6·0% (4·4–7·6; 49 of 810 individuals) to 18·7% (12·5–24·9; 28 of 150 individuals) during the 5 month period. Regression analyses showed that IgG seropositivity was significantly lower in men than women and in people with diabetes or chronic diseases for CoronaVac vaccine recipients ($p<0·0001$), and for individuals aged 60 years and

older compared with people aged 18–39 years for both vaccines (p<0·0001), 3–16 weeks after the second dose.

*Interpretation*: IgG seropositivity was lower after CoronaVac than after BNT162b2 and declined over time since vaccination for CoronaVac recipients but not BNT162b2 recipients. Prolonged IgG monitoring will allow further evaluation of seropositivity overtime, providing data, in conjunction with effectiveness studies, for possible future re-assessment of vaccination strategies.

**Reference**

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00479-5/fulltext

# REPORT

**Publication Date: Sep 14, 2021**

## Identification of resident memory CD8+ T cells with functional specificity for SARS-CoV-2 in unexposed oropharyngeal lymphoid tissue

Cross-reactive CD4+ T cells that recognize severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are more commonly detected in the peripheral blood of unexposed individuals compared with SARS-CoV-2–reactive CD8+ T cells. However, large numbers of memory CD8+ T cells reside in tissues, feasibly harboring localized SARS-CoV-2–specific immune responses. To test this idea, we performed a comprehensive functional and phenotypic analysis of virus-specific T cells in tonsils, a major lymphoid tissue site in the upper respiratory tract, and matched peripheral blood samples obtained from children and adults before the emergence of COVID-19 (coronavirus disease 2019). It was found that SARS-CoV-2–specific memory CD4+ T cells could be found at similar frequencies in the tonsils and peripheral blood in unexposed individuals, whereas functional SARS-CoV-2–specific memory CD8+ T cells were almost only detectable in the tonsils. Tonsillar SARS-CoV-2–specific memory CD8+ T cells displayed a follicular homing and tissue-resident memory phenotype, similar to tonsillar Epstein-Barr virus–specific memory CD8+ T cells, but were functionally less potent than other virus-specific memory CD8+ T cell responses. The presence of preexisting tissue-resident memory CD8+ T cells in unexposed individuals could potentially enable rapid sentinel immune responses against SARS-CoV-2.

**Reference**

https://www.science.org/doi/10.1126/sciimmunol.abj2901

**Publication Date: Sep 09, 2021**

## Early cross-coronavirus reactive signatures of humoral immunity against COVID-19

The introduction of vaccines has inspired hope in the battle against SARS-CoV-2. However, the emergence of viral variants, in the absence of potent antivirals, has left

the world struggling with the uncertain nature of this disease. Antibodies currently represent the strongest correlate of immunity against SARS-CoV-2, thus we profiled the earliest humoral signatures in a large cohort of acutely ill (survivors and nonsurvivors) and mild or asymptomatic individuals with COVID-19. Although a SARS-CoV-2–specific immune response evolved rapidly in survivors of COVID-19, nonsurvivors exhibited blunted and delayed humoral immune evolution, particularly with respect to S2-specific antibodies. Given the conservation of S2 across β-coronaviruses, we found that the early development of SARS-CoV-2–specific immunity occurred in tandem with preexisting common β-coronavirus OC43 humoral immunity in survivors, which was also selectively expanded in individuals that develop a paucisymptomatic infection. These data point to the importance of cross-coronavirus immunity as a correlate of protection against COVID-19.

**Reference**

https://www.science.org/doi/10.1126/sciimmunol.abj2901

## Molecular basis of immune evasion by the Delta and Kappa SARS-CoV-2 variants

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission leads to the emergence of variants, including the B.1.617.2 (Delta) variant of concern which is causing a new wave of infections and has become globally dominant. We show that these variants dampen the in vitro potency of vaccine-elicited serum neutralizing antibodies and provide a structural framework for describing their immune evasion. Mutations in the B.1.617.1 (Kappa) and B.1.617.2 (Delta) spike glycoproteins abrogate recognition by several monoclonal antibodies via alteration of key antigenic sites, including remodeling of the B.1.617.2 (Delta) N-terminal domain. The ACE2 binding affinities of the B.1.617.1 (Kappa) and B.1.617.2 (Delta) receptor-binding domains are comparable to the Wuhan-Hu-1 isolate whereas B.1.617.2+ (Delta+) exhibits markedly reduced affinity.

**Reference**

https://www.science.org/doi/10.1126/science.abl8506