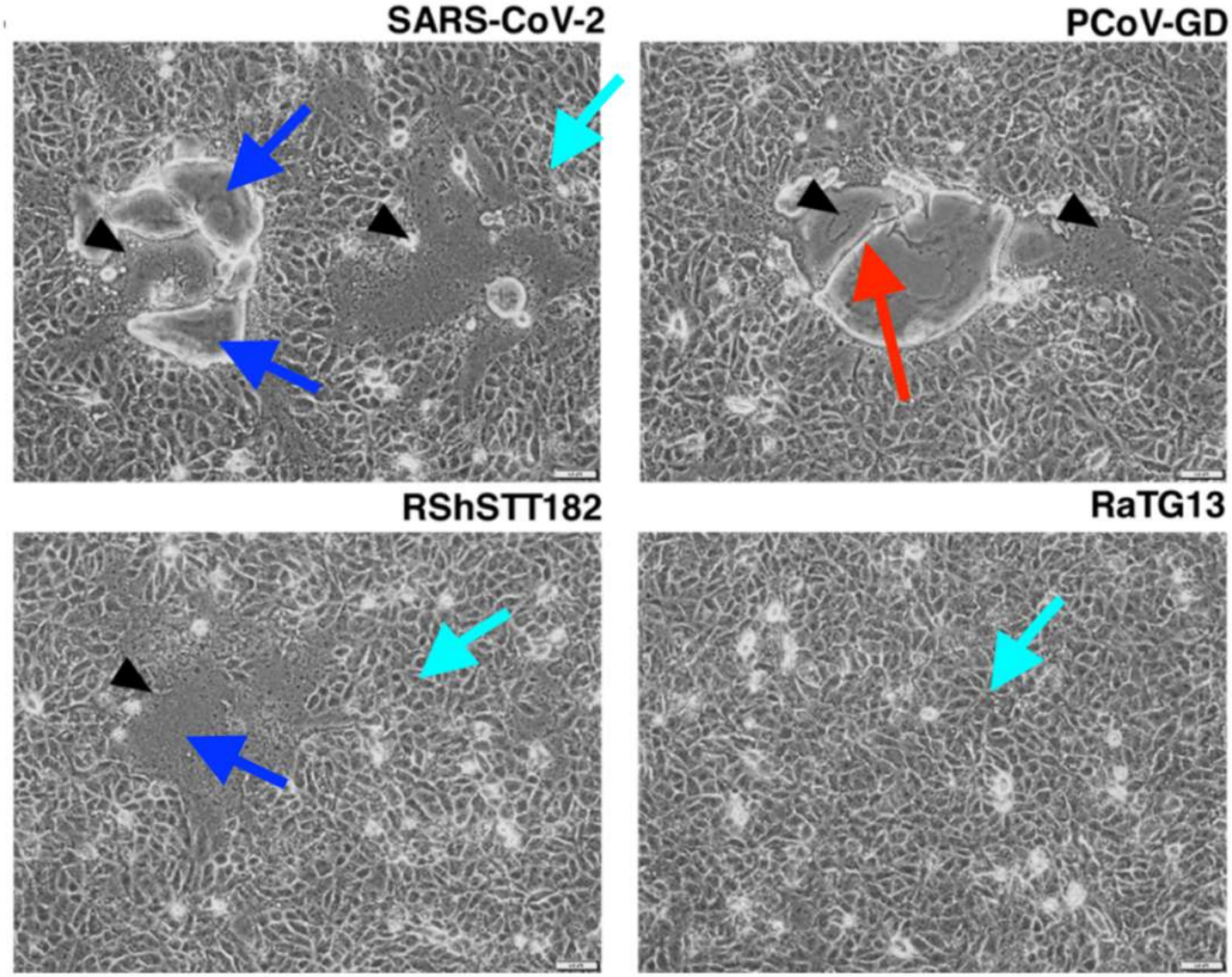

Expression and cell-cell fusion activity of sarbecovirus spikes in VeroE6 cells.

Cell–cell fusion in VeroE6 cells transfected with each spike variant in the presence of trypsin. Images were taken under an inverted light microscope 24 h after transfection (100-μm scale bars). Black arrows mark representative areas where cell–cell fusion was observed.

The RaTG13 RBD Is Responsible for Its Inability to Induce Cell–Cell Fusion in VeroE6 Cells

Cross-Neutralization of SARS-CoV-2-Specific Antibodies in Convalescent and Immunized Human Sera against the Bat and Pangolin Coronaviruses

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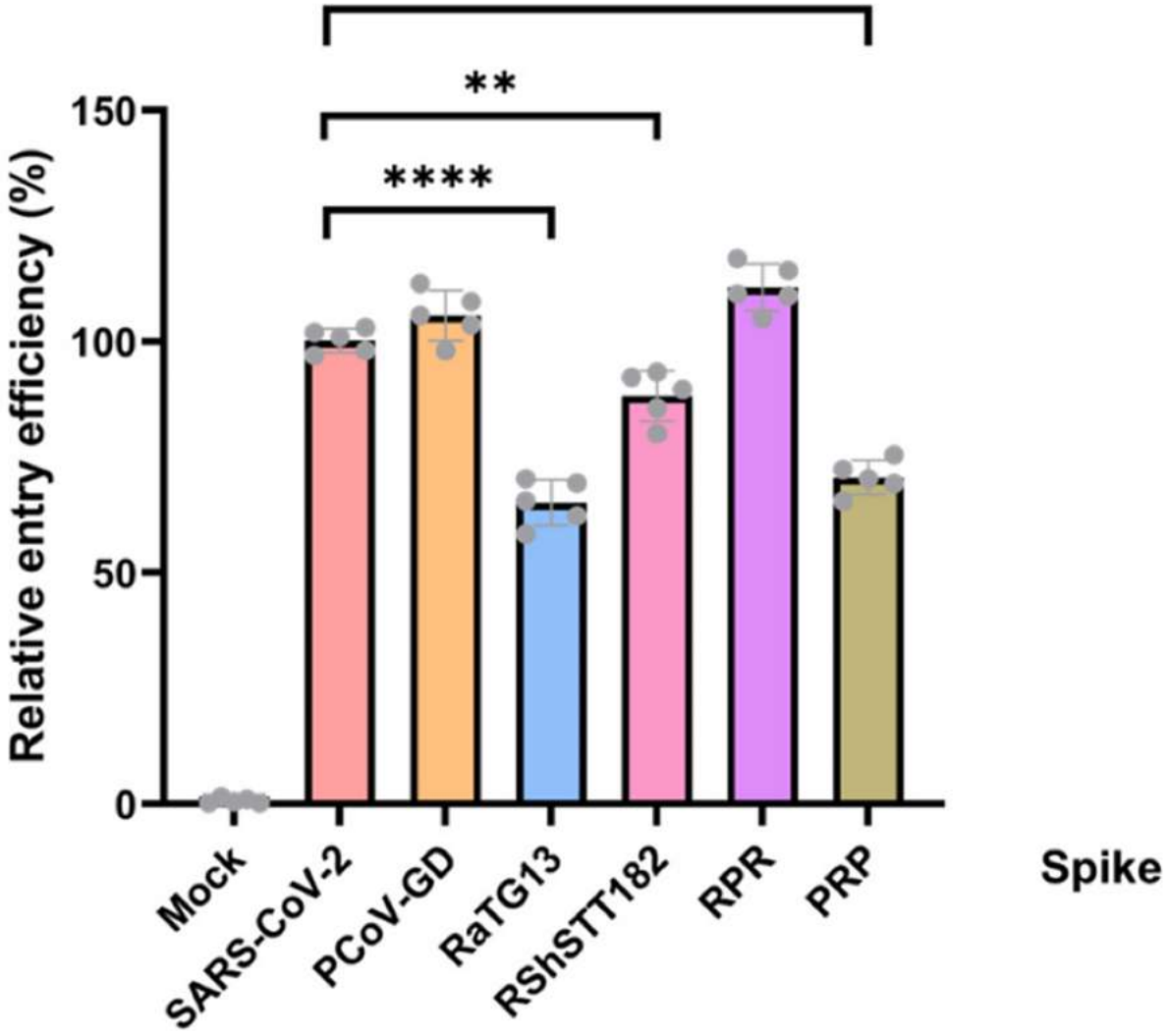
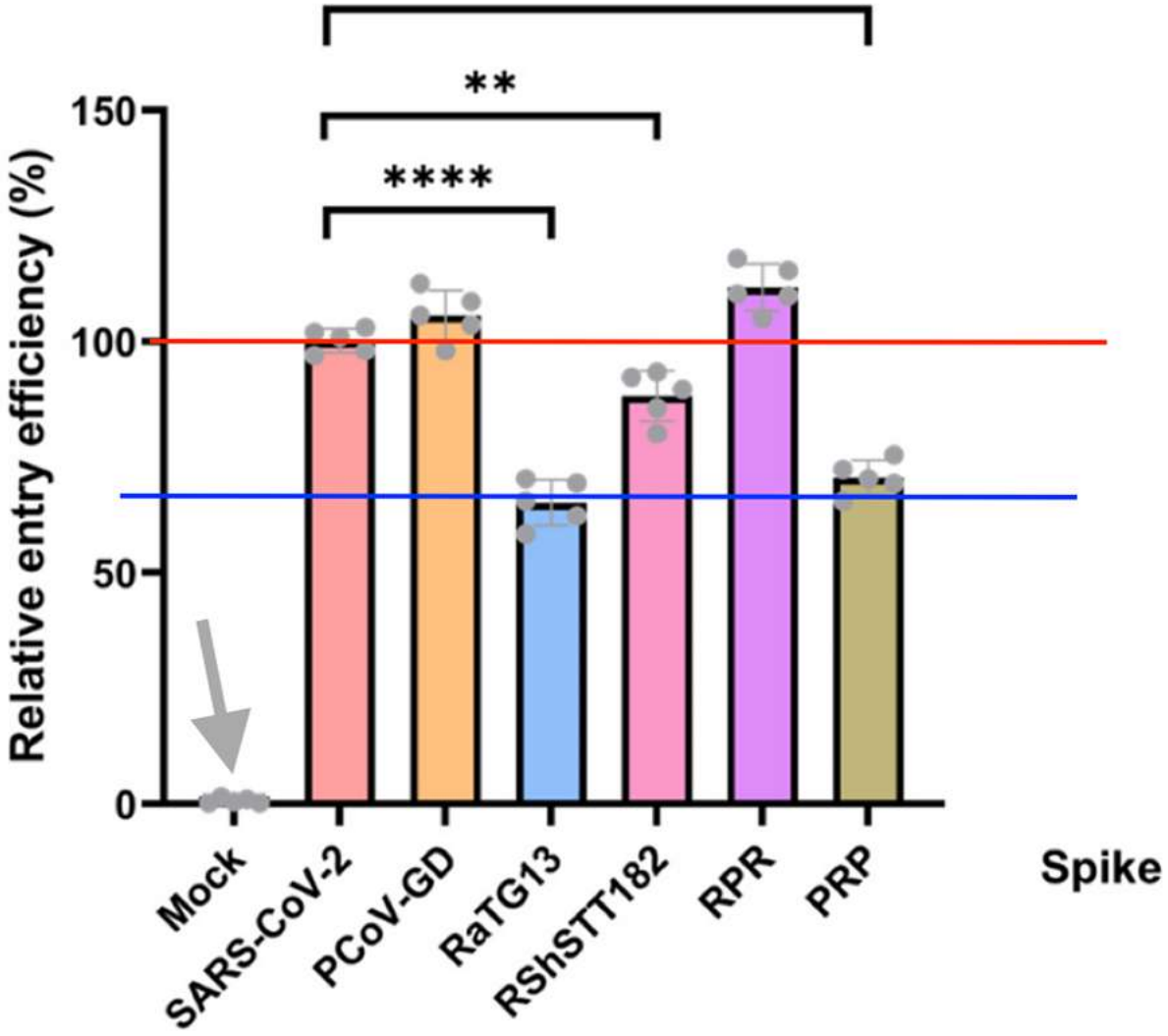
Abstract: Coronaviruses isolated from bats and pangolins are closely related to SARS-CoV-2, the causative agent of COVID-19. These so-called sarbecoviruses are thought to pose an acute pandemic threat. As SARS-CoV-2 infection and vaccination have become more widespread, it is not known whether neutralizing antibodies to SARS-CoV-2 can cross-neutralize coronaviruses transmitted by bats or pangolins. In this study, we analyzed antibody-mediated neutralization with serum samples from COVID-19 patients ($n = 31$) and those immunized with inactivated SARS-CoV-2 vaccines ($n = 20$) against lentivirus-based pseudo-viruses carrying the spike derived from ancestral SARS-CoV-2, bat (RaTG13 or RshSTT182), or pangolin coronaviruses (PCoV-GD). While SARS-CoV-2, PCoV-GD, and RshSTT182 spikes could promote cell-cell fusion in VeroE6 cells, the RaTG13 spike did not. RaTG13, on the other hand, was able to induce cell-cell fusion in cells overexpressing ACE2. Dramatic differences in neutralization activity were observed, with the highest level observed for RaTG13, which was even significantly higher than SARS-CoV-2, PCoV-GD, and RshSTT182 pseudo-viruses. Interestingly, pseudo-viruses containing the chimeric protein in which the receptor-binding domain (RBD) of PCoV-GD spike was replaced by that of RaTG13 could be strongly neutralized, whereas those carrying RaTG13 with the RBD of PCoV-GD were significantly less neutralized.



Entry of pseudo-viruses carrying each spike into HEK-293T-ACE2 cells. After pseudo-virus entry, the luciferase signal was used to evaluate the entry efficiency. The entry efficiency of SARS-CoV-2 wild-type pseudo-viruses was taken as 100%. The error bars depict the standard deviation (n = 5) with each dot representing each replication. Normalization of the relative luminescence unit (RLU) of Luc reporter gene expression to the p24 content of the pseudo-viruses. Adjusted p values were calculated using one-way ANOVA: ** p 0.01, **** p 0.0001.

SARS-CoV-2 Positive Sera Exhibit Varying Levels of Neutralizing Activity against Bat and Pangolin CoVs



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