# A Fc-enhanced non-neutralizing antibody delays SARS-CoV-2 induced death in mice

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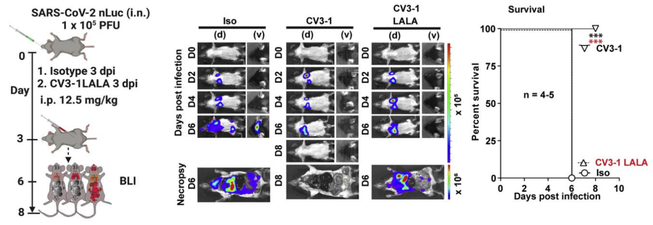
## BACKGROUND

Since the beginning of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic, a major emphasis has been put on studying the neutralizing responses of monoclonal antibodies and of convalescent and vaccinated individuals. However, multiple studies showed that between 25% and 45% of people who resolve infection had a low or undetectable neutralizing response suggesting that other antibody functions might play an important role in contributing in fighting SARS-CoV-2 infection. In a previous study, we showed that, in addition to neutralization, Fc-mediated effector functions were necessary in order to protect K18-hACE2 mice from a lethal SARS-CoV-2 challenge. However, it is unclear if Fc-effector functions alone could protect against SARS-CoV-2 infection. Here, we sought to determine if Fc-effector functions alone could offer any level of protection against a lethal SARS-CoV-2 challenge in K18-hACE2 mice.

**Neutralization alone is insufficient to protect K18-hACE2 mice from a lethal SARS-CoV-2 challenge**




Ullah I, Prévost J, Ladinsky MS, et al. *Immunity.* 2021.

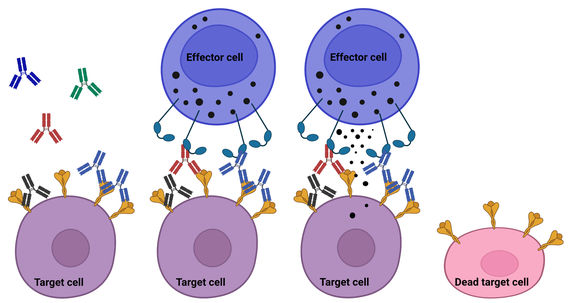
**Antibody-dependent cellular cytotoxicity (ADCC)**

Antibodies bind antigens at the surface of target cells (SARS-CoV-2 infected cells)

Effector cells recognize the bound antibodies by their CD16a receptors

Cross-linking of CD16a induces degranulation of the effector cells in the lytic synapse

Target cells die by apoptosis




## ACKNOWLEDGMENTS

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The ADCC figure and the schematics for showing experimental designs in figures were created with Biorender.com.

**Figure 1. CV3-13 is a non-neutralizing antibody with potent Fc-mediated effector functions**

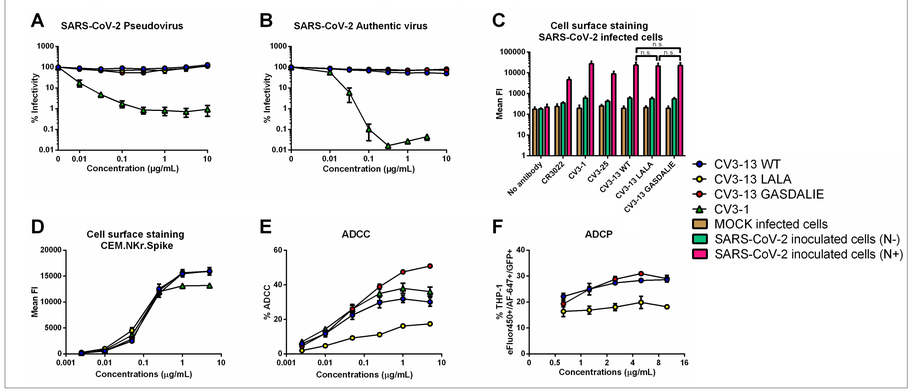
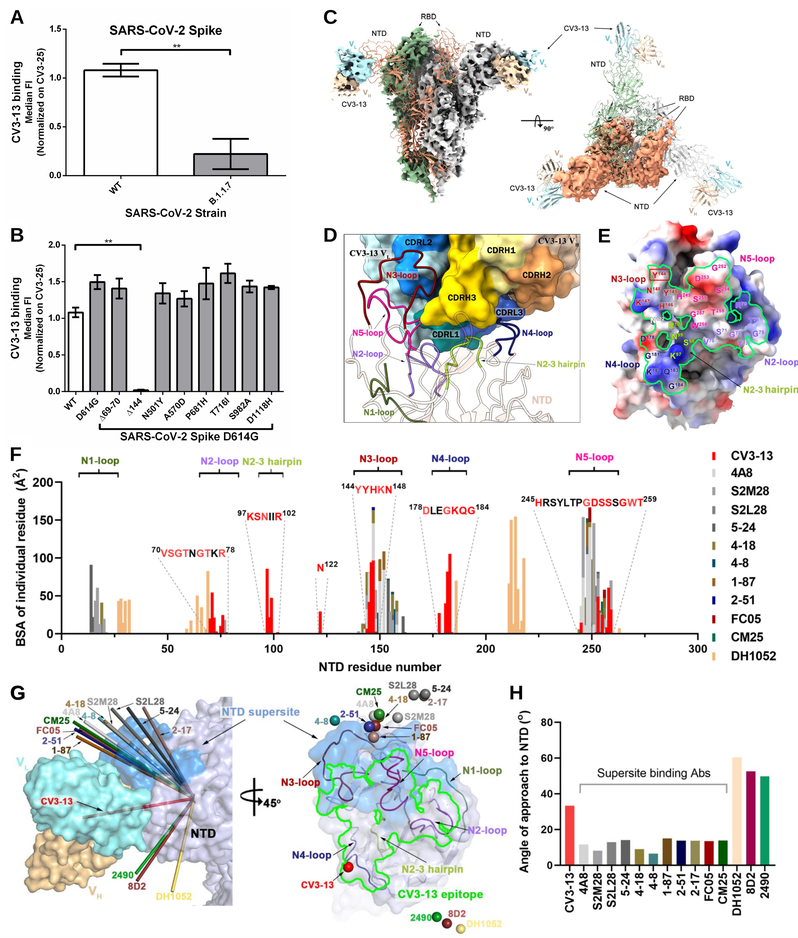
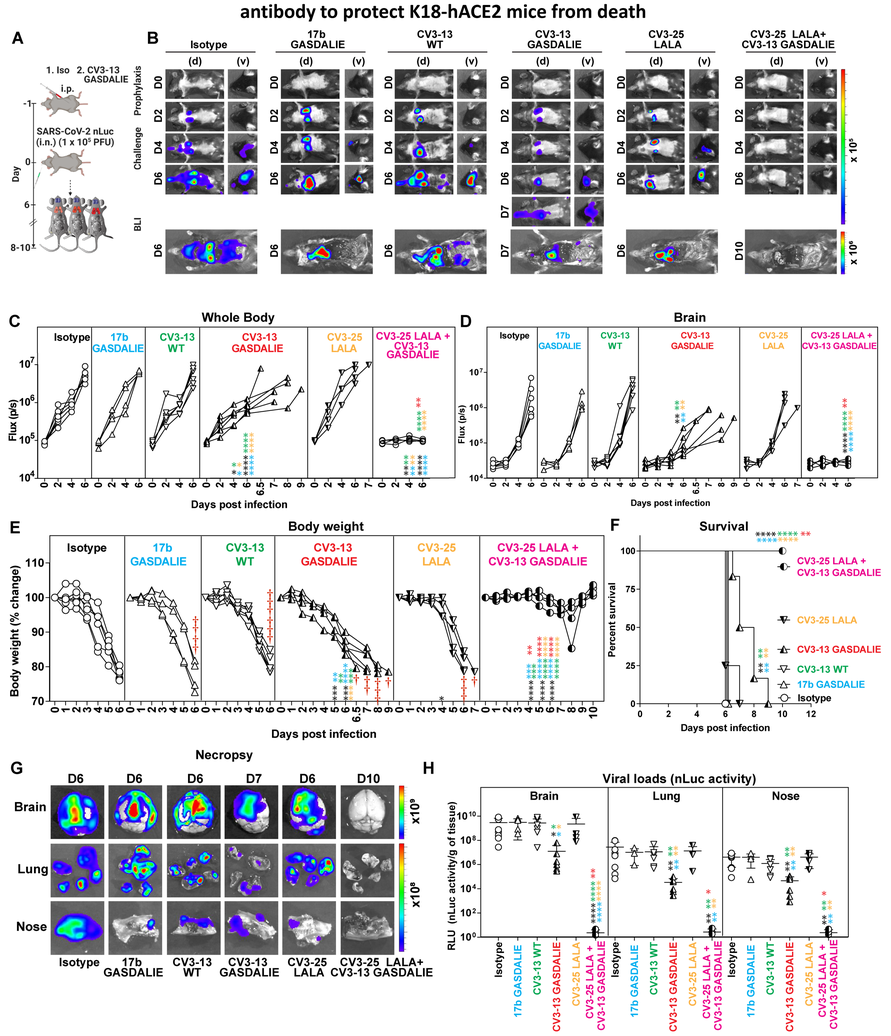



**Figure 2. CV3-13 binds the NTD of the SARS-CoV-2 Spike with a unique angle of approach**




## RESULTS

**Figure 3. An enhanced version of CV3-13 delays death and synergizes with a Fc-impaired neutralizing antibody to protect K18-hACE2 mice from death**




## CONCLUSIONS

- CV3-13 is a non-neutralizing antibody with Fc-effector functions.
- A Fc-enhanced version of CV3-13 induced significant delay of death.
- The enhanced version of CV3-13 synergizes with a Fc-impaired neutralizing antibody to completely protect mice from death.

➢ **Fc-effector functions play an important role in protection against SARS-CoV-2.**