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Modeling Viral Resistance to Monotherapy with Monoclonal Antibody Treatment for SARS-CoV-2

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MODELING VIRAL RESISTANCE TO MONOTHERAPY WITH MONOCLONAL ANTIBDOY TREATMENT FOR SARS-COV-2. *Tin Phan, Carolin Zitzmann, Alan S. Perelson, Ruy M. Ribeiro, Ruian Ke. Theoretical Biology and Biophysics, Los Alamos National Laboratory, Los Alamos, NM.

The COVID-19 pandemic has led to approximately 400 million cases and 6 million deaths. To mitigate the loss of lives, emergency authorization was given to several monoclonal antibody therapies for the treatments of mild-to-moderate SARS-CoV-2 patients with high risks of progressing to severe disease.

Neutralizing monoclonal antibody treatments target the virus's spike proteins to block its ability to enter and infect target cells. Monoclonal antibody therapy can thus accelerate the decline in viral load, which results in a lower hospitalization rate among high-risk patients. However, viral resistance can develop and lead to the occurrence of transient viral rebound in some patients. This raises an urgent concern regarding drug resistance that could compromise the efficacy of monoclonal antibody therapy.

In this study, we develop mathematical models and fit them to data from SARS-CoV-2 patients. Our fitting results show that either a model with innate and adaptive immune responses (Model A) or a model with antibody-dependent enhancement of infection (Model B) can fit the data well across all patients. Model A suggests that the main factor leading to viral rebound is an ineffective immune response, while Model B suggests antibody-dependent enhancement of the infection is the driving force. Additional simulations support the notion that viral recrudescence is due in part to antibody treatment at low dose.