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mRNA-1273 Efficacy in a Severe COVID-19 Model: Attenuated Activation of Pulmonary Immune Cells After Challenge

Dr. Meyer obtained her PhD in Virology and Microbiology at the University of Queensland, Australia. While completing her degree, she joined Panbio as a R&D Scientist to successfully develop a Dengue virus early rapid diagnostic test. Overseeing its development through to market release sparked her interest in conducting translational research. Dr. Meyer went on to do her post-doctoral research at the GNL BSL4 high containment facility at the University of Texas Medical Branch, Galveston, in the laboratory of Alexander Bukreyev, PhD. Dr. Meyer studied the immune responses and protective efficacy of an aerosolized virus-vectored respiratory vaccine against Ebola virus. She is currently a Research Scientist II focusing on novel vaccine development for emerging pathogens and elucidating the correlates of vaccine-mediated protection. Overall, her expertise encompasses a broad spectrum of RNA viruses.

Abstract: The mRNA-1273 vaccine was recently shown to be highly efficacious against symptomatic COVID-19 disease in a large Phase 3 study and was authorized for emergency use by the Food and Drug Administration. Human studies, however, cannot provide the controlled response to infection and complex immunological insight that are possible with preclinical studies. The golden Syrian hamster is the only model that reliably exhibits severe COVID-19 disease similar to hospitalized patients, making it pertinent for vaccine evaluation. We demonstrate that prime-boost dose regimens of mRNA-1273 in hamsters provides more robust neutralizing antibody responses and effective SARS-CoV-2 clearance in the airways compared to a single dose. Among all regimens tested, the highest prime-boost dose conferred better protection against clinical disease and lung injury. Unlike results from previous preclinical studies on mRNA-1273, the infection-permissive immunity coincided with an anamnestic response. Single-cell RNA sequencing of lung tissue isolated from vaccinated hamsters during acute infection permitted high resolution analysis at the transcriptional level which is not possible in vaccinated humans and has not been performed in other challenge models. mRNA-1273-established immunity prevented the influx of inflammatory cells and the reduction of lymphocyte proportions. The transcriptional

programs of immune cells from vaccinated hamsters appeared to promote pulmonary homeostasis following infection while supporting virus clearance. Surprisingly, transcriptional programs activated in some myeloid and lymphoid cells after infection were shared in vaccinated and mock-vaccinated hamsters. These findings indicate core effector immunological responses are stimulated by transient viral replication in the lungs of vaccinees. Our results highlight the importance of a two-dose mRNA-1273 schedule to protect against severe disease and provides insight into the potential responses within the lungs of vaccinated humans who are exposed to SARS-CoV-2.