

Prof. Grant MacGregor







BUILDING A BETTER MOUSE MODEL TO UNDERSTAND SARS-COV-2

COVID-19 has profoundly affected humanity both through its severe toll and its rapid spread. As it emerged, researchers quickly began developing animal models to help uncover its mechanisms and fight the symptoms. Scientists from the UCI School of Biological Sciences and the UCI School of Medicine are working together on this effort, which is crucial to understand how SARS-CoV-2 causes COVID-19.

For over a century, the use of animal models has led to significant advances in our understanding and treatment of human disease. Many animal species share a remarkable similarity to humans, making them suitable for studying a wide range of pathologies. The models can help scientists understand the processes that cause disease and develop treatments.

The UCI team is a collaboration between Developmental and Cell Biology Professor Grant MacGregor, Neurobiology and Behavior Professor Kim Green, Neurobiology and Behavior Chancellor's Professor Thomas Lane and Ophthalmology Professor Eric Pearlman. Their research teams are working to produce mice with a humanized version of the receptor ACE2 (hACE2), which is short for angiotensin-converting enzyme 2.

As with previous SARS infections, the SARS-CoV-2 virus binds to the ACE2 receptor to enter human cells to cause COVID-19.

Their work is significant because existing mouse models available to scientists to investigate SARS-CoV-2 disease produce much higher and non-physiological amounts of hACE2 in different organs, which can affect the outcomes and interpretations of SARS-CoV-2 experiments.

The BioSci/School of Medicine team is generating a genetically engineered mouse model that produces

human ACE2 at a level, and in organs, that is more consistent with humans. The researchers have also used CRISPR to eliminate the gene making the native mouse ACE2 receptor, so it does not interfere with research results. Once completed, the new model is expected to be a valuable tool for scientists investigating mechanisms of COVID-19's complex disease outcomes as well as future SARS outbreaks.

