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(54) Title: TRANSGENIC MOUSE LINES EXPRESSING HUMAN ACE2 AND USES THEREOF

(57) Abstract: Animal models for severe acute respiratory syndrome (SARS)-coronavirus infection of humans are needed to elucidate SARS pathogenesis and develop vaccines and antivirals. Transgenic mice were developed expressing human angiotensin-converting enzyme 2, a functional receptor for the virus, under the regulation of a global promoter. A transgenic lineage, designated AC70, was among the best characterized against SARS coronavirus infection, showing weight loss and other clinical manifestations before reaching 100% mortality within 8 days after intranasal infection. High virus titers were detected in the lungs and brains of transgene-positive mice on days 1 and 3 after infection. Inflammatory mediators were also detected in these tissues, coinciding with high levels of virus replication. In contrast, infected transgene-negative mice survived without showing any clinical illness. The severity of the disease developed in these transgenic mice, AC70 in particular, makes these mouse models valuable not only for evaluating the efficacy of antivirals and vaccines, but also for studying SARS coronavirus pathogenesis and infection by other coronaviruses utilizing human ACE2 for viral entry into cells.



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