

For evaluating the potential of vaccines and therapeutics against CoVs, including SARS-CoV, MERS-CoVs, and the presently emerging SARS- CoV-2, suitable animal models that can mimic the clinical disease are needed (211, 212). Various animal models were assessed for SARS- and MERS- CoVs, such as mice, guinea pigs, golden Syrian hamsters, ferrets, rabbits, nonhuman primates like rhesus macaques and marmosets, and cats (185, 213-218). The specificity of the virus to hACE2 (receptor of SARS-CoV) was found to be a significant barrier in developing animal models. Consequently, a SARS-CoV transgenic mouse model has been developed by inserting the hACE2 gene into the mouse genome (219). The inability of MERS-CoV to replicate in the respiratory tracts of animals (mice, hamsters, and ferrets) is another limiting factor. However, with genetic engineering, a 288-330/* MERS-CoV genetically modified mouse model was developed and now is in use for the assessment of novel drugs and vaccines against MERS-CoV (220). In the past, small animals (mice or hamsters) have been targeted for being closer to a humanized structure, such as mouse DPP4 altered with human DPP4 (hDPP4), hDPP4-transduced mice. and hDPP4-Tg mice (transgenic for expressing