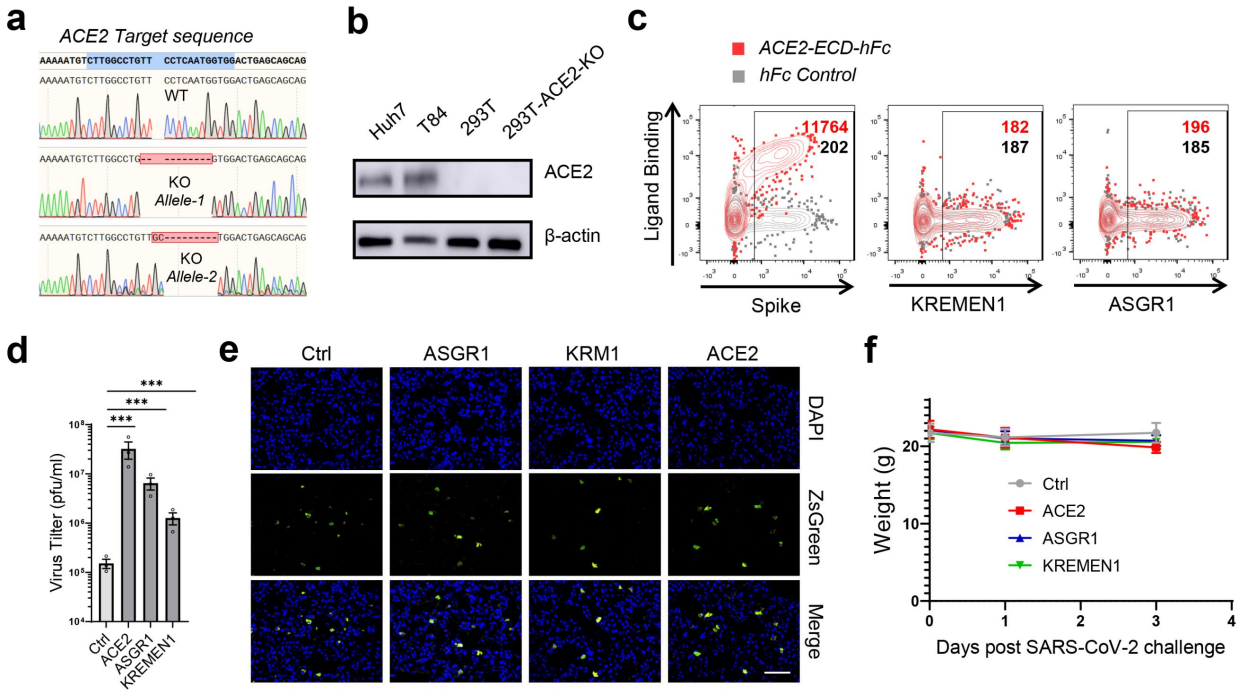

Fig. S4. KREMEN1 and ASGR1 as alternative functional receptors of SARS-CoV-2.

a, ACE2 exon1 was PCR amplified from ACE2-WT/KO HEK293T cells for sequencing. Gene editing at ACE2 locus on both alleles resulting in frame-shift were shown. **b,** Western blot showing the expression of ACE2 in the indicated cells. **c,** KREMEN1, ASGR1 or SARS-CoV-2 Spike expressing HEK293E cells were incubated with ACE2-ECD-hFc (10μg/ml final concentration), and the binding of ACE2-ECD was determined by flow cytometry. **d,** KREMEN1-, ASGR1-, or ACE2-transfected ACE2-KO HEK293T cells were infected with authentic SARS-CoV-2, the viral titers in the cell supernatants 72 hrs post-infection were measured by plaque assay. **e,** Mice were transduced intranasally with 2.5×10^7 FFU of ASGR1- or KREMEN1- expressing lentivirus with a ZsGreen reporter, and sacrificed at the fifth day after transduction to detect ZsGreen expression in lungs. (Bar = 100μm). **f,** Lenti-ACE2/ASGR1/KREMEN1- transduced mice were challenged with authentic SARS-CoV-2, mice weights were measured at the indicated time after challenge. Statistical significance was evaluated by unpaired two-tailed Student's *t*-tests, **P* < 0.05, ***P*<0.01, ****P*<0.001.