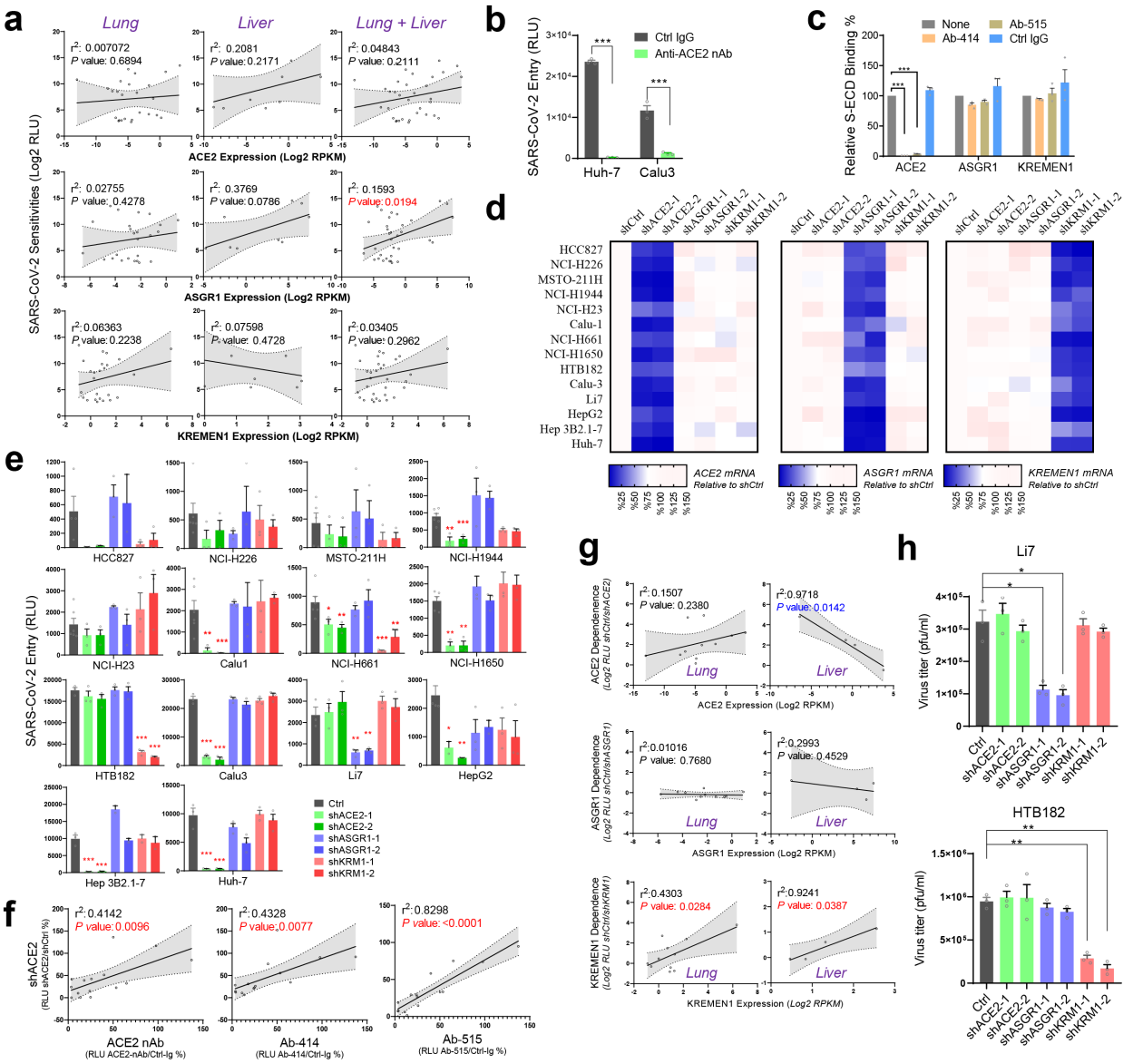

Fig. S7. KREMEN1 and ASGR1 play essential roles in ACE2-independent SARS-CoV-2 entry.

a, 29 lung cancer cell lines and 10 liver cancer cell lines were infected with or without pseudotyped SARS-CoV-2. Correlations of virus sensitivities with the expression levels of individual ASK receptors in the tested cell lines from lung, liver or both (two-sided *Pearson correlation* analysis). **b**, Huh-7 and Calu3 cell lines were infected with S-pseudotyped SARS-CoV-2 in the presence ACE2-S blocking antibody at a final concentration of 2ug/ml. Luciferase activity relative to control antibody treatment was measured 60 hr post-infection (mean ± SEM, n=3, unpaired two-tailed Student's *t*-tests, ***$P < 0.001$). **c**, ACE2, ASGR1 or KREMEN1expressing HEK293E cells were incubated with SARS-CoV2 S-ECD-hFc in the presence of neutralizing antibody Ab-414 or Ab-515, that we isolated from convalescent COVID-19 patients, at final concentration of 5μg/mL.

Relative S-ECD binding to no treatment was measured (mean ± SEM, n=3, unpaired two-tailed Student's *t*-tests, ***$P < 0.001$). **d**, Lentivirus encoding shRNA against ACE2, KREMEN1 or ASGR1 were transduced into the indicated cells respectively, gene expression levels relative to control shRNA were measured by real time RT-qPCR and shown as heatmap (n=2). **e and f**, Knock-down (KD) of ACE2, ASGR1 or KREMEN1 in the indicated cell lines followed by infection with S-pseudotyped SARS-CoV-2. **e**, Luciferase activity relative to control was measured 60 hr post-infection (mean ± sem, n=3, unpaired two-tailed Student's *t*-tests, *P< 0.05, **$P<0.01$, ***$P < 0.001$). **f**, Logarithm of the effect of ACE2 shRNA-mediated KD on virus entry was corelated with the effect of different ACE2-targeting antibodies on virus entry (two-sided *Pearson correlation* analysis). **g**, Logarithm of the effect of receptor KD on virus entry was corelated with expression level of corresponding receptors in the tested cell lines from lung and liver (two-sided *Pearson correlation* analysis). **h**, KD of ACE2, ASGR1 or KREMEN1 in HTB-182 and Li7 cells followed by infection with authentic SARS-CoV-2 at a MOI of 1. The viral titers in the cell supernatants 72 hr post-infection were measured by plaque assay (mean ± SEM, n=3). The statistical significance was evaluated by unpaired two-tailed Student's *t*-tests, *$P<0.05$, **$P<0.01$, ***$P<0.001$.