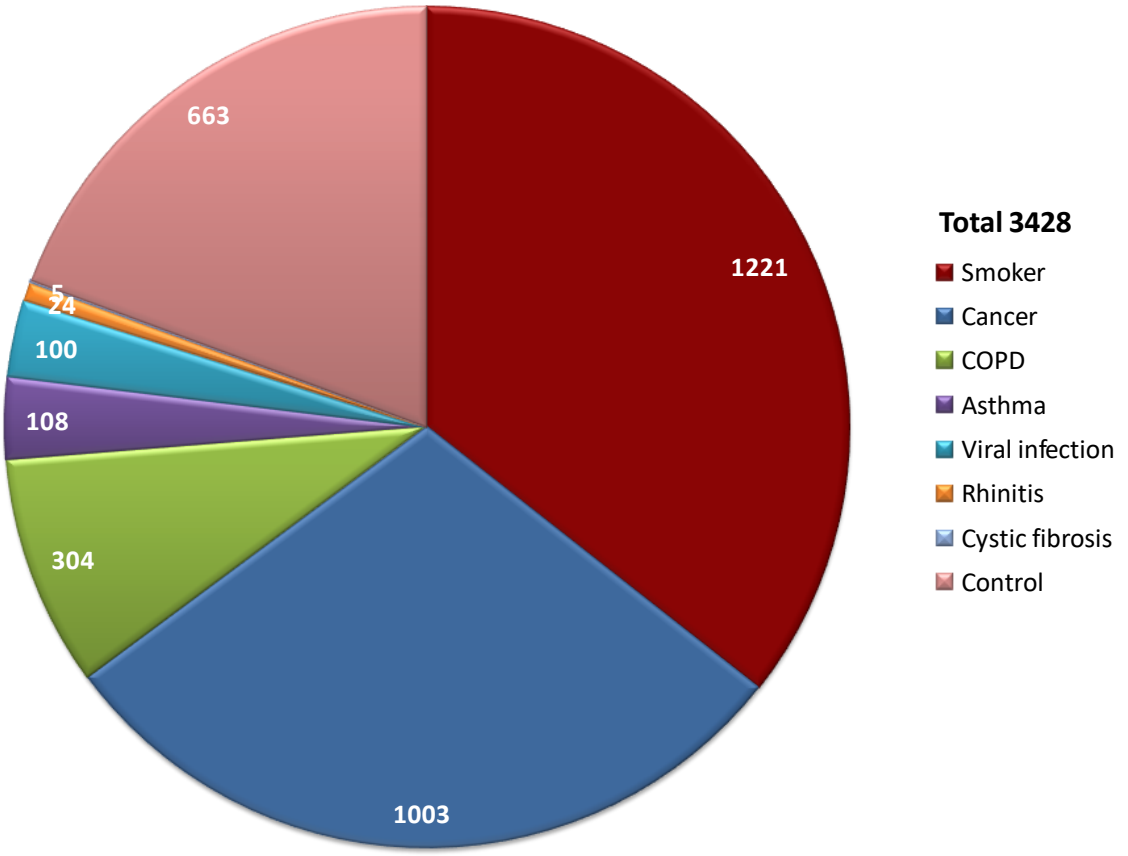
Supplementary information

Supplementary table 1: List of datasets recruited in this study

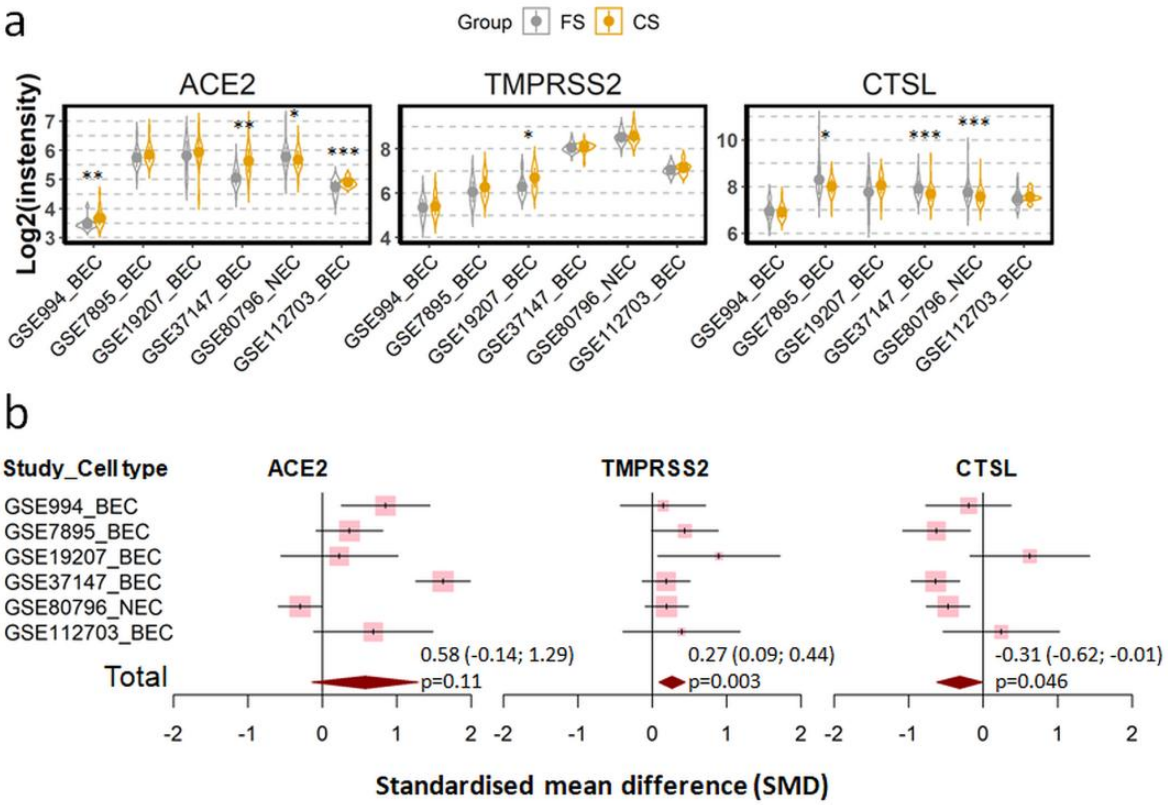
Datasets	Platform	Ref. (PMID)	Studying focus	Submitted time (year)	Cell type	Sample sizes
Crystal et al. Group 01 (GSE4498, GSE5058, GSE5059, GSE7832, GSE8545, GSE10006, GSE10135, GSE11784, GSE11906, GSE11952, GSE13931, GSE13933, GSE17905, GSE18385, GSE19407, GSE19667, GSE20250, GSE20257)	GPL570 [HG-U133_Plus_2]	18339782, 17108109, 18832735, 21829517, 19852842, 20693378	Smoking and COPD	2006-2010	AEC	49 COPD, 124 NS ,167 CS
Crystal et al. Group 02 (GSE22047, GSE24337, GSE30063, GSE34450, GSE43939, GSE53537, GSE63127, GSE64614, GSE76324, GSE77658)	GPL570 [HG-U133_Plus_2]	21325429, 22855713, 24465567, 26927796	Smoking and COPD	2010-2016	AEC	36 COPD, 98 NS, 129 CS
GSE994	GPL96 [HG-U133A]	15210990	Smoking	2004	BEC	34 CS, 18 FS, 23 NS
GSE4115	GPL96 [HG-U133A]	17334370	Lung cancer	2006	BEC	102 LC, 90 NC
GSE4302	GPL570 [HG-U133_Plus_2]	17898169	Smoking and athma	2006	BEC	42 baseline asthma, 13 placebo treated asthma, 19 Flovent treated asthma, 16 smoker, 28 HC
GSE7895	GPL96 [HG-U133A]	17894889	Smoking	2007	BEC	52 CS, 31 FS, 21 NS
GSE8987	GPL571 [HG-U133A_2]	18513428	Smoking	2007	NEC	7 CS, 8 NS
GSE11348	GPL570 [HG-U133_Plus_2]	18658112	Human rhinovirus infection	2008	NEC	48 Control 45 HRV
GSE13396	GPL570 [HG-U133_Plus_2]	19710636	Human rhinovirus infection	2008	BEC	11 Control 11 HRV
GSE14633	GPL5175 [HuEx-1_0-st]	19168627	Smoking	2009	BEC	11 CS, 11 NS
GSE18965	GPL96 [HG-U133A]	20110557	Asthma	2009	BEC	9 Asthma, 7 HC
GSE19027	GPL96 [HG-U133A]	20689807	Smoking and lung cancer	2009	BEC	CA: 9 CS, 12 FS; HC: 20 CS 9 FS 9 NS
GSE19187	GPL6244 [HuGene-1_0-st]	22005912	Allergic rhinitis and asthma	2009	NEC	7 Controled asthma,, 6 uncontroled asthma, 11 HC, 14 Rhinitis
GSE28835	GPL13447 [HG-U133A_2]	21636547	Lung cancer	2011	LAEC	8 LC ,5 NC
GSE37147	GPL13243 [HuGene10stv1_Hs_ENSG]	23471465	COPD	2012	BEC	COPD: 30 CS, 57 FS; HC: 69 CS, 82 FS
GSE40445	GPL10097 [HsAirwaya520108F]	23537407	Cystic fibrosis	2012	NEC	5 CF, 5 HC
GSE44037	GPL13158 [HT_HG-U133_Plus_PM]	24282527	Allergic rhinitis and asthma	2013	BEC	12 Asthma ,12 HC, 10 Rhinitis
GSE51392	GPL13158 [HT_HG-U133_Plus_PM]	24475887	Poly(I:C) stimulation	2013	BEC	34 Control 34 Poly(I:C)
GSE54495	GPL570 [HG-U133_Plus_2]	25705890	Lung cancer	2014	Peripheral AEC	17 LC, 13 Smoker

GSE56341	GPL6244 [HuGene-1_0-st]	24298892	COPD	2014	Small AEC	8 COPD, 14 FS
GSE66499	GPL6244 [HuGene-1_0-st]	25981554	Lung cancer	2015	BEC	490 LC ,190 HC
GSE67061	GPL17077 [Agilent-039494]	26308599	Lung cancer	2015	AEC	56 LC ,17 HC
GSE70190	GPL20609 [PrimeView]	26810609	Human rhinovirus infection	2015	BEC	10 Control, 10 rhinovirus infection
GSE80796	GPL6244 [HuGene-1_0-st]	28376173	Smoking and lung cancer	2016	NEC	CA: 113 CS, 196 FS; HC: 73 CS, 123 FS
GSE84101	GPL570 [HG-U133_Plus_2]	28273093	Smoking	2016	Small AEC	7 SM ,7 NS
GSE97010	GPL17244 [HuGene-1_0-st]	29932825	Smoking	2017	BEC	63 baseline ,63 post ASE
GSE112073	GPL17556 [HuGene-1_0-st]	31233743	Smoking	2018	BEC	9 CS, 21 FS
GSE128708	GPL570 [HG-U133_Plus_2]	32432483	COPD	2019	Small AEC	124 COPD smoker, 84 NS

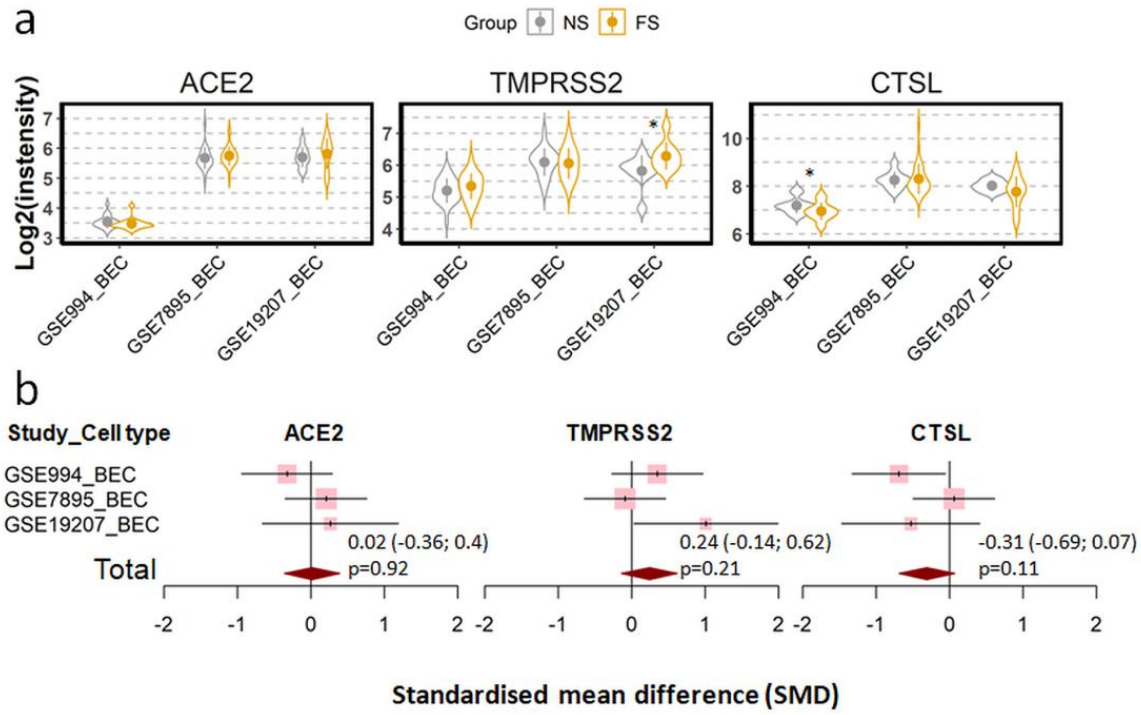
AEC, Airway epithelial cells; BEC, Bronchial and nasal epithelial cells; LAEC, Large airway epithelial cells; NEC, Nasal epithelial cells; NS, Never smoker; SM, Smoker; CS, Current smoker; FS, Former smoker; LC, Lung cancer; HC, Healthy control; COPD,. Chronic obstractive pulmonary disease; ASE, Acute smoking exposure.



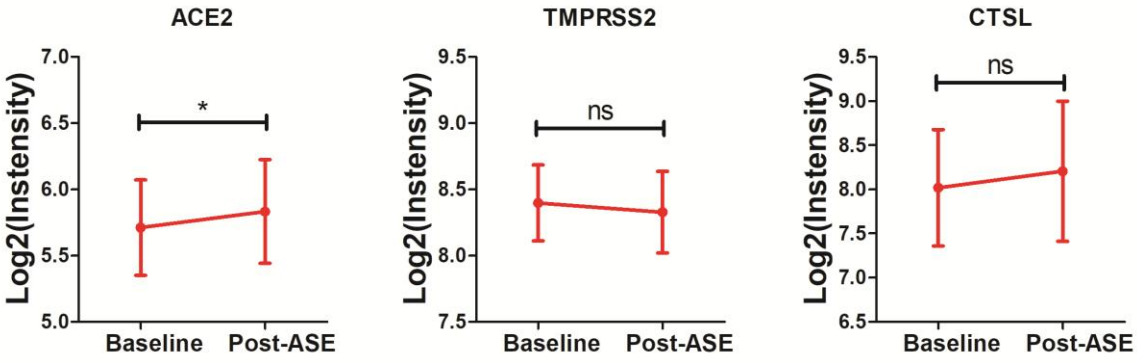
Supplementary fig.1: Pie chart showing the composition of samples. Control group consists of healthy never smokers, healthy subjects without information of smoking status and control samples in *in vitro* studies, while the smoker group contains healthy smokers, including both current smokers and former smokers.



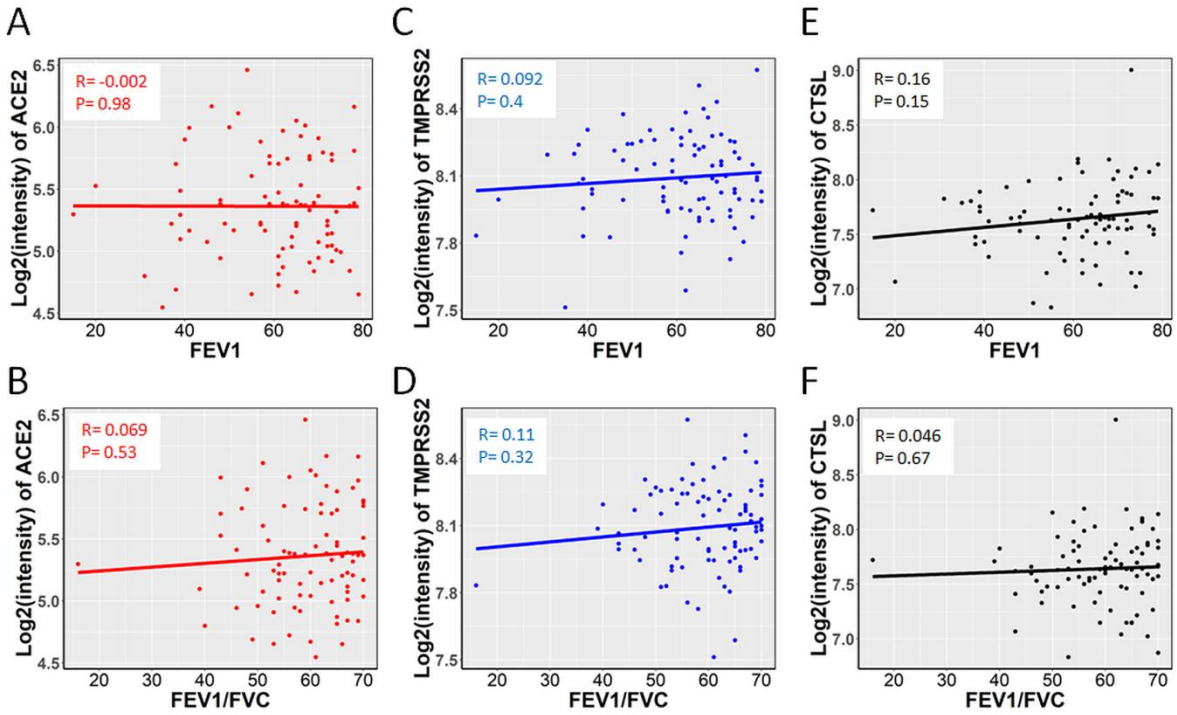
Supplementary Fig. 2. Expression of ACE2, TMRPSS2 and cathepsin L (CTSL) in airway epithelial cells of healthy current smokers (CS) and former smokers (FS). a) Violin plot of expression levels of ACE2, TMPRSS2 and CTSL in 6 datasets which contain current smokers and former smoker. The mean and standard deviation (SD) of each group were presented as dot and line, respectively. BEC, bronchial epithelial cells; NEC, nasal epithelial cells. Statistical differences were calculated by Student's t test. *p<0.05, **p<0.01, ***p<0.001. **b)** Forest plot of 6 datasets examining expression of ACE2, TMPRSS2 and CTSL in current smokers and former smokers. The x-axis indicates the standardized mean difference (SMD), while the y-axis shows GEO datasets and cell types. Each square in the plots represents the SMD in corresponding datasets and the 95% confidence interval (CI) is showed by the error bar. The size of each square represents the weight of the individual dataset in the meta-analysis. The diamonds in the bottom represent the SMD of the meta-analysis. The SMD, 95% CI and *P* values of meta-analysis are depicted.



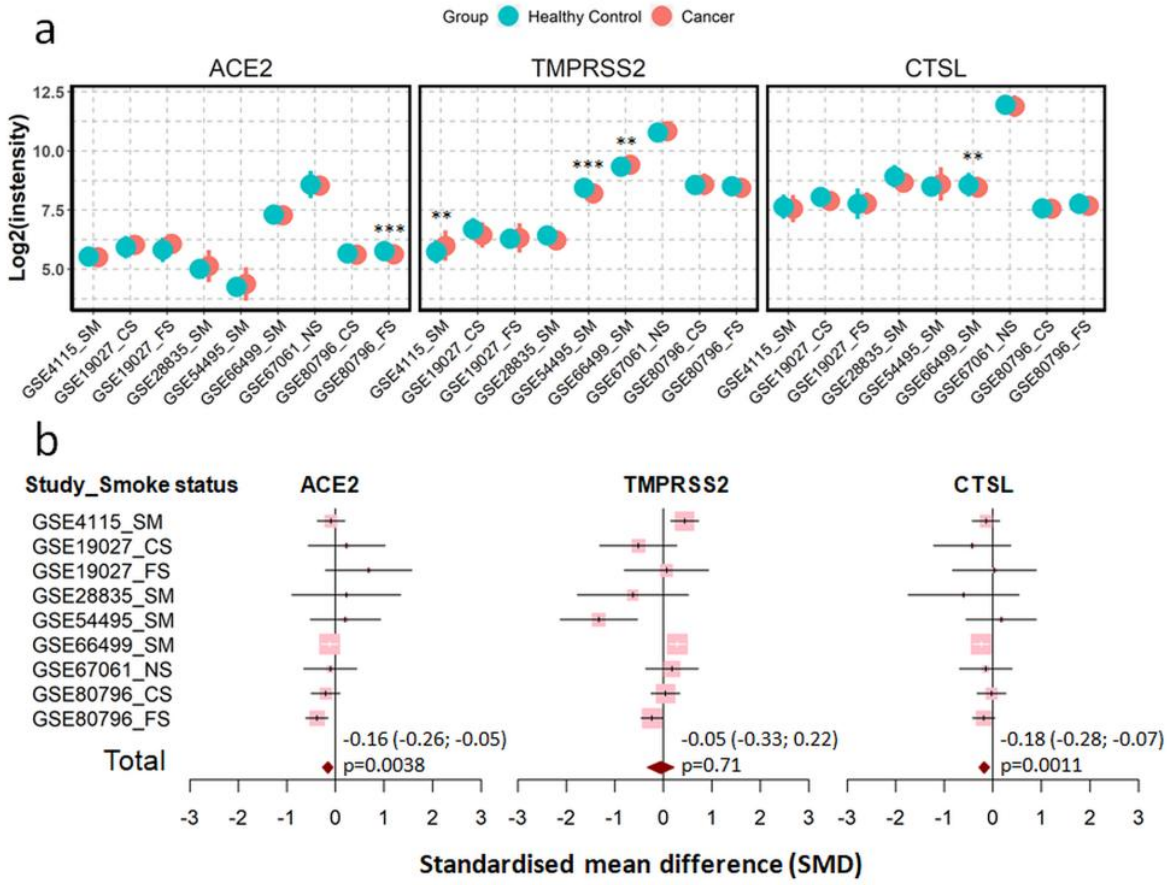
Supplementary Fig. 3. Expression of ACE2, TMRPSS2 and cathepsin L (CTSL) in the airway epithelial cells of healthy never smokers (NS) and former smokers (FS) . a) Violin plot of expression levels of ACE2, TMPRSS2 and CTSL in 3 datasets which contain current smokers and former smoker. Statistical difference was calculated by Student's t test. *p<0.05. **b)** Forest plot of 3 datasets examining expression of ACE2, TMPRSS2 and CTSL in never smokers and former smokers. The x-axis indicates the standardized mean difference (SMD), while the y-axis shows GEO datasets and cell types. The SMD, 95% CI and *P* values of meta-analysis are depicted.



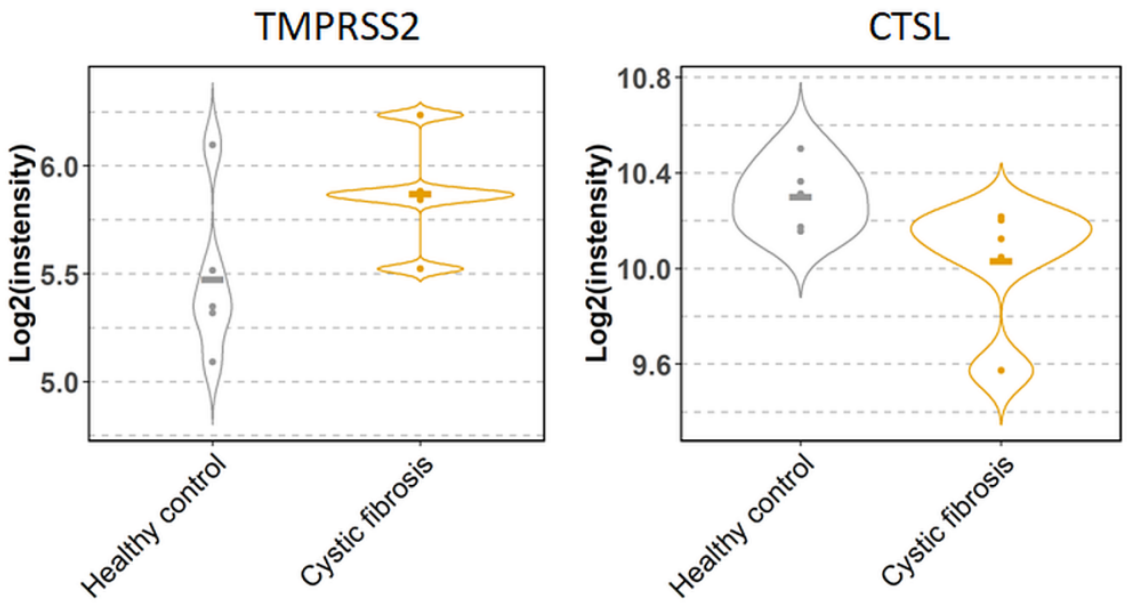
Supplementary Fig. 4. Expression of ACE2, TMPRSS2 and cathepsin L (CTSL) in airway epithelial cells before and after acute smoke exposure (ASE) in healthy smokers in dataset GSE97010. The post-ASE group stands for 63 smokers who were asked to refrain from cigarette smoking for at least 2 days and then subjected to ASE, while the 63 subjects obtained from smoking and underwent bronchoscopy at a separate time at least 6 wks from the post-smoking bronchoscopy to serve as an unexposed baseline group. Statistical difference was analyzed by paired Student t test. * $p<0.05$, ns. not significant.



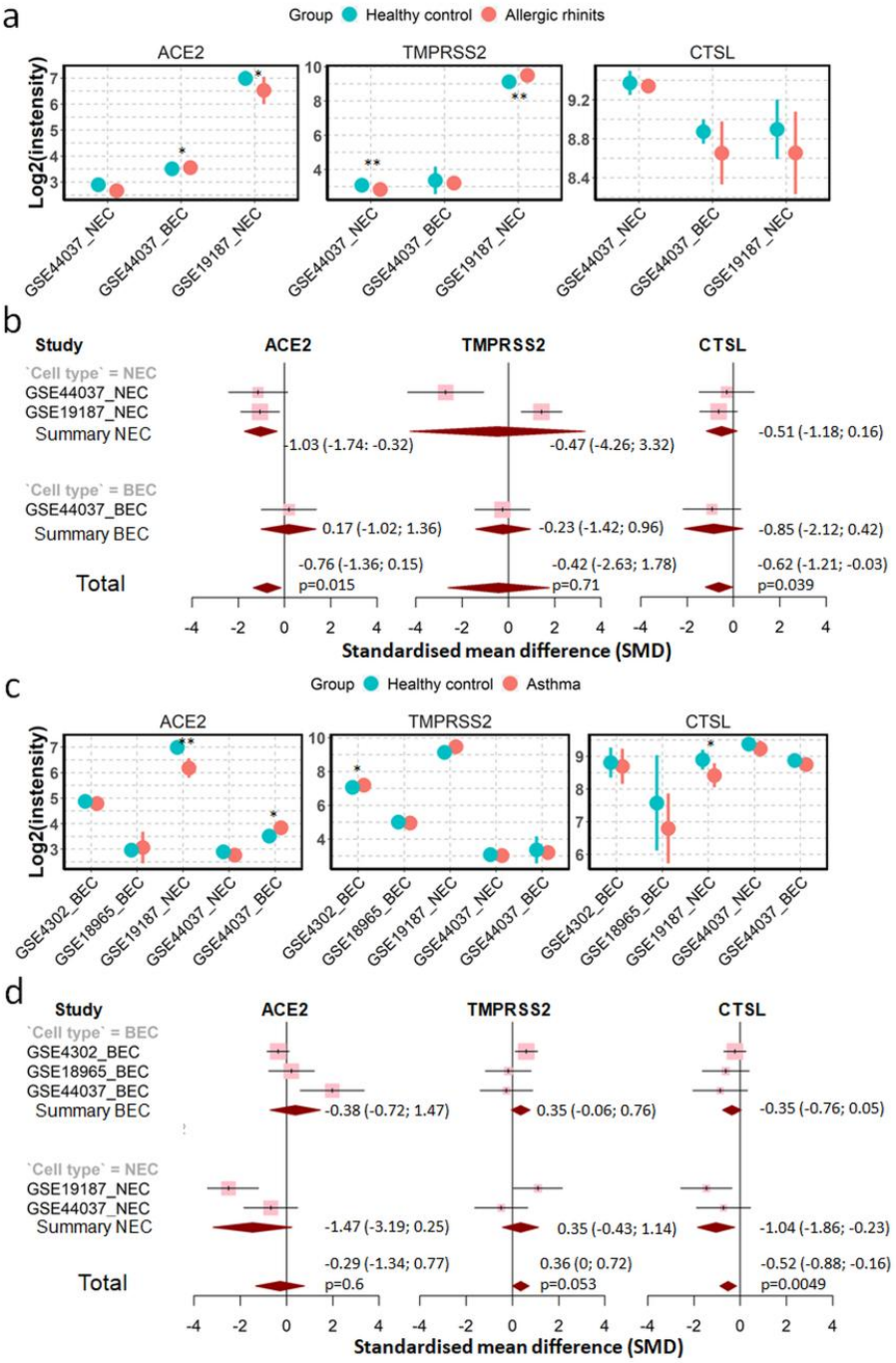
Supplementary Fig. 5. Correlation between SARS-CoV-2 entry related genes with lung function indexes in COPD patients. Linear regression of FEV1 (A,C,E) and FEV1/FVC (B,D,F) with expression of ACE2 (A,B), TMPRSS2 (C,D) and cathepsin L (CTSL) (E,F). Data are from dataset GSE37147. FEV1, the first second of forced expiration to the full; FVC, forced vital capacity; FEV1/FVC, ratio of FEV1 and FVC. *P* values and correlation coefficient (R) calculated by pearson method are depicted.



Supplementary Fig. 6. Expression of ACE2, TMRPSS2 and cathepsin L (CTSL) in airway epithelial cells of healthy controls and patients with lung cancer. a) Plot of expression levels of ACE2, TMPRSS2 and CTSL in 9 datasets which contain healthy control and patients with lung cancers. Statistical difference was calculated by Student's t test. *p<0.05, **p<0.01, ***p<0.001. **b)** Forest plot of 9 datasets examining expression of ACE2, TMPRSS2 and CTSL in healthy controls and patients with lung cancer. The x-axis indicates the standardized mean difference (SMD), while the y-axis shows GEO datasets and cell types. The SMD, 95% CI and p values of meta-analysis are depicted. BEC, bronchial epithelial cells; NEC, nasal epithelial cells; CS, Current smokers; FS, Former smokers; SM, Smokers.

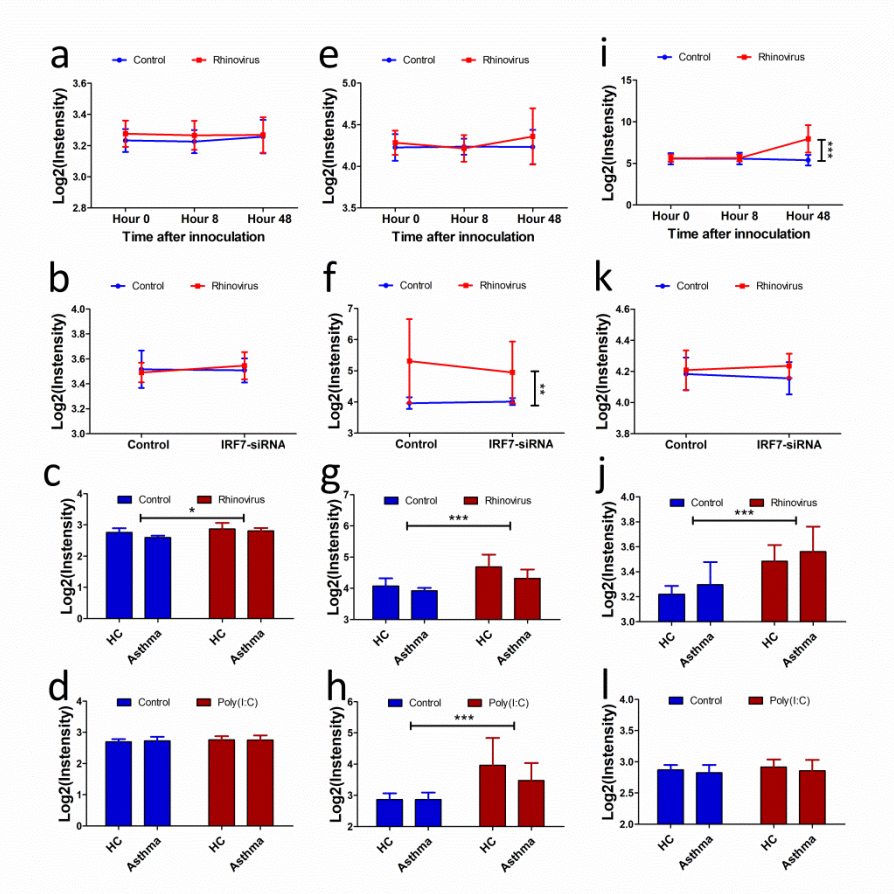


Supplementary Fig. 7. Expression of TMPRSS2 and cathepsin L (CTSL) in airway epithelial cells of healthy controls (n=5) and patients with cystic fibrosis (n=5) in dataset GSE40445. No significant difference has been observed between the two groups.



Supplementary Fig. 8. Expression of ACE2, TMPRSS2 and cathepsin L (CTSL) in airway epithelial cells of healthy controls, patients with asthma and patients with allergic rhinitis. a) Plot of expression levels of ACE2, TMPRSS2 and CTSL in 3 datasets which contain healthy control and patients with allergic rhinitis. Statistical difference was calculated by Student' t test. *p<0.05, **p<0.01, ***p<0.001. **b)** Forest plot of 3 datasets examining expression of ACE2, TMPRSS2 and CTSL in healthy controls and patients with allergic rhinitis. The x-axis indicates the standardized mean difference (SMD), while the y-axis shows GEO datasets and cell types. The SMD, 95% CI and p values of meta-analysis are depicted. **c)** Plot of expression levels of ACE2, TMPRSS2 and CTSL in 5 datasets which contain healthy control and patients with asthma. **d)** Forest plot of 5 datasets examining

expression of ACE2, TMPRSS2 and CTSL in healthy controls and patients with asthma. BEC, bronchial epithelial cells; NEC, nasal epithelial cells.



Supplementary Fig. 9. Expression of IFN-α, IFN-β and IFN-γ in airway epithelial cells after rhinoviral infection or TLR3 activation. Kinetics of expression of IFN-α (a), IFN-β (e), and IFN-γ (i) in airway epithelial cells of healthy subjects artificially infected with rhinovirus or saline control (data from GSE11348). Expression of IFN-α (b), IFN-β (f), and IFN-γ (j) in airway epithelial cells isolated from healthy subjected and stimulated in vitro with or without rhinovirus in presence or absence of IRF-siRNA (data from GSE70190). Expression of IFN-α (c), IFN-β (g), and IFN-γ (k) in airway epithelial cells isolated from healthy subjected or patients with asthma and stimulated in vitro with rhinovirus or saline control (data from GSE13396). Expression of IFN-α (d), IFN-β (h), and IFN-γ (l) in airway epithelial cells isolated from healthy subjected or patients with asthma and stimulated in vitro with polyI:C or or saline control (data from GSE13396). Statistical analysis was performed using two-way ANOVA, Tukey's test for post hoc analysis was performed after two-way ANOVA analysis. *, $p<0.05$, **, $p<0.01$, ***, $p<0.001$. HC, healthy control; NS, not significant.