Pathway	Genes
P1	BCL2L1, PTGS2, CDKN1A, NFKBIA, EGFR, BAX, BID, JUN, MAPK3, MAPK1, NFKB1, MYC, BIRC5, CHUK, PPARG, VEGFA, MAPK8, IL2RA, TP53, CASP3, CCND1, CASP8, CASP9, IL6, CDK4, MMP9, MMP2, IL8, BCL2
P2	CCL2, PTGS2, CDKN1A, NFKBIA, EGFR, BAX, IL1B, BID, IFNB1, MAPK3, MAPK1, NFKB1, MYC, CHUK, TNF, VEGFA, TP53, CASP3, CCND1, CASP8, CASP9, IL6, CDK4, IL8
P3	BIRC5, NFKBIA, BAX, BID, JUN, IFNB1, MAPK3, MAPK1, NFKB1, MYC, CDKN1A, CHUK, TNF, MAPK8, TP53, CASP3, CASP8, CASP9, IL6, MMP9, IL8, BCL2
P4	PTGS2, CDKN1A, NFKBIA, BAX, BID, JUN, IFNB1, MAPK3, MAPK1, NFKB1, MYC, CHUK, VEGFA, MAPK8, TP53, CASP3, CCND1, CASP8, CASP9, IL6, CDK4, IL8
P5	BCL2L1, TP53, CASP3, BID, NFKBIA, JUN, CHUK, CASP8, CASP9, MAPK3, PARP1, MAPK1, MCL1, BAX, NFKB1, MAPK8, BIRC5, TNF, BCL2
P6	BCL2L1, IL2RA, TP53, CASP3, CCND1, BID, NFKBIA, JUN, CHUK, CASP8, IFNB1, IL6, CDK4, BAX, NFKB1, IL1B, CASP9, MAPK8, BCL2
P7	CCL2, TNF, CASP3, CDK4, JUN, BAX, CCND1, IL6, MAPK3, MAPK1, VEGFA, NFKB1, IL1B, MMP2, MAPK8, IL8, BCL2
P8	TP53, CASP3, CCND1, CDKN1A, NFKBIA, JUN, CHUK, CASP8, BID, IL6, TNF, CDK4, BAX, CASP9, NFKB1, MYC, IFNB1, MAPK8, BCL2
P9	TP53, CASP3, CCND1, CDKN1A, NFKBIA, EGFR, CHUK, CASP8, IFNB1, MAPK3, MAPK1, CDK4, BAX, NFKB1, MYC, CASP9, BID, TNF
P10	CCL2, CASP3, NLRP3, CDK4, BID, NFKBIA, CHUK, CASP8, IFNB1, IL6, MAPK3, MAPK1, TNF, BAX, NFKB1, IL1B, CASP9, IL8
P11	BCL2L1, CCL2, NLRP3, NFKBIA, JUN, CHUK, CASP8, IFNB1, IL6, MAPK3, MAPK1, TNF, P2RX7, NFKB1, IL1B, MAPK8, IL8, BCL2
P12	CCL2, PTGS2, CASP3, NFKBIA, JUN, CHUK, CASP8, IL6, MAPK3, MAPK1, TNF, MMP9, NFKB1, IL1B, MAPK8, IL8
P13	CCL2, PTGS2, CASP3, NFKBIA, JUN, CHUK, CASP8, IFNB1, IL6, MAPK3, MAPK1, MMP9, NFKB1, IL1B, MAPK8, TNF
P14	BCL2L1, IL2RA, TP53, CCND1, CDKN1A, NFKBIA, JUN, CHUK, BAX, IL6, MAPK3, MAPK1, CDK4, NFKB1, MYC, MAPK8, TNF
P15	BCL2L1, TP53, CDK4, CDKN1A, EGFR, CHUK, BAX, CASP9, CCND1, MAPK3, MAPK1, VEGFA, NFKB1, MAPK8

Fig. S1 The list of genes in top 15 pathways

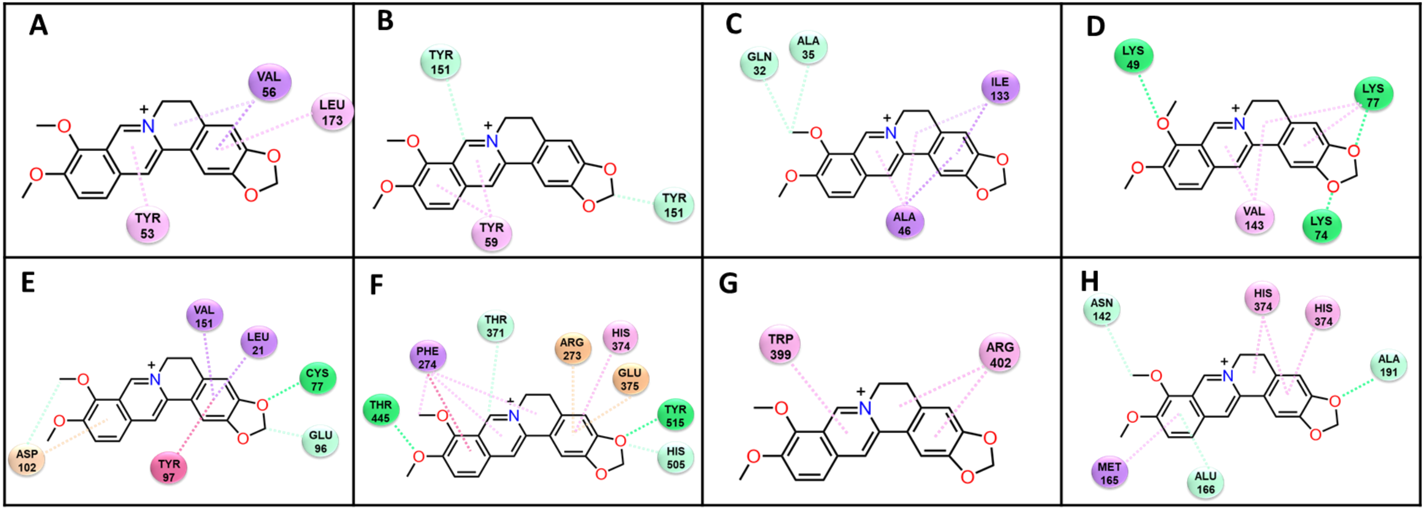

Fig. S2 Binding interactions in complex MAPK3-berberine, TNF-Berberine, BAX-berberine, BAX-berberine, NFκB1-berberine, CHUK-berberine, ACE2-berberine, TMPRSS2 -berberine, 3CLpro-berberine. Predicted lowest-energy binding mode of berberine with the following proteins in 2-dimensional images: (A) MAPK3; (B) TNF; (C) BAX ; (D) NFκB1; (E) CHUK; (F) ACE2 ; (G)TMPRSS2; (F) 3CLpro. The green, purple, and orange lines stand for hydrogen binding, hydrophobic interaction, and anion-π interaction between berberine and residues, respectively.

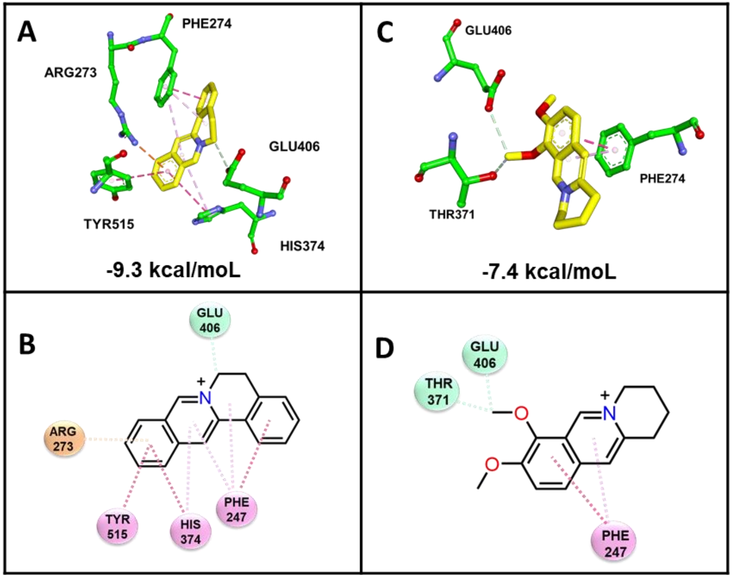

Fig. S3 Binding explorations of complex ACE2-anolog1 and ACE2-anolog1 . Predicted lowest-energy binding mode of ACE2-anolog1 in 3-dimensional image (A) and 2-dimensional image (B); ACE2-anolog2 in 3-dimensional image (C) and 2-dimensional image (D). For analogs, the C, O and N are highlighted in yellow, red and blue, respectively. For residues of proteins, the green, red and blue stand for C, O and N, respectively. The green, purple, orange lines stand for hydrogen binding, hydrophobic interaction and anion-π interaction between BBR and related residents, respectively.

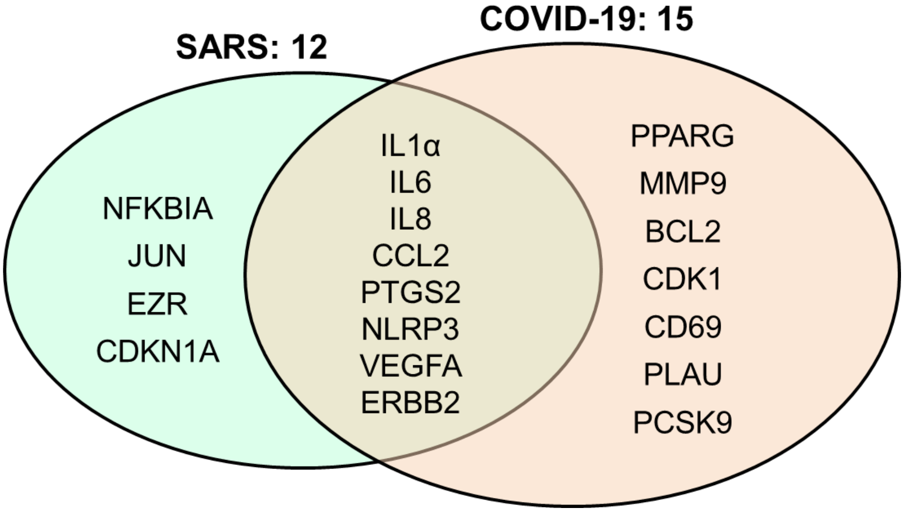

Fig. S4 Comparison of regulated targets of berberine on the lung for SARS and COVID-19. There are 12 and 15 pharmacological targets for SARS and COVID-19 respectively. Among them, 8 shared targets were displayed in overlap area.