Supplementary Fig. 1: Human constraint scores for host proteins involved in SARS-CoV-2 viral entry

TMPRSS2

Category	Exp. SNVs	Obs. SNVs	Constraint metrics	
Synonymous	143.6	132	Z = 0.76 o/e = 0.92 (0.8 - 1.06)	0 —o— 1
Missense	323.2	303	Z = 0.4 o/e = 0.94 (0.85 - 1.03)	0 —o— 1
pLoF	30.9	20	pLI = 0 o/e = 0.65 (0.46 - 0.94)	0 —o— 1

ACE2

Category	Exp. SNVs	Obs. SNVs	Constraint metrics	
Synonymous	101	84	Z = 1.33 o/e = 0.83 (0.7 - 1)	0 —o— 1
Missense	281.8	223	Z = 1.25 o/e = 0.79 (0.71 - 0.88)	0 —o— 1
pLoF	31	3	pLI = 1 o/e = 0.1 (0.04 - 0.25)	0 o—— 1

Cathepsin B (CTSB)

Category	Exp. SNVs	Obs. SNVs	Constraint metrics	
Synonymous	82.6	168	Z = -7.39 o/e = 2.03 (1.73 - 1.99)	0 ——▷1
Missense	207.9	344	Z = -3.35 o/e = 1.65 (1.51 - 1.81)	0 ——▷1
pLoF	19.2	17	pLI = 0 o/e = 0.89 (0.61 - 1.33)	0 —o— 1

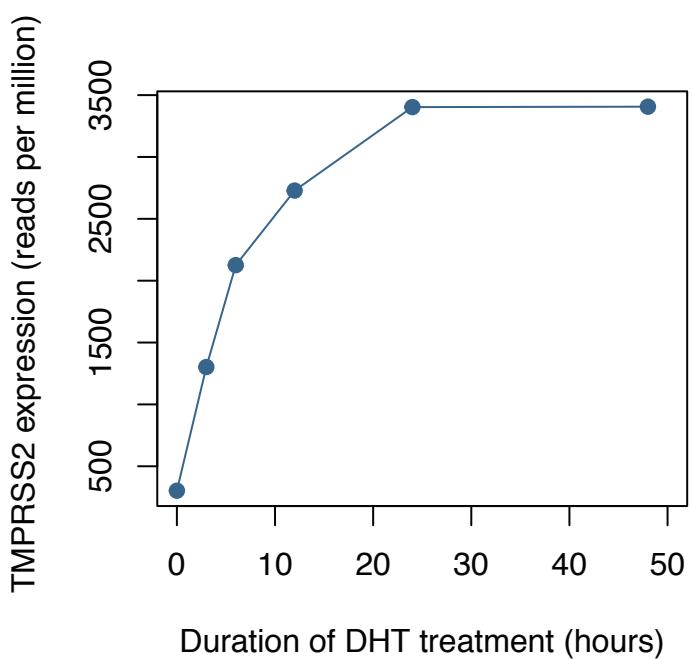
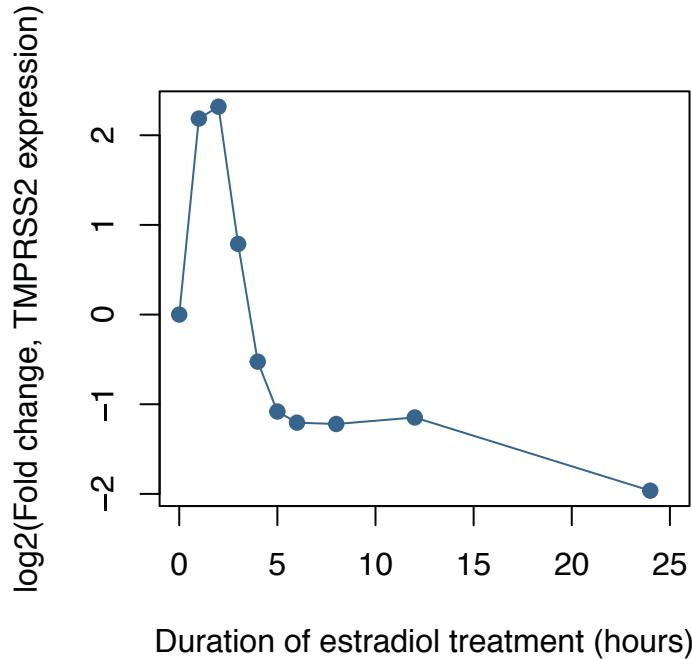
Note Too many missense variants; missense z score < -5

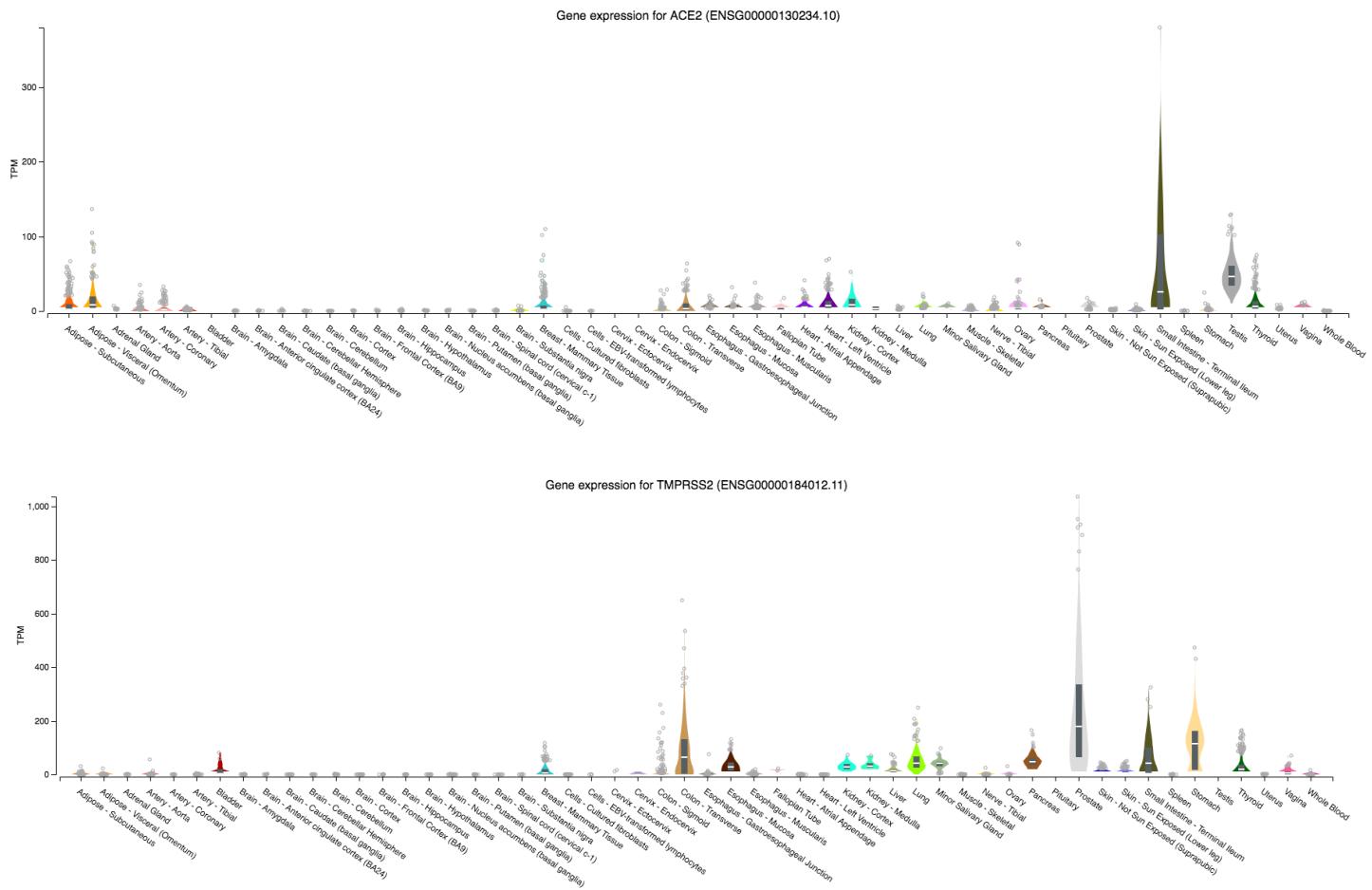
Note Too many or too few synonymous variants; synonymous z score < -5 or synonymous z score > 5

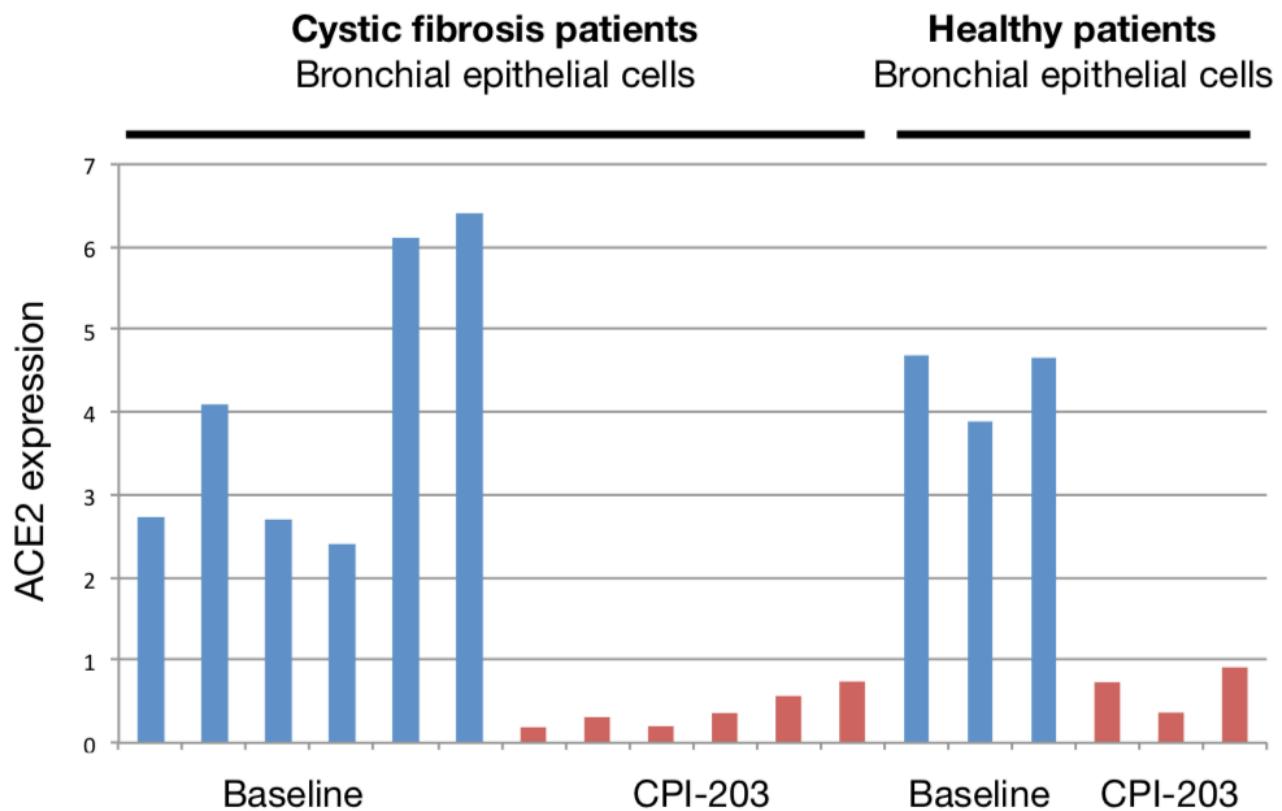
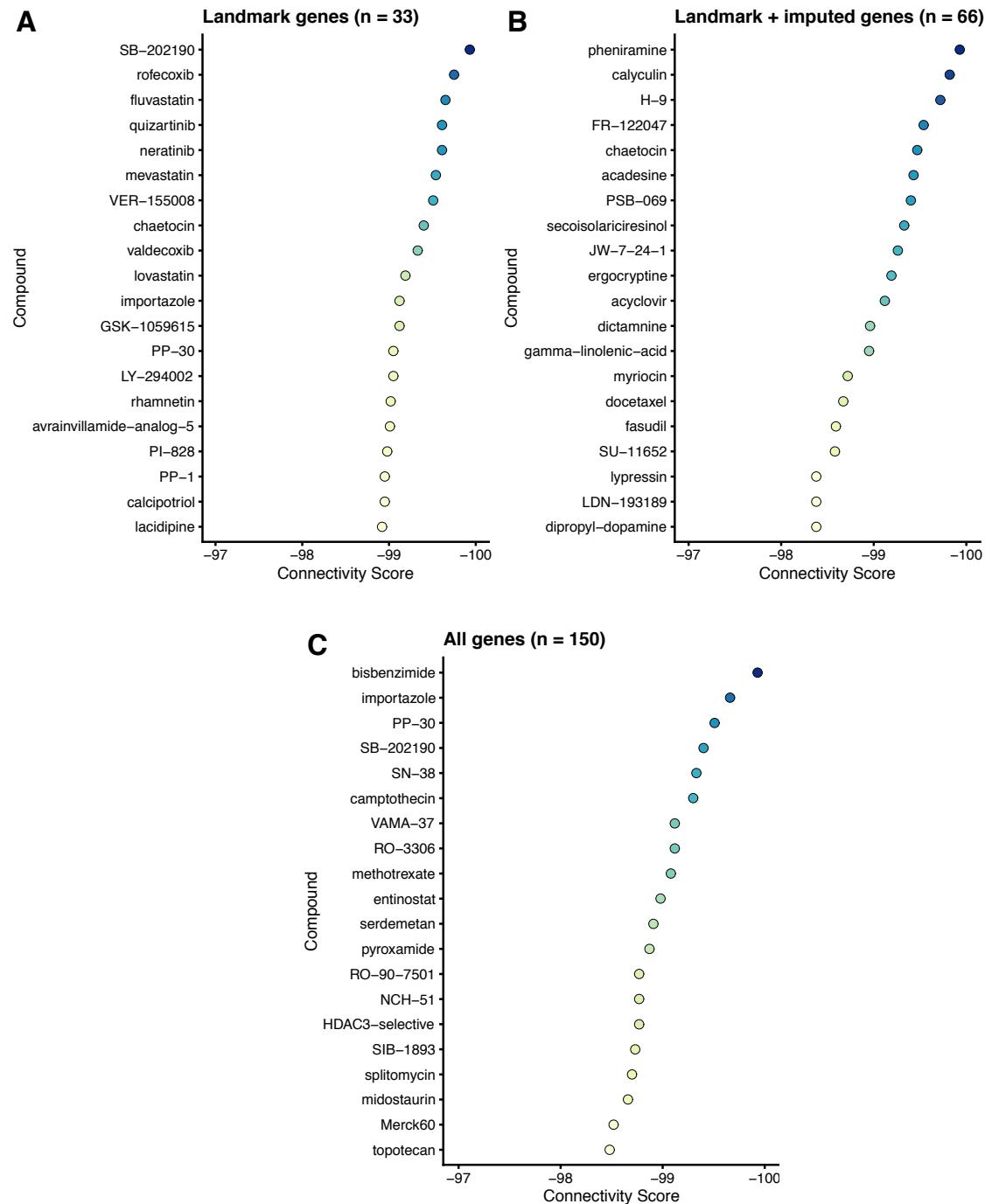
Cathepsin L (CTSL)

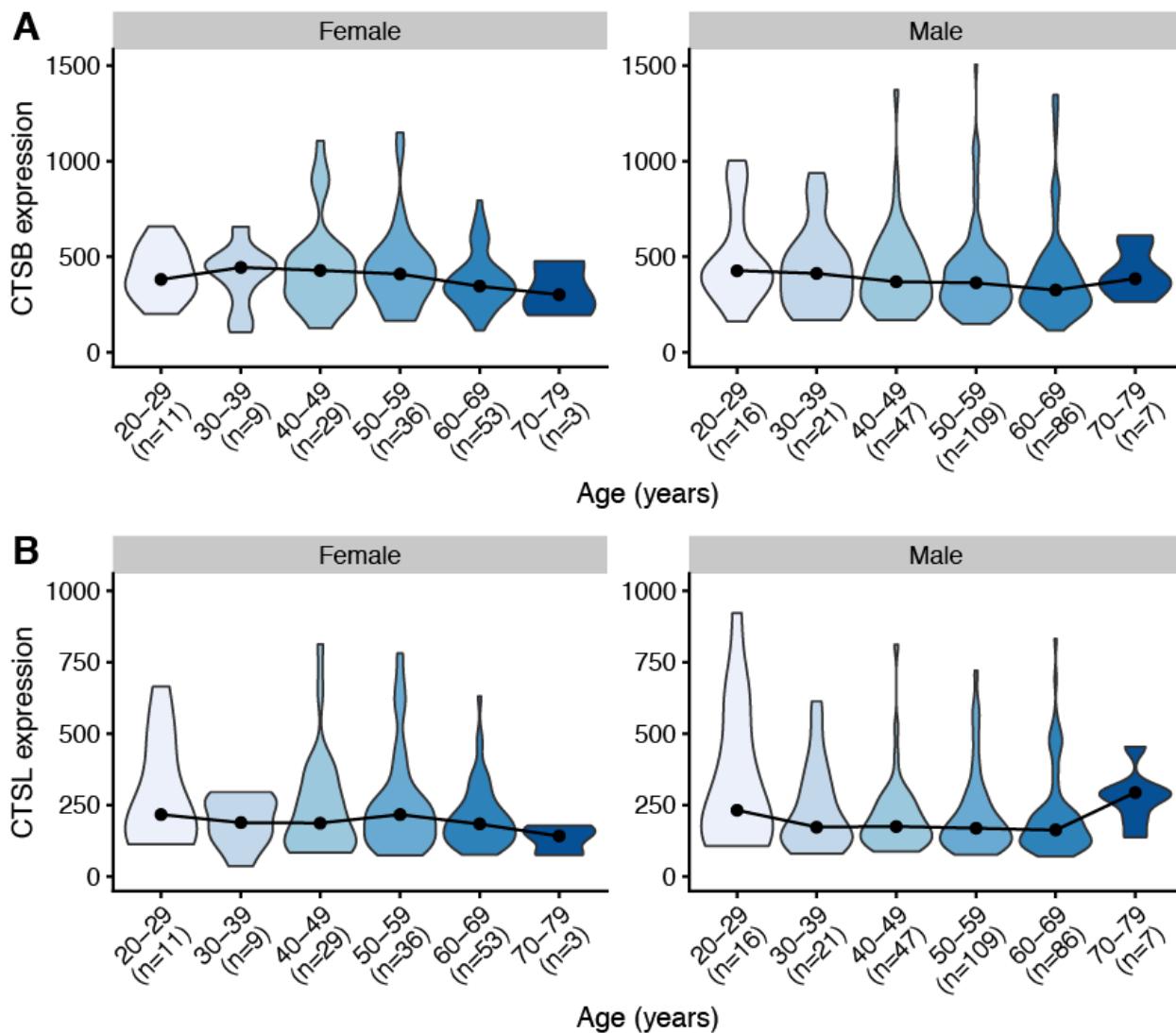
Category	Exp. SNVs	Obs. SNVs	Constraint metrics	
Synonymous	64.2	59	Z = 0.51 o/e = 0.92 (0.74 - 1.14)	0 —o— 1
Missense	180.7	167	Z = 0.36 o/e = 0.92 (0.81 - 1.05)	0 —o— 1
pLoF	15.2	6	pLI = 0.01 o/e = 0.4 (0.22 - 0.78)	0 —o— 1

Supplementary Fig. 1: Human population-based constraint scores for TMPRSS2, ACE2, Cathepsin B and Cathepsin L. Data taken from the gnomAD browser (v2.1.1). Of the four host proteins, only ACE2 is strongly intolerant of loss-of-function mutations

Supplementary Fig. 2: Time-dependent effects of estradiol and DHT on TMPRSS2 expression

Supplementary Fig. 2: Time-dependent effects of estradiol and DHT on TMPRSS2 expression. Estradiol data from Baran-Gale et al. (SRP070657), DHT data from GEO accession GSE70150.

Supplementary Fig. 3: ACE2 and TMPRSS2 have restricted expression patterns across human tissues

Supplementary Fig. 3: ACE2 and TMPRSS2 have restricted expression patterns across human tissues.
Data taken from the GTEx project (v8).

Supplementary Fig. 4: CPI-203 treatment in bronchial epithelial cells reduces ACE2 expression

Supplementary Fig. 5: Top hits from Connectivity Map for compounds that down-regulate host proteins that interact with SARS-CoV-2 proteins

Supplementary Fig. 5: Top hits from Connectivity Map for compounds that down-regulate host proteins that interact with SARS-CoV-2 proteins. Top compounds shown for three comparisons: landmark genes (panel A, directly assayed by L1000 array), landmark + top imputed genes (panel B), and all genes (top 150 by fold-change). Gene number per analysis listed in plot titles, strongest down-regulator compounds have scores closest to -100.

Supplementary Fig. 6: Expression of CTSB and CTSL in lung across demographic groups

Supplementary Fig. 7: Expression of ACE2 and TMPRSS2 across developmental time using LungMap RNA-seq data