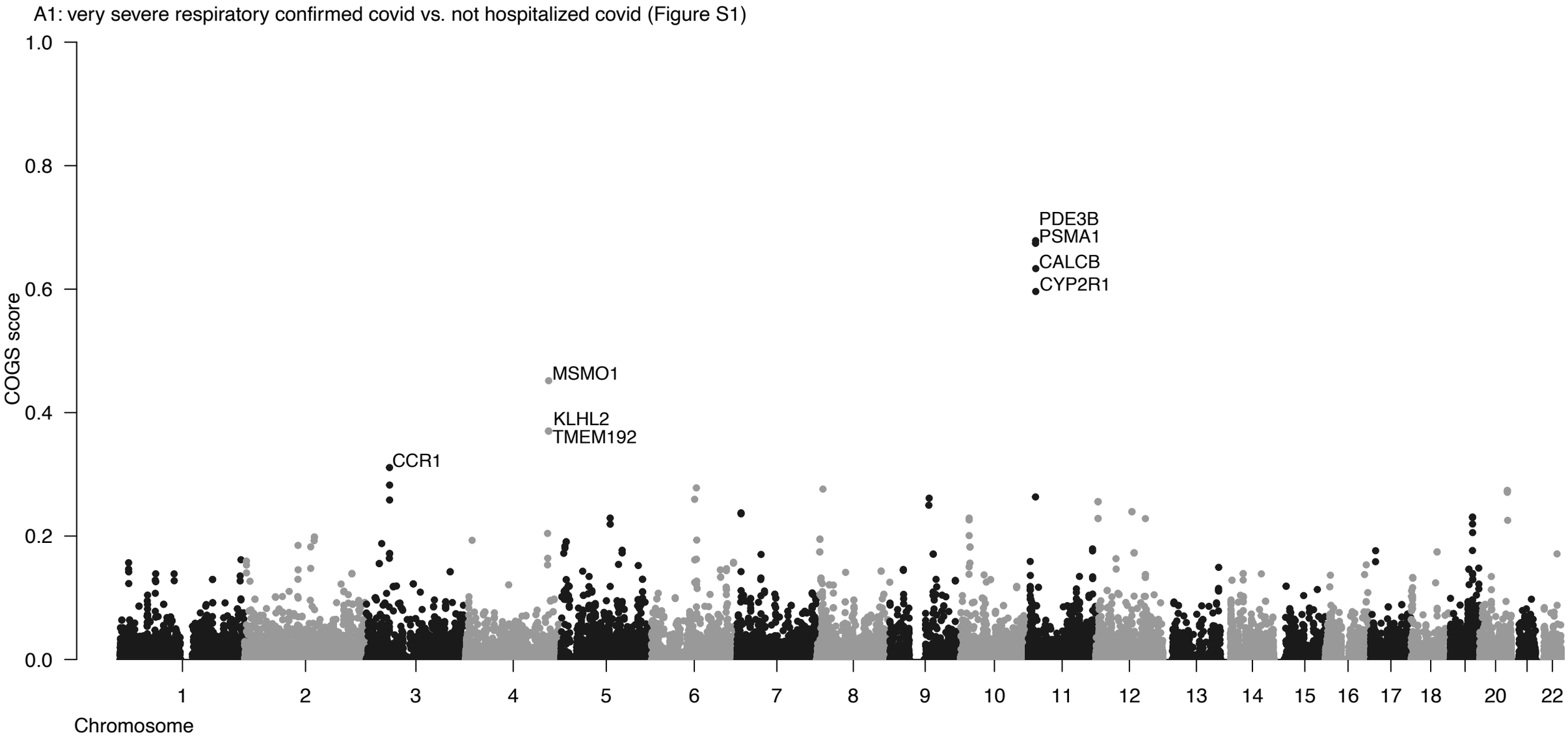
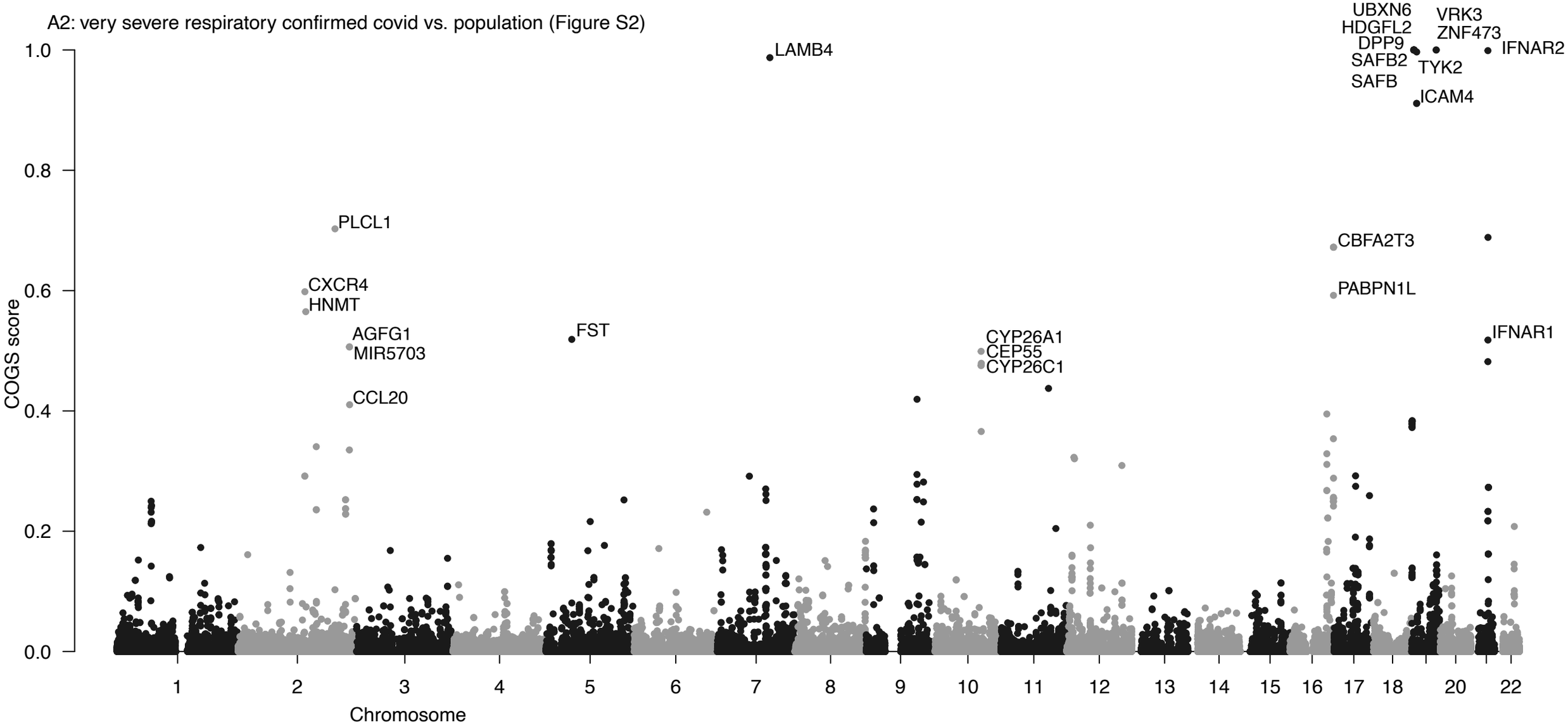
Prioritization of putative target genes underpinning COVID-19 host GWAS traits based on high-resolution 3D chromosomal topology

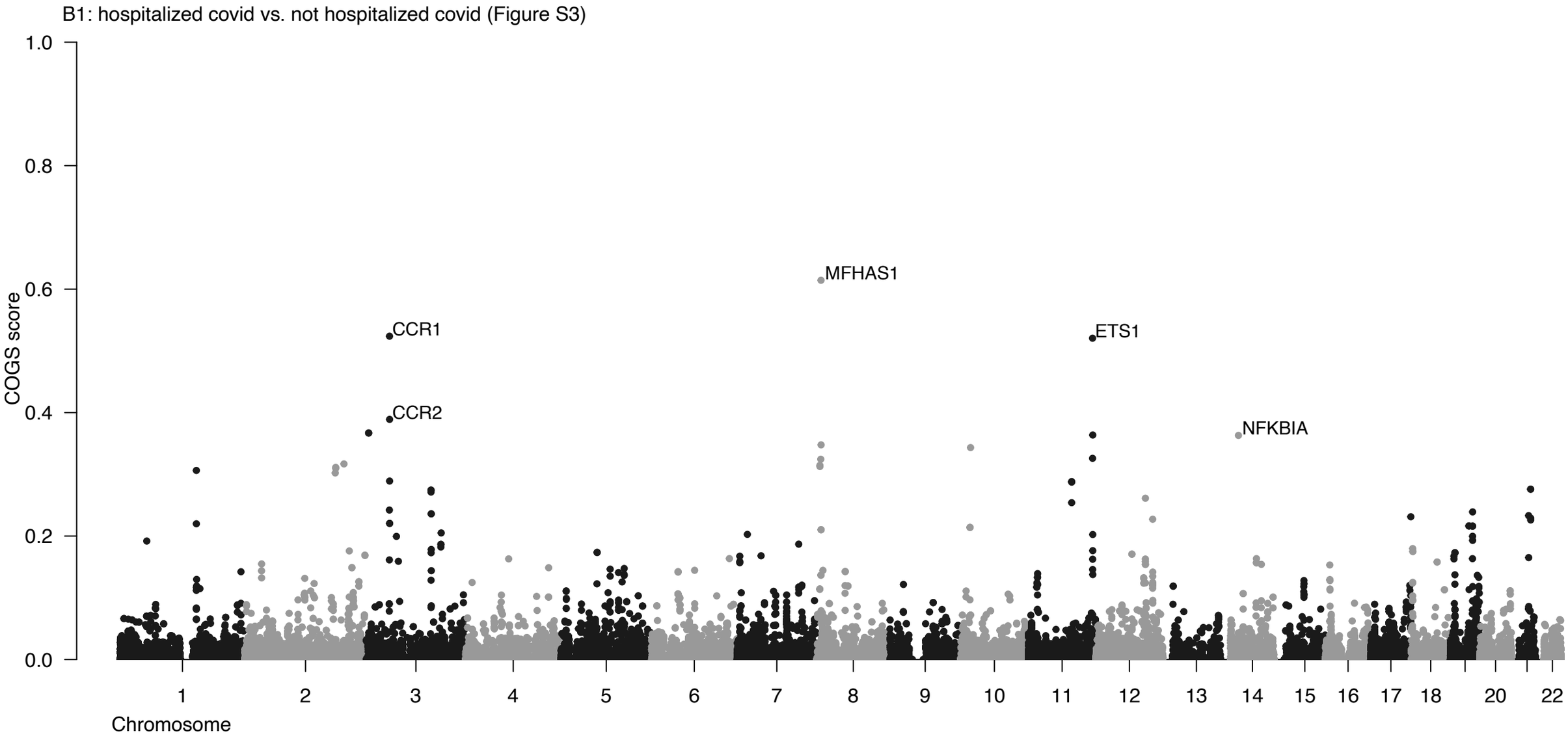
Supplementary figures S1-S11 and Table S2

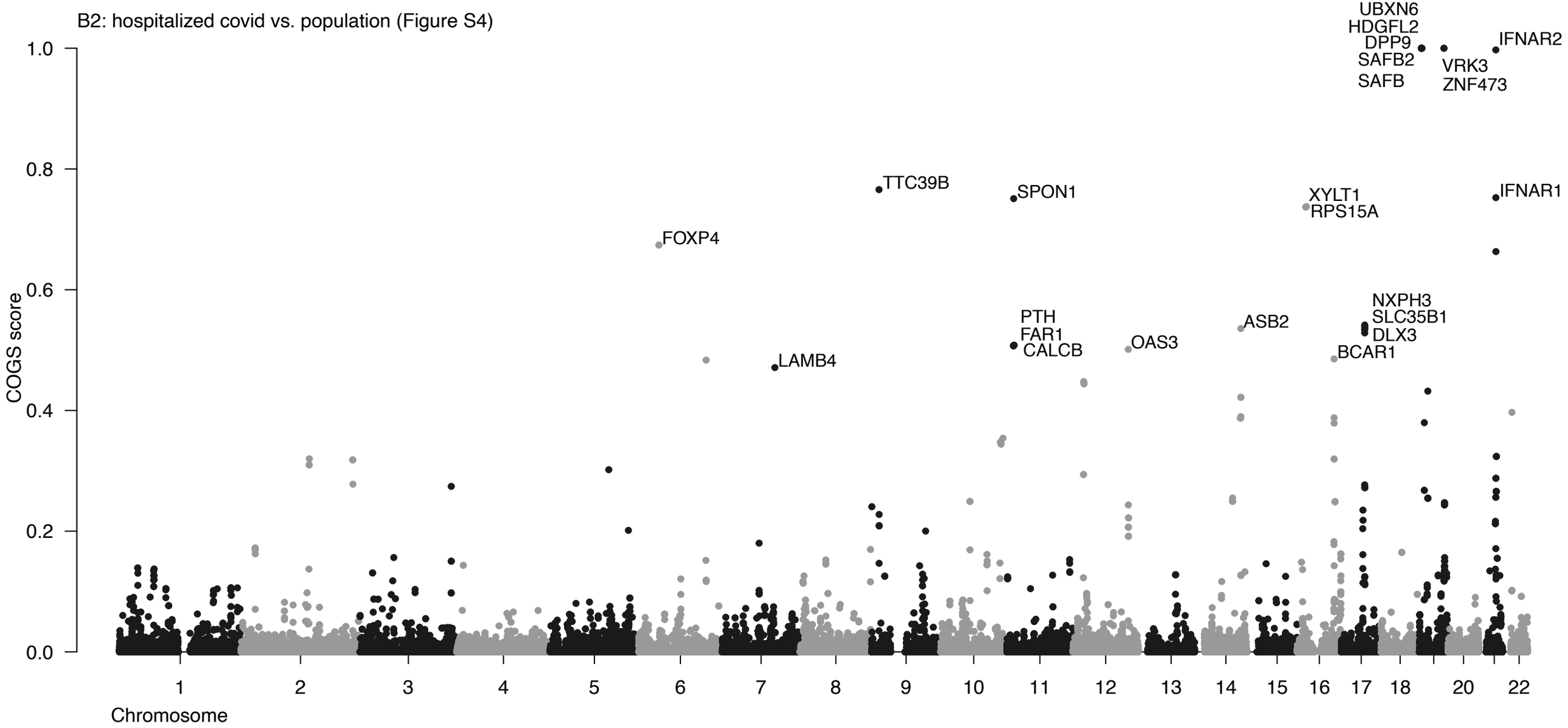
Figures S1 – S7. Manhattan plots showing COGS gene prioritisation scores for the seven COVID-19 host GWAS.

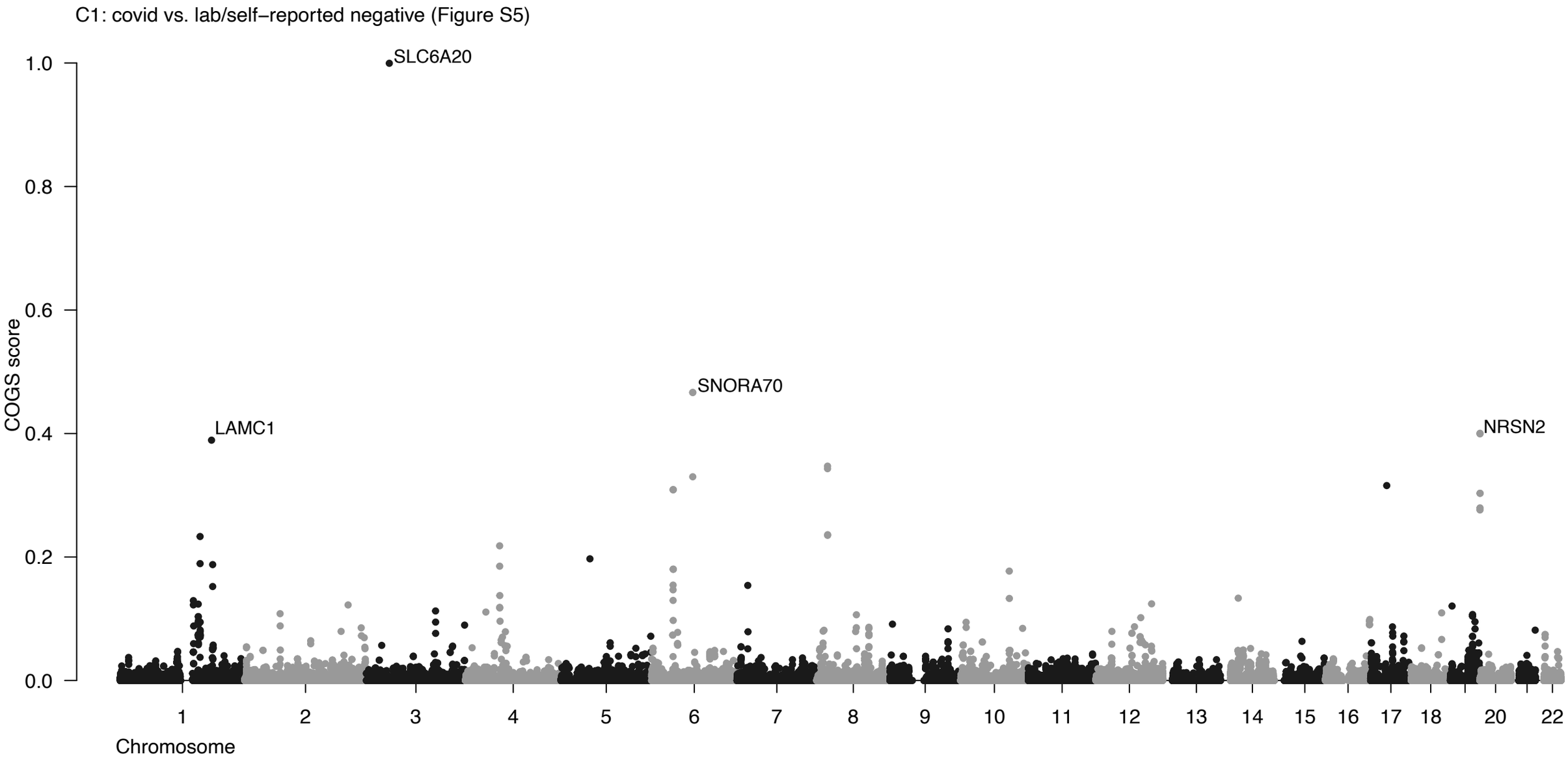
Dots represent genes, and selected genes exceeding a lenient COGS prioritisation score cutoff of 0.3 are labelled, based on Promoter Capture Hi-C data from 17 human primary blood cell types (including endothelial precursors). Some labels were removed to avoid overprinting, and most genes without conventional names were not labelled. Please refer to Table S1 for full information.

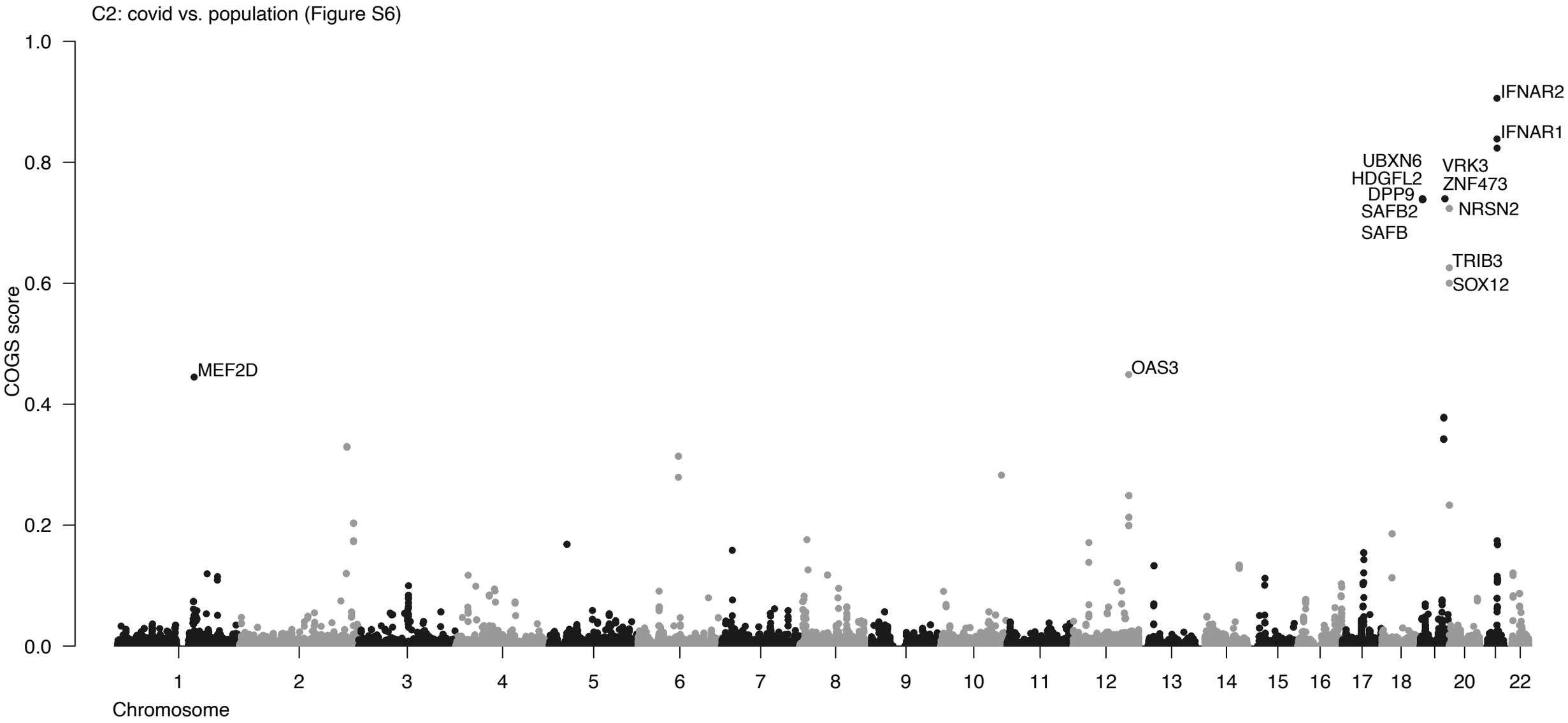

A1: very severe respiratory confirmed covid vs. not hospitalized covid (Figure S1)
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
PDE3B
PSMA1
CALCB
CYP2R1
MSMO1
KLHL2
TMEM192
CCR1
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome

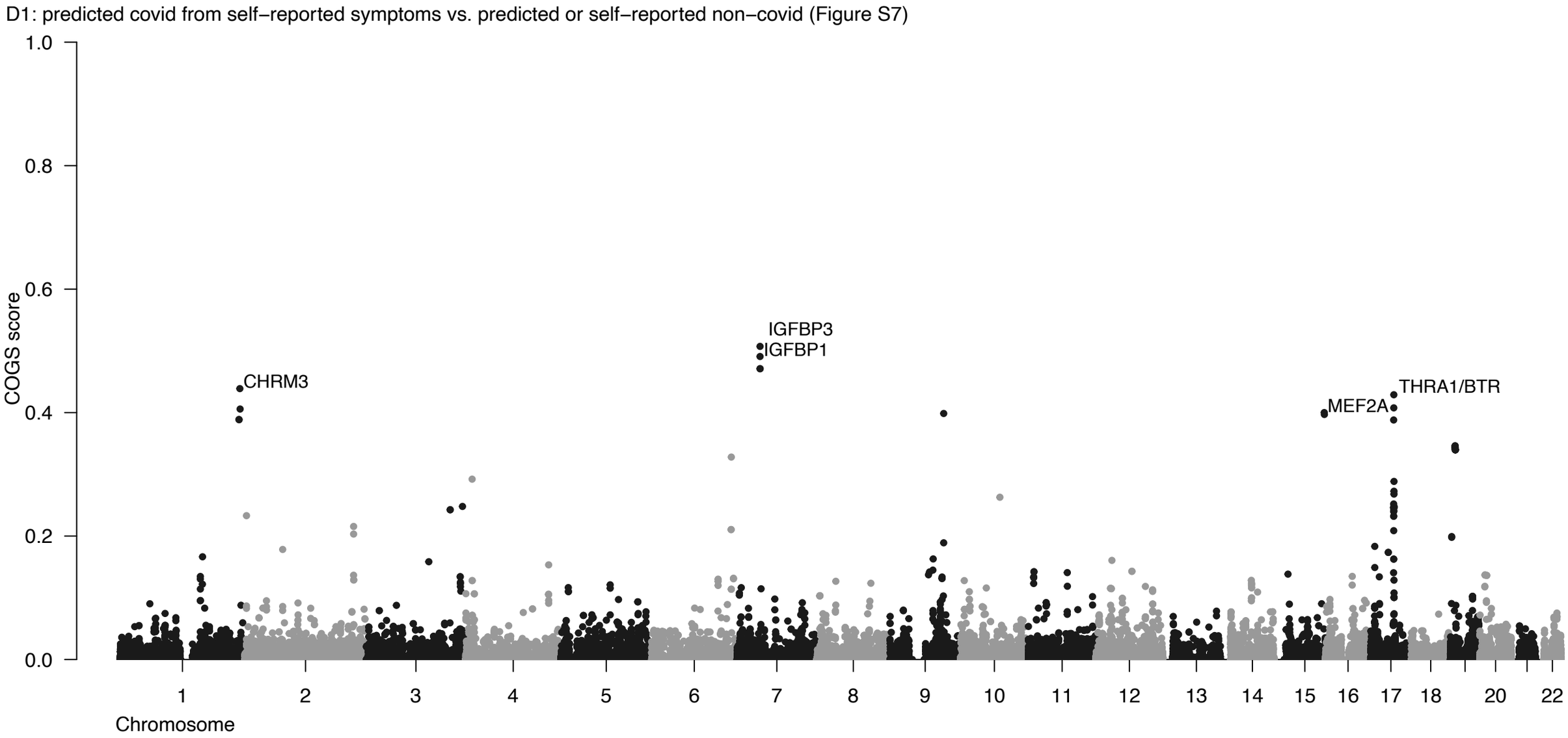

A2: very severe respiratory confirmed covid vs. population (Figure S2)
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
LAMB4
UBXN6
HDGFL2
DPP9
SAFB2
SAFB
VRK3
ZNF473
TYK2
ICAM4
IFNAR2
PLCL1
CBFA2T3
CXCR4
HNMT
PABPN1L
AGFG1
MIR5703
FST
CYP26A1
CEP55
CYP26C1
IFNAR1
CCL20
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome


B1: hospitalized covid vs. not hospitalized covid (Figure S3)
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
MFHAS1
CCR1
ETS1
CCR2
NFKBIA
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome


B2: hospitalized covid vs. population (Figure S4)
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
Chromosome
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
UBXN6
HDGFL2
DPP9
SAFB2
SAFB
VRK3
ZNF473
IFNAR2
TTC39B
SPON1
XYLT1
RPS15A
IFNAR1
FOXP4
NXPH3
SLC35B1
DLX3
PTH
FAR1
CALCB
ASB2
OAS3
BCAR1
LAMB4


C1: covid vs. lab/self−reported negative (Figure S5)
SLC6A20
SNORA70
LAMC1
NRSN2
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome


C2: covid vs. population (Figure S6)
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
IFNAR2
IFNAR1
UBXN6
HDGFL2
DPP9
SAFB2
SAFB
VRK3
ZNF473
NRSN2
TRIB3
SOX12
MEF2D
OAS3
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome


D1: predicted covid from self−reported symptoms vs. predicted or self−reported non−covid (Figure S7)
COGS score
1.0
0.8
0.6
0.4
0.2
0.0
CHRM3
IGFBP3
IGFBP1
MEF2A
THRA1/BTR
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome

Figures S8 – S11. Example profiles of SNP-level posterior probabilities, promoter interactions and H3K27ac signals in potentially causal cell types for three prioritised genes

Top: –log10-p-values from the summary statistics of GWAS meta-analysis produced by COVID-19hg consortium (Figure S8: B2 [hospitalized covid vs. population]; Figure S9: A2 [very severe respiratory confirmed covid vs. population]; Figure S10: B1 [hospitalized covid vs. not hospitalized covid]; Figure S11: A1 [very severe respiratory confirmed covid vs. not hospitalized covid], respectively).

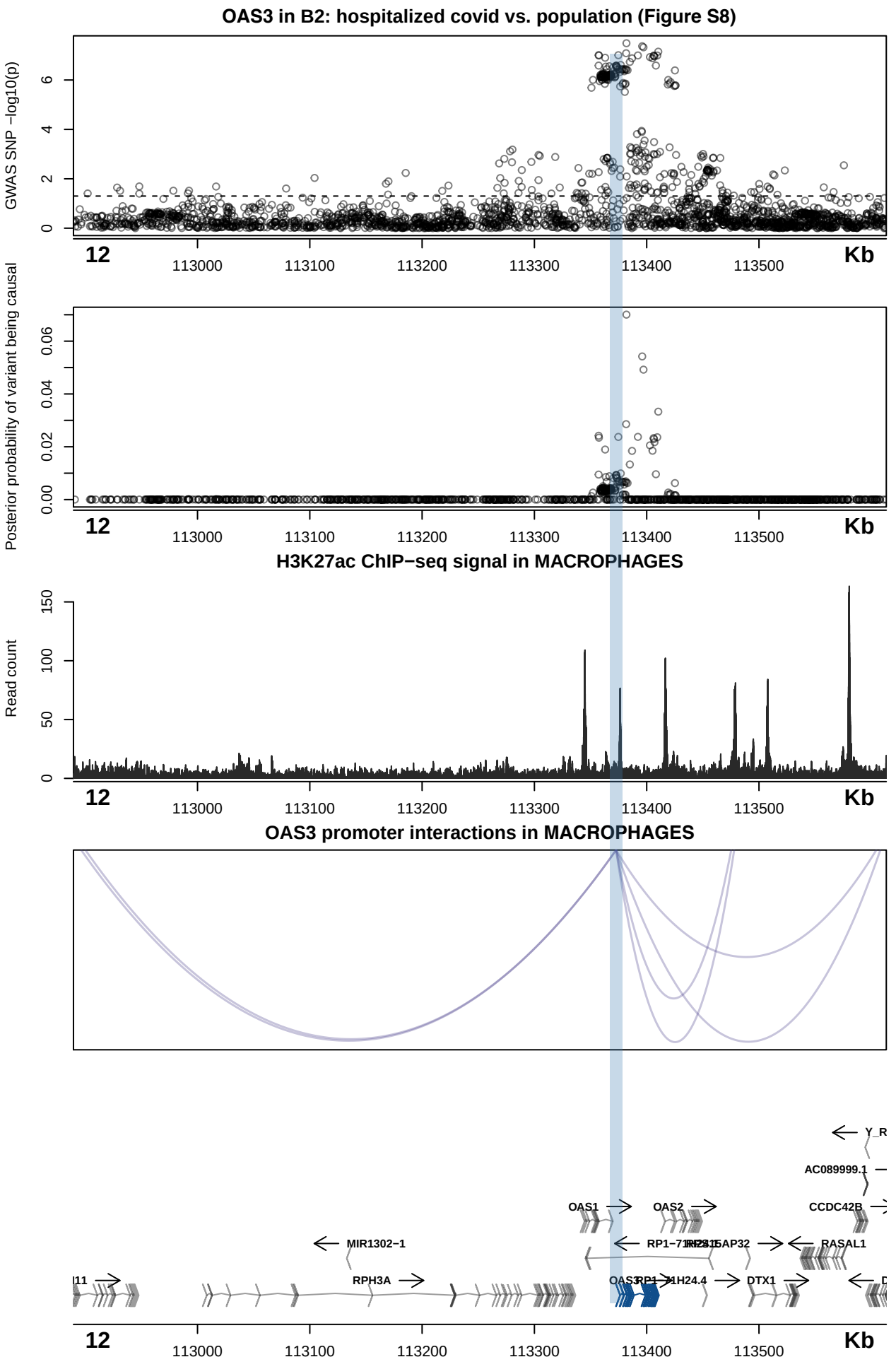
Second from top: SNP-level posterior probabilities of variant being causal for the respective GWAS generated by Wakefield's Bayesian prioritisation procedure.

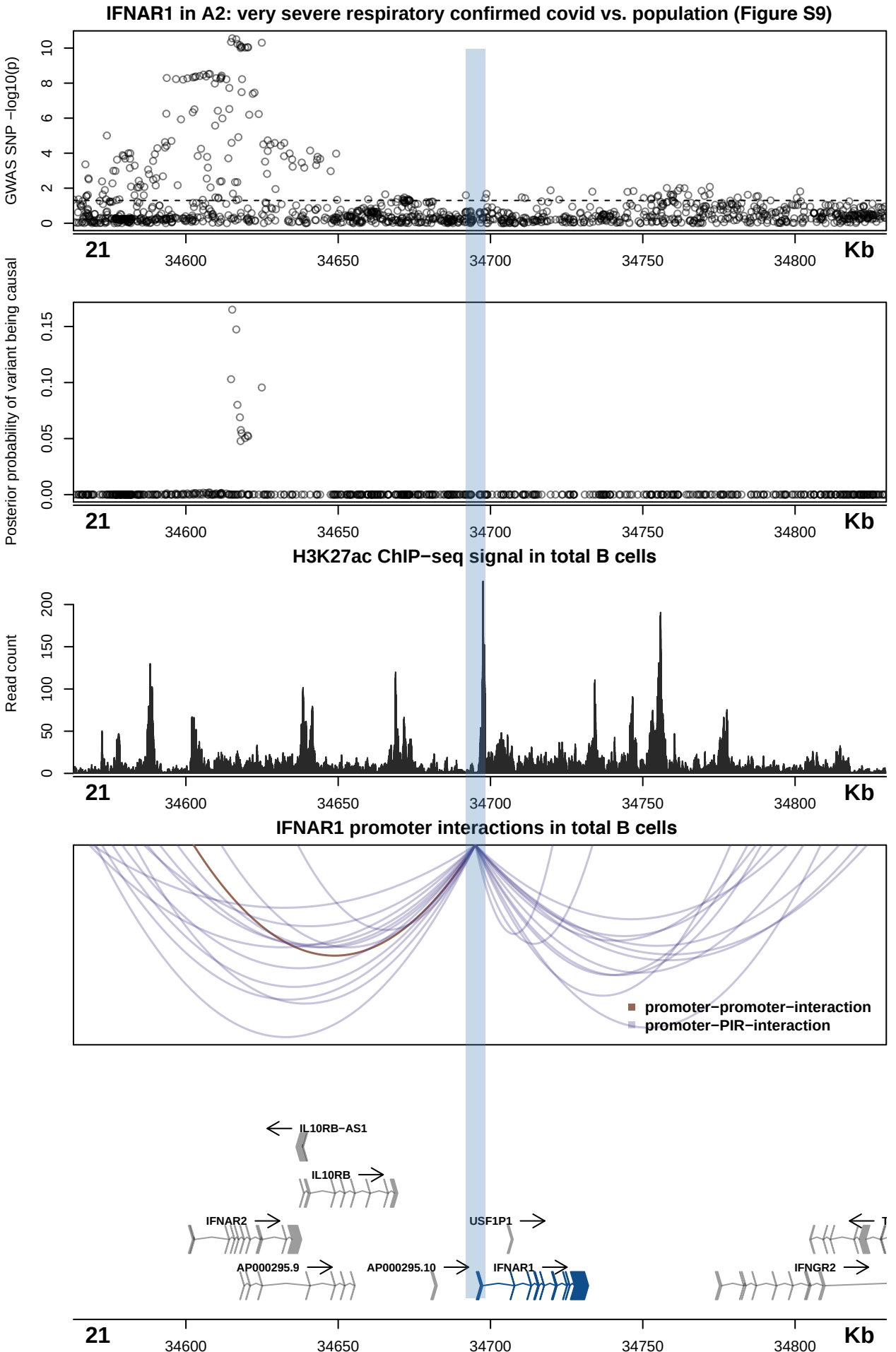
Third from top: Arcs showing promoter interactions detected for the prioritised gene (Figure S8: *OAS3*; Figure S9: *IFNAR1*; Figure S10: *ETS1*; Figure S11: *CCR1*, respectively) in one of the 17 human primary blood cell types from Javierre et al. (2016) used in the COGS prioritisation procedure.

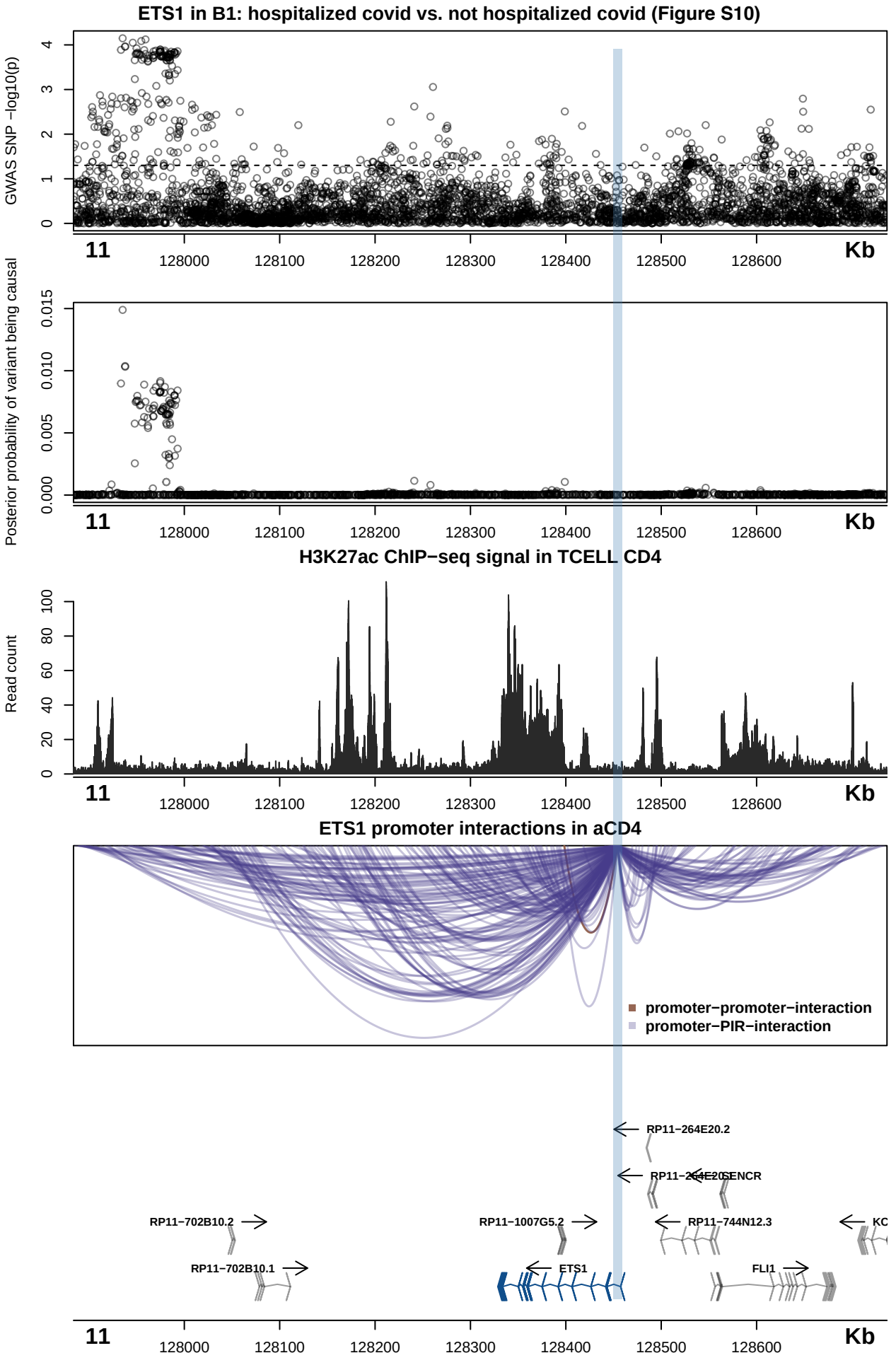
Fourth from top: Pileups of H3K27ac ChIP-seq signal for the same cell type as above in the analysed locus (*OAS3* and *CCR1:* macrophages from Pacheco et al., *BMC Genomics* 2015, accession GSE68798; *IFNAR1:* B cells from Andersson, *Nature* 2017, accession GSE40668; *ETS1:* CD4+ T cells, *ENCODE* project, accession ENCSR561KOM).

Bottom panel: The locations of the annotated genes in the analysed locus.

The genomic coordinates are on the GRCh37 assembly.


OAS3 in B2: hospitalized covid vs. population (Figure S8)
GWAS SNP −log10(p)
0
2
4
6
12
113000
113100
113200
113300
113400
113500
Kb
Posterior probability of variant being causal
0.00
0.02
0.04
0.06
H3K27ac ChIP−seq signal in MACROPHAGES
Read count
0
50
100
150
OAS3 promoter interactions in MACROPHAGES
Y_R
AC089999.1
OAS1
OAS2
CCDC42B
MIR1302−1
RASAL1
RPH3A
DTX1


IFNAR1 in A2: very severe respiratory confirmed covid vs. population (Figure S9)
GWAS SNP −log10(p)
0
2
4
6
8
10
21
34600
34650
34700
34750
34800
Kb
Posterior probability of variant being causal
0.00
0.05
0.10
0.15
H3K27ac ChIP−seq signal in total B cells
Read count
0
50
100
150
200
IFNAR1 promoter interactions in total B cells
promoter−promoter−interaction
promoter−PIR−interaction
IL10RB−AS1
IL10RB
IFNAR2
USF1P1
AP000295.9
AP000295.10
IFNAR1
IFNGR2


ETS1 in B1: hospitalized covid vs. not hospitalized covid (Figure S10)
GWAS SNP −log10(p)
0
1
2
3
4
11
128000
128100
128200
128300
128400
128500
128600
Kb
Posterior probability of variant being causal
0.000
0.005
0.010
0.015
H3K27ac ChIP−seq signal in TCELL CD4
Read count
0
20
40
60
80
100
ETS1 promoter interactions in aCD4
promoter−promoter−interaction
promoter−PIR−interaction
RP11−264E20.2
RP11−264E20GENCR
RP11−702B10.2
RP11−1007G5.2
RP11−744N12.3
RP11−702B10.1
ETS1
FLI1

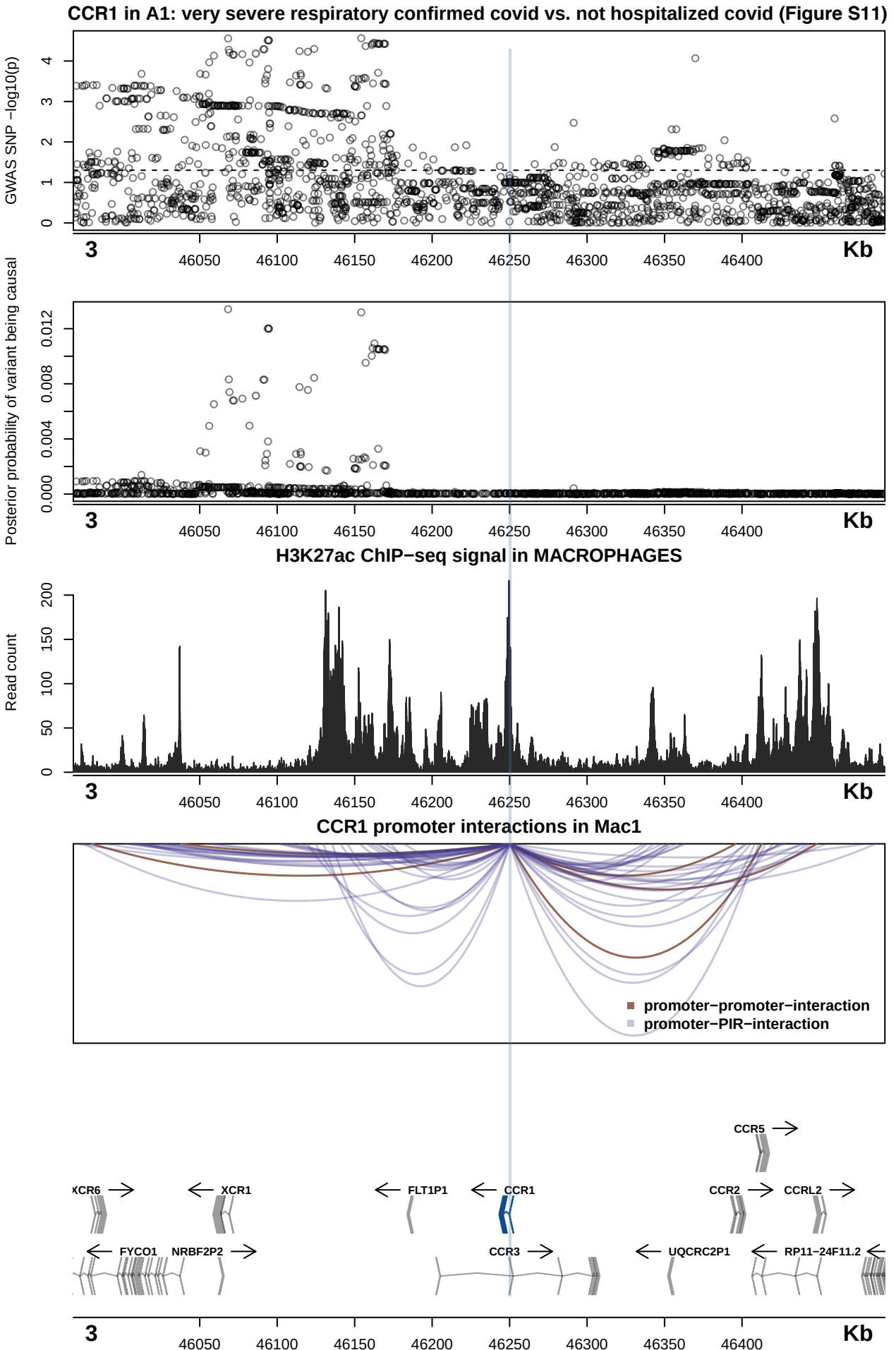

CCR1 in A1: very severe respiratory confirmed covid vs. not hospitalized covid (Figure S11)
GWAS SNP −log10(p)
0
1
2
3
4
3
46050
46100
46150
46200
46250
46300
46350
46400
Kb
Posterior probability of variant being causal
0.000
0.004
0.008
0.012
H3K27ac ChIP−seq signal in MACROPHAGES
Read count
0
50
100
150
200
CCR1 promoter interactions in Mac1
promoter−promoter−interaction
promoter−PIR−interaction
CCR5
XCR6
XCR1
FLT1P1
CCR1
CCR2
CCRL2
FYCO1
NRBF2P2
CCR3
UQCRC2P1
RP11−24F11.2

Table S2. The numbers of genes showing elevated COGS prioritisation scores per GWAS

	Number of genes		**Examples of prioritised coding genes**
GWAS	COGS>=0.75	0.3<COGS<0.75	
A1	0	8	PDE3B, CCR1
A2	16	42	DPP9, IFNAR2, TYK2, ICAM4
B1	0	19	MFHAS1, CCR1, CCR2, ETS1, KCNJ5, NFKBIA
B2	15	50	DPP9, IFNAR2, FOXP4, OAS3
C1	1	14	SLC6A20
C2	3	28	IFNAR2, IFNAR1, DPP9
D1	0	28	IGFBP3, IGFBP1