

TITLE: Imiquimod increases interferon response, and decreases ACE2 and pro-inflammatory response of human bronchial epithelium in asthma.

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SUPPLEMENTARY TABLES

Supplementary Table 1. List of primers used in qPCR assays.		
Primer	Provider	Cat. No or sequence
ACE2	Qiagen	#PPH02572A-200
CCL-5	Primer Design	Sense: -AACCCAGCAGTCGTCTTTGTC- Anti-sense: -AGCAAGCAGAAACAGGCAAAT-
GAPDH	Qiagen	#PPH00150F-200
IFN-β	Qiagen	#PPH00384F-200
IL-1β	Qiagen	#PPH00171C-200
IL-33	Primer Design	Sense: -AAAGAAAGATAAGGTGTTACTGAGTTA- Anti-sense: -GCAACCAGAAGTCTTTGTAGG-
MDA5	Qiagen	#PPH18927A-200
RIG-I	Qiagen	#PPH20774A-200
TLR3	Qiagen	#PPH01803E-200
TMPRSS2	Qiagen	#PPH02262C-200
TNF-α	Primer Design	Sense: -AGGTTCTCTCCTCTCACATAC- Anti-sense: -ATCATGCTTTCAGTGCTCATG-

Supplementary Table 2. Differentially expressed proteins in imiquimod treated HBECs compared with unstimulated cells.

Proteins	Log2 Fold-Change	SE of difference	P value	t ratio	df
SNRPE	-6,56171	0,89168	0,005187	7,35881	3
SRSF3	-6,21941	0,382767	0,003766	16,2486	2
HIST1H1D	-5,04973	1,19302	0,02413	4,23273	3
LSM3	-4,99512	1,49896	0,04464	3,33239	3
LRRC47	-4,58984	1,03937	0,047644	4,416	2
KPNA2	-3,9309	0,815816	0,008533	4,81837	4
UNC45A	-3,92184	0,995889	0,029174	3,93803	3
DDB1	-3,91515	0,672336	0,028247	5,82321	2
MYO1E	-3,85071	0,889308	0,049416	4,33001	2
RPLP0	-3,84009	0,622533	0,008576	6,16849	3
FAU	-3,82132	1,11485	0,041609	3,42765	3
PDLIM5	-3,81022	0,760234	0,015292	5,0119	3
PPP2R2A	-3,80562	0,826075	0,019235	4,60687	3
RPS16	-3,7158	1,0621	0,024929	3,49854	4
SERPINH1	-3,58003	0,62466	0,010546	5,73117	3
IARS	-3,56413	0,406114	0,003116	8,77618	3
GLOD4	-3,52306	0,744378	0,017879	4,73289	3
POLR1C	-3,43976	0,53216	0,023108	6,46378	2
PC	-3,33423	0,184187	0,003038	18,1024	2
H2AFY	-3,32857	1,17777	0,04753	2,82615	4
KYAT3	-3,29688	0,394455	0,003591	8,35806	3
NME2	-3,20386	0,901682	0,02373	3,55321	4
PPM1G	-3,08191	0,813783	0,032286	3,78714	3
OLA1	-3,04894	0,6011	0,007119	5,07226	4
ALDH2	-2,92441	0,387685	0,00483	7,54328	3
SART1	-2,91746	0,837691	0,039976	3,48274	3
RPS15	-2,91108	0,310919	0,00258	9,36281	3
SSRP1	-2,86601	0,48037	0,009421	5,96625	3
PARP9	-2,80669	0,270853	0,009185	10,3624	2
HADHA	-2,7977	0,844861	0,029615	3,31144	4
EPHA2	-2,79283	0,40058	0,006055	6,97197	3
PRDX4	-2,74692	0,500466	0,031627	5,48873	2
MRPL12	-2,74321	0,690695	0,028534	3,97167	3
DYNLRB1	-2,72754	0,693046	0,029222	3,93558	3
FGFBP1	-2,68276	0,603694	0,0113	4,44391	4
RABGGTB	-2,652	0,342202	0,016246	7,74981	2

EHP1L1	-2,55026	0,725696	0,039079	3,51423	3
ACTR1A	-2,50933	0,468417	0,012727	5,35704	3
CSTB	-2,48053	0,377541	0,002777	6,57021	4
PARK7	-2,474	0,53713	0,009986	4,60596	4
BAG6	-2,45961	0,48795	0,037176	5,04069	2
PYGB	-2,45741	0,540879	0,01047	4,54337	4
AK1	-2,37158	0,274356	0,01312	8,64419	2
ACO2	-2,36188	0,319264	0,005108	7,3979	3
DNM1L	-2,34205	0,795705	0,042247	2,94337	4
SRPK1	-2,32568	0,526564	0,04763	4,41672	2
ARPC1B	-2,29883	0,342638	0,006757	6,70923	3
GOT2	-2,1734	0,307206	0,002107	7,07473	4
FUBP1	-2,1709	0,444056	0,008109	4,88881	4
MTCH2	-2,11918	0,388677	0,032031	5,45229	2
PPAT	-2,06297	0,217776	0,010961	9,4729	2
CKAP5	-2,03639	0,58553	0,025401	3,47786	4
TUBB6	-2,01976	0,264456	0,004661	7,63741	3
PCYT1A	-1,99888	0,555935	0,022849	3,59553	4
ATP5F1C	-1,96519	0,58294	0,043373	3,37117	3
PARP4	-1,95957	0,152864	0,00603	12,8191	2
SSB	-1,95447	0,57453	0,027231	3,40186	4
CTSZ	-1,88564	0,450758	0,024894	4,18327	3
DNAJB1	-1,8711	0,659607	0,047025	2,83669	4
LRPPRC	-1,85979	0,439302	0,013332	4,23352	4
ANXA5	-1,81793	0,456096	0,016321	3,98585	4
CHMP4A	-1,80368	0,244101	0,001789	7,38909	4
STK26	-1,79284	0,51221	0,039475	3,5002	3
AKR1D1	-1,7871	0,207206	0,013178	8,62474	2
IRGQ	-1,76979	0,554029	0,049544	3,19441	3
BUB3	-1,74554	0,177051	0,010132	9,85898	2
TCOF1	-1,74135	0,402874	0,012425	4,32232	4
PRDX1	-1,7398	0,559818	0,035949	3,10779	4
CTSD	-1,70007	0,595924	0,046264	2,85282	4
YME1L1	-1,69816	0,0536669	0,000997	31,6427	2
CCT5	-1,68679	0,601648	0,048632	2,80361	4
TUBG2	-1,66527	0,471709	0,038631	3,5303	3
RAB8A	-1,6408	0,450583	0,035704	3,64151	3
TES	-1,58368	0,400785	0,028917	3,95144	3
MAGOHB	-1,56455	0,244117	0,023491	6,409	2
PCBP1	-1,49743	0,330137	0,010531	4,53578	4
COL17A1	-1,48815	0,465558	0,033011	3,19649	4
EIF4G1	-1,44462	0,432599	0,028852	3,33939	4

CCT2	-1,42648	0,443983	0,032499	3,21291	4
RPL7	-1,40494	0,441398	0,033441	3,18293	4
STRN4	-1,38507	0,00536675	0,000015	258,083	2
CHMP2A	-1,38029	0,458552	0,039546	3,01012	4
TSTA3	-1,3568	0,29575	0,019453	4,58765	3
RPSA	-1,35606	0,481385	0,047974	2,817	4
UGDH	-1,3109	0,265262	0,007806	4,94188	4
NCL	-1,29884	0,465118	0,049187	2,79249	4
H1FX	-1,28915	0,34366	0,033088	3,75125	3
ZPR1	-1,28088	0,145179	0,012604	8,82276	2
RPL15	-1,27365	0,371481	0,041582	3,42857	3
AARS	-1,27151	0,434016	0,042829	2,92964	4
RPL35	-1,22423	0,356583	0,026457	3,43323	4
PMPCB	-1,20445	0,0837988	0,004806	14,3731	2
ZC3H18	-1,19632	0,342199	0,039596	3,49597	3
CCT3	-1,18026	0,363484	0,031463	3,24706	4
S100A14	-1,17765	0,379394	0,03608	3,10403	4
LUC7L2	-1,1344	0,32618	0,040118	3,47782	3
TAGLN2	-1,11943	0,136366	0,0012	8,20901	4
MTHFD1	-1,09515	0,31604	0,025695	3,46523	4
NCEH1	-1,06112	0,0488548	0,002113	21,72	2
CAPRIN1	-0,995311	0,140708	0,019406	7,07358	2
HNRNPK	-0,979516	0,289114	0,027581	3,38799	4
PTMA	-0,97186	0,335491	0,044259	2,89682	4
ANXA1	-0,961044	0,344685	0,049404	2,78818	4
EHD1	-0,861052	0,242568	0,038098	3,54973	3
PCBP2	-0,839867	0,300174	0,048914	2,79794	4
RPS4X	-0,7765	0,259901	0,040431	2,98768	4
HSPB1	-0,755001	0,240647	0,034936	3,13738	4
EZR	-0,719886	0,23859	0,039269	3,01725	4
NOLC1	-0,692483	0,173517	0,016253	3,99087	4
APEX1	-0,673531	0,227833	0,041709	2,95625	4
NUP93	-0,59549	0,136017	0,011893	4,37806	4
GOLGA3	-0,566146	0,113512	0,037928	4,98754	2
KPNA1	-0,540556	0,0812648	0,021862	6,65178	2
SFN	-0,52892	0,182967	0,044528	2,89079	4
PAPOLA	0,190326	0,0360134	0,033989	5,28487	2
ITGA3	0,301182	0,0592206	0,01469	5,08577	3
ASPH	0,628595	0,207584	0,038851	3,02815	4
MTHFS	0,719578	0,11672	0,025316	6,16498	2
KIF2A	0,773129	0,277441	0,049482	2,78664	4
LSM12	0,889807	0,204151	0,048817	4,35858	2

ESYT2	0,997048	0,14355	0,006121	6,94567	3
MAPK3	1,03331	0,27319	0,032391	3,78238	3
LPCAT1	1,08621	0,0139707	0,000165	77,7491	2
GNG12	1,10427	0,276352	0,016185	3,99588	4
FAM120A	1,19085	0,287768	0,025616	4,13823	3
OXR1	1,33251	0,448985	0,041233	2,96782	4
CUL4B	1,34495	0,382956	0,039141	3,51202	3
SDC4	1,48367	0,28102	0,013251	5,27959	3
BLMH	1,67269	0,0776476	0,002148	21,5421	2
PRRC2A	2,55132	0,455423	0,030418	5,60208	2

Supplementary Table 3. Reactome pathways overrepresented in imiquimod downmodulated proteins.

#term ID	term description	observed gene count	background gene count	strength	FDR	matching proteins in your network
HSA-1430728	Metabolism	19	2032	0.39	0.0296	ACO2,PYGB,AKR1D1,GOT2,RPS16,CCBL2,LRPPRC,ALDH2,PPAT,PCYT1A,ATP5C1,PARP9,AK1,IARS,HADHA,PARP4,PC,RPLP0,RPS15
HSA-2408522	Selenoamino acid metabolism	4	112	0.97	0.0296	RPS16,IARS,RPLP0,RPS15
HSA-71291	Metabolism of amino acids and derivatives	6	354	0.65	0.0471	GOT2,RPS16,CCBL2,IARS,RPLP0,RPS15
HSA-2022377	Metabolism of Angiotensinogen to Angiotensins	2	17	1.49	0.0471	CTSZ,CTSD
HSA-1852241	Organelle biogenesis and maintenance	7	287	0.8	0.0296	CCT5,RAB8A,TUBB6,ATP5C1,DYNLRB1,ACTR1A,CKAP5
HSA-380320	Recruitment of NuMA to mitotic centrosomes	4	91	1.06	0.0296	TUBG2,TUBB6,ACTR1A,CKAP5
HSA-68877	Mitotic Prometaphase	5	190	0.84	0.0296	TUBG2,TUBB6,BUB3,ACTR1A,CKAP5
HSA-69275	G2/M Transition	6	189	0.92	0.0296	TUBG2,RAB8A,TUBB6,PPP2R2A,ACTR1A,CKAP5
HSA-68886	M Phase	6	343	0.66	0.0471	TUBG2,TUBB6,PPP2R2A,BUB3,ACTR1A,CKAP5
HSA-69278	Cell Cycle, Mitotic	7	483	0.58	0.0471	TUBG2,RAB8A,TUBB6,PPP2R2A,BUB3,ACTR1A,CKAP5
HSA-75153	Apoptotic execution phase	3	51	1.19	0.0296	HIST1H1D,MST4,DNM1L
HSA-3371497	HSP90 chaperone cycle for steroid hormone receptors (SHR)	3	53	1.17	0.0297	DNAJB1,TUBB6,ACTR1A
HSA-168254	Influenza Infection	4	148	0.85	0.0471	RPS16,KPNA2,RPLP0,RPS15
HSA-5663205	Infectious disease	6	363	0.63	0.0471	RPS16,SSRP1,CHMP4A,KPNA2,RPLP0,RPS15
HSA-8953854	Metabolism of RNA	9	652	0.56	0.0296	RPS16,LSM3,SART1,MAGOHB,PPP2R2A,SRSF3,SNRPE,RPLP0,RPS15

HSA-73856	RNA Polymerase II Transcription Termination	3	65	1.08	0.0471	MAGOHB,SRSF3,SNRPE
HSA-975957	Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	5	112	1.07	0.0296	RPS16,MAGOHB,PPP2R2A,RPLP0,RPS15
HSA-109688	Cleavage of Growing Transcript in the Termination Region	3	65	1.08	0.0471	MAGOHB,SRSF3,SNRPE
HSA-72163	mRNA Splicing - Major Pathway	5	178	0.86	0.0296	LSM3,SART1,MAGOHB,SRSF3,SNRPE
HSA-197264	Nicotinamide salvaging	2	19	1.44	0.0471	PARP9,PARP4
HSA-5617833	Cilium Assembly	6	195	0.9	0.0296	CCT5,RAB8A,TUBB6,DYNLRB1,ACTR1A,CKAP5

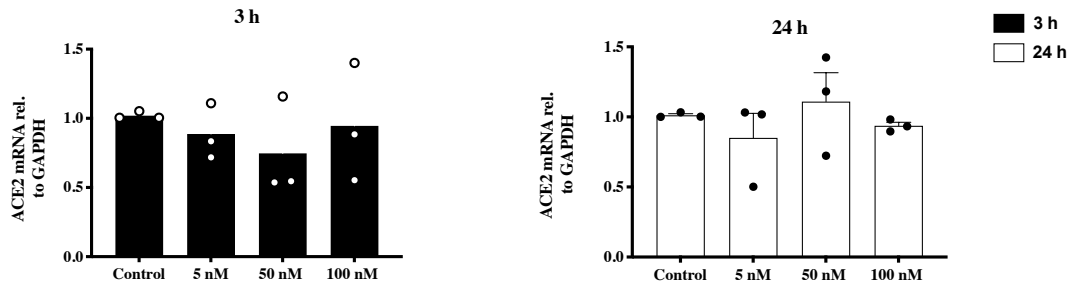
Supplementary Table 4. Differentially expressed genes (p-value < 0.1) in poly(I:C) stimulated cells treated with imiquimod vs. poly(I:C) stimulated cells.

mRNA	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	P-value	BY.p.value	probe.ID
CTNNB1	1.01	0.083	0.846	1.17	1.89e-05	0.0225	NM_001098210.1:1815
BCAP31	0.547	0.0484	0.453	0.642	2.84e-05	0.0225	NM_005745.7:495
ITGA5	1.46	0.143	1.18	1.74	5.13e-05	0.0262	NM_002205.2:925
JAK1	0.976	0.104	0.771	1.18	8.47e-05	0.0262	NM_002227.1:285
PTAFR	1.72	0.188	1.35	2.09	9.75e-05	0.0262	NM_000952.3:1035
CD9	1.21	0.134	0.949	1.47	0.000103	0.0262	NM_001769.2:405
C1QBP	-0.831	0.0945	-1.02	-0.645	0.00012	0.0262	NM_001212.3:745
CD82	1.19	0.139	0.919	1.46	0.000137	0.0262	NM_002231.3:1211
IKBKG	1.02	0.124	0.773	1.26	0.000175	0.0262	NM_003639.2:470
STAT2	1.1	0.134	0.836	1.36	0.000179	0.0262	NM_005419.2:1965
CDKN1A	1.43	0.176	1.08	1.77	0.000189	0.0262	NM_000389.2:1975
PTK2	0.833	0.104	0.63	1.04	2E-04	0.0262	NM_005607.3:1005
CD24	1.19	0.151	0.897	1.49	0.000216	0.0262	NM_013230.2:95
BCL3	1.33	0.172	0.993	1.67	0.000247	0.0279	NM_005178.2:450
TAPBP	0.852	0.118	0.621	1.08	0.000356	0.0367	NM_003190.4:1536
CD99	0.701	0.0978	0.51	0.893	0.000371	0.0367	NM_002414.3:625
TGFB1	0.948	0.134	0.686	1.21	0.000394	0.0367	NM_000660.3:1260
CD46	0.992	0.143	0.712	1.27	0.000443	0.0389	NM_172350.1:365
IGF2R	1.08	0.158	0.772	1.39	0.00048	0.0399	NM_000876.1:2605
NT5E	1.06	0.157	0.752	1.37	0.000521	0.0411	NM_002526.2:1214
IL6ST	0.904	0.135	0.639	1.17	0.000545	0.0411	NM_002184.2:2505
IRF1	1.59	0.242	1.11	2.06	0.000605	0.0435	NM_002198.1:510
SIGIRR	1.64	0.254	1.15	2.14	0.000638	0.0439	NM_021805.2:469
POU2F2	-1.39	0.218	-1.82	-0.962	0.000702	0.0449	NM_002698.2:908
RUNX1	1.1	0.172	0.757	1.43	0.00071	0.0449	NM_001754.4:635
BCL10	0.723	0.118	0.493	0.954	0.00085	0.0517	NM_003921.2:1250
STAT6	0.35	0.0578	0.236	0.463	0.000925	0.0529	NM_003153.3:2030
ARG2	1.07	0.177	0.72	1.41	0.000936	0.0529	NM_001172.3:1150
PLAU	1.09	0.184	0.725	1.45	0.00105	0.0573	NM_002658.2:793
IL13RA1	0.853	0.146	0.567	1.14	0.00111	0.0574	NM_001560.2:1230
TGFR1	1.45	0.249	0.961	1.94	0.00113	0.0574	NM_004612.2:4280
MYD88	0.93	0.162	0.613	1.25	0.00121	0.0589	NM_002468.3:2145

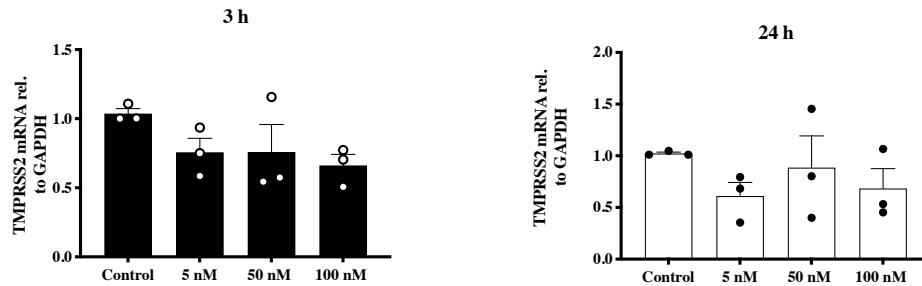
NOTCH2	0.87	0.152	0.571	1.17	0.00125	0.0589	NM_024408.3:2842
MAPK1	0.566	0.0994	0.371	0.761	0.00127	0.0589	NM_138957.2:430
ICAM1	2.02	0.362	1.31	2.73	0.00142	0.0641	NM_000201.2:2253
ITGB1	0.749	0.136	0.482	1.02	0.00151	0.0657	NM_033666.2:2000
MCL1	0.669	0.122	0.43	0.909	0.00154	0.0657	NM_021960.3:1260
IRF5	2.51	0.463	1.6	3.41	0.00165	0.0685	NM_002200.3:1845
IFNAR1	0.979	0.182	0.622	1.33	0.00169	0.0685	NM_000629.2:3123
PTGS2	-1.13	0.212	-1.55	-0.717	0.00175	0.069	NM_000963.1:495
CD3EAP	-2.03	0.381	-2.77	-1.28	0.00179	0.069	NM_012099.1:555
C14orf166	0.112	0.0212	0.0707	0.154	0.00185	0.0695	NM_016039.2:210
CD44	0.713	0.135	0.447	0.978	0.00189	0.0696	NM_001001392.1:429
PRKCD	0.839	0.161	0.523	1.15	0.00199	0.0706	NM_006254.3:2165
PSMB7	0.306	0.0589	0.191	0.422	0.00202	0.0706	NM_002799.2:420
EGR1	1.83	0.356	1.14	2.53	0.00211	0.0706	NM_001964.2:1505
STAT1	0.745	0.145	0.461	1.03	0.00214	0.0706	NM_007315.2:205
FYN	1.23	0.238	0.758	1.69	0.00214	0.0706	NM_002037.3:765
NFKBIA	0.946	0.187	0.579	1.31	0.00232	0.0746	NM_020529.1:945
RELB	0.968	0.194	0.588	1.35	0.00247	0.0746	NM_006509.2:250
ILF3	-0.308	0.0618	-0.429	-0.187	0.00249	0.0746	NM_001137673.1:730
CD164	0.545	0.11	0.329	0.761	0.00258	0.0746	NM_006016.4:2575
CASP3	0.422	0.0853	0.254	0.589	0.0026	0.0746	NM_032991.2:685
STAT3	0.737	0.149	0.444	1.03	0.00263	0.0746	NM_139276.2:4535
SMAD3	0.628	0.128	0.377	0.88	0.00272	0.0746	NM_005902.3:4220
CSF1	1.29	0.264	0.773	1.81	0.00273	0.0746	NM_000757.4:823
MALT1	0.728	0.149	0.436	1.02	0.00276	0.0746	NM_006785.2:909
STAT4	1.17	0.239	0.7	1.64	0.00276	0.0746	NM_003151.2:789
IFNAR2	1.13	0.232	0.675	1.58	0.00278	0.0746	NM_000874.3:631
TNFSF15	1.58	0.332	0.927	2.23	0.00314	0.0829	NM_001204344.1:2338
PECAM1	0.866	0.184	0.505	1.23	0.00332	0.0855	NM_000442.3:1365
CD58	0.606	0.129	0.353	0.86	0.00338	0.0855	NM_001779.2:478
RELA	0.714	0.153	0.415	1.01	0.00341	0.0855	NM_021975.2:360
LTB4R2	-1.04	0.222	-1.47	-0.6	0.00346	0.0855	NM_019839.4:1250
LITAF	0.734	0.159	0.421	1.05	0.00368	0.0895	NM_004862.3:1000
HLA-DMA	1.03	0.225	0.587	1.47	0.00384	0.0919	NM_006120.3:380
TRAF6	0.659	0.146	0.373	0.945	0.00404	0.0954	NM_145803.1:1839
CCL20	1.79	0.399	1.000	2.57	0.0042	0.0977	NM_004591.1:35

SUPPLEMENTARY FIGURES

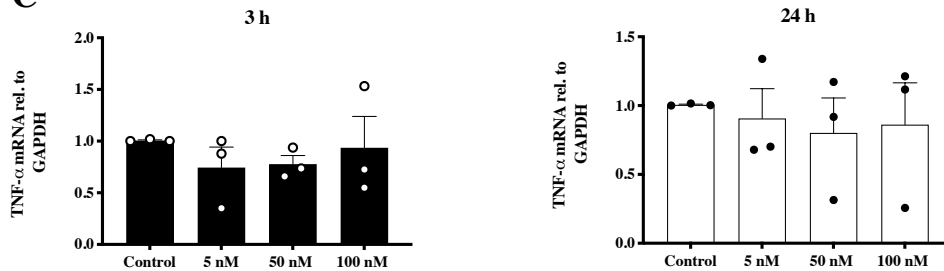
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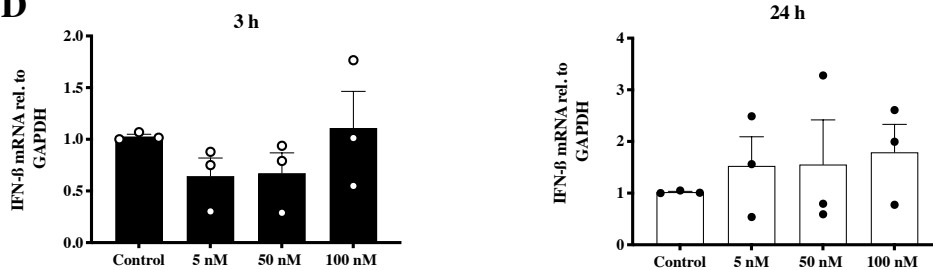
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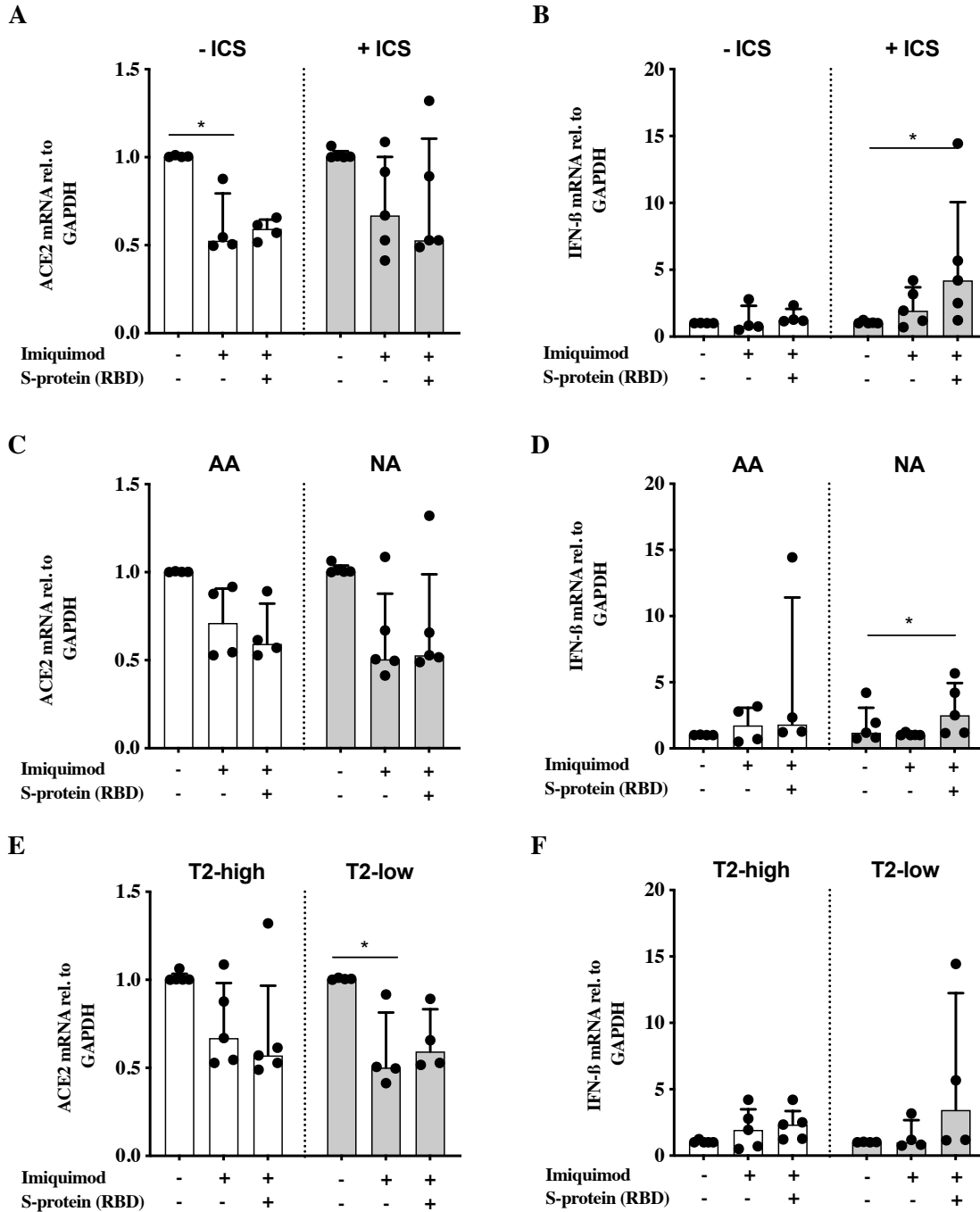
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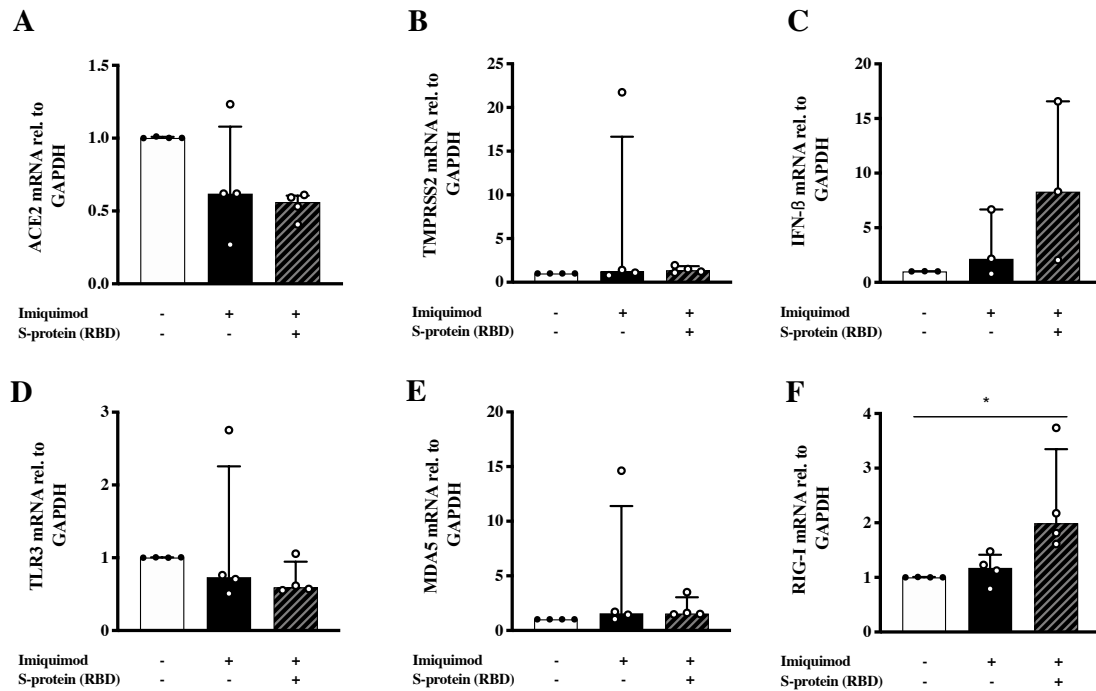
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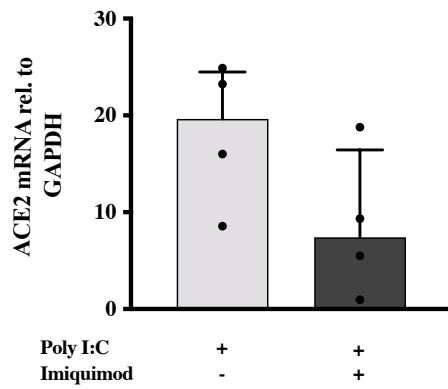
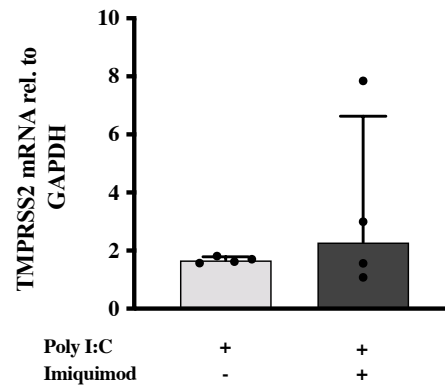
Supplementary Figure 1. SARS-CoV-2 S-protein 1 (SP1) effect on human bronchial epithelial cells from asthmatic donors. Dose response (5-100 nM) mRNA expression of the SARS-CoV-2 receptor ACE2 (A), the host protease TMPRSS2 (B), the proinflammatory cytokine TNF- α (C), and the type I interferon IFN- β (D) after 3h (left) and 24h (right) stimulation with SP1. N = 3.



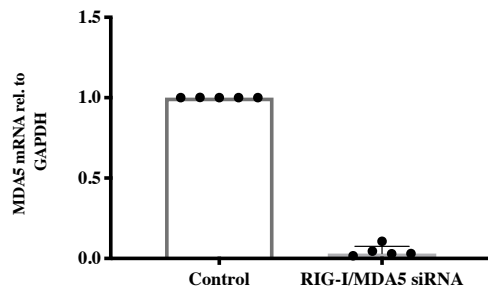
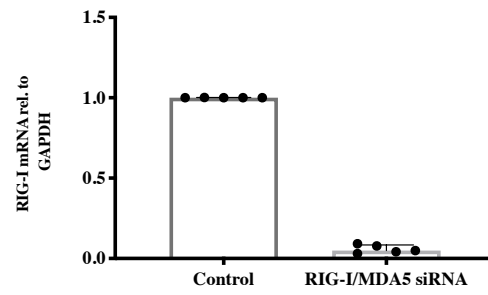
Supplementary Figure 2. Imiquimod trend to decrease the expression of ACE2 receptor and trend to increase IFN- β response independently of asthma phenotype. mRNA expression of ACE2 (A) and IFN- β (B) in HBECs from patients with asthma (cohort 2) treated (N = 5) or not (N = 4) with inhaled corticosteroids (ICS) in response to imiquimod treatment alone or in combination with SP1. mRNA expression of ACE2 (C) and IFN- β (D) in HBECs from patients with allergic (AA; N = 4) or non-allergic asthma (NA; N = 5) phenotypes in response to imiquimod treatment alone or in combination with SP1. mRNA expression of ACE2 (E) and IFN- β (F) in HBECs from patients with T2-high (N = 5) or T2-low (N = 4) phenotypes in response to imiquimod treatment alone or in combination with SP1. * $p < 0.05$, Friedman test followed by Dunn's multiple comparison test.



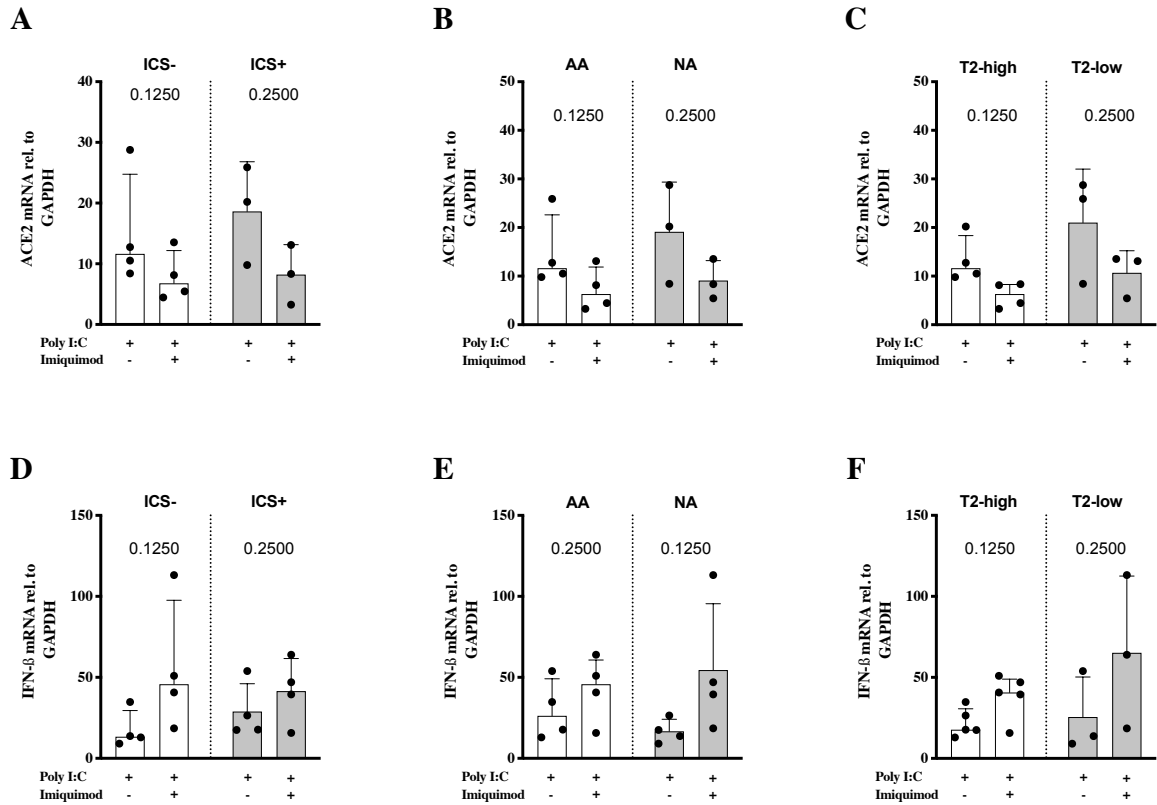
Supplementary Figure 3. S-protein 1 (SP1) from SARS-CoV-2 in combination with imiquimod trend to decrease the expression of ACE2 receptor and increase the anti-viral response in human bronchial epithelial cells (HBECs) from healthy subjects. mRNA expression of ACE2 (A), TMPRSS2 (B), IFN-β (C), and the pattern recognition receptors TLR3 (D), MDA5 (E), and RIG-I (F) in HBECs in response to imiquimod treatment alone (black bars) or in combination with SP1 (striped bars). * p < 0.05, Friedman test followed by Dunn's multiple comparison test. N = 4.

A**B**

Supplementary Figure 4. Imiquimod trends to decrease the poly(I:C)-induced expression of ACE2 receptor, but not TMPRSS2 on human bronchial epithelial cells (HBECs) from healthy subjects. Effect of imiquimod treatment in the poly(I:C) induced ACE2 (A) and TMPRSS2 (B) expression in HBECs from healthy subjects (N = 4).

A**B**

Supplementary Figure 5. siRNA knock-down of MDA5 and RIG-I mRNA. MDA5 (A) and RIG-I (B) mRNA expression in HBECs relative to control cells after siRNA-mediated downmodulation of MDA5 and RIG-I. N = 5.



Supplementary Figure 6. Imiquimod trend to decrease the poly(I:C)-induced expression of ACE2 receptor, whereas trend to increase the poly(I:C)-induced IFN-β response independently of asthma phenotype. (A) mRNA expression of ACE2 after poly(I:C) stimulation of HBECs from patients with asthma (cohort 2) treated (N = 3) or not (N = 4) with inhaled corticosteroids (ICS) in response to imiquimod treatment. (B-C) mRNA expression of ACE2 after poly(I:C) stimulation of HBECs from patients with allergic (AA; N = 4) / non-allergic asthma (NA; N = 4) (B) or T2-high (N = 4) / T2-low (N = 3) asthma (C) in response to imiquimod treatment. (D) mRNA expression of IFN-β after poly(I:C) stimulation of HBECs from patients with asthma treated or not with ICS in response to imiquimod treatment. (E-F) mRNA expression of IFN-β after poly(I:C) stimulation of HBECs from patients with AA / NA asthma (B) or T2-high / T2-low asthma (C) in response to imiquimod treatment. Number on the graph represent p-values (Wilcoxon test).