

Supplementary Table 1 Reagents and instruments

Reagents / instruments	Product Code	Manufacturer
LPS	L2880	Sigma, St. Louis, USA
isoflurane	R510-22-10	RWD Life Science Co., Ltd., Shenzhen, China
pentobarbital sodium	P3761	Sigma, St. Louis, USA
Acupuncture needles	0.25mm×15mm	Suzhou Medical Supplies Co. Ltd, China
EA apparatus	HuaTuo SDZ-V type	Suzhou Medical Supplies Co. Ltd, China
Xylene	-	Chengdu Kolon Chemical Co., Ltd, China
HE Staining Kit	DH0020	Leagene, China
(HRP-labeled) secondary antibodies	BL003A	Biosharp, China
RIPA lysis buffer	G2002-100mL	Servicebio, Wuhan, China
phenylmethylsulfonyl fluoride (100mM)	CR2202124	Servicebio, Wuhan, China
Phosphatase Inhibitor	CR2202004-1	Servicebio, Wuhan, China
BCA Protein Concentration Assay Kit	BL521A	Servicebio, Wuhan, China
SDS-PAGE Gel	CR2203049	Servicebio, Wuhan, China

Preparation Kit

PVDF Membrane, 0.45µm RISB97908 Immobilon-P, Germany

HRP-Goat anti Rabbit JAC-111-035-003 JacKson, America

HRP-Goat anti Mouse JAC-115-035-003 JacKson, America

Ultra-sensitive ECL CR2108094 Servicebio, Wuhan, China

Chemiluminescent

Substrate

Embedding Machine JB-P5 Wuhan Junjie Electronic Co., Ltd,
China

Tissue Rapid Dehydrator STP420 ES Thermo Scientific/Thermo Fisher
Scientific, America

Slicer HM325 Thermo Scientific/Thermo Fisher
Scientific, America

Automatic Staining Varistain™ Gemini ES Thermo Scientific/Thermo Fisher
Machine Scientific, America

digital panoramic scanner PANNORAMIC 3D-HISTECH, Hungary
DESK/MIDI/250/1000

microscope DM500 Leica, Germany

Agilent 2100 Bioanalyzer G2939A Agilent Technologies, Palo Alto, CA

Supplementary Table 2 Primer information

Primer name	The sequence(5' to 3')
ACTIN F	TCAGGTCATCACTATCGGCAAT
ACTIN R	AAAGAAAGGGTGTAAAACGCA
Mrc1 F	CAAGGAAGGTTGGCATTGT
Mrc1 R	GGAACGTGTGCTCTGAGTT
Gpnmb F	CCAGGTAGCAGATGTCCCAA
Gpnmb R	TTGCAGGTCACAATGAAGTCC
Aqp9 F	GATGGACTCATGGCCTTTGCTG
Aqp9 R	CAATCATAGGACCCACGACAGG
Trem1 F	AAGTATGCCAGAAGCAGGAAGG
Trem1 R	GGTAGGGTCATCTTTCAGGGTGT
Pde3a F	TCACAGGGCCTTAACTTACAC3
Pde3a R	GGAGCAAGAATTGGTTTGTC
Bmp6 F	GACAGCAGAGTCGCAATCG
Bmp6 R	AGCTCACGTAAAGCTCATGC
Slc26a4 F	GTGGGGTCCGTTGTTC
Slc26a4 R	CCGTTGTAGTTTTTGGTTGAG
Msr1 F	TGTGGGCCAGATGCTGAAAT
Msr1 R	AGGGATGCTGTCATGGAACG

Supplementary Table 3 The list of 27 genes downregulated in the COPD vs. NC group, and inversely upregulated after EA treatment.

Gene ID	Gene name	Description	1mA vs	log2FC	P value	3mA vs	log2FC	P value	COPD vs	log2FC	P value
			COPD			COPD			Normal		
ENSRNOG00000018268	Hhip	Hedgehog-interacting protein	UP	1.23	3.34E-05	UP	1.50	4.61E-07	DOWN	-2.55	1.01E-16
ENSRNOG00000019120	Hmgcs2	3-hydroxy-3-methylglutaryl-CoA synthase 2	UP	1.06	3.19E-04	UP	1.37	3.69E-06	DOWN	-1.39	2.62E-06
ENSRNOG00000069899	-	-	UP	3.69	2.20E-26	UP	3.79	8.84E-28	DOWN	-4.40	9.71E-36
ENSRNOG00000011901	Rrad	RRAD, Ras related glycolysis inhibitor and calcium channel regulator	UP	1.08	2.93E-04	UP	1.43	1.93E-06	DOWN	-1.48	7.70E-07
ENSRNOG00000028624	Kif26b	kinesin family member 26B	UP	1.15	1.08E-04	UP	1.21	4.59E-05	DOWN	-1.15	1.08E-04
ENSRNOG00000039571	Glod5	glyoxalase domain containing 5	UP	1.04	7.51E-04	UP	1.16	1.39E-04	DOWN	-1.43	3.07E-06
ENSRNOG00000020424	Plpp4	phospholipid phosphatase 4	UP	1.55	9.17E-07	UP	2.08	4.10E-11	DOWN	-2.64	1.10E-16
ENSRNOG00000015473	Phactr2	phosphatase and actin regulator 2	UP	1.07	2.68E-04	UP	1.06	3.08E-04	DOWN	-1.30	9.70E-06
ENSRNOG00000014030	Sym	synemin	UP	1.09	1.98E-04	UP	1.00	6.14E-04	DOWN	-1.50	4.12E-07
ENSRNOG00000005700	Nsg1	neuronal vesicle trafficking associated 1	UP	1.04	4.03E-04	UP	1.17	7.46E-05	DOWN	-1.62	5.07E-08
ENSRNOG00000010280	Pde8b	phosphodiesterase 8B	UP	1.18	8.26E-05	UP	1.72	1.22E-08	DOWN	-1.65	4.49E-08
ENSRNOG00000067538	-	-	UP	1.13	1.68E-04	UP	1.05	4.16E-04	DOWN	-1.41	2.38E-06
ENSRNOG00000010447	Tmod2	tropomodulin 2	UP	1.57	6.00E-07	UP	1.43	5.70E-06	DOWN	-1.72	4.56E-08
ENSRNOG00000018557	Cdh22	cadherin 22	UP	1.22	6.14E-05	UP	1.57	2.86E-07	DOWN	-1.35	8.61E-06
ENSRNOG00000003762	Smarca1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1	UP	1.34	7.44E-06	UP	1.22	4.18E-05	DOWN	-1.61	7.21E-08
ENSRNOG00000001652	Erg	ETS transcription factor ERG	UP	1.11	1.59E-04	UP	1.16	8.10E-05	DOWN	-1.60	6.90E-08
ENSRNOG00000054013	Clec4g	C-type lectin domain family 4, member G	UP	2.12	9.46E-12	UP	1.91	6.04E-10	DOWN	-2.56	3.64E-16
ENSRNOG00000003209	Pcp4l1	Purkinje cell protein 4-like 1	UP	1.28	2.03E-05	UP	1.18	7.91E-05	DOWN	-1.62	6.93E-08
ENSRNOG00000063400	Shisa9	shisa family member 9	UP	1.14	1.58E-04	UP	1.42	2.81E-06	DOWN	-1.51	5.54E-07
ENSRNOG00000019549	Akap12	A-kinase anchoring protein 12	UP	1.07	2.73E-04	UP	1.66	2.25E-08	DOWN	-1.68	1.70E-08
ENSRNOG00000031211	Acsm5	acyl-CoA synthetase medium-chain family member 5	UP	1.24	2.71E-05	UP	1.31	8.95E-06	DOWN	-2.02	1.94E-11
ENSRNOG00000019365	Ablim3	actin binding LIM protein family, member 3	UP	1.69	1.27E-08	UP	1.37	3.20E-06	DOWN	-1.53	2.46E-07
ENSRNOG00000028743	Gal3st3	galactose-3-O-sulfotransferase 3	UP	1.09	2.37E-04	UP	1.95	9.50E-11	DOWN	-1.56	1.76E-07
ENSRNOG00000007370	Rnf144a	ring finger protein 144A	UP	1.07	3.71E-04	UP	1.79	3.41E-09	DOWN	-1.61	1.01E-07
ENSRNOG00000013408	Npas2	neuronal PAS domain protein 2	UP	1.45	1.07E-06	UP	1.82	1.21E-09	DOWN	-2.97	1.85E-21
ENSRNOG00000063594	-	-	UP	1.05	4.48E-04	UP	1.20	6.63E-05	DOWN	-1.52	4.46E-07
ENSRNOG00000058202	Ppp2r2c	protein phosphatase 2, regulatory subunit B, gamma	UP	1.24	4.36E-05	UP	1.35	8.70E-06	DOWN	-1.79	4.52E-09

Supplementary Table 4 The list of 63 genes upregulated in the COPD vs. NC group, and inversely downregulated after EA treatment.

Gene ID	Gene name	Description	1mA vs	log2FC	P value	3mA vs	log2FC	P value	COPD vs	log2FC	P value
			COPD			COPD			Normal		
ENSRNOG00000058337	Plcb2	phospholipase C, beta 2	DOWN	-1.18	5.93E-05	DOWN	-1.04	3.92E-04	UP	1.41	1.72E-06
ENSRNOG00000054964	Aoah	acyloxyacyl hydrolase	DOWN	-1.67	2.10E-08	DOWN	-1.27	1.54E-05	UP	1.54	2.01E-07
ENSRNOG00000021310	Slc36a3	solute carrier family 36, member 3	DOWN	-1.48	5.35E-06	DOWN	-1.64	2.81E-07	UP	2.31	2.07E-11
ENSRNOG00000013747	Sh3bp2	SH3-domain binding protein 2	DOWN	-1.33	6.07E-06	DOWN	-1.03	4.38E-04	UP	1.18	5.94E-05
ENSRNOG00000024115	C6	complement C6	DOWN	-2.25	1.19E-13	DOWN	-1.81	1.40E-09	UP	4.02	1.56E-34
ENSRNOG00000024346	Plet1	placenta expressed transcript 1	DOWN	-1.15	8.39E-05	DOWN	-1.04	3.74E-04	UP	1.92	1.44E-10
ENSRNOG00000004226	Irak3	interleukin-1 receptor-associated kinase 3	DOWN	-1.05	3.52E-04	DOWN	-1.07	2.69E-04	UP	1.26	1.89E-05
ENSRNOG00000022975	Nfam1	NFAT activating protein with ITAM motif 1	DOWN	-1.21	3.71E-05	DOWN	-1.05	3.25E-04	UP	1.45	9.13E-07
ENSRNOG00000002385	Prg4	proteoglycan 4	DOWN	-1.55	1.54E-07	DOWN	-1.04	3.92E-04	UP	1.48	5.22E-07
ENSRNOG00000020136	Tgm1	transglutaminase 1	DOWN	-1.62	5.50E-08	DOWN	-1.26	1.87E-05	UP	1.27	1.63E-05
ENSRNOG00000026203	Pax8	paired box 8	DOWN	-1.33	1.02E-05	DOWN	-1.19	7.32E-05	UP	1.69	2.78E-08
ENSRNOG00000018251	Mrc1	mannose receptor, C type 1	DOWN	-1.75	4.51E-09	DOWN	-1.32	7.39E-06	UP	1.55	1.54E-07
ENSRNOG00000016826	Pla2g2d	phospholipase A2, group IID	DOWN	-1.50	3.98E-07	DOWN	-1.06	2.90E-04	UP	1.37	3.36E-06
ENSRNOG00000020716	Axl	Axl receptor tyrosine kinase	DOWN	-1.40	2.02E-06	DOWN	-1.00	6.06E-04	UP	1.31	7.99E-06
ENSRNOG00000011107	Pcsk1	proprotein convertase subtilisin/kexin type 1	DOWN	-1.42	1.53E-06	DOWN	-1.38	3.05E-06	UP	2.06	8.03E-12
ENSRNOG00000067740	-	-	DOWN	-1.78	2.75E-09	DOWN	-1.59	9.01E-08	UP	2.47	7.08E-16
ENSRNOG00000029179	Cyp2d3	cytochrome P450, family 2, subfamily d, polypeptide 3	DOWN	-1.33	9.52E-06	DOWN	-1.04	4.89E-04	UP	1.50	5.73E-07
ENSRNOG00000013641	Myo7a	myosin VIIA	DOWN	-1.56	1.67E-07	DOWN	-1.07	3.03E-04	UP	2.12	4.39E-12
ENSRNOG00000053430	Slco4a1	solute carrier organic anion transporter family, member 4a1	DOWN	-1.96	1.58E-10	DOWN	-1.51	5.66E-07	UP	1.61	9.77E-08
ENSRNOG00000034190	Ighm	immunoglobulin heavy constant epsilon	DOWN	-1.51	3.31E-07	DOWN	-1.32	7.04E-06	UP	2.82	7.63E-20
ENSRNOG00000065128	Naip5	NLR family, apoptosis inhibitory protein 5	DOWN	-1.27	1.92E-05	DOWN	-1.55	1.88E-07	UP	1.89	3.36E-10
ENSRNOG00000026306	Clec5a	C-type lectin domain containing 5A	DOWN	-1.45	1.11E-06	DOWN	-1.20	4.70E-05	UP	1.87	5.60E-10
ENSRNOG00000071194	-	-	DOWN	-1.25	2.58E-05	DOWN	-1.13	1.40E-04	UP	1.25	2.87E-05
ENSRNOG00000003170	Nlrp3	NLR family, pyrin domain containing 3	DOWN	-1.22	3.80E-05	DOWN	-1.18	6.24E-05	UP	1.38	3.51E-06
ENSRNOG00000042237	Tm6sf2	transmembrane 6 superfamily member 2	DOWN	-1.21	5.39E-05	DOWN	-1.15	1.14E-04	UP	1.31	1.14E-05
ENSRNOG00000010935	Cpb2	carboxypeptidase B2	DOWN	-1.16	1.36E-04	DOWN	-1.50	1.60E-06	UP	3.50	7.67E-24
ENSRNOG00000037331	Cd33	CD33 molecule	DOWN	-1.61	6.03E-08	DOWN	-1.35	4.55E-06	UP	1.94	1.18E-10
ENSRNOG00000034038	AABR07005844.1	deleted in malignant brain tumors 1 protein-like	DOWN	-1.65	3.54E-08	DOWN	-1.27	1.92E-05	UP	2.09	4.91E-12
ENSRNOG00000030877	Htr2c	5-hydroxytryptamine receptor 2C	DOWN	-1.49	7.96E-07	DOWN	-1.09	2.67E-04	UP	1.20	7.19E-05
ENSRNOG00000061883	Aqp9	aquaporin 9	DOWN	-1.14	1.71E-04	DOWN	-1.28	2.93E-05	UP	1.67	9.71E-08
ENSRNOG00000026235	Hk3	hexokinase 3	DOWN	-1.59	8.65E-08	DOWN	-1.33	6.35E-06	UP	2.61	1.95E-17
ENSRNOG00000018790	Kcnh4	potassium voltage-gated channel subfamily H member 4	DOWN	-1.44	1.17E-06	DOWN	-1.20	4.90E-05	UP	1.98	6.99E-11
ENSRNOG00000037563	Cd68	Cd68 molecule	DOWN	-1.44	1.12E-06	DOWN	-1.23	3.01E-05	UP	2.09	4.29E-12
ENSRNOG00000005246	Tfap2c	transcription factor AP-2 gamma	DOWN	-1.09	2.16E-03	DOWN	-1.05	2.01E-03	UP	1.18	6.53E-04
ENSRNOG00000027739	Cndp1	carnosine dipeptidase 1	DOWN	-1.37	3.23E-06	DOWN	-1.10	1.84E-04	UP	1.51	3.39E-07

ENSRNOG00000004704	Dstamp	dendrocyte expressed seven transmembrane protein	DOWN	-1.71	1.03E-08	DOWN	-1.35	5.30E-06	UP	1.59	9.41E-08
ENSRNOG00000039390	Slc37a2	solute carrier family 37 member 2	DOWN	-1.17	7.41E-05	DOWN	-1.05	3.61E-04	UP	1.67	2.37E-08
ENSRNOG00000008588	Batf	basic leucine zipper ATF-like transcription factor	DOWN	-1.12	1.68E-04	DOWN	-1.13	1.53E-04	UP	1.81	2.63E-09
ENSRNOG00000057827	Lmln2	leishmanolysin like peptidase 2	DOWN	-1.35	1.59E-05	DOWN	-1.36	1.43E-05	UP	1.33	2.90E-05
ENSRNOG00000070924	-	-	DOWN	-1.14	2.74E-04	DOWN	-1.19	1.27E-04	UP	1.36	1.67E-05
ENSRNOG00000028016	Ncf2	neutrophil cytosolic factor 2	DOWN	-1.37	3.28E-06	DOWN	-1.10	1.87E-04	UP	1.50	4.50E-07
ENSRNOG00000036726	Cd300e	Cd300e molecule	DOWN	-1.70	1.74E-08	DOWN	-1.70	1.73E-08	UP	1.83	2.27E-09
ENSRNOG00000018748	Slc16a11	solute carrier family 16, member 11	DOWN	-2.34	2.76E-14	DOWN	-1.68	2.29E-08	UP	3.07	2.29E-22
ENSRNOG00000017521	Gpr55	G protein-coupled receptor 55	DOWN	-1.61	2.75E-07	DOWN	-1.81	6.70E-09	UP	1.87	2.16E-09
ENSRNOG00000050672	Ervfrd-1	endogenous retrovirus group FRD member 1, envelope	DOWN	-1.64	9.82E-07	DOWN	-1.27	8.20E-05	UP	1.65	5.61E-07
ENSRNOG00000004150	Slc9a7	solute carrier family 9 member A7	DOWN	-1.33	1.22E-05	DOWN	-1.14	1.67E-04	UP	1.60	2.04E-07
ENSRNOG00000014653	Arl11	ADP-ribosylation factor like GTPase 11	DOWN	-1.30	9.96E-06	DOWN	-1.03	4.19E-04	UP	1.72	8.64E-09
ENSRNOG00000022859	Trem1	triggering receptor expressed on myeloid cells 1	DOWN	-1.65	2.90E-08	DOWN	-1.45	1.10E-06	UP	1.98	5.93E-11
ENSRNOG00000017381	Itih4	inter-alpha-trypsin inhibitor heavy chain 4	DOWN	-1.56	2.34E-07	DOWN	-1.26	2.05E-05	UP	1.38	3.55E-06
ENSRNOG00000047367	Card14	caspase recruitment domain family, member 14	DOWN	-1.63	4.39E-08	DOWN	-1.07	2.56E-04	UP	2.16	9.51E-13
ENSRNOG00000066785	-	-	DOWN	-1.31	8.76E-06	DOWN	-1.23	3.07E-05	UP	1.93	1.31E-10
ENSRNOG00000015774	Mreg	melanoregulin	DOWN	-1.00	6.23E-04	DOWN	-1.10	2.02E-04	UP	2.75	1.73E-18
ENSRNOG00000033064	Edil3	EGF like repeats and discoidin domains 3	DOWN	-1.13	1.13E-04	DOWN	-1.16	7.82E-05	UP	1.52	3.37E-07
ENSRNOG00000064228	-	-	DOWN	-1.11	1.51E-04	DOWN	-1.16	8.64E-05	UP	1.26	2.20E-05
ENSRNOG00000000815	Smpd3a	sphingomyelin phosphodiesterase, acid-like 3A	DOWN	-1.44	1.13E-06	DOWN	-1.35	4.33E-06	UP	2.17	6.95E-13
ENSRNOG00000013748	Trem3	triggering receptor expressed on myeloid cells 3	DOWN	-1.10	1.86E-04	DOWN	-1.48	6.69E-07	UP	1.30	1.23E-05
ENSRNOG00000036692	Gcgr	glucagon receptor	DOWN	-1.11	2.30E-04	DOWN	-1.09	3.14E-04	UP	2.84	3.18E-18
ENSRNOG00000014956	Slc11a1	solute carrier family 11 member 1	DOWN	-1.25	2.20E-05	DOWN	-1.04	3.69E-04	UP	1.96	6.02E-11
ENSRNOG00000008816	Gpnmb	glycoprotein nmb	DOWN	-1.33	5.74E-06	DOWN	-1.18	5.50E-05	UP	2.33	1.79E-14
ENSRNOG00000008839	Pparg	peroxisome proliferator-activated receptor gamma	DOWN	-1.35	4.79E-06	DOWN	-1.02	4.69E-04	UP	1.28	1.42E-05
ENSRNOG00000021243	Siglec1	sialic acid binding Ig like lectin 1	DOWN	-1.77	2.87E-09	DOWN	-1.54	2.03E-07	UP	2.23	1.95E-13
ENSRNOG00000000187	Csf2rb	colony stimulating factor 2 receptor subunit beta	DOWN	-1.61	6.35E-08	DOWN	-1.26	2.00E-05	UP	2.13	2.10E-12
ENSRNOG00000023214	Il20rb	interleukin 20 receptor subunit beta	DOWN	-1.15	8.47E-05	DOWN	-1.03	4.83E-04	UP	1.08	2.50E-04

Supplementary Table 5 The respective GO functional analyzes by pairwise group comparisons

COPD vs NC													
Category	Term	Count	%	P Value	Log P value	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
GOTERM_BP_DIRECT	GO:0006954 inflammatory response	39	4.29	2.40E-08	-7.62	ENSRNOG00000031930, ENSRNOG00000070382, ENSRNOG00000019077, ENSRNOG00000046834, ENSRNOG00000065935, ENSRNOG00000017819,	778	346	19234	2.79	9.82E-05	6.30E-05	6.23E-05
						ENSRNOG00000009848, ENSRNOG00000028548, ENSRNOG0000007989, ENSRNOG00000020716, ENSRNOG00000033693, ENSRNOG00000016945, ENSRNOG0000001480, ENSRNOG00000013717, ENSRNOG00000022067, ENSRNOG00000007159,							

GOTERM_BP_DIRECT	GO:0042554 superoxide anion generation	10	1.10	3.08E-08	-7.51	ENSRNOG0000004404, ENSRNOG0000005810, ENSRNOG0000002723, ENSRNOG00000013014, ENSRNOG00000070745, ENSRNOG00000003170, ENSRNOG00000021166, ENSRNOG00000028016, ENSRNOG00000046261, ENSRNOG0000004063, ENSRNOG0000001480, ENSRNOG00000009848, ENSRNOG00000025051, ENSRNOG00000054695, ENSRNOG00000050190, ENSRNOG00000027357, ENSRNOG00000029768, ENSRNOG0000001414, ENSRNOG00000014117, ENSRNOG00000021166, ENSRNOG00000021004, ENSRNOG00000009848, ENSRNOG00000042905, ENSRNOG00000047706, ENSRNOG00000013280, ENSRNOG00000013717, ENSRNOG00000012749, ENSRNOG00000004647, ENSRNOG00000011478, ENSRNOG00000067968, ENSRNOG00000067740, ENSRNOG00000054008, ENSRNOG00000070745, ENSRNOG00000017625, ENSRNOG00000014956, ENSRNOG00000046216, ENSRNOG00000003442, ENSRNOG00000000940, ENSRNOG00000053550, ENSRNOG00000060087, ENSRNOG00000046829, ENSRNOG00000017208,	ENSRNOG00000029768, ENSRNOG0000004249, ENSRNOG00000029949, ENSRNOG00000013231, ENSRNOG00000016535, ENSRNOG00000043451, ENSRNOG00000009131, ENSRNOG00000003622, ENSRNOG00000025117, ENSRNOG00000019048, ENSRNOG0000007865, ENSRNOG00000056836, ENSRNOG00000021318, ENSRNOG00000008313, ENSRNOG00000008990, ENSRNOG00000028713, ENSRNOG00000046829, ENSRNOG00000013887, ENSRNOG00000008587, ENSRNOG00000009131, ENSRNOG00000004067, ENSRNOG00000050898, ENSRNOG00000050430, ENSRNOG00000049829, ENSRNOG00000021155, ENSRNOG0000007002, ENSRNOG00000047571, ENSRNOG0000004249, ENSRNOG00000032596, ENSRNOG0000004062, ENSRNOG00000025100, ENSRNOG0000004647, ENSRNOG00000018445, ENSRNOG00000022975, ENSRNOG00000024931, ENSRNOG00000017819, ENSRNOG00000032247, ENSRNOG00000010853, ENSRNOG00000011054, ENSRNOG00000018445, ENSRNOG00000020369, ENSRNOG00000015603,	ENSRNOG0000002227, ENSRNOG00000018390, ENSRNOG00000053272, ENSRNOG00000014156, ENSRNOG00000017208, ENSRNOG00000014956, ENSRNOG00000033348, ENSRNOG00000020353, ENSRNOG00000013014, ENSRNOG0000004712, ENSRNOG00000010233, ENSRNOG00000016248, ENSRNOG00000066008, ENSRNOG00000062882, ENSRNOG00000000940, ENSRNOG0000006281, ENSRNOG00000017208, ENSRNOG00000069521, ENSRNOG00000000855, ENSRNOG00000010031, ENSRNOG00000065254, ENSRNOG00000021157, ENSRNOG0000002385, ENSRNOG00000054129, ENSRNOG00000030712, ENSRNOG00000070745, ENSRNOG00000045595, ENSRNOG00000026310, ENSRNOG0000004226, ENSRNOG00000019336, ENSRNOG00000026306, ENSRNOG00000008588, ENSRNOG0000002227, ENSRNOG0000004517, ENSRNOG00000070745, ENSRNOG00000027938, ENSRNOG00000013887, ENSRNOG00000065935,	778	20	19234	12.36	1.26E-04	6.30E-05	6.23E-05
GOTERM_BP_DIRECT	GO:0001525 angiogenesis	30	3.30	8.43E-08	-7.07	ENSRNOG00000007865, ENSRNOG00000056836, ENSRNOG00000021318, ENSRNOG00000008313, ENSRNOG00000008990, ENSRNOG00000028713, ENSRNOG00000046829, ENSRNOG00000013887, ENSRNOG00000008587, ENSRNOG00000009131, ENSRNOG00000004067, ENSRNOG00000050898, ENSRNOG00000050430, ENSRNOG00000049829, ENSRNOG00000021155, ENSRNOG0000007002, ENSRNOG00000047571, ENSRNOG0000004249, ENSRNOG00000032596, ENSRNOG0000004062, ENSRNOG00000025100, ENSRNOG0000004647, ENSRNOG00000018445, ENSRNOG00000022975, ENSRNOG00000024931, ENSRNOG00000017819, ENSRNOG00000032247, ENSRNOG00000010853, ENSRNOG00000011054, ENSRNOG00000018445, ENSRNOG00000020369, ENSRNOG00000015603,	ENSRNOG0000004712, ENSRNOG00000010233, ENSRNOG00000016248, ENSRNOG00000066008, ENSRNOG00000062882, ENSRNOG00000000940, ENSRNOG0000006281, ENSRNOG00000017208, ENSRNOG00000069521, ENSRNOG00000000855, ENSRNOG00000010031, ENSRNOG00000065254, ENSRNOG00000021157, ENSRNOG0000002385, ENSRNOG00000054129, ENSRNOG00000030712, ENSRNOG00000070745, ENSRNOG00000045595, ENSRNOG00000026310, ENSRNOG0000004226, ENSRNOG00000019336, ENSRNOG00000026306, ENSRNOG00000008588, ENSRNOG0000002227, ENSRNOG0000004517, ENSRNOG00000070745, ENSRNOG00000027938, ENSRNOG00000013887, ENSRNOG00000065935,	778	234	19234	3.17	3.45E-04	6.90E-05	6.83E-05	
GOTERM_BP_DIRECT	GO:0006955 immune response	33	3.63	2.17E-07	-6.66	ENSRNOG00000013717, ENSRNOG00000012749, ENSRNOG00000004647, ENSRNOG00000011478, ENSRNOG00000067968, ENSRNOG00000067740, ENSRNOG00000054008, ENSRNOG00000070745, ENSRNOG00000017625, ENSRNOG00000014956, ENSRNOG00000046216, ENSRNOG00000003442, ENSRNOG00000000940, ENSRNOG00000053550, ENSRNOG00000060087, ENSRNOG00000046829, ENSRNOG00000017208,	ENSRNOG0000007002, ENSRNOG00000047571, ENSRNOG0000004249, ENSRNOG00000032596, ENSRNOG0000004062, ENSRNOG00000025100, ENSRNOG0000004647, ENSRNOG00000018445, ENSRNOG00000022975, ENSRNOG00000024931, ENSRNOG00000017819, ENSRNOG00000032247, ENSRNOG00000010853, ENSRNOG00000011054, ENSRNOG00000018445, ENSRNOG00000020369, ENSRNOG00000015603,	ENSRNOG0000002385, ENSRNOG00000054129, ENSRNOG00000030712, ENSRNOG00000070745, ENSRNOG00000045595, ENSRNOG00000026310, ENSRNOG0000004226, ENSRNOG00000019336, ENSRNOG00000026306, ENSRNOG00000008588, ENSRNOG0000002227, ENSRNOG0000004517, ENSRNOG00000070745, ENSRNOG00000027938, ENSRNOG00000013887, ENSRNOG00000065935,	778	287	19234	2.84	8.87E-04	1.48E-04	1.46E-04
GOTERM_BP_DIRECT	GO:0001819 positive regulation of cytokine production	15	1.65	5.45E-06	-5.26	ENSRNOG00000017625, ENSRNOG00000014956, ENSRNOG00000046216, ENSRNOG00000003442, ENSRNOG00000000940, ENSRNOG00000053550, ENSRNOG00000060087, ENSRNOG00000046829, ENSRNOG00000017208,	ENSRNOG0000004647, ENSRNOG00000018445, ENSRNOG00000022975, ENSRNOG00000024931, ENSRNOG00000017819, ENSRNOG00000032247, ENSRNOG00000010853, ENSRNOG00000011054, ENSRNOG00000018445, ENSRNOG00000020369, ENSRNOG00000015603,	ENSRNOG0000004226, ENSRNOG00000019336, ENSRNOG00000026306, ENSRNOG00000008588, ENSRNOG0000002227, ENSRNOG0000004517, ENSRNOG00000070745, ENSRNOG00000027938, ENSRNOG00000013887, ENSRNOG00000065935,	778	83	19234	4.47	2.21E-02	2.23E-03	2.21E-03
GOTERM_BP_DIRECT	GO:0043410 positive regulation of MAPK cascade	22	2.42	6.28E-05	-4.20	ENSRNOG00000000940, ENSRNOG00000053550, ENSRNOG00000060087, ENSRNOG00000046829, ENSRNOG00000017208,	ENSRNOG00000010853, ENSRNOG00000011054, ENSRNOG00000018445, ENSRNOG00000020369, ENSRNOG00000015603,	ENSRNOG0000004517, ENSRNOG00000070745, ENSRNOG00000027938, ENSRNOG00000013887, ENSRNOG00000065935,	778	200	19234	2.72	2.27E-01	1.28E-02	1.26E-02

						ENSRNOG00000008587, ENSRNOG00000007002, ENSRNOG00000027894												
						ENSRNOG00000031930, ENSRNOG00000009848, ENSRNOG00000004712,												
						ENSRNOG00000027030, ENSRNOG00000036942, ENSRNOG00000050697,												
						ENSRNOG00000052510, ENSRNOG00000010031, ENSRNOG00000018445,												
						ENSRNOG00000020369, ENSRNOG00000016945, ENSRNOG00000004033,												
						ENSRNOG00000013717, ENSRNOG00000066008, ENSRNOG00000053675,												
						ENSRNOG00000028896, ENSRNOG00000006720, ENSRNOG00000053272,												
						ENSRNOG00000033564, ENSRNOG00000033444, ENSRNOG00000001955,												
						ENSRNOG00000032596, ENSRNOG00000070745, ENSRNOG00000017409,												
						ENSRNOG00000003172, ENSRNOG00000067740, ENSRNOG00000010935,												
						ENSRNOG00000009826, ENSRNOG00000020380, ENSRNOG00000030625,												
						ENSRNOG00000011107, ENSRNOG00000028548, ENSRNOG00000003969,												
						ENSRNOG00000001827, ENSRNOG00000030462, ENSRNOG00000030187,												
						ENSRNOG00000013973, ENSRNOG00000014426, ENSRNOG00000065935,												
						ENSRNOG00000050190, ENSRNOG00000023257, ENSRNOG00000017819,												
						ENSRNOG00000007002, ENSRNOG00000006033, ENSRNOG00000043387,												
						ENSRNOG00000026650, ENSRNOG00000047571, ENSRNOG00000010645,												
						ENSRNOG00000029768, ENSRNOG00000004404, ENSRNOG00000004647,												
						ENSRNOG00000002227, ENSRNOG00000001414, ENSRNOG00000017381,												
						ENSRNOG00000042326, ENSRNOG00000019689, ENSRNOG00000067968,												
GOTERM_CC	GO:0005615	1.22E	13.42	2.70E-11	-10.57	ENSRNOG00000001092, ENSRNOG00000024115, ENSRNOG00000008680,	808	1609	19758	1.85	1.46E-08	8.96E-09	8.75E-09					
_DIRECT	extracellular space	+02				ENSRNOG00000003666, ENSRNOG00000050898, ENSRNOG00000042905,												
						ENSRNOG00000004517, ENSRNOG00000011320, ENSRNOG00000020716,												
						ENSRNOG00000020206, ENSRNOG00000049829, ENSRNOG00000013064,												
						ENSRNOG00000046834, ENSRNOG00000017438, ENSRNOG00000025332,												
						ENSRNOG00000025581, ENSRNOG00000006368, ENSRNOG00000004222,												
						ENSRNOG00000006802, ENSRNOG00000046261, ENSRNOG00000005679,												
						ENSRNOG00000000940, ENSRNOG00000050767, ENSRNOG00000002723,												
						ENSRNOG00000029949, ENSRNOG00000014171, ENSRNOG00000059579,												
						ENSRNOG00000050761, ENSRNOG00000009350, ENSRNOG00000017206,												
						ENSRNOG00000009597, ENSRNOG00000004062, ENSRNOG00000006641,												
						ENSRNOG00000022353, ENSRNOG00000032569, ENSRNOG00000001469,												
						ENSRNOG00000003649, ENSRNOG00000000815, ENSRNOG00000012110,												
						ENSRNOG00000003807, ENSRNOG00000047706, ENSRNOG00000015675,												
						ENSRNOG00000013280, ENSRNOG00000021155, ENSRNOG00000023576,												
						ENSRNOG00000021157, ENSRNOG00000005386, ENSRNOG00000062101,												
						ENSRNOG00000002385, ENSRNOG00000007159, ENSRNOG00000030712,												
						ENSRNOG00000017063, ENSRNOG00000051235, ENSRNOG00000018952,												
						ENSRNOG00000016535, ENSRNOG00000028072, ENSRNOG00000013668,												
						ENSRNOG00000043451, ENSRNOG00000021166, ENSRNOG00000045595,												
						ENSRNOG00000005770												
GOTERM_CC	GO:0043020	6.00E	0.66	7.00E-05	-4.16	ENSRNOG00000028016, ENSRNOG00000003622, ENSRNOG00000033348,	808	12	19758	12.23	3.69E-02	3.83E-03	3.74E-03					

_DIRECT	NADPH oxidase complex GO:0016176 superoxide-generating	+00				ENSRNOG00000025117, ENSRNOG00000013014, ENSRNOG00000001480									
GOTERM_MF_DIRECT	NADPH oxidase activator activity GO:0016175	5	0.55	1.67E-04	-3.78	ENSRNOG00000028016, ENSRNOG00000025117, ENSRNOG00000020353, ENSRNOG00000004063, ENSRNOG00000001480	724	8	17765	15.34	1.54E-01	3.62E-02	3.57E-02		
GOTERM_MF_DIRECT	superoxide-generating NADPH oxidase activity	5	0.55	4.69E-04	-3.33	ENSRNOG00000028016, ENSRNOG00000003622, ENSRNOG00000033348, ENSRNOG00000013014, ENSRNOG00000001480	724	10	17765	12.27	3.74E-01	5.21E-02	5.14E-02		

EA-1mA vs COPD

Category	Term	Count	%	P Value	Log P value	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
GOTERM_BP_DIRECT	GO:0045087 innate immune response	18	5.81	3.27E-05	-4.48	ENSRNOG00000003622, ENSRNOG00000005810, ENSRNOG00000009912, ENSRNOG00000010347, ENSRNOG00000004249, ENSRNOG00000051235, ENSRNOG00000046834, ENSRNOG00000022859, ENSRNOG00000013973, ENSRNOG00000034190, ENSRNOG00000026306, ENSRNOG00000003170, ENSRNOG00000024159, ENSRNOG00000024115, ENSRNOG00000065128, ENSRNOG00000009331, ENSRNOG00000006033	254	410	19234	3.32	6.08E-02	3.13E-02	3.11E-02
GOTERM_BP_DIRECT	GO:0001819 positive regulation of cytokine production	8	2.58	1.11E-04	-3.95	ENSRNOG00000018445, ENSRNOG00000022975, ENSRNOG00000004647, ENSRNOG00000004226, ENSRNOG00000009912, ENSRNOG00000026306, ENSRNOG00000014956, ENSRNOG00000008588	254	83	19234	7.30	1.92E-01	5.32E-02	5.28E-02
GOTERM_BP_DIRECT	GO:0071222 cellular response to lipopolysaccharide	14	4.52	1.53E-04	-3.81	ENSRNOG00000003244, ENSRNOG00000004763, ENSRNOG00000024382, ENSRNOG00000004647, ENSRNOG00000019120, ENSRNOG00000018251, ENSRNOG00000020716, ENSRNOG00000018598, ENSRNOG00000037563, ENSRNOG00000022859, ENSRNOG00000013973, ENSRNOG00000003170, ENSRNOG00000009131, ENSRNOG00000006033	254	295	19234	3.59	2.55E-01	5.87E-02	5.83E-02
GOTERM_BP_DIRECT	GO:0050776 regulation of immune response	6	1.94	9.83E-04	-3.01	ENSRNOG00000024382, ENSRNOG00000001425, ENSRNOG00000037339, ENSRNOG00000024159, ENSRNOG00000007664, ENSRNOG00000049422	254	58	19234	7.83	8.48E-01	1.88E-01	1.87E-01
GOTERM_BP_DIRECT	GO:0001818 negative regulation of	5	1.61	1.67E-03	-2.78	ENSRNOG00000008816, ENSRNOG00000004647, ENSRNOG00000014956, ENSRNOG00000008839, ENSRNOG00000020716	254	39	19234	9.71	9.60E-01	2.25E-01	2.23E-01

GOTERM_BP_DIRECT	cytokine production GO:0006909 phagocytosis GO:0050728	6	1.94	2.43E-03	-2.61	ENSRNOG00000028016, ENSRNOG00000013641, ENSRNOG00000014956, ENSRNOG00000020716, ENSRNOG00000009331, ENSRNOG00000050430	254	71	19234	6.40	9.91E-01	2.39E-01	2.37E-01
GOTERM_BP_DIRECT	negative regulation of inflammatory response GO:0030593	8	2.58	2.17E-03	-2.66	ENSRNOG00000004763, ENSRNOG00000054964, ENSRNOG00000042326, ENSRNOG00000011071, ENSRNOG00000004647, ENSRNOG00000003170, ENSRNOG00000012972, ENSRNOG00000008839	254	136	19234	4.45	9.84E-01	2.39E-01	2.37E-01
GOTERM_BP_DIRECT	neutrophil chemotaxis GO:0030593	6	1.94	3.09E-03	-2.51	ENSRNOG00000022859, ENSRNOG00000029768, ENSRNOG00000024159, ENSRNOG00000013748, ENSRNOG00000049422, ENSRNOG00000050430	254	75	19234	6.06	9.97E-01	2.57E-01	2.55E-01
GOTERM_CC_DIRECT	plasma membrane GO:0005886	107	34.52	5.68E-06	-5.25	ENSRNOG00000003622, ENSRNOG00000017072, ENSRNOG00000058337, ENSRNOG00000019412, ENSRNOG00000054013, ENSRNOG00000013674, ENSRNOG00000058692, ENSRNOG00000018606, ENSRNOG00000004150, ENSRNOG00000004393, ENSRNOG00000002372, ENSRNOG00000028930, ENSRNOG00000000187, ENSRNOG00000026592, ENSRNOG00000052064, ENSRNOG00000053430, ENSRNOG00000017521, ENSRNOG00000043478, ENSRNOG00000013564, ENSRNOG00000014653, ENSRNOG00000011071, ENSRNOG00000045816, ENSRNOG00000019549, ENSRNOG00000024578, ENSRNOG00000009797, ENSRNOG00000001270, ENSRNOG00000009033, ENSRNOG00000029740, ENSRNOG00000061883, ENSRNOG00000057703, ENSRNOG0000005465, ENSRNOG00000011901, ENSRNOG00000030625, ENSRNOG00000036726, ENSRNOG0000001425, ENSRNOG00000010375, ENSRNOG00000020939, ENSRNOG00000010094, ENSRNOG00000016685, ENSRNOG00000018748, ENSRNOG00000003280, ENSRNOG00000068001, ENSRNOG00000024346, ENSRNOG00000004763, ENSRNOG00000052880, ENSRNOG00000004249, ENSRNOG00000030877, ENSRNOG00000017381, ENSRNOG00000051950, ENSRNOG00000020706, ENSRNOG00000004928, ENSRNOG00000042326, ENSRNOG00000036692, ENSRNOG00000022859, ENSRNOG00000019606, ENSRNOG00000043416, ENSRNOG00000014956, ENSRNOG00000021243, ENSRNOG00000007866, ENSRNOG00000054219, ENSRNOG00000012779, ENSRNOG00000004517, ENSRNOG00000020716, ENSRNOG00000012098, ENSRNOG00000046834, ENSRNOG00000018644, ENSRNOG00000026704, ENSRNOG00000026306, ENSRNOG00000007345, ENSRNOG00000006410, ENSRNOG00000049422, ENSRNOG00000003136, ENSRNOG00000019183, ENSRNOG00000004226, ENSRNOG00000009912, ENSRNOG00000010347, ENSRNOG00000018251, ENSRNOG00000011550, ENSRNOG00000037563, ENSRNOG00000027808, ENSRNOG00000021424, ENSRNOG00000003095, ENSRNOG00000015948, ENSRNOG00000004067, ENSRNOG00000026310, ENSRNOG00000006116, ENSRNOG00000005388, ENSRNOG00000008816, ENSRNOG00000024382, ENSRNOG00000037339,	268	5376	19758	1.47	1.70E-03	8.53E-04	8.41E-04

						ENSRNOG00000018268, ENSRNOG00000037331, ENSRNOG00000017976, ENSRNOG00000013280, ENSRNOG00000014227, ENSRNOG00000023214, ENSRNOG00000046972, ENSRNOG00000001571, ENSRNOG00000012628, ENSRNOG00000008409, ENSRNOG00000011016, ENSRNOG00000058422, ENSRNOG00000018790, ENSRNOG00000051235, ENSRNOG00000034075, ENSRNOG00000024159, ENSRNOG00000009331									
GOTERM_MF_DIRECT	GO:0004888 transmembrane signaling receptor activity	9	2.90	3.68E-04	-3.43	ENSRNOG00000003136, ENSRNOG00000024382, ENSRNOG00000022975, ENSRNOG00000021424, ENSRNOG00000036726, ENSRNOG00000004249, ENSRNOG00000004393, ENSRNOG00000018251, ENSRNOG00000049422	239	130	17765	5.15	1.72E-01	1.89E-01	1.88E-01		

EA-3mA vs COPD

Category	Term	Count	%	P Value	Log P value	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
GOTERM_BP_DIRECT	GO:0001525 angiogenesis	19	5.05	5.06E-08	-7.30	ENSRNOG00000007865, ENSRNOG00000003587, ENSRNOG00000007830, ENSRNOG00000028713, ENSRNOG00000007726, ENSRNOG00000056836, ENSRNOG00000003984, ENSRNOG00000012991, ENSRNOG00000013683, ENSRNOG00000060381, ENSRNOG00000046829, ENSRNOG00000021536, ENSRNOG00000017208, ENSRNOG00000055293, ENSRNOG00000050190, ENSRNOG00000021166, ENSRNOG00000021004, ENSRNOG00000008313, ENSRNOG00000008990	311	234	19234	5.02	1.06E-04	1.06E-04	1.06E-04
GOTERM_BP_DIRECT	GO:0071560 cellular response to transforming growth factor beta stimulus	9	2.39	4.11E-04	-3.39	ENSRNOG00000025042, ENSRNOG00000007302, ENSRNOG00000028713, ENSRNOG00000056836, ENSRNOG0000001469, ENSRNOG00000004704, ENSRNOG00000018598, ENSRNOG00000052510, ENSRNOG00000012660	311	110	19234	5.06	5.79E-01	1.44E-01	1.44E-01
GOTERM_BP_DIRECT	GO:0032496 response to lipopolysaccharide	14	3.72	6.76E-04	-3.17	ENSRNOG00000028016, ENSRNOG00000000187, ENSRNOG00000010997, ENSRNOG00000027030, ENSRNOG00000011107, ENSRNOG00000004226, ENSRNOG00000012840, ENSRNOG00000030285, ENSRNOG00000000838, ENSRNOG00000009260, ENSRNOG00000014443, ENSRNOG00000019549, ENSRNOG00000014956, ENSRNOG00000008680	311	281	19234	3.08	7.59E-01	1.78E-01	1.77E-01
GOTERM_BP_DIRECT	GO:0019934 cGMP-mediated signaling	5	1.33	1.14E-03	-2.94	ENSRNOG00000025042, ENSRNOG00000010997, ENSRNOG00000012060, ENSRNOG00000030877, ENSRNOG00000053728	311	29	19234	10.66	9.10E-01	2.41E-01	2.41E-01
GOTERM_BP_DIRECT	GO:0071260 cellular response to mechanical stimulus	8	2.13	7.11E-03	-2.15	ENSRNOG00000038483, ENSRNOG00000032973, ENSRNOG00000033090, ENSRNOG00000056836, ENSRNOG00000050190, ENSRNOG00000018598, ENSRNOG00000013717, ENSRNOG00000038784	311	138	19234	3.59	1.00E+00	6.07E-01	6.05E-01
GOTERM_BP	GO:0007267	6	1.60	6.11E-03	-2.21	ENSRNOG00000053675, ENSRNOG00000060087, ENSRNOG00000008816,	311	72	19234	5.15	1.00E+00	6.07E-01	6.05E-01

GOTERM_CC_DIRECT	GO:0098978 glutamatergic synapse	22	5.85	2.51E-03	-2.60	ENSRNOG00000012344, ENSRNOG00000013781, ENSRNOG00000010161, ENSRNOG00000060054, ENSRNOG00000016412, ENSRNOG00000066033, ENSRNOG00000024712, ENSRNOG00000046683, ENSRNOG00000009177, ENSRNOG00000006611, ENSRNOG00000007865, ENSRNOG00000005700, ENSRNOG00000006877, ENSRNOG00000004810, ENSRNOG00000005519, ENSRNOG000000050767, ENSRNOG00000012840, ENSRNOG00000019365, ENSRNOG00000020839, ENSRNOG00000065255, ENSRNOG00000060054, ENSRNOG00000016412, ENSRNOG00000019018, ENSRNOG00000012060, ENSRNOG00000064362, ENSRNOG00000021984, ENSRNOG00000008970, ENSRNOG00000017606, ENSRNOG00000009862, ENSRNOG00000043085, ENSRNOG00000063400, ENSRNOG00000007302, ENSRNOG00000009949, ENSRNOG00000028627, ENSRNOG00000004810, ENSRNOG00000013324, ENSRNOG00000012058, ENSRNOG00000058337, ENSRNOG00000001827, ENSRNOG00000015675, ENSRNOG00000033090, ENSRNOG00000008970, ENSRNOG00000016826, ENSRNOG00000008135, ENSRNOG00000043085, ENSRNOG00000053675, ENSRNOG00000028335, ENSRNOG00000004346, ENSRNOG00000054964, ENSRNOG00000006565, ENSRNOG00000033348, ENSRNOG00000003998, ENSRNOG00000012840, ENSRNOG00000032350, ENSRNOG00000033064, ENSRNOG00000018557, ENSRNOG00000060054	322	655	19758	2.06	5.40E-01	6.45E-02	6.27E-02
GOTERM_MF_DIRECT	GO:0005509 calcium ion binding	26	6.91	1.95E-04	-3.71	ENSRNOG00000008135, ENSRNOG00000043085, ENSRNOG00000053675, ENSRNOG00000028335, ENSRNOG00000004346, ENSRNOG00000054964, ENSRNOG00000006565, ENSRNOG00000033348, ENSRNOG00000003998, ENSRNOG00000012840, ENSRNOG00000032350, ENSRNOG00000033064, ENSRNOG00000018557, ENSRNOG00000060054	287	705	17765	2.28	1.02E-01	1.07E-01	1.07E-01
GOTERM_MF_DIRECT	GO:0016175 superoxide-generating NADPH oxidase activity	3	0.80	1.07E-02	-1.97	ENSRNOG00000028016, ENSRNOG00000033348, ENSRNOG00000001480	287	10	17765	18.57	9.97E-01	9.48E-01	9.48E-01

Supplementary Table 6 The DEGs validated with published animal studies

Gene ID	Description	1mA vs COPD	log2FC	P value	3mA vs COPD	log2FC	P value	COPD vs Normal	log2FC	P value	Database	PMID
Npas2	neuronal PAS domain protein 2	UP	1.45	1.07E-06	UP	1.82	1.21E-09	DOWN	-2.97	1.85E-21	DOWN	29765063;28575117
Clec5a	C-type lectin domain containing 5A	DOWN	-1.45	1.11E-06	DOWN	-1.20	4.70E-05	UP	1.87	5.60E-10	UP	24663285
Dcstamp	dendrocyte expressed seven transmembrane protein	DOWN	-1.71	1.03E-08	DOWN	-1.35	5.30E-06	UP	1.59	9.41E-08	UP	24663285
Mrc1	mannose receptor, C type 1	DOWN	-1.75	4.51E-09	DOWN	-1.32	7.39E-06	UP	1.55	1.54E-07	UP	28575117
Cry1	cryptochrome circadian regulator 1	NC	-	-	DOWN	-1.15	8.92E-05	NC	-	-	UP	25346222;19926613
Csf2rb	colony stimulating factor 2 receptor subunit beta	DOWN	-1.61	6.35E-08	DOWN	-1.26	2.00E-05	UP	2.13	2.10E-12	UP	36218263
Plet1	placenta expressed transcript 1	DOWN	-1.15	8.39E-05	DOWN	-1.04	3.74E-04	UP	1.92	1.44E-10	UP	28575117
Gpnmb	glycoprotein nmb	DOWN	-1.33	5.74E-06	DOWN	-1.18	5.50E-05	UP	2.33	1.79E-14	UP	28575117;35319981
Akap12	A-kinase anchoring protein 12	UP	1.07	2.73E-04	UP	1.66	2.25E-08	DOWN	-1.68	1.70E-08	DOWN	19698101

Arntl	aryl hydrocarbon receptor nuclear translocator-like	NC	-	-	UP	1.34	6.42E-06	DOWN	-2.57	5.75E-17	DOWN	29765063;28575117;24025728;19926613
Adm	adrenomedullin	NC	-	-	UP	1.27	2.12E-05	DOWN	-1.39	3.28E-06	DOWN	28575117
Slc39a2	solute carrier family 39 member 2	DOWN	-1.38	2.74E-06	DOWN	-1.13	1.22E-04	NC	-	-	UP	28575117
Serpina10	serpin family A member 10	NC	-	-	DOWN	-1.19	7.85E-05	UP	1.05	4.34E-04	UP	28575117
Per2	period circadian regulator 2	NC	-	-	DOWN	-1.48	5.46E-07	UP	2.81	1.14E-19	UP	28575117;25346222;19926613
Eln	elastin	NC	-	-	UP	2.16	8.64E-13	DOWN	-2.81	1.21E-19	DOWN	28575117
Foxa3	forkhead box A3	DOWN	-1.68	5.95E-08	NC	-	-	UP	1.72	1.33E-08	UP	28575117
Fcamr	Fc fragment of IgA and IgM receptor	DOWN	-1.15	1.47E-04	NC	-	-	NC	-	-	UP	28575117
Msr1	macrophage scavenger receptor 1	DOWN	-1.18	6.13E-05	NC	-	-	UP	2.10	3.60E-12	UP	35319981
Lcn2	lipocalin 2	DOWN	-1.09	1.98E-04	NC	-	-	UP	3.17	6.30E-24	UP	24663285
Vsig1	V-set and immunoglobulin domain containing 1	DOWN	-1.33	1.38E-05	NC	-	-	UP	1.30	1.49E-05	UP	28575117
Aldoc	aldolase, fructose-bisphosphate C	DOWN	-1.11	1.73E-04	NC	-	-	UP	1.51	4.07E-07	UP	28575117
Nt5e	5' nucleotidase, ecto	DOWN	-1.22	3.27E-05	NC	-	-	UP	1.41	1.99E-06	UP	28575117
Alas2	aminolevulinic acid synthase 2, erythroid	DOWN	-1.34	7.83E-06	NC	-	-	NC	-	-	DOWN	28575117
Tubb1	tubulin, beta 1 class VI	UP	1.00	1.59E-03	NC	-	-	NC	-	-	DOWN	28575117
Spon2	spondin 2	UP	1.25	2.43E-05	NC	-	-	DOWN	-3.13	2.36E-23	DOWN	29765063

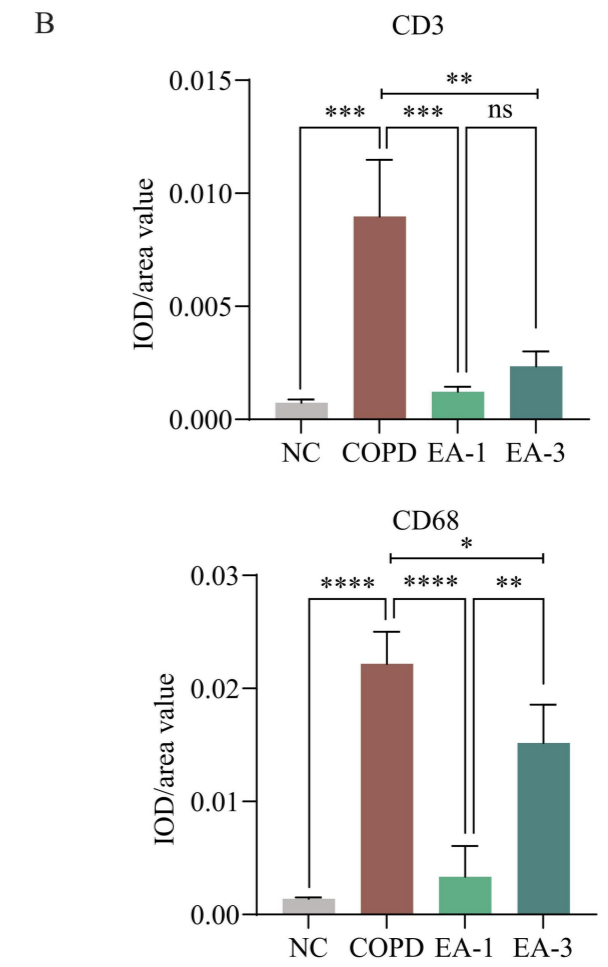
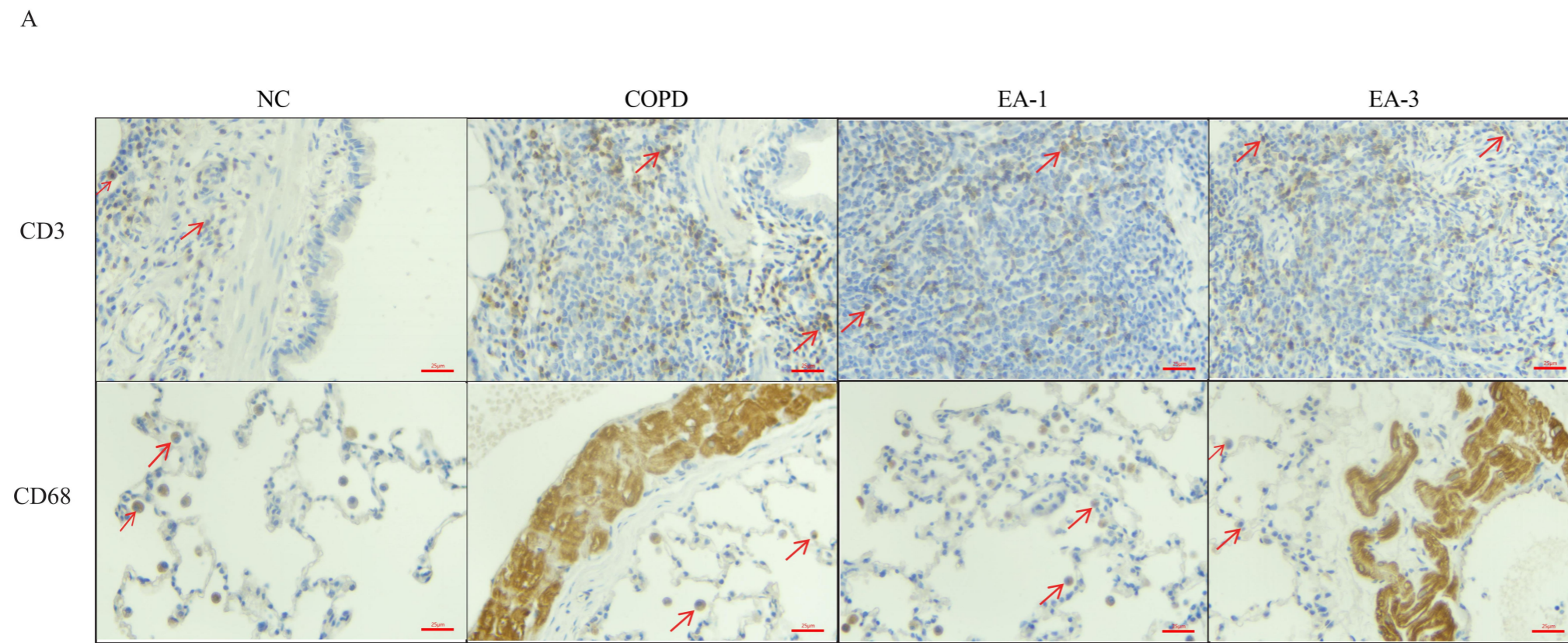
Supplementary Table 7 The DEGs validated with published clinical studies

Gene ID	Description	1mA vs COPD	log2FC	P value	3mA vs COPD	log2FC	P value	COPD vs Normal	log2FC	P value	Database	PMID
Ednrb	endothelin receptor type B	NC	-	-	UP	1.21	3.98E-05	DOWN	-1.40	2.29E-06	DOWN	28287180;32470642
Cox4i2	cytochrome c oxidase subunit 4i2	NC	-	-	UP	1.53	2.79E-07	DOWN	-1.10	1.99E-04	DOWN	25834810;32470642

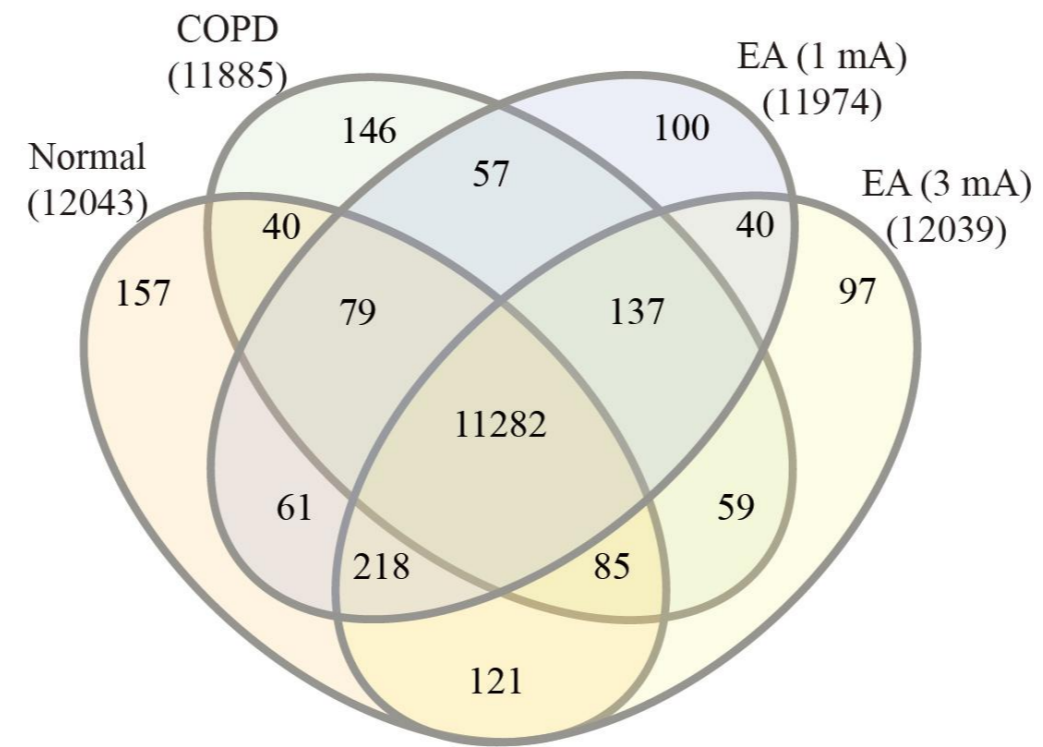
Slco4a1	solute carrier organic anion transporter family, member 4a1	DOWN	-1.96	1.58E-10	DOWN	-1.51	5.66E-07	UP	1.61	9.77E-08	UP	25834810
Ldb2	LIM domain binding 2	NC	-	-	UP	1.17	7.26E-05	DOWN	-1.28	1.34E-05	DOWN	32470642
Slc7a2	solute carrier family 7 member 2	DOWN	-2.11	2.61E-12	DOWN	-1.60	6.81E-08	NC	-	-	UP	32470642
Cdh5	cadherin 5	NC	-	-	UP	1.41	1.67E-06	DOWN	-1.60	6.86E-08	DOWN	32470642
Fst	follicle-stimulating hormone receptor 1	UP	1.24	3.21E-05	UP	1.65	3.59E-08	NC	-	-	DOWN	32470642
Ncf1	neutrophil cytosolic factor 1	NC	-	-	DOWN	-1.31	8.35E-06	UP	1.92	1.30E-10	UP	36217144
Phactr2	phosphatase and actin regulator 2	UP	1.07	2.68E-04	UP	1.06	3.08E-04	DOWN	-1.30	9.70E-06	DOWN	32470642
Edil3	EGF like repeats and discoidin domains 3	DOWN	-1.13	1.13E-04	DOWN	-1.16	7.82E-05	UP	1.52	3.37E-07	UP	25834810
Pde5a	phosphodiesterase 5A	NC	-	-	UP	1.35	4.60E-06	DOWN	-1.01	5.78E-04	DOWN	32470642
Arpp19	cAMP-regulated phosphoprotein 19	NC	-	-	UP	1.05	9.39E-04	NC	-	-	DOWN	28287180
Erg	ETS transcription factor ERG	UP	1.11	1.59E-04	UP	1.16	8.10E-05	DOWN	-1.60	6.90E-08	DOWN	32470642
Slc11a1	solute carrier family 11 member 1	DOWN	-1.25	2.20E-05	DOWN	-1.04	3.69E-04	UP	1.96	6.02E-11	UP	36217144
Aqp9	aquaporin 9	DOWN	-1.14	1.71E-04	DOWN	-1.28	2.93E-05	UP	1.67	9.71E-08	UP	25834810
Efnb2	ephrin B2	NC	-	-	UP	1.50	3.86E-07	DOWN	-1.69	1.30E-08	DOWN	32470642
Cd68	Cd68 molecule	DOWN	-1.44	1.12E-06	DOWN	-1.23	3.01E-05	UP	2.09	4.29E-12	UP	36217144
Cpa3	carboxypeptidase A3	NC	-	-	DOWN	-1.45	1.70E-06	NC	-	-	UP	35983043
Insc	INSC, spindle orientation adaptor protein	NC	-	-	UP	1.21	6.06E-05	NC	-	-	DOWN	32470642
Mrc1	mannose receptor, C type 1	DOWN	-1.75	4.51E-09	DOWN	-1.32	7.39E-06	UP	1.55	1.54E-07	UP	25834810
Ptprb	protein tyrosine phosphatase, receptor type, B	NC	-	-	UP	1.05	3.50E-04	NC	-	-	DOWN	32470642
Card14	caspase recruitment domain family, member 14	DOWN	-1.63	4.39E-08	DOWN	-1.07	2.56E-04	UP	2.16	9.51E-13	UP	32470642
Trem1	triggering receptor expressed on myeloid cells 1	DOWN	-1.65	2.90E-08	DOWN	-1.45	1.10E-06	UP	1.98	5.93E-11	UP	25834810
Samsn1	SAM domain, SH3 domain and nuclear localization signals, 1	NC	-	-	DOWN	-1.07	2.64E-04	NC	-	-	UP	36217144
Rrad	Ras related glycolysis inhibitor and calcium channel regulator	UP	1.08	2.93E-04	UP	1.43	1.93E-06	DOWN	-1.48	7.70E-07	DOWN	25542208
Gpnmb	glycoprotein nmb	DOWN	-1.33	5.74E-06	DOWN	-1.18	5.50E-05	UP	2.33	1.79E-14	UP	36217144
Cav1	caveolin 1	NC	-	-	UP	1.08	2.36E-04	DOWN	-1.39	2.47E-06	DOWN	25834810;32470642
Sema6a	semaphorin 6A	NC	-	-	UP	1.09	2.14E-04	DOWN	-1.34	5.59E-06	DOWN	32470642
Ms4a1	membrane spanning 4-domains A1	NC	-	-	DOWN	-1.14	1.12E-04	NC	-	-	UP	28287180;25542208

Ak4	adenylate kinase 4	NC	-	-	DOWN	-1.02	5.61E-04	UP	1.38	3.76E-06	UP	32470642
Itih4	inter-alpha-trypsin inhibitor heavy chain 4	DOWN	-1.56	2.34E-07	DOWN	-1.26	2.05E-05	UP	1.38	3.55E-06	UP	25542208
Fcrla	Fc receptor-like A	DOWN	-1.48	5.71E-07	DOWN	-1.36	4.15E-06	NC	-	-	UP	25542208
Pcdh17	protocadherin 17	NC	-	-	UP	1.18	6.31E-05	NC	-	-	DOWN	32470642
Trpv3	transient receptor potential cation channel, subfamily V, member 3	DOWN	-2.07	4.37E-11	DOWN	-1.04	5.27E-04	NC	-	-	UP	32470642
Armcx6	armadillo repeat containing, X-linked 6	NC	-	-	UP	1.45	1.77E-06	DOWN	-1.40	3.73E-06	DOWN	25834810
Rasip1	Ras interacting protein 1	NC	-	-	UP	1.05	3.14E-04	DOWN	-1.12	1.38E-04	DOWN	32470642
Tnfrsf13c	TNF receptor superfamily member 13C	DOWN	-1.02	8.29E-04	DOWN	-1.44	2.64E-06	NC	-	-	UP	32470642
Kdr	kinase insert domain receptor	NC	-	-	UP	1.34	5.62E-06	DOWN	-1.72	7.35E-09	DOWN	32470642
Myo10	myosin X	NC	-	-	UP	1.06	3.07E-04	DOWN	-1.19	4.74E-05	DOWN	32470642
Chst2	carbohydrate sulfotransferase 2	NC	-	-	UP	1.12	1.41E-04	DOWN	-1.25	2.20E-05	DOWN	32470642
Amotl1	angiomin-like 1	NC	-	-	UP	1.07	2.62E-04	DOWN	-1.01	6.00E-04	DOWN	32470642
Tmem26	transmembrane protein 26	NC	-	-	UP	1.08	2.33E-04	NC	-	-	DOWN	32470642
Ncf2	neutrophil cytosolic factor 2	DOWN	-1.37	3.28E-06	DOWN	-1.10	1.87E-04	UP	1.50	4.50E-07	UP	36217144
Myo7a	myosin VIIA	DOWN	-1.56	1.67E-07	DOWN	-1.07	3.03E-04	UP	2.12	4.39E-12	UP	25542208;32470642
Cd300e	Cd300e molecule	DOWN	-1.70	1.74E-08	DOWN	-1.70	1.73E-08	UP	1.83	2.27E-09	UP	25834810
Pdzd2	PDZ domain containing 2	NC	-	-	UP	1.09	1.94E-04	NC	-	-	DOWN	32470642
Fcrlg	Fc fragment of IgE receptor Ig	DOWN	-1.03	4.55E-04	NC	-	-	UP	1.32	7.80E-06	UP	35071459;32470642;21940491
Sostdc1	sclerostin domain containing 1	UP	1.72	3.08E-08	NC	-	-	DOWN	-1.41	5.11E-06	DOWN	21940491
Egl3	egl-9 family hypoxia-inducible factor 3	DOWN	-1.37	4.23E-06	NC	-	-	UP	1.30	1.11E-05	UP	32470642
Parvg	parvin, gamma	DOWN	-1.14	1.02E-04	NC	-	-	UP	1.50	3.74E-07	UP	25542208
Msr1	macrophage scavenger receptor 1	DOWN	-1.18	6.13E-05	NC	-	-	UP	2.10	3.60E-12	UP	36217144
Alox5	arachidonate 5-lipoxygenase	DOWN	-1.52	2.89E-07	NC	-	-	NC	-	-	UP	36217144

Igf1	insulin-like growth factor 1	DOWN	-1.25	2.03E-05	NC	-	-	UP	1.49	4.45E-07	UP	25834810
Alox15	arachidonate 15-lipoxygenase	DOWN	-1.79	3.35E-09	NC	-	-	NC	-	-	UP	32470642
Hey2	hes-related family bHLH transcription factor with YRPW motif 2	UP	1.27	2.10E-05	NC	-	-	DOWN	-1.94	1.72E-10	DOWN	32470642
Cfb	complement C2	DOWN	-1.10	1.71E-04	NC	-	-	UP	1.17	6.92E-05	UP	32470642
Lif	LIF, interleukin 6 family cytokine	DOWN	-1.17	8.43E-05	NC	-	-	UP	1.33	8.14E-06	UP	25834810;32470642
Slc12a8	solute carrier family 12, member 8	DOWN	-1.10	2.66E-04	NC	-	-	NC	-	-	UP	32470642
Cybb	cytochrome b-245, beta polypeptide	DOWN	-1.43	1.28E-06	NC	-	-	UP	1.68	1.58E-08	UP	23117565;25265030;36217144
Chrm2	cholinergic receptor, muscarinic 2	UP	1.10	2.91E-04	NC	-	-	NC	-	-	DOWN	32470642
Cgrefl	cell growth regulator with EF hand domain 1	DOWN	-1.42	4.22E-06	NC	-	-	UP	1.81	7.49E-09	UP	32470642
Gria1	glutamate ionotropic receptor AMPA type subunit 1	UP	1.77	4.39E-08	NC	-	-	DOWN	-2.01	4.71E-10	DOWN	32470642
Cdc42bpg	CDC42 binding protein kinase gamma	UP	1.35	4.41E-06	NC	-	-	NC	-	-	DOWN	32470642
Snrpn	SNRPN upstream reading frame	UP	1.17	7.43E-05	NC	-	-	NC	-	-	DOWN	25834810
C3	complement C3	DOWN	-1.01	5.63E-04	NC	-	-	UP	2.06	7.30E-12	UP	25834810



Supplementary Figure 1 Expression of CD3 (marker of T lymphocytes) and CD68 (marker of macrophages) in lung tissues of each group. (A) Representative images of IHC stained lung sections from each group (n=3 per group). The cell nucleus appears blue after staining with hematoxylin, while the positive expression revealed by DAB staining appears tan. The red arrows indicate the cells positive for CD3 and CD68. Scale bar: 25µm. (B) IOD/area values in NC, COPD, EA-1, and EA-3 group. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, ns, not significant.



Supplementary Figure 2 Genes distributed in the NC, COPD, EA-1mA and EA-3mA groups