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Supplemental information

A myeloid program associated with COVID-19 severity is decreased by therapeutic blockade of IL-6 signaling

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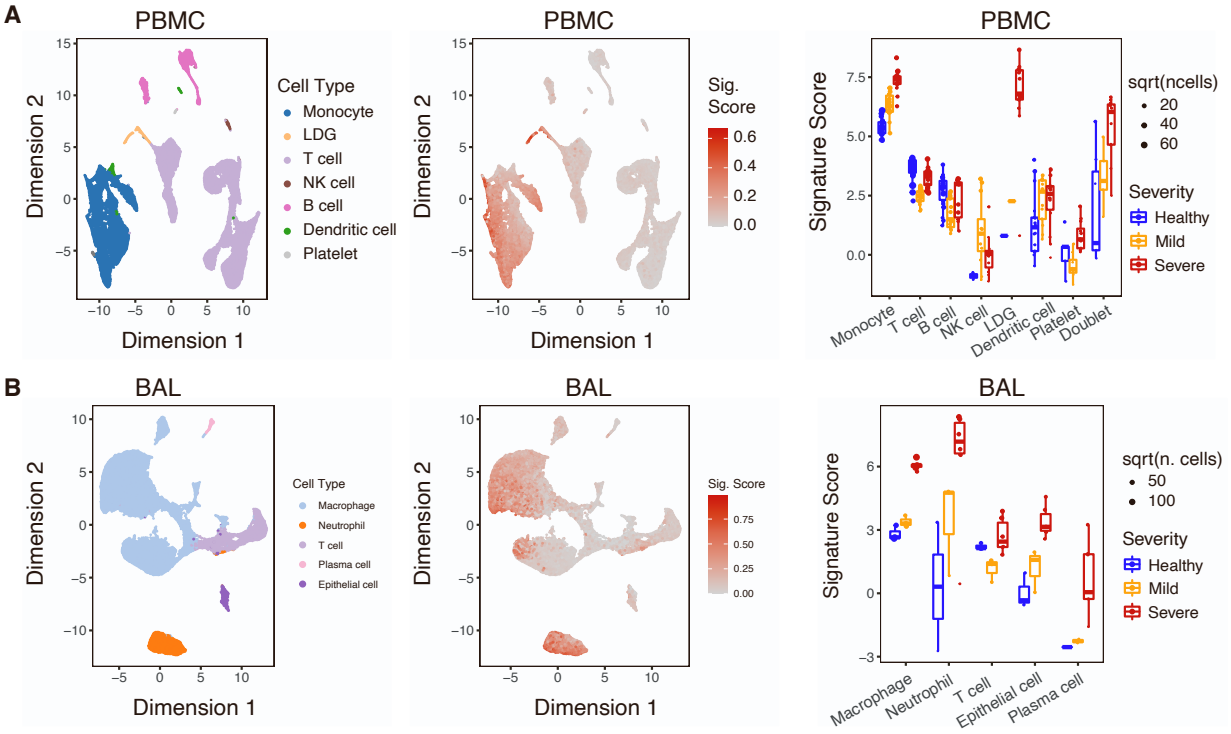
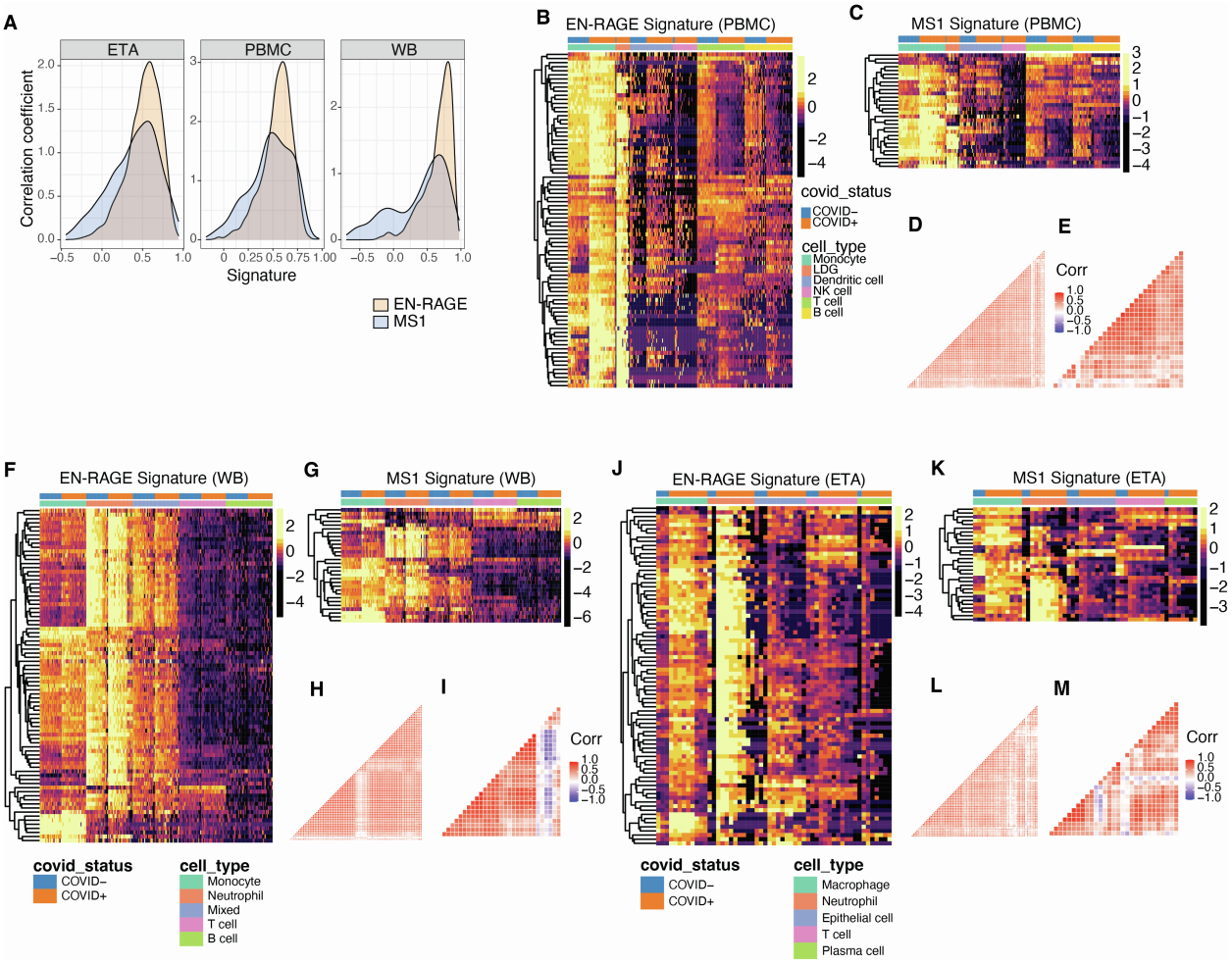
Supplemental Data

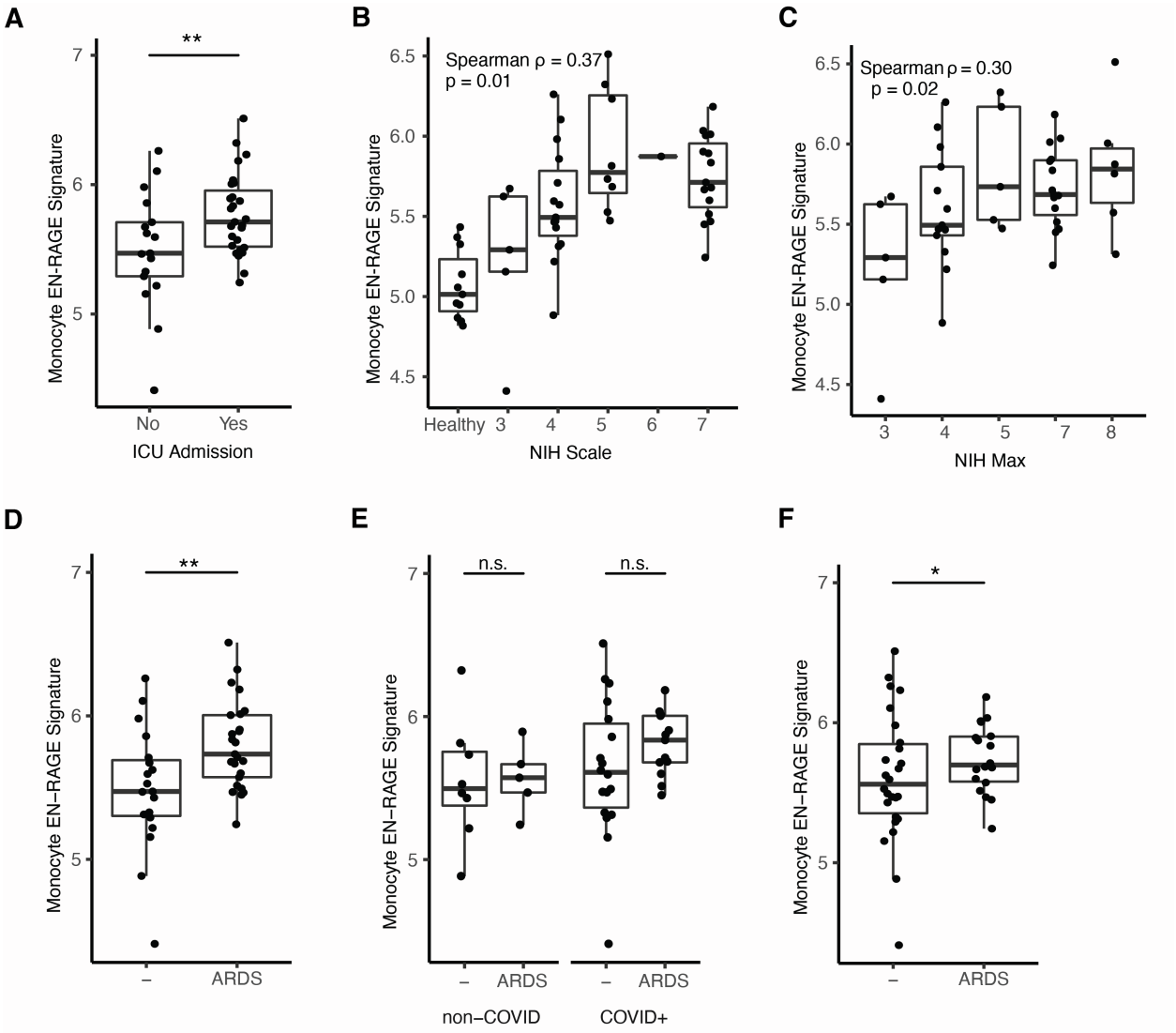
Supplementary Figure 1. Further characterization of the EN-RAGE signature within PBMC and BAL, related to Figure 1. A.) Expression of EN-RAGE signature in PBMC[11] single cell RNA-seq data. Left panel: UMAP projection of cells colored by cell types. Each point represents a single cell, and points are colored by annotated cell types. Middle panel: UMAP projection of cells colored by EN-RAGE signature score. Each point represents a single cell, colored by the signature score value. Right panel: pseudo-bulk expression profiles including non-myeloid cell types. Each point represents the pseudo-bulk signature score for a cell type in a patient sample. Blue=healthy (BAL n = 3; PBMC, n = 3), orange=moderate (BAL, n = 3; PBMC, n = 8; hospitalized +/- supplemental O_2), red=critical (BAL, n = 6; PBMC, n = 10; requiring mechanical ventilation), with severity defined within each published dataset by the original authors. B.) EN-RAGE signature expression in BAL[7] single cell RNA-seq data. Left panel: UMAP project of cells colored by cell type. Middle panel: cells colored by expression of the EN-RAGE signature. Right panel: pseudo-bulk expression of EN-RAGE including non-myeloid cells; colored as in A above. (C-F**)**. Heatmaps of ENRAGE (C-D) and MS1 (E-F) signature genes in pseudo-bulk expression profiles in BAL and PBMC. Each row is a gene, each column is a cell cluster. Each row is z-score normalized within each dataset. LDG=low density granulocytes.


A
PBMC
Dimension 2
Dimension 1
Cell Type
Monocyte
LDG
T cell
NK cell
B cell
Dendritic cell
Platelet
PBMC
Sig. Score
PBMC
Signature Score
sqrt(ncells)
Severity
Healthy
Mild
Severe
Monocyte
T cell
B cell
NK cell
LDG
Dendritic cell
Platelet
Doublet
B
BAL
Macrophage
Neutrophil
T cell
Plasma cell
Epithelial cell
BAL
BAL
sqrt(n. cells)
Macrophage
Neutrophil
T cell
Epithelial cell
Plasma cell
C
PBMC
COVID status
COVID−
COVID+
Cell Type
Monocyte
LDG
Dendritic cell
NK cell
T cell
B cell
D
BAL
Macrophage
Neutrophil
Epithelial cell
T cell
Plasma cell
E
PBMC
F
BAL

Supplementary Figure 2. Expression of EN-RAGE signature, compared to the MS1 signature across multiple sample types from the COMET cohort, related to Figure 2. A.) Pairwise Spearman correlation coefficients between genes within the EN-RAGE and MS1 gene signatures across three different compartments: ETA (n = 55), PBMC (n = 279), and whole blood (n = 245). B-E.) Heatmaps of gene expression (B-C) and pairwise gene correlations (D-E) of EN-RAGE and MS1 within the PBMC compartment. (11). F-I.) Heatmaps of gene expression (F-G) and pairwise gene correlations (H-I) of the whole blood compartment (11). J-M.) Heatmaps of gene expression (J-K) and pairwise gene correlations (L-M) of EN-RAGE and MS1 within the ETA compartment (7). Gene expression values were pseudobulked for each cell population (sample + cell type) and the pairwise Spearman correlation coefficients were calculated using the pseudobulked gene expression values. LDG=low-density granulocytes.



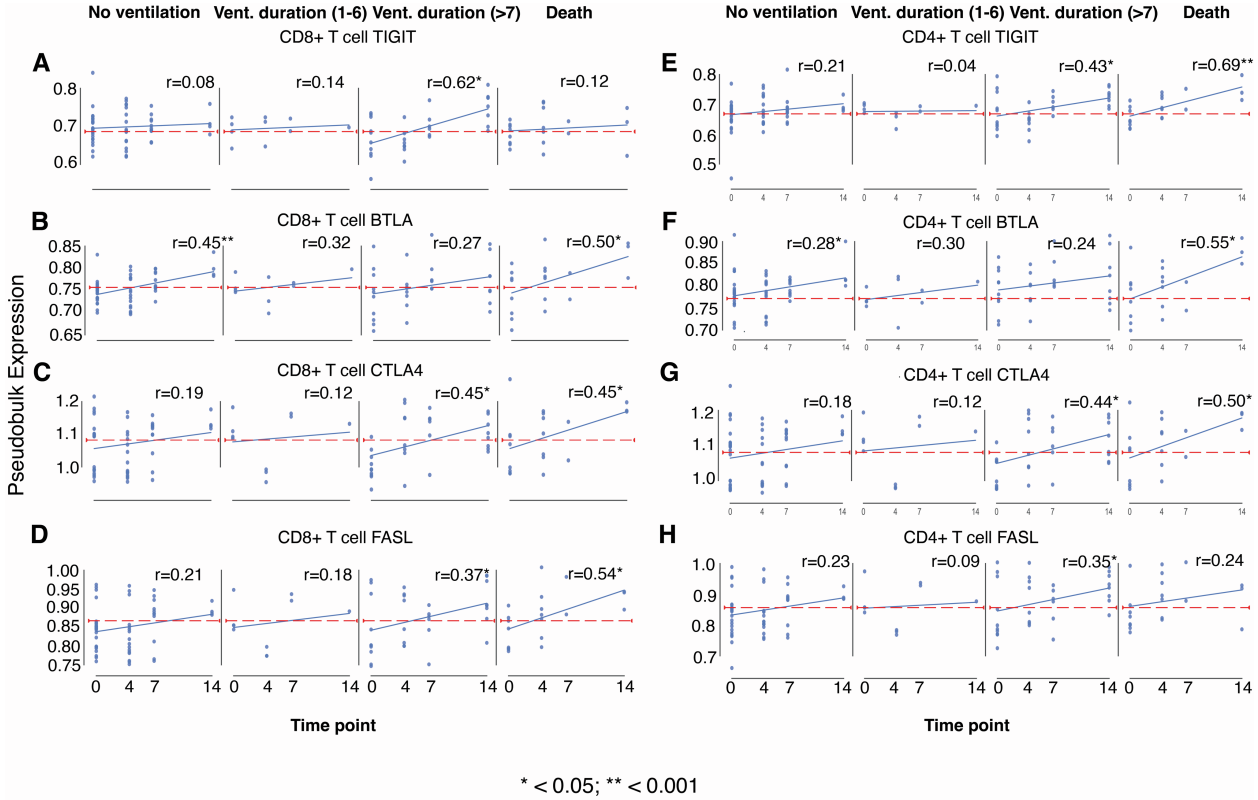
Supplementary Figure 3. EN-RAGE gene set expression in PBMCs is associated with increased clinical severity and poor outcomes in the COMET cohort, related to Figure 3. A.) Comparison of EN-RAGE signature in monocytes from patients admitted to ICU compared to those not. B-C.) Correlation between baseline pseudobulk EN-RAGE gene set expression in myeloid cells and (B) baseline NIH scale, and (C) maximal NIH scale (worst score recorded during hospitalization, excluding healthy controls). Each dot represents one patient, n=49. D-F.) Myeloid EN-RAGE gene set expression by ARDS diagnosis. D.) ARDS diagnosed using AECC criteria. E.) ARDS diagnosed using Berlin criteria. F.) Berlin ARDS subset by COVID-19 status. Boxes represent first and third quartiles, the centerline shows the median. Two-tailed t-test p-values are shown: n.s.= not significant, *$p<0.05$, **$p<0.01$. G.) Spearman correlation coefficients comparing unadjusted or baseline severity-adjusted EN-RAGE signature expression with clinical severity, outcomes, or plasma protein measures. To adjust for baseline severity, a linear model was fit between EN-RAGE expression and baseline NIH scale. Residuals from this model were then compared to each of the severity or protein measures. Correlation with NIH scale is meaningless in this context, so has been omitted.



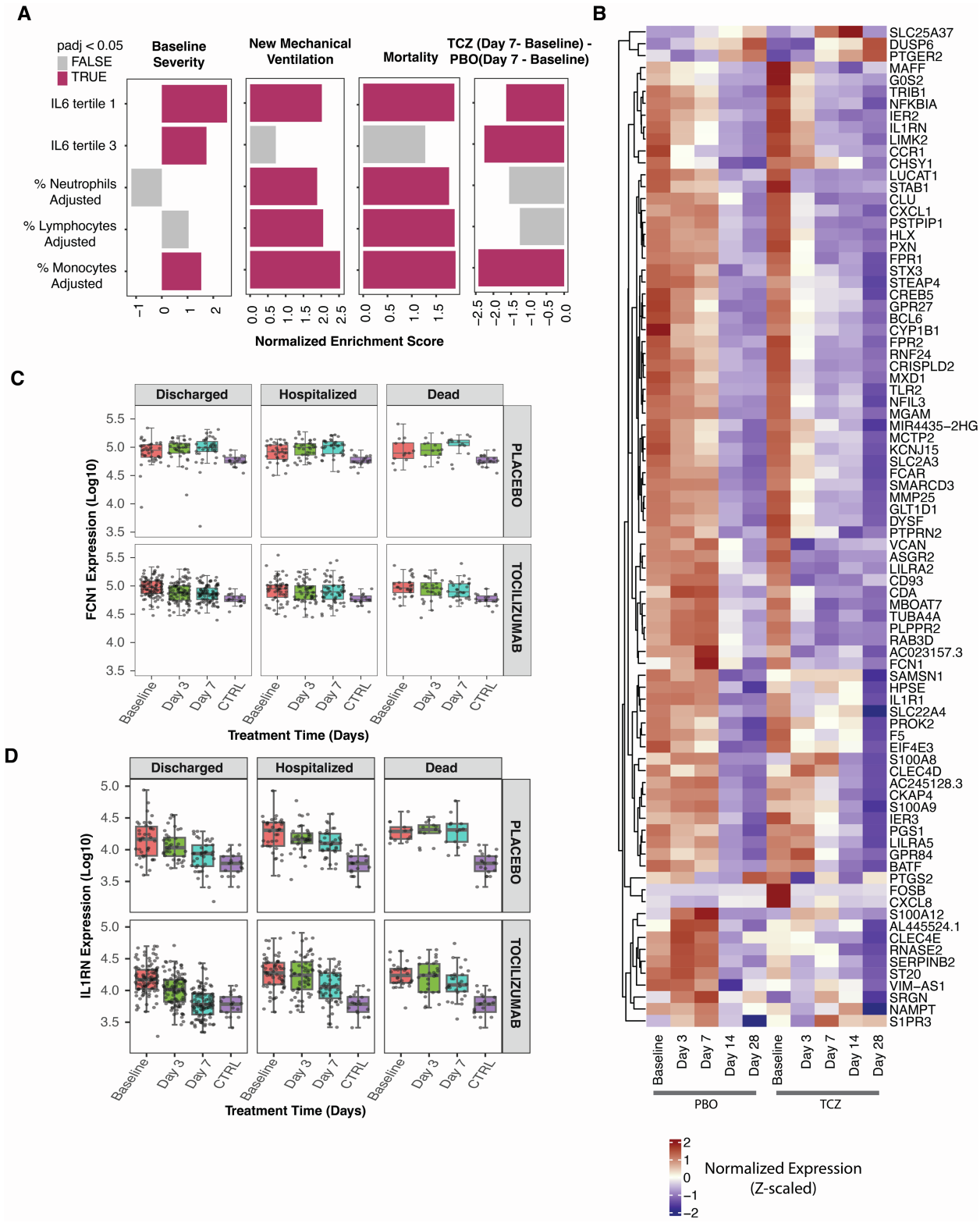
G

PBMC		Clinical severity		Clinical outcome		Plasma protein	
		NIH	SOFA	NIH MAX	VFDS	IL-6	IL-10
Unadjusted	r	0.37	0.22	0.30	-0.25	0.41	0.29
	p	0.010	0.15	0.02	0.10	0.005	0.05
Severity-adjusted	r	NA	0.03	0.20	-0.08	0.3	0.28
	p	NA	0.85	0.20	0.60	0.051	0.07

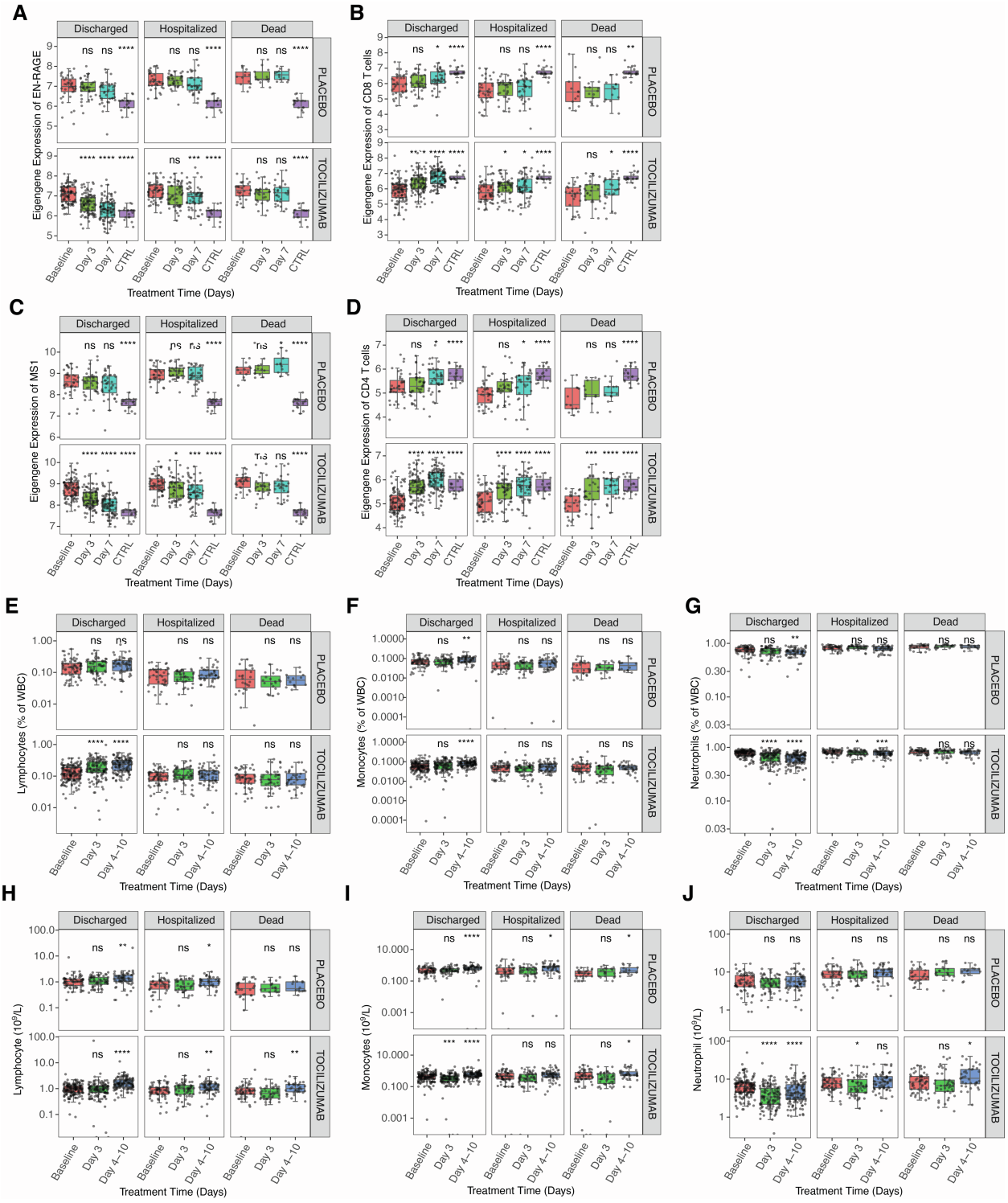
Supplemental Figure 4. Comparison of EN-RAGE signature expression with T cell immunosuppression phenotypes in the COMET PBMC cohort, related to Figure 4. A-H.) Pseudobulked surface protein expression in 128 PBMC samples from 60 patients over 14 days, grouped by clinical outcomes. A-D.) Expression in pseudobulked $CD8^+$ T cells. E-H.) Expression in pseudobulked $CD4^+$ T cells. Blue line denotes the linear regression trend for gene expression over time. Red line denotes the average expression level in 11 healthy controls. Vent. duration = days of mechanical ventilation in survivors. Pearson correlation coefficients (r) are indicated, stars represent significant correlations: * = $p < 0.05$, ** = $p < 0.01$.



Supplemental Figure 5. Myeloid and T cell gene sets are associated with poor outcome in COVID-19 patients and decreased following tocilizumab treatment, related to Figure 6. A.) GSEA enrichments are consistent with those in Figure 6B-E for the ENRAGE gene set following adjustment for blood % monocytes, % neutrophils, or % lymphocytes. The effect of tocilizumab treatment is not affected by baseline tertile of serum IL-6 protein levels, with 1= lowest tertile and 3=highest tertile. GSEA are shown in red when FDR<0.05. NES=normalized enrichment score. B.) Heatmap showing normalized expression of EN-RAGE gene set at baseline, day 3, 7, 14 and 28 for placebo (First 5 columns) and Tocilizumab treatment arms (Last 5 columns). C-D.) Box plots showing normalized expression of FCN1 (C) and IL1RN (D) for healthy controls and patients in placebo or Tocilizumab study arm at baseline, Day 3 and 7 faceted by their clinical status by day 28.


A
padj < 0.05
FALSE
TRUE
Baseline Severity
New Mechanical Ventilation
Mortality
TCZ (Day 7- Baseline) - PBO(Day 7 - Baseline)
IL6 tertile 1
IL6 tertile 3
% Neutrophils Adjusted
% Lymphocytes Adjusted
% Monocytes Adjusted
Normalized Enrichment Score
B
SLC25A37
DUSP6
PTGER2
MAFF
G0S2
TRIB1
NFKBIA
IER2
IL1RN
LIMK2
CCR1
CHSY1
LUCAT1
STAB1
CLU
CXCL1
PSTPIP1
HLX
PXN
FPR1
STX3
STEAP4
CREB5
GPR27
BCL6
CYP1B1
FPR2
RNF24
CRISPLD2
MXD1
TLR2
NFIL3
MGAM
MIR4435–2HG
MCTP2
KCNJ15
SLC2A3
FCAR
SMARCD3
MMP25
GLT1D1
DYSF
PTPRN2
VCAN
ASGR2
LILRA2
CD93
CDA
MBOAT7
TUBA4A
PLPPR2
RAB3D
AC023157.3
FCN1
SAMSN1
HPSE
IL1R1
SLC22A4
PROK2
F5
EIF4E3
S100A8
CLEC4D
AC245128.3
CKAP4
S100A9
IER3
PGS1
LILRA5
GPR84
BATF
PTGS2
FOSB
CXCL8
S100A12
AL445524.1
CLEC4E
RNASE2
SERPINB2
ST20
VIM–AS1
SRGN
NAMPT
S1PR3
Baseline
Day 3
Day 7
Day 14
Day 28
PBO
TCZ
Normalized Expression (Z-scaled)
C
Discharged
Hospitalized
Dead
PLACEBO
TOCILIZUMAB
FCN1 Expression (Log10)
Treatment Time (Days)
D
IL1RN Expression (Log10)
Treatment Time (Days)

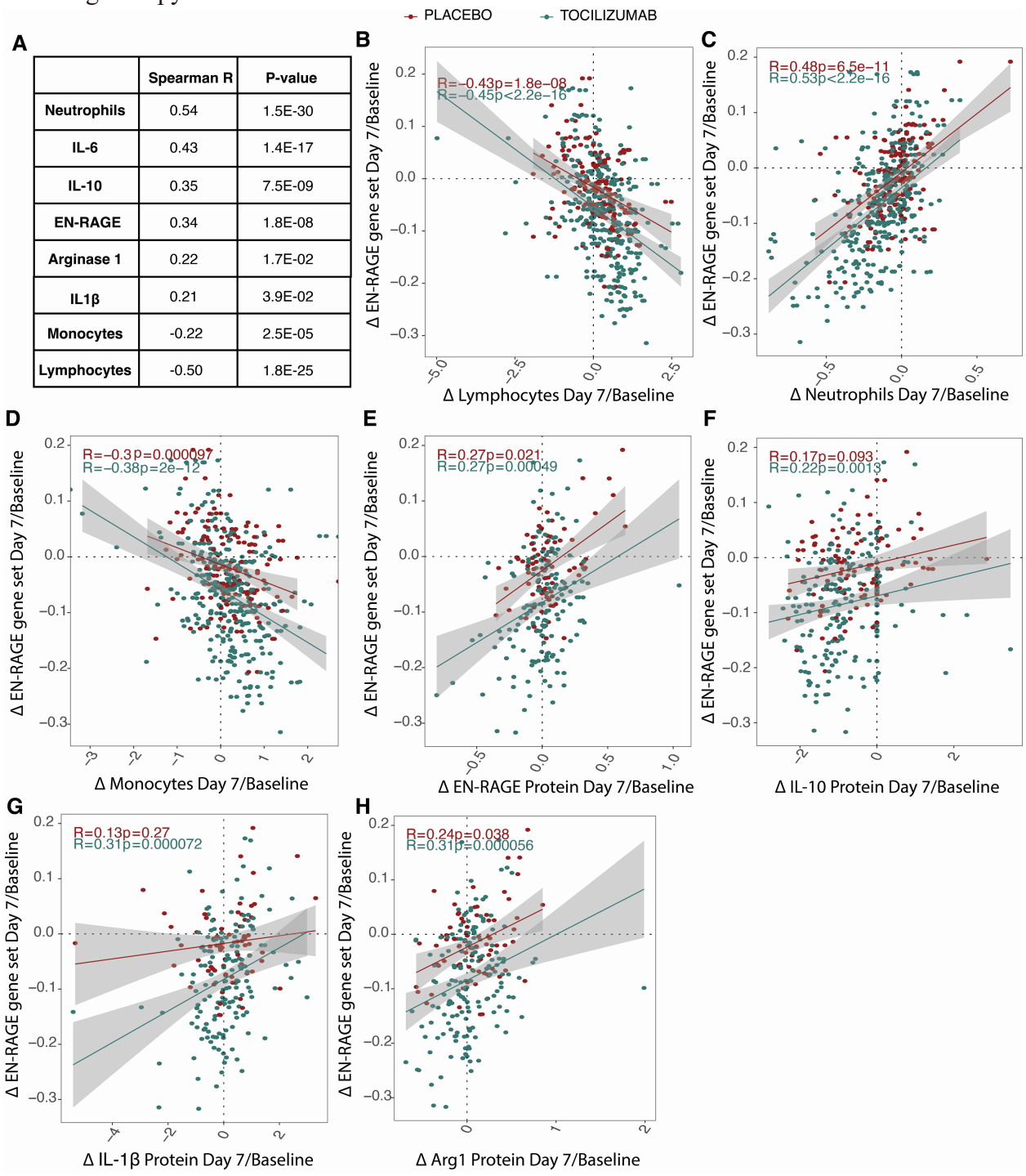
Supplemental Figure 6. Tocilizumab modulates expression of blood myeloid and T cell signature genes and cell composition more than placebo over 7 days of treatment, related to Figure 6 and Figure 7. A-D.) Signature scores are shown within each day, split by treatment arm and disease course and compared with healthy controls (CTRL). Patients are split into those that were discharged before D28, those who remained hospitalized, or subjects who died by day 28. Average signature scores are shown across the first 7 days of treatment for patients with measurements at all 3 time points. Tocilizumab treatment decreased expression of (A) EN-RAGE signature and increased expression of (B) CD8 T cell signature in survivors. Tocilizumab treatment decreased expression of (C) MS1 signature and increased expression of (D) $CD4^+$ T cell signature in survivors. E-J.) Tocilizumab normalizes blood cell composition more rapidly than placebo. Blood cell percentage (E-G) and absolute cell counts (H-J) are shown at baseline (pre-treatment) and D3 and D4-D10 (post-treatment); FDR calculated relative to baseline * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$, **** = $p < 0.0001$, ns = non-significant. Significance testing was performed using either t-test (A-D) or Wilcoxon rank-sum test (E-J). SOC = standard of care drug therapy. For box plots, each point represents a patient sample, center lines depict the median value, the bottom and top of the boxes show the first and third quartile, and whiskers show the most extreme point <1.5x the interquartile range (IQR) from the bottom or top of the box.


A
Discharged
Hospitalized
Dead
PLACEBO
TOCILIZUMAB
Eigengene Expression of EN-RAGE
Baseline
Day 3
Day 7
CTRL
Treatment Time (Days)
B
Eigengene Expression of CD8 T cells
C
Eigengene Expression of MS1
D
Eigengene Expression of CD4 T cells
E
Lymphocytes (% of WBC)
Day 4–10
F
Monocytes (% of WBC)
G
Neutrophils (% of WBC)
H
Lymphocyte (10⁹/L)
I
Monocytes (10⁹/L)
J
Neutrophil (10⁹/L)

Supplemental Figure 7. Effect of tocilizumab on blood cell counts and serum protein levels relative to ENRAGE gene set expression Day 7 vs baseline, related to Figure 7. A.) Correlation of blood ENRAGE gene set expression with serum proteins and blood cell counts at baseline prior to treatment. IL-10 was measured by Protein Simple and IL-1β, ENRAGE, and Arg1 were measured by Olink. B-H.) Spearman correlations between change in blood ENRAGE gene set expression and change in blood cell counts (B-D) and serum proteins (E-H) between baseline and D7. Each dot represents a patient with available samples at baseline and D7, SOC = standard of care drug therapy.

A

	Spearman R	P-value
Neutrophils	0.54	1.5E-30
IL-6	0.43	1.4E-17
IL-10	0.35	7.5E-09
EN-RAGE	0.34	1.8E-08
Arginase 1	0.22	1.7E-02
IL1β	0.21	3.9E-02
Monocytes	-0.22	2.5E-05
Lymphocytes	-0.50	1.8E-25



Supplemental Table 1. Definition of the EN-RAGE gene set, related to Figure 1.

ID	Gene symbol	ID	Gene symbol	ID	Gene symbol	ID	Gene symbol
ENSG00000276900	AC023157.3	ENSG00000163412	EIF4E3	ENSG00000248323	LUCAT1	ENSG00000101236	RNF24
ENSG00000268734	AC245128.3	ENSG00000198734	F5	ENSG00000185022	MAFF	ENSG00000163221	S100A12
ENSG00000233461	AL445524.1	ENSG00000186431	FCAR	ENSG00000125505	MBOAT7	ENSG00000143546	S100A8
ENSG00000161944	ASGR2	ENSG00000085265	FCN1	ENSG00000140563	MCTP2	ENSG00000163220	S100A9
ENSG00000156127	BATF	ENSG00000125740	FOSB	ENSG00000257335	MGAM	ENSG00000213694	S1PR3
ENSG00000113916	BCL6	ENSG00000171051	FPR1	ENSG00000172965	MIR4435-2HG	ENSG00000155307	SAMSN1
ENSG00000163823	CCR1	ENSG00000171049	FPR2	ENSG00000008516	MMP25	ENSG00000197632	SERPINB2
ENSG00000125810	CD93	ENSG00000123689	G0S2	ENSG00000059728	MXD1	ENSG00000197208	SLC22A4
ENSG00000158825	CDA	ENSG00000151948	GLT1D1	ENSG00000105835	NAMPT	ENSG00000147454	SLC25A37
ENSG00000131873	CHSY1	ENSG00000170837	GPR27	ENSG00000165030	NFIL3	ENSG00000059804	SLC2A3
ENSG00000136026	CKAP4	ENSG00000139572	GPR84	ENSG00000100906	NFKBIA	ENSG00000082014	SMARCD3
ENSG00000166527	CLEC4D	ENSG00000136630	HLX	ENSG00000087157	PGS1	ENSG00000122862	SRGN
ENSG00000166523	CLEC4E	ENSG00000173083	HPSE	ENSG00000105520	PLPPR2	ENSG00000180953	ST20
ENSG00000120885	CLU	ENSG00000160888	IER2	ENSG00000163421	PROK2	ENSG00000010327	STAB1
ENSG00000146592	CREB5	ENSG00000137331	IER3	ENSG00000140368	PSTPIP1	ENSG00000127954	STEAP4
ENSG00000103196	CRISPLD2	ENSG00000115594	IL1R1	ENSG00000125384	PTGER2	ENSG00000166900	STX3
ENSG00000163739	CXCL1	ENSG00000136689	IL1RN	ENSG00000073756	PTGS2	ENSG00000137462	TLR2
ENSG00000169429	CXCL8	ENSG00000157551	KCNJ15	ENSG00000155093	PTPRN2	ENSG00000173334	TRIB1
ENSG00000138061	CYP1B1	ENSG00000239998	LILRA2	ENSG00000089159	PXN	ENSG00000127824	TUBA4A
ENSG00000139318	DUSP6	ENSG00000187116	LILRA5	ENSG00000105514	RAB3D	ENSG00000038427	VCAN
ENSG00000135636	DYSF	ENSG00000182541	LIMK2	ENSG00000169385	RNASE2	ENSG00000229124	VIM-AS1

Supplementary Table 2. Reproducibility of EN-RAGE+ myeloid cell gene expression across cohorts and sample types, related to Figure 3. Spearman correlation coefficients are shown for pseudo-bulk EN-RAGE signature score and genes encoding myeloid functions within specific myeloid populations across scRNA-seq datasets. Positive correlations are shaded red and negative correlations shaded blue, with increasing darkness of shading indicating two tailed p values of $p<0.05$, $p<0.01$, and $p<0.001$. TA=tracheal aspirate, BAL=bronchoalveolar lavage. Blanks indicate transcript in below detection. Datasets: Liao et al.[7], Grant et al.[6], Delorey et al.[5], Schulte-Schrepping et al.[11], Silvin et al.[12], COMET PBMC[2], whole blood[39], and ETA[38].

	Spearman rho		HLA.DRA	HLA.DRB1	CD14	STAT3	S100A12	S100A9	IL10	PDL1	PTGER2	TGFB1	IL1B	IDO1	CCR5	CYBB	ARG1	CCR2
	Monocyte	n																
Airway samples	TA MonoMac COMET	41	0.11	-0.23	0.10	0.75	0.70	0.76	0.74	0.59	0.72	0.13	0.86	0.33	0.36	0.14	0.31	0.26
	BAL monocyte Liao	12	-0.90	-0.97	0.73	0.71	0.92	0.38	0.82	0.58	0.89	0.89	0.74	0.69	0.80	0.07		0.73
	BAL myeloid Grant	19	0.52	0.43	0.41	0.48	0.53	0.16	0.36	0.47	0.66	0.29	0.47	0.34	0.37	0.06		-0.05
	BAL macrophage Grant	19	-0.26	-0.33	0.32	0.83	0.93	0.89	0.65	0.76	0.81	0.38	0.55	0.61	0.46	-0.19	0.30	0.15
	Lung myeloid Delorey	24	-0.01	0.00	-0.02	0.65	0.76	0.32	0.77	0.85	0.74	0.29	0.87	0.65	0.43	-0.15	0.53	0.28
	Neutrophil																	
	TA neutrophil COMET	40	0.05	-0.16	0.58	0.63	0.74	0.85	0.53	0.61	0.35	0.54	0.78	0.30	-0.02	0.21	0.59	-0.09
	BAL neutrophil Liao	11	0.34	0.35	0.82	0.84	0.89	0.96		0.99	0.87	0.96	0.83	0.93	0.80	0.85		0.15

	Spearman rho		HLA.DRA	HLA.DRB1	CD14	STAT3	S100A12	S100A9	IL10	PDL1	PTGER2	TGFB1	IL1B	IDO1	CCR5	CYBB	ARG1	CCR2
	Monocyte	n																
Blood samples	Blood monocyte COMET	18	-0.01	0.19	0.62	0.79	0.67	0.74	0.57	0.31	0.52	0.37	0.34	0.37	0.07	0.60	0.43	0.53
	Blood monocyte Schulte	33	-0.54	-0.41	0.81	0.75	0.67	0.67	0.05	0.27	0.51	0.36	-0.16	0.09	0.05	0.56	-0.01	0.23
	Blood monocyte Silvin	6	-0.77	-0.89	0.94	0.54	1.00	0.77		0.68	-0.03	0.31	-0.43		0.43	0.94		0.60
	PBMC monocyte COMET	44	-0.45	-0.48	0.65	0.15	0.73	0.79	0.15	0.02	0.38	0.18	0.34	-0.08	-0.44	0.52	-0.09	0.25
	PBMC monocyte Schulte	16	-0.73	-0.54	0.75	0.86	0.57	0.71	0.66	0.43	0.77	-0.20	0.64	0.02	-0.40	0.40	0.65	-0.56
	Neutrophil																	
	Blood neutrophil COMET	18	-0.53	-0.52	0.78	0.94	0.72	0.87	0.30	0.78	-0.48	0.91	0.70	0.37	0.06	0.28	0.77	-0.21
	Blood neutrophil Schulte	33	-0.23	-0.05	0.71	0.79	0.57	0.62		0.50	0.22	0.80	-0.08		0.33	0.19	0.19	-0.01
	Blood neutrophil Silvin	6	-0.37	-0.77	1.00	0.20	1.00	0.94		0.60	0.82	0.60	-0.03			-0.09	0.54	-0.85
	PBMC neutrophil Schulte	16	0.21	0.46	0.54	0.74	0.63	0.68		0.62	-0.11	0.91	0.80	0.55		0.23	0.47	

Supplementary Table 3. Differential expression analysis of IL-6 treated monocytes, related to Figure 5. Summary statistics (log2 fold change, p-value and FDR) are shown for genes identified in the EN-RAGE signature, myeloid function genes, and T cell modulatory genes.

ID	Symbol	Gene Name	P-Value	FDR	Log2 Fold Change
ENSG00000276900	AC023157.3	NA	0.0002558	0.00688289	-0.946526
ENSG00000268734	AC245128.3	NA	0.00068357	0.01282159	1.37033234
ENSG00000233461	AL445524.1	NA	0.00011969	0.00434596	1.11062331
ENSG00000161944	ASGR2	asialoglycoprotein receptor 2 [Source:HGNC Symbol;Acc:HGNC:743]	0.00101507	0.01623308	0.7888026
ENSG00000156127	BATF	basic leucine zipper ATF-like transcription factor [Source:HGNC Symbol;Acc:HGNC:958]	2.25E-05	0.00154798	0.77230429
ENSG00000113916	BCL6	B-cell CLL/lymphoma 6 [Source:HGNC Symbol;Acc:HGNC:1001]	0.34096017	0.59700076	0.30265759
ENSG00000163823	CCR1	C-C motif chemokine receptor 1 [Source:HGNC Symbol;Acc:HGNC:1602]	0.0002279	0.00639216	1.11822664
ENSG00000125810	CD93	CD93 molecule [Source:HGNC Symbol;Acc:HGNC:15855]	0.00675866	0.05468667	0.56329649
ENSG00000158825	CDA	cytidine deaminase [Source:HGNC Symbol;Acc:HGNC:1712]	0.08780946	0.27327715	-0.6961891
ENSG00000131873	CHSY1	chondroitin sulfate synthase 1 [Source:HGNC Symbol;Acc:HGNC:17198]	0.05249982	0.20065662	0.52522326
ENSG00000136026	CKAP4	cytoskeleton associated protein 4 [Source:HGNC Symbol;Acc:HGNC:16991]	0.25426105	0.50725658	0.18099133
ENSG00000166527	CLEC4D	C-type lectin domain family 4 member D [Source:HGNC Symbol;Acc:HGNC:14554]	3.80E-05	0.00213636	1.29276817
ENSG00000166523	CLEC4E	C-type lectin domain family 4 member E [Source:HGNC Symbol;Acc:HGNC:14555]	0.00062178	0.01211745	0.66621281
ENSG00000120885	CLU	clusterin [Source:HGNC Symbol;Acc:HGNC:2095]	0.25681528	0.51016731	-0.7074343
ENSG00000146592	CREB5	cAMP responsive element binding protein 5 [Source:HGNC Symbol;Acc:HGNC:16844]	0.00034248	0.00829596	0.95498353
ENSG00000103196	CRISPLD2	cysteine rich secretory protein LCCL domain containing 2 [Source:HGNC Symbol;Acc:HGNC:25248]	0.9550075	0.98294597	0.02830623
ENSG00000163739	CXCL1	C-X-C motif chemokine ligand 1 [Source:HGNC Symbol;Acc:HGNC:4602]	0.09385064	0.28517184	1.09058755
ENSG00000169429	CXCL8	C-X-C motif chemokine ligand 8 [Source:HGNC Symbol;Acc:HGNC:6025]	0.15309532	0.38208223	-0.8591684
ENSG00000138061	CYP1B1	cytochrome P450 family 1 subfamily B member 1 [Source:HGNC Symbol;Acc:HGNC:2597]	0.057066	0.21144762	0.2970168
ENSG00000139318	DUSP6	dual specificity phosphatase 6 [Source:HGNC Symbol;Acc:HGNC:3072]	0.0019424	0.02504931	0.6022381
ENSG00000135636	DYSF	dysferlin [Source:HGNC Symbol;Acc:HGNC:3097]	0.12850349	0.34489034	1.04938142
ENSG00000163412	EIF4E3	eukaryotic translation initiation factor 4E family member 3 [Source:HGNC Symbol;Acc:HGNC:31837]	0.01868306	0.10516259	0.51182583
ENSG00000198734	F5	coagulation factor V [Source:HGNC Symbol;Acc:HGNC:3542]	0.04059769	0.17130637	1.13549923
ENSG00000186431	FCAR	Fc fragment of IgA receptor [Source:HGNC Symbol;Acc:HGNC:3608]	0.00120478	0.01823671	1.2267336
ENSG00000085265	FCN1	ficolin 1 [Source:HGNC Symbol;Acc:HGNC:3623]	0.91792301	0.96843436	-0.0132796
ENSG00000125740	FOSB	FosB proto-oncogene, AP-1 transcription factor subunit [Source:HGNC Symbol;Acc:HGNC:3797]	0.00057552	0.01150973	-1.5571324
ENSG00000171051	FPR1	formyl peptide receptor 1 [Source:HGNC Symbol;Acc:HGNC:3826]	0.00214927	0.02687908	2.46797774
ENSG00000171049	FPR2	formyl peptide receptor 2 [Source:HGNC Symbol;Acc:HGNC:3827]	7.16E-05	0.0031548	2.95300415
ENSG00000123689	G0S2	G0/G1 switch 2 [Source:HGNC Symbol;Acc:HGNC:30229]	0.03136987	0.14585339	1.04079477
ENSG00000151948	GLT1D1	glycosyltransferase 1 domain containing 1 [Source:HGNC Symbol;Acc:HGNC:26483]	4.52E-07	0.00015703	0.86549295
ENSG00000170837	GPR27	G protein-coupled receptor 27 [Source:HGNC Symbol;Acc:HGNC:4482]	0.24301613	0.49524341	0.97088636
ENSG00000139572	GPR84	G protein-coupled receptor 84 [Source:HGNC Symbol;Acc:HGNC:4535]	0.4274837	0.67643793	0.13717464
ENSG00000136630	HLX	H2.0 like homeobox [Source:HGNC Symbol;Acc:HGNC:4978]	0.63656708	0.82485607	0.16023166
ENSG00000173083	HPSE	heparanase [Source:HGNC Symbol;Acc:HGNC:5164]	0.00229917	0.02804157	0.63249147

ENSG00000160888	IER2	immediate early response 2 [Source:HGNC Symbol;Acc:HGNC:28871]	0.87002609	0.94693555	0.02568598
ENSG00000137331	IER3	immediate early response 3 [Source:HGNC Symbol;Acc:HGNC:5392]	0.01223604	0.08091413	0.83494161
ENSG00000115594	IL1R1	interleukin 1 receptor type 1 [Source:HGNC Symbol;Acc:HGNC:5993]	0.41204952	0.66304842	0.15820301
ENSG00000136689	IL1RN	interleukin 1 receptor antagonist [Source:HGNC Symbol;Acc:HGNC:6000]	0.57218936	0.78432026	0.23559381
ENSG00000157551	KCNJ15	potassium voltage-gated channel subfamily J member 15 [Source:HGNC Symbol;Acc:HGNC:6261]	6.28E-06	0.00074343	1.75942985
ENSG00000239998	LILRA2	leukocyte immunoglobulin like receptor A2 [Source:HGNC Symbol;Acc:HGNC:6603]	0.03706315	0.16193569	0.24452248
ENSG00000187116	LILRA5	leukocyte immunoglobulin like receptor A5 [Source:HGNC Symbol;Acc:HGNC:16309]	3.45E-05	0.00202174	1.69784191
ENSG00000182541	LIMK2	LIM domain kinase 2 [Source:HGNC Symbol;Acc:HGNC:6614]	7.24E-06	0.00080663	0.97543978
ENSG00000248323	LUCAT1	lung cancer associated transcript 1 (non-protein coding) [Source:HGNC Symbol;Acc:HGNC:48498]	0.1459313	0.37162743	0.33464446
ENSG00000185022	MAFF	MAF bZIP transcription factor F [Source:HGNC Symbol;Acc:HGNC:6780]	0.1380025	0.35875242	-0.7571991
ENSG00000125505	MBOAT7	membrane bound O-acyltransferase domain containing 7 [Source:HGNC Symbol;Acc:HGNC:15505]	9.86E-06	0.00095036	0.89812172
ENSG00000140563	MCTP2	multiple C2 and transmembrane domain containing 2 [Source:HGNC Symbol;Acc:HGNC:25636]	4.51E-05	0.00234434	1.51782517
ENSG00000257335	MGAM	maltase-glucoamylase [Source:HGNC Symbol;Acc:HGNC:7043]	0.22226083	0.47035084	-0.2806996
ENSG00000172965	MIR4435-2HG	MIR4435-2 host gene [Source:HGNC Symbol;Acc:HGNC:35163]	0.03076242	0.14425059	-0.7820365
ENSG00000008516	MMP25	matrix metallopeptidase 25 [Source:HGNC Symbol;Acc:HGNC:14246]	0.34632146	0.60227409	0.24510192
ENSG00000059728	MXD1	MAX dimerization protein 1 [Source:HGNC Symbol;Acc:HGNC:6761]	1.30E-07	7.39E-05	1.71771187
ENSG00000105835	NAMPT	nicotinamide phosphoribosyltransferase [Source:HGNC Symbol;Acc:HGNC:30092]	1.42E-07	7.39E-05	1.8905536
ENSG00000165030	NFIL3	nuclear factor, interleukin 3 regulated [Source:HGNC Symbol;Acc:HGNC:7787]	0.69490948	0.85894369	0.08469961
ENSG00000100906	NFKBIA	NFKB inhibitor alpha [Source:HGNC Symbol;Acc:HGNC:7797]	0.15140542	0.37964501	0.2329592
ENSG00000087157	PGS1	phosphatidylglycerophosphate synthase 1 [Source:HGNC Symbol;Acc:HGNC:30029]	2.98E-05	0.00181119	0.5554646
ENSG00000105520	PLPPR2	phospholipid phosphatase related 2 [Source:HGNC Symbol;Acc:HGNC:29566]	0.00670735	0.05430312	0.47712892
ENSG00000163421	PROK2	prokineticin 2 [Source:HGNC Symbol;Acc:HGNC:18455]	0.06829251	0.2364142	1.31956596
ENSG00000140368	PSTPIP1	proline-serine-threonine phosphatase interacting protein 1 [Source:HGNC Symbol;Acc:HGNC:9580]	0.15621382	0.38693619	-0.1396252
ENSG00000125384	PTGER2	prostaglandin E receptor 2 [Source:HGNC Symbol;Acc:HGNC:9594]	0.00054456	0.0110989	0.90132869
ENSG00000073756	PTGS2	prostaglandin-endoperoxide synthase 2 [Source:HGNC Symbol;Acc:HGNC:9605]	0.02402345	0.12330904	0.50030344
ENSG00000155093	PTPRN2	protein tyrosine phosphatase, receptor type N2 [Source:HGNC Symbol;Acc:HGNC:9677]	0.1438039	0.36808873	-1.4315168
ENSG00000089159	PXN	paxillin [Source:HGNC Symbol;Acc:HGNC:9718]	9.72E-06	0.00094201	1.03358085
ENSG00000105514	RAB3D	RAB3D, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:9779]	0.05566382	0.20791312	0.46673696
ENSG00000169385	RNASE2	ribonuclease A family member 2 [Source:HGNC Symbol;Acc:HGNC:10045]	0.04112826	0.17267452	0.82801537
ENSG00000101236	RNF24	ring finger protein 24 [Source:HGNC Symbol;Acc:HGNC:13779]	0.64963761	0.8322104	0.03995637
ENSG00000163221	S100A12	S100 calcium binding protein A12 [Source:HGNC Symbol;Acc:HGNC:10489]	0.00025289	0.00683886	1.24344981
ENSG00000143546	S100A8	S100 calcium binding protein A8 [Source:HGNC Symbol;Acc:HGNC:10498]	8.09E-05	0.00343381	0.85722886
ENSG00000163220	S100A9	S100 calcium binding protein A9 [Source:HGNC Symbol;Acc:HGNC:10499]	1.38E-07	7.39E-05	1.63614409

ENSG00000213694	S1PR3	sphingosine-1-phosphate receptor 3 [Source:HGNC Symbol;Acc:HGNC:3167]	0.43363103	0.68202843	0.53490736
ENSG00000155307	SAMSN1	SAM domain, SH3 domain and nuclear localization signals 1 [Source:HGNC Symbol;Acc:HGNC:10528]	0.00018746	0.00568941	0.44680548
ENSG00000197632	SERPINB2	serpin family B member 2 [Source:HGNC Symbol;Acc:HGNC:8584]	0.00829877	0.06226309	1.8308051
ENSG00000197208	SLC22A4	solute carrier family 22 member 4 [Source:HGNC Symbol;Acc:HGNC:10968]	0.42821242	0.67691335	0.22695657
ENSG00000147454	SLC25A37	solute carrier family 25 member 37 [Source:HGNC Symbol;Acc:HGNC:29786]	0.23118103	0.48141237	0.23100506
ENSG00000059804	SLC2A3	solute carrier family 2 member 3 [Source:HGNC Symbol;Acc:HGNC:11007]	8.15E-05	0.00344058	1.43809499
ENSG00000082014	SMARCD3	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3 [Source:HGNC Symbol;Acc:HGNC:11108]	0.00012868	0.00451911	0.87426808
ENSG00000122862	SRGN	serglycin [Source:HGNC Symbol;Acc:HGNC:9361]	0.00450854	0.04210837	0.35254964
ENSG00000180953	ST20	suppressor of tumorigenicity 20 [Source:HGNC Symbol;Acc:HGNC:33520]	0.48338386	0.72221243	0.19612312
ENSG00000010327	STAB1	stabilin 1 [Source:HGNC Symbol;Acc:HGNC:18628]	0.0238392	0.12274581	0.32872072
ENSG00000127954	STEAP4	STEAP4 metalloreductase [Source:HGNC Symbol;Acc:HGNC:21923]	0.0031347	0.03384836	2.41419201
ENSG00000166900	STX3	syntaxin 3 [Source:HGNC Symbol;Acc:HGNC:11438]	0.48226411	0.72124343	0.05193184
ENSG00000137462	TLR2	toll like receptor 2 [Source:HGNC Symbol;Acc:HGNC:11848]	0.00354142	0.03629353	0.37560024
ENSG00000173334	TRIB1	tribbles pseudokinase 1 [Source:HGNC Symbol;Acc:HGNC:16891]	0.01676227	0.09806768	0.77869291
ENSG00000127824	TUBA4A	tubulin alpha 4a [Source:HGNC Symbol;Acc:HGNC:12407]	0.13874694	0.36006242	0.43569793
ENSG00000038427	VCAN	versican [Source:HGNC Symbol;Acc:HGNC:2464]	3.74E-08	3.39E-05	1.84828714
ENSG00000229124	VIM-AS1	VIM antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44879]	0.29642929	0.55244352	0.10496826
ENSG00000120217	CD274	CD274 molecule [Source:HGNC Symbol;Acc:HGNC:17635]	0.19742761	0.44184669	0.58942095
ENSG00000204287	HLA-DRA	major histocompatibility complex, class II, DR alpha [Source:HGNC Symbol;Acc:HGNC:4947]	0.00472144	0.04334815	0.34541003
ENSG00000121807	CCR2	C-C motif chemokine receptor 2 [Source:HGNC Symbol;Acc:HGNC:1603]	0.00082997	0.01429496	0.62233716
ENSG00000163220	S100A9	S100 calcium binding protein A9 [Source:HGNC Symbol;Acc:HGNC:10499]	1.38E-07	7.39E-05	1.63614409
ENSG00000168610	STAT3	signal transducer and activator of transcription 3 [Source:HGNC Symbol;Acc:HGNC:11364]	3.16E-07	0.00012453	0.81921988
ENSG00000165168	CYBB	cytochrome b-245 beta chain [Source:HGNC Symbol;Acc:HGNC:2578]	2.26E-05	0.00154798	0.50282461
ENSG00000136634	IL10	interleukin 10 [Source:HGNC Symbol;Acc:HGNC:5962]	0.00047859	0.01029886	1.2355798
ENSG00000125384	PTGER2	prostaglandin E receptor 2 [Source:HGNC Symbol;Acc:HGNC:9594]	0.00054456	0.0110989	0.90132869
ENSG00000163221	S100A12	S100 calcium binding protein A12 [Source:HGNC Symbol;Acc:HGNC:10489]	0.00025289	0.00683886	1.24344981
ENSG00000160791	CCR5	C-C motif chemokine receptor 5 (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:1606]	4.77E-05	0.00241612	1.12530733
ENSG00000170458	CD14	CD14 molecule [Source:HGNC Symbol;Acc:HGNC:1628]	0.0007962	0.0139324	0.65225493
ENSG00000125538	IL1B	interleukin 1 beta [Source:HGNC Symbol;Acc:HGNC:5992]	0.01035649	0.07225619	0.9626091
ENSG00000073756	PTGS2	prostaglandin-endoperoxide synthase 2 [Source:HGNC Symbol;Acc:HGNC:9605]	0.02402345	0.12330904	0.50030344
ENSG00000196126	HLA-DRB1	major histocompatibility complex, class II, DR beta 1 [Source:HGNC Symbol;Acc:HGNC:4948]	0.02832988	0.13728513	0.31377178
ENSG00000131203	IDO1	indoleamine 2,3-dioxygenase 1 [Source:HGNC Symbol;Acc:HGNC:6059]	0.01104881	0.07560173	-1.7425979
ENSG00000105329	TGFB1	transforming growth factor beta 1 [Source:HGNC Symbol;Acc:HGNC:11766]	0.02323542	0.1210483	-0.2886977
ENSG00000118520	ARG1	arginase 1 [Source:HGNC Symbol;Acc:HGNC:663]	NA	NA	NA