iScience, Volume *25*

Supplemental information

Coagulation factor V is a T-cell inhibitor expressed by leukocytes in COVID-19

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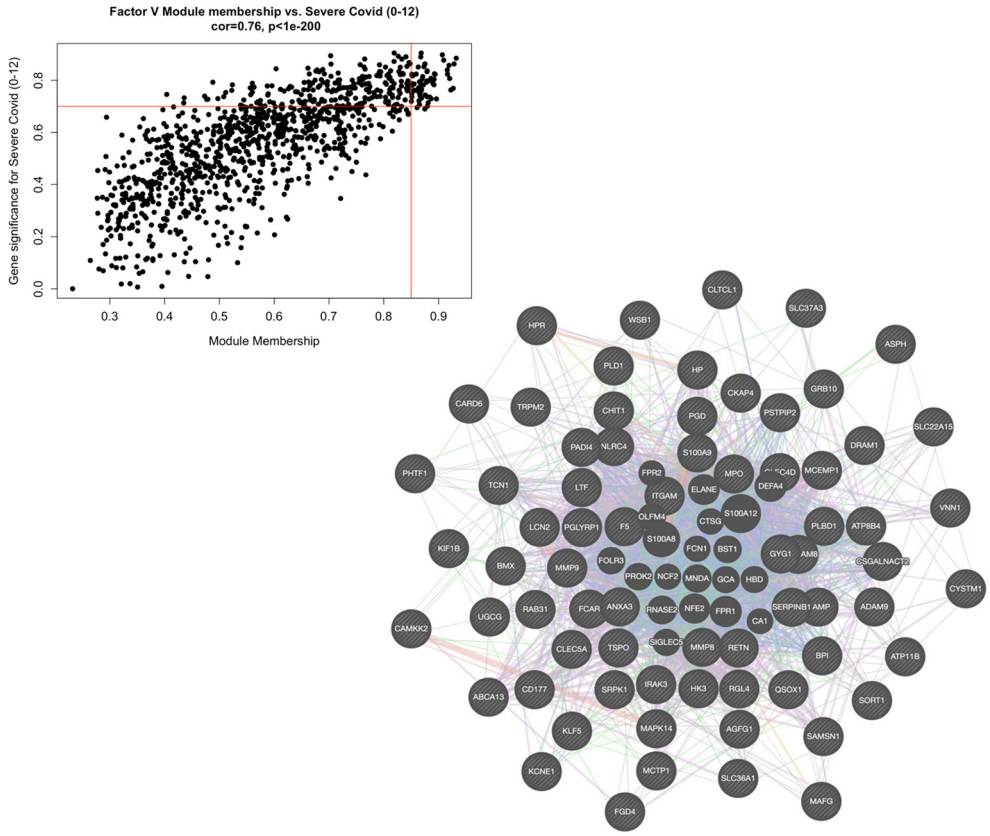

Figure S1. Factor V module membership identifies genes that correlate with severe COVID-19. Related to Figure 1 and Figure 2. Genes comprising the Factor V module are graphed. The x axis represents the correlation of a given gene's expression with the module eigenvalue. The higher the correlation, the more representative the module expression is of the gene. The Y axis represents the correlation between a gene's expression and disease status (HC versus severe COVID-19 at 0-12 days post symptom onset). The higher the correlation, the more able a given gene can distinguish severe COVID-19 from health. The red lines demarcate the "hub genes" which represent genes that strongly model the module and disease status. The genes illustrated are: KIF1B; PGD; PADI4; SORT1; PHTF1; SLC22A15; S100A9; F5; QSOX1; CHIT1; MTARC1; NLRC4; AGFG1; LTF; CAMP; GYG1; PLD1; ATP11B; ANXA3; CARD6; MCTP1; CYSTM1; SLC36A1; HK3; SERPINB1; SRPK1; MAPK14; VNN1; ABCA13; GRB10; SLC37A3; CLEC5A; BMX; ADAM9; ASPH; UGCG; LCN2; TCN1; MMP8; CSGALNACT2; CLEC4D; PLBD1; FGD4; IRAK3; DRAM1; CKAP4; CAMKK2; KLFV; ATP8B4; ITGAM; HP; HPR; WSB1; MPO; MAFG; RAB31; PSTPIP2; BPI; MMP9; RETN; MCEMP1; CEACAM8; CD177; PGLYRP1; FCAR; CLTCL1; RGL4; TSPO; SAMSN1; KCNE1; TRPM2.

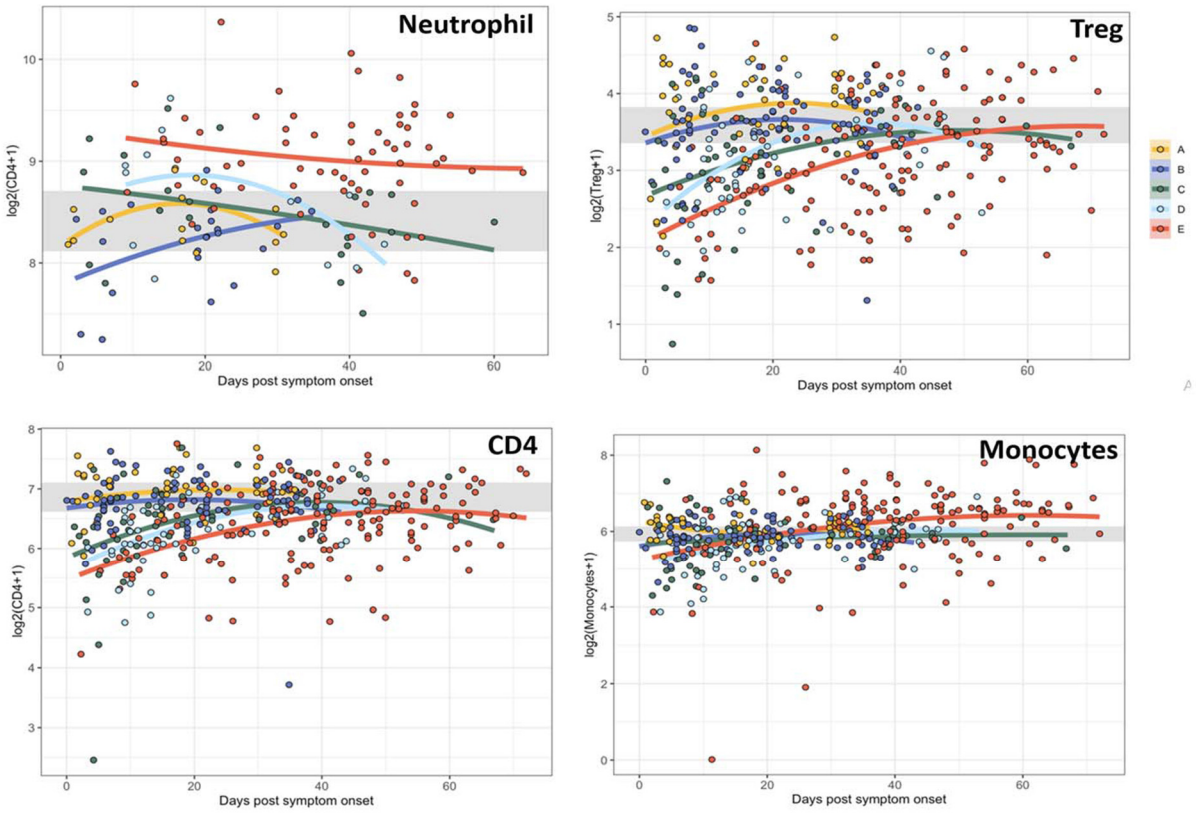

Figure S2. Leukocyte cell types have different trajectories over time. Related to Figure 2. Mixed-effect model with quadratic time trend showing the longitudinal trajectories for neutrophils, Tregs, CD4 and monocytes over time. A, HCW screening asymptomatic; B, HCW screening symptomatic; C, hospitalised mild disease; D, hospitalised requiring oxygen; E, hospitalised, intensive care.

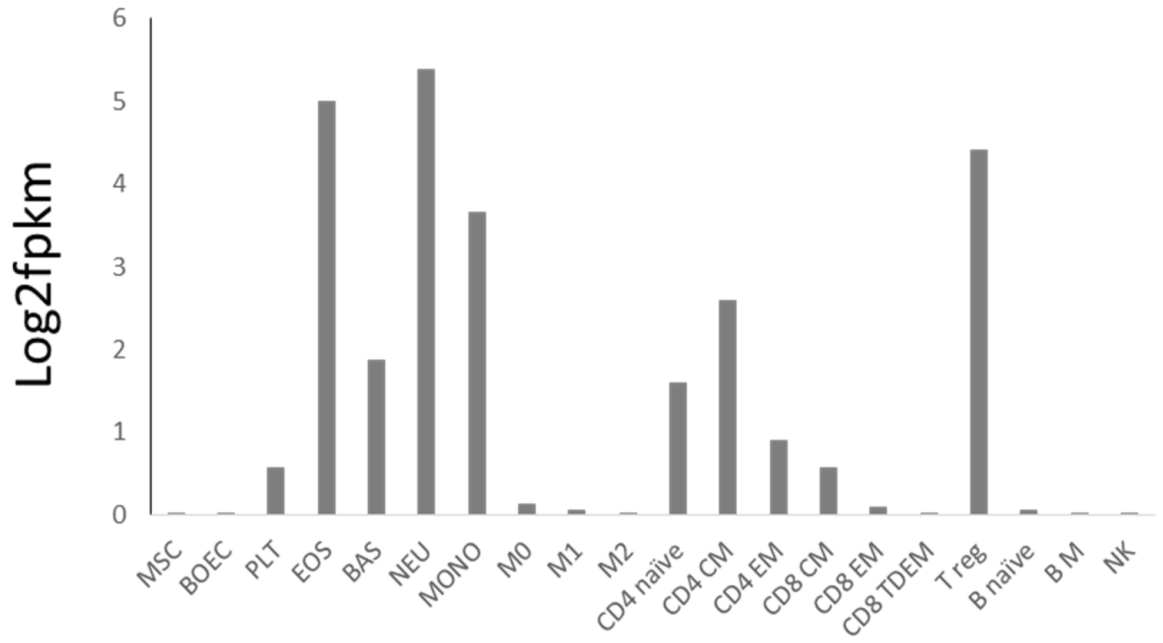

Figure S3. FV is expressed in peripheral blood leukocytes. Related to Figure 1.

Analysis of the Blueprint (https://www.blueprint-epigenome.eu/) database identified FV expression in peripheral blood cell subsets in healthy individuals, with the highest expression in neutrophils, eosinophils, monocytes and Tregs derived from healthy individuals. fpkm - fragments per kilobase of transcript per million mapped reads. MSC: mesenchymal stem cells, BOEC: blood outgrowth endothelial cells, PLT: platelet, EOS: eosinophil, BAS: basophil, NEU: neutrophil, MONO: monocyte, M0, M1 and M2: macrophages, CM: central memory, EM: effector memory, TDEM: terminally differentiated effector memory, T reg: regulatory T cells, B M: B memory
NK: natural killer.

Table S1. Gene Ontology (GO) enrichment analysis of FV module genes. Related to Figure 1.

Name	p-value	Adjusted p-value	Odds ratio	Combined score
Neutrophil mediated immunity (GO:0002446	6.500E-49	1.433E-45	13.97	1549.67
Neutrophil degranulation (GO:0043312)	3.299e-48	3.636e-45	13.92	1521.46
Neutrophil activation involved in immune response (GO:0002283)	5.879e-48	4.319e-45	13.78	1498.52
Innate immune response in mucosa (GO:0002227)	1.773e-8	0.000005583	32.91	587.37
Mucosal immune response (GO:0002385)	1.647e-7	0.00004537	21.93	342.56
Defense response to Gram-negative bacterium (GO:0050829)	1.061E-9	4.675e-7	13.14	271.47