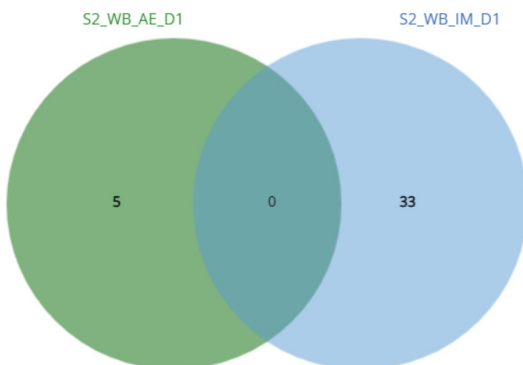


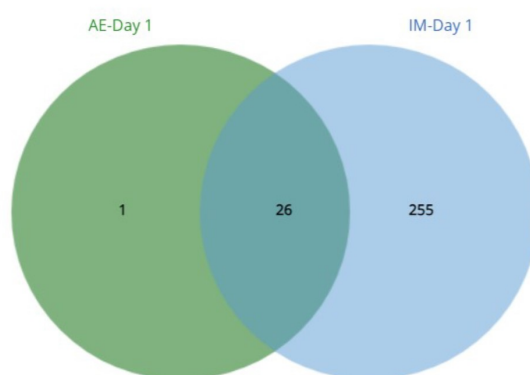
A.

Day 1-Whole Blood



C.

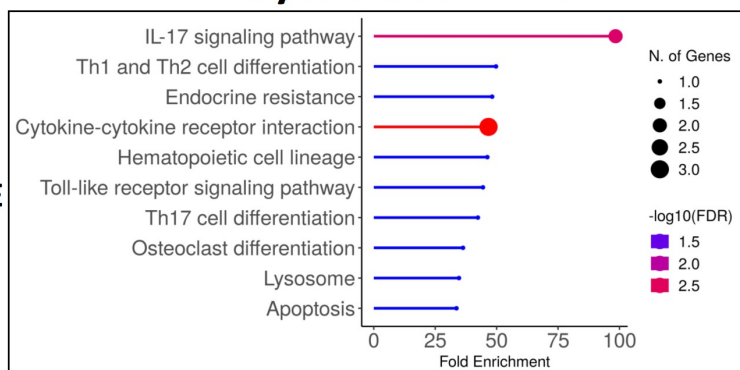
Day 1-Lung



B.

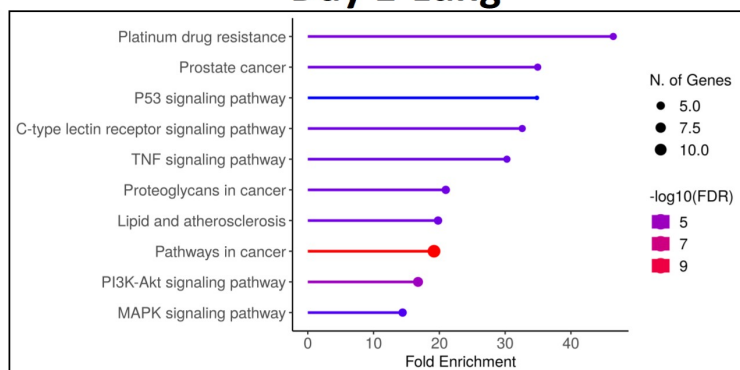
Day 1-Whole Blood

AE

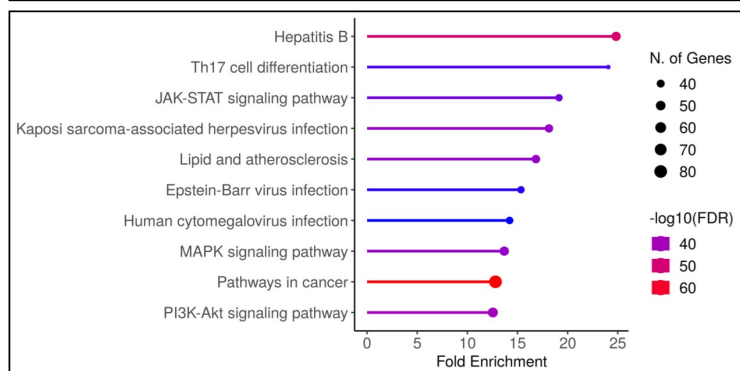
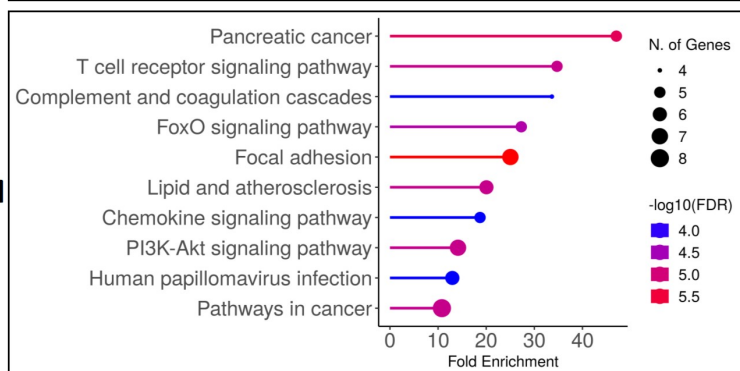


D.

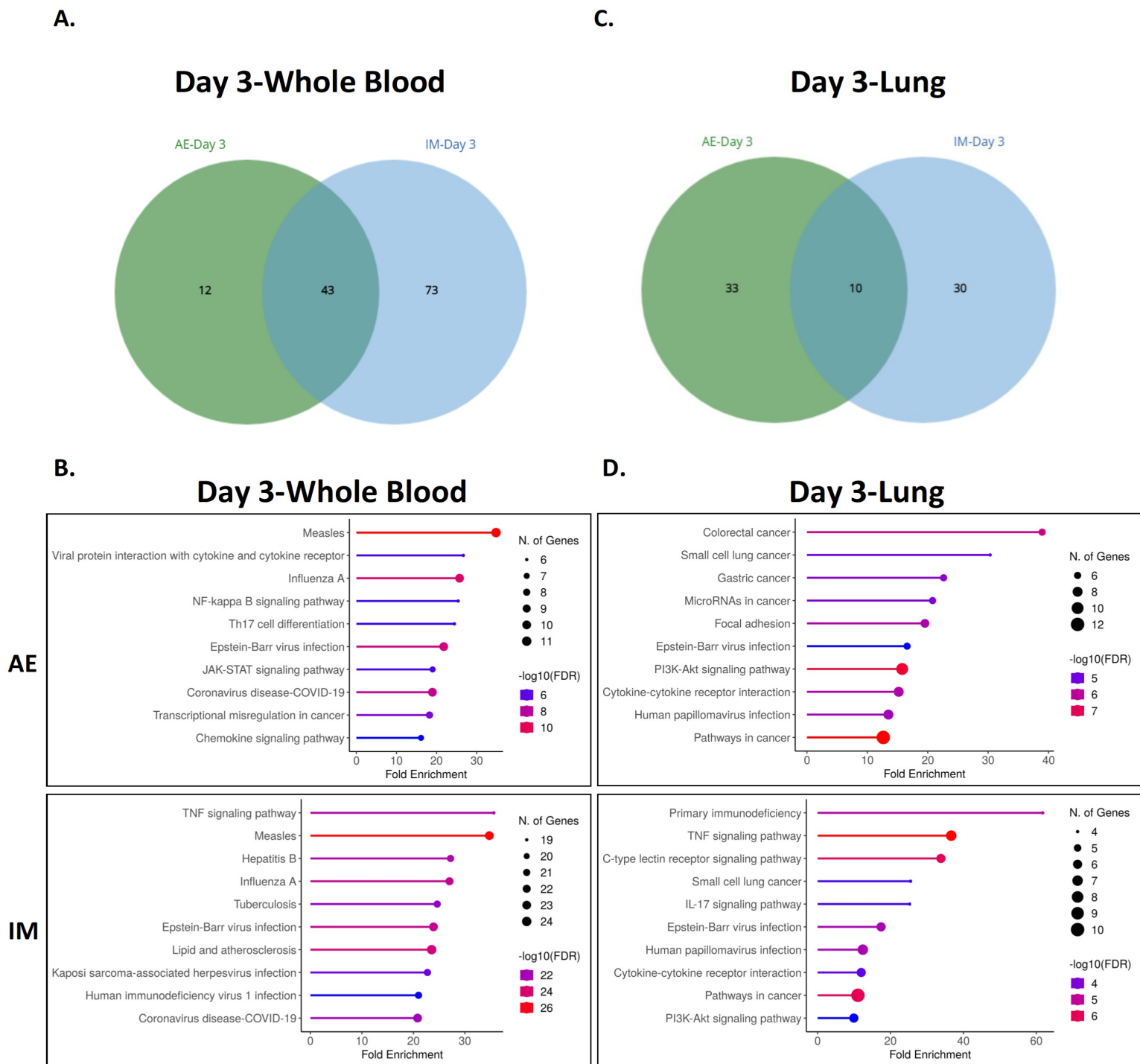
Day 1-Lung



IM



Supplementary Figure 1. Transcriptomic analysis of whole blood and lung 1 day post-EBOV exposure. Whole blood analysis at 1 dpi of (A) Challenge route-associated overlap of DEGs at 1 dpi, and (B) KEGG pathway analysis of significantly enriched pathways. Lung homogenate analysis at 1 dpi of (C) Challenge-route associated overlap of DEGs, and (D) KEGG pathway analysis of significantly enriched pathways. All of the above differential analysis is based on aggregate analysis of 4 ferrets per group time point.



Supplementary Figure 2. Transcriptomic analysis of whole blood and lung 3 day post-EBOV exposure. Whole blood analysis at 3 dpi of (A) Challenge route-associated overlap of DEGs, and (B) KEGG pathway analysis of significantly enriched pathways. Lung homogenate analysis at 3 dpi of (C) Challenge-route associated overlap of DEGs, and D) KEGG pathway analysis of significantly enriched pathways. All of the above differential analysis is based on aggregate analysis of 4 ferrets per group time point.

Supplementary Table 1. Significant differentially expressed mRNAs in ferret whole blood, 1 dpi.

	IM		AE	
	Gene	Log ₂ Diff (<i>p</i> value)	Gene	Log ₂ Diff (<i>p</i> value)
Upregulated	SMAD3	5.13 (0.0065)	CD68	4.46 (0.0024)
	C1QBP	4.70 (0.0018)	IL17RB	4.46 (0.038)
	CCR3	4.13 (0.024)	IL1RL1	3.46 (0.026)
	NLRP3	4.05 (0.0022)	—	—
	NOX1	3.64 (0.030)	—	—
	ATG10	3.46 (0.0055)	—	—
	RFXAP	3.17 (0.047)	—	—
	PTPN22	2.36 (0.0011)	—	—
	CASP7	2.04 (0.0074)	—	—
	CDC42	1.49 (0.0072)	—	—
Downregulated	CD55	-1.94 (0.0039)	CSF3R	-2.35 (0.0072)
	EGR1	-2.04 (0.045)	FOS	-5.34 (0.011)
	FANCD2	-2.29 (0.0038)	—	—
	VWF	-2.37 (0.0057)	—	—
	GP6	-2.48 (0.00052)	—	—
	THBS1	-4.22 (0.00081)	—	—
	IGF1	-5.36 (0.0014)	—	—
	CXCL6	-6.15 (0.00031)	—	—
	EGF	-7.69 (0.00077)	—	—
	CLU	-7.93 (0.020)	—	—

Top 10 of most upregulated and downregulated genes included. Inclusion criteria were a linear 2-fold difference and p-value ≤ 0.05 .

Supplementary Table 2. Significant differentially expressed mRNAs in ferret whole blood, 3 dpi.

	IM		AE	
	Gene	Log ₂ Diff (<i>p-value</i>)	Gene	Log ₂ Diff (<i>p-value</i>)
Upregulated	IDO1	8.42 (0.018)	IDO1	7.92 (0.030)
	DHX58	8.11 (0.012)	IL27	6.90 (0.041)
	IL27	7.97 (0.014)	CCL8	6.08 (0.046)
	OASL	7.34 (0.036)	IFIT1	4.89 (0.011)
	ISG15	5.56 (0.0034)	ISG15	4.68 (0.018)
	IFIT1	5.22 (0.0047)	IFIH1	4.56 (0.012)
	MX1	5.17 (0.0057)	MX1	4.42 (0.020)
	CLEC7A	5.10 (0.0107)	IFIT3	4.27 (0.011)
	SOCS1	4.93 (0.0017)	DDX58	3.90 (0.014)
	IFIH1	4.70 (0.0050)	SOCS1	3.76 (0.030)
Downregulated	CD4	-1.58 (0.00052)	FYN	-1.095 (0.023)
	EPOR	-1.74 (0.0046)	IL6ST	-1.15 (0.013)
	LCK	-1.75 (0.0014)	CD3E	-1.23 (0.022)
	NPC1	-1.85 (0.030)	IL2RB	-1.30 (0.0038)
	PRF1	-2.05 (0.046)	CCND2	-1.33 (0.022)
	VTN	-2.078 (0.021)	TRIM33	-1.34 (0.0011)
	PLCG1	-2.30 (0.013)	CD5	-1.56 (0.0029)
	LTA	-3.21 (0.039)	KLRD1	-1.60 (0.0041)
	C8A	-4.09 (0.011)	CD84	-1.61 (0.0051)
	FOS	-6.60 (0.0026)	CCR7	-1.69 (0.0075)

Top 10 of most upregulated and downregulated genes included. Inclusion criteria were a linear 2-fold difference and p-value ≤ 0.05.

Supplementary Table 3. Significant differentially expressed mRNAs in ferret lung homogenate, 1 dpi.

	IM		AE	
	Gene	Log ₂ Diff (<i>p-value</i>)	Gene	Log ₂ Diff (<i>p-value</i>)
Upregulated	IL17B	4.48 (0.0067)	COL1A1	3.71 (0.00071)
	IFNL1	4.22 (0.0082)	IFNL1	3.20 (0.044)
	GAST	3.64 (0.040)	IGF2	2.64 (0.044)
	POMC	3.47 (0.015)	RPLP0	1.41 (0.0091)
	PTX3	3.26 (0.0052)	—	—
	TCF3	3.25 (0.0078)	—	—
	CD4	3.038 (0.018)	—	—
	IGF2	2.91 (0.027)	—	—
	C8A	2.80 (0.032)	—	—
	C1QB	2.74 (0.038)	—	—
Downregulated	PIK3C3	-6.98 (0.00013)	FANCD2	-3.91 (0.029)
	NFATC3	-7.25 (0.0029)	IFNLR1	-3.95 (0.013)
	MFGE8	-7.57 (0.0013)	MMP9	-4.13 (0.035)
	PTPN2	-7.59 (6.68E-05)	IL17RD	-4.49 (0.020)
	ABL1	-7.65 (0.018)	ATG12	-4.52 (0.029)
	P2RX7	-7.68 (0.00077)	IKBKG	-4.73 (0.019)
	PRKDC	-7.69 (0.018)	IGF1R	-4.82 (0.018)
	PLD1	-8.047 (0.00069)	PMAIP1	-5.11 (0.018)
	IL6ST	-8.43 (0.00010)	MDM2	-5.70 (0.015)
	PDGFRA	-8.51 (0.0072)	CFH	-6.24 (0.0073)

Top 10 of most upregulated and downregulated genes included. Inclusion criteria were a linear 2-fold difference and *p-value* ≤ 0.05.

Supplementary Table 4. Significant differentially expressed mRNAs in ferret lung homogenate, 3 dpi.

	IM		AE	
	Gene	Log ₂ Diff (<i>p-value</i>)	Gene	Log ₂ Diff (<i>p-value</i>)
Upregulated	ISG15	5.14 (0.0052)	CCL4	6.62 (0.016)
	IL17B	4.27 (0.0097)	CCL5	5.73 (0.049)
	GAST	3.91 (0.028)	MX1	4.79 (0.019)
	IGF2	3.75 (0.0043)	CCL22	4.28 (0.025)
	IFNL1	3.72 (0.020)	CXCL10	4.12 (0.038)
	POMC	3.32 (0.020)	CCL8	3.77 (0.042)
	COL1A1	3.13 (0.0039)	CDKN1A	3.53 (0.041)
	TCF3	2.96 (0.015)	PTX3	2.90 (0.012)
	CD19	2.59 (0.033)	IL1RN	2.80 (0.030)
	PTX3	2.59 (0.025)	COL1A1	2.47 (0.020)
Downregulated	IL23A	-3.392 (0.047)	FLT1	-1.88 (0.026)
	PTPN22	-3.555 (0.036)	HGF	-2.04 (0.033)
	FCER1A	-3.807 (0.044)	GHR	-2.06 (0.050)
	ATG10	-3.845 (0.038)	ENTPD1	-2.20 (0.013)
	FANCD2	-3.907 (0.029)	PDGFRB	-2.30 (0.037)
	MMP9	-4.129 (0.035)	VEGFC	-2.54 (0.039)
	IL17RD	-4.492 (0.020)	PTGS2	-2.87 (0.029)
	ATG12	-4.524 (0.029)	ATG10	-3.68 (0.046)
	IKBKG	-4.728 (0.019)	CCL24	-4.17 (0.016)
	HMGB1	-5.285 (0.0063)	IL17RD	-4.49 (0.020)

Top 10 of most upregulated and downregulated genes included. Inclusion criteria were a linear 2-fold difference and *p-value* ≤ 0.05.