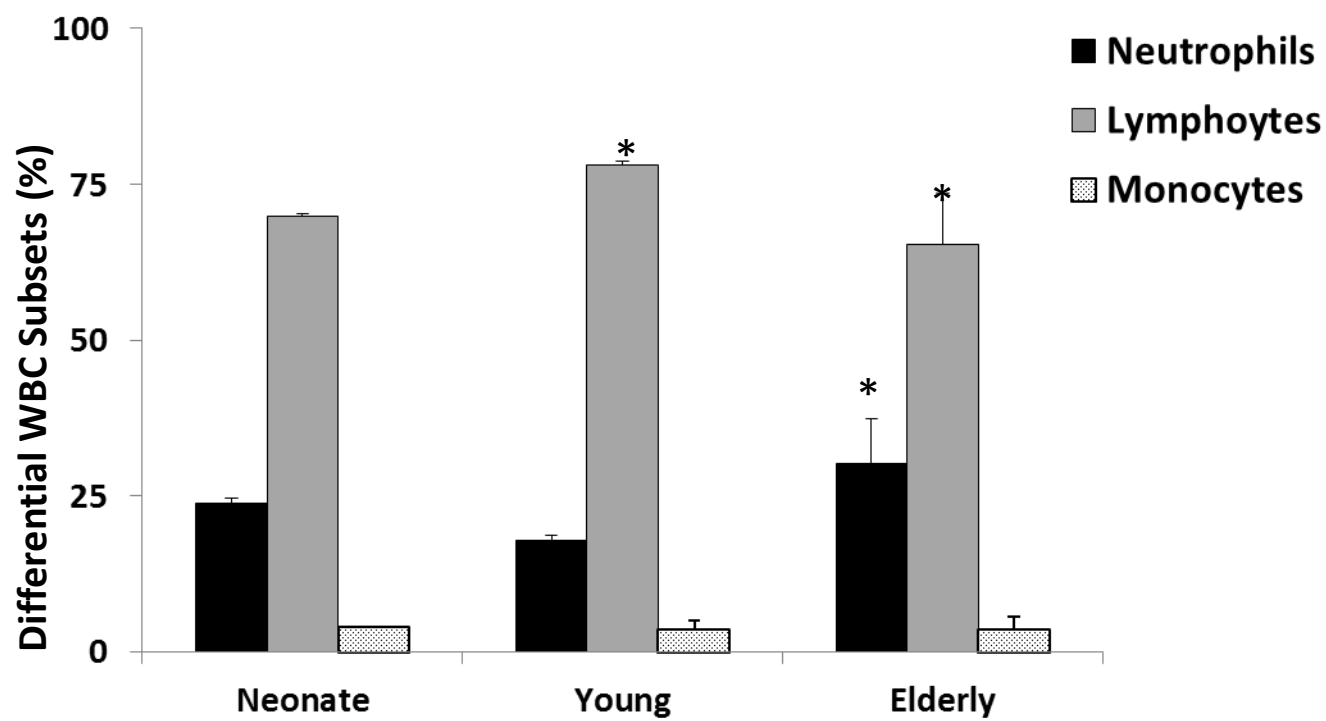


Supplemental Table I. Genes of Interest Over Time

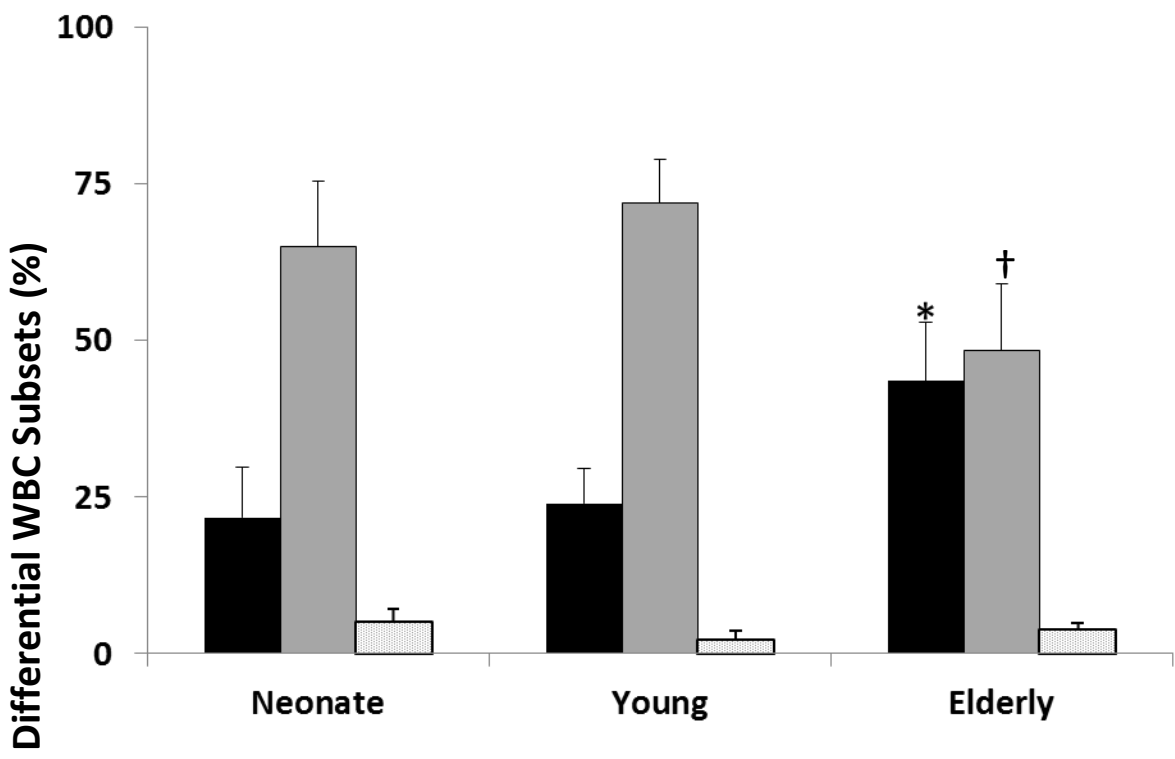
2 Hour				1 Day				3 Day			
Gene	Neonate	Adult	Elderly	Gene	Neonate	Adult	Elderly	Gene	Neonate	Adult	Elderly
<b>Chemotaxis</b>											
Cxcl10	2.1	4.6	6.2	Cxcl10	1.3	7.8	1.5				
Cxcl2	147.1	210.6	170					Cxcl2	5.8	13.1	1.5
				Cxcl3	5.8	396.0	145.8	Cxcl3	1.5	2.5	1.6
				Cxcl13	4.8	17.4	2.9	Cxcl13	1.6	2.4	-1.5
<b>Antimicrobial Peptides/Proteins</b>											
Ltf	1.5	7.0	29	Ltf	-3.1	12.0	11.0	Ltf	-1.2	53.7	5.3
				Arg1	3.7	19.6	10.7	Arg1	2.2	19.4	4.9
<b>Co-Stimulatory Molecules on Leukocytes</b>											
Cd28	-2.4	2.0	-2.0	Cd28	-4.0	1.0	-2.6	Cd28	-6.4	-3.4	1.5
Cd40	-1.2	4.3	-2.2	Cd40	2.1	-1.4	-2.9	Cd40	1.4	-3.6	-2.0
Btla	-1.3	2.3	1.3	Ctla4	1.4	3.3	1.8	Cd27	-7.3	-3.0	-1.3
Ctla2a	1.9	-1.4	1.5					Ctla2a	1.3	1.4	1.4
<b>PAMP Detection</b>											
Cd14	10	14.2	29.5	CD14	-3.3	8.4	7.0	Tlr4	1.1	2.8	1.6
<b>Inflammation Related Peptides/Proteins</b>											
Il-10	1.9	5.3	1.9	Il-10	1.6	19.7	2.5	Il-10	1.6	1.8	-1.4
Tnfaip3	4.1	14	18.6	Tnfaip3	-1.3	11.2	2.4	IfnG	1.2	-1.5	-2.9
Irg1	31.5	109	124.3	Irg1	1.3	36	22.6	Irg1	7.3	4.8	2.6
Casp1	-1.1	-3.5	-1.6	Casp1	-1.8	-1.9	-1.6	Casp1	1.0	-2.0	1.5
Il-6	13.9	11.4	6.4	Il-6	-1.2	51.6	1.7	Socs3	2.6	8.5	5.8
Il-1B	7.8	2.3	8.6	Il-1B	-1.4	1.0	1.5	Il-1B	1.1	-1.3	3.0
Hmgb1	-1.4	2.3	1.3					Hmgb1	-2.5	-1.9	1.4
<b>Other Immune Related Genes</b>											
Cd69	-1.4	2.4	1.4	Cd69	-1.1	1.5	-2.6	Cd69	-2.3	-2.9	-1.3
Cd44	1.7	3.2	2.1	Cd44	-3	1.5	1.4	Cd44	1.5	1.5	2.9
Trem1	7	2.8	9.7	Trem1	2	4	3.4	Trem1	1.7	3	2.3
Tf	-38.2	-3.3	-1.5	Tf	-13	-2.1	-4.5	Tf	-4.6	-4.3	-2.3
Mhc2-Q1	-10.5	1.6	-1.0	Mhc2-Q1	-12.7	1.4	1.4	Mhc2-Q1	-19.5	1.7	-1.1

Table showing the fold changes of selected genes from neonatal, adult, and elderly mice 2 hours, 1 day, and 3 days after cecal slurry as compared to control mice ( $p < 0.001$ ).

### A. WBC Differential in Healthy Naïve Mice



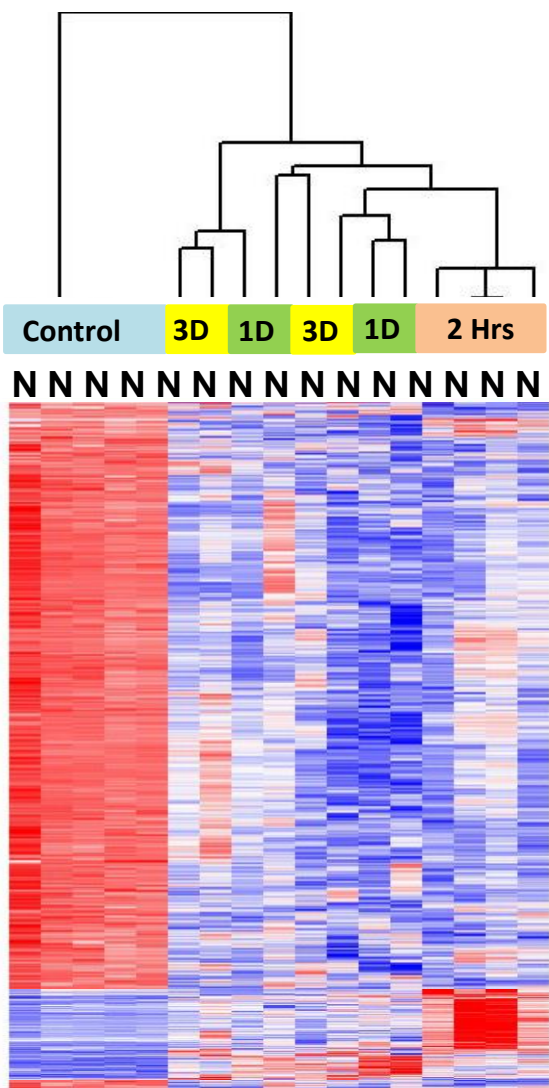
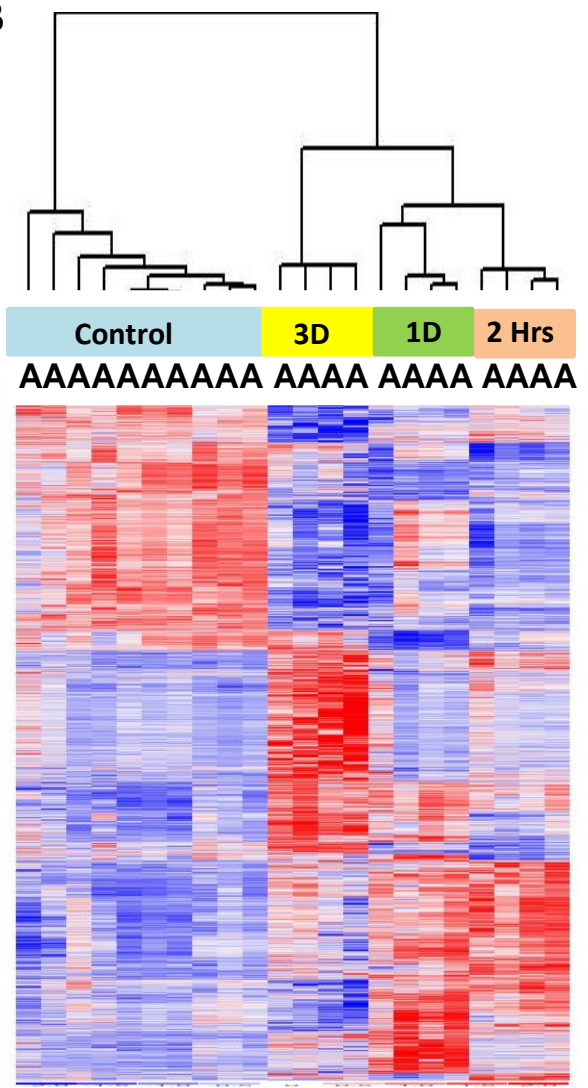
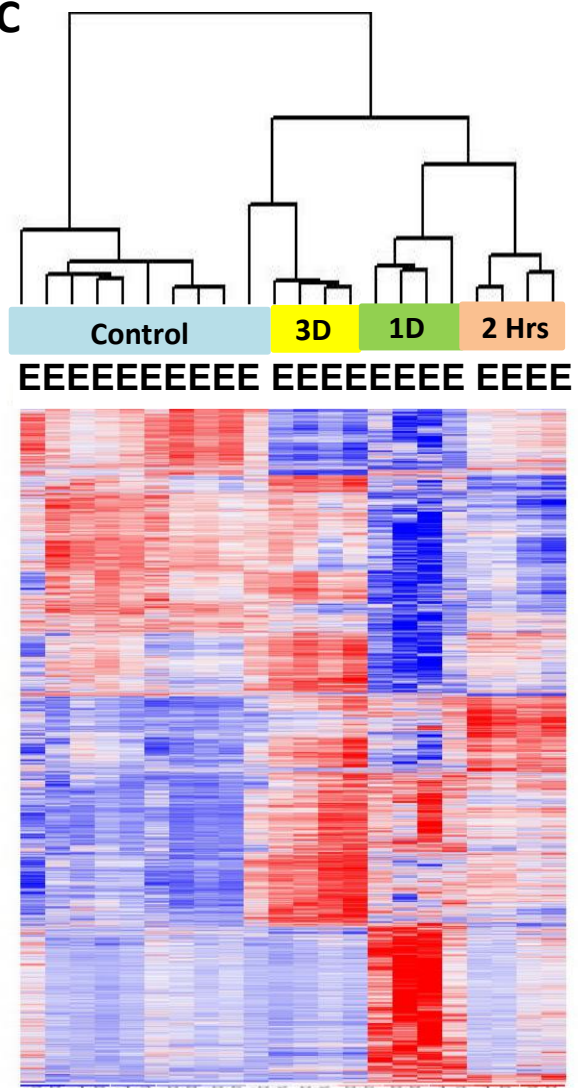
### B. WBC Differential 24 Hours after Sepsis



**Supplemental Figure 1 A.** Differential WBC subsets in naïve animals. n=3-6, (\* p<0.05). **B.** Differential WBC subsets 24 hours after sepsis. N=3-6. (\*p<0.05) (†p= 0.004).

**Supplemental Table 2. Immune Cell Trafficking-Activation** Table contains complete list of genes included in the functional category 'Immune Cell Trafficking-Activation.'

Genes	Neo	Young Adult	Elderly
AIP		-1.6	-3.7
BCL11B	-6	-1.5	-3.5
BCL2	1	2.2	3.6
BCL2L11	-1.44	4.9	4.6
BCL3	1.5	3.8	2.2
BCR	1.3	-1.9	1.8
C5AR1	-1.4	4	3.4
CALR	-1.5	2.1	-2.5
CAMP	-1.1	16.1	11.3
CARD11		-2.3	-1.3
CCL2		83.9	4.9
CCL4	1.5	10.8	2.1
CD14	-3.3	8.4	6.9
CD180	-1.5	-1.2	-2.5
CD48	-5.3	-4.5	-10.1
Cd55/Daf2	1.8	-11.8	-8.6
CLEC4E	-1.1	7.4	2.1
CMAHP		-2.9	-3.5
CNR2	-1.1	-4.1	-4.1
CPB2		-1.2	2.7
CSF1	1.7	2.3	-1.9
CSF1R		1.5	1.6
CSF2RB	-1.7	2.9	3.4
CSF3	1.8	8.7	1.6
CXCL1	5.8	395.9	145.8
CXCL10	1.3	7.8	1.5
CXCL3	8.2	231.8	115.6
CXCL6	1.3	5.9	1.9
CXCR5	-1.4	-5	-8.5
FCGR2B	-4	5.7	2.7
HLA-DMA	-1.8	-3.4	-6.7
HLA-DMB	1	-5.5	-17.4
HLA-DOA	1	-3	-5.3
HLA-DQB1		-7.5	-9
ICAM1	-1.1	3.7	1
IL10	1.4	18.7	2.5
IL1A	1.5	5.2	2.9
IL6	-1.2	54.3	1.7
ITK		2.7	1.4
KLF4		1.2	-1.6
LCN2	-1.72	22.1	11.8
LTF	-3.3	12	11.1
MALT1	1.3	2.1	-1.8
NFKB2	1.9	2	4.3
NFKBID		1.5	-1
NFKBIZ	-1.2	5.3	2.7
PLSCR1		8	4.2
PPP3CB	1.7	-1.2	-4
PRKCI	-1.8	1.4	-2
PTPRC		1.5	-2.1
PTPRJ	1.9	2	4.6
PYCARD	-2.4	1.8	2.3
RABGEF1	1.7	3.9	2.2
RHOA	1.5	2.2	3.7
RHOB		2.7	1.5
SMAD3		1.7	1
SMPD1	-1.2	-1.4	-2.1
SNCA	1.14	-2.5	-1.8
SOCS2	-1.4	6.7	2.1
STAT1	-1.54	3.8	-6.5
STAT3		2.5	3.3
TLR7	1.5	3.3	-1.9
TNF	1.6	2.8	1.6
TNFSF13		-3.7	-3.3
TNFSF9	1.3	2.6	1
TRAF5	-1.1	-3.2	-4.9
TREM1	2	4	3.4
VCAN	1.7	5.9	3.6
ZAP70	-1	-1.3	-2.2

**A****Neonates****B****Young Adults****C****Elderly**

**Supplemental Figure 2. Neonatal and elderly mice have significantly different gene expression patterns in response to CS polymicrobial sepsis over time.** **A.** Heat map showing the neonatal murine response to CS sepsis as compared to neonate control mice over time, with 1183 probe sets significantly changed compared to control ( $p < 0.001$ ). Neonates are unable to up regulate gene expression like adults and remain in a relatively unresponsive genomic state over a 3 day course of sepsis compared to baseline, and only have significant gene expression changes in one-sixth of their genome compared to young adult and elderly mice. **B.** Heat map showing the young adult murine response to CS sepsis as compared to adult control mice over time, with 6,973 probe sets significant at  $p < 0.001$ . **C.** Heat map showing the elderly murine response to CS sepsis as compared to adult control mice over time, with 6,486 probe sets significant at  $p < 0.001$ .