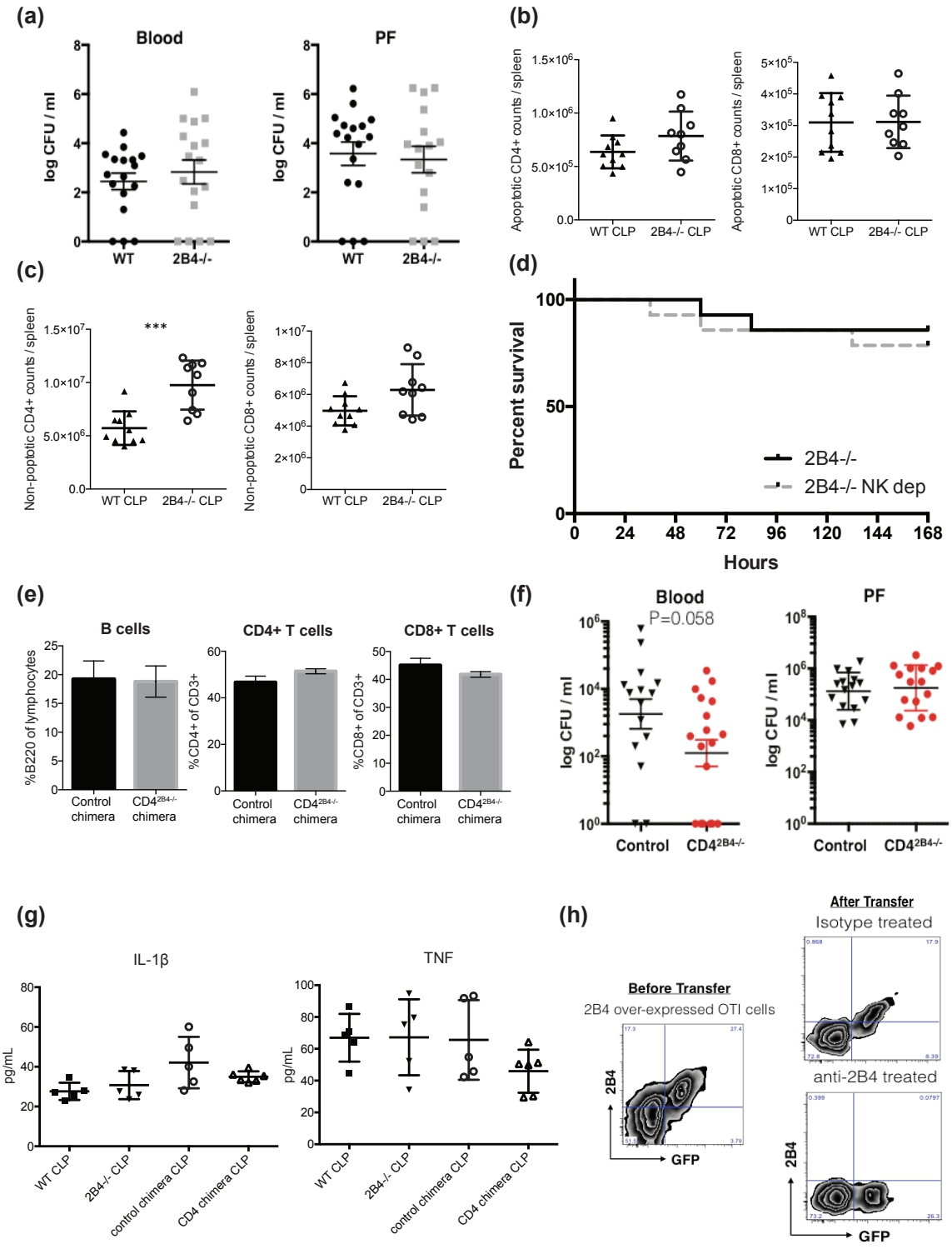

Supplemental Figure 1a. Bacterial cultures showed no difference between WT and 2B4$^{-/-}$ animals. WT and 2B4$^{-/-}$ animals were subjected to CLP. After 24 hours post-surgery, blood was collected by cardiac puncture and peritoneal fluid was obtained by injection of 2mL 0.9% sterile saline into the mouse peritoneum at 24 hours post-sepsis. Samples were serially diluted and a 100 µl aliquot of each sample was plated on sheep's blood agar plates and incubated at 37°C in 5% CO2

for 24 hours. Bacterial colony counts were obtained from plates containing fewer than 300 colonies and the colony-forming units (CFUs) per ml of original specimen were determined.

Supplemental Figure 1b. 2B4$^{-/-}$ and WT animals exhibited similar numbers of apoptotic cell after CLP. Age and gender matched WT and 2B4$^{-/-}$ animals were subjected to CLP and sacrificed at 24 hours. Apoptotic cells were identified as Caspase3/7^{+}SYTOX^{-} and the absolute cell counts are determined.

Supplemental Figure 1c. 2B4$^{-/-}$ animals retained higher number of non-apoptotic cell numbers after CLP. Age and gender matched WT and 2B4$^{-/-}$ animals were subjected to CLP and sacrificed at 24 hours. Non-apoptotic and non-necrotic cells were identified as Caspase3/7^{-}SYTOX^{-} and the absolute cell counts are determined.

Supplemental Figure 1d. NK depletion in 2B4$^{-/-}$ animals displayed no survival disadvantages. 2B4$^{-/-}$ animals were treated with anti-asialoGM1 one day before surgery to deplete NK cell population. NK cells depletion has confirmed by flow cytometer (data not shown). The CLP survival was performed on 2B4$^{-/-}$ animals and 2B4-/- animals with NK cells depletion.

Supplemental Figure 1e. The lymphocyte compositions of chimera animals are the same. Blood samples collected from control chimera and CD4$^{2B4-/-}$ chimera mice prior to CLP and composition of individual immune cell compartments was analyzed.

Supplemental Figure 1f. Bacterial cultures showed no difference between CD4$^{2B4-/-}$ chimeric animals and control chimera. The control chimera and CD4$^{2B4-/-}$ chimeric animals were subjected to CLP. The blood and peritoneal fluid were collected and bacterial load was determined at 24 hours post-surgery.

Supplemental Figure 1g. Serum cytokine levels are similar between chimeric animals. Serum were collected and the level of TNF and IL-1β at 24 h post-CLP in WT, 2B4$^{-/-}$, control WT chimeric and CD4$^{2B4-/-}$ chimeric animals were measured by Bio-Plex Pro™ (BIO-RAD).

Supplemental Figure 1h. Monoclonal anti-2B4 antibody (clone: 2B4) displayed no depletion effect on 2B4-expressing retrogenic OT-I cells. 2B4 over-expressed retrogenic OTI cells were generated by a previously described method [19]. Two million 2B4 over-expressed OTI cells were adoptively transferred into WT animals which were treated with intraperitoneal anti-2B4 mAB (250μg) to determine the depletion effect. Animals were sacrificed 24 hours after mAb treatment and transferred OTI T cells were analyzed by flow cytometry.

Table 1 — Septic Patients Demographics

Patient	Age	Gender	Weight (kg)	Race	Hospital LOS* (Days)	ICU LOS* (Days)	Intubated	Discharge status	Sepsis source	Sepsis Organism	WBC**	ALC***	2B4% of CD4+ T cells	2B4% of CD8+ T cells
#1	74	M	78	Black	4	3	Y	Dead	Respiratory	Bacillus species- not anthracis and coagulase negative Staphylococcus	25.5	2.5	22.0	31.8
#2	32	M	61.7	Black	18	2	N	Home	Urine	Escherichia coli and Stenotrophomonas maltophilia	3.3	0.1	1.5	65.4
#3	52	M	65.9	Black	17	7	Y	Skilled Nursing	Respiratory	Methicillin resistant staphylococcus aureus and Escherichia coli	14.9	0.4	5.6	65.5
#4	79	M	77	Black	10	4	Y	Skilled Nursing	Respiratory	Escherichia coli, Enterococcus faecalis, and Klebsiella pneumoniae ssp pneumoniae and Haemophilus influenzae	4.8	0.2	10.6	82.9
#5	87	F	82	Black	28	2	N	Skilled Nursing	Respiratory	Not identified	7.5	1	13.4	54.0
#6	19	F	64	Other	7	4	Y	Home	Respiratory	MSSA	7.5	0.8	61.6	96.8
#7	47	M	70	Caucasian	31	8	Y	Home	Urine	Staphylococcus aureus	12.5	0.4	2.5	16.3
#8	51	F	65	Black	11	10	Y	Hospice	Respiratory	Escherichia coli, yeast, Staphylococcus aureus, and Coagulase negative Staphylococcus	18.6	1.1	5.6	49.9
#9	49	M	90	Black	49	25	Y	Home	Respiratory	Klebsiella pneumonae	13.9	1	6.0	33.7
#10	33	M	136	Black	11	4	Y	Rehab	Blood	Not identified	7.1	1.4	0.9	45.9
#11	59	M	106	Black	21	2	Y	Home	Respiratory	Staphylococcus aureus, Alpha (Viridans) Streptococcus, Enterobacter aerogenes, Staphylococcus aureus	9.1	0.5	6.8	56.0
#12	46	M	121	Caucasian	30	16	Y	Rehab	Respiratory	Acinetobacter calcoaceticus-baumannii complex	11.2	2.1	1.6	26.9

Table 1: Septic Patients Demographics * Length of stay (LOT) **White Blood cell Counts (WBC), ***Absolutely Lymphocyte Counts (ALC)