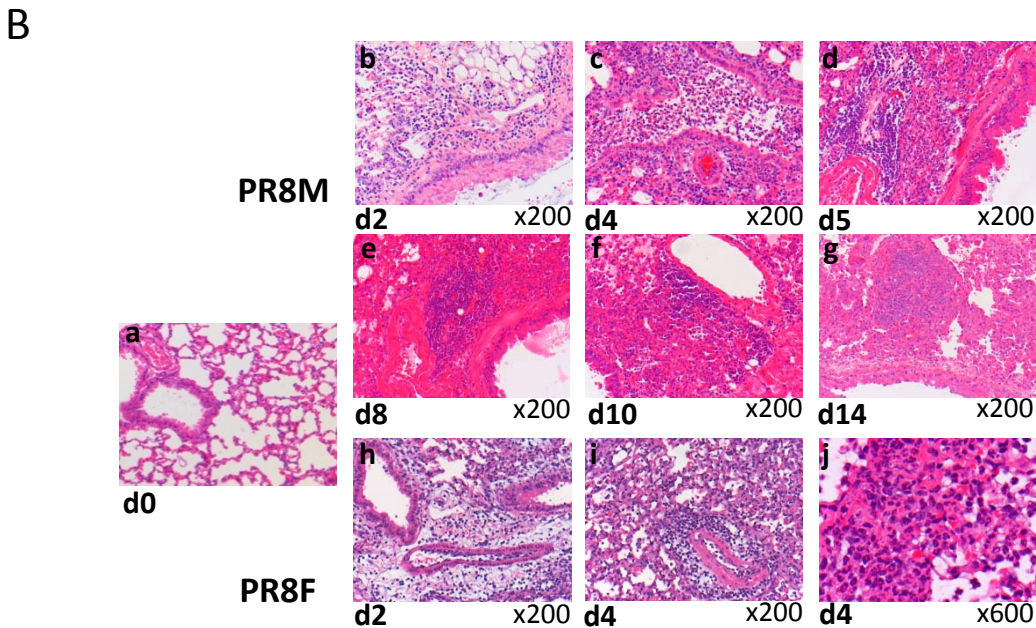
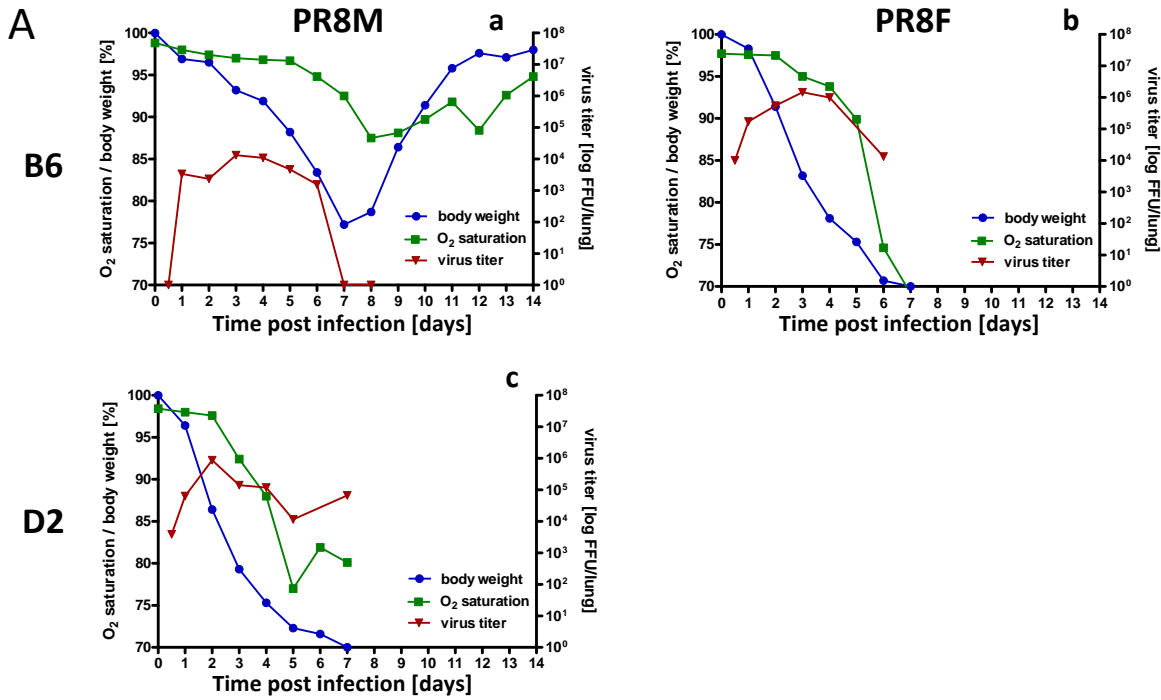


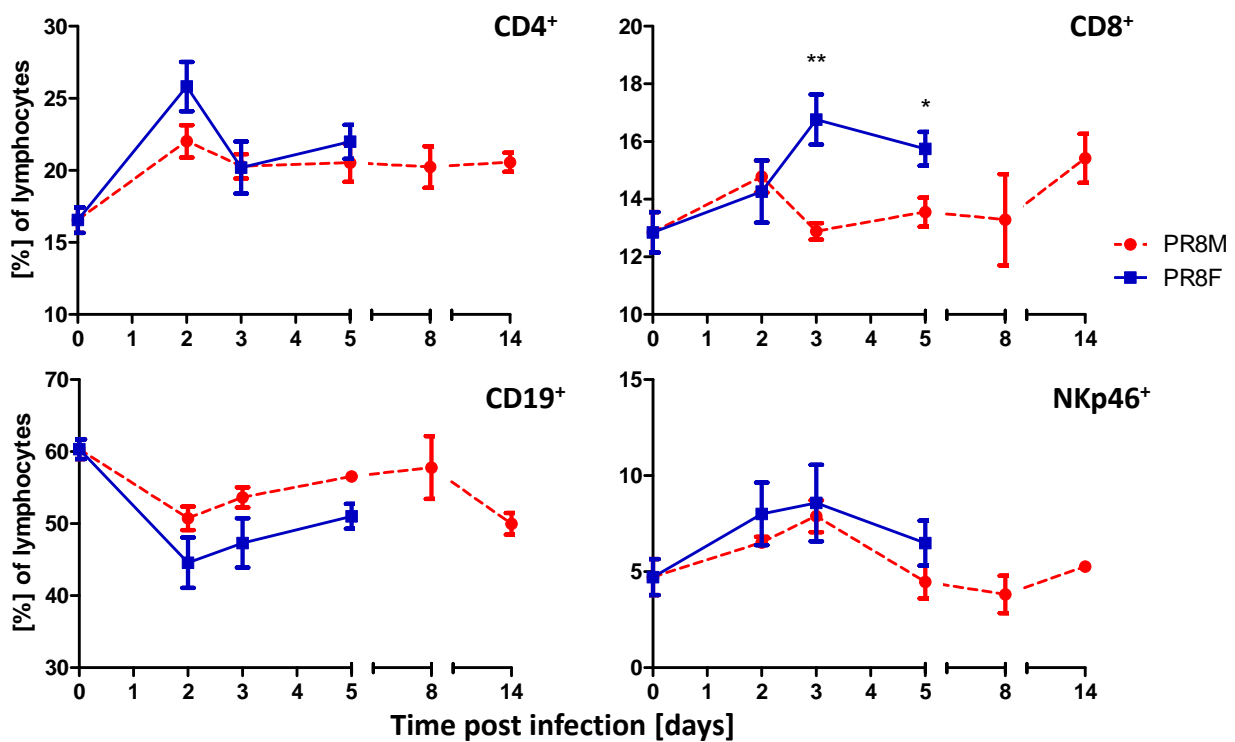
Supporting information: Figure I: general phenotypes

Female C57BL/6J & DBA/2J mice were infected intra-nasally with 2×10^3 FFU. Body weight loss (n=9), virus titer (n=3) and oxygen saturation (n=9) were monitored until day 14 p.i. in surviving animals (a: B6 - PR8M) or until death (b: B6 - PR8F & c: D2 - PR8M) (A). Representative histological sections of lungs (B) from non-infected controls (a) and mice infected with PR8M (b-g; days (d) 2, 4, 5, 8, 10, 14) or PR8F (h-j; d 2, 4) were prepared and stained with HE (n=3).



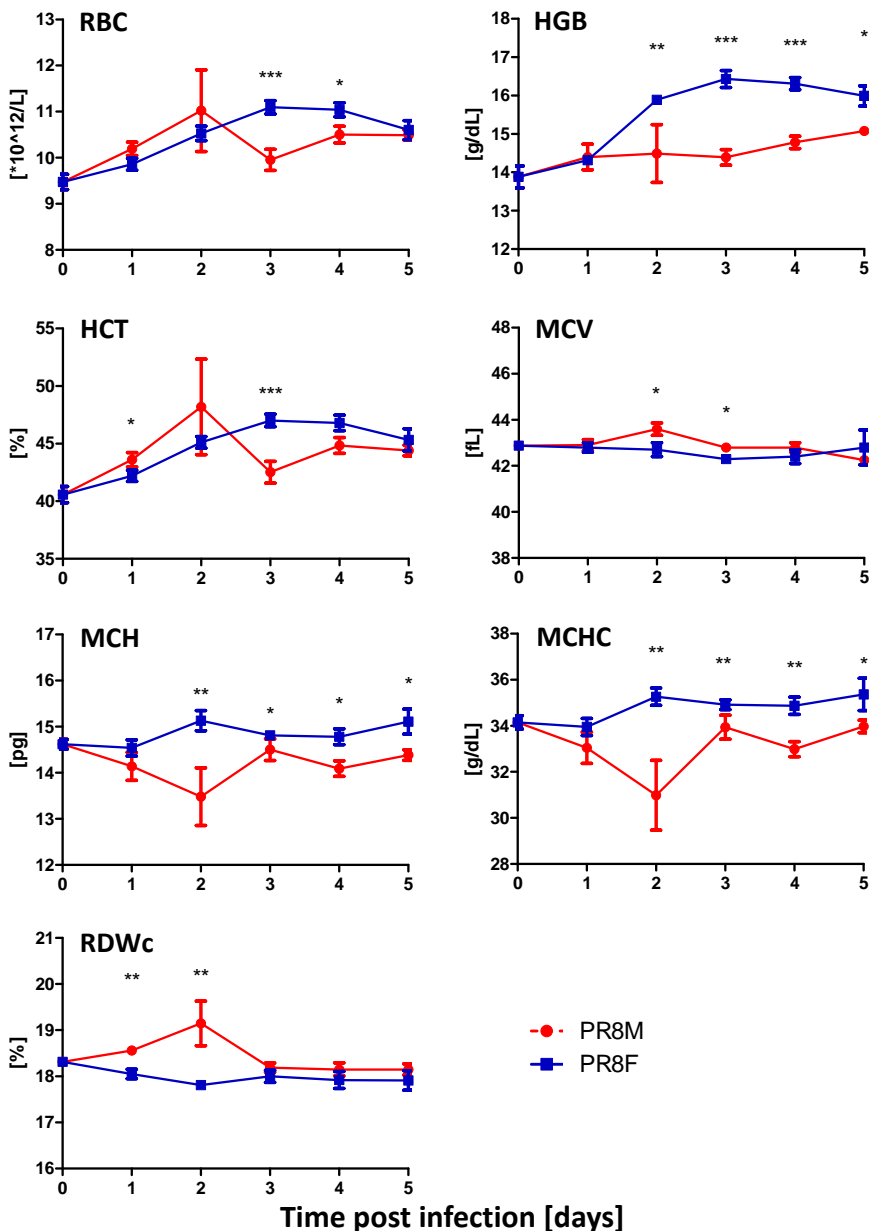
Supporting information: Figure II: Flow cytometry of blood

Lymphocytes from infected C57BL/6J mice (2×10^3 FFU) were differentiated by flow cytometry with respect to the expression of various cell surface markers: CD19 (B cells), NKp46 (NK cells), CD4 (T helper cells) and CD8 (cytotoxic T cells). The percentage of the individual cell populations gated in relation to all lymphocytes is depicted for days 1 to 14 (PR8M) or for days 1 to 5 (PR8F) p.i., respectively. Mean \pm SEM values were calculated from two independent experiments ($n=6$). Data were analyzed for statistically significant differences using non-parametric Mann-Whitney-U-test. *: p -value < 0.05 ; **: p -value < 0.01 .



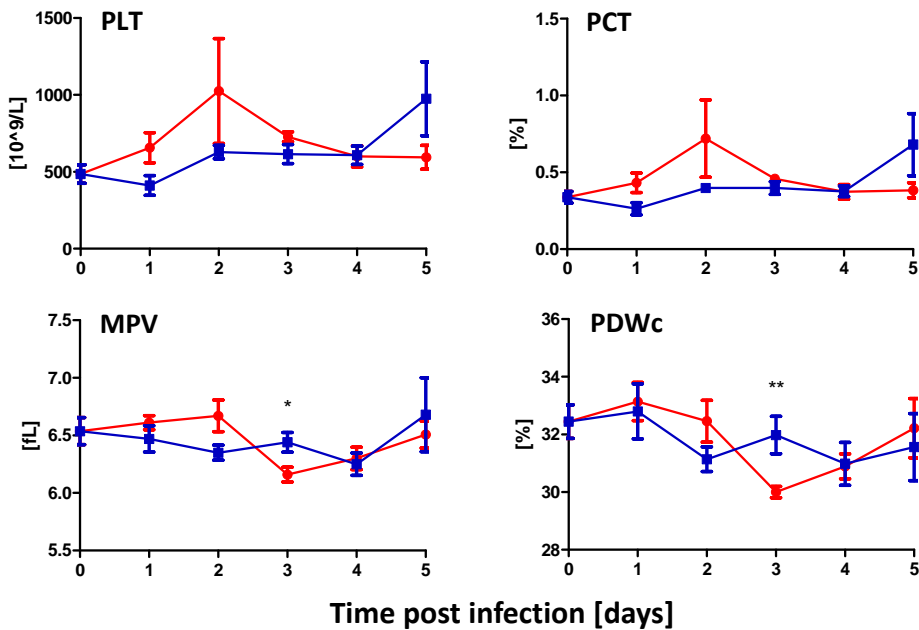
Supporting information: Figure III: red blood cell parameters

Several hematological parameters were determined from PR8M (red) and PR8F (blue) infected C57BL/6J mice (2×10^3 FFU) on days 1 to 5 p.i.: red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red blood cell distribution width (RDWc). Data were collected from two independent experiments (total $n=10$) for the first five days p.i. Data were analyzed for statistically significant differences using non-parametric Mann-Whitney-U-test. *: p value <0.05 ; **: p value <0.01 ; ***: p value <0.001 .



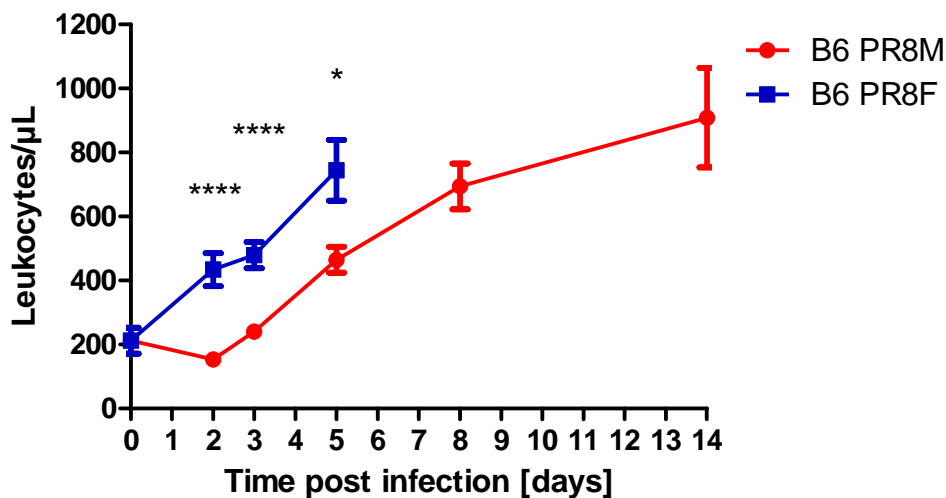
Supporting information: Figure IV: platelet parameters

Various platelet associated parameters were determined in the blood of PR8M (red) and PR8F (blue) infected C57BL/6J mice (2×10^3 FFU) during the course of infection: platelets (PLT), plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDWc). Data were collected from two independent experiments (total $n=10$) for the first five days p.i. Data were analyzed for statistically significant differences using non-parametric Mann-Whitney-U-test. *: p value < 0.05 ; **: p -value < 0.01 .



Supporting information: Figure V: Flow cytometry – absolute leukocyte counts

Flow cytometric analyses revealed quantitative differences of immune cell infiltration after PR8M versus PR8F infection. Lungs from infected C57BL/6J mice (2×10^3 FFU) were extracted and cell suspensions were analyzed by flow cytometry on days 0, 2, 3, 5, 8 and 14 p.i. After excluding dead cells leukocytes ($CD45^+$) were gated. For each measurement two to three lungs were pooled and data from two independent experiments were combined ($n=12-26$). Data were analyzed for statistically significant differences using non-parametric Mann-Whitney-U-test. *: p -value <0.05 ; ****: p -value <0.0001 .



Supporting information: Table I – C57BL/6J mice infected with PR8M, 2x10³FFU

	0		1		2		3		4		5		6		8		10		12		14			
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM		
B6 PR8M2x10³																								
day post infection																								
n	33		10		10		10		10		12		5		5		5		5		5		5	
WBC [10⁹/L]	12.31	0.96	7.15	0.54	7.73	1.09	6.83	0.49	10.04	1.54	13.53	1.40	18.89	1.50	21.89	1.02	16.73	1.11	16.29	0.81	15.45	2.08		
Lym [10⁹/L]	9.66	0.66	6.31	0.49	6.23	0.97	5.46	0.39	7.54	0.97	9.99	0.79	13.25	1.55	16.85	1.03	13.02	1.16	13.26	0.80	11.29	1.74		
Mon [10⁹/L]	0.36	0.08	0.15	0.04	0.27	0.08	0.17	0.04	0.40	0.15	0.49	0.16	0.99	0.41	0.13	0.00	0.34	0.24	0.46	0.25	1.11	0.44		
Neu [10⁹/L]	2.48	0.36	0.69	0.10	1.22	0.19	1.21	0.12	2.10	0.54	3.05	0.66	4.64	0.50	4.32	0.61	3.37	0.26	2.57	0.36	3.06	0.40		
Lym [%]	80.92	1.41	88.20	1.24	79.37	2.02	80.01	1.39	78.00	2.64	75.80	2.15	69.16	3.82	76.74	1.07	77.36	1.90	81.28	1.29	71.86	2.76		
Mon [%]	2.61	0.46	2.27	0.55	3.67	0.90	2.31	0.45	3.21	0.74	3.33	0.83	4.84	1.85	0.60	0.00	2.24	1.64	2.84	1.52	6.24	2.30		
Neu [%]	16.47	1.38	9.54	1.02	16.95	2.02	17.68	1.20	18.78	2.44	20.87	2.23	26.00	5.12	22.66	1.07	20.46	2.03	15.88	2.25	21.86	4.86		
RBC [*10¹²/L]	9.47	0.17	10.20	0.15	11.02	0.88	9.95	0.23	10.50	0.18	10.49	0.11	9.65	0.43	10.71	0.12	11.27	0.98	9.65	0.10	10.08	0.33		
HGB [g/dL]	13.88	0.28	14.40	0.33	14.49	0.75	14.39	0.20	14.78	0.16	15.08	0.11	15.04	0.20	16.36	0.17	15.56	0.21	14.70	0.11	15.28	0.25		
HCT [%]	40.58	0.70	43.61	0.62	48.20	4.15	42.52	0.95	44.85	0.68	44.40	0.47	40.57	1.79	45.43	0.57	42.39	0.77	39.68	0.55	41.60	1.17		
MCV [fL]	42.88	0.16	42.90	0.23	43.60	0.27	42.80	0.13	42.80	0.20	42.25	0.13	42.20	0.20	42.20	0.20	41.20	0.37	41.00	0.32	41.40	0.24		
MCH [pg]	14.62	0.10	14.14	0.30	13.48	0.63	14.50	0.23	14.09	0.17	14.38	0.11	15.76	0.94	15.30	0.04	15.14	0.17	15.22	0.08	15.16	0.32		
MCHC [g/dL]	34.15	0.29	33.05	0.68	30.99	1.52	33.94	0.52	32.99	0.32	33.98	0.27	37.50	2.26	36.00	0.12	36.68	0.40	37.06	0.42	36.74	0.63		
RDWc	18.32	0.08	18.56	0.09	19.15	0.48	18.19	0.10	18.15	0.14	18.15	0.12	18.32	0.19	21.24	2.70	18.64	0.10	19.30	0.51	19.00	0.15		
PLT	511.32	54.33	656.30	98.67	1025.20	341.42	727.10	32.03	601.10	68.62	594.25	77.16	343.60	49.11	378.00	44.71	284.60	27.91	199.20	9.32	214.80	28.53		
PCT	0.33	0.04	0.43	0.07	0.71	0.25	0.45	0.02	0.38	0.04	0.38	0.05	0.27	0.05	0.31	0.04	0.22	0.03	0.15	0.01	0.16	0.03		
MPV	6.54	0.12	6.61	0.06	6.67	0.14	6.16	0.06	6.30	0.10	6.51	0.12	7.66	0.27	8.10	0.35	7.42	0.32	7.52	0.18	7.50	0.32		
PDWc	32.44	0.58	33.14	0.66	32.46	0.72	30.00	0.20	30.89	0.43	32.22	1.03	37.04	0.70	37.26	0.90	35.42	0.82	35.40	0.37	34.44	1.31		

Supporting information: Table II- C57BL/6J mice infected with PR8M, 2x10⁵FFU

B6 PR8M 2x10⁵												
day post infection	0		1		2		3		4		5	
n	33		10		10		10		10		10	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
WBC [10⁹/L]	12.31	0.96	12.25	1.35	9.85	1.20	14.20	1.00	16.35	1.95	16.22	1.52
Lym [10⁹/L]	9.66	0.66	8.70	0.89	6.33	0.65	8.37	0.66	11.33	1.28	10.68	0.96
Mon [10⁹/L]	0.36	0.08	0.45	0.13	0.44	0.14	1.00	0.19	0.86	0.21	0.77	0.24
Neu [10⁹/L]	2.48	0.36	3.09	0.46	3.05	0.54	4.79	0.34	4.16	0.57	4.77	0.66
Lym [%]	80.92	1.41	71.61	1.53	66.35	2.97	59.11	1.78	70.16	1.34	66.41	2.02
Mon [%]	2.61	0.46	3.85	0.86	3.82	0.82	6.80	1.19	4.97	0.81	4.93	1.37
Neu [%]	16.47	1.38	24.53	1.56	29.80	2.68	34.08	1.55	24.82	1.33	28.73	2.14
RBC [*10¹²/L]	9.47	0.17	9.58	0.27	10.52	0.23	10.78	0.16	10.72	0.09	9.96	0.26
HGB [g/dL]	13.88	0.28	14.55	0.11	16.14	0.16	16.28	0.09	15.56	0.16	15.35	0.15
HCT [%]	40.58	0.70	40.86	1.20	44.58	1.07	45.59	0.72	45.37	0.41	42.48	1.06
MCV [fL]	42.88	0.16	42.70	0.21	42.30	0.26	42.30	0.21	42.20	0.29	42.70	0.30
MCH [pg]	14.62	0.10	15.35	0.57	15.39	0.32	15.13	0.26	14.53	0.14	15.51	0.46
MCHC [g/dL]	34.15	0.29	35.96	1.39	36.35	0.86	35.79	0.65	34.32	0.33	36.37	1.11
RDWc [%]	18.32	0.08	18.11	0.07	18.34	0.32	18.08	0.22	18.04	0.14	17.64	0.18
PLT [10⁹/L]	511.32	54.33	428.30	50.46	718.30	75.15	570.60	68.51	618.70	61.47	618.8	99.18
PCT [%]	0.33	0.04	0.28	0.03	0.46	0.05	0.37	0.05	0.38	0.04	0.38	0.06
MPV [fL]	6.54	0.12	6.55	0.20	6.36	0.06	6.44	0.13	6.23	0.10	6.16	0.11
PDWc [%]	32.44	0.58	33.13	1.02	32.37	0.74	32.34	0.70	31.62	0.82	29.94	1.18

Supporting information: Table III- C57BL/6J mice infected with PR8F,2x10³FFU

B6 PR8F2x10 ³	0		1		2		3		4		5	
day post infection	0		1		2		3		4		5	
n	33		10		10		10		10		12	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
WBC [10 ⁹ /L]	12.31	0.96	13.39	1.52	10.27	0.74	14.00	1.06	11.33	1.79	14.26	1.70
Lym [10 ⁹ /L]	9.66	0.66	10.18	1.07	7.24	0.53	7.01	0.67	6.13	1.18	8.70	1.11
Mon [10 ⁹ /L]	0.36	0.08	0.39	0.16	0.47	0.09	0.94	0.22	0.76	0.22	1.08	0.23
Neu [10 ⁹ /L]	2.48	0.36	2.82	0.59	2.56	0.28	5.75	0.52	4.45	0.51	4.48	0.68
Lym [%]	80.92	1.41	77.01	2.37	70.64	1.62	53.13	2.16	52.21	1.98	60.49	3.20
Mon [%]	2.61	0.46	3.13	1.20	4.58	0.82	6.07	1.17	5.70	1.03	7.39	1.18
Neu [%]	16.47	1.38	19.86	3.01	24.79	1.91	40.80	1.75	42.10	2.66	32.11	3.47
RBC [*10 ¹² /L]	9.47	0.17	9.86	0.13	10.53	0.16	11.10	0.14	11.04	0.15	10.60	0.20
HGB [g/dL]	13.88	0.28	14.32	0.07	15.89	0.08	16.43	0.22	16.31	0.16	15.99	0.26
HCT [%]	40.58	0.70	42.21	0.49	45.11	0.50	47.02	0.54	46.80	0.67	45.32	0.97
MCV [fl]	42.88	0.16	42.80	0.20	42.70	0.30	42.30	0.15	42.40	0.31	42.80	0.76
MCH [pg]	14.62	0.10	14.54	0.17	15.13	0.22	14.81	0.09	14.78	0.17	15.11	0.27
MCHC [g/dL]	34.15	0.29	33.95	0.37	35.26	0.38	34.92	0.21	34.87	0.38	35.36	0.70
RDWc	18.32	0.08	18.05	0.10	17.81	0.08	18.00	0.13	17.92	0.18	17.91	0.21
PLT	511.32	54.33	411.10	64.69	628.00	44.20	614.90	62.29	607.80	59.24	975.00	241.15
PCT	0.33	0.04	0.26	0.04	0.40	0.03	0.40	0.04	0.38	0.03	0.68	0.20
MPV	6.54	0.12	6.47	0.11	6.35	0.07	6.44	0.09	6.25	0.10	6.68	0.32
PDWc	32.44	0.58	32.80	0.96	31.14	0.43	31.98	0.65	30.98	0.74	31.56	1.16

Supporting information: Table IV-C57BL/6J mice infected with hvPR8, 2x10³FFU

B6 hvPR8 2x10 ³												
day post infection	0		1		2		3		4		5	
n	33		10		10		10		10		10	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
WBC [10 ⁹ /L]	12,31	0,96	15,50	1,19	9,90	1,13	14,51	1,67	12,78	1,97	11,36	2,24
Lym [10 ⁹ /L]	9,66	0,66	10,98	0,73	5,74	0,72	7,46	1,03	6,66	1,17	6,12	1,23
Mon [10 ⁹ /L]	0,36	0,08	1,05	0,17	0,50	0,10	1,62	0,76	1,12	0,24	1,13	0,27
Neu [10 ⁹ /L]	2,48	0,36	3,47	0,51	3,67	0,44	6,15	0,55	5,00	0,64	4,11	0,82
Lym [%]	80,92	1,41	71,59	1,99	57,44	2,16	51,04	1,87	50,56	2,65	53,74	3,30
Mon [%]	2,61	0,46	6,84	1,08	5,20	0,89	5,47	1,22	8,37	0,95	8,93	0,65
Neu [%]	16,47	1,38	21,57	2,44	37,37	2,31	43,50	2,18	41,08	2,48	37,35	3,29
RBC [*10 ¹² /L]	9,47	0,17	9,92	0,13	10,75	0,12	11,11	0,10	11,11	0,21	11,64	0,24
HGB [g/dL]	13,88	0,28	14,69	0,12	15,83	0,21	16,36	0,14	16,62	0,13	17,44	0,22
HCT [%]	40,58	0,70	42,58	0,54	45,82	0,55	47,16	0,41	47,02	0,94	50,11	0,93
MCV [fL]	42,88	0,16	43,10	0,10	42,60	0,16	42,40	0,16	42,50	0,34	43,22	0,97
MCH [pg]	14,62	0,10	14,81	0,16	14,73	0,16	14,73	0,14	15,03	0,28	15,03	0,26
MCHC [g/dL]	34,15	0,29	34,49	0,37	34,58	0,44	34,72	0,38	35,48	0,66	34,87	0,44
RDWc	18,32	0,08	18,04	0,11	18,00	0,13	18,03	0,12	17,94	0,24	18,26	0,15
PLT	511,32	54,33	435,90	49,60	642,90	81,85	656,20	70,10	786,90	49,68	1015,65	334,18
PCT	0,33	0,04	0,28	0,03	0,41	0,05	0,42	0,05	0,52	0,03	0,93	0,19
MPV	6,54	0,12	6,61	0,17	6,42	0,12	6,37	0,14	6,70	0,16	6,84	0,30
PDWc	32,44	0,58	32,04	0,86	32,36	0,83	31,89	0,76	31,75	0,92	33,26	0,69

Supporting information: Table V- DBA/2J mice infected with PR8M, 2x10³FFU

D2 PR8M2x10 ³	0		1		2		3		4		5	
day post infection	24-29		10		9		10		10		12	
n	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
WBC [10 ⁹ /L]	16.15	0.77	8.25	0.59	7.72	0.88	7.35	0.25	11.85	1.87	15.48	1.75
Lym [10 ⁹ /L]	11.15	0.53	6.73	0.42	4.38	0.62	3.82	0.21	6.75	1.12	8.99	1.12
Mon [10 ⁹ /L]	0.51	0.12	0.21	0.03	0.33	0.05	0.41	0.07	0.52	0.14	0.69	0.18
Neu [10 ⁹ /L]	4.50	0.29	1.29	0.18	3.02	0.31	3.13	0.18	4.57	0.78	5.80	0.76
Lym [%]	69.39	1.14	82.40	1.26	55.41	2.91	51.87	2.22	57.13	2.10	57.99	3.25
Mon [%]	3.05	0.68	2.62	0.38	4.24	0.61	5.55	0.82	4.88	0.96	4.46	0.88
Neu [%]	27.56	1.25	14.98	1.32	40.33	2.64	42.61	2.16	37.99	1.46	37.54	3.46
RBC [*10 ¹² /L]	10.89	0.13	11.11	0.18	10.34	0.68	11.93	0.12	12.11	0.20	12.87	0.20
HGB [g/dL]	14.70	0.06	14.53	0.23	13.13	0.85	15.64	0.13	15.99	0.20	16.95	0.34
HCT [%]	45.48	0.54	47.12	0.70	44.37	2.76	49.78	0.48	50.00	0.71	52.42	0.82
MCV [fL]	41.75	0.25	42.30	0.33	42.89	0.45	41.80	0.25	41.30	0.26	40.70	0.21
MCH [pg]	13.55	0.17	13.08	0.12	12.74	0.15	13.10	0.14	13.21	0.16	13.16	0.07
MCHC [g/dL]	32.44	0.42	30.84	0.33	29.61	0.39	31.41	0.30	32.02	0.34	32.34	0.27
RDWc	19.88	0.15	20.38	0.12	20.52	0.23	20.04	0.22	19.95	0.44	19.77	0.29
PLT	342.79	59.22	683.20	103.20	680.78	112.85	937.20	68.67	692.30	126.79	706.10	136.73
PCT	0.23	0.04	0.47	0.07	0.49	0.09	0.66	0.05	0.48	0.09	0.51	0.10
MPV	6.68	0.11	6.76	0.15	7.11	0.14	6.97	0.19	6.76	0.20	7.09	0.18
PDWc	34.01	0.47	34.33	0.50	35.56	0.74	34.65	0.97	34.84	0.98	36.61	0.90