

**Fairhurst et al Supplementary Table 1.**

**Summary of splenic leukocytes.** Flow Cytometry Analysis of Splenic leukocyte lineage and activation in 9 month old male mice. 1-way ANOVA was used to analyse data as described in Experimental Procedures. Significant differences between B6.*Sle1Yaa* and B6.*Sle1YaaTLR7* are shown; \*p=0.05, \*\*p=0.01, \*\*\*p=0.001. Bold indicates percentage of the total. Normal font is a subgroup of the bolded font.

	<b>B6 (n=5)</b>	<b>B6.<i>Sle1</i> (n=5)</b>	<b>B6.<i>Sle1Yaa</i> (n=5)</b>	<b>B6.<i>Sle1YaaTLR7</i>- (n=5)</b>
	<b>Mean ± SE</b>	<b>Mean ± SE</b>	<b>Mean ± SE</b>	<b>Mean ± SE</b>
<b>Total Cell count (x10<sup>7</sup>)</b>	11.4 ± 1.4	13.3 ± 0.9	50.4 ± 13.1	12.9 ± 0.7
<b>CD19+</b>	58.4 ± 2.7	53.2 ± 2.5	27.9 ± 4.7	51.5 ± 1.7***
% CD69+	8.8 ± 1.6	9.9 ± 1.7	19.5 ± 1.8	10.1 ± 1.0*
CD86 MFI	39.1 ± 8.4	64.3 ± 5.9	90.1 ± 5.0	68.6 ± 7.3
<b>Follicular B (CD23<sup>+</sup>CD21<sup>+</sup>IgM<sup>lo</sup>)</b>	39.7 ± 1.2	36.9 ± 1.5	17.6 ± 3.0	36.3 ± 1.0***
CD86 MFI	45.5 ± 6.9	70.2 ± 6.5	62.1 ± 4.4	73.2 ± 5.8
<b>T1 (CD23<sup>-</sup>CD21<sup>-</sup>IgM<sup>+</sup>)</b>	3.2 ± 0.3	2.0 ± 0.1	1.5 ± 0.3	2.1 ± 0.2
<b>T2 (CD23<sup>+</sup>CD21<sup>hi</sup>IgM<sup>hi</sup>)</b>	1.9 ± 0.3	1.9 ± 0.3	0.9 ± 0.3	1.6 ± 0.2
<b>MZ (CD23<sup>+</sup>CD21<sup>-</sup>IgM<sup>+</sup>)</b>	2.0 ± 0.1	2.2 ± 0.1	1.0 ± 0.2	1.5 ± 0.2
<b>B1a (CD5<sup>+</sup>CD23<sup>-</sup>B220<sup>+</sup>)</b>	1.1 ± 0.1	1.1 ± 0.1	1.6 ± 0.3	1.0 ± 0.1
<b>B1b (CD5<sup>-</sup>CD23<sup>-</sup>B220<sup>+</sup>)</b>	8.4 ± 0.6	7.7 ± 0.4	6.1 ± 0.6	7.1 ± 0.2
<b>B2 (CD5<sup>-</sup>CD23<sup>+</sup>B220<sup>+</sup>)</b>	43.9 ± 1.6	39.9 ± 1.8	17.8 ± 3.4	39.7 ± 1.4***
<b>Plasmablast (B220<sup>+</sup>CD138<sup>+</sup>)</b>	2.0 ± 0.4	2.0 ± 0.3	1.9 ± 0.7	1.9 ± 0.5
<b>Plasma (B220<sup>-</sup>CD138<sup>+</sup>)</b>	1.4 ± 0.2	1.6 ± 0.2	4.0 ± 0.4	2.4 ± 0.2
<b>CD4+</b>	20.9 ± 0.7	21.9 ± 1.7	17.1 ± 1.6	21.1 ± 1.7*
%CD69+	15.8 ± 1.5	21.5 ± 2.3	39.3 ± 2.4	24.8 ± 3.1**
CD62L <sup>+</sup> CD44 <sup>lo</sup>	55.7 ± 0.8	42.1 ± 6.3	17.5 ± 3.7	41.3 ± 6.5*
CD62L <sup>-</sup> CD44 <sup>h</sup>	38.9 ± 0.7	51.8 ± 6.3	77.0 ± 3.5	51.3 ± 5.5**
CD25 <sup>+</sup> CD127 <sup>-</sup>	10.4 ± 0.8	11.9 ± 0.6	14.2 ± 0.5	12.3 ± 1.0
CD25 <sup>+</sup> CD127 <sup>+</sup>	1.4 ± 0.2	1.6 ± 0.3	3.7 ± 0.3	1.7 ± 0.3***
ICOS MFI	419 ± 14	603 ± 60	1482 ± 19	719 ± 114
PD-1 MFI	115 ± 7	188 ± 30	429 ± 65	188 ± 41
CXCR5 MFI	22 ± 4.2	65 ± 19.7	117 ± 7.9	68 ± 20.9
<b>CD8+</b>	12.4 ± 0.5	12.7 ± 0.7	4.9 ± 1.4	12.0 ± 1.5**
%CD69+	11.8 ± 1.0	14.2 ± 2.7	27.1 ± 1.8	14.9 ± 1.6
CD62L <sup>+</sup> CD44 <sup>lo</sup>	87.1 ± 1.5	76.4 ± 9.3	50.4 ± 7.9	86.5 ± 2.4
CD62L <sup>-</sup> CD44 <sup>h</sup>	8.3 ± 0.8	13.7 ± 4.2	38.4 ± 6.2	7.7 ± 1.3*
PD-1 MFI	210.6 ± 19.2	293.2 ± 57.1	430.9 ± 29.1	258.5 ± 31.0*

<b>Total Myeloid (CD11b+)</b>	3.0 ± 0.3	5.0 ± 0.3	29.1 ± 5.3	5.4 ± 0.5***
%CD69+	10.0 ± 3.0	7.7 ± 1.0	20.1 ± 2.5	10.8 ± 1.1*
CD11b MFI	1006 ± 21.9	1236 ± 44.1	2292 ± 214.7	1301 ± 64.0***
MHC II MFI	4786 ± 735	1557 ± 288	429 ± 145	1789 ± 440***
CD62L MFI	3428 ± 226	2074 ± 396	737 ± 116	2376 ± 155
CXCR4 MFI	97 ± 15	174 ± 27	642 ± 58	217 ± 17***
CD86 MFI	798 ± 44	599 ± 46	331 ± 95	675 ± 97*
<b>PMNs</b>	1.4 ± 0.9	2.2 ± 0.8	8.0 ± 2.0	1.9 ± 0.6***
CD11b MFI	3351 ± 188	2386 ± 120	3987 ± 704	4458 ± 334
MHC II MFI	442 ± 30	267 ± 35	127 ± 21	201 ± 30
CD62L MFI	3834 ± 178	2479 ± 588	888 ± 244	2321 ± 148
CXCR4 MFI	303 ± 26	247 ± 42	471 ± 65	220 ± 9**
CD86 MFI	315 ± 16	140 ± 20	86 ± 31	113 ± 23
<b>Gr1+monocytes</b>	1.0 ± 0.2	1.9 ± 0.2	8.9 ± 1.6	1.6 ± 0.2***
CD11b MFI	1873 ± 36	2026 ± 107	2717 ± 228	2327 ± 91
MHC II MFI	882 ± 78	587 ± 97	183 ± 28	418 ± 69
CD62L MFI	2749 ± 188	1903 ± 338	927 ± 93	1776 ± 62
CXCR4 MFI	210 ± 41	156 ± 23	440 ± 65	197 ± 8**
CD86 MFI	592 ± 42	425 ± 40	173 ± 59	361 ± 30**
<b>Gr1lo/-monocytes</b>	1.7 ± 0.1	2.8 ± 0.1	12.9 ± 3.6	2.7 ± 0.2**
CD11b MFI	1526 ± 22	1596 ± 37	2086 ± 72	1624 ± 17**
MHC II MFI	9689 ± 548	5917 ± 498	1959 ± 830	7438 ± 1038**
CD62L MFI	2634 ± 482	1139 ± 128	328 ± 71	150 ± 195*
CXCR4 MFI	66 ± 10	189 ± 30	671 ± 76	178 ± 20
CD86 MFI	1142 ± 89	977 ± 36	732 ± 120	1102 ± 143

**Fairhurst et al: Supplementary Table 2.**

**Summary of splenic leukocytes in the kidney.** Flow Cytometry Analysis of leukocyte lineage

and activation in 9 month old male mice. 1-way ANOVA was used to analyse data as described

in Experimental Procedures. Significant differences between B6.*Sle1Yaa* and B6.*Sle1YaaTLR7*

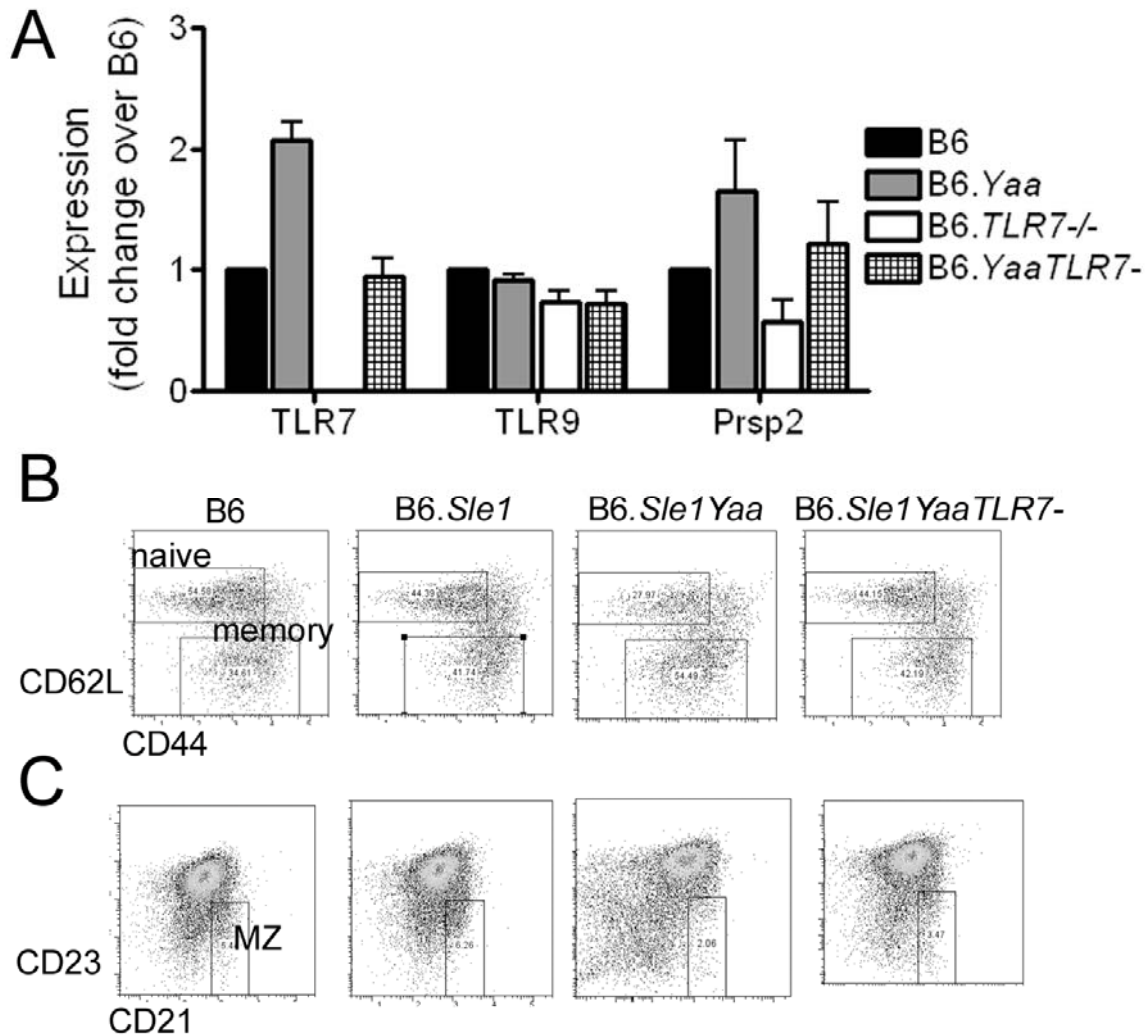
are shown; \*p=0.05, \*\*p=0.01, \*\*\*p=0.001

	<b>B6 (n=5)</b>	<b>B6.<i>Sle1</i> (n=5)</b>	<b>B6.<i>Sle1Yaa</i> (n=5)</b>	<b>B6.<i>Sle1YaaTLR7</i>- (n=5)</b>
	<b>Mean ± SE</b>	<b>Mean ± SE</b>	<b>Mean ± SE</b>	<b>Mean ± SE</b>
<b>Total Cell count (x10<sup>7</sup>)</b>	16.7 ± 1.7	14.0 ± 0.9	22.6 ± 4.7	16.0 ± 1.9
<b>CD19+</b>	9.0 ± 1.2	8.6 ± 2.0	2.9 ± 0.6	7.3 ± 0.8
% CD69+	18.0 ± 1.0	22.9 ± 4.9	48.5 ± 7.9	17.8 ± 2.2**
CXCR4 MFI	201 ± 49	227 ± 84	670 ± 162	172 ± 33**
<b>CD4+</b>	12.3 ± 1.4	12.4 ± 1.3	22.1 ± 2.5	12.6 ± 1.3**
%CD69+	34.0 ± 1.4	33.1 ± 2.2	35.5 ± 2.7	38.5 ± 2.6
CD62L <sup>+</sup> CD44 <sup>lo</sup>	15.7 ± 3.4	17.0 ± 3.5	12.5 ± 5.7	8.8 ± 1.3
CD62L <sup>-</sup> CD44 <sup>h</sup>	77.2 ± 4.7	74.7 ± 5.0	61.1 ± 6.9	86.0 ± 1.8
ICOS MFI	610 ± 60	592 ± 25	1253 ± 123	635 ± 38***
PD-1 MFI	280 ± 55	453 ± 121	626 ± 162	259 ± 44
<b>CD8+</b>	13.7 ± 1.1	11.0 ± 1.8	8.1 ± 1.2	6.6 ± 0.8
%CD69+	50.0 ± 1.3	44.4 ± 2.3	56.8 ± 7.4	47.8 ± 0.5
CD62L <sup>+</sup> CD44 <sup>lo</sup>	20.7 ± 1.9	29.4 ± 8.7	16.7 ± 2.6	19.3 ± 3.2
CD62L <sup>-</sup> CD44 <sup>h</sup>	50.8 ± 10.8	33.2 ± 13.6	65.0 ± 5.5	71.4 ± 2.9*
<b>Total Myeloid (CD11b+)</b>	56.7 ± 1.3	61.1 ± 2.3	70.3 ± 2.7	67.4 ± 1.3
CD11b MFI	1818 ± 58	2068 ± 150	3773 ± 124	2292 ± 94
MHC II MFI	9906 ± 346	8075 ± 1599	2327 ± 1308	10182 ± 752*
CD62L MFI	82.6 ± 9.9	74.8 ± 5.4	42.7 ± 33.4	24.3 ± 14.1
CXCR4 MFI	430 ± 19	417 ± 49	448 ± 46	365 ± 25
CD86 MFI	1504 ± 39.0	1463 ± 122	1218 ± 204	1450 ± 82
<b>PMNs</b>	1.8 ± 1.0	1.9 ± 0.7	1.7 ± 1.0	1.3 ± 0.2
CD11b MFI	12584 ± 506	12580 ± 1605	19249 ± 1223	14815 ± 520
MHC II MFI	123 ± 71	91 ± 76	325 ± 298	136 ± 49
<b>Gr1<sup>++</sup>monocytes</b>	2.0 ± 0.4	2.4 ± 0.3	3.7 ± 0.3	1.7 ± 0.1***
CD11b MFI	6659 ± 216	6641 ± 210	8171 ± 277	6889 ± 71**
MHC II MFI	276 ± 77	365 ± 108	662 ± 342	429 ± 54
CXCR4 MFI	21 ± 9.9	42.6 ± 27	262.9 ± 63.1	8.4 ± 21.6**
CD86 MFI	531 ± 42	692 ± 127	1145 ± 107	551 ± 45
%CD69+	29.2 ± 1.6	29.0 ± 3.0	39.2 ± 5.1	24.9 ± 1.6*

<b>Gr1+monocytes</b>	21.9 ± 0.4	24.2 ± 1.3	29.2 ± 1.2	28.0 ± 1.3
CD11b MFI	1437 ± 42	1674 ± 141	2977 ± 124	1866 ± 75
MHC II MFI	10754 ± 288	9121 ± 1530	2635 ± 1266	10018 ± 603***
CD62L MFI	139 ± 16	112 ± 7	88 ± 37	52 ± 22
CXCR4 MFI	639 ± 26	591 ± 72	592 ± 55	504 ± 31
CD86 MFI	1633 ± 73	1613 ± 101.2	1227 ± 181	1495 ± 107
%CD69+	70.5 ± 1.1	65.0 ± 3.6	59.4 ± 5.8	62.8 ± 1.8
<b>Gr1+monocytes</b>	29.3 ± 0.6	30.9 ± 1.1	32.7 ± 1.8	34.5 ± 0.9
CD11b MFI	1740 ± 53	1955 ± 173	3716 ± 132	2386 ± 118
MHC II MFI	11721 ± 268	9689 ± 1818	2693 ± 1704	11859 ± 923
CXCR4 MFI	507 ± 18	489 ± 55	436 ± 45	411 ± 26
CD86 MFI	1712 ± 70	1637 ± 126	1234 ± 212	1557 ± 69
%CD69+	62.7 ± 1.3	58.1 ± 3.7	47.3 ± 6.3	55.3 ± 2.2

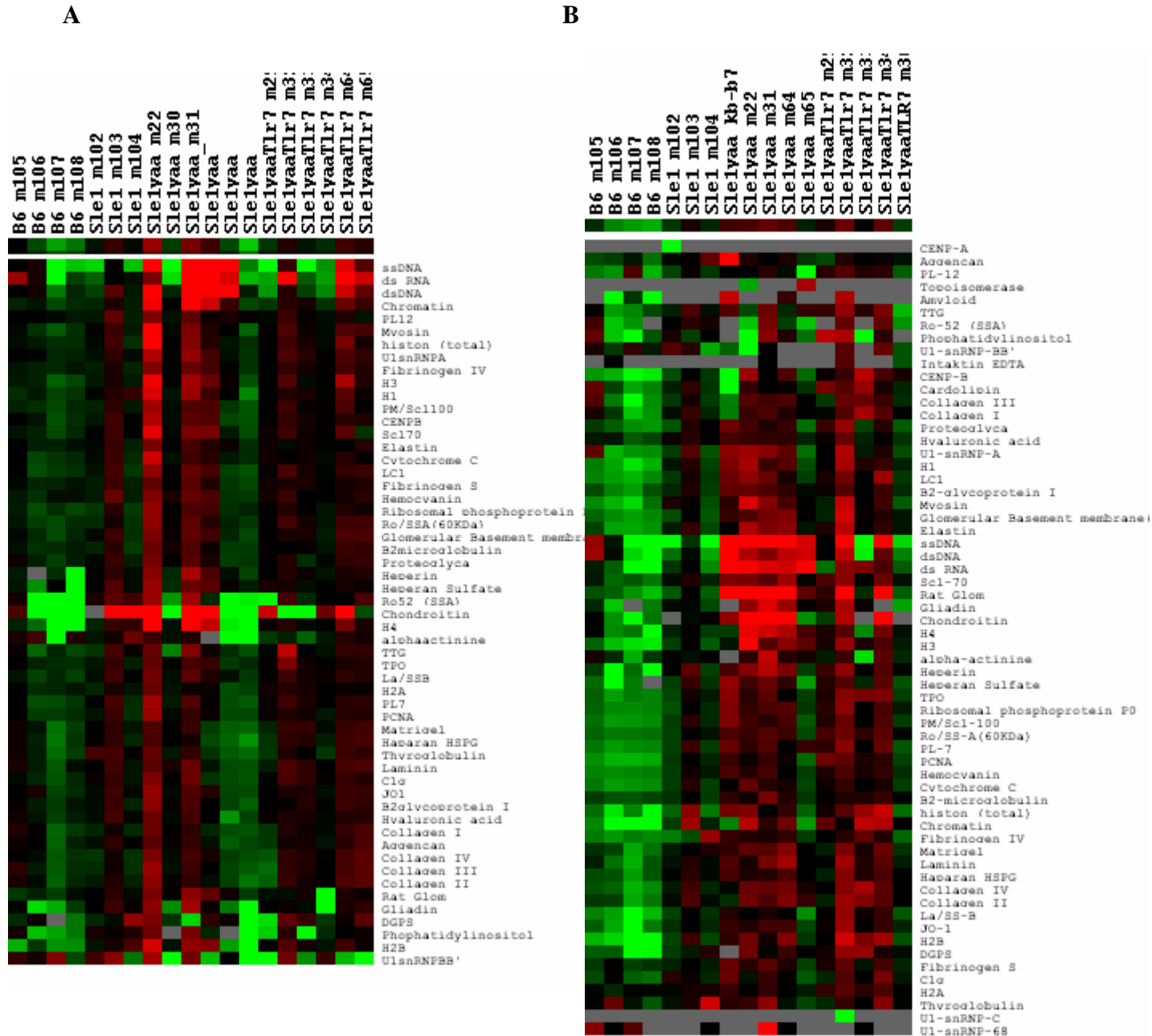
Fairhurst et al: Supplemental Figure 1:

**Deletion of an additional copy of TLR7 in B6.Yaa Mice.** B6.Yaa mice were backcrossed to TLR7 deficient mice and the mRNA expression examined using RT-PCR with Primer sets from Applied Biosystems (A). Flow cytometry plots of 9 month old male B6, B6.Sle1, B6.Sle1Yaa and B6.Sle1YaaTLR7- mice demonstrate a resolution of phenotypes. (B&C). The CD4+ memory population is restored to normal levels on TLR7 deletion (B). Marginal Zone B cell depletion is also restored on TLR7 deletion (C).



Fairhurst et al: Supplemental Figure 2:

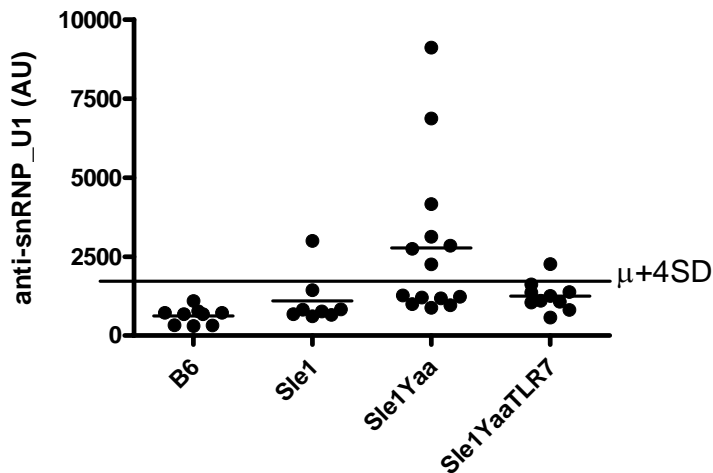
**Serum Analysis of Ig in a separate cohort of 9 month mice.** The autoantigen was repeated in a separate cohort of 9 month old mice at the UT Southwestern Microarray Core facility. The autoantigen specificity of these antibodies is shown for IgM (a) and IgG (b)



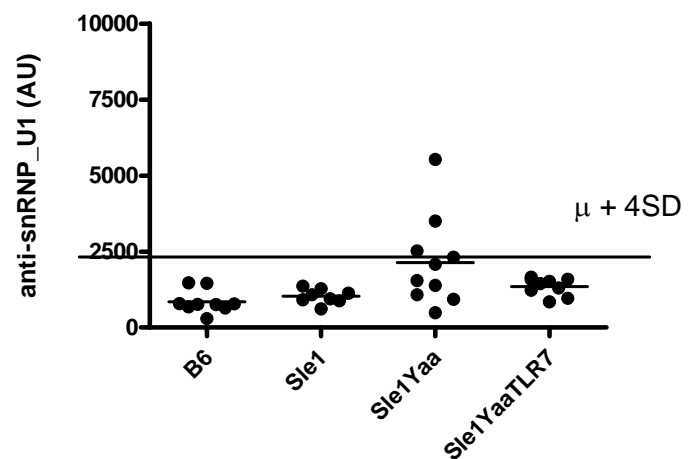
Fairhurst et al: Supplemental Figure 3:

**U1snRNP levels in aged mice.** Immulon II plates (Dynatech Laboratories, Chantilly, VA), precoated with methylated BSA, were coated with 0.4 $\mu$ g/ml each of U1-snRNP C Protein, U1-snRNP C A Protein and U1-snRNP C 68 Protein, as recommended by the manufacturer (Diarect, Germany). After blocking with PBS/3% BSA/0.1% gelatin/3mM EDTA, 1/800 dilutions of the test sera were incubated in duplicate for 2h at room temperature (Optimization of this dilution was determined using 5 MRLlpr mice in an initial experiment). Bound IgG was detected with alkaline phosphatase (AP)-conjugated anti-mouse IgG (Jackson ImmunoResearch Laboratories, West Grove, PA or IgM-AP (Southern Biotech)) using pNPP as a substrate. Raw OD was converted to U/ml using positive control serum from an MRLlpr mouse. Positive sera were determined to be values over B6 (mean+ 4 SD).

A. U1snRNP levels in mice aged 5-6 months



B. U1snRNP levels in mice aged 9 months







Fairhurst et al: Supplemental Figure 5

**Gating Strategy for the Myeloid lineage.** Spleens and kidneys from 9 month old male B6, B6.*Sle1*, B6.*Sle1Yaa* and B6.*Sle1YaaTLR7*<sup>-</sup> mice were processed for flow cytometry as described in Experimental Procedures. Live splenic cells were gated on CD4 and CD8 and the non-T population was analyzed for CD19 expression (A). Non B cells were then gated and examined for expression of Gr1 and CD11b. PMNs have high Gr1<sup>+</sup> expression (G1, A). Myeloid cells are gated into Gr1<sup>high</sup> (G2), and Gr1<sup>lo/-</sup> (G3). Kidney leukocytes were gated on using CD45<sup>+</sup> and forward scatter (FSC) (B). Leukocytes were then gated on nonT and nonB, as for splenic gating. The resultant CD11b vs Gr1 plot showed 4 main populations that were CD11b<sup>+</sup>. PMNs are Gr1<sup>+</sup> (G1 side scatter high). Remaining myeloid cells are gated into Gr1<sup>++</sup> monocytes (G2) and Gr1<sup>+</sup> (G3) and Gr1<sup>-</sup> myeloid cells (G4).

