

### Supplemental Table 1

Demographic characteristics of the healthy control group

Category	Feature	Healthy Controls (n=16)
Demographic	Age, mean $\pm$ SD	36.48 $\pm$ 8.32
	No. (%) female	12 (75.0)
	No. (%) male	4 (25.0)
	Race/Ethnicity, No (%)	
	Asian	6 (37.5)
	Black or African American	0 (0)
	Caucasian	8 (50.0)
	Hispanic	2 (12.5)
	Native Hawaiian/PI	0 (0)
	unknown/other	0

## Supplemental Table 2

*TLR7* expression and *TLR7* rs385839 genotype of SLE subject and healthy controls used in the study

study ID	gender	<i>TLR7</i> genotype	<i>TLR7</i> expression*
<b>SLE <i>TLR7</i><sup>hi</sup> group</b>			
SLE-1059	female	C/G	121.89
SLE-1077	male	G	99.69
SLE-1078	female	G/G	85.53
SLE-1074	male	C	59.68
SLE-870	female	G/G	55.49
SLE-941	female	G/G	54.61
SLE-985	female	C/G	45.27
SLE-1079	female	C/G	45.18
SLE-1075	female	G/G	35.82
SLE-1073	female	C/G	35.46
SLE-921	female	C/C	31.99
SLE-1020	female	C/G	30.33
SLE-1070	female	C/G	26.45
SLE-1004	female	G/G	25.50
SLE-1027	female	C/C	25.15
SLE-1069	female	C/C	24.94
SLE-1089	female	C/C	24.76
SLE-1076	female	C/G	24.36
SLE-984	female	C/G	24.30
<b>SLE <i>TLR7</i><sup>hi</sup> group</b>			
SLE-922	female	C/C	21.30
SLE-840	female	C/C	18.73
SLE-1001	female	G/G	18.11
SLE-929	female	G/G	18.05
SLE-1090	male	G	17.78
SLE-828	female	C/C	17.33
SLE-1019	female	G/G	16.50
<b>SLE <i>TLR7</i><sup>norm/lo</sup> group</b>			
SLE-1098	female	C/G	15.82
SLE-1071	female	C/C	14.08
SLE-1086	female	G/G	12.79
SLE-824	female	G/G	10.03
SLE-1015	female	G/G	9.42
SLE-1097	female	C/C	8.81
SLE-845	female	C/C	8.57
SLE-1018	male	C	7.19
SLE-991	female	C/C	7.19
SLE-946	female	G/G	6.86
SLE-1085	female	C/C	6.28
SLE-1072	male	C	5.59
SLE-1034	female	G/G	5.09
SLE-1024	female	C/G	4.47
SLE-1933	female	C/C	4.49
SLE-1092	female	C/C	4.05
SLE-1023	male	G	3.79
SLE-1088	female	C/C	3.72
SLE-1055	female	C/C	2.86
SLE-872	female	C/C	1.91
SLE-1033	female	G/G	1.52

study ID	gender	<i>TLR7</i> genotype	<i>TLR7</i> expression*
<b>Healthy controls (HC)</b>			
HC1	female	G/G	17.28
HC2	female	C/G	13.70
HC3	female	C/G	20.22
HC4	female	C/G	16.57
HC5	female	C/C	14.07
HC6	female	C/C	15.89
HC7	female	C/G	15.22
HC8	female	C/C	22.62
HC9	female	C/C	13.17
HC10	female	C/C	13.80
HC11	male	C	13.00
HC12	male	G	19.10
HC13	female	C/C	19.85
HC14	female	C/G	18.00
HC15	male	C	11.15
HC16	male	C	16.40

\* *TLR7* expression levels are presented as  $2^{-\Delta CT} \times 10^3$

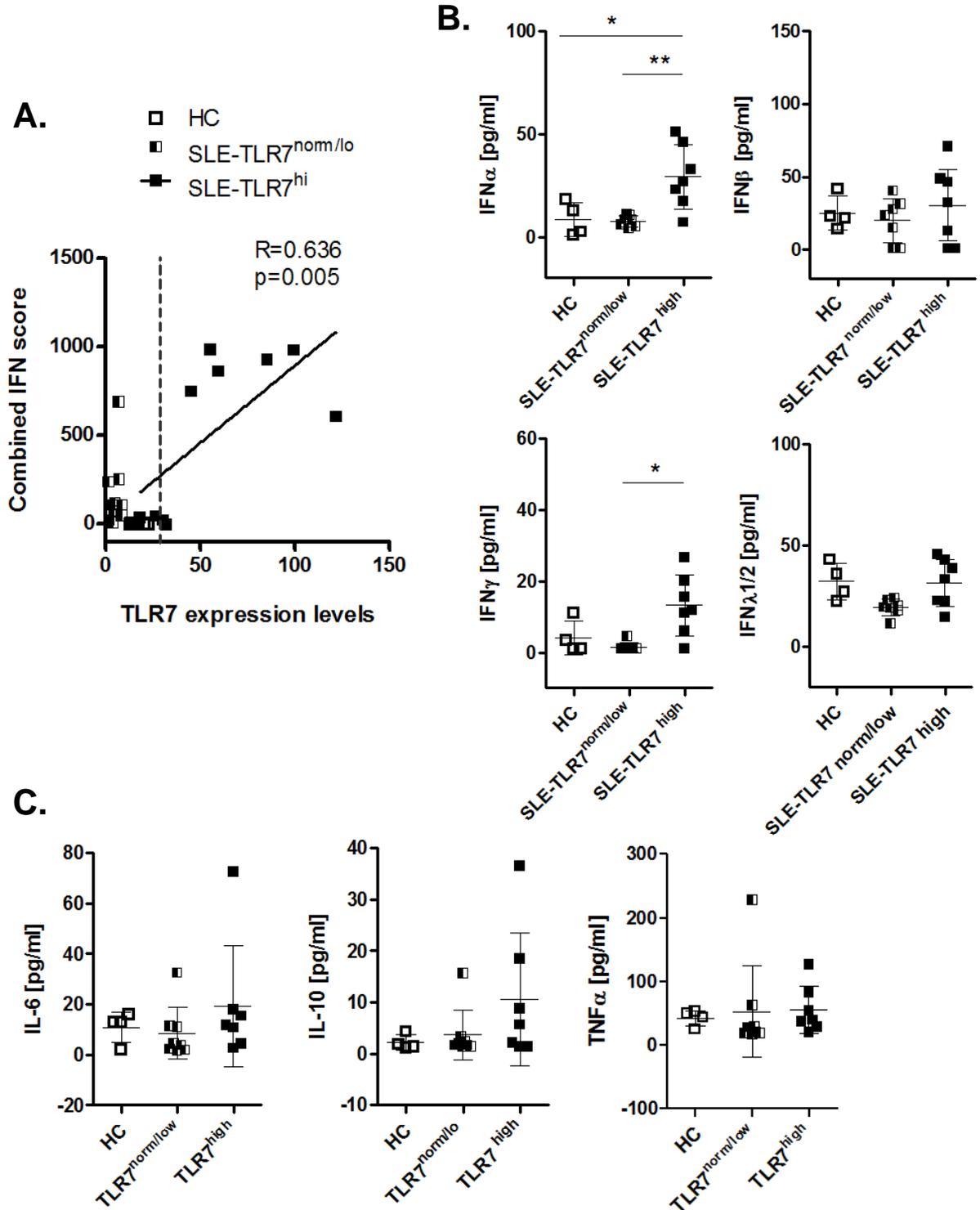
**Supplemental Table 3**  
Antibodies used for flow cytometry

<b>Antibodies</b>	<b>Clone</b>	<b>Company</b>
CD10	CB-CALLA	E-Bioscience
CD19	HIB19	Bio Legend
CD24	SN3	Invitrogen
CD27	LG.7F9	E-Bioscience
CD38	HB7	E-Bioscience
IgD	IA6-2	Bio Legend
TLR7	533707	R&D Systems
Mouse IgG2a isotype	MOPC-173	Bio Legend
Fc Block	Human TruStain FcX™	Bio Legend

**Supplemental Table 4**  
Primer Sequences used for RT-PCR

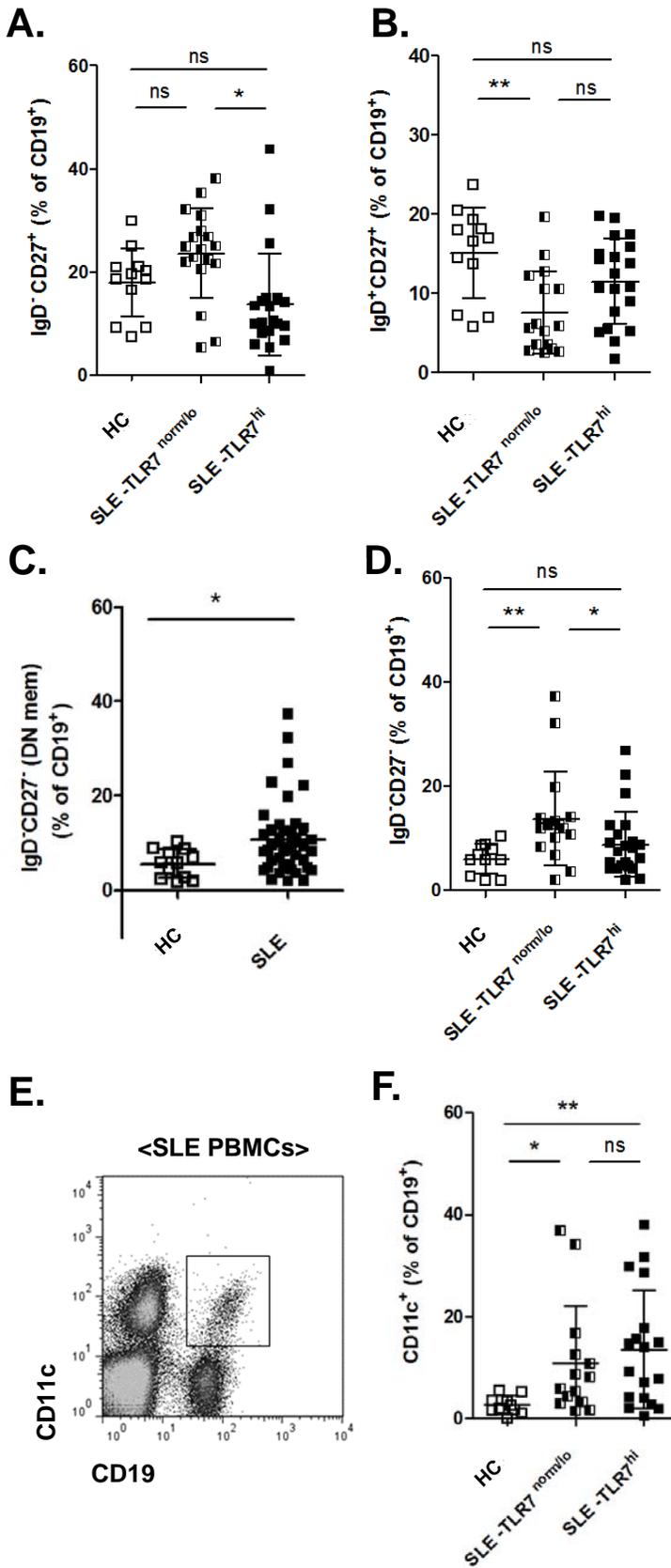
<b>Gene</b>	<b>Forward (5' to 3')</b>	<b>Reverse (3' to 5')</b>
<i>GAPDH</i>	CAACGGATTTGGTCGTATT	GATGGCAACAATATCCACTT
<i>IFI27</i>	CTCTAGGCCACGGAATTAACC	CTCCTCCAATCACAACCTGTAGC
<i>IFI44L</i>	GAAGTGGACCCCATGAAGG	ACTCTCATTGCGGCACACC
<i>IFIT1</i>	CTCCTTGGGTTTCGTCTACAAATTG	AGTCAGCAGCCAGTCTCAG
<i>IRF7</i>	TGGTCCTGGTGAAGCTGGA	GATGTCGTCATAGAGGCTGTTGG
<i>MX1</i>	AGCCACTGGACTGACGACTT	ACCACGGCTAACGGATAAG
<i>PKR</i>	CTTCCATCTGACTCAGGTTT	TGCTTCTGACGGTATGTATTA
<i>TLR7</i>	CATGCTCTGCTCTCTTCAACCAG	AGTGACATCACAGGGCAGAGTT
<i>TLR9</i>	GAAGGGACCTCGAGTGTGAA	CTGGAGCTCACAGGGTAGGA
<i>UBC</i>	GTCGCAGTTCTTGTGGTGG	CAGCAAAGA TCAGCCTCTGC

## Supplemental Figure 1



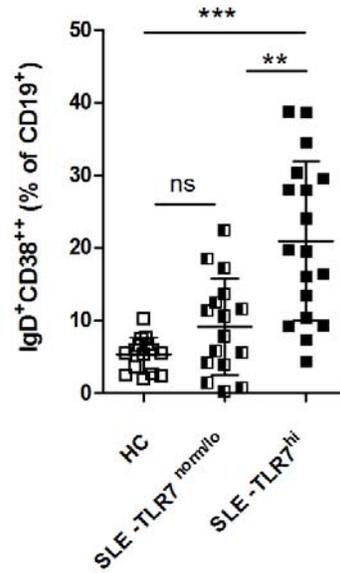
**Supplemental Figure 1. Increased *TLR7* expression correlates with ISGs expression and IFN $\alpha$  and  $\gamma$  production. (A)** Correlation between combined IFN scores and *TLR7* mRNA expression in PBMCs from HC (n=10) or SLE patients (*TLR7*<sup>norm/lo</sup> (n=10) and *TLR7*<sup>hi</sup> (n=10)), defined by Spearman's correlation. IFN scores were calculated based on the relative expression of IFN-inducible genes (PKR, MX1, IFI1, IFI27, and IFI44L). **(B and C)** Cytokine levels, measured in serum samples from HC (n=4), *TLR7*<sup>norm/lo</sup> (n=8) and *TLR7*<sup>hi</sup> (n=7) SLE groups. Each symbol represents an individual, and horizontal lines indicate mean  $\pm$  SD. \* $p<0.05$  and \*\* $p<0.01$ , significance determined by Kruskal-Wallis, Dunn's post-test.

## Supplemental Figure 2



**Supplemental Figure 2. Changes in peripheral B cells, associated with high *TLR7* expression in SLE patients. (A-B)** Summary flow data of the frequencies of IgD<sup>-</sup>CD27<sup>+</sup> (switched memory), IgD<sup>+</sup>CD27<sup>+</sup> (un-switched memory) of CD19<sup>+</sup> cells in HC (n=12), TLR7<sup>norm/lo</sup> (n=16) and TLR7<sup>hi</sup> (n=18) SLE groups. **(C-D)** Summary flow data of the frequencies of IgD<sup>-</sup>CD27<sup>-</sup> double-negative (DN) memory B cells in HCs and SLE patients, or HC, TLR7<sup>norm/lo</sup> and TLR7<sup>hi</sup> SLE groups **(E-F)** Representative flow cytometry plots of SLE PBMCs showing staining of CD19<sup>+</sup>CD11c<sup>+</sup> B cells **(E)**. Summary flow data of the frequencies of CD11c<sup>+</sup> cells of CD19<sup>+</sup> cells in HC, TLR7<sup>norm/lo</sup> and TLR7<sup>hi</sup> SLE groups **(F)**. **(G)** Summary flow data of the frequencies of CD38<sup>++</sup>CD27<sup>++</sup> plasma cells in HC, TLR7<sup>norm/lo</sup> and TLR7<sup>hi</sup> SLE groups. Differences between groups were determined by Mann-Whitney test (C) or Kruskal-Wallis, Dunn's post-test (A, B, D, F, and G). Data are shown as the mean ± SD. \*p<0.05 and \*\*p<0.01.

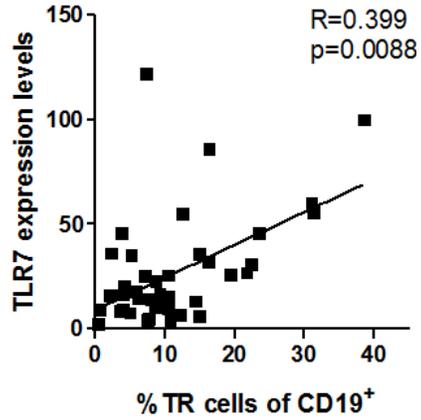
### Supplemental Figure 3



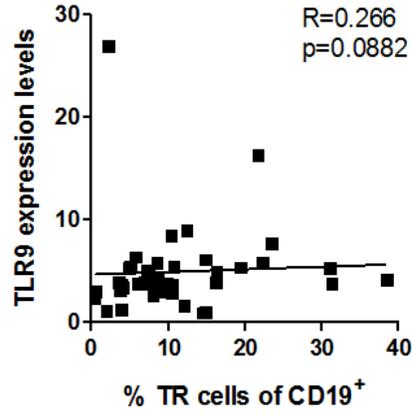
**Supplemental Figure 3.** Summary flow data of the frequency of TR B cells defined as IgD<sup>+</sup> CD38<sup>++</sup> of CD19<sup>+</sup> cells in HC (n=12), TLR7<sup>norm/lo</sup> (n=16) and TLR7<sup>hi</sup> (n=18) SLE groups. Data are shown as the mean  $\pm$  SD. \*\*p<0.01 and \*\*\*p<0.001 by Kruskal-Wallis, Dunn's post-test.

## Supplemental Figure 4

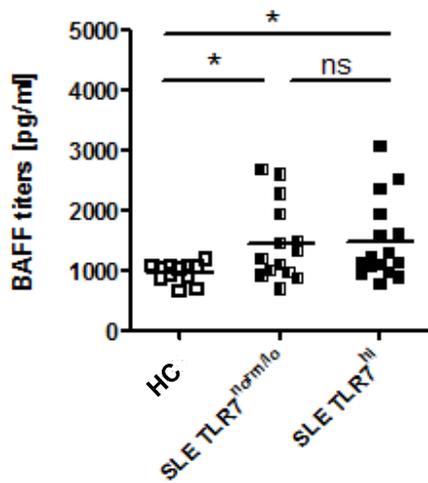
**A.**



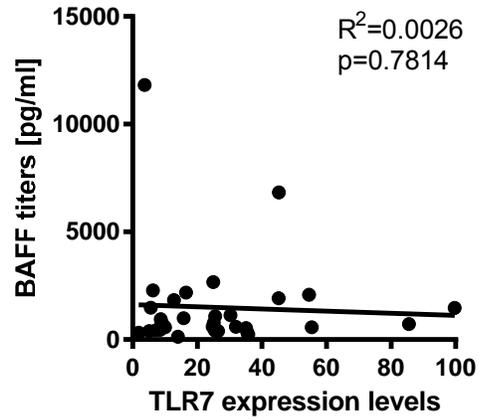
**B.**



**C.**

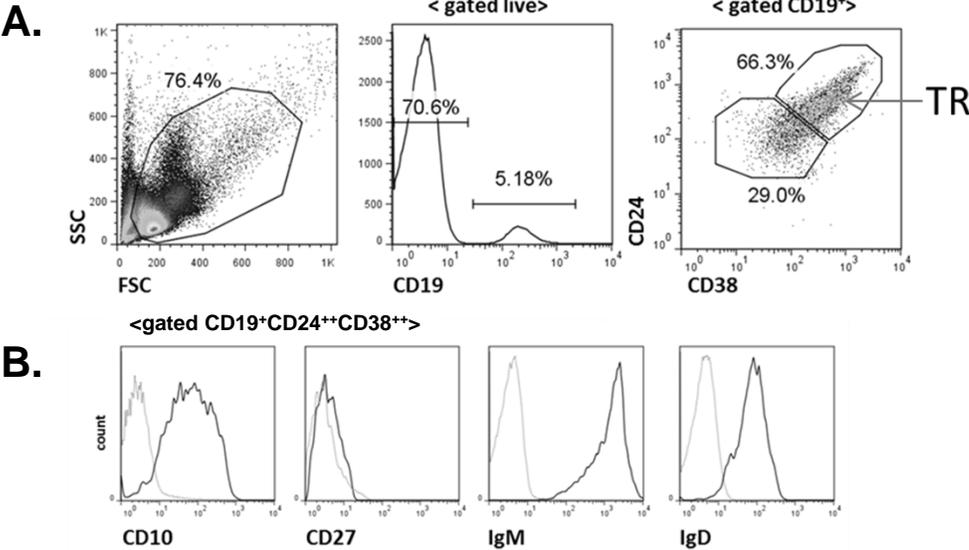


**D.**



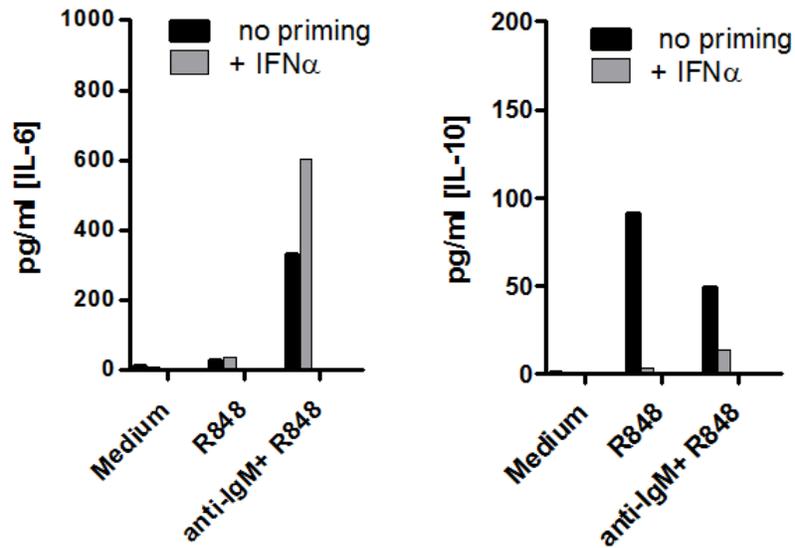
**Supplemental Figure 4. (A and B)** Correlations between TR B cell frequency and TLR7 or *TLR9* expression in SLE PBMCs (n=40). **(C)** BAFF levels in serum samples from HC (n=12), TLR7<sup>norm/lo</sup> (n=15) and TLR7<sup>hi</sup> (n=17) SLE patients. **(D)** Correlation between BAFF serum titers and *TLR7* expression in SLE patients (n=32). Data are shown as the mean  $\pm$  SD. \* $p<0.05$  by Kruskal-Wallis, Dunn's post-test. Associations determined by Spearman's correlation.

# Supplemental Figure 5



**Supplemental Figure 5. Representative flow analysis of cord blood (CB) TR B cells. (A)** Gating strategy used to identify CB-TR B cells using CD19, CD38, and CD24 staining. **(B)** CB-TR B cell phenotype. Histograms show staining with anti-CD10, anti-CD27, anti-IgM and anti-IgD Abs of gated CD19<sup>+</sup>CD24<sup>++</sup>CD38<sup>++</sup> CB-TR B cells (black lines), or Ab-isotype controls (grey lines).

## Supplemental Figure 6



**Supplemental Figure 6. IFN priming alters cytokine production by CB-TR B cells.** Purified CB-TR B cells were primed with IFN $\alpha$  and cultured in cell medium, or, stimulated with R848 (50 ng/ml), or a combination of R848 plus F(ab')<sub>2</sub> anti-human IgM (anti-IgM) (10 $\mu$ g/ml) for 5 days. Concentrations of IL-6 and IL-10 were measured in cell culture supernatants. Representative data from one of three independent experiments.