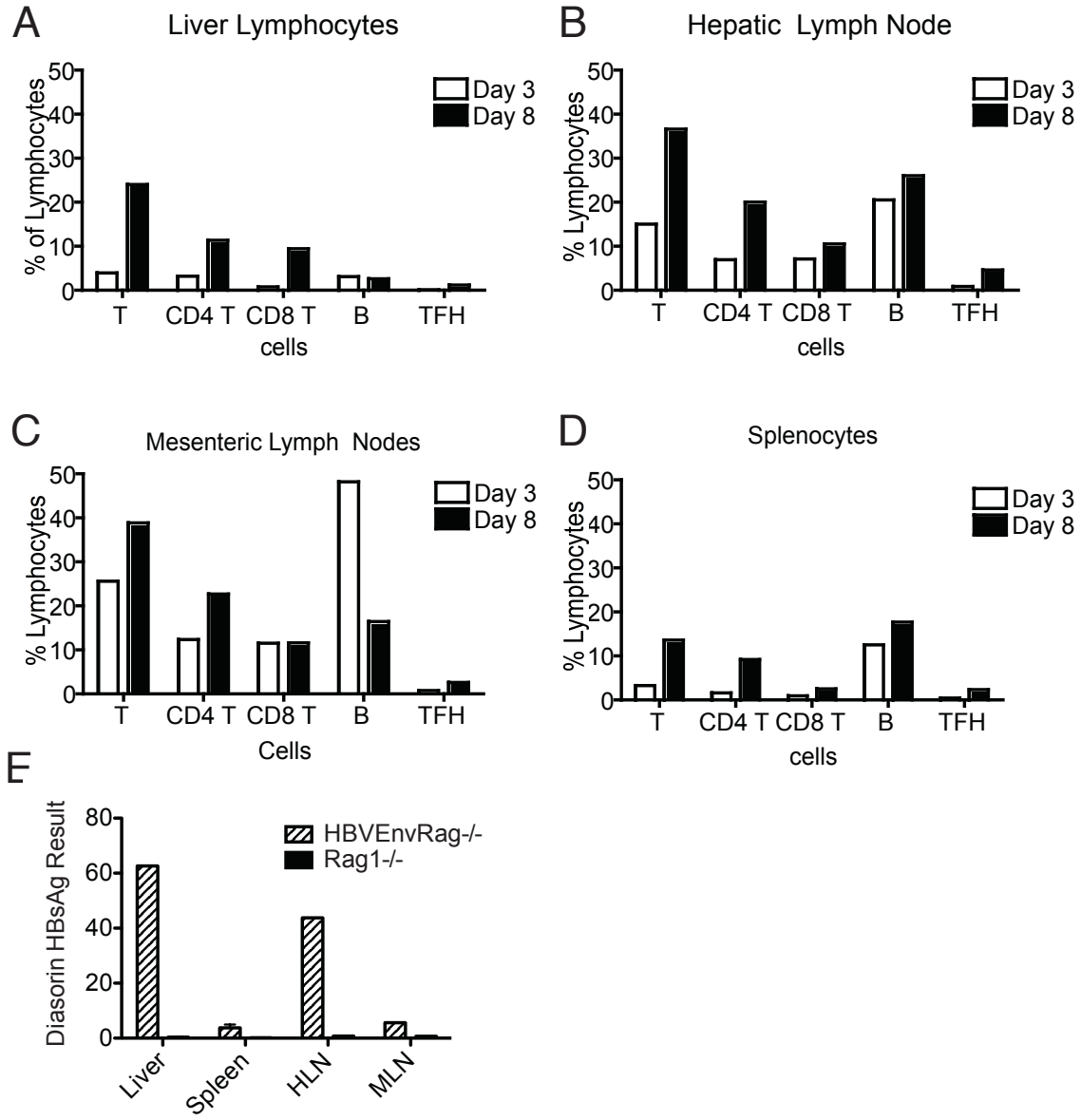
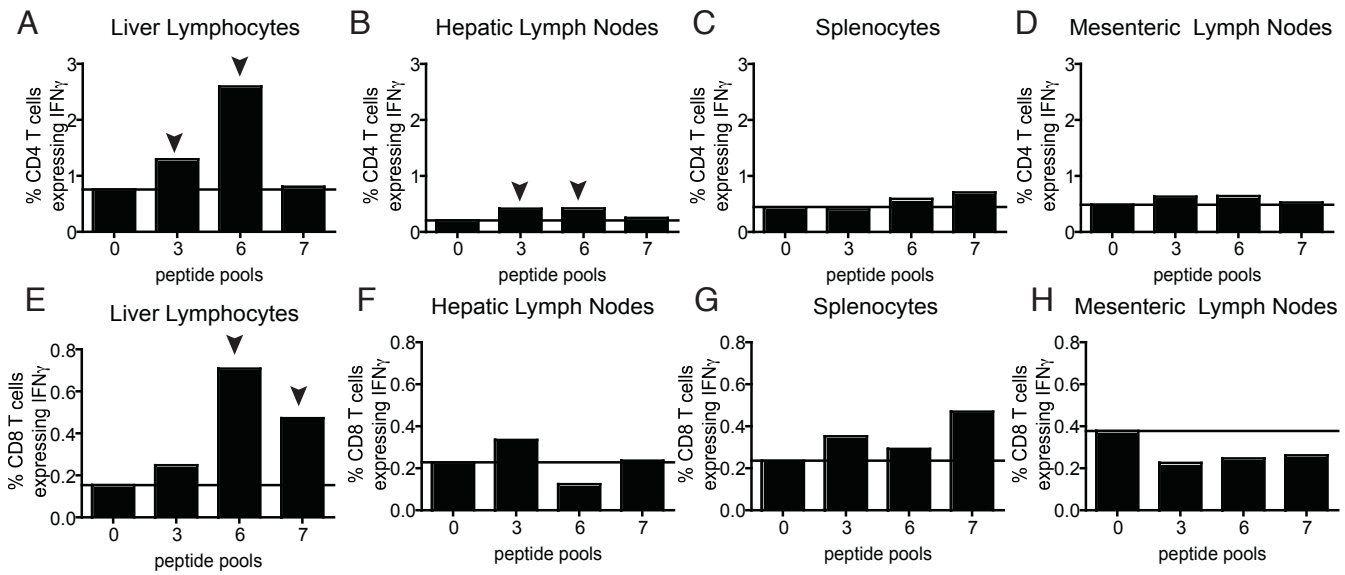
Publicover et al, Supplemental Figure 1



Supplemental Figure 1

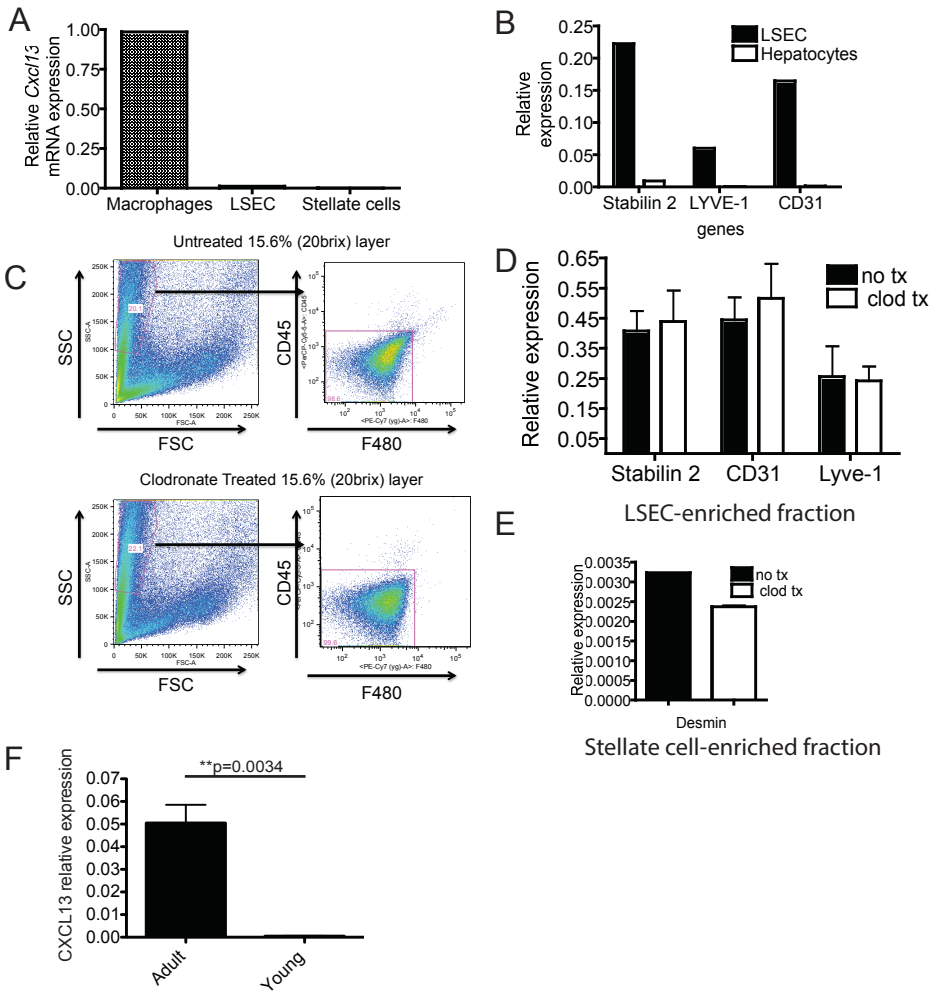
Percentage of lymphocyte populations at day 3 and 8 post adoptive transfer in HBVEnvRag-/- mice, and HBsAg expression before adoptive transfer. Lymphocytes isolated from liver (**A**) hepatic lymph nodes (**B**), spleen (**C**) and mesenteric lymph nodes (**D** were isolated from adult HBVEnvRag-/- mice 3 days (open bars) and 8 days (solid bars) after adoptive transfer and percentages of T cells (TCRβ), CD4 T cells (CD4+ TCRβ+), CD8 T cells (CD8+, TCRβ+), B cells (CD19+) and T follicular helper cells (TFH; CD4+, CXCR5+, ICOS+) were determined by flow cytometry. Lymphocytes pooled from N=4 mice. (**E**) Presence of HBsAg was determined in homogenized liver, spleen, HLN or MLN from HBVEnvRag-/- (striped bar) or *Rag1-/-* (solid bar) mice. N=4 mice; liver and spleen were processed individually and HLN and MLN were pooled. Tissue weight ranged from 20mg-33mg for spleen, 15mg-30mg for liver, 2.0mg-8.0mg for HLN and 42mg-46mg for MLN. Result was determined by Diasorin HBsAg Plus and reported as "result" calculated from 450, 630 OD reading using Diasorin preprogramed plate reader. All Rag1-/- organs were reported as "negative" and all HBVEnvRag-/- organs were reported as "positive."

Publicover et. al, Supplemental Figure 2



Supplemental Figure 2
CD4 and CD8 T cell responses appear at day 8 in the liver of HBVEnvRag-/- mice; CD4 T cell responses appear in the hepatic lymph node at day 8. Lymphocytes from liver (**A, E**) hepatic lymph nodes (**B, F**), spleen (**C, G**) and mesenteric lymph nodes (**D, H**) were isolated from adult HBVEnvRag-/- mice 8 days after adoptive transfer and incubated with no HBV peptides (0), peptides from pools 3, 6, 7 (composed of 11-14 14mer HBV peptides and described in methods and Publicover et. al 2011, JCI.) Following a four hour incubation with peptide pools described earlier and in Publicover et. al 2011, lymphocytes were stained for IFNγ secretion by IFNγ capture assay (Miltenyi Biotec) using standard protocol along with anti-CD4, anti-CD8 and anti-TCRβ. Percentage of CD4 and CD8 T cells that produce IFNγ were determined and displayed above. Arrows indicate a positive response determined by ≥2X background (no stimulation, 0). Lymphocytes were pooled from N=4 mice.

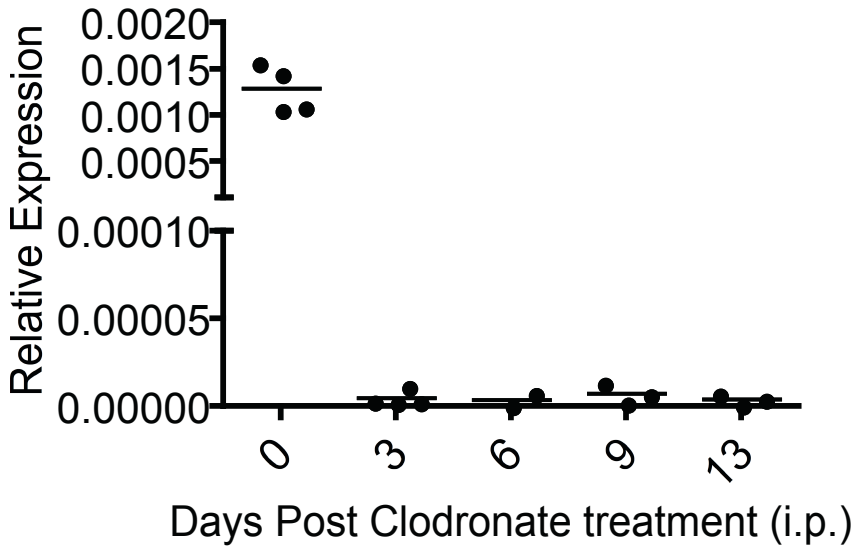
Publicover et al Supplemental Figure 3



Supplemental Figure 3

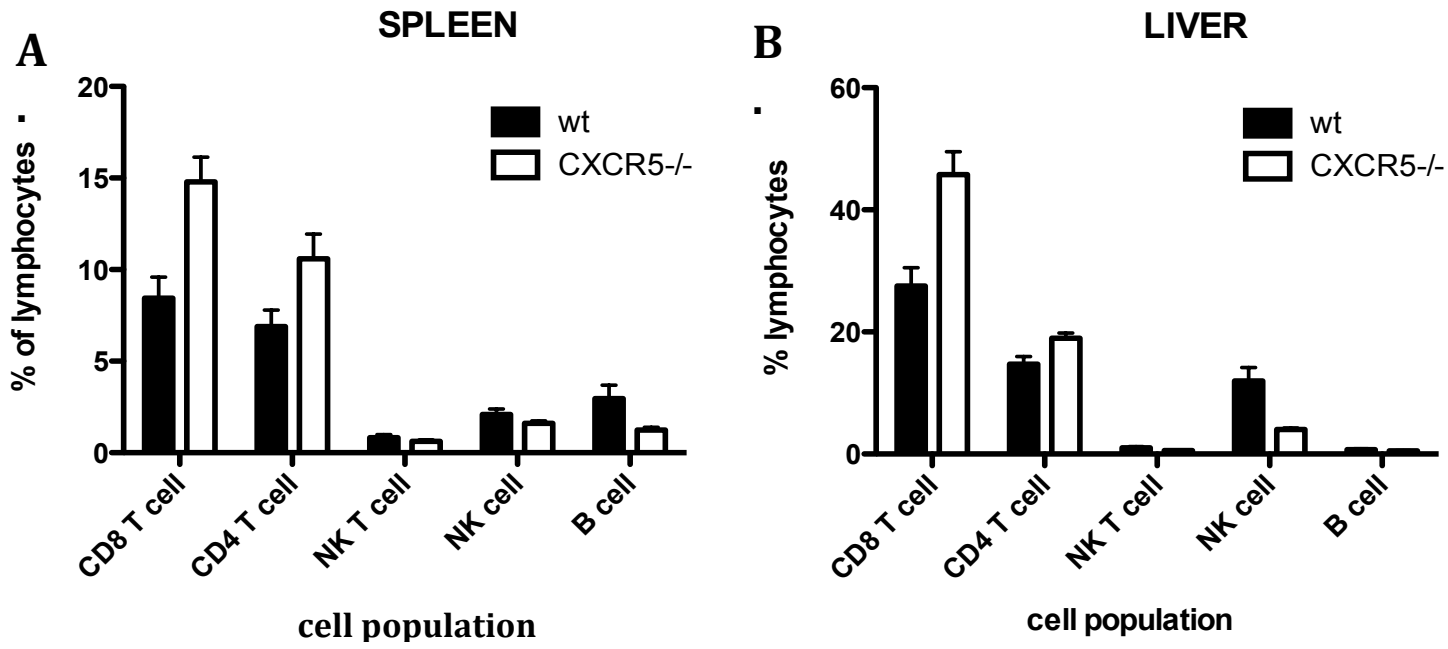
CXCL13 is not expressed by liver sinusoid endothelial cells (LSEC) or stellate cells and LSEC and stellate cells are not affected by clodronate liposome treatment; and CXCL13 expression in the liver 8 days after adoptive transfer does not change from pre-adoptive transfer levels (**A**) Macrophages were isolated as described in Figure 4. LSEC and stellate cells were isolated using the previously described collagenase/Dnase media perfusion and Pronase digest followed by an Accudenz gradient (20 brix/10 brix Accudenz followed by 20,000 rpm ultracentrifugation for 25 min). LSEC were collected from the 20Brix/10Brix interface and sorted for CD45-, DAPI+. (**B**) The LSEC population was confirmed to be positive for LSEC by 24-, 105-, and 109-fold increased mRNA transcripts of Stabilin 2, Lyve-1 and CD31 (relative to GAPDH,) respectively compared to sorted hepatocytes. Stellate cells were isolated from the 20 Brix/10 Brix and the 10 Brix/0 Brix interfaces since stellate cells were present in both interfaces. (**C**) Stellate cells were isolated from wild-type C57Bl/6 mice treated with clodronate liposomes (clod tx) by i.p. injection 24 hrs prior or untreated (no tx) and further confirmed to be unaffected by clodronate liposome treatment by FACS analysis by size and granularity, followed by an absence of CD45 and F4/80. (**D-E**) RNA was obtained from LSEC and stellate cells isolated from mouse livers untreated or treated with clodronate liposomes 24hrs prior, and analyzed for presence of (**D**) Stabilin 2, CD31, and Lyve-1, and (**E**) Desmin transcripts respectively relative to GAPDH by real time PCR. Clodronate treated and untreated mice showed equivalent expression of LSEC and stellate cell associated transcripts (N=2). (**F**) CXCL13 transcript levels relative to GAPDH in mouse livers eight days post adoptive transfer of wild-type splenocytes into HBVEnvRag-/- adult or young mice. N=4, statistics determined by unpaired student t-test.

Publicover et. al, Supplemental Figure 4



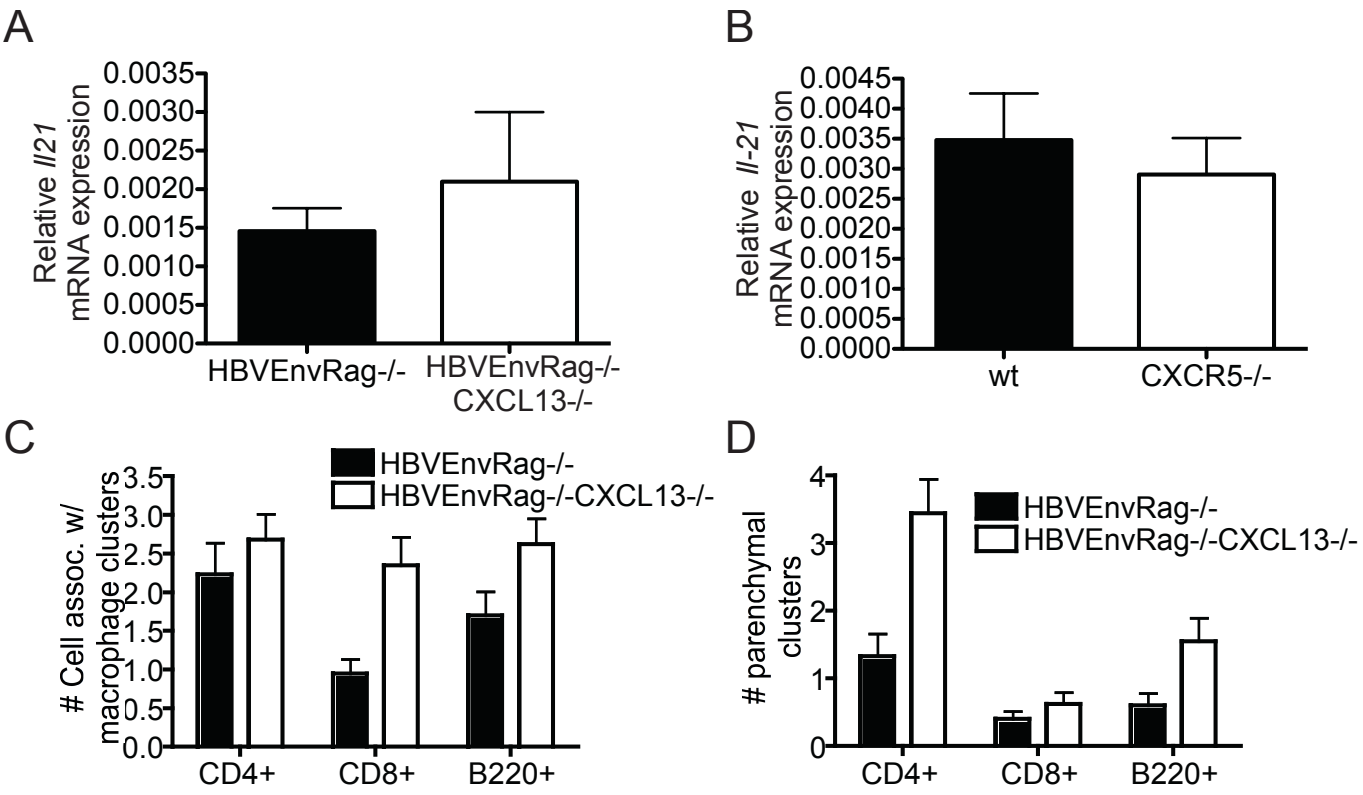
Supplemental Figure 4
Injection of clodronate liposomes decreases levels of CXCL13 long-term. Wild-type C57BL/6 mice were given clodronate liposomes via intraperitoneal (i.p.) injection at day 0, 3, 6, 9 and 13. RNA was extracted from liver tissue taken prior to injection and levels of CXCL13 relative to GAPDH were determined using real-time PCR.

Publicover et. al, Supplemental Figure 5



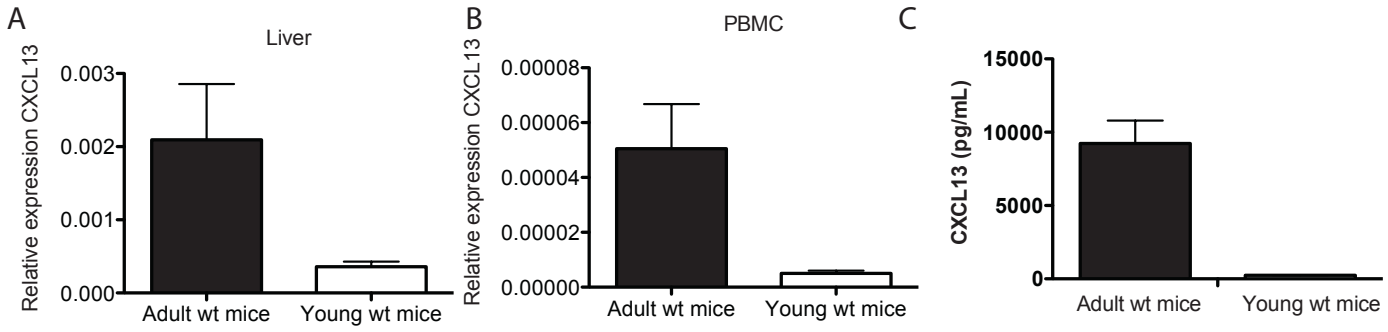
Supplemental Figure 5
Percentage of lymphocyte populations in the spleen and liver at day 8 post adoptive transfer of wild-type or CXCR5-/- splenocytes into HBVEnvRag-/- mice. Lymphocytes isolated from spleen (**A**) and liver (**B**) were isolated from adult HBVEnvRag-/- mice 8 days after adoptive transfer of wildtype (solid bars) or CXCR5-/- splenocytes (open bars). Percentages of CD8 T cells (CD8+, TCRβ+), CD4 T cells (CD4+ TCRβ+), NK T cells (TCRβ+, NK1.1+), NK cells (NK1.1+), and B cells (CD19+) were determined by flow cytometry. Lymphocytes pooled from N=4 mice.

Publicover et. al, Supplemental Figure 6



Supplemental Figure 6

IL-21 response, macrophage-associated lymphocyte organization and parenchymal lymphocyte clustering is not dependent on CXCL13-CXCR5 interactions. IL-21 transcription levels relative to GAPDH in (**A**) HBVEnvRag-/- (solid bar) and HBVEnvRag-/- CXCL13-/- (open bar) mice eight days after adoptive transfer of wt, syngeneic splenocytes and (**B**) HBVEnvRag-/- mice eight days after adoptive transfer of wt splenocytes (solid bar) or CXCR5-/- (open bar) splenocytes. HBVEnvRag-/- (solid bar) and HBVEnvRag-/- CXCL13-/- (open bar) mouse liver was obtained eight days after adoptive transfer of wt, syngeneic splenocytes and stained for macrophage (F4/80), nuclei and either CD4, CD8 or B220 as previously described. Fifteen random frames from each section (N≥3) were scored by an unbiased pathologist for (**C**) number of CD4, CD8 or B220 cells interacting with macrophage cluster (defined as ≥ 4 macrophages) per frame, (**D**) number of parenchymal lymphocyte clusters (≥2 cells within 0.5 inches of 10X magnification frame) of CD4, CD8, B220 cells per frame. Bars indicate average incidents per frame ±SEM.



Supplemental Figure 7

Plasma and PBMC expression of CXCL13 reflects hepatic levels of CXCL13 expression. CXCL13 mRNA levels were determined in adult and young wt C56Bl/6 mouse (**A**) liver and (**B**) PBMC relative to GAPDH by RTPCR. (**C**) Plasma levels of CXCL13 were determined by ELISA in young and adult wt C56Bl/6 mice.