**Supplemental Experimental Procedures**

***Mice***

All mice were obtained from JAX. B6.Cg-*Il21tm1.1Hm*/HmDcr;  B6.129S2-*Ifnar1tm1Agt*; B6.129(Cg)-*Il21rtm1Wjl*; B6.129S2-*Il6tm1Kopf*/J; B6.129S2-*Igh6tm1Cgn*/J; B6.129P2-*Il10tm1Cgn*/J; B6.Cg-Tg(TcraTcrb)425Cbn/J; B6.129S2-*Tcratm1Mom*/J; B6.129S1-*Il12btm1Jm*/J; B6.129S2(Cg)-*Cxcr5tm1Lipp*/J; B6.Cg-*Foxp3sf*/J; B6.Cg-*Foxp3tm2Tch*/J, B6(Cg)-*Il10tm1Karp*/J, B6.129S4-*Ifngtm3.1Lky*/J, C57BL/6-*Il17atm1Bcgen*/J; B6.129S2-*Airetm1.1Doi/J*; B6.129S(FVB)-*Bcl6Ttm1.1Dent/*J; and B6.SJL-*Ptprca Pep3b*/BoyJ (Ly5.1). PCR genotyping was performed using oligonucleotide primers recommended at the JAX MICE website. IL21-VFP mice carrying conditional knockouts of *Bcl6* were produced crossing B6.129S(FVB)-*Bcl6tm1.1Dent*/J mice with B6.Cg-Tg(CD4-cre)1Cwi/BfluJ with B6.IL21-VFP reporter mice to generate *Cd4-cre+/?* *Bcl6fl/fl*mice.

***Quantitative RT-PCR***

Total RNA was extracted with the RNeasy Micro kit (Qiagen) followed by cDNA synthesis using the QuantiTect Reverse Transcription kit (Qiagen) according to the manufacturer’s protocol. SuperScript III Platinum Two-Step qRT-PCR Kit with SYBR Green (Invitrogen) was used for quantification. Samples were run in technical triplicates on the ViiA Real Time PCR system (Life Technologies) and mean expression was normalized to 18sRNA using the Ct method. Primer sequences: *Il21* F-GAA GAT GGC AAT GAA AGC CTG T, R-AGG ATG TGG GAG AGG AGA CTG A; *VFP1* F-AAG CTG ACC CTG AAG TTC ATC TGC, R-CTT GTA GTT GCC GTC GTC CTT GAA; *VFP2* F-CAA CAG CCA CAA CGT CTA TAT CAT, R-CAA CAG CCA CAA CGT CTA TAT CAT; *VFP3* F-TG CTG CCC GAC AA, R-TCA CGA ACT CCA GCA G.

**Antibodies used for flow cytometric analysis and cell sorting:**

**Antigen Clone Fluorochrome Company**

B220 RA3-6B2 PB Biolegend

B220 RA3-6B2 Biotin BD Bioscience

CD11b M1/70 PE cy7 Biolegend

CD11b M1/70 Biotin BD Bioscience

CD11c HL3 Biotin BD Bioscience

CD11c HL3 PE BD Bioscience

CD4 GK 1.5 Pacific Orange Made at JAX

CD4 GK 1.5 A650 BD Bioscience

CD44 IM7.8.1 APC cy7 BD Bioscience

CD62L MEL-14 PE cy7 BD Bioscience

CD8 53-6.7 A700 BD Bioscience

CD8 53-6.7 Biotin BD Bioscience

CXCR5 L138D7 Biotin Biolegend

GR1 RB6-8C5 APC cy7 BD Bioscience

ICOS C398.4A A647 Biolegend

NK 1.1 PK136 PE BD Bioscience

PD1 RMP1-30 PE Cy7 Biolegend

Streptavidin BV421 Biolegend

Cd3e 145-2C11 PE-CF594 BD Bioscience

CD5 53-7.3 BV421 BD Bioscience

CD45.1 A201.7 PE Biolegend

CD45.2 1042.1 Unconjugated The Jackson Laboratory

Pacific Orange Life Technologies

**ELISA**

Supernatants were added to plates coated with purified anti-mouse IL2 (BD; clone JES6-1A12), anti-mouse IL10 (BD; clone JES5-2A5), anti-mouse IL17(BD; clone TC11-18H10), anti-mouse IFN gamma (BD; clone R4-6A2) and anti-mouse IL21 (Peprotech; polyclonal rabbit) (2ug/ml). Respective purified recombinant murine cytokines were used as standards. Cytokines were detected by biotinylated secondary antibodies and anti-mouse IL2 (BD; clone JES6-5H4), anti-mouse IL10 (BD; clone JES5-16H3), anti-mouse IL17( BD; clone TC11-8H4), anti-mouse IFN gamma (BD; clone XMG1.2) or  anti-mouse IL21 (Peprotech; polyclonal rabbit) (1ug/ml) as revealed by colorimetry using avidin-HRP (Sigma; 1:1000) and TMB (Invitrogen) after the reaction was stopped using 7% sulphuric acid (Sigma). Absorbance was measured at 450nm and concentrations were calculated using respective standard curves.

***Comparison of RNAseq profiles with antigen-induced TFH microarray and RNAseq datasets***

Gene expression profiles of the 8-day Naïve CD 4 T cells, TH1 cells, TFH cells, GC TFH cells (Yusuf et al., 2010) and the 3-day TFH, TH1 cells (Choi et al., 2015) were downloaded from gene expression omnibus (GSE21380 and GSE67334). The 8-day and 3-day samples were measured by microarray and RNA-seq, respectively. To compare the gene expression profiles of these cell populations with our N, ACT, and IL21-ACT cells: firstly, gene expression levels by microarray and RNA-seq were transformed into log2 intensity and log2 TPM scales; secondly, platform and study differences were corrected by subtracting the first principle component of the combined samples for each transcript; and thirdly hierarchical clustering was performed on the combined samples based on the residual transcript levels.

***Immunohistochemisty***

Formalin fixed paraffin embedded sections of spleens and lymph nodes of IL21-VFP mice were treated with Proteinase K (DAKO) for 5’ at RT then stained with a rabbit polyclonal anti-GFP antibody (Abcam; ab6556) followed by biotinylated goat anti-rabbit IgG (Vector Labs) and ABC Elite Reagent (Vector Labs).  Detection with DAB was followed by hematoxylin counterstain. Histology images were viewed with an Olympus BX41 microscope (10-100X objectives) and photographed with an Olympus DP71 camera. DP controller software (Version 3.3.1.292) was used for image acquisition.