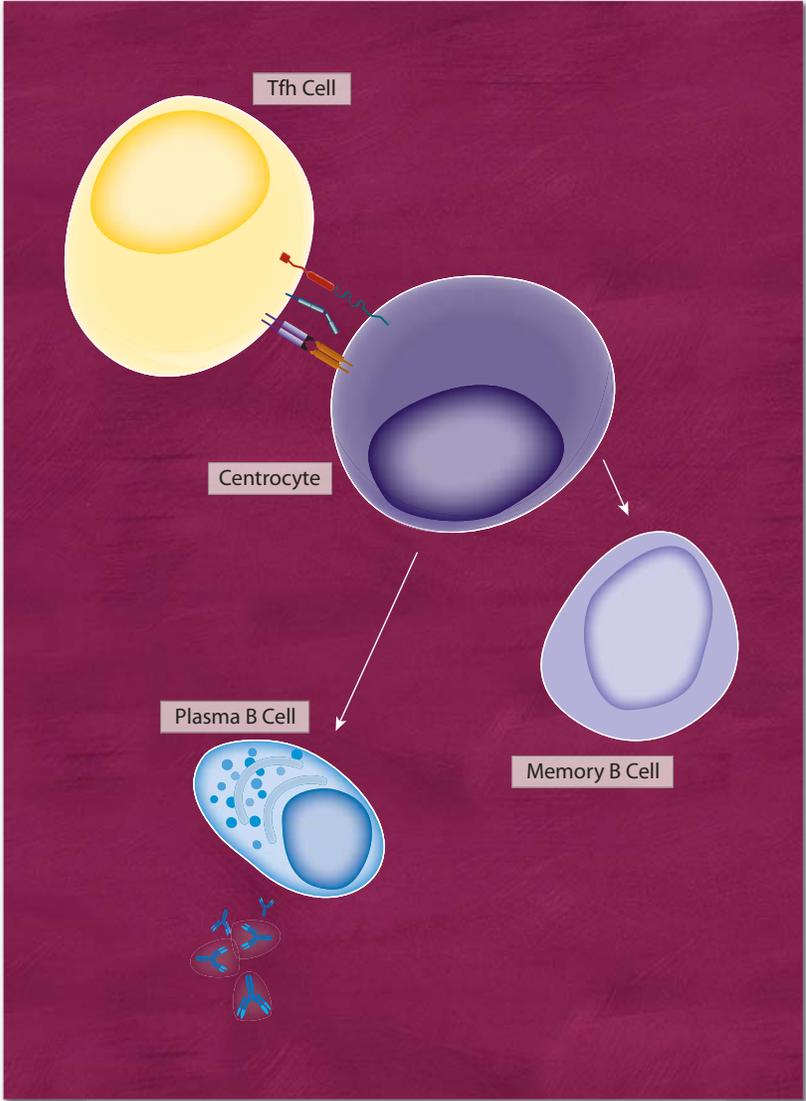


Follicular Helper T Cells

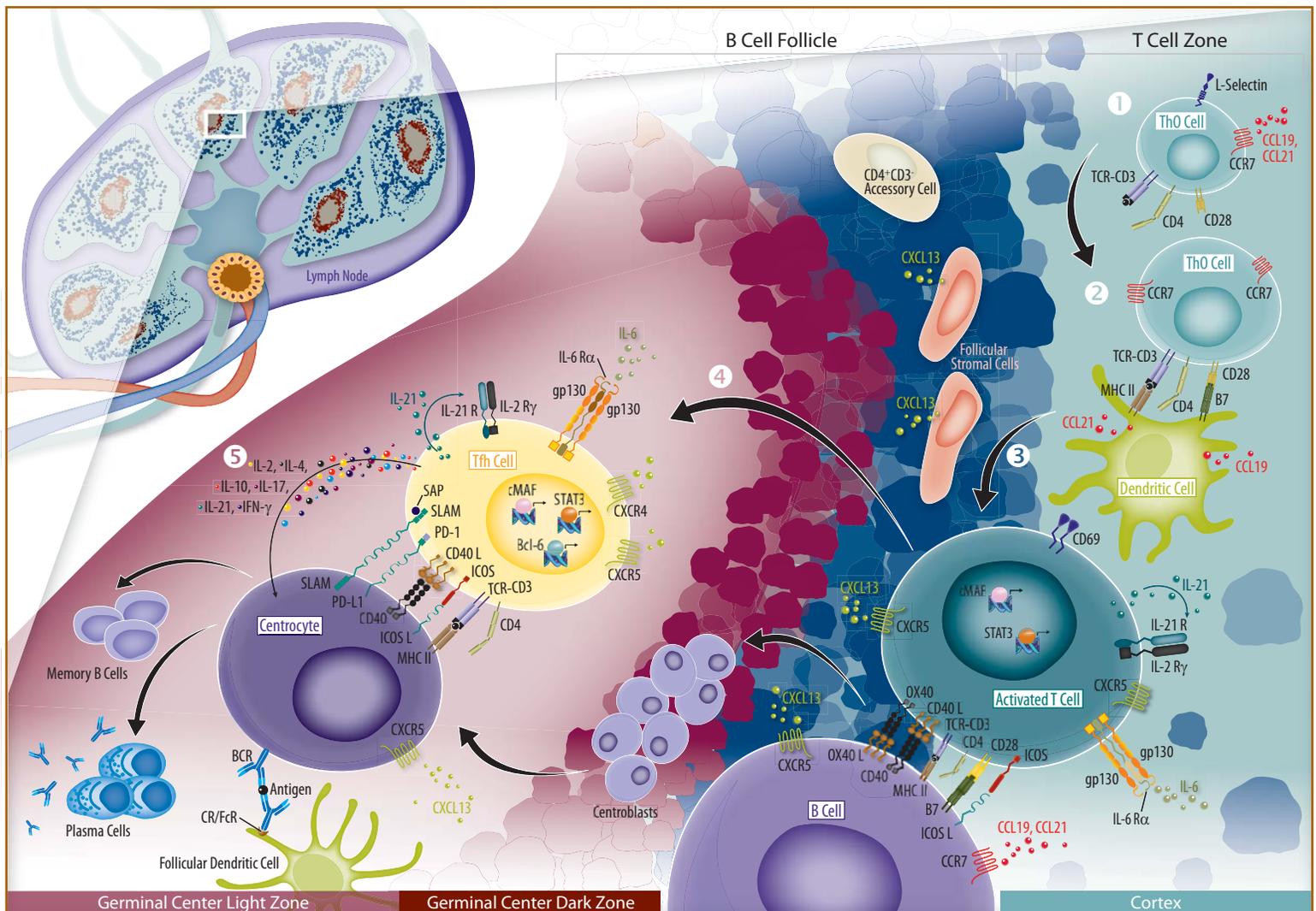


Follicular Helper T Cells & Regulation of B Cell Immunity

Follicular helper T (Tfh) cells represent a functional subset of CD4⁺ helper T (Th) cells that provides help for B cells to allow the formation of plasma cells and long-lived memory B cells. Tfh cells are characterized by the elevated expression of CXCR5, CD40L, OX40, ICOS, PD-1, Bcl-6, SLAM family of receptors (SLAM, SLAMF3, SLAMF5, SLAMF6), and IL-21. Though other Th subsets express these proteins, it is the relatively high expression levels that delineates Tfh cells and enhances their capacity to facilitate antibody production. Tfh cells are believed to be involved in angioimmunoblastic T cell lymphoma and several autoimmune diseases, including systemic lupus erythematosus and Sjogren's syndrome.

Though the complete differentiation process for Tfh cells is still being investigated, it has been shown that naïve CD4⁺ T (Th0) cells expressing CCR7 chemokine receptor are chemoattracted to the T cell zone of the secondary lymphoid tissue by CCL19 and CCL21 (1). In the T cell zone, Th0 cells are activated by antigen-presenting dendritic cells and express CD40L,

OX40, and ICOS (2). These activated T cells migrate to the edge of the B cell follicle where they interact with antigen-primed B cells (3). The T cells also respond to IL-6 with the activation of the transcription factors cMAF and STAT3, and the induction of IL-21 expression. IL-6 and the autocrine action of IL-21 stimulate activated T cells to express Bcl-6, the master transcription factor that controls Tfh cell differentiation. Bcl-6, a transcriptional repressor, suppresses factors that mediate the differentiation of Th1, Th2, and Th17 cells. In addition, Bcl-6 indirectly induces the expression of accessory proteins, such as CXCR4 and PD-1, by repressing clusters of microRNAs that negatively regulate these molecules. The synergistic actions of Bcl-6 and cMAF, in conjunction with CD28, OX40, and ICOS stimulation in Tfh cells, induce a sustained increase in CXCR5 expression. CXCR5 directs migration into B cell follicles where Tfh cells interact with germinal center B cells called centrocytes (4). Tfh cells secrete IL-10, IL-21, and small amounts of IL-2, IL-4, IL-17, and IFN- γ , to stimulate centrocytes to generate antibody-producing plasma cells and memory B cells (5).



This illustration represents general pathways suggested in the scientific literature and is not to be considered comprehensive nor definitive.

Abbreviation Key

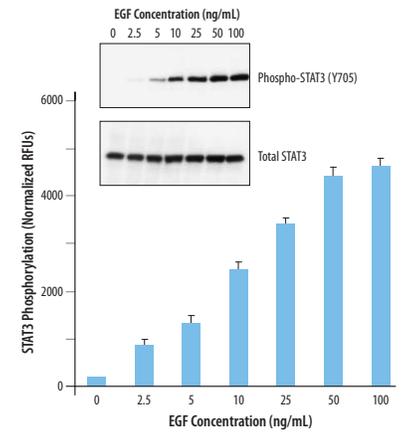
Bcl-6 B cell lymphoma-6
 CD40 L CD40 Ligand
 CR Complement Receptor
 FcR Fc Receptor

ICOS Inducible T cell Co-stimulator
 ICOS L ICOS Ligand
 OX40 L OX40 Ligand
 PD-1 Programmed Death-1

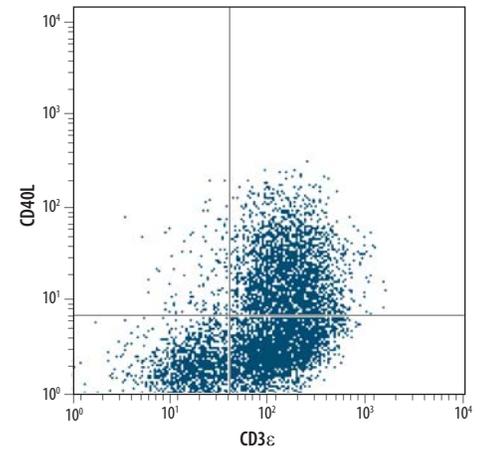
PD-L1 Programmed Death Ligand-1
 SAP SLAM-associated Protein
 SLAM Signaling Lymphocytic Activation Molecule Receptor Family Members
 STAT3 Signal Transducer and Activator of Transcription 3

Follicular Helper T Cell-Related Products

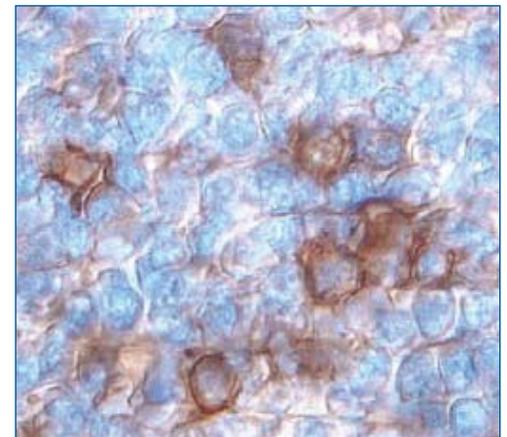
Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs	Other Kits*
Akt		H M R	H M R	
Bcl-6		H M		
BLIMP1		H M		
BTLA/CD272	M	H M		
CCL19/MIP-3β	H M	H M	H M	
CCL21/6CKine	H M	H M	H M	
CCR7		H M		
CD4	H	H M Ca F		H M R
CD10/Nepriylisin	H M	H M	H M	
CD21/Complement Receptor 2	H	H		
CD28	H M	H M		
CD30/TNFRSF8	H M	H M	M	
CD30 Ligand/TNFSF8	H M	H M	M	
CD35/Complement Receptor 1	H	H		
CD40/TNFRSF5	H M	H M	M	
CD40 Ligand/TNFSF5	H M	H M	H M	
CD69		H M		
CD80/B7-1	H M R	H M R	H M	
CD86/B7-2	H M R	H M R	R	
CD200	H M	H M	H	
CD200 R1	H M	H M		
Common γ chain/IL-2 Rγ	H M	H M		
CXCL13/BLC/BCA-1	H M	H M	H M	
CXCR4		H M F		H
CXCR5		H		
Fas/TNFRSF6/CD95	H M R F	H M R F	H M	
Fcγ RII		M		
GATA-3	H			
gp130	H M R	H M	H M	
ICOS	H M	H M		
ICOS Ligand/B7-H2	H M	H M		
IFN-γ	H M R P B Ca C R E F R M	H M R P B Ca C R E F R M	H M R P B Ca C R E F Pr	
IL-2	H M R P B Ca C R E F	H M R P B Ca C R E F	H M R B Ca E F	
IL-4	H M R P B Ca C R E F R M	H M R P B Ca C R E F	H M R P C R E F	
IL-4 Rα	H M	H M		
IL-5	H M R B Ca E F P R M	H M R Ca E F P	H M	H M
IL-6	H M R P Ca C R E F	H M R P Ca C R E F	H M R P Ca F	
IL-6 Rα	H M	H M	H M	
IL-10	H M R P Ca C R E F V	H M R P Ca C R E F V	H M R P Ca E F	
IL-13	H M R Ca R M	H M R	H M	H M
IL-17	H M Ca	H M	H M	
IL-21	M Ca	M	M	
IL-21 R	H M	H M		
Jak1		H M R		
Jak2		M R		
NFATC1		H		
OX40/TNFRSF4	H M	H M		
OX40 Ligand/TNFSF4	H M	H M	M	
PD-1	H M	H M	H	
PD-L1/B7-H1	H M	H M		
PD-L2	H M	H M		
PI 3-Kinase p55γ		H M R		
PI 3-Kinase p85α		H M R		
PI 3-Kinase p110β		H		
PI 3-Kinase p110δ		H		
PI 3-Kinase p110γ		H		
PTEN	H	H M R	H M R	
SHIP		H M R		
SHIP2		H M R		
SLAM/CD150	M	H M		
SLAMF3/CD229	H	H M		
SLAMF5/CD84	H	H		
SLAMF6/Ly-108/NTB-A	H M	H M		
STAT3		H M R	H M	
Tyk2		H		
Vav-1		H		



EGF-induced STAT3 Phosphorylation on Y705 in Human Epithelial Carcinoma Cells. A431 human epithelial carcinoma cells were treated with the indicated concentrations of Recombinant Human EGF (Catalog # 236-EG). STAT3 phosphorylation on Y705 was determined using the Human/Mouse Phospho-STAT3 (Y705) Cell-Based ELISA (Catalog # KCB4607) and normalized to total STAT3 in the same wells (bar graph). Detection of STAT3 phosphorylation on Y705 by Western blot is shown for comparison (inset).



Detection of CD40L and CD3ε on Human Activated PBMCs. Activated human peripheral blood mononuclear cells (PBMCs) were stained with PerCP-conjugated Human CD40 Ligand Monoclonal Antibody (Catalog # FAB617C) and Fluorescein-conjugated Human CD3ε Monoclonal Antibody (Catalog # FAB100F). The dot plot shows the relative CD3ε⁺/CD40L⁺ cell population. Quadrants were set based on isotype controls.



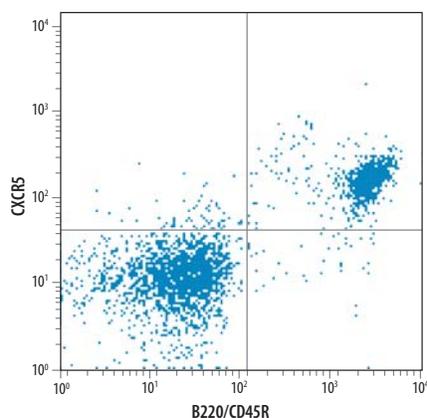
ICOS in Human Tonsil. ICOS was detected in paraffin-embedded human tonsil tissue sections using the Human ICOS Antigen Affinity-purified Polyclonal Antibody (Catalog # AF169). The tissue was stained using the Anti-Goat HRP-DAB Cell and Tissue Staining Kit (Catalog # CTS008; brown) and counterstained with hematoxylin (blue).

Key: H Human M Mouse R Rat B Bovine Ca Canine CR Cotton Rat E Equine F Feline P Porcine Pr Primate RM Rhesus Macaque V Viral
Other kits include: ELISpot Kits & Development Modules, Cell Selection & Detection Kits & Reagents, Multiplex/Array Assay Kits & Reagents.

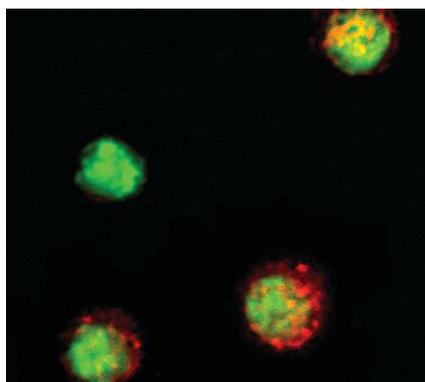


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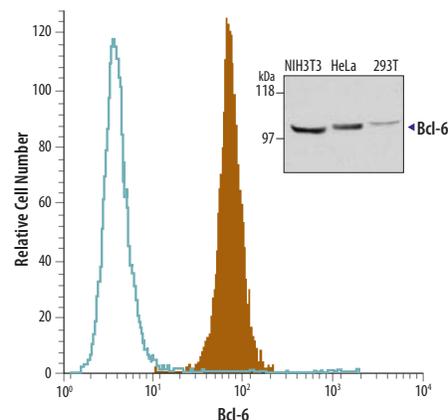
FL103MAR_Tfh_August



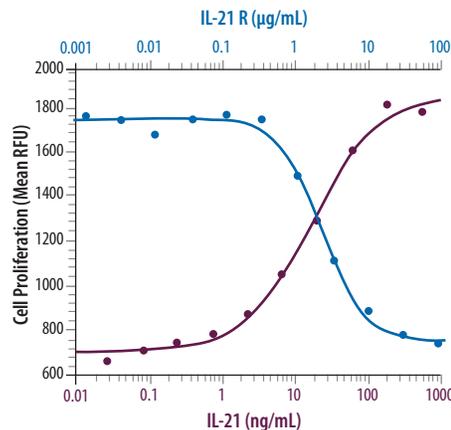
Detection of CXCR5 and B220/CD45R on Mouse Splenocytes. Mouse splenocytes were stained for CXCR5 and B220/CD45R expression using the PE-conjugated Mouse CXCR5 Monoclonal Antibody (Catalog # FAB6198P) and PerCP-conjugated Mouse B220/CD45R Monoclonal Antibody (Catalog # FAB1217A). The dot plot shows the relative B220/CD45R⁺ cell population. Quadrants were set based on isotype controls.



Detection of IL-21 in Mouse Splenocytes. Mouse splenocytes were stimulated with Concanavalin A. IL-21 was detected using the Mouse IL-21 Antigen Affinity-purified Polyclonal Antibody (Catalog # AF594) followed by staining with NorthernLights 557-conjugated Anti-Goat IgG Secondary Antibody (Catalog # NL001; red). Cells were counterstained green.



Detection of Bcl-6 by Flow Cytometry and Western Blot. A20 mouse B lymphoma cells were stained using PE-conjugated Human/Mouse Bcl-6 Monoclonal Antibody (Catalog # IC5046; filled histogram) or PE-conjugated Isotype control (Catalog # IC013P; open histogram). Bcl-6 was also detected by Western blot in lysates from NIH-3T3 mouse embryonic fibroblasts, HeLa human cervical epithelial carcinoma cells, and 293T human embryonic kidney cells using the Human/Mouse Bcl-6 Antigen Affinity-purified Polyclonal Antibody (Catalog # AF5046; inset).



Inhibition of IL-21 Activity by Soluble IL-21 Receptor. Recombinant Mouse IL-21 (Catalog # 594-ML) stimulates the proliferation of N1186 HTLV-1-infected human T cells (red line), measured by resazurin fluorescence (Catalog # AR002). The stimulatory effect induced by 100 ng/mL IL-21 was inhibited in a dose-dependent manner by soluble Recombinant Mouse IL-21 R (Catalog # 596-MR; blue line).