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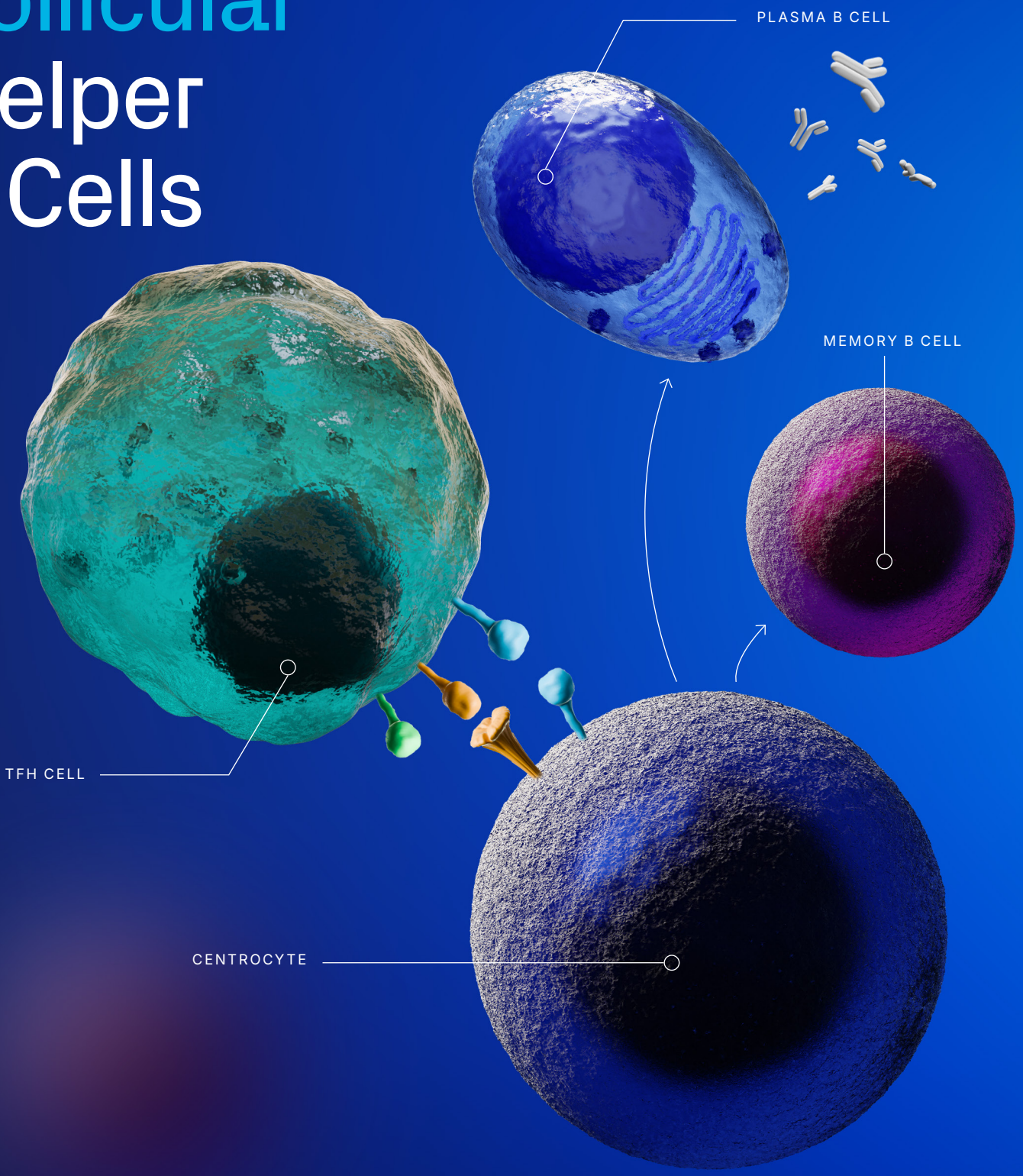
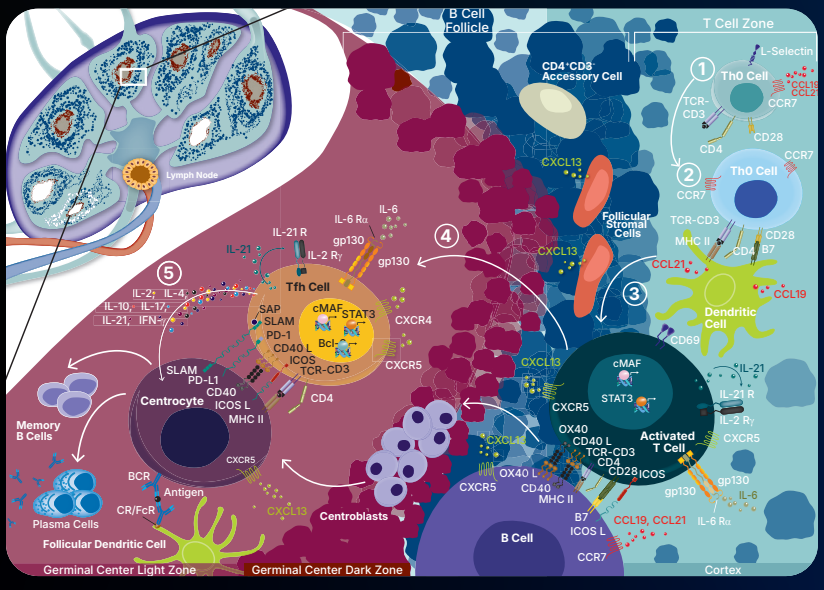
Follicular Helper T Cells



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 receptors, 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.



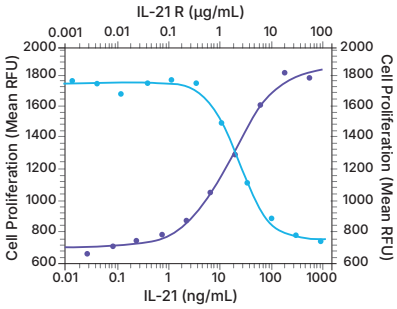
This illustration represents general pathways suggested in the scientific literature and is not to be considered comprehensive nor definitive.

ABBREVIATION KEY

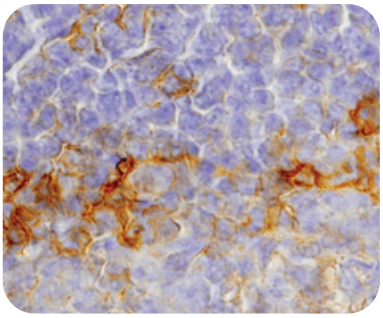
Bcl-6	B cell lymphoma-6
CD40 L	CD40 Ligand
CR	Complement Receptor
FcR	Fc Receptor
ICOS	Inducible T cell Co-stimulator
ICOS L	ICOS Ligand
OX40 L	OX40 Ligand
PD-1	Programmed Death-1
PD-L1	Programmed Death Ligand-1
SAP	SLAM-associated Protein
SLAM	Signaling Lymphocytic Activation Molecule Receptor Family
STAT3	Signal Transducer and Activator of Transcription 3

Follicular Helper T Cell-Related Products

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
2B4/CD244/SLAMF4	H M	H M	
Akt		H M R	H M R
B7-H2/ICOS Ligand	H M	H M	
Bcl-6		H M	
BLAME/SLAMF8	H	H M	
BLIMP1		H M	
BTLA/CD272	H M	H M	
CCL19/MIP-3β	H M R	H M R	H M
CCL21/6Ckine	H M R	H M	H M
CCR7		H M	
CD2F-10/SLAM9	H M	M	
CD4	H R CR F	H M R Ca CR F	
CD10/Neprilysin	H M	H M	H M
CD21	H	H	
CD28	H M	H M	
CD30/TNFRSF8	H M	H M	H M
CD30 Ligand/TNFSF8	H M	H M	M
CD35	H	H	
CD40/TNFRSF5	H M R	H M	H M
CD40 Ligand/TNFSF5	H M R	H M	H M
CD48/SLAMF2	H M	H M	M
CD69	H M	H M	
CD84/SLAMF5	H M	H	
CD200	H M	H M R	H
CD200 R1	H M	H M	
CD229/SLAMF3	H M	H M	
CRACC/SLAMF7	M	H M	
CXCL13/BLC/BCA-1	H M	H M	H M
CXCR4		H M F	
CXCR5		H M	
Fas/TNFRSF6/CD95	H M R F	H M R F	H M
Fcγ RII/CD32		H M	
GATA-3		H M	
ICOS	H M	H M	
IFN-γ	H M R P B Ca CR E F RM V	H M R P B Ca CR E F RM	H M R P B Ca CR E F Pr
IL-4	H M R P B Ca CR E F Rb RM	H M R P B Ca CR E F Rb	H M R P Ca CR E F Rb
IL-4 Rα	H M	H M	
IL-5	H M R P B Ca E F RM	H M R P Ca E F	H M F
IL-6	H M R P Ca CR E F	H M R P Ca CR E F Pr	H M R P B Ca CR F Rb
IL-6 Rα	H M	H M	H M
IL-10	H M R P Ca CR E F V	H M R P Ca CR E F V	H M R P Ca E F GP
IL-13	H M R Ca CR RM	H M R Ca	H M
IL-17/IL-17A	H M R Ca	H M Ca Pr	H M Ca
IL-21	H M Ca Rb	M Ca	M
IL-21 R	H M R	H M	
Jak1		H M R	
Jak2		M R	
NFATC1		H	
NTB-A/SLAMF6/Ly-108	H M	H M	
OX40/TNFRSF4	H M R	H M	
OX40 Ligand/TNFSF4	H M R	H M	M
PD-1	H M CM	H M	H M
PD-L1/B7-H1	H M	H M	H CM
PD-L2	H M CM	H M	H
PI 3-Kinase p55γ		H M R	
PI 3-Kinase p85α		H M R	
PI 3-Kinase p85β		H	
PI 3-Kinase p110β		H	
PI 3-Kinase p110δ		H	
PI 3-Kinase p110γ		H	
PTEN	H	H M R	
SHP-1	H	H M R	
SHP-2	H	H M R	H M R
SLAM/CD150	H M	H M	H M
STAT3		H M R	H M
Tyk2		H	
Vav-1		H M	



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 (purple 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).



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).

H Human **M** Mouse **R** Rat **B** Bovine
Ca Canine **CM** Cynomolgus Monkey
CR Cotton Rat **E** Equine **F** Feline
GP Guinea Pig **P** Porcine **Pr** Primate
Rb Rabbit **RM** Rhesus Macaque **V** Viral

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