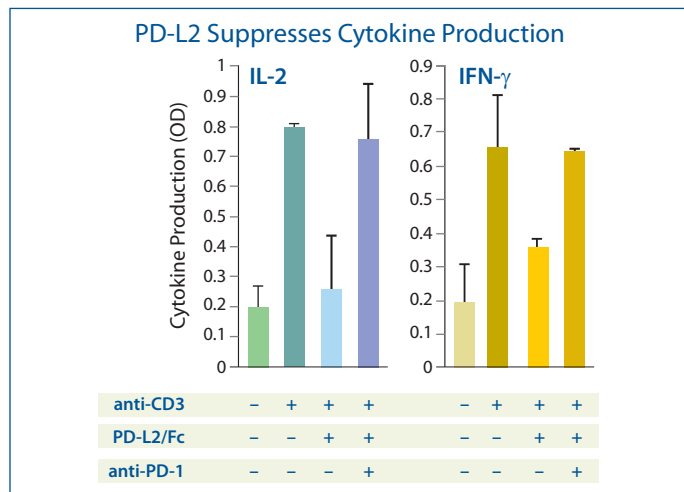


# T-Cell Co-Stimulation/-Inhibition: The B7 Family & Associated Molecules

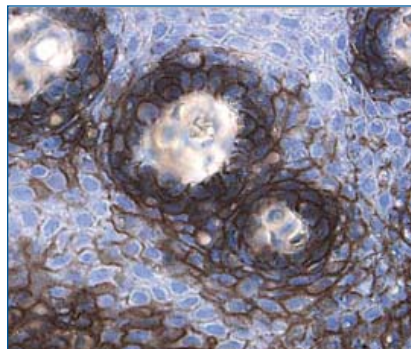
The spectrum of B7 family co-regulatory molecules has expanded since the original members, B7-1 (CD80) and B7-2 (CD86), were described. It now includes seven members with roles inside and outside of lymphoid tissues. PD-L1 (B7-H1) and PD-L2 (B7-DC) play important roles in regulating T cell activation and tolerance by delivering mainly inhibitory signals through T cell programmed death-1 (PD-1). B7-H2 (B7h, ICOSL) is a ligand for inducible co-stimulator (ICOS), an effector of T cell responses and T cell-dependent B cell responses. ICOS engagement stimulates the production of cytokines including IL-10, indicating B7-H2 might influence CD4<sup>+</sup>CD25<sup>+</sup> T regulatory cells, tolerance, and autoimmunity. Two more B7 homologs, B7-H3 and B7-H4 (B7x, B7-S1), bind to and influence activated T cells, although the receptors they engage are not yet known. B7-H3 shows both stimulatory and inhibitory actions, while B7-H4 is an unequivocal negative regulator of T cell responses. B7-1 and B7-2 act through CD28 as co-stimulators and CTLA-4 as a co-inhibitor.



**Figure 1.** The co-inhibitory ligand PD-L2 suppresses cytokine production in stimulated T cells. PHA human T cell blasts were stimulated with an anti-CD3 antibody, or stimulated with anti-CD3 supplemented with R&D Systems recombinant PD-L2/Fc chimera (Catalog # 1224-PL), or treated with anti-CD3, recombinant PD-L2/Fc, and R&D Systems human anti-PD-1 monoclonal antibody (Catalog # MAB1086). After a 2 day incubation, supernatants were collected and assessed using R&D Systems IL-2 (Catalog # D2050) or IFN- $\gamma$  (Catalog # DIF50) Quantikine<sup>®</sup> ELISA kits. Cytokine stimulation is suppressed by PD-L2, which is in turn inhibited by a blocking antibody to its receptor, PD-1.

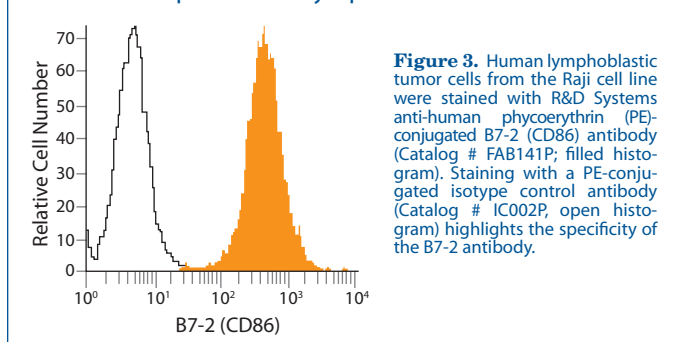
Figure used with permission: Saunders, P.A. et al. (2005) Eur. J. Immunol. 35:3561.

## CD58/LFA-3 in Human Tonsil



**Figure 2.** Detection of CD58 in paraffin-embedded human tonsil tissue sections using R&D Systems anti-human CD58 affinity-purified polyclonal antibody (Catalog # AF1689). Tissues were stained using anti-goat HRP-DAB Cell and Tissue Staining Kit (brown; Catalog # CTS008) and counterstained with hematoxylin (blue).

## B7-2 Expression in Lymphoblastic Tumor Cells



**Figure 3.** Human lymphoblastic tumor cells from the Raji cell line were stained with R&D Systems anti-human phycoerythrin (PE)-conjugated B7-2 (CD86) antibody (Catalog # FAB141P; filled histogram). Staining with a PE-conjugated isotype control antibody (Catalog # IC002P, open histogram) highlights the specificity of the B7-2 antibody.

## Co-Stimulation/Co-Inhibition Research Reagents

MOLECULE	ANTIBODIES	PROTEINS	ELISAs/ASSAYS	PRIMER PAIRS
2B4/SLAMF4	H M	H M		
4-1BB/TNFRSF9	H M	H M	H M	
4-1BB Ligand/TNFSF9	H M	H M		
B7-1/CD80	H M R	H M R	H M	
B7-2/CD86	H M R	H M R		
B7-H1/PD-L1	H M	H M		
B7-H2	H M	H M		
B7-H3	H M	H M		
B7-H4	M	M		
BLAME/SLAMF8	H M			
BTLA	H M			
CD2F-10/SLAMF9	M			
CD27/TNFRSF7	H M	H M	M	H
CD27 Ligand/TNFSF7	H M	M	M	M
CD28	H M	H M		
CD30/TNFRSF8	H M	H M	M	H M R
CD30 Ligand/TNFSF8	H M	H M	M	H
CD40/TNFRSF5	H M	H M	M	H
CD40 Ligand/TNFSF5	H M	H M	H M	H M R
CD48/SLAMF2	H M	H M		
CD58/LFA-3	H	H		
CD84/SLAMF5	H	H		
CD229/SLAMF3	H M			
CRACC/SLAMF7	H			
CTLA-4	H M	H M		
GITR/TNFRSF18	H M	H M	H M	H
GITR Ligand/TNFSF18	H M	H M	H	
HVEM/TNFRSF14	H M	H		
ICOS	H M	H M		
LAG-3	H M	H		
LIGHT/TNFSF14	H M	H M	H	H
NTB-A/SLAMF6	H			
OX40/TNFRSF4	M	H M		
OX40 Ligand/TNFSF4	H M	H M	H	
PD-1	H M	H M		
PD-L2	H M	H M		
SLAM	H			
TIM-1/KIM-1/HAVCR	H M R	H M R		
TIM-4	H M	H M		

Key: H Human M Mouse R Rat