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The B7:CD28 Superfamily: Starting, Stopping and Attenuating T Cell Responses

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Pathways within the B7:CD28 superfamily play key roles in regulating T cell activation and tolerance. These pathways not only provide critical positive second signals that augment and sustain T cell responses, but also contribute key negative second signals that downregulate T cell responses. The B7-1/B7-2:CD28/CTLA-4 costimulatory pathway is the best characterized costimulatory pathway, but is complex due to the dual specificity of the B7 ligands, B7-1(CD80) and B7-2(CD86), for the stimulatory CD28 receptor and inhibitory CTLA-4 (CD152) receptors, and the opposing outcomes of CD28 and CTLA-4 engagement. Recently, two new pathways within the B7:CD28 superfamily have been defined: one pathway involving the CD28 homologue ICOS that interacts with a ligand which will be called ICOS ligand (B7h, GL50, B7RP-1, LICOS, B7-H2), and a second pathway involving the PD-1 receptor that interacts with two new B7 family members, PD-L1 (B7-H1) and PD-L2 (B7-DC). The discovery of these pathways has revealed new means by which T cell responses are regulated and raised questions about the roles of these pathways in regulating T cell activation and tolerance. Studies defining the functions of these two new pathways and investigating their functional relationships with the B7-1/B7-2:CD28/CTLA-4 pathway will be presented.

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