

CD148 is excluded from the immunologic synapse and downregulates prolonged signals

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CD148 is a receptor-like tyrosine phosphatase involved in signal transduction of many cell types. Resting T cells express low levels of CD148 on the cell surface, however upon stimulation, it is upregulated. To further examine the role of CD148 in T cells, we expressed CD148 in Jurkat T cells which do not have endogenous CD148. Expression of CD148 inhibits the NFAT response induced by soluble anti-T cell receptor (TCR) antibody stimulation. However, when CD148 expressing cells are stimulated with either antigen presenting cells (APC) loaded with super-antigen (SAg) or immobilized anti-TCR antibodies, the inhibition of NFAT activation is no longer seen. Upon closer examination by immunofluorescence, CD148 appears to be excluded from the central region of the T cell-APC contact termed the immunologic synapse and therefore potential substrates. The CD148 extracellular domain mediates the exclusion out of the synapse. When the phosphatase domain of CD148 is targeted to the synapse, NFAT activation is potently inhibited by all means of triggering through the TCR. This data leads us to propose a model where CD148 activity is regulated by exclusion from the immunologic synapse. Upon APC-T cell disengagement, CD148 can then access potential downstream substrates to downregulate the prolonged response after T cell stimulation.