

THE MIDWINTER CONFERENCE OF IMMUNOLOGISTS POSTER ABSTRACT - 2005

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Regulation of the receptor-like tyrosine phosphatase CD148 on hemopoietic cells.

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Protein tyrosine phosphatases can both positively and negatively regulate lymphocyte activation. One such example is the CD45 receptor like tyrosine phosphatase, which is required for initiation of TCR signaling by dephosphorylating a regulatory tyrosine in Lck. CD148 is a receptor-like protein tyrosine phosphatase expressed on a wide variety of cell types. Through the use flow cytometry and immunofluorescence microscopy on tissue sections, we examined the expression of CD148 on multiple murine hemopoietic cell lineages. We found that CD148 is moderately expressed during all stages of B cell development, as well as peripheral mature B cells. In contrast, CD148 expression on thymocytes and mature T cells is substantially lower. However, stimulation of peripheral T cells through the TCR leads to an increase of CD148 expression. This up-regulation on T cells can be partially inhibited by reagents that block the activity of src family kinases, calcineurin, MEK, or PI3K. Using a tetracycline inducible expression system, our lab has shown that TCR mediated activation of both Ras and Ca²⁺ pathways are inhibited by expression of CD148. Importantly, LAT and PLC γ are specifically dephosphorylated, while most phosphoproteins are unaffected by CD148 expression. These results indicate that CD148 regulates TCR signaling by targeting LAT and PLC γ . However, it is not clear if LAT and PLC γ are direct substrates of CD148. To further explore the mechanism of CD148 function, we have generated substrate-trapping mutant of CD148. We have identified number of phosphoproteins interact with CD148. Their identification may provide new insights into the role of CD148 in antigen receptor signaling. In addition, we have also generated CD148 mutant WEHI 231 B cell line. The function of CD148 on BCR mediated signaling pathways were examined.