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Title

Wc1 Mediates T Cell Activation And Is Required For The Response Of Bovine $\gamma\delta$ T Cells To Leptospira Antigen

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Abstract

Workshop cluster 1 (WC1) molecules are exclusively expressed on the surface of $\gamma\delta$ T cells. They belong to the scavenger receptor cysteine-rich (SRCR) superfamily and are encoded by a multiple-gene family. WC1 molecules are divided into three major groups, WC1.1, WC1.2 and WC1.3, on the basis of antibody reactivity. The expression of WC1 molecules from these groups correlates with differences in $\gamma\delta$ T cell responses. Particularly, the expression of receptors within the serologically-defined WC1.1 group correlates with the capacity to respond to *Leptospira* antigen. The potential role of WC1 as a co-stimulatory molecule for the $\gamma\delta$ TCR is suggested by the presence of several tyrosine-based motifs in their intracellular domains. In this study, we found that WC1 was constitutively phosphorylated in ex vivo bovine $\gamma\delta$ T cells and associated with src family tyrosine kinases. Crosslinking of WC1 molecules resulted in an increase in WC1 phosphorylation and co-crosslinking of WC1 and $\gamma\delta$ TCR together prolonged WC1 phosphorylation. We identified the second tyrosine residue on the WC1 intracellular tail as the primary phosphorylation target in WC1.1 and WC1.2 intracellular sequences in both in vitro and in vivo assays. And phosphorylation of the second tyrosine was required for the WC1-mediated potentiation of TCR-induced T cell proliferation, suggesting that WC1 acts as a co-stimulatory molecule for $\gamma\delta$ TCR. The cytoplasmic tails of WC1.1 and WC1.2 were also phosphorylated on serine and PKC activity was required for phosphorylation-dependent endocytosis of WC1.1 or WC1.2. Finally, we used RNA interference to directly investigate the role of WC1 expression in the response to *Leptospira borgpetersenii*. We found that when a subset of WC1 transcripts were down-regulated by RNA interference, the proliferation of cells in response to *Leptospira* antigen and the production of IFN- γ was significantly reduced. Our data directly demonstrate that the co-receptors in the WC1 family act as an essential component for *Leptospira* recognition and/or activation of $\gamma\delta$ T cells.

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