

# ScholarWorks@UMass Amherst

## DOCTORAL DISSERTATIONS 1896 - FEBRUARY 2014

Off-campus UMass Amherst users: To download campus access dissertations, please use the following link to [log into our proxy server](#) with your UMass Amherst user name and password.

Non-UMass Amherst users: Please talk to your librarian about requesting this dissertation through interlibrary loan.

Dissertations that have an embargo placed on them will not be available to anyone until the embargo expires.

### **Title**

WC1 Functions as a Co-Receptor and A Pattern Recognition Receptor In Bovine Gamma delta T Cells

### **Author**

Hao-Ting Hsu, *University of Massachusetts - Amherst*

### **Date of Award**

9-2013

### **Document Type**

Campus Access

### **Degree Name**

Doctor of Philosophy (PhD)

### **Degree Program**

Molecular and Cellular Biology

## First Advisor

Janice Telfer

## Second Advisor

Cynthia Baldwin

## Third Advisor

Wilmore Webley

## Subject Categories

Immunology and Infectious Disease

## Abstract

WC1 proteins specifically expressed on the surface of  $\gamma\delta$  T cells are members of group B Scavenger Receptor Cysteine Rich (SRCR) superfamily, in which receptors contain several SRCR domains in the extracellular region. WC1+  $\gamma\delta$  T cells play a critical role in bridging innate and adaptive immunity, organizing granulomas in response to *Mycobacterium* and producing IFN $\gamma$  in response to *Leptospira*. The serologically-defined WC1.1+  $\gamma\delta$  T cells exclusively respond to spirochete *Leptospira*; the serologically-defined WC1.2+ subpopulation responds to rickettsias *Anaplasma*; shRNA silencing three WC1.1+ proteins significantly reduced  $\gamma\delta$  T cell response to *Leptospira* antigen. Co-ligation of WC1 with TCR/CD3 potentiates T cell activation, and tyrosine phosphorylation of the WC1 cytoplasmic domain is required for WC1 co-receptor activity. We hypothesized that WC1 receptors encode antigen specificity and contribute to T cell activation in response to leptospirosis. Our data showed SRCR domains from a WC1.1 type receptor, WC1-3, directly interact with vaccines and liquid cultures of leptospires. Vaccine *Leptospira* interacts with more SRCR domains as compared to liquid cultures, suggesting that vaccine preparation may enhance ligand accessibility to SRCR domains. Importantly, we did not observe any *Leptospira* binding from WC1-4 SRCR domains, a representative WC1.2 type receptor. The binding assay showed that SRCR a1 domains from WC1.1 type proteins contribute to *Leptospira* recognition, but none from WC1.2 proteins does. Alkaline phosphatase treatment suggests that a phosphorylation pattern is recognized by SRCR a1 domain, supporting that WC1 functions as a pattern recognition receptor. PMA-induced CD4/WC1-3 endocytosis is mediated by a membrane-proximal dileucine motif, which is essential for the recruitment of AP2 complexes. The disruption of the dileucine motif greatly accumulates the overall levels of CD4/WC1-3 molecules on the cell surface and in the cytoplasm. Co-crosslinking CD4/WC1-3 and TCR/CD3 indicates that the dileucine motif acts as a negative regulator for downstream cytokine production. Moreover, a double serine motif upstream the dileucine motif mediates signaling through WC1-3 for the downstream event. Taken together, the data support that co-ligation of WC1 and the  $\gamma\delta$  TCR by pathogen-associated molecular patterns (PAMPs) induces specific  $\gamma\delta$  T cell activation.

## Recommended Citation

Hsu, Hao-Ting, "WC1 Functions as a Co-Receptor and A Pattern Recognition Receptor In Bovine Gamma delta T Cells" (2013). *Doctoral Dissertations 1896 - February 2014*. 514.  
[https://scholarworks.umass.edu/dissertations\\_1/514](https://scholarworks.umass.edu/dissertations_1/514)

[Download](#)

DOWNLOADS

Since June 25, 2014

Share

COinS