FCΓ RECEPTOR BINDING BREADTH OF RV144 ANTIBODIES

Chung AW[1], McLean MW[1], Madhavi V[1], Wines BD[2,3,4], Hogarth PM[2,3,4], Kent SJ[1,5,6]

[1] Department of Microbiology and Immunology, Peter Doherty Institute for Infection and Immunity, University of Melbourne
[2] Centre for Biomedical Research, Burnet Institute
[3] Department of Immunology, Monash University Central Clinical School
[4] Department of Pathology, The University of Melbourne
[5] Melbourne Sexual Health Centre, Infectious Diseases Department, Alfred Health, Central
Clinical School, Monash University
[6] ARC Centre of Excellence in Convergent Bio-Nano Science and Technology

Background: Immune correlates analysis of the partially protective RV144 vaccine trial identified antibodies that recognize the V1V2 region as a correlate of protection, while Antibody dependent cellular cytotoxicity (ADCC) responses was a secondary correlate of protection. Thus understanding the protective mechanisms behind V1V2 antibodies, along with ADCC responses are of growing interest in the HIV vaccine field.

Methods: We developed an ELISA and multiplex assay to model the cross-linking of Fcγ-receptors (FcγR) by antibodies which is required to initiate an ADCC response. The high-throughput multiplex assay allowed us to simultaneously measure FcγR dimer binding antibodies to 32 different HIV antigens across 7 different HIV-1 clades, providing a measure of the breadth of FcγR-binding antibodies induced by the RV144 trial. RV144 plasma samples were also profiled for their IgG subclasses and functional ADCC activity.

Results: The FcγR dimer binding antibodies induced by the RV144 regimen correlated well with functional ADCC assays as well as IgG subclasses. FcγR-binding antibodies specific to V1V2 were strongly associated with increased breadth of recognition of different Env proteins.

Conclusions: Taken together our results describe a robust high throughput assay to predict ADCC responses. This FcγR dimer binding multiplex assay has the potential to screen large panels of HIV proteins for ADCC breadth and reduce the need to run cell-based assays for the early recognition of ADCC functional antibodies, thus accelerating the identification of immune responses that may contribute to an effective HIV-1 vaccine. In addition, we further characterize the immunity of the RV144 trial, suggesting that the anti-V1V2 antibodies induced by RV144 may be a marker of increased ADCC breadth.