

DETECTION AND CHARACTERIZATION OF ANTI-IFN- γ AUTOANTIBODY IN PATIENTS WITH ADULT-ONSET IMMUNODEFICIENCY SYNDROME

Dyah Ika Krisnawati

Graduate Institute of Medical Sciences, College of Medicine, Taipei Medical University

Email : dyah_krisna@ymail.com

Abstract

Interferon (IFN)- γ , a type II IFN produced by natural killer cells, dendritic cells, and T cells, confers crucial functions for inducing immunomodulation (such as macrophage activation, antigen presentation, and helper T cell differentiation), causing antimicrobial (such as antiviral replication, microbial killing, and MHC induction), and promoting anticancer activity (such as growth inhibition, cytotoxicity, and immune priming). An emerging type of immune disorder, called adult-onset immunodeficiency syndrome, has currently reported in patients who show defects in IFN- γ signaling commonly resulted from the generation of anti-IFN- γ autoantibody and partly due to mutations in IFN- γ signaling molecules. In these cases, tuberculosis and non-tuberculosis mycobacteria infection are frequently identified regarding IFN- γ is potent anti-tuberculosis cytokine. Until now, the detection of anti-IFN- γ autoantibody is not recurrently in clinical and the immunopathogenesis of anti-IFN- γ autoantibody remains unclear. This study aims to develop methods for the detection of anti-IFN- γ autoantibody in patients with adult-onset immunodeficiency and plans to characterize the immunopathogenic effects of anti-IFN- γ autoantibody. Specific Aim 1 of this study is to develop methods for detecting anti-IFN- γ autoantibody. ELISA and western blot are utilized in this study. The possible binding site is next evaluated by using synthetic peptide binding assay. According to the results, we propose that the generation of anti-IFN- γ autoantibody may neutralize IFN- γ effectively. Specific Aim 2 is to perform those all functional assay to check IFN- γ -activated STAT-IRF1 signaling pathway as well as IFN- γ -mediated nitric oxide generation, cytokine/chemokine production, T cell activation, and anti-tuberculosis activity. These results provide methods for autoantibody detection and characterize the blockade effects of autoantibody on IFN- γ signaling and bioactivity.

Keywords: Anti-IFN- γ autoantibody, Adult-onset immunodeficiency syndrome, Immunopathogenesis, Signaling, Bioactivity

