

IL-17 is dispensable for inflammatory myocarditis but essential for the progression to dilated cardiomyopathy

G. Christian Baldeviano^{1,2}, Sachin Srinivasan², Jobert G. Barin¹, Dongfeng Zheng¹, Monica Talor¹, Djahida Bedja³, Kathleen Gabrielson³, Noel R Rose^{1,2} and Daniela Cihakova¹

1 Department of Pathology, the Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA

2 W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

3 Department of Molecular and Comparative Pathobiology, the Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.

Myocarditis and dilated cardiomyopathy (DCM) are significant causes of sudden death in young adults. Whereas CD4⁺ helper lymphocytes are essential for myocarditis induction, the subset(s) and effector function(s) mediating inflammation in the heart are not well defined. We sought to determine the role of Th17 CD4⁺ T cells in the induction of myocarditis, and the progression to DCM using a murine model of myocarditis (EAM). Gene knockout studies revealed that IL-12p40, but not IL-12p35, is essential for myocarditis induction, underscoring a critical role for IL-23 dependent Th17 cells in the initiation of myocarditis. However, deficiency in IL-17A, a major cytokine secreted by Th17 cells, did not abrogate heart inflammation, nor did it abolish the production of myosin-specific autoantibodies. Remarkably, echocardiography analysis revealed that IL-17A deficient mice were completely protected from DCM, which correlated with decreased deposition of collagen in the myocardium. Thus, IL-17 is dispensable for myocarditis inflammation but is a critical mediator of tissue fibrosis and cardiac remodeling leading to post-inflammatory heart dysfunction.