Cooperation of Th1 and Th17 cells determines transition from autoimmune myocarditis to dilated cardiomyopathy

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Myocarditis is a potentially lethal inflammatory heart disease of children and young adults that frequently leads to dilated cardiomyopathy (DCM). Since diagnostic procedures and efficient therapies are lacking, it is important to characterize the critical immune effector pathways underlying the initial cardiac inflammation and the transition from myocarditis to DCM. We describe here a T-cell receptor (TCR) transgenic mouse model with spontaneously developing autoimmune myocarditis that progresses to lethal DCM. Cardiac magnetic resonance imaging revealed early inflammation-associated changes in the ventricle wall including transient thickening of the left ventricle wall. Furthermore, we found that IFN-γ was a major effector cytokine driving the initial inflammatory process and that the cooperation of IFN-γ and IL-17A was essential for the development of the progressive disease. This novel TCR transgenic mouse model permits the identification of the central pathophysiological and immunological processes involved in the transition from autoimmune myocarditis to DCM.