Molecular mapping of autoimmune B cell responses in experimental myocarditis

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Autoimmune responses directed against heart-specific antigens most likely play a key role in the pathogenesis of myocarditis. Although autoantibodies against cardiac determinants are frequently detected both in human patients and mice suffering from myocarditis, the immunological mechanisms for their induction have not yet been fully explored. We used here the SEREX approach (serological identification of recombinantly expressed proteins) to molecularly dissect heart-specific autoimmune B cell responses that develop in the course of experimentally induced myocarditis. Screening of a heart cDNA library with sera of cardiac myosin heavy chain alpha (myhcalpha) peptide-immunized BALB/c mice revealed a strong focusing of the B cell response on the myhcalpha protein. The vast majority of the myhcalpha transcripts coded for regions other than the sequence of the immunogenic myhcalpha peptide, indicating extensive intramolecular epitope spreading. Importantly, we found that the infection with cardiotropic viruses such as MCMV and Coxsackievirus B3 elicited specific autoantibody pattern with a particular skewing to the myhcalpha protein. The induction of myhcalpha peptide-specific Th cells in the course of both infections suggests that infection-associated determinant spreading on the Th cell level paves the way for a focused and dominant anti-myhcalpha B cell response.