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SmD1 83-119 peptide accelerates disease in lupus prone mice

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Keywords

Anti-dsDNA antibodies, lupus mice, SmD1 peptides, systemic lupus erythematosus

Context

Among antibodies found in sera from patients with systemic lupus erythematosus (SLE), those directed against DNA and Sm proteins are specific and have been included as one of the American College of Rheumatology classification criteria for SLE. The authors have previously identified a polypeptide (83-119) of SmD1 protein recognized by 70% of SLE patients' sera. They observed that reactivity to 83-119 polypeptide is higher in anti-dsDNA antibody positive sera than anti-dsDNA antibody negative sera. The present study was undertaken to analyze the influence of the SmD1 83-119 polypeptide on the generation of pathogenic anti-dsDNA antibodies. The authors immunized female lupus-prone prenephritic (NZB x NZW) F_1 mice (NZB/NZW mice) with keyhole limpet hemocyanin (KLH)-coupled SmD1 83-119 peptide and measured survival, proteinuria, renal function and anti-dsDNA production.

Significant findings

Immunization of NZB/NZW mice with KLH-SmD1 83-119-but not with control peptide and protein-resulted in decreased survival, increased anti-dsDNA antibody production, enhanced proteinuria and immune complex nephritis, and accelerated production of autoantibodies directed against various self antigens. None of these manifestations were observed in other control mouse strains immunized with KLH-SmD1 83-119. The authors also found that splenocytes from unmanipulated NZB/NZW mice, unlike those from normal mice, proliferated in response to peptide 83-119; this response was further amplified after immunization. Cells from both untreated and treated NZB/NZW mice seldom recognized the recombinant SmD1 protein used as a control.

Comments

This study showed that injection of polypeptide 83-119 of SmD1, previously identified as a B-cell epitope in SLE patients, induced an accelerated disease in prenephritic NZB/NZW mice. As shown with cellular experiments, 83-119 polypeptide seems to be also a T-cell epitope in NZB/NZW mice. Based on unpublished observations (i.e. that the highly positively charged C-terminal SmD1 peptide binds to DNA) the authors proposed that SmD1-DNA complexes could activate T cells via SmD1 peptides and B cells via DNA. This mechanism suggests a role for SmD1 83-119 polypeptide in accelerating the production of anti-dsDNA antibodies via T-cell stimulation. Indeed, this hypothesis seems very attractive. Application to the human disease, however, would require the identification of T-cell epitopes in SLE patients. A recent study identified regions of SmD1 recognized by T-cell clones from SLE patients in residues 35-53 and 53-67 (see Additional information [1]). Such sequences have also been well documented as B-cell epitopes in lupus-prone mice (see Additional information [2]) and in humans.

Methods

Immunization, ELISA, immunohistology, T-cell proliferation

Additional information

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