

**Characterization of human DNA
topoisomerase II as an autoantigen
recognized by patients with IDDM**

商惠芳

Chang YH;Hwang Jaulang;Shang HF and Tsai ST

摘要

Abstract

Autoantibodies against several cytoplasmic autoantigens such as glutamic acid decarboxylase, heat shock protein 65, insulin, and carboxypeptidase H have been identified in the sera of patients with IDDM. To investigate whether type II DNA topoisomerase (TopII) is an autoantigen in IDDM patients, we have constructed a series of overlapping DNA TopII fragments that covered the entire length of this enzyme. These fragments were used as antigens to screen sera of IDDM patients. We have examined 195 Chinese IDDM patients (mean age 14.2 +/- 7.5 years, age at onset 9.2 +/- 6.4 years, duration of diabetes 4.6 +/- 3.4 years) and 51 nondiabetic individuals. The results showed that DNA TopII autoantibodies were detected in 49.2 and 47.2% of IDDM patients using purified TopII fragments and full-length TopII as antigens, respectively. The frequency of anti-TopII positivity was relatively stable irrespective of sex and disease duration. The patients were slightly older at onset and the prevalence of anti-thyroglobulin/anti-microsomal autoantibodies was twice that in the IDDM subgroup positive for anti-TopII than in IDDM patients who were negative for anti-TopII. We also characterized the epitopes of DNA TopII that were recognized by IDDM sera. Those epitopes resided mostly in three distinct domains. One resided in amino acid residues 1-147, another in amino acid residues 286-472, and the third in the COOH-terminal one-third of DNA TopII. Intriguingly, we found that these epitopes shared similarity (up to 36% identity and 63.6% homology) to previously identified epitopes of IDDM autoantigens