098

Interleukin (IL) 10 gene promoter polymorphism in systemic lupus erythematosus

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Background : IL10 is an anti-inflammatory cytokine produced by TH_2 lymphocytes, B cells, monocytes and macrophages. In contrast to its inhibitory effect on the functions of T helper cells and antigen presenting cells, it is a potent cytokine promoting the proliferation and growth of B cells and hence antibody production. Three biallelic polymorphisms at positions -1087 (A or G), -824 (C or T) and -597 (A or C) have been identified in the IL10 gene promoter region. Preliminary studies have revealed that these polymorphisms may have a function effect on IL10 transcription. Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by B cell hyperactivity leading to pathological antibody production. IL10 level is increased in patients with SLE and the level fluctuates with clinical and serological activity. The aim of the present project is to study the IL10 promoter polymorphisms in our local Chinese SLE population.

Methods : DNA was extracted from patients with SLE and age-matched controls. The promoter region of the IL10 gene from -1120 to -533 position was expanded by polymerase chain reaction (PCR). Polymorphic alleles at the -1087, -824 and -597 positions were studied by restriction enzyme cleavage (mnlI, MaeIII, RsaI respectively).

Results :

-597 position

	CC	CA	AA	Total
SLE	2	12	14	28
Normal	4	9	15	28

Fisher's exact test p>0.05

-824 position

	TT	TC	CC	Total
SLE	2	12	14	28
Normal	4	9	15	28

p>0.05

Conclusions : Nucleotide C at the -597 position is linked to C at the -824 position wheras A at the -597 position is linked to T at the -824 position in all the samples studied. There is no significant difference in the distribution of alleles between normal controls and SLE patients at the -597 and -824 positions. More patients and controls are being studied and the polymorphism at the -1087 position is going to be evaluated soon.

099

PERIPHERAL LYMPHOCYTE APOPTOSIS AND bcl-2 EXPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: CORRELATION WITH DISEASE ACTIVITY.

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Defective apoptosis has been suggested to be of pathogenic significance in autoimmune diseases such as systemic lupus erythematosus (SLE). However, previous studies have shown contrasting results. In this study, we investigated the correlation between the rate of apoptosis of peripheral blood lymphocytes and disease activity in patients with SLE.

Cytoplasmic bcl-2, which has been correlated with cell survival, was measured by a specific monoclonal antibody after permeation of plasma membrane. Cells were also cultured without stimulation for 2 days and apoptotic cells were detected by a commercial kit which labelled cells with DNA fragmentation. Disease activity was scored by the SLE disease activity index (SLEDAI). Fewer peripheral lymphocytes were bcl-2^+ in SLE patients than in controls (medians 90.6% vs 97.1%, $p<0.05$). The difference between patients and controls was more marked in those with active disease (SLEDAI>10) (84.9%) and no difference was found between normal and patients with inactive disease (SLEDAI<5) (95.3%). The rate of apoptosis of cultured cells was significantly higher in SLE patients than controls (34.2% vs 11.5%, $p<0.05$). The differences between active disease (62%) and normal and between inactive disease (27.5%) and controls were both significant ($p<0.005$).

We did not find defective apoptosis in our patients with SLE. Indeed, a higher rate of apoptosis and a lower percentage of *bcl-2*$^+$ lymphocytes were found in patients with active SLE. It is possible that SLE disease flare is due to failure to clear apoptotic cells.