

## **Increased expression of c-rel, from the NF-KB/Rel family, in T cells from patients with systemic lupus erythematosus**

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### **Abstract**

#### **OBJECTIVE:**

To explore the role of the NF-kappaB/Rel transcription factor family in autoimmunity, we investigated whether peripheral blood mononuclear cells (PBMC) and T cells from the blood of patients with systemic lupus erythematosus (SLE) exhibit abnormal expression of c-rel, both when recently isolated and/or during in vitro activation.

#### **METHODS:**

Total RNA and protein extracts were prepared from PBMC and T cells isolated by immunoadsorption with magnetic beads. The relative concentrations of c-rel mRNA and of c-Rel protein were determined by semiquantitative assays of competitive reverse transcriptase-polymerase chain reaction and chemiluminescent immunoblots, respectively. Activity of NF-kappaB/Rel was studied by electrophoretic mobility shift assay of nuclear extracts.

#### **RESULTS:**

Significantly increased levels of c-rel mRNA were found (1) in PBMC from SLE patients (n = 48; p<0.0000001), even during inactive disease (n = 11; p<0.001), compared to controls (n = 54), and (2) in T cells isolated from a subgroup of these patients (n = 11; p<0.00002) and controls (n = 12). c-Rel protein was found increased in the cytosol but not in the nucleus of PBMC of patients with SLE (n = 12; p<0.02) compared to controls (n = 12). No evidence of NF-kappaB/Rel nuclear activity was detected. In vitro stimulation of T cells by incubating PBMC with concanavalin A showed that less c-Rel entered the nucleus in lupus cells than healthy cells, correlating with lower interleukin 2 production. However, the same stimulating conditions provoked an increase in c-rel mRNA to higher levels in lupus cells from 2 patients compared with 2 controls. Increased levels of both IkappaB alpha and IkappaB beta could account for c-Rel cytosolic retention.

#### **CONCLUSION:**

Our data suggest that T cells from patients with SLE possess altered regulatory mechanisms of c-rel expression and nuclear import that might potentially determine conditions for developing autoimmunity. Other cells present in the PBMC could also be affected.