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Release of autoantigens from apoptotic cells

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Keywords

Apoptosis, histones, systemic lupus erythematosus

Context

Autoantibodies found in SLE sera are frequently directed towards antigens exposed during the "blebbing" phase of apoptosis. These blebs contain nucleosomes - DNA wound around a histone core, which have been cleaved by an endonuclease induced by caspases. To investigate the spectrum of autoantibodies to proteins induced by apoptosis in normal human serum and in sera from five patients with SLE.

Significant findings

Autoantibodies to 13, 21 and 33 kDa antigens were only seen in apoptotic lysates, and at much higher concentrations in SLE sera than in normal controls. These were identified as histone H4 (13 kDa band), H3, H2b and H2a (21 kDa), and H1a and H1b (33 kDa band). Blocking steps were used to confirm specificity. An immune complex precipitation step ensured that anti-DNA antibodies in DNA/histone complexes were not detected.

Comments

This finding confirms previous reports of autoantibodies to antigens generated during apoptosis. Since such antibodies were also detected in normal controls, it is suggested that the immune dysregulation of lupus may result from inefficient clearance of apoptotic cells. It would be interesting to confirm the low levels of such antibodies in individual normal subjects (rather than using pooled serum) and also to relate levels of such antibodies to disease activity or manifestations. If poor clearance of apoptotic cells is an important feature of lupus, then methods of enhancing clearance may be of therapeutic importance.

Methods

Apoptosis was induced in cell lines (Jurkat and U937) using a variety of techniques, and confirmed by both electron microscopy and annexin V/PI staining. Apoptosis-induced proteins were isolated by cell lysis in buffer solutions that preserved cytoplasmic but not nuclear antigens, ultracentrifuged and then electrophoresed. The proteins separated by electrophoresis were blotted onto nitrocellulose and probed with human sera.

References

1. Huggins ML, Todd I, Cavers MA, Pavuluri SR, Tighe PJ, Powell RJ: Antibodies from systemic lupus erythematosus (SLE) sera define differential release of autoantigens from cell lines undergoing apoptosis. Clin Exp Immunol. 1999, 118: 322-328.