THE EXPRESSION OF AUTOANTIBODIES TO MITOCHONDRIA IN THE BLOOD OF PATIENTS WITH SLE

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Background Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease characterized by the expression of antibodies to extracellular vesicles (EVs). These vesicles can arise from dead and dying cells and display nuclear and cytoplasmic molecules. Since EV preparations contain mitochondria, we performed experiments to test directly the binding of SLE antibodies to mitochondria.

Methods Mitochondria were prepared from mouse liver and immobilized on microtiter plates pre-coated with poly-L-lysine at 0.5 µg/ml. Bound antibodies were detected using a peroxidase-conjugated anti-IgG reagent. To determine whether DNA contributed to the antigenicity of the mitochondria, the ability of DNA to inhibit binding was tested. The binding of sera from 211 SLE patients who met 1982 ACR criteria for classification was determined by ELISA and results compared with an ELISA for M2 antimitochondrial antibodies (AMA).

Results Using an ELISA assay with immobilized mitochondria, 60.2% of SLE sera showed positive responses defined as greater than two standard deviations above the mean of control sera. Samples were also analyzed using a commercial AMA ELISA (Euroimmun US, Morris Plains, New Jersey) for IgG antibodies to the M2 antigen. With this kit, 5.7% of the SLE samples tested positive. To determine the relationship of antibodies to anti-DNA, the ability of calf thymus (CT) DNA to inhibit binding to mitochondria was investigated for a subset of samples. In the ELISA, CT DNA at 50 µg/ml inhibited binding for 7 of 8 SLE plasmas, with inhibition ranging from 7.7%–59.3%.

Conclusion These results indicate that blood of patients with SLE contains antibodies to mitochondria. Among these antibodies, some may react to DNA as shown by the ability of soluble DNA to inhibit ELISA binding. While binding mitochondria, these antibodies differ from AMA found in primary biliary cholangitis since few reacted in the ELISA for M2 AMA. Since studies using flow cytometry have demonstrated that IgG positive EVs in the blood of patients contain mitochondria as shown by MitoTracker Deep Red, these results suggest that, like nuclei, mitochondria may be a subcellular organelle that can display autoantigenic determinants to form immune complexes in SLE.