

This Week's Citation Classic

Koffler D, Schur P H & Kunkel H G. Immunological studies concerning the nephritis of systemic lupus erythematosus. *J. Exp. Med.* **126**:607-24, 1967. [Rockefeller Univ., and Dept. Pathol., Mt. Sinai Sch. Med., New York, NY]

Anti-DNA and several other antinuclear antibodies were eluted from glomeruli of kidneys showing SLE nephritis. Deposits of DNA antigen associated with immunoglobulin and complement were observed using immunofluorescence. These results suggest a pathogenetic role for DNA-anti-DNA immune complexes. [The SCI® indicates that this paper has been cited over 465 times since 1967.]

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"These studies were performed in my first year as a postdoctoral fellow studying immunology in the laboratory of Henry Kunkel at Rockefeller University. I had come to this laboratory for training in immunology having had some experience in immunopathology acquired during a pathology residency. A strong interest in SLE had developed as a result of my own immunopathology studies of this disease and conversations with Paul Klemperer, retired chairman of pathology at the Mount Sinai Hospital, who had devoted many years to the study of this disease. I was most impressed by the insights into potential pathogenetic mechanisms that he had obtained by simple light microscopic studies, which were thoughtfully and critically analyzed.

"When I moved to the laboratory at the Rockefeller University, I became associated with investigators who had a major interest in the immunology of SLE. The serological studies of Kunkel and his colleagues had

provided compelling evidence that anti-DNA antibodies were closely related to the pathogenesis of the disease. It appeared reasonable, therefore, that complexes containing both antibody and antigen were present in the kidneys of patients affected by glomerulonephritis. Prior attempts to demonstrate the antigen in tissue had not been successful probably because the antigen was concealed in a complex with antibody. Acid buffer elution of tissue sections removed sufficient antibody to permit demonstration of the antigen. Deoxyribonuclease enzyme treatments of the isolated glomeruli facilitated the preferential release of anti-DNA antibody from tissue providing further support for the immune complex hypothesis involving DNA.

"The evidence obtained from these studies was one of the early demonstrations that a specific antigen (DNA) and antibody were associated with renal glomerular injury. The techniques utilized were of potential importance for the identification of antigens and antibodies in other forms of immune complex type glomerulonephritis. Subsequently, similar techniques were utilized to demonstrate DNA antigen and antibodies in a murine model of human SLE. Although the precise mechanism of immune injury in this disease remains to be established, a large number of investigators have continued to evaluate, characterize and demonstrate the importance of the DNA system for the pathogenesis of SLE. The disease is of considerable interest, not only as an entity more common than originally believed, but because it serves as a prototype of immune manifestations of several other human diseases. These factors have probably contributed to the frequent citation of this study."