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This Week's Citation Classic

Pincus T, Schur P H, Rose J A, Decker J L & Talal N. Measurement of serum DNA-binding activity in systemic lupus erythematosus.
N. Engl. J. Med. 281:701-5, 1969. [Labs. Viral Dis. and Biol. Viruses, Natl. Inst. Allergy and Infect. Dis., Arthritis and Rheumatism Br., Natl. Inst. Arthritis and Metabolic Dis., NIH, Bethesda, MD and Robert Breck Brigham Hosp., Boston, MA]

The Farr ammonium sulfate technique was applied to measurement of antibodies to double-stranded DNA found in patients with systemic lupus erythematosus (SLE). The method provides an easily performed specific clinical test for diagnosis and management of SLE. [The *SCI*® indicates that this paper has been cited in over 335 publications since 1969.]

Theodore Pincus
Division of Rheumatology & Immunology
Department of Medicine
Vanderbilt University
Nashville, TN 37232

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"DNA antibodies were recognized in active systemic lupus erythematosus (SLE) in 1957, but measurement of these antibodies was largely confined to research laboratories in 1967. The possibility of using the Farr ammonium sulfate precipitation technique to provide a simple clinical measure of DNA antibodies was raised initially in a discussion with Norman Talal at a social gathering in the home of Ron Lamont-Havers. I had learned this technique as a medical student in the laboratory of Charles Christian, and was invited by Talal to work on the assay as a spare-time project, despite my background as a surgical intern and affiliation with a tumor virus laboratory. There were many other sources of help, including Jim Rose, who taught me how to prepare radiolabeled DNA, and Peter Schur, who provided well-characterized SLE sera. After about three months of informal experimentation, it became apparent that the research might lead to a useful clinical test. My supervisor, Wallace Rowe, generously allowed me to spend nine months away from tumor virus studies, while John Decker kindly provided space in the Arthritis Branch to complete the work. I then returned to more basic research on endogenous murine retroviruses with Rowe, which has continued over the years, and have not pursued further research on DNA antibodies. I did enjoy introducing the technique to colleagues, including Alfred Steinberg,[1] and Graham Hughes and Rob Lightfoot,[2] whose studies were responsible for its wide use.

"In retrospect, the resources and unstructured environment at NIH provided an optimal environment for problem solving, under the enlightened leadership of Rowe, Talal, and Decker. I had no formal affiliation with the Arthritis Branch nor identity as a rheumatology trainee during this entire period, though eight studies with six members of the Branch were completed during the year of informal collaboration. These studies did not result from well-articulated planning, but rather from empirical 'hands on' intuitive probing, as has been the case in most of my interesting research as well as in many advances from other laboratories far more important than my work. Yet it remains curious that scientific progress is frequently described as resulting primarily from orderly predictable planning rather than unstructured high-risk intuition, prior expertise rather than a will to solve a problem, the number of workers or dollars involved rather than the enthusiasm of the workers, and formal administrative organization rather than ideas and a positive environment.

"I believe the relatively trivial observation in this study has been highly cited because it was published in a most respected and well-read journal, and contains clinically significant diagnostic, management, and pathogenetic observations in a single source—it is unfortunate that consolidation of data into potentially important papers may be discouraged by a tendency to assess scientific accomplishment in terms of the quantity rather than quality of publications. My experiences at NIH led to reorientation of my career from surgery to rheumatology, with continued study of host variables in disease in a milieu of inquiry at Vanderbilt University under Grant Liddle, involving the two themes which provided so much satisfaction during that period, i.e., basic research on regulatory mechanisms involving endogenous retroviruses,[3] and clinical research toward better assessment in diagnosis and therapy of inflammatory rheumatic diseases. My recent clinical research has been outside the laboratory, toward assessment of patient function, demographic variables, and attitudes in the course of chronic rheumatic diseases, as limitations to the use of laboratory data in optimally defining patient status which were apparent in 1969 are even more appreciated today. Basic laboratory research, including recent elegant studies of nucleic acid antibodies,[4] will provide ultimate solutions, but improved clinical measurements are needed to advance ongoing patient care in chronic rheumatic diseases."

1. **Steinberg A D, Raveche E S, Laskin C A, Miller M L & Steinberg R T.** Genetic, environmental, and cellular factors in the pathogenesis of systemic lupus erythematosus. *Arthritis Rheum.* 25:734-43, 1982.
2. **Lightfoot R W, Jr. & Hughes G R V.** Significance of persisting serologic abnormalities in SLE. *Arthritis Rheum.* 19:837-43, 1976.
3. **Pincus T.** Studies regarding a possible function for viruses in the pathogenesis of systemic lupus erythematosus. *Arthritis Rheum.* 25:847-56, 1982.
4. **Koffler D,** ed. Current perspectives on the immunology of systemic lupus erythematosus. (Whole issue.) *Arthritis Rheum.* 25(7), 1982. p. 721-910.