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## This Week's Citation Classic

Erlanger B F, Borek F, Beiser S M & Lieberman S. Steroid-protein conjugates: I. Preparation and characterization of conjugates of bovine serum albumin with testosterone and with cortisone. J. Biol. Chem. 228:713-27, 1957. [Departments of Microbiology, Biochemistry, Obstetrics, & Gynecology, College of Physicians & Surgeons, Columbia University, New York, NY]

This paper describes novel methods used to prepare immunogenic protein conjugates of testosterone and cortisone. Antibodies elicited by immunization with these and subsequent steroid-protein conjugates have found wide use in radioimmunoassay procedures and in studies on steroid action in biological systems. [The SCI® indicates that this paper has been cited in over 695 publications.]

> Bernard F. Erlanger Department of Microbiology **Cancer Center College of Physicians & Surgeons Columbia University** New York, NY 10032

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Three of the coauthors of this paper, Seymour Lieberman, Sam M. Beiser, and I, lived near one another and, at a time when a twocar family was not so common, organized a car pool to take us to and from our respective laboratories at Columbia. During one of these trips, the subject of steroid antagonists was brought up by Lieberman, a steroid biochemist, who foresaw a possible use for them as contraceptive agents. Beiser, an immunologist, thought in terms of antisteroid antibodies, and I, a protein and peptide biochemist who happened to be familiar with K. Landsteiner's work,<sup>1</sup> suggested that we proceed by preparing immunogenic steroid-protein conjugates. Felix Borek was recruited as a postdoctoral fellow to assist us in the work.

The result is this paper, which describes some relatively simple procedures to make these conjugates, procedures that since then have been adopted by many laboratories for the preparation of antibodies to other hormones and to pharmacological, active molecules in general.

Subsequent papers<sup>2,3</sup> described other steroid-protein conjugates and their use in preparing steroid-specific antibodies, many of which are now routinely used in radioimmunoassays (RIAs) to determine steroid levels in sera and other biological fluids. Prior to the advent of RIAs, however, we had published the results of what was probably the first steroid immunoassay.4

Shortly after we published this Citation Classic, we approached the Schering Corporation for help in carrying out animal studies. They were cooperative but raised the question of patent protection should they discover prac-tical uses for these antibodies. We approached the dean of the Columbia University medical school, William Rappelye, concerning the possibility of patenting our procedures. He informed us, in no uncertain terms, that the medical school considered it unethical to patent biomedical discoveries.

Needless to say, times have changed. Universities, including Columbia, are now hungry for patents. The old policy shortened our collaboration with Schering and, although we did not know it at that time, deprived us of a very lucrative patent indeed.

Beiser died tragically at the age of 49, depriving the field of immunology of a very talented, creative scientist. He is coauthor of one of two other highly cited papers of mine,5,6 one of which has been designated a Citation Classic.<sup>6</sup> Lieberman is still at Columbia, as am

The popularity of this paper stems, to a con-siderable extent, from the rather simple, systematic procedures developed for the preparation of hapten-protein conjugates of biological interest.7 Still, its widespread applicability is owed primarily to the introduction of RIA procedures by Solomon A. Berson and Rosalyn S. Yalow.8

1. Landsteiner K. The specificity of serological reactions. Cambridge, MA: Harvard University Press, 1946. 310 p. (Cited 110 times since 1955.)

- 2. Erlanger B F, Borek F, Beiser S M & Lieberman S. Steroid-protein conjugates: II. Preparation and characterization of conjugates of bovine serum albumin with progesterone, deoxycorticosterone and estrone. J. Biol. Chem. 234:1090-4, 1959. (Cited 300 times.)
- 3. Lieberman S, Erlanger B F, Beiser S M & Agate F. Steroid-protein conjugates: their chemical, immunochemical and endocrinological properties. Recent Prog. Hormone Res. 15:165-200, 1959. (Cited 140 times.)
- 4. Beiser S M & Erlanger B F. Estimation of steroid hormones by an immunochemical technique. Nature 214:1044-5, 1967.
- 5. Erlanger B F & Beiser S M. Antibodies specific for ribonucleosides and ribonucleotides and their reaction with DNA.
- Proc. Nat. Acad. Sci. USA 52:68-74, 1964. (Cited 445 times.) 6. Erlanger B F, Kokowsky N & Cohen W. The preparation and properties of two new chromogenic substrates of trypsin. Arch. Biochem. Biophys. 95:271-8, 1961. (Cited 1,405 times.) [See also: Erlanger B F. Citation Classic. (Barrett J T, comp.) Contemporary classics in the life sciences. Volume 2: the molecules of life. Philadelphia: ISI Press, 1986. p. 143.]
- 7. Erlanger B F. The preparation of antigen hapten-carrier conjugates: a survey. Meth. Enzymology 70:85-104, 1980.
- 8. Yalow R S. Radioimmunoassay methodology: application to problems of heterogeneity of peptide hormones.
- (Cotten M deV, ed.) New York Heart Association Symposium on Immunopharmacology. Baltimore, MD: Williams & Wilkins, 1973. p. 161-78.

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