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This Week's Citation Classic

Kessler S W. Rapid isolation of antigens from cells with a staphylococcal protein A-antibody adsorbent: parameters of the interaction of antibody-antigen complexes with protein A. *J. Immunology* **115**:1617-24, 1975.
[Dept. Microbiology and Immunology, UCLA Sch. Med., Los Angeles, CA]

This paper introduced the concept of using fixed protein A-bearing staphylococci as an adsorbent for antibodies complexed with radiolabeled antigens from cell lysates. Antigen isolation procedures using this immunoprecipitation system were shown to be considerably faster and more quantitative, specific, versatile, and economical than conventional methods. [The *SCI*® indicates that this paper has been cited in over 1,390 publications since 1975.]

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"In the early-1970s, relatively few workers had sufficient faith in the potential of immunoaffinity techniques for isolation of antigenic cell proteins to devote much time to the technology. I was convinced that it was just a matter of time until most details of membrane protein structure would be made accessible by this approach, and I had chosen a PhD project on the characterization of lymphocyte immunoglobulins that obliged me to justify my convictions. Most of my colleagues were more comfortable with their 'brute force' isolation methods, and felt duty-bound to remind me of all the problems inherent in the double antibody immunoprecipitation system which reflected the current state of the art (see this and subsequent papers[1,2] for the grim details). Although my own system seemed to work as well as anyone's who published in my field, the results were typically and frustratingly variable.

" 'Salvation' came one day (my birthday) in the wake of a particularly grueling and largely inconclusive experiment. Making the best of a gloomy situation, I absentmindedly began to read an article on a subject that over the years I had studiously avoided, due to its apparent irrelevance to my interests. The topic was the affinity of staphylococcal protein A for IgG.[3] The realization that protein A-bearing staphylococci might substitute for my second antibody came immediately and seemed so logical that it simply had to work. Within a few weeks I had located a source for the appropriate strain (Cowan I) of *S. aureus* (at the time it wasn't listed in the ATCC catalog), obtained a seed culture, and prepared a test batch. My first experiment, designed purely empirically, gave the cleanest polyacrylamide gel patterns of lymphocyte immunoglobulins I had ever seen.

"As one of the first demonstrations of staphylococcal protein A being put to some practical use, this paper helped to hasten an awareness of the molecule's myriad other applications. Simplifying the immunoprecipitation approach to antigen isolation created opportunities for more workers to enter the field. Ultimately, it may have to accept some blame as well for having helped to spawn a generation of immunochemical 'experts' who have never mastered antigen-antibody equivalence point titrations."

1. **Kessler S W.** Cell membrane antigen isolation with the staphylococcal protein A-antibody adsorbent. *J. Immunology* **117**:1482-90, 1976.
2. ----------. Use of protein A-bearing staphylococci for the immunoprecipitation and isolation of antigens from cells. *Meth. Enzymology* **73**:442-58, 1981.
3. **Kronvall G, Quie P G & Williams R C, Jr.** Quantitation of staphylococcal protein A: determination of equilibrium constant and number of protein A residues on bacteria. *J. Immunology* **104**:273-8, 1970.