

Voller A, Bidwell D & Bartlett A. Microplate enzyme immunoassays for the immunodiagnosis of virus infections. (Rose N R & Friedman H, eds.) *Manual of clinical immunology*. Washington, DC: American Society for Microbiology, 1976. p. 506-12.  
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This paper described various theoretical approaches and applications of enzyme immunoassays. The paper was also one of the first "cookery-book" style guides to the practical aspects of enzyme immunoassays. This enabled many workers to establish the method in their own laboratories. [The *SCI*® indicates that this chapter has been cited in over 640 publications.]

## Better Health Care with Microplate ELISA

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Our laboratory was instrumental in developing and establishing many immunodiagnostic tests for parasitic diseases in the 1960s and early 1970s. At an early stage we became convinced of the merits of labelled reagent methods, and we set up the immunofluorescent technique for diagnosis and seroepidemiology in many countries in Africa, Asia, and South America. However, our field experience told us that the demands for large-scale testing could not be met by immunofluorescence, which was a subjective, time-consuming method requiring skilled staff, carefully preserved reagents, and expensive equipment. We toyed with radioimmunoassay but rejected it because of the short life of the reagents and the necessity for sophisticated equipment.

Quite fortuitously, one of us met Eva Engvall in Stockholm in 1972 at the time she was working on the enzyme-linked immunosorbent assay (ELISA). Anglo-Scandinavian collaboration followed, and it became evident that the ELISA method could have wide applications.

We soon realized that the original coated tube method of ELISA was cumbersome and wasteful and

was inappropriate for routine use. Because of this we adapted the ELISA to a microplate format. This permitted easy batch processing of about 100 samples together. We were also able to show that this method had convenience and reliability, which, together with long-life reagents and easy-to-read results, made it suitable for both diagnostic and screening applications in virtually all parts of the world.

We were able to establish the microplate ELISA method for a variety of antibodies and antigens relevant to major parasitic and viral diseases of man (e.g., trypanosomiasis, malaria, rubella). Many other workers have followed in our footsteps, and now the microplate ELISA is the major immunodiagnostic method for virtually all viral diseases (including hepatitis B and HIV) as well as being used for many other infectious diseases, tumour markers, hormone measurements, autoimmune indicators, and so on.<sup>1</sup>

In addition, the microplate ELISA method established an industry standard. The microplate format and all the subunits (e.g., strips 2 x 8, 1 x 12 wells, and so on), once accepted, permitted the rational development of pipetting devices, dedicated photometers, and washing machines. The establishment of such industry standards also permitted further developments such as luminescence and fluorescence substrate systems. Although hailed (by the commercial producers) as major advances, these developments are, in reality, minor amendments to the basic microplate ELISA.

A further result of the microplate ELISA was to extend immunoassays to the veterinary<sup>2</sup> and agricultural<sup>3</sup> areas. Now pregnancy testing of cattle and viral testing of plants are just two of the many large-scale applications in this area.

We believe this paper is a *Citation Classic* for several reasons. It showed in simple hieroglyphics how antibodies, antigens, and haptens could be measured. It gave practical details so that any laboratory workers could carry out their own tests and even make and standardize all their own reagents. This enabled wide application of the method in spite of the attempted limitations by patent claims of various commercial enterprises. In fact this was one of the last major generic methodologies to develop unhindered by commercial secrecy. This paper showed that highly sensitive methods could be very simple and could be used both within and outside the conventional laboratory. We believe that this paper contributed towards better health care of millions of people, animals, and plants throughout the world.

1. Avrameas S, Druet P, Masseyeff R & Feldmann G. *Immunoenzymatic techniques*. Amsterdam, The Netherlands: Elsevier, 1983. 410 p. (Cited 5 times.)
2. Wardley R C & Crowther J R, eds. *The ELISA: enzyme-linked immunosorbent assay in veterinary research and diagnosis*. The Hague, The Netherlands: Martinus Nijhoff, 1982. 319 p.
3. Clark M F & Bar-Joseph M. Enzyme immunosorbent assays in plant virology. (Maramorosch K & Koprowski H, eds.) *Methods in virology*. New York: Academic Press, 1984. p. 51-85. (Cited 10 times.)

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