

This Week's Citation Classic

Ada G L, Nossal G J V, Pye J & Abbot A. Antigens in immunity. 1. Preparation and properties of flagellar antigens from *Salmonella adelaide*. *Aust. J. Exper. Biol. Med. Sci.* 42:267-82, 1964. [Walter and Eliza Hall Institute of Medical Research, Melbourne. Australia]

The paper describes the preparation and physical and chemical properties of the monomeric protein flagellin and of the formation *in vitro* of polymerised forms which appear similar in appearance to the parent flagella particles. [The SCI[®] indicates that this paper has been cited over 240 times since 1964.]

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"This work, together with the subsequent papers in the series, came about for two reasons. Spurred on by Burnet's concepts, my own interests were switching from virology to immunology. G.J.V. Nossal had recently returned to the Walter and Eliza Hall Institute after a two year period in Joshua Lederberg's new department at Stanford. After numerous discussions, Nossal and I were struck by the lack in the literature of experiments which attempted to determine how small, 'physiological' amounts of a bacterial or viral antigen might stimulate an antibody response. It seemed to us that the time had come to attempt to describe such events in molecular terms.

"The sort of questions we wished to answer included: Did the immunogen react directly with the precursor of the antibody forming cell? Did it become

associated with the protein synthesizing units in the cell as a template, as many thought at that time? If so, how many molecules were involved? To answer such questions, we needed to use an antigen which had well-defined chemical and physical properties, was highly immunogenic, and could readily be labelled with a radioisotope to high specific activity.

"Fortunately for us, Hunter and Greenwood had recently described a direct oxidation method of iodination using a carrier-free preparation of iodide-131.¹ Two candidates for choice of immunogen were the influenza virus and the flagellar proteins isolated from *Salmonella*. The influenza virus, though highly immunogenic, was known to contain a number of different proteins so was less suitable. So the flagellar protein won the day. The paper describes the chemical and physical properties of the monomeric flagellin, and the original finding that it could readily be polymerised *in vitro* to form rod-shaped structures similar in appearance to the parent flagellin particles. Some of the immediate results from using this antigen were the demonstration of particular patterns of antigen localization in lymphoid tissues, factors which affected these patterns, and the failure to find antigen in antibody forming cells. The availability of the antigen led later to an appreciation of the role of multivalency in cell surface reactions.

"A major reason for the subsequent frequent citation of the paper was that the protein became widely used in immunological work, particularly by the many scientists who at some time or another worked at the Hall Institute."

1. Hunter W M & Greenwood F C. Preparation of iodine-131 labelled human growth hormone of high specific activity. *Nature* 194:495-6. 1962.