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Basten A, Miller J F A P, Sprent J & Pye J. A receptor for antibody on B lymphocytes. I. Method of detection and functional significance. *J. Exp. Med.* 135:610-26, 1972.

[Walter and Eliza Hall Inst. Med. Res., Melbourne, Victoria, Australia]

This paper contains the first description of the Fc receptor as a marker for B lymphocytes. The original method, or modifications of it, now forms the basis of standard assays for detection of the receptor and has been used to obtain enriched populations of B lymphocytes from mixed cell populations. [The SC¹® indicates that this paper has been cited in over 550 publications since 1971.]

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"The experiments described in this paper were carried out when I was a postdoctoral research fellow with Jacques Miller at the Walter and Eliza Hall Institute. At the time, I was sharing a laboratory with Jonathan Sprent, who was, and still is, the doyen of thoracic duct cannulation in the mouse. We were all interested in the phenomenon of immunological memory and, like others, wished to establish whether it was a manifestation of a qualitative or quantitative change in the recirculating lymphocyte pool. The obvious experiment was therefore to compare the proportion of thoracic duct lymphocytes from normal versus primed mice which bound radiolabelled antigen. Using ¹²⁵I FyG (fowl immunoglobulin G), autoradiographs were prepared and, to our great surprise, revealed that no less than 15 percent of the primed cells bound antigen, whereas less than one percent of normal cells did so. The immediate conclusion was that immunological memory represented a quantitative increase in the number of antigen binding cells. However, after a little reflection, and bearing in mind the rules of clonal selection, the result, we decided, was impossible. If true, then either clonal selection was wrong or the animals should have expired early in life from a surfeit of

memory cells of various specificities. Not surprisingly, the decision was made to repeat the experiment and on three separate occasions the original finding could not be reproduced.

"As a prelude to discarding the results as an unexplained artifact, each step in the experimental protocol was analysed with care. This revealed the only difference between the first and subsequent experiments to be the number of times the thoracic duct lymphocytes were washed before exposure to ¹²⁵I labelled antigen. When the cells were spun down and labelled immediately, as was done originally, 15 percent bound antigen. This figure dropped sharply following sequential washes. Since lymph plasma is known to contain antibodies, the possibility arose that a subpopulation of thoracic duct lymphocytes carried cytophilic antibody and therefore labelled spuriously with antigen. The subsequent studies which form the basis of this much cited paper confirmed the above hypothesis and provided conclusive proof for the existence of Fc receptors on B cells but not T cells.

"The major reason the paper is frequently cited is the fact that it was published at a time when the concept of Fc receptors was in its infancy and great interest was being shown in phenotypic differences between B cells and T cells. Subsequently, numerous groups have confirmed the original observations¹ although both we¹ and others² have found Fc receptors, albeit at lower density, on T cells as well. The receptor probably plays a key role in modulation of B cell responses since it serves as a trap for immune complexes irrespective of their specificity. In retrospect, it is amusing to note that the original work, as so often happens in research, was not directed toward discovering Fc receptors on B cells but had a completely different goal (i.e., memory). Interestingly, the original goal has yet to be achieved despite the fact that Fc receptors and perhaps even B cells have been relegated to second place behind the T cell and its antigen specific receptor."

1. Basten A, Miller J F A P, Warner N L, Abraham R, Chia E & Gamble J. A subpopulation of T cells bearing Fc receptors. *J. Immunology* 115:1159-65, 1975. (Cited 90 times.)

2. Dikler H B. Lymphocyte receptors for immunoglobulin. *Advan. Immunol.* 24:167-214, 1976. (Cited 290 times.)