

**Papamichail M, Brown J C & Holborow E J.** Immunoglobulins on the surface of human lymphocytes. *Lancet* 2:850-2, 1971.  
[MRC Rheumatism Res. Unit, Canadian Red Cross Mem. Hosp., Taplow, Maidenhead, Berkshire, England]

By a membrane-staining technique, fluorescein-conjugated antisera to immunoglobulins were reacted with purified human blood lymphocyte suspensions. A proportion of peripheral-blood and lymph-node lymphocytes were shown to have immunoglobulins on their surfaces. The clinical observations suggest that they belong to the bone marrow-derived B-cell population. Patients with active rheumatoid arthritis show an increased proportion in their peripheral blood, and nearly all the lymphocytes from three patients with chronic lymphocytic leukemia bore immunoglobulin determinants suggesting the B-cell origin of these leukemic cells. [The SCI® indicates that this paper has been cited over 425 times.]

Michael Papamichail  
Department of Immunology  
Hellenic Anticancer Institute  
Athens 11522  
Greece

January 21, 1985

In 1970, as a newcomer in immunology, I was working with my colleagues J.C. Brown and E.J. Holborow in the MRC Unit in Taplow, England, on the presence of Fc receptors (FcR) on mouse and human B cells. The method we used for detecting FcR was the incubation of human mononuclear cells with aggregated human  $\gamma$ -globulin and then with an antiserum to human IgG conjugated with fluorescein. We observed that approximately 20-30 percent of human mononuclear cells were positively stained using this methodology. However, when the second conjugated antiserum was used alone, as a control, the percentage of positive cells did not change considerably. Also, a proportion (30 percent) of lymph-node lymphocytes stained for surface Ig. Thus, it was evident that a percentage of mononuclear cells bear

on their surfaces immunoglobulin-like structures.

At that time, we were not aware of M.C. Raff's<sup>1</sup> paper in *Immunology* in which he described the existence of two distinct populations of peripheral lymphocytes in mice using immunofluorescence. The B-cell nature of these lymphocytes was substantiated by their positive reaction with anti-immunoglobulin antibodies and by their failure to form sheep erythrocyte rosettes (a T-cell marker). In the majority of cases of chronic lymphocytic leukemia, the leukemic cells were shown to have a B-cell origin by these same tests. The obvious clinical material (leukemia and immunodeficiency cases) to be studied at that time was not readily available since our unit was involved in the study of immunological disturbances of rheumatic diseases. An increased proportion of Ig-bearing blood-lymphocytes in patients with rheumatoid arthritis in an active phase of the disease was also reported in our paper. However, in a more detailed subsequent study, this finding was not found to be statistically significant, and it was probably due to the presence of passively absorbed Igs, through Fc receptors, on the surface of lymphocytes. Further, due to the lack of specificity of the commercial antibodies used at this time, we were not able to detect precisely the Ig class present on the surface of malignant lymphocytes. A paper by J.D. Wilson and G.J.V. Nossal on the same subject was also published in *Lancet* at approximately the same time.<sup>2</sup>

The manuscript was accepted by *Lancet*, which was the first journal to which it was submitted.

I believe that the paper is cited frequently for the following reasons: (1) it was the first time human B lymphocytes could be distinguished by a surface marker; (2) enumeration of T and B human lymphocytes has been studied extensively ever since in various diseases; and (3) the entire field of lymphocyte surface markers proliferated enormously in the 1970-1980 period, giving us the hope of understanding the cellular defects of the lymphoid system in various diseases.

1. Raff M C. Two distinct populations of peripheral lymphocytes in mice distinguishable by immunofluorescence. *Immunology* 19:637-50, 1970. [See also: Raff M C. Citation Classic. *Current Contents/Life Sciences* 27(27):21, 2 July 1984.]
2. Wilson J D & Nossal G J V. Identification of human T and B lymphocytes in normal peripheral blood and in chronic lymphocytic leukemia. *Lancet* 2:788-91, 1971. (Cited 420 times.)
3. Holborow E J & Papamichail M. The lymphoid system and lymphocyte subpopulations. (Holborow E J & Reeves W G, eds.) *Immunology in medicine*. London: Academic Press, 1983. p. 17-34.