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This Week's Citation Classic

Bianco C, Patrick R & Nussenzweig V. A population of lymphocytes bearing a membrane receptor for antigen-antibody-complement complexes. I. Separation and characterization. *J. Exp. Med.* **132**:702-20, 1970.
[Dept. Pathology, New York Univ. Sch. Med., New York, NY and Dept. Pathology, Health Center, Univ. Connecticut, Farmington, CT]

Lymphocytes were divided into two discrete subpopulations: those bearing complement receptors (CRL) and those without the receptor (non-CRL). The two populations were physically separated using rosette formation and density gradients. CRL carried membrane immunoglobulin and adhered to nylon wool. They are known today as B-lymphocytes; non-CRL are known as T-lymphocytes. [The *SCI*® indicates that this paper has been cited over 1,170 times since 1970.]

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"This was my first scientific paper. I came to the laboratory of Victor Nussenzweig for a postdoctoral fellowship 22 months before its publication. The timing was right. Waltraut Lay had just finished her fellowship with Victor. They had shown that some white blood cells carried plasma membrane receptors for a complement component bound to immune complexes.[1] At that time, immunologists were starting to recognize a sharp functional division among lymphocytes. It seemed that lymphocytes which matured in the thymus participated in cell-mediated immune responses (delayed hypersensitivity reactions, transplantation immunity), while those derived from the bone marrow differentiated into antibody secreting plasma cells. (Presently these subpopulations are known as T and B lymphocytes.) My initial experiments were directed specifically to one question: Were the lymphocytes bearing complement receptors (CRL) a discrete cell population? I had to show that the observed percentage of CRL (for instance, 40 percent of spleen lymphocytes) was not the result of an artificial threshold created by limited sensitivity of the assays. I spent several months developing procedures for the physical separation of the lymphocyte subpopulations. The successful method employed rosette formation between lymphocytes and complement coated red cells, and differential flotation in an albumin gradient. The procedures were reproducible and did not require unusual skills or reagents. We were then able to show that CRL expressed membrane associated immunoglobulins, and adhered to nylon wool. Two subsequent papers[2,3] confirmed that the complement receptor was a marker for bone marrow derived, thymus independent lymphocytes, later called B cells.

"During our attempts to reproduce in humans some of the results obtained in mice we made another observation. One of our control reagents, sheep erythrocytes without added antibodies or complement, produced ;osettes with a large population of human peripheral blood lymphocytes. I was deeply involved in the study of CRL and had no time to pursue this observation. We decided to call Waltraut, who had returned to Brazil. She worked intensively to standardize the assay and characterize the cell population. Another Brazilian immunologist. Nelson Mendes, searched for clinical materials, including thymuses of children undergoing cardiac surgery. After a few months we were all exultant. We had found a marker for human T cells (or, as we used to call them, non-CRL). We wrote a paper for *Nature,* hoping to have it published fast.[4] Meanwhile, Victor went to a conference in Finland, where he presented the findings on CRL. In a discussion period he presented our preliminary data on rosettes with human lymphocytes. Then everything went wrong. In the next year, two papers described the new T cell marker.[5,6] Our *Nature* paper was collecting dust in the printing office. It was published almost a year after submission. Probably, in our eagerness to divulge the findings, we lost our place in the pages of the *Science Citation Index®.*

"Waltraut is still in Brazil, now working in the immunology of *Trypanosoma cruzi.* Victor remained at New York University. I left the lymphocyte receptor area seven years ago to work on monocytes and macrophages. We are extremely happy with our *Citation Classic.* I recently published a review of this field."[7]

1. **Lay W H & Naussenzweig V**. Receptors for complement on leukocytes. *J. Exp. Med.* **128**:991-1009, 1968.
2. **Bianco C & Nanssenzweig V.** Theta-bearing and complement-receptor lymphocytes are distinct populations of cells. *Science* **173**:154-6, 1971.
3. **Dukor P, Bianco C & Nanssenzweig V**. Bone marrow origin of complement-receptor lymphocytes. *Eur. J. Immunol.* **1:**491-4, 1971.
4. **Lay W H, Mendes N F, Biaaco C & Nanssenzweig V.** Binding of sheep red blood cells to a large population of human lymphocytes. *Nature* **230**:531-2, 1971. [The *SCI*® indicates that this paper has been cited over 430 times since 1971.]
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6. **Coombs R R A, Gurner B W, Wllson A B, Hoim G & Lindgren B .** Rosette-formation between human lymphocytes and sheep red cells not involving immunoglobulin receptors. *Int. Arch. Allergy* **39**:658-63, 1970.
7. **Blanco C**. Plasma membrane receptors for complement. (Day N K & Good R A, eds.) *Biological amplification systems in immunology.* New York: Plenum, 1977.'p. 69-84.