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This Week's Citation Classic™

Lay W H & Nussemweig V. Receptors for complement on leukocytes.
J. Exp. Med. **128**:991-1009, 1968.
[Department of Pathology. New York University School of Medicine, NY]

Sheep red blood cells (SRBC), sensitized by 7S but not by 19S rabbit anti-SRBC antibodies, adhere to mouse macrophages. When, however, C factors are added to the antigen-19S antibody complex, the SRBC adhere to the membranes of most mouse peritoneal macrophages and blood polymorphonuclear cells ('rosette' formation) Similar rosettes are formed on 15 to 25 percent of lymph node lymphocytes but not on thymus lymphocytes. Rosette formation by AgAb C on macrophages and neutrophils depends on Mg^{+} $^{+}$. Adherence to lymphocytes is independent of divalent ions and occurs in the presence of EDTA Mouse serum deficient in C_5 can be used as a source of C components. [The *SCI*® indicates that this paper has been cited in over 660 publications since 1968.]

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"This was a paper that preceded another *Citation Classic* by Celso Bianco, R. Patrick, and Victor Nussenzweig on lymphocytes bearing complement receptors.[1,2] Both emerged under Victor's guidance in Baruj Benacerraf's pathology department at New York University and involved Brazilian fellowship holders: Bianco and me. It is perhaps worthwhile to note how often papers that become *Citation Classics* are the products of beginners under expert supervision.

"In 1966, I began working in P. Miescher's laboratory, where preliminary assays on the phenomenon of phagocytosis had led to the curious observation that human leukocytes fed with complement-coated erythrocytes stubbornly refused to engulf the meal, in spite of the tight adherence of the erythrocytes on their membranes. When I moved over to Victor's laboratory, this was the item chosen to be worked on in my scientific apprenticeship. We changed from human leukocytes to mouse macrophages mainly because mice do not charge $10 for volunteering. A secondary reason was that mouse complement is poorly lytic, and we could work in an entirely homologous system. Once again, the over-classic SRBC-anti-SRBC system was the tool used in our daily attack on the questions of how, when, and why complement-coated erythrocytes stuck to the membrane of phagocytic cells. Victor had been working on the immunochemical aspect of immunology, and this subject marked his 'debut' in cellular immunology. A previous paper by Berken and Benacerraf on cytophilic antibodies[3] and the contemporaneous work of Michel Rabinovitch on phagocytosis of aldehyde-fixed erythrocytes[4] guided our thoughts during our meticulous and slowly progressing work.

"No great discoveries led to the inclusion of our paper among the *Citation Classics,* just the priority of description and characterization of the complement receptors at the right moment, when people were concerned with the recognition functions of cell membranes. Bianco, who later worked out the subject of the complement receptors of lymphocytes, wrote a review of this field[5] and so did Victor.[6] I only enjoy the glory of being cited so often."

1. **Blanco C, Patrick R & Nussenzweig V.** A population of lymphocytes bearing a membrane receptor for antigen-antibody-complement complexes. Separation and characteriation. *J. Exp. Med.* **132.7**02-20. 1970.
2. **Blanco C.** Citation Classic. Commentary on *J. Exp. Med.* **132**:702-20. 1970. *Current Contents'Life Sciences* 24(20):21. 12 May 1981.
3. **Berken A & Benacerraf B.** Properties of antibodies cytophilic for macrophages. *J. Exp. Med.* **123**:119-44. 1966. (Cited 540 times.)
4. **Rablnovitch M.** Phagocytosis: the engulfment stage. *Semin. Hematnl* **5**:134-55, 1968. (Cited 100 times.)
5. **Bianco C.** Plasma membrane receptors for complement. (Day N K & Good R A. eds.) *Biological amplification systems in immunology.* New York: Plenum Press. 1977. p. 69-84.
6. **Nussenzwelg V.** Receptors for immune-complexes on lymphocytes. *Advan. Immunol.* **19**:217-58. 1974. (Cited 175 times.)