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Foon K A & Todd R F III. Immunologic classification of leukemia and lymphoma. *Blood* 68:1-31. 1986. (Division of Hemaiology & Oncology, Dept. Internal Medicine. Univ. Michigan, Ann Arbor, MI]

This manuscript reviewed the literature on the rapidly growing field of immunophenotyping and molecular diagnostics of leukemia and lymphoma, organizing the lymphoid and myeloid leukemias and lymphomas as well as Hodgkin's disease, and correlating immunophenotypes with morphologic classification. [The *SCI*® indicates that this paper has been cited in more than 610 publications.]

Hematologic Malignancies: Correlating Morphology with Immunology

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During my training in hematology and oncology at the University of California, Los Angeles (UCLA), I became fascinated by the potential use of monoclonal antibodies to dissect the various subtypes of hematologic malignancies. This field began to grow exponentially shortly after the discovery of the hybridoma technology for which G. Kohler and C. Milstein received the Nobel Prize in medicine in 1984,' Even more fascinating was the finding that not only could we subset the various leukemias and lymphomas by phenotype, but also we could actually correlate some of these subsets with their functional activity in vitro.[2] Such insights could lead to a better understanding of the clinical behavior of the various ieukemias and lymphomas.

In the late 1970s my UCLA colleague, Robert Schroff, and I generated a panel of monoclonal antibodies for subsetting leukemias and lymphomas. Schroff later used this panel of antibodies to study the peripheral blood from a variety of patients at UCLA, which led to an important historical observation: He was the first to identify decreased T cells with a reversal of the CD4/CD8 ratio in patients with a newly recognized immunodeficiency disorder.[3] This disease, of course, later became known as the acquired immune deficiency syndrome.

Through the late 1970s, as new monoclonal antibodies were being generated, there was difficulty in correlating data from various laboratories because there was no standard for comparison of antibodies, and so there was little basis for a uniform criterion for an immunologic classification of leukemias and lymphomas. Fortunately, the international workshop which cluster-designated monoclonal antibodies began to organize these data in the early 1980s, and we were able to incorporate these data into our classification scheme.

I first began to review the literature while I was at the National Cancer Institute; when I moved to the University of Michigan in 19851 asked Robert Todd to cowrite the paper. Todd had trained at the Dana Farber Cancer Institute in the laboratory of Stuart Schlossman, where he developed many of the first monoclonal antibodies that identified monocytes, granulocytes, and myeloid progenitor cells.'We spent the greater part of one year compiling data and attempting to present it in a practical and logical fashion that could be followed by pathologists and clinicians. It was an exhaustive effort to which Todd gave meticulous attention. At the completion of the project he didn't hesitate to inform me that if I should ever decide to update the manuscript to please *not* ask him to be involved.

After publication, I received a note from Schlossman (Todd's mentor) complimenting us on the article. In truth, I probably should have dedicated the paper to Schlossman and his colleagues, as I cited them in the references 51 times. It was a great tribute to his laboratory that their work represented over 10 percent of the total number of references in the manuscript.

As ii turned out, this manuscript was among the very first papers to try to "make sense" of the myriad of data and information regarding the immunologic classification of leukemias and lymphomas. Although there remained significant gaps, where possible, we correlated molecular diagnostics with immunophenotyping: While the classification of leukemia and lymphoma has not changed dramatically since the publication of this article, multicolor flow cytometry, fluorescent in situ hybridization, and the polymerase chain reaction have led to refinements in classification as well as identification of as few as 1 in 100,000 malignant cells.

Interestingly, in addition to the receipt of many reprint requests (over 2,000), I often received personal requests to send bulk quantities of reprints because the manuscript was being used as a teaching vehicle in a variety of formal and informal courses. This was most gratifying—perhaps the ultimate compliment: To be judged good enough to be taught!

1. **Köhler** G & **Milstein** C. Continued cultures of fused cells segregating antibodies of predefined specificities. *Nature* 256:495-7. 1975. (Cited 7,935 times.)

2 **Broder S. Edelson R L, Lutzner M A. Nelson D L, MacDermott R P. Dunn M E, Goldman C K. Meade B D** & Waldmann T A. The Sezary syndrome: a malignant proliferation of helper T cells. *J. Clin. Invest.* 58:1297-306. 1976. (Cited 500 limes.)

3. **Gottlieb M S, Schroff R, Schanker H M, Weisman J D, Fan P T, Wolf R A & Saxon A.** *Pneumocysns carinu* pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency *N. Engl. J. Med,* 305.1425-31, 1981. (Cited 1,435 times.) [See also: **Gottlieb M** S. AIDS: die discovery. Citation Classic® *Current Contents*[1]*/Clinical Medicine* 21(30):8, 26 July 1993.]

4 Todd R F, Nadler L M & Schlossman S **F.** Antigens on human monocyles identified by monoclonal antibodies. *J. Immunol,* 126:1435-42. 1981. (Cited 630 times.)

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