

This Week's Citation Classic™

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Edelson R L, Kirkpatrick C H, Shevach E M, Schein P S, Smith R W, Green I & Lutzner M. Preferential cutaneous infiltration by neoplastic thymus-derived lymphocytes: morphologic and functional studies.

Ann. Intern. Med. 80:685-92, 1974.

[Dermatol., Med., and Immunol. Branches, Natl. Cancer Inst., and Labs. Clin. Invest. and Immunol. Natl. Inst. Allergy and Infectious Dis., NIH, Bethesda, MD]

Malignant lymphocytes from each of seven patients with widespread involvement of skin were shown to be of T- (thymus-derived) cell lineage. These cells had a characteristic tissue distribution: preferential infiltration of skin and T-cell zones of lymph nodes and sparing of bone marrow. These findings suggested that lymphomas and leukemias with widespread cutaneous infiltration are frequently T-cell malignancies with several distinguishing features. [The *SCI*® indicates that this paper has been cited in over 225 publications since 1974.]

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"At the time of my arrival as a clinical associate at the National Institutes of Health (NIH) in 1972, the discipline of human cellular immunology was in its early infancy. Techniques for identification of human B (bone marrow-derived) and T (thymus-derived) lymphocytes had recently been established. I was fortunate to receive substantial guidance from four senior investigators who had already made major contributions to this new science (Ira Green, Michael Frank, Ethan Shevach, and Charles Kirkpatrick).

"The above mentioned paper was actually only the second one which I published. We were quite surprised to discover that malignancies of lymphocytes with a tendency to invade broad expanses of skin were almost invariably T-cell lymphomas or leukemias. In marked contrast, lymphomas and leukemias in which the skin was not significantly infiltrated were almost always malignancies of B lymphocytes. One particularly unusual finding in the patients with T-cell leukemias was the sparing of the bone marrow, a finding explained by the circulatory patterns of T cells.

"This paper was the point of departure for much of my research over the next ten years, which is summarized in two recent editorials.^{1,2} It permitted unification, under the classification 'cutaneous T-cell lymphoma' (CTCL),³ of an artificially splintered group of lymphocytic malignancies that previously went by such noncontributory names as 'mycosis fungoides,' 'Sézary syndrome,' or 'leukemia cutis.' CTCL is now being studied in many laboratories around the world and is widely recognized to be a malignancy of phenotypic helper T cells with an extraordinary affinity for epidermis. It may, in fact, be the most common form of adult lymphoma with an incidence greater than that of Hodgkin's disease. It is noteworthy that CTCL was identified as a single disease with diverse clinical manifestations only through T-cell marker studies.

"On the basis of this work at the NIH, I received an Irma T. Hirsch Career Investigator Award (1976-1981), which is given to promising junior faculty members at research institutes in New York City. This early support, along with subsequently obtained NIH grants, has permitted me to continue to study the basic biology of CTCL. In collaboration with my close colleague, Carole Berger, at Columbia University, monoclonal antibodies with specificity for CTCL cells have been produced and are useful as diagnostic and investigational tools. The affinity of the malignant T cells for epidermis led to the initial suggestion of a role for this tissue in normal T-cell maturation,³ which is now being supported by the finding that this tissue produces thymic-like factors.

"The number of citations which this paper received is almost certainly a reflection of the clinical significance of CTCL. It is far more common than we anticipated and remains a devastating disease for those afflicted with it. Hopefully, exciting new observations, such as Robert Gallo's that CTCL is associated with an RNA retrovirus (human T lymphoma virus), will contribute to elucidation of its pathogenesis. The subject is one of ever-increasing excitement, and I am privileged to have been there at the beginning."

1. Patterson J A K & Edelson R L. Interaction of T cells with the epidermis. (Comment.)

Brit. J. Dermatol. 107:117-22, 1982.

2. Edelson R L. Pathogenesis of T cell lymphoma of skin. (Editorial.) *J. Amer. Acad. Dermatol.* 9:957-60, 1983.

3. Cutaneous T cell lymphomas: clues of a skin-thymus interaction. *J. Invest. Dermatol.* 67:419-24, 1976.