

**Brouet J C, Flandrin G & Seligmann M.** Indications of the thymus-derived nature of the proliferating cells in six patients with Sézary's syndrome.  
*N Engl J Med.* 289:341-4, 1973.  
[Research Institute on Blood Diseases, Hôpital Saint-Louis, Paris, France]

Abnormal cells from six cases of Sézary syndrome<sup>1</sup> were shown to be of T-cell origin, i.e., formed E rosettes and featured T-cell antigens in the three cases that were studied. The small and large Sézary cells had the same immunological phenotype as well as ultrastructural and chromosomal characteristics [The SCJ® indicates that this paper has been cited in over 305 publications since 1973.]

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About 15 years ago, the availability of membrane markers that define the two broad subsets of lymphocytes—T and B cells—prompted extensive phenotypic studies of human lymphoid malignancies. Two major concepts emerged at that time, namely, the monoclonality of B-cell diseases and the existence of a maturation arrest of leukemic cells. On the other hand, phenotyping of human malignancies was disappointing at first glance from a clinical point of view since most chronic lymphoid disorders appeared to be of B-cell origin. However, the systematic survey performed in our laboratory by Jean-Louis Preud'homme and Maxime Seligmann<sup>2</sup> indicated that some malignant cells were devoid of B-cell markers and were therefore good candidates to delineate T-cell diseases. Sézary syndrome fell within this group of non-B malignancies. As T-cell markers (E-rosette formation and T-cell-specific antigens revealed by hetero rabbit antisera) became available, it was of obvious interest to study those patients whose disease is characterized by erythrodermia and circu-

lating abnormal cells. Therefore, we had to select only six Sézary patients with high white blood cell counts (to be sure to phenotype the malignant cells), and all the work was done within four hours! I always wondered whether these six erythrodermic patients who met in my office on the same day guessed that some new study was going on.

Everything was easy because for some months our hematology department had been studying the cytological and ultrastructural features of cells from Sézary patients. These patients had been referred by several dermatology departments at the request of M. Lutzner, who was in Paris at that time.

Results indicated in all cases a clearcut T-cell phenotype. Therefore, it is not surprising that this paper has been highly cited since all papers dealing with a T-cell malignancy in the next years referred to this original report. Both physicians and immunologists were interested in these findings. It was a great help to physicians in classifying what is now called cutaneous T-cell lymphomas, including the various aspects of Sézary syndrome and mycosis fungoides.<sup>3</sup> The spectrum of T-cell malignancies now extends to a percentage of acute lymphoblastic leukemias and non-Hodgkin lymphomas. The biology of these T-cell malignancies was recently enlightened by the discovery of a retrovirus (HTLV-I) that is associated with some T-cell diseases and was first characterized in cells from a Sézary patient.<sup>4</sup>

Finally, immunologists used these homogeneous cell populations from Sézary patients to study T-cell function. In most cases, Sézary cells have a helper phenotype and indeed may behave as helper T cells for antibody production in coculture experiments with B cells.<sup>5</sup> Presently, many studies are devoted to the biochemical characterization of various lymphokines, and undoubtedly Sézary cells will provide a unique opportunity to characterize B-cell differentiation factors.

Respectively, it is probably rare that such a relatively limited study of six patients turned out to be so useful in clinical medicine and revealed such a large domain of investigation to fundamental immunologists.

- 1 Sézary A & Bouvraïn Y. Érythrodermie avec présence de cellules monstrueuses dans le derme et le sang circulant *Bull Soc Fr Dermatol Syphiligr* 45 254-60, 1938 (Cited 135 times since 1955.)
- 2 Preud'homme J L & Seligmann M. Surface bound immunoglobulins as a cell marker in human lymphoproliferative diseases *Blood* 40 777-94, 1972 [See also Preud'homme J L. Citation Classic *Current Contents/Clinical Practice* 10(47) 18, 22 November 1982.]
- 3 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 [See also Edelson R L. Citation Classic *Current Contents/Clinical Practice* 12(14) 20, 2 April 1984.]
- 4 Polesz B J, Ruscetti F W, Gazdar A F, Bunn P A, Minna J D & Gallo R C. Detection and isolation of type-C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. *Proc Nat Acad Sci US* 77 7415-19, 1980 (Cited 375 times.)
- 5 Broder S, Edelson R L, Lutzner M A, Nelson D L, MacDermott R P, Durm M E, Goldman C K, Meade B D & Waldmann T A. The Sézary syndrome—a malignant proliferation of helper T cells. *J Clin Invest* 58 1297-306, 1976 (Cited 370 times.)