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# Immunological Classification of Acute Lymphatic Leukemia

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Lymphocytes have conventionally been classified as T, B, and null cells, based on their characteristic surface membrane markers. Such membrane features can be revealed by rosette assays and by immunofluorescence using heterologous and/or monoclonal antibodies. Studies of these characteristics can provide important insight into the differentiation scheme of normal lymphocytes and can be applied to the classification of leukemic cells. This is a preliminary report on the studies of immunological markers of leukemic cells from acute lymphocytic leukemia (ALL) patients in an attempt to classify these cells into specific subtypes and to correlate these membrane features with prognostic and pathogenic characteristics.

Leukemic cells from 54 patients could be classified into eight subtypes, based on immunological phenotypic criteria as listed in Table 1. The percent distribution of the different subtypes were: null (0%), Ia (17%), cALL (52%), pre-B (4%), B (4%), defective B (8%), pre-T (4%), early T (8%), and T1 (5%). There were no apparent differences among the cALL, Ia, and the various types of B-ALL in clinical findings and in general, Ia, cALL, pre-B, and defective B patients had higher remission rates and better responses to chemotherapy while the others had poorer prognosis and higher incidences of drug resistance as reported elsewhere [2].

There has been some controversy over the classification criteria of our non-T non-B cells and pre-T ALL. Our standard criteria for non-T non-B (null, Ia, cALL) cells are those proposed by Chessells et al. [3] and Brouet and Seligmann [1], and our definition for pre-T cells is based on reac-

**Table 1.** Identification of ALL leukemic cells by surface marker analysis

| Type | Subtype | Ia | cALL | OKT9 | 10 | 11A | S33 | WT1 | SIg[a] | CmIg | E(h/c) | EA/EAC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Monoclonal antibodies | | | | | | | | |
| Non-T, non-B | Null | – | – | – | – | – | – | – | – | – | – | – |
| | Ia | + | – | – | +/– | – | – | – | – | – | – | – |
| | cALL | + | + | – | +/– | – | – | – | – | – | – | – |
| B | Pre-B | + | +/– | – | – | – | – | – | – | + | – | – |
| | Def B | + | – | – | – | – | – | – | – | – | – | + |
| | B1 | + | – | – | – | – | – | – | + | – | – | + |
| T | Pre-T | +/– | +/– | – | + | +/– | + | + | – | – | – | – |
| | Early T | +/– | – | + | + | +/– | +/– | + | – | – | – | – |
| | T1 | – | – | – | + | + | + | + | – | – | + | – |

[a] SIg, surface immunoglobulin; CmIg, cytoplasmic immunoglobulin; E(h/c), hot/cold E rosette; EA/EAC, EA and EAC rosettes

**Table 2.** Percentage of T-ALL leukemic cells reactive to a selected panel of monoclonal antibodies and other assays

| Case No. | Subtype | E(h/c) | OKT3 | 9 | 10 | 11A | S33 | WT1 | SIg | cALL | Ia | Thymic mass |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Monoclonal antibodies | | | | | | | | | |
| 1[a] | pre-T | 0/5 | 7 | 0 | 90 | 92 | 90 | 99 | 0 | 0 | 94 | – |
| 2 | pre-T | 0/1 | 0 | 0 | 42 | 3 | 63 | 95 | 0 | 32 | 0 | + |
| 3 | early T | 0/2 | 1 | 78 | 99 | 99 | 99 | 99 | 0 | 0 | 0 | – |
| 4 | early T | 0/3 | 3 | 45 | 90 | 3 | 99 | 99 | 0 | 9 | 0 | + |
| 5 | early T | 0/3 | 3 | 79 | 90 | 7 | 7 | 99 | 0 | 0 | 90 | + |
| 6 | early T | 0/2 | 2 | 72 | 90 | NT | NT | NT | 0 | 0 | 0 | + |
| 7 | T1 | 40/96 | NT | NT | NT | NT | NT | NT | 0 | 0 | 0 | + |
| 8 | T1 | 20/58 | 20 | NT | NT | 32 | 23 | NT | 0 | 2 | 8 | + |
| 9 | T1 | 31/81 | 81 | NT | NT | 18 | 33 | 23 | 1 | 7 | 4 | + |

NT, not tested

[a] Based on our previous classification criteria (see text for description), cases 1 and 5 were diagnosed as Ia subtype; case 2 was cALL and cases 3, 4, and 6 were null subtype

tivity to OKT10 but not to other OKT monoclonal antibodies as reported by Reinherz et al. [4]. However, further analysis with additional monoclonal antibodies OKT11A, S33, and WT1 have shown that (1) at least some of our non-T non-B cases can be reclassified into the T-cell category and (2) pre-T and early T subtypes of ALL can be better defined with the aid of OKT11A, S33, and WT1. Together with OKT9/10, this panel of monoclonal antibodies defines pre-T ALL as $OKT9^-/10^+$ and $OKT11A^{\pm}/S33^+/WT1^+$ while early T-ALL can be distinguished as $OKT9^+/10^+$ and $OKT11A^{\pm}/S33^{\pm}/WT1^+$ (Table 2). Based on these new criteria, all of our null-ALL, one of cALL, and two of our Ia-ALL have been reclassified as either pre-T or early T-ALL as shown in Table 2. Our data thus suggest that OKT11A, S33, and WT1 monoclonal antibodies should be included in the OKT regiment for the phenotypic studies of T and stem (non-T non-B) cell subtypes. Furthermore, the characteristic markers of the "null" cell subtype should be reexamined or the term "null cell" be abandoned.

In conclusion, we have been able to classify 54 acute lymphocytic leukemic cases into eight subtypes based on surface marker analysis and a panel of monoclonal antibodies. Our preliminary data have casted some doubts on the immunological classification criteria of some subtypes of ALL. Furthermore, we have shown that the use of monoclonal antibodies OKT11A, S33, and WT1 may be very useful in defining pre-T and early T subtypes of ALL and in differentiating between stem cells and pre-T cells. Attempts are in progress to further substantiate these suggestions.

## References


1. Brouet JC, Seligmann M (1978) The immunological classification of acute lymphoblastic leukemias. Cancer 42:817–827
2. Chen PM, Ho CK, Hwang TS (1982) Preliminary report on classification of acute lymphocytic leukemia using heteroantisera. Chin Med J (ROC) 29:425–429
3. Chessells JM, Hardisty RM, Rapson NT (1977) Acute lymphoblastic leukemia in children: Classification and prognosis. Lancet 2:1307–1309
4. Reinherz EL, Kung PC, Goldstein G, Levey RH, Schlossman SF (1980) Discrete stages of human intrathymic differentiation. Analysis of normal thymocytes and leukemic lymphoblasts of T cell lineage. Proc Natl Acad Sci USA 77:1588–1592