

Leukemia is the unchecked proliferation of an abnormal clone of haematopoietic cells. Typically, leukemic cells respond poorly or inappropriately to regulatory signals, display aberrant patterns of differentiation, or even fail to differentiate. Furthermore, they sometimes suppress the growth of normal lymphoid and myeloid cells. Leukemia can arise at any maturational stage of any one of the haematopoietic lineages.

Lymphocytic leukemias display many characteristics of cells of the lymphoid lineage; another broad group, myelogenous leukemias, have attributes of members of the myeloid lineage. Aside from lineage, many leukemias can be classified as acute or chronic. Some examples are acute lymphocytic leukemia (ALL), the most common childhood leukemia; acute myelogenous leukemia (AML), found more often in adults than in children; and chronic lymphocytic leukemia (CLL), which is rarely seen in children but is the most common form of adult leukemia in the Western world. A fourth type, chronic myelogenous leukemia (CML), occurs much more often in older adults than in children.

The diagnosis of leukemia is made on the basis of two findings. One is the detection of abnormal cells in the bloodstream, and the other is observation of abnormal cells in the bone marrow. Clinical experience has shown that designing the most appropriate therapy for the patient requires knowing which type of leukemia is present. In this regard, two of the important questions are: (1) What is the lineage of the abnormal cells and (2) What is their maturational stage?

A variety of approaches, including cytologic examination of cell morphology and staining characteristics, immunophenotyping, and, in some cases, an analysis of gene rearrangements, are useful in answering these questions. One of the most powerful of these approaches is immunophenotyping, the determination of the profile of selected cell-surface markers displayed by the leukemic cell. Although leukemia-specific antigens have not yet been found, profiles of expressed surface antigens often can establish cell lineage, and they are frequently helpful in determining the maturational stages present in leukemic cell populations.

For example, an abnormal cell that displays surface immunoglobulin would be assigned to the B-cell lineage and its maturational stage would be that of a mature B cell. On the other hand, a cell that had cytoplasmic heavy chains, but no surface immunoglobulin, would be a B-lineage leukemic cell, but at the maturational stage of a pre-B cell. The most efficient and precise technology for immunophenotyping uses flow cytometry and monoclonal antibodies. The availability of monoclonal antibodies specific for each of the scores of antigens found on various types and subtypes of haematopoietic cells has made it possible to identify patterns of antigen expression that are typical of cell lineages, maturational stages, and a number of different types of leukemia.

Most cancer centers are equipped with flow cytometers that are capable of performing and interpreting the multiparameter analyses necessary to provide useful profiles of surface markers on tumour cell populations. Flow cytometric determination of immuno-phenotypes allows:

- Confirmation of diagnosis;

- Diagnosis when no clear judgement can be made based on morphology or patterns of cytochemical staining;

- Identification of aberrant antigen profiles that can help identify the return of leukemia during remission;

- Improved prediction of the course of the disease.

*Clinical Focus* is extracted from Kuby's Textbook of Immunology.

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