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Rethinking How to Classify Hematopoietic and Lymphoid Neoplasms

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Cancers were originally named and classified for their anatomic site and cell of origin. Epidemiologists, pathologists and oncologists have somewhat different goals with respect to disease classification: epidemiologists want to predict causal factors, pathologists predict the natural history, and oncologists want to predict outcome and response to treatment.

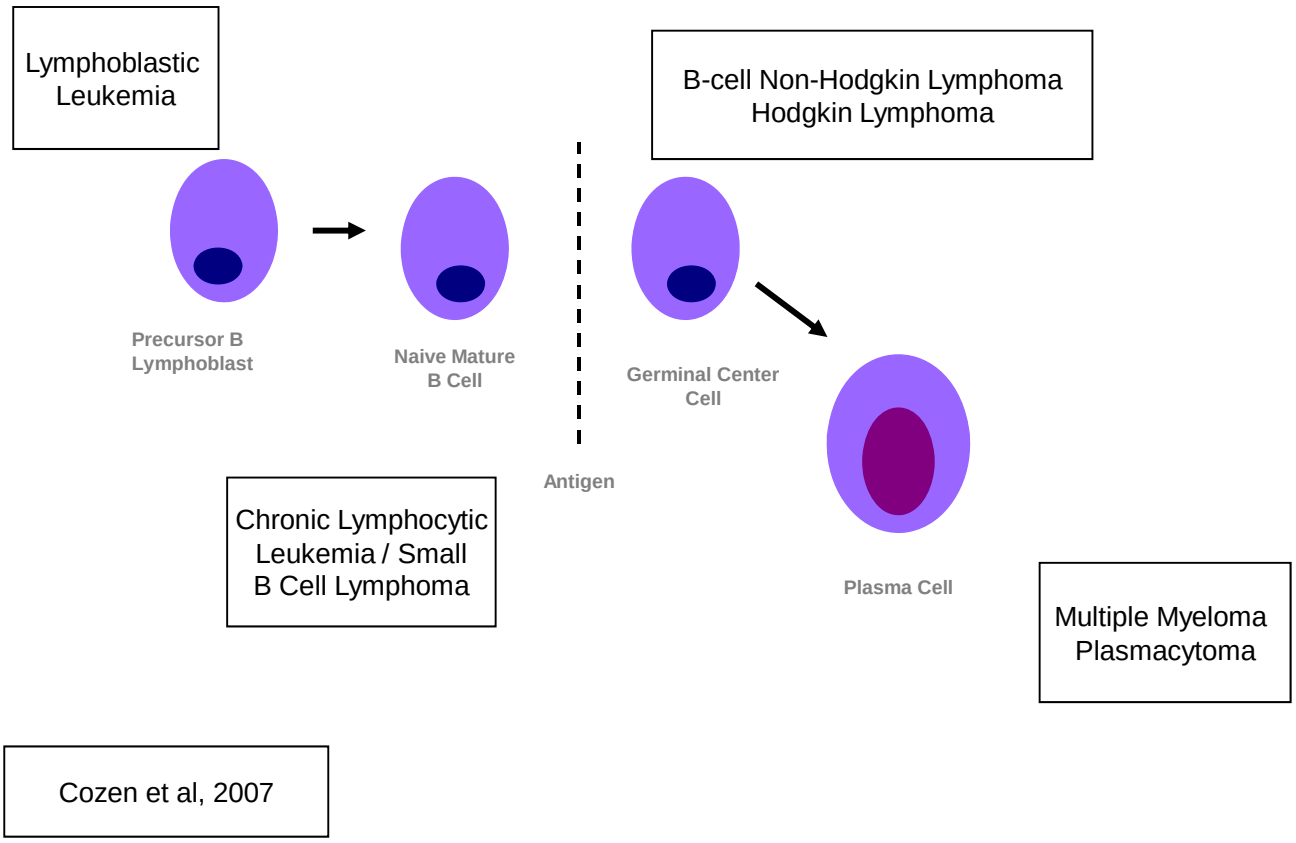
For most cancers, the process is fairly straightforward but the classification of hematological neoplasms has always been more difficult. The unique characteristic of hematologic neoplasms is that different cancers arise from different stages of the same cell (Figure 1 on page 2).

For example, B-cell lymphocytes arise from a precursor cell, migrate from the bone marrow to lymphocytes (in adults), and along the way they mature in stages while acquiring more sophisticated and complex activities such as responding to antigen and making antibodies (end stage plasma cell).

The classification of hematologic neoplasms continues to evolve as new technologies allow us to better determine the exact stage of maturation for each type of cell. As cells mature, they express different markers (usually called CD's for "Cluster of Differentiation, now up to CD 338) on their surface. These markers can be used to identify lineage and type. Subtypes are continuously being reclassified in the face of increasing molecular data.

For example, natural killer cells are a type of lymphocyte that are indistinguishable from T and B-cell lymphocytes by light microscopy, so these were always lumped in with T-cell lymphocyte tumors. Once CD cell surface markers were found that were specific to natural killer cells, the cancers associated with them were split off as coming from a different origin (Grade Rule G9). It is now considered more important to classify lymphoid neoplasms by the cell of origin rather by where they occur in the body (blood or lymph node), so Burkitt's leukemia is now considered the same entity as Burkitt's lymphoma, and chronic lymphocytic leukemia is the same entity as small lymphocytic lymphoma because they both derive from a mature but naïve (has never encountered an antigen) B-cell lymphocyte (Figure 1 on page 2)

Figure 1. Stage of B-Lymphocyte and Correlation with Tumor Type



Classifications can also be altered because of new clinical research on natural history of the disease. A good example is the work that has been done by Dr. Robert Kyle and colleagues at Mayo Clinic and Dr. Ola Landgren at the National Cancer Institute on the natural history of plasma cell myeloma (formerly multiple myeloma). These investigators found that a benign clone of identical plasma cells precedes the development of (malignant) plasma cell myeloma and is thus the precursor stage of the cancer. Only a small proportion of people with this precursor stage, monoclonal gammopathy of undetermined significance (MGUS), progress to active plasma cell myeloma, in which the plasma cells become neoplastic and metastasize causing symptoms. Other clinical investigators found that there is often an intermediate stage between MGUS and active plasma cell myeloma called smoldering plasma cell myeloma which is slow-growing and asymptomatic. At this time, smoldering and active plasma cell myeloma are reportable.