CD MARKERS AND LYMPHOMA
by Sue Herms

Not too many years ago, most lymphomas were diagnosed by using a few simple stains and looking at the appearance of cells under the microscope. But there were only a few types of lymphoma that could easily be distinguished in this way, and it often appeared that tumors of the same cell type behaved very differently in different individuals. It was obvious that something else was going on at the molecular level to account for these differences.

As medical diagnosis progressed to the study of molecules, new techniques such as flow cytometry were devised to identify specific molecules, located on the surface of white blood cells. Such molecules are referred to as cluster of differentiation (CD) markers. The system of CD classification was established in 1982; while originally intended only for white blood cell markers, its use has since expanded to many other cell types. At last count, over 350 CD markers have been identified. It is now understood that each cell type has its own distinct markers that can serve as "identification tags." Many of these CD markers have helped physicians to understand why there is so much variation among the different types of lymphoma.

Antibodies have been developed that are specific for each CD surface marker. These antibodies can be tagged with fluorescent stains and allowed to combine with their corresponding markers on the cells. If a particular CD marker is present, the CD-antibody combination will fluoresce; if the marker is not present, the antibody will not attach and there will be no fluorescence. The presence or absence of fluorescence allows cells to be defined with a + or − symbol to indicate whether they express (that is, exhibit) or lack a particular CD marker. For example, a CD20+, CD5- cell is one that expresses CD20 but does not express CD5. The degree of fluorescence is also important in designating some cells as exhibiting strong expression of markers and others as exhibiting weak expression. It should be noted that, while we commonly think of CD molecules as markers or "identification tags" for specific types of cells, they do function in numerous ways that are important to a cell's maturation and survival. These functions include acting as receptors for various substances or serving as signals to initiate or alter cell behavior.

As both B- and T-lymphocytes mature, they go through several stages of development. During these stages, lymphocytes will acquire new CD markers, while other CD markers will diminish in their expression or be lost altogether. But if a lymphocyte mutates and forms a clone of lymphoma cells, the mutated cells will express the same CD markers (indicating cell type and stage of development) as the normal cell from which they mutated. When the pathologist makes a lymphoma diagnosis, he first determines the CD pattern of a particular patient's cells and then compares it with known patterns of cell populations for a whole range of different types of lymphoma. It is the variation in CD expression found among different lymphomas that assists the pathologist in making a lymphoma diagnosis.

For example, the typical CD pattern for the majority of WM clonal cells is CD5-, CD10-, CD19+, CD20+, CD23-, CD38-. Although this is the norm, there can be slight variations in the WM pattern as well as in the CD patterns of other B-cell lymphomas. Therefore, a whole range of test results, such as cell morphology, IgM expression, etc., must be considered in the diagnosis.

In another example, the typical pattern for B-cell chronic lymphocytic leukemia (B-cell CLL), is CD5+, CD10-, CD19+, CD20+, CD23+, CD38-. Notice that the major CD differences between the two are usually CD5 and CD23 expression. Also, whereas WM has very strong expression of CD20, B-cell CLL typically shows weaker expression of this particular marker.

Multiple myeloma is generally CD19-, CD20-, CD38+. This occurs because, as B-cells mature into plasma cells, they lose the CD19 and CD20 markers and begin to strongly express the CD38 marker. Consequently, these markers are frequently used in the differential diagnosis of certain B-cell lymphomas vs. multiple myeloma.

T-cell lymphocytes have their own unique CD markers, such as CD3, CD4, and CD8.

CD markers are not only important in the diagnosis of lymphoma—they are also useful for predicting the types of treatment that might be successful and for monitoring the effectiveness of treatment. The fact that the CD20 marker is positive for almost all non-Hodgkin's B-cell lymphomas makes it a good target for the use of rituximab, which is a well-known anti-CD20 antibody treatment. It has been speculated that rituximab treatment is more effective in lymphomas with stronger CD20 expression than in those with weaker expression. Rituximab is not generally used for multiple myeloma because these cells typically no longer express CD20. Interestingly, while the CD20 marker is a very important one, not much is known about its activity in the B-cell. It is suspected to act as a calcium channel in the cell membrane.

The use of CD markers has been a revolution in the diagnosis and treatment of various cancers, including lymphoma. Stem cell transplantation relies on detection of the CD34 marker present on harvested stem cells to determine how successful the harvesting process has been. New CD markers are being discovered, and new antibody therapies against various CD targets are being developed in the hope of improving cancer outcomes.

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