MORE ON THE ORIGIN OF THE REED-STERNBERG CELL

To the Editor:

In his recent “Letter to the Editor,” Dr Hsu arrived at the conclusion that “Hodgkin/Reed-Sternberg (H-RS) cells must be viewed as derived from cells of histiocyte rather than of lymphoid lineage.” However, I feel that this conclusion is based mainly on circumstantial evidence and that a number of other findings clearly contradict this assumption.

1. Can we extrapolate in vitro results to in vivo H-RS cells? To my knowledge, the direct descendancy of the KM-H2 and HDLM-1/HDLM-2 cells from the in vivo H-RS cells of the respective patients has not been demonstrated. Therefore, it is quite conceivable that these cell lines do not represent H-RS cells at all. Hence, the description of “Hodgkin’s disease derived cell lines” is more appropriate than the misnomer “Hodgkin cell lines” or “H-RS cell lines.”

2. Which feature represents inappropriate expression and which one genuine expression? Dr Hsu dismisses the lymphoid characteristics of the cell lines as “aberrant or inappropriate expression occurring in leukemias and lymphomas” and describes features promoted by various agents during induction of differentiation as specific lineage markers. But why not see it the other way around and assign these artificially induced properties of the cells to the category of aberrant, inappropriate marker expression? Are the genes encoding the proteins listed (cytokines, surface antigens, etc) not in lymphoid cells as well as in histiocytes and simply have to be turned on? There have been reports of the induction of macrophage phenotypes in genuine lymphoid leukemia cell lines. Furthermore, I should mention that while some of the parameters cited are indeed “shared” by histiocytes, they are found on lymphocytes as well.

3. Nature of the giant polynucleated cells. The formation of multinucleated giant cells of monocyte/macrophage/histiocyte origin occurs via fusion of mononuclear cells resulting in syncytia. In contrast, studies on fresh H-RS cells and Hodgkin’s disease derived cell lines showed that here multinucleated giant cell formation involved nuclear endomitosis without cell division and not cell fusion.

4. Precedence of results on in vivo H-RS cells. Finally, when speculating on the origin of H-RS cells, results from the direct analysis of fresh H-RS cells should take priority over indirect data from in vitro studies of a panel of Hodgkin’s disease derived cell lines. This group of cell lines includes quite different types of cell cultures with regard to morphologic, immunologic, molecular genetic, functional, and other criteria. Most recent evidence coming from the study of freshly explanted H-RS cells points to a lymphoid-type cell.

However, the data of these and other Hodgkin’s disease derived cell lines cannot and should not be dismissed out of hand. The previously forwarded concept of a hybrid cell fusing a B cell with a histiocyte-type cell would have one great advantage in that it would conciliate both camps, and thereby this theory becomes a bit more attractive.

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REFERENCES


More on the origin of the Reed-Sternberg cell [letter; comment]

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