Fifty Years of Tart Cells

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On January 21, 1948, a seminal report by Dr Malcolm M. Hargraves (Figure 1) and associates appeared in the Proceedings of the Staff Meetings of the Mayo Clinic. This publication, entitled “Presentation of Two Bone Marrow Elements: The ‘Tart’ Cell and the ‘L. E.’ Cell,” marked the first time the phenomenon of nucleophagocytosis in bone marrow preparations was described. The terms LE cell and Tart cell were both coined by Hargraves et al in that report.

The observation of the lupus erythematosus cell led to important gains in understanding the pathogenesis of systemic lupus erythematosus (SLE), but this cell is now considered by most pathologists as being “largely of historical interest.” However, the presence of LE cells was considered important enough to be included as a criterion in the most recent (1982) revised criteria for the classification of systemic lupus erythematosus, prepared by the American Rheumatism Association (now the American College of Rheumatology). There are still rare instances in which the presence of LE cells may be important in the diagnosis of SLE. For example, a case report published in 1992 described 2 brothers with symptoms suggestive of SLE in whom immunologic studies, including antinuclear antibody assays, were unrevealing. An LE cell preparation showed positive results in both patients and helped support the diagnosis of SLE. The history of the LE cell and its role in furthering the understanding of SLE were recently reviewed.

While the LE cell has diminished in importance since its original description in 1948, the Tart cell has fallen into complete obscurity. Seven major textbooks on clinical hematology and 7 on immunology published since 1980 were reviewed, but none mentioned the Tart cell. Relatively few pathologists and immunologists are aware of the existence of the Tart cell, especially those trained within the past decade.

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Original Description of the Tart Cell

In their 1948 report, Hargraves and colleagues presented the Tart cell as a finding that “can occur in practically all bone marrows” but especially in patients with conditions such as lymphoblastoma, pulmonary infection or metastatic carcinoma. The cell was thought to represent either a “histiocyte” (tissue macrophage) or a “monocytoid reticulo-endothelial cell” (monocyte) containing a pyknotic secondary nucleus nestled within its perinuclear hof (Figure 2). (Hof, a German word for court or yard, denotes the clear area in the cytoplasm next to a cell’s nucleus.) Sometimes, more than 1 secondary nucleus was observed in a single monocyte (an illustration of this phenomenon accompanied the original article).

“The distinguishing feature of this Tart cell … is that the secondary nucleus has retained a definite chromatin structure.” Hargraves et al considered this to be the most important feature distinguishing the Tart cell from the LE cell, which by contrast contained a “homogeneous, purple-staining mass in the vacuole” in which the nuclear chromatin pattern was no longer visible. The fact that the phagocytic cell component of the LE cell was “practically always a mature neutrophilic polymorphonuclear leukocyte” instead of a monocyte or macrophage was also noted in the original description.

From the perspective of 50 years, the explanation suggested by Hargraves et al concerning the origin of the Tart cell is incorrect: “We have the impression that this is probably an abortive nucleus resulting from a previous incomplete mitotic division of the cell.” The investigators admitted that they had seen the secondary nucleus partially outside the cell and wrote that “it is impossible to say whether it is being extruded from the cell or is in the process of being taken into the cell.” By contrast, Hargraves et al originally thought that the LE cell represented “one of two things: either phagocytosis of free nuclear material … or, second, an actual autolysis of one or more lobes of the nucleus of the involved cell.”

Some atlases on hematopathology still include the Tart cell. The distinctions first made by Hargraves et al between the Tart cell and the LE cell—namely, that the Tart cell is a monocyte (not a polymorphonuclear leukocyte) and that its secondary nucleus contains chromatin
Figure 1. Malcolm M. Hargraves, discoverer of the lupus erythematosus cell and the Tart cell.

Figure 2. Tart cell phenomenon: a monocyte has phagocytized another nucleated cell. The pyknotic secondary nucleus in the monocyte's perinuclear hof retains vestiges of its chromatin structure (redrawn from Diggs and associates§65).

material—are still considered important, as described by Diggs§65 in The Morphology of Human Blood Cells:

Structureless red-staining cytoplasmic inclusions of the type demonstrable in stained smears of bone marrow and body fluids in patients with lupus erythematosus are to be differentiated from linear and/or lumpy nuclei that stain dark blue and that are contained in the cytoplasm of monocytes. Monocytes that have ingested nonlysed nuclei are designated as "Tart cells," so named because they resemble the cells that were observed and reported in smears of bone marrow of Mr. Tart who was a patient at the Mayo Clinic.

Origin of the Name "Tart"

The fact that the Tart cell is actually named after a patient was not mentioned in the original report by Hargraves et al. At a 1969 symposium on the discovery of the LE cell, published in the Mayo Clinic Proceedings, Hargraves commented on the confusion surrounding the name:

For many years there was much curiosity about our choice of the name, "tart cell." Many people felt, and understandably so, that it was named after a small pastry in which the decorative effect of pieces of fruit on the surface was sometimes mimicked by the two nuclei of the "tart cell." However, the truth is that the cell was named after a patient in whose bone marrow preparation we first found tremendous numbers of these cells.

Naming the cell after Tart was consistent with a vogue during the 1940s and 1950s for eponyms derived from patients in whom a disease or abnormality was first described, rather than the names of the original investigators. Other examples include clotting factors such as Hageman factor (also known as factor XII, first described in 1955§5) and Christmas factor (also known as factor IX, first described in 1952§5), as well as the antibiotic bacitracin (named after Margaret Tracy, a young girl whose compound fracture site yielded the "Tracy I" strain of Bacillus subtilis from which the antibiotic was isolated in 1945§5). Such eponymic derivations are rare today, perhaps because of increased respect for the privacy of patients.

Although Hargraves did not capitalize the word tart in either his 1948 or 1969 publication, most other references on the subject have, and I chose to capitalize the word in this article because it represents a proper name.

Decline of the Tart Cell

Rarely, studies involving Tart cells are reported by investigators; a careful electronic database search uncovered only a few publications.11,12 In the late 1960s, rheumatology trainees were still taught to recognize Tart cells and to distinguish them from LE cells, but this skill is no longer a valued or regular part of the fellowship curriculum (S. E.
Walker, personal communication, May 1998). Textbooks of laboratory hematology written as late as the 1970s often included a paragraph warning trainees not to mistake Tart cells for LE cells, but, of the 5 laboratory textbooks published since 1980 that I consulted, only 1 discussed this problem.

The decline of the Tart cell reflects the diminishing importance of its "big sister," the LE cell. The main importance of the Tart cell was the possibility that it might be mistaken for an LE cell; its presence in isolation proved to be of little diagnostic value. As the LE cell assay gave way to various immunologic assays for antinuclear antibodies in the diagnosis of rheumatologic disease, the Tart cell yielded importance also.

Many reference laboratories such as the Mayo Medical Laboratories no longer perform the LE cell assay because it is labor-intensive and is generally viewed as obsolete, having been replaced by more specific immunologic assays such as those for IgG anti-double-stranded DNA (H. A. Homburger, personal communication, November 1997). Nevertheless, there are still rare occasions in which an LE preparation can be clinically important, and in such instances, the interpreting physician must be able to recognize the false-positive phenomenon of a Tart cell.

Conclusion

Relatively few physicians today have heard of the Tart cell; indeed, it is the rare person who recognizes this cell and realizes that it represents the phenomenon of nucleophagocytosis. Nonetheless, the Tart cell is of interest, both as a part of the history of rheumatology, hematology, and immunology and as a false-positive LE cell phenomenon.

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REFERENCES