

Brief Notes

Electron Microscopy of Emperipolesis. BY EMMA SHELTON AND A. J. DALTON. (*From the National Institutes of Health, Bethesda, Maryland.*)*

In a previous communication (1), one of us described the propensity for emperipolesis exhibited by the cells of the mouse ascites lymphocytic tumor, Lymphoma No. 1 (L #1). Emperipolesis, a term coined by Humble, Jayne, and Pulvertaft (2) to describe the "inside round about wandering" of lymphocytes within cells, has been observed by several investigators to occur under a variety of conditions (*cf.* reference 1). The question that presents itself when cells are observed to be existing within other cells is—what are the relationships between the engulfing cell and the engulfed cells? Are the engulfed cells in intimate contact with the cytoplasm of the engulfing cell or are membranes present which separate one cell from the other?

These questions are answered in part by the micrographs accompanying this note. The macrophage shown in the phase photomicrograph (Fig. 1) contains five living L #1 tumor cells and one dead cell. The very granular cytoplasm of the macrophage can readily be distinguished from the clear cytoplasm of the tumor cells contained in it, but the nature of the boundary between the two cytoplasm cannot be determined by phase microscopy.

A thin section of a similar group of cells, fixed in chrome-osmium and photographed with the electron microscope, shows that for the most part the malignant lymphocytes are separated from the cytoplasm of the macrophage by two membranes, one belonging to the lymphocytes and one belonging to the macrophage (Figs. 2 and 4). Thus, the macrophage cytoplasm is not only enclosed in an outer membrane but in an inner membrane as well. While the plasma membrane of each of the

lymphocytes is intact, there are areas where the inner membrane of the macrophage is not so distinct and in these areas macrophage cytoplasm appears to be in contact with the lymphocyte membrane (Figs. 3 and 5). The continuity of the outer membrane shows that at the level of the section, at least, the tumor cells are indeed entirely within the macrophage.

Although the nature of the plasma membrane of cells is only poorly understood, there is no reason to think that the inner membrane of the macrophage is different from the outer one. It is more interesting to speculate on the reason for its existence. The macrophage shown here has reacted to the presence of living lymphocytes within it by forming another membrane, so that the relationship between the two cell types at the point in time shown here, at least, is not very different from the contact between two contiguous cells. There is support for the belief that it is the lymphocyte that brings about this situation. It was noted in a recent review (3) that lymphocytes have been found within liver cells, amphibian ova, fibroblasts in culture, in the epithelium of the liver, kidney, intestine, trachea, and thyroid. Thus the macrophage is but one of many cells in which lymphocytes can be found. With what peculiar immunity is the lymphocyte endowed that permits it to wander in and out of cells and to undergo mitosis within them? The lymphocyte is perhaps the least understood of all metazoan cells.

REFERENCES

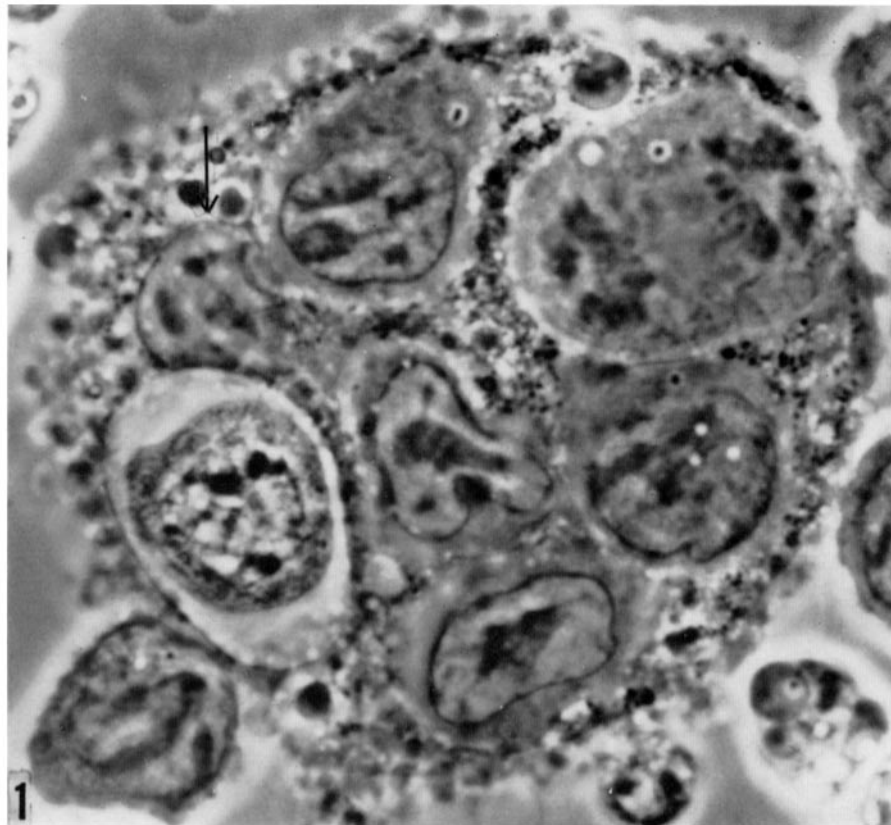
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EXPLANATION OF PLATES

PLATE 247

FIG. 1. Phase photomicrograph of L # 1 tumor cells within a macrophage. The arrow points to the macrophage nucleus. $\times 2000$.



(Shelton and Dalton: Emperipolesis)

PLATE 248

The horizontal bars on the figures equal 1 micron.

FIG. 2. Thin section through a macrophage containing five tumor cells; unfortunately, the macrophage nucleus is not in the plane of the section. Note the continuity of the outer macrophage membrane. The tumor cell on the extreme right has a "tail" characteristic of a lymphocyte in motion. Approximately $\times 2000$.

FIG. 3. Detail of the junction of four of the lymphocytes. Note what appears to be macrophage cytoplasm in the spaces between the tumor cells. Approximately $\times 16,000$.

FIG. 4. Detail of the macrophage membranes and their relation to the tumor cell plasma membrane. Approximately $\times 16,000$.

FIG. 5. Detail of area where macrophage inner membrane is less well delineated. "Naked" macrophage cytoplasm is in contact with the tumor cell plasma membrane at this point. Approximately $\times 16,000$.

