

## Malignolipin

In this day, with biochemistry emerging as a highly complex and incompletely understood area of inquiry, it is particularly disconcerting to see publications in this field which jump to hasty and obviously unjustified conclusions.

I am thinking specifically of the report on malignolipin, by Kôzaki *et al.*, which appeared in the 16 May issue of *Science* [127, 1176 (1958)]. On the basis of the data presented (purely qualitatively), these authors report that malignolipin was isolated from every malignant tumor on which the extraction procedure was used, in greatest amounts from active tumors and in least amounts from necrotizing tumors. They further report that no malignolipin could be isolated from cattle brain or whole mouse bodies.

From these scanty data the five authors conclude that malignolipin is present in all malignant tumors, is not present in any other tissue, and is intimately connected with the malignancy of the tumors.

It seems almost needless to point out that until data on the percentage of recovery of malignolipin by the method used are presented, one cannot conclude that failure to isolate any from a tissue is indicative that none is present. The obvious suggestion to be deduced from the results of these authors is that the lipid may be associated with tissues of high growth rates. Yet, without investigating gonadal, regenerating, or embryonic tissue, the authors state that malignolipin is present only in the tumors. Obviously, considerably more facts must be presented before any such generalizations can be made.

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In the report published in the 16 May issue of *Science* [127, 1176 (1958)], I and my coworkers stated the existence of a new phospholipid in human malignant tumors and the nonexistence of such a lipid in normal tissues, such as cattle brain or whole bodies of normal mice, and we also mentioned the supposition that malignolipin is intimately related to the malignancy of tumor cells.

Fresh normal human tissues cannot be obtained in sufficiently large amounts to give conclusive evidence that such tissues do not contain malignolipin. Therefore we have attempted to detect malignolipin in the fresh whole bodies of normal mice, including of course gonadal tissues, and also in fresh cattle brain. Besides, we have attempted to isolate malignolipin from the stomach, brain, and liver of normal persons autopsied. In examination of these tissues no malignolipin could be detected.

Malignant tumors show a very marked affinity for protoporphyrin, an affinity



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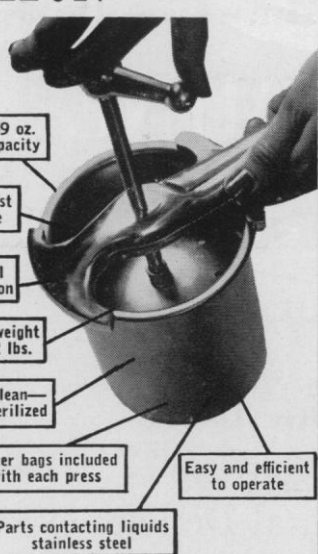
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which is confined chiefly to small extracellular bodies in the tumors. In normal tissues, only sphingomyelin has the affinity for protoporphyrin (1). How to isolate the substance with the affinity for porphyrin from human malignant tumors, excluding sphingomyelin, constituted the basis of our discovery.

On the same basis, we originated a histological method for detecting malignolipin, excluding sphingomyelin, and ascertained that malignolipin could never be found in such tissues as normal liver, kidney, alimentary tract, lung, heart, pancreas, spleen, urinary bladder, and prostate, or in noncancerous tissues from individuals with hepatitis, liver cirrhosis, stomach ulcer, renal tuberculosis, and prostate hypertrophy, but could be found always in cancerous tissues. We studied one cancer of the esophagus, 12 stomach cancers, one cancer of the cecum, three cancers of the rectum, one uterine cancer, one renal adenocarcinoma, one Grawitz' tumor, one breast cancer, two urethral cancers, two seminomata, five cancers of the urinary bladder, one prostate cancer, one Hodgkin's malignant granuloma, and one reticulosarcoma (2).

No malignolipin could be detected histologically in human testicles, in tissues of 2- to 3-month human fetuses, or in chicken embryos of various stages of development (3).

Since malignolipin could be isolated from the blood and ascites of cancer-bearing plants as well as from Ehrlich's cancer ascites of mice, a sensitive method for exact detection of malignolipin in blood was devised. Tests, made in accordance with this method, of the blood of 18 normal persons and of eight patients not bearing malignant tumors were uniformly negative with respect to malignolipin, but tests were positive, without exception, for 25 patients bearing cancer. This method has been stated to be an excellent clinical method for the diagnosis of malignant tumors, especially for their early discovery (2).

Since malignolipin was thus supposed to be intimately related to the malignancy of tumor cells, its effect on the growth of Ehrlich's ascites cancer was examined to test the validity of this supposition and it was ascertained that malignolipin increased the intraperitoneal growth of Ehrlich's ascites cancer and the rate of mitosis of Ehrlich's ascites cancer cells (2).

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#### References and Notes

1. See reports No. 6 and 13 of the studies of T. Kôzaki *et al.* on the affinity of tissue elements for porphyrin, *J. Mie Med. Coll. (Japan)* 5, 29 (1955); 7, 313 (1957).
2. These results have been reported in *Proc. Japan Acad. No. 5* (1958).
3. A paper describing the particulars of these results is in preparation.

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