LETTERS TO THE EDITORS

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Electron Microscope Studies of Normal and Malignant Tissues of High- and Low-Breast-Cancer Strains of Mice

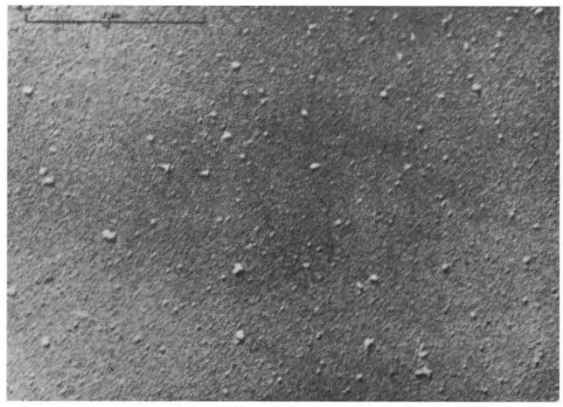
MAMMARY cancer in high-breast-cancer strains of mice has been shown by Bittner[1] to be transmissible to the offspring through the milk of the mother, and furthermore he has claimed[2] that all the tissues except the liver of high-cancer strains contain the same tumour-inducing factor as is found in the milk.

Barnum, Ball, Bittner and Visscher[3] described some of the physical properties of the milk factor present in tissues of mice of high-cancer strains. They found that petroleum ether does not destroy the tumour-inducing properties of tissues derived from high-cancer strains. They also observed that these properties remain unchanged at *p*H values between 5·0 and 10·2. According to Bittner[4], and confirmed by one of us (Dmochowski), extraction of breast-tumour tissue with distilled water is more efficient than with saline.

In June 1946, experiments were undertaken in order to examine with the electron microscope normal and malignant tissues obtained from high- and low-cancer strains.

Extracts of normal and malignant tissues from mice of *C3H*, Strong *A*, and *R3* high-cancer strains, as well as of *C57* black and *CBA* (which in this laboratory is a low-cancer strain), were prepared in the following way. Dried tissues were treated with petroleum ether, extracted with distilled water, treated with trypsin for 30 min. at 37° C., and filtered through Berkefeld *N* candles. The following tissue extracts were made: lactating breasts and breast tumours of *C3H*, Strong *A* and *R3* strains; lactating breasts of *C57* and *CBA* strains; breast tumours induced in *C57* and in *IF* low-cancer-strain mice by methylcholanthrene; and also 37*S* transplantable sarcoma of the Imperial Cancer Research Fund, and a sarcoma induced in *C57* by methylcholanthrene. In each case extracts of the same concentration were made, starting from equal amounts of dried tissue. Usually several tumours or lactating breasts from several mice of each strain were minced together and desiccated in the usual way[5]. In a few cases breast tumours and lactating breasts, each derived from a single mouse, were also examined. All extracts for electron microscopy were further diluted with filtered distilled water to a strictly comparable concentration, micro-drops were placed on filmed specimen grids, and the drops were drained immediately with a strip of filter paper to bring about rapid drying. After shadowing with metallic gold, the suspensions were photographed.

Results. Extracts of lactating breast tissues and of breast tumour tissues of *C3H*, Strong *A* and *R3* strains were found to contain approximately spherical particles about 200 A. in diameter (see photograph). Extracts of lactating breast tissues from mice of *C57* and *CBA* low-cancer strains, extracts of breast tumours induced in *C57* and *IF* low-cancer strains by methylcholanthrene, and extracts of 37*S* sarcoma, were found to be free from such particles. Our results showed, therefore, that particles of about 200 A. diameter were consistently present in breast tissues and tumours of high-cancer strains, and consistently absent from those of low-cancer strains.



EXTRACT (PETROLEUM ETHER, DISTILLED WATER, TRYPSIN, BERKEFELD *N* CANDLE) OF *C3H* HIGH-CANCER STRAIN LACTATING BREAST TISSUE. GOLD-SHADOWED ON COLLODION FILM

Concurrently, all extracts were inoculated into *C57* × *R3* hybrid mice, susceptible to the development of breast cancer. The results of these biological tests are awaited.

Since this letter was ready for publication, it has come to our notice that Graff, Moore, Stanley *et al.*[6] have examined the milk of a high- and a low-cancer strain of mice and report finding a "characteristic material of large particle size" from the milk of their high-cancer strain and its absence or low concentration in their low-cancer strain. The significance of the difference in size between the particles encountered in the two laboratories is not clear at present, nor is the relationship between these particles and the tumour-inducing factor.

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[2] Bittner, J. J., *U.S. Pub. Health Rep.*, **54**, 1827 (1939).
[3] Barnum, C. P., Ball, Z. B., Bittner, J. J., and Visscher, M. B., *Science*, **100**, 575 (1944).
[4] Bittner, J. J., Amer. Assoc. Adv. Sci., Research Conference on Cancer, Washington, p. 80 (1945).
[5] Dmochowski, L., *Brit. J. Exp. Path.*, **25**, 138 (1944); **26**, 192 (1945); **26**, 267 (1945).
[6] Graff, G., Moore, D. H., Stanley, W. M., Randall, H. T., and Haagensen, C. D., 4th Intern. Cancer Research Congress, Sept. 2–7, 144 (1947).

Specimen Changes due to Electron Bombardment in the Electron Microscope

WE have recently observed changes in a number of substances, chiefly ionic crystals, when subject to intense electron bombardment in the electron microscope. While the results are not readily interpretable, they do suggest that the effects may not be entirely due to the heating effect of the electron bombardment. It is for this reason, as well as for recording a type of artefact that has hitherto received little attention in the literature, that we report them here.