exerted on metabolic processes early in malignancy. The inhibitor was ineffective when used under a wide spectrum of biological conditions against spontaneous and transplanted tumours.

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Electronmicroscopy of Friend Tumour Cell with Special Reference to the Influence of Friend Virus Immunity on Friend Tumour Cell

TRANSPLANTABLE tumour (Friend tumour) was inoculated into mice immunized with Friend virus formalin vaccine and the resultant changes were studied electronmicroscopically, with special reference to the intracellular distribution and morphological changes of the Friend virus particles which are the cause of the tumour.

The Friend tumour in question has been carried for approximately two hundred generations since its establishment, and has been continuously transplanted as an ascites tumour in mice of the strain *dd/Om*[1]. One of the characteristics of this Friend tumour is that it is still a host for the Friend virus, and while it continues to produce Friend virus it also continues to proliferate as a malignant tumour. Electronmicroscopic observations by Kodama (report in preparation) of Friend tumour show the presence of extracellular Friend virus and it is also known that the course of the maturation of virus from the Friend tumour cell can be seen as a process of budding from the tumour cell membrane. The presence of intracellular Friend virus in the tumour cell can, however, scarcely be seen.

When 10^5–10^6 Friend tumour cells were inoculated into *dd/Om* mice immunized with Friend virus formalin vaccine (the virus is centrifuged and separated by Moloney's method[2] and immunized by Friend's method[3]) intraperitoneally and subcutaneously, a remarkable degeneration of the tumour cells as compared with those inoculated into non-immunized mice, a decrease in the rate of mortality caused by the tumour in mice, and a lengthening of the time of survival were seen[4].

The almost complete disappearance of virus particles from the outside of cells (electronmicroscopically and biologically) and an extraordinary accumulation of intracellular virus particles (Figs. 1 and 2) is interesting. The majority of intracellular virus particles are concentrated in the cytoplasmic matrix, with a higher concentration in the concave area of the eccentric nucleus, and at times these are seen surrounding the endoplasmic vacuoles, arranged in parallel rows directly under the endoplasmic membrane. These virus particles are round or almost round with diameters of 750 Å–850 Å. The virus has a double shell membrane structure in a concentric form with a dense nucleoid area in the central part and is classified as Bernhard's[5] type *A* particle. As compared with the typical mixture of Friend virus *C* and *A* as seen in Friend disease or Friend tumour, *A* alone is characteristic of the present case.

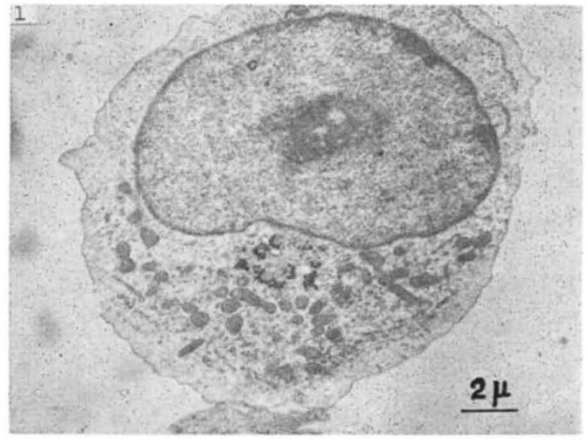

Fig. 1.

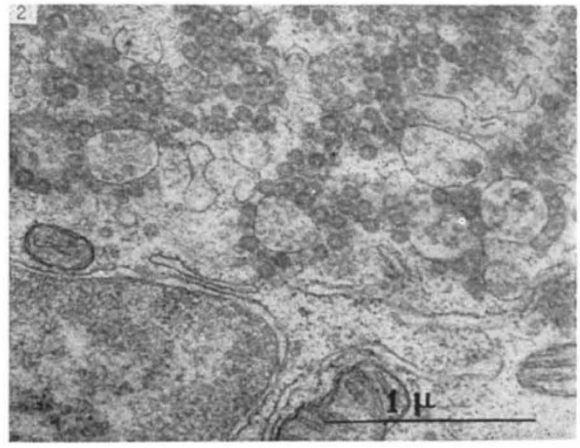

Fig. 2.

The relationship of the intracellular virus particles in question with Friend virus may be explained as follows: The particles are morphologically identical to Friend virus *A*; an inoculation of these virus particles into non-immunized mice produces slight Friend disease and such a phenomenon is only seen with the immunization of Friend virus or Friend tumour cell and not with the immunization of other cells.

The mechanism of the intracellular accumulation of virus particles in such an immunization procedure is not certain; it may involve a shift of the site of virus production so that virus replication under the influence of the virus immunity at the cell membrane occurs at a site where the influence of immunity is smallest. This problem must be investigated further in relation to the mechanism of the selective appearance of *A* particles within the cell. It is probable that, as in the case of virus induction by such procedures as X-ray irradiation, this phenomenon may be considered as a case in which intracellular virus accumulation can be seen in immunized but not in non-immunized mice.

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