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Multinucleated Giant Cell Formation by Fusion of Two Different Strains of Cells

In the previous papers, Okada *et al.*¹⁾, and Okada²⁾, have reported that Ehrlich's ascites tumor cells (ETC) fuse together and many multinucleated giant cells appear under the action of HVJ virus *in vivo* or *in vitro*. The fusion reaction is completed *in vitro* within 60 minutes by incubation of a mixture of HVJ and ETC, suspended in Hanks' solution not containing glucose, at 37°C with shaking.

The possibility of whether multinucleated giant cells could be derived from the fusion of two different strains of tumor cells by HVJ was examined. Two new mouse ascites tumor cell strains, Sarcoma 180 cells and SN-36 cells as well as ETC were used. The latter is a strain of lymphocytic ascites tumor cell derived from a Nitromin induced leukaemia mouse by Dr. Nakamura of the Sasaki Institute, Tokyo. Both cell strains were kindly supplied by Dr. Tadashi Yamamoto of the Institute for Infectious Diseases, Tokyo University. All these three strains have been individually passaged in the abdominal cavity of ddO stock mice.

In the first experiment, ETC and Sarcoma 180 cells were used. The latter cell strain can produce fused cells with HVJ virus like ETC. A 1:1 (cell number) mixture of ETC and Sarcoma 180 cells, also produced typical giant cells on the addition of HVJ. The rate of cell fusion in this cell mixture was about equal as that of ETC alone or Sarcoma 180 cells alone. This suggests that some giant cells are derived from the fusion of these two different types of cells. If it were not so, the efficiency of fusion of the mixture would be lower than that of ETC or Sarcoma 180 cells alone, because it is known that cells which do not take part in the fusion reaction must be excluded from the cell aggregate formed in the early stage of the reaction.

In the second experiment, ETC and SN-36 cells were used. SN-36 cells have the capacity to produce fused cells with HVJ virus but the capacity is lower than that of ETC. When an ETC and SN-36 cell mixture was examined, both typical fused cells and rugged surfaced abnormal giant cells appeared on HVJ virus treatment and much cell debris was also found. Balloon-like membranes covered part of the abnormal giant cell surface. The internal structure is not clear, and only a large number of fine granules can be seen. This type of cell may have abnormal metabolism. The abnormal giant cell must have been formed from complexes of ETC and SN-36 cells, since the frequency of appearance of cell was highest when ETC and SN-36 cells were mixed in a 1:1 ratio.

The cause of the abnormal giant cell formation is not yet clear but at least two factors must be considered: first, the cell membrane structure of ETC and SN-36 cells are so different that the cell membrane can not be organized

together and as a result cell metabolism is distorted; secondary, there may be some kinds of incompatibility between the two kinds of cells, and the cytoplasm of ETC is not maintained normally when mixed with the cytoplasm of SN-36 cells, or vice versa, when the abnormal reaction takes place between the two heterogeneous cytoplasms.

The results may suggest that mixing or connecting the cytoplasms of two kinds of cells is possible by the fusion reaction. If so, it seems that it would be possible to classify cell strains by the possibility of such a compatibility (in the first experiment), or incompatibility (in the second experiment) between the cytoplasm of two different kinds of cells.

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EXPLANATION OF PHOTOGRAPHS

- Fig. 1. A. Ehrlich's tumor cell (ETC) control
B. Typical fused cells of ETC produced by HVJ virus
- Fig. 2. A. Sarcoma 180 cell control
B. Typical fused cells of Sarcoma 180 cells produced by HVJ virus
- Fig. 3. A. ETC and Sarcoma 180 cell mixture control (mixing ratio 1:1)
B. Typical fused cells in ETC and Sarcoma 180 cell mixture, at a mixing ratio of 1:1, produced by HVJ virus
- Fig. 4. A. SN-36 cell control
B. Typical fused cells of SN-36 produced by HVJ virus
- Fig. 5. A. ETC and SN-36 cell mixture control (mixing ratio 1:1)
B. Abnormal giant cells in ETC and SN-36 cell mixture, at a mixing ratio of 1:1, produced by HVJ virus
- Fig. 6. An abnormal giant cell in ETC and SN-36 cell mixture at higher magnification
- All photographs were taken by a phase contrast microscope with a dark contrast objective lense.



