Discussion to d-8.

Antitumor Effect of Heterologous Immune Lymphocytes
in Experimental Gliomas and Fibrosarcomas

Preliminary Report

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There have been many reports which suggest the presence of tumor specific antigens. Their precise localization and chemical nature are, however, unfortunately obscure. As the tumor cells are arisen from the corresponding normal cells by unknown process of malignant transformation, their antigenicity is usually extremely weak. The immune reactions to weak antigens, such as antigens of transplantation type including tumor antigens, are reported to be mainly mediated by so-called cell bound antibodies, that is, sensitized lymphoid cells.

Alexander et al. have treated primary fibrosarcomas in rats with immune lymphocytes derived from syngeneic, allogeneic or heterologous sources.

We attempted to show the antitumor effect of heterologous immune lymphocytes, because of some possibilities that this type of method may eventually become clinically useful for eliminating malignant cells left behind after removal of major part of the tumor. We do not believe, however, that this type of procedure is likely to be of value when the bulk of the tumor remains in situ or tumor metastases are extensive.

Animals, available in the experiments, were randomly bred C57BL mice in closed colony and rats of Wister strain. Transplantable gliomas and fibrosarcomas were induced in mice by the intracerebral and subcutaneous implantations of MC powder. Rats were sensitized with a piece of mouse tumor in the route of subcutaneous implantation. Thoracic duct lymphocytes of these rats were obtained by cannulation 7 and 14 days later. Lymph was collected over a period of 24 hrs. into a refrigerated flask containing heparin and tissue culture medium. The number of lymphocytes usually amounted to \(10^7-10^9/24\) hrs. per rat, and 15 to 25% of the collected lymphocytes were lymphoblasts. These sensitized lymphocytes, 10 to 1000 times as many as the tumor cells, were injected intravenously in mice and at the same time the tumor cells were transplanted subcutaneously.

This preliminary work might suggest that antitumor effect of heterologous lymphocytes was stronger at 7 days than at 14 days after sensitization and the more immune lymphocytes to tumor cells, the stronger the antitumor effect. There was no remarkable difference in the antitumor effect of sensitized lymphocytes between gliomas and sarcomas.

C57BL mice used were randomly bred in closed colony and showed the
transplantation rate of about 80% on the subcutaneous inoculation of trypsinized viable $10^6$ tumor cells. The mice which had rejected the first tumor grafts showed the complete resistance to subsequent challenge of the same dose of the same tumor. The main mechanism of this rejection, however, is probably due to the transplantation immunity. Experiments using inbred animals are now in progress.

d-9. Classification of Glioma Groups

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Classification of glioma arranged by Bailey and Cushing in 1926 was based upon histogenesis. After Bailey & Cushing, many scholars reported their own way of classification, which were somehow different each other, but most of them were based upon histogenesis.

Contemporary science shows that mutation, anaplasia, metaplasia, kataplasia of the cells result in tumor formation and brain tumors cannot be of exception. Kernohan and Willis reported their own classification based on the idea that tumors arose from adult cells.

I have seen many histological specimens of brain tumors, (about 1,000 cases at Kyoto University Hospital, about 1,500 cases at Montefiore Hospital in New York and about 200 cases at Kansai Medical College Hospital nd others) and tried to design a new classification of glioma groups with background of my own experience of histopathology, tissue culture and electron microscopic study. Our experience of tissue culture of medulloblastoma proved only axon formation and no clear glial cells were found to emigrate at any stage of the culture. Therefore this tumor is to be classified not as a glioma but is to be treated as a neurogenic tumor.

The word “spongioblastoma plare” is inadequate from many reasons. Tumors consisting of cells resembling astroblast, oligodendroblast and ependymoblast seems to be not clear.

Some scholars believe that all of glioblastoma are astrocytic tumors, but I do not believe that glioblastoma is always of astrocytic origin. Some of glioblastoma seems either of ependymal cell origin or of oligodendrogial origin. With electron microscope some glioblastmas are definitely of ependymal origin, in which cilia, desmosome and blepharoblast are observed in tumor cells.

Judging from above-mentioned study a simplified classification of glioma based upon cancer classification is designed as follows: Benign form is consisted of 3 groups in which tumor cells look like normal glial cells. Malignant tumor with cell pattern of unknown origin is classified as glioblastoma. All other glial tumors are classified in between and put a simple word of “malignant” in front.