F. Tumor Diagnosis

Distribution of Tumor Seeking Substances in Tumor Tissue

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This study was performed to investigate the distribution of ^{67}Ga-citrate, ^{111}In-citrate, ^{169}Yb-citrate, ^{167}Tm-citrate, ^{32}P-sodium phosphate, ^{131}I-albumin and ^{125}I-fibrinogen in tumor tissue by macroautoradiography. These labeled compounds were injected intravenously to the rats subcutaneously transplanted Yoshida sarcoma and were injected intraperitoneally to the mice subcutaneously transplanted Ehrlich tumor. These animals were sacrificed at 24 hours after injection, and tumor tissues were frozen in n-hexane (−70°C) cooled with dry ice acetone. After this, these frozen tumor tissues were cut to thin sections (10μm) in the cryostat (−20°C). First slice of these sections was then placed on X-ray film and this film was developed after exposure of several days. On the other hand, next slice of these sections were then stained using the hematoxylin and eosin. From observing these autoradiogram and H.E. stained slice, the following results were obtained. The uptake of ^{67}Ga, ^{111}In, ^{169}Yb, ^{167}Tm and ^{32}P was predominant in viable tumor tissue rather than in necrotic tumor tissue, but the uptake of ^{131}I-albumin and ^{125}I-fibrinogen was predominant in necrotic tumor tissue rather than in viable tumor tissue. These results were very similar each other in two stains of tumor (Yoshida sarcoma and Ehrlich tumor).

"A Biochemical study on ^{67}Ga Accumulation in Morris Hepatoma"

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In purpose to investigate the basic accumulation mechanism of ^{67}Ga in malignant tumor tissue, one of minimum deviation hepatoma of Morris 7316 A was used. Tumor tissues were preparated in about 48 hours after intraperitoneal injection of ^{67}Ga citrate and fractionated following the method of C. de Duve et al. (1955). Normal rat livers were also treated simultaneously as a control. Light mitochondrial fractions, which contained mainly lysosomes, revealed the highest relative specific

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radioactivity of ^{67}Ga both in tumor and in normal livers. These results indicated that ^{67}Ga was highly concentrated in lysosomes.

The light mitochondrial fractions were treated by various procedures to disrupt the lysosomes gradually. Marker enzyme of lysosomes (acid phosphatase) was activated stepwise at the same rate of solubilization of ^{67}Ga from lysosomes. So it is conclusive that ^{67}Ga was contained in lysosomal granules.

Cytosol of tumor tissue accumulated not only the highest counts of ^{67}Ga ($36.3\pm2.5\%$ of all acounts), but also the highest activity of lysosomal marker enzyme (acid phosphatase) ($41.6\pm1.7\%$ of all activities) And the correlation coefficient between the two activities (^{67}Ga and acid phosphatase) was 0.97. From this result, it is clear that most counts of lysosomes move into cytosols through subfractionation probably because lysosomes of tumors are liable to break and move into cytosols.

Similar results were also obtained in case of normal rat livers. The highest counts of ^{67}Ga and relative radioactivity were found out in light mitochondrial fraction. The fact that accumulation mechanism of ^{67}Ga exists in lysosomal fraction, is more clear than in case of tumor tissue. From these observations we must not discuss the accumulation mechanism without saying lysosomal function of tumors.

Effects of Cold Gallium on Cultured Cancer Cells: A Biological Approach to the Study of Mechanisms of Gallium Tumor Affinity

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In spite of its clinical usefulness, the mechanisms of ^{67}Ga tumor affinity remains controversial. The present investigations were undertaken in order to obtain an insight into this problem by studying probable biological effects on cultured mammalian cancer cells of cold gallium.

Results:

1. EM3A mouse mammary cancer cells were shown capable of extracting ^{67}Ga from the surrounding culture medium when they were exposed to the radioelement during the logarhythmic growth period.
2. Cold, nonradioactive gallium was found quite less toxic to the cells than the x-rays as studies by the colony formation technic.
3. The biological effectiveness of gallium on the logarhythmically multiplying cells was evidenced by plateau formation, reduced growth rate, reduced saturation density, development of locomotion and phagocytic function as well as morphological maturation. Similar morphological changes were observed in B-16 melanotic and amelanotic melanoma cells of C57B1 mouse origin, too. These changes appear to suggest an attainment of reduction in malignancy of these cells and their phenotypic acquisition of the normal cell morphology and function.
4. The rat ascitic hepatoma cells, AH 7974F, are free cells of malignancy and cell membrane negative charge much greater than their sibling cell line, AH 7974, an island-former. An

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