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UPTAKE OF Ga-67 CITRATE IN VARIOUS KINDS OF EXPERIMENTAL TUMORS. —MORPHOLOGIC INVESTIGATION—

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Ehrlich's tumor(mouse), sarcoma 180 (mouse) and 3'-Me-DAB hepatoma(rat) were compared each other autoradiographically and histologically to investigate the uptake of Ga-67 citrate in tumor. In order to evaluate the associations between the growth of tumor and the uptake of Ga-67, animals were killed at 3, 5, 7 and 10 days after injection of Ehrlich's and sarcoma 180 tumor cells.
Following results were obtained. Accumulation of Ga-67 was seen in all experimental tumors. RI uptake ratio(tumor/normal tissue counts ratio, T/N ratio) was increased according to the growth of tumor in Ehrlich's tumor and sarcoma 180. T/N ratio calculated about 5 in the mice tumor at 10 days after injection of tumor cells. On the other hand, RI uptake ratio(hepatoma/normal liver tissue) calculated 1.62-3.31 in 3'-Me-DAB hepatoma. In all tumors, the evident accumulation of Ga-67 was demonstrated into the site of dense tumor cells without degeneration and necrosis. Ehrlich's tumor and sarcoma 180 showed a tendency to uptake Ga-67 into the granulation tissues around the tumor and most of them showed also higher uptake than that of tumor cells.

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UPTAKE OF GA-67 BY AH-130 TUMOR CELLS.

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Uptake of Ga-67 by AH-130 ascite tumor cells (AH-130) and effect of heparan sulfate (HS) addition were studied.

AH-130 were suspended in 1mL of 0.9 % NaCl-0.01 M MOPS buffer (pH 5.5-8.0),and incubated with Ga-67-citrate (0.05 μCi, containing 1.4 μg sodium citrate). After the incubation, each suspension was centrifuged for 10 min at 400g, and sediment was washed with buffer described above (twice), then the radioactivity in the sediment was counted. Moreover, HS was added (1-20 μg) to above incubation mixture.

Uptake of Ga-67 by AH-130 showed an inverse dependence on the pH of incubation mixture. The uptake was increased with adding HS, and that that uptake and HS uptake by AH-130 both were significantly increased at lower pH. Moreover, we measured the pH levels in AH-130 solid tumor, CCl_4 damaged liver, and, normal tissues by using with pH electrode for tissue and cell. Tumor and CCl_4 damaged liver tissues pH were low values compared with normal tissues.

These results indicated that the HS related to the Ga-67 uptakes in tumor and inflammatory lesions and the decreased pH in their tissues stimulates to the Ga-67 uptake.

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THE RELATIONSHIPS BETWEEN GA-67 AND FE-59 UPTAKE AND CELL CYCLE OF SYNCHRONIZED CULTURED TUMOR CELLS.

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It is said that the uptake of Ga-67 in malignant tumor cells was preceded by binding of Ga-67 to transferrin like iron, but the localization or binding substance of Ga-67 in malignant tumor cells is different from iron.

In the present study I have attempted to examine the relationship between cell cycle using synchronized mouse tumor cells and Ga-67 and Fe-59 accumulation into malignant tumor cells. Cells were synchronized by a modified method of Shinohara. Mouse leukemia L5178Y were cultured in Fischer's medium with 10% horse serum. The synchronization of L5178Y cells was essentially produced by a combination of excess thymidine and colcemid, except that mixture of deoxycytidine and colcemid was added directly to the cell suspension without removing excess thymidine. The uptake of Ga-67 and Fe-59 into malignant tumor cells was gradually increased 9 or 10 hours after syncronization, afterwards the Ga-67 and Fe-59 uptake was gradually decreased. The Ga-67 uptake in G_2 phase of cell cycle was greater than that of other phase of cell cycle.

From these results, it may be concluded that the accumulation of Ga-67 into synchronized cultured cells was almost simillary as well as the accumulation of Fe-59.

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EXPERIMENTAL STUDY ON Ga-67 ACCUMULATION AND ATP METABOLISM IN CULTURED TUMOR CELLS.

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In order to clarify the molecular mechanism of Ga-67 uptake in malignant tumor cells,the effects of NaF on Ga-67 uptake in mouse leukemia cells were examined. The uptake of Ga-67 in control cells had gradually increased during incubation with a concomitant cell proliferation.
However,when NaF was added to these cell suspensions,Ga-67 uptake did not increase and kept a constant level,and ATP content of these NaF treated cells was much lower than that of control cells,because NaF is a potent inhibitor of glycolysis.
Therefore the process of Ga-67 uptake in these cells is considered to be dependent on intracellular ATP content.