D. Tumor

1201

ROLE OF TRANSFERRIN ON Ga-67 ACCUMULATION IN CELLS IN VITRO. A. Muranaka, Y. Ito, N. Otsuka and H. Terashima Division of Nuclear Medicine, Kawasaki Medical School. Kurashiki

In previous studies, we reported that there was another accumulation mechanism of Ga-67 involved in Ga-complex, being not mediated by transferrin (Tf). In present studies, the kinetics of Ga-67 and I-125-Tf in various cells were studied to assess the role of Tf on Ga-67 accumulation in tumors in vitro. Ga-67 uptake by cells in MEM containing 100 μg/ml of human Tf increased with contact time. But, I-125-Tf uptake showed no marked increase in the contact time of 30 min to 24 hr. The retention rates of Ga-67 in Yoshida sarcoma cells followed by trypsinization increased with contact time and were about 90 % in 24 hr. In contrast, the retention rates of I-125-Tf were 20-30 % irrespective of the contact time. The excretion of Ga-67 from HeLa S3 was about 10 % during 12 hrs, while the excretion of I-125-Tf was extremely rapid. The results indicate that the kinetics of Ga-67 are different from those of I-125-Tf. Namely, Ga-67 is gradually taken up by the cells and is hardly excreted. In constant, I-125-Tf mainly binds to cell surface membrane and is rapidly turned over. Therefore, it is suggested that "Tf-receptor theory"is not exclusive.

1202

THE INFLUENCE OF IRON ON GA-67 DISTRIBUSION IN TUMOR-BEARING MICE. H. Wakao, K. Furukawa, A. Shimura and T. Higashi Department of Radiology, Kanagawa Dental College, Yokosuka

It has been recently found that the clearance of Ga-67 from blood and the attainment of high ratios of the tumor to normal soft-tissue concentrations are accelerated, if the serum iron concentration is high. The present investigation was, therefore, undertaken in order to study the effect of administered iron after injection of Ga-67 on the accumulation of Ga-67 in the tumor tissue of mice bearing Ehrlich ascites tumor. The following results were obtained. The accumulations of Ga-67 in the tumor and soft-tissues were slightly decreased compared with controls after ferric acid saccharated (Fesin) administration 3, 6 and 24 hours after injection of Ga-67. Furthermore, the accumulation of Ga-67 in Ehrlich ascites tumor in mice was clearly decreased compared with controls after Fesin administration 1, 4 and 24 hours post injection of Ga-67. This result suggest Ga-67 excretion from not only suppernate of Ehrlich ascites tumor but the tumor cells as well. However, the tumor to blood ratio in each group treated with Fesin was considerably increased because the clearance of Ga-67 from the blood is accelerated. The large tumor to blood ratio would be advantageous for tumor scanning.

1203

ACCUMULATION MECHANISM OF GALLIUM IN TUMOR CELLS (6). H. Orii, K.Nakamura & K.Samezima Dept. of Radiology, Tokyo Mtropol.Inst. Med.Sci., Tokyo

We previously reported that Ga-67 appeared in "5S" fraction of liver cell supenatant shortly after iv injection of Ga-67 citrate, and that almost all of Ga-67 transfered to lysosome within 24 h. Now we have developed the zonal ultracentrifugation method applied to ascites hepatoma without destroying its lysosomes. Using this method, Ga-67 has turned out to be distributed into lysosomes of ascites hepatoma,which was divided into two parts depending on their weights. The activity of Ga-67 in lysosomes of ascites hepatoma even 3 h post injection was larger than that from liver 24 h post injection, indicating that ascites hepatoma uptaken Ga-67 rapider than liver. However, as was in the case of liver, Ga-67 was not observed in ferritin fraction of ascites hepatoma. When I-125 transferrin-Ga-67 was injected to ascites hepatoma and subcellular separation(zonal) was carried out, I-125 activity, as well as Ga-67, was detected in both heavier and lighter lysosomes. Considering from the activities of Ga-67 and I-125, heavier and lighter lysosomes have estimated to uptake ca. 20 % and 55 % of Ga-67 togather with transferrin, respectively. These results have suggested that pynocytosis might be partly involved in the accumulation of Gallium in lysosomes.

1204

ACCUMULATION MECHANISM OF GALLIUM IN CELLS (7). K.Nakamura, K.Samezima, H.Kawaguchi & H.Orii Dept. of Radiology, Tokyo Metropol. Inst. Med. Sci., Tokyo

We've proved that Ga-67 is finally distributed into lysosomes of tumor as well as liver, using the continuous ultracentrifugation method. Of all cell fractions obtained from liver or ascites hepatoma with this method, Fe content and Fe binding capacity (Fe-B.C.) were investigated. Experiments have indicated that; (1) Any fraction where Ga-67 was accumulated have Fe-B.C. (2) Among fractions of Fe-B.C., the ratio of lysosome fraction from ascites hepatoma was larger than those from normal liver. (3) Fe content in acites hepatoma, and particularly, Fe saturation ratio in its lighter lysosomes were small. (4) In normal liver, most of Fe was distributed into ferritin fraction, whereas either Ga-67 or Fe was scarcely observed in the ferritin of ascites hepatoma. These results have suggested that; (1) Ga-67 is accumulated into lysosome with higher Fe-B.C. and with less Fe saturation ratio, i.e., more Fe binding sites, than liver. (3) Ga-67, which is distinct from Fe, is accumulated into lysosomes without involving ferritin. Thus, we have proposed hypothesis about the gallium accumulation mechanism closely related to chemical behavior of iron.