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Sub Title	
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Publisher	共立薬科大学
Publication year	1987
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.32 (1987.) ,p.52- 52
JaLC DOI	
Abstract	
Notes	抄録
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000032-0052

No. 32 (1987)

Zn and Cu Accumulation and Isometallothionein Induction in Mouse Ascites Cells

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We are interested in the relationship between Cu and Zn metabolism and the biological role of metallothionein (MT) in growing cells. In the present study, we investigated Zn and Cu accumulation, and MT indiction, in growing, compared with post-mitotic, cells ; mouse ascitic sarcoma S 180 A cells and host mouse liver were used. Furthermore, iso-MTs induced in the tumor cells were examined by h. p. l. c. on an anion-exchange column.

To investigate Zn and Cu accumulation and iso-MT induction in ascites sarcoma S 180 A cells, 5 μg of Zn^{2+} or Cu^{2+}/g body weight was administered to tumor-bearing mice intraperioneally. In the tumor cells the Zn or Cu concentration increased more than in the host liver, which is the target organ for those metals ; the maximum Zn or Cu levels was about 2—3 times that in the hose liver. The amounts of Zn-MT or Cu-MT accumulated in the tumor cells and host liver were proportional to such dose accumulation levels in the each cytosol ; the maximum level of Zn-MT or Cu-MT was 4 or 2 times higher than in the host liver.

MT accumulated in the tumor cells showed two subfractions (MT-1 and MT-2); the ratio of Zn (or Cu) bound to MT-1 to that bound to MT-2 in the host liver and tumor cells was 1. 0 (or 1. 0) and 0. 7 (or 0. 25) respectively, suggesting that the induction level of MT-2 in the tumor cells is more than that of MT-1. The h. p. l. c. profiles (using an anion-exchange column) of the isolated MT-1 and MT-2 subfractions from Zn-treated normal mouse liver showed a single peak (MT-1-1) and two peaks (MT-2-1 and MT-2-2) respectively ; mouse MTs were separated into three isoforms. In the ascites cells, the MT fraction obtained by a gel filtration was also separated into three isoforms ; however, the amount of MT-2-1 isoform was three times that in the Zn-treated normal mouse liver. Although we are unable to explain the difference in iso-MTs between the tumor cells and liver, it is interesting that the MT-2-1 isoform, which is a minor component in post-mitotic cells, increases in growing cells. The MT-2-1 isoform might be related to cell growth or cancerous stress.

本報告は *Biochem. J.*, 249(1) 69～75 (1988) に発表.