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Author	小林, 静子(Kobayashi, Shizuko) 鈴木, 純子(Suzuki, Junko) 遠山, 千春(Toyama, Chiharu)
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Effects of Epidermal Growth Factor on Metallothionein Induction in Mammalian Cells

Shizuko KOBAYASHI, Junko SUZUKI and Chiharu TOHYAMA*

小林静子，鈴木純子，遠山千春*

Recently, it has been demonstrated that metallothionein (MT) gene expression is regulated not only by serum cell growth factors and proteinkinase C activators, but also by cAMP, Metallothionein has been localized mainly in the cytoplasm of hepatocytes of adult rats. In the fetal and neonatal kidney, however, MT has been found mainly in the nucleus and cytoplasm of the proximal tubular epithelial cells of human and rat, Although the exact functions of MT in cell metabolism are unknown, these results suggest that there is a close relation between cellular proliferation and MT synthesis.

In order to elucidate possible physiological roles of isoforms of MT in cellular growth, we have studied effects of zinc, glucocorticoid and epidermal growth factor (EGF) on biosynthesis of isoMTs in a mouse mammary carcinoma cell line (FM3A) by the use of an anion exchange high performance liquid chromatography (HPLC).

In the presence of both Zn^{2+} (15 μM) and glucocorticoid (dexamethasone; 1 nM), MTs were either induced in very small amounts of not induced at all. Addition of EGF (10 ng/ml) to the culture medium resulted in significant induction of MTs. Mouse MTs were separated into three isoforms, designated as MT-1, MT-2-1 and MT-2-2. In the growing cells, the HPLC profile of isoMTs induced by EGF and physiological concentrations of both glucocorticoid and Zn^{2+} showed a single Zn-associated peak, corresponding to MT-2-2 subfraction. Induction of MT-2-2 isoform may be related to cellular proliferation.

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* 国立環境研究所