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High Invasiveness of Tumor Cells After Host Exposure to Heavy Metals

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The invasiveness of tumor cells to heavy metal-exposed host cells or tissues was investigated. Human fibrosarcoma cell invasion of heavy metal-treated fibroblast or endothelial cells was enhanced in a treatment-time-dependent fashion, though tumor cell attachment to host cells was not affected. This enhancement was correlated with an increase in metallothioneins in the cytosol of fibroblasts or endothelial cells. Mouse melanoma cell invasion of organ samples obtained from syngeneic mice who had been administered heavy metals was also enhanced. The results suggest that heavy metal-induced metallothioneins serve as a host-derived factor in malignant disease and closely relate to metastasis.

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Effect of Metallothioneins on Transformation of Gelatinase A From Human Fibroblast WI-38 Cells

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The effect of metallothioneins (MTs) on gelatinase A activity was investigated. The collagenolytic activity of gelatinase A from human fibroblast WI-38 cells was enhanced by the addition of MTs. This enhancement may be caused by the transformation of the inactive 62kDa intermediate species of gelatinase A to the 59kDa active enzyme. This enhancement was also observed in the conditioned medium of WI-38 cells exposed to heavy metals, but intracellular 72kDa pro-gelatinase A did not change. Furthermore, degradation of gelatinase A occured in the reaction between gelatinase A with substrate and MTs. Our results suggest that MTs may be an endogenous activator of gelatinase A, and may provide a host factor in cancer metastasis.

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Effect of Metallothioneins on Collagenolytic Activity of Tumor Gelatinase B

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The activity of pro-gelatinase B(92kDa type IV collagenase, Matrix metalloproteinase-9) purified from conditioned medium of human fibrosarcoma HT-1080 cells was enhanced in a concentration- and time-dependent fashion by addition of metallothioneins (MTs), purified from livers of $CdCl_2$ treated male Wistar rats but not by addition of zinc or cadmium as binding metals. MTs may act by converting latent enzyme to active form. Activation of pro-gelatinase B by rat Cd MTs occurred rapidly, but this reaction was incomplete and may have been reversible. Complete activation of pro-gelatinase B, however quickly progressed in the presence of substrate. The MTs, on the other hand, did not change. MTs could be host factors related to cancer cell invasion and metastasis and to inflammatory disease.