[*Cancer Biochem. Biophys.*, **16**, 31-43 (1998)] [Lab. of Hygienics]

Inhibition Effect of Propargylglycine on Human Fibrosarcoma HT-1080 Cell Invasiveness Propargylglycine Inhibit Tumor Invasiveness.

Arayo HAGA, Hisamitsu NAGASE,* Hideaki KITO and Takahiko SATO

Effect of propargylglycine (2-Amino-4-pentynoic acid, PPG) on invasive property of human fibrosarcoma HT-1080 cell was investigated. PPG treatment of HT-1080 significantly reduced the total cellular metallothioneins (MTs) contents, and the resistance of HT-1080 against heavy metals toxicity decreased with the decrease of the MTs contents. The HT-1080 cell invasion to reconstituted basement membrane Matrigel (MG) was inhibited by the PPG treatment in a PPG concentration-dependent fashion. The inhibition was due to the lowering of HT-1080 cells attachment to MG and degradation activity of matrix metalloproteinases (MMPs) secreted from HT-1080 by the PPG treatment. However the chemotactic ability of the PPG treated HT-1080 was enhanced. Our results suggest that MTs concentration levels in a malignant tumor cell are closely related to its invasiveness, and if MTs level of tumor cell can be controlled, cancer metastasis may be under the control.

[*Cancer Res. Ther. Control*, **5**, 181-187 (1998)] [Lab. of Hygienics]

Heavy Metal Loading Enhances the Murine Tumor Metastasis.

Arayo HAGA, Hisamitsu NAGASE,* Hideaki KITO and Takahiko SATO

Experimental (tumor cells injected i.v.) and spontaneous (tumor cells injected s.c.) metastasis of tumor cell lines in heavy metal-treated mice were investigated. The number of lung metastases in heavy metal-treated mice given an *i.v.* injection of murine melanoma B16-BL6 cells did not differ significantly from that in untreated mice. Heavy metal-treatment caused obvious metastatic enhancement, accompanied by extensive necrosis, in the liver-spleen experimental metastasis model with murine T-lymphoma L5178Y-ML25 cells. Heavy metal-treatment also enhanced invasiveness in the spontaneous metastasis model with B16-BL6 cells, but tumor mass was not affected. The results suggest that heavy metal-induced metallothioneins as a host-derived factor is closely related to metastasis.

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Correlation Between Host Metallothioneins and Collagenases in Murine Metastasis Models.

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The biological significance of the relationship of metallothioneins (MTs) and collagenases activity to experimental metastasis was investigated in mouse models. M5076 reticulum cell sarcoma metastasis in C57BL/6 mice was significantly enhanced by cadmium-treatment, and metastatic volume correlated significantly with tissue MT content. Tissue MT levels and collagenolytic activity also correlated significantly in this model. MT induction in liver and spleen increased the retention of L5178Y-ML25 lymphoma cells injected i.v. into CDF1 mice. Treatment with a MT induction inhibitor restored cell retention to the control level. Liver MT or Zn levels were increased by *s.c.* injection of B16-BL6 melanoma cells and by i.v. injection of M5076 reticulum cell sarcoma cells into Zn-treated C57BL/6 mice. Our results suggest that host-derived MTs promote metastasis, and inhibitors of MT induction may be a promising anti-metastasis approach.

[*Toxicology*, **126**, 41-53 (1998)] [Lab. of Hygienics]

Augmentation of Allergic Reactions by Several Pestisides.

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The augumentative effect of several pesticides on histamine release from mast cells of rats that had been sensitised passively by anti-denitrophenol (DNP) monoclonal IgE antibodies were investigated *in vitro*. Various pesticides, especially phentoate (PAP), chlornitrophen (CNP) and paraquat (PQ), increased histamine release. This increase was not observed in histamine release with non-antigen or induction by calcium ionophore A23187 or compound 48/80. Passive cutaneous anaphylaxis (PCA) was examined, and an increase of PCA was observed with PAP and PQ, but not with CNP, while an increase of tumor necrosis factor-α production was observed with CNP and PQ, but not PAP. These results suggest that various pesticides as environmental pollutants exacerbate allegic diseases.