parallelism of the log dose-response lines. It was found that there was no significant difference in the potency between the two analytical methods. The weighted geometric mean of each of the laboratory geometric mean (95% confidence interval) was 3,370,219 IU (3,265,821~3,477,954) by the participants' own methods and 3,289,187 IU (3,202,000~3,330,752) by parallel line analysis.

[PC1-45] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Effect of lawsone methyl ether on the release of glycosylphospatidylinositol-anchored renal dipeptidase and alkaline phosphatase

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Detergent-insoluble microdomains (rafts) may play crucial roles in many cellular functions such as membrane trafficking, cell signaling and human diseases. The variant surface glycoproteins are localized in microdomains and anchored to the cell surface via a glycosylphosphatidylinositol (GPI) anchor. Renal proximal tubules (PTs) were used to compare the release between GPI-anchored renal dipeptidase (RDPase, EC 3.4.13.19) related with cellular signaling pathway and GPI-anchored alkaline phosphatase (APase EC 3.1.3.1) of ubiquitous location. Cell viability was evaluated using a MTT assay and was shown to be intact. The RDPase was released by endogenous GPI-specific phospholipase C (GPI-PLC). Although APase is also a target of GPI-PLC, it showed different activity as compared with RDPase when released from renal PTs in the presence of lawsone methyl ether (LME), a naphtoquinone compound isolated from a Tai medicinal plant. Incubating PTs with various concentration of LME, RDPase activity was increased to 300% (500μM LME) of the control whereas APase activity was not affected significantly. Such increase was also confirmed as a function of time. The results suggest that the release mechanism of RDPase was different from that of APase.

[PC1-46] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Retrovirus-mediated Gene Delivery of TIMP-2 Inhibits Invasion, Migration and Angiogenesis

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The matrix metalloproteases (MMPs) play important roles in invasion, metastasis and angiogenesis in various cell types. An endogenous inhibitor of MMP, tissue inhibitor of metalloprotease-2 (TIMP-2), has high specificity for MMP-2. An imbalance between MMP-2 and TIMP-2 causes the degradation of the extracellular matrix associated with pathological events including invasion, metastasis and angiogenesis. Since TIMPs are secreted molecules, they have the potential to be used for gene therapy of certain tumors. In the present study, we have studied the retrovirus-mediated delivery of TIMP-2 in H-ras MCF10A cells in which MMP-2 was shown to be responsible for the H-ras-induced invasive phenotype. Recombinant retrovirus containing TIMP-2 gene was used to infect PG13 cells (packaging cell line). When the H-ras MCF10A cells were treated with the conditioned media of PG13/TIMP-2, a dose-dependent inhibition of MMP-2 secretion was observed by gelatin zymography. TIMP-2 overexpression mediated by retrovirus significantly reduced the invasiveness and migration of H-ras MCF10A cells in a dose-dependent manner. In addition, retroviral delivery of TIMP-2 efficiently inhibited angiogenesis of HUVEC cells in a dose-dependent manner as evidenced by in vitro tube formation assay. Taken together, we show that the down-regulation of MMP-2 by TIMP-2 overexpression inhibits invasive and migrative properties of H-ras MCF10A cells and angiogenesis of HUVEC cells. Our data showing efficient inhibition of cancer progression by retrovirus-mediated delivery of TIMP-2 suggest a possible application for gene therapy to prevent and treat cancer.

[PC1-47] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]