dependent manner. In addition, DA-125 inhibited cancer cell migration and colony formation, and also exhibited the inhibitory activities of invasion and motility with a matrigel and type I collagen assay. These results suggest that DA-125 inhibits tumor cell invasion and metastasis by suppression of MMPs and TIMPs in tumor cells. Further, cell adhesion molecules (CAMs) such as vascular cell adhesion molecule-1 (VCAM-1) and intercellular cell adhesion molecule (ICAM) have been reported to play an important role in cancer metastasis via the adhesive interaction between tumor cells and endothelial cells. We examined the effects of DA-125 on CAMs expression and its transcriptional regulatory mechanism in human microvascular endothelial cells (HMEC-1). Dose-dependent suppression of CAMs mRNA levels was observed in DA-125-treated HMEC–1. Taken together, anti-metastatic and anti-invasive effect of DA-125 might be an additional mechanism as a promising anticancer agent.

[OA4-1] [2003-10-11 09:45 - 10:00 / ASEM Hall Meeting Room 208]

Dihydrosphingosine 1-phosphate: New Biomarker for Fumonisin B1 Toxicity

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Fumonisins are a family of mycotoxins produced from Fusarium verticillioides. Most of fumonisin B1 (FB1) toxicities can be explained by its ability to alter sphingolipid metabolism by inhibiting ceramide synthase. At least, the elevation in dihydrosphingosine (DHS) mediates the earliest toxicity of FB1. Some tissues such as kidney and liver, may be most affected by FB1 because they shows high rates of de novo sphingolipid synthesis. Recent review on FB1 toxicity by A.H. Merrill Jr. et al. suggested the possible role of dihydrosphingosine 1-phosphate (dihydroS1P), which sometimes elevated in cell- or tissue specific manners. In this study, we demonstrated that FB1 accumulated not only DHS but dihydroS1P, which was typically observed in FB1-sensitive pig kidney epithelial cells (LLC-PK1 cells). Moreover, dihydroS1P was suggested as a new indicator for FB1 exposure in rat plasma while sphingoid bases ratio was still useful in other organ tissues. For further study to elucidate the toxic mediator of FB1, we used mouse F9 embryonal carcinoma cells, which exhibits SPL -/- stable transformant (SPL lyase KO) and murine S1P phosphohydrolyase (mSPP1) stably overexpressed transformant (SPL lyase KO + mSPP1). Surprisingly, overexpression of mSPP1 in SPL -/- stable transformant showed strong resistance to FB1. Conclusively, the FB1 toxicity may be mainly mediated by endogenous dihydroS1P, which possibly exerted antagonistic action to S1P in intracellular mode.

[OB3-1] [2003-10-11 10:00 - 10:15 / ASEM Hall Meeting Room 208]

In vivo evidence for brain-to-blood efflux transport of taurine and regulation of this transport by tumor necrosis factor-α at the blood-brain barrier

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The purpose of this study is to examine whether the efflux system for taurine from brain to blood is present on the blood-brain barrier (BBB) using the brain efflux index (BEI) method and taurine transport system is regulated by CNS cell damage with oxidative stress agent such as diethyl maleate (DEM) or tumor necrosis factor-α (TNF-α) in vivo. [^{3}H]Taurine was microinjected into parietal cortex area 2 (Par2) of the rat brain, and was eliminated from the brain with efflux transport rate of 1.22 10^{-2}/min, and the process is saturable with a K_m of 43.5 μM. This process was significantly inhibited by taurine transport inhibitors, such as unlabeled taurine, β-alanine, betaine, nipecotic acid and γ-aminobutyric acid (GABA). In addition, the effect of DEM or TNF-α on [^{3}H]taurine transport was investigated. [^{3}H]Taurine uptake was increased and efflux was reduced by pre-treatment with DEM or TNF-α. Also, [^{3}H]taurine efflux was decreased by TNF-α in time- and dose-dependent manner. In conclusion, the efflux pump for taurine at the BBB reduced taurine concentration in the brain interstitial fluid and this process was carrier mediated and also, was regulated by oxidative cell damage.

[OC1-1] [2003-10-11 10:15 - 10:30 / ASEM Hall Meeting Room 208]

Augmentation of constitutive nf-κb activation by bcl-2 in pc12 cells: implications for