proposed to undergo redox cycling that could lead to the generation of reactive oxygen species (ROS) that would subsequently cause oxidative damage to DNA associated with hormonal carcinogenesis. The effects of TCDD on expression of CYP1A1 and CYP1B1 were measured by Western Blot analysis in human breast epithelial MCF10A cells. DNA strand breaks induced by $2OHE_2$ and $4OHE_2$ and in the presence of Cu(II) were assured by the conversion of supercoiled phage ΦX-174 DNA into open circular one. Furthermore, in MCF10A cells these catechol estrogens showed cytotoxic and antiproliferative effects. $2OHE_2$ induced intracellular accumulation of ROS in MCF10A cells as assessed by DCF-DA staining. MCF10A cells treated with $2OHE_2$ underwent apoptotic death as determined by morphological features, positive in situ terminal nick end-labeling (TUNEL) and poly(ADP-ribose)polymerase (PARP) cleavage. Concomitant with the apoptosis, $2OHE_2$ activated the c-Jun N-terminal protein kinase (JNK) pathway via phosphorylation and induced JNK expression. $4OHE_2$ increased DNA binding activity of nuclear factor-kappaB (NF-kappaB), but not of activator protein-1 (AP-1). In another experiment expression of cyclooxygenase-2, one of the target genes regulated by NF-kappaB, was induced by $4OHE_2$. In addition, $4OHE_2$ induced the activation of extracellular-signal regulated protein kinase (ERK) and p38 MAPK.

[PC1-42] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Activation of p38 mitogen-activated protein kinase in H-ras MCF10A cells: Possible role in H-ras-induced invasive phenotype

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One of the most frequent defects in human cancer is the uncontrolled activation of the ras-signaling pathways. We have previously shown that H-ras, but not N-ras, induces an invasiveness in human breast epithelial cells (MCF10A), while both H-ras and N-ras induce transformed phenotype. Since migration plays a crucial role in invasion, we examined motility of MCF10A cells transformed with H-ras or N-ras. Here, we show that cell motility was greatly increased by H-ras, but not N-ras, suggesting that H-ras-induced invasive phenotype may be mainly due to enhanced cell motility. It has been recently shown that p38, a member of the mitogen activated protein (MAP) kinase family, is important for cell migration. We wished to investigate the functional role of p38 MAP kinase in H-ras-induced invasive phenotype. We show that p38 is prominently activated in H-ras MCF10A cells comparing to the parental MCF10A cells or N-ras MCF10A cells, while no significant difference was found in the activation of stress-activated protein kinase-1/c-Jun N-terminal protein kinase (SAPK-1/JNK). Extracellular signal-regulated protein kinase (ERK)-1,2 were activated in both H-ras and N-ras MCF10A cells. These results suggest a possible involvement of p38 in H-ras-induced invasiveness/motility. Effect of a specific p38 inhibitor, SB203580, on the H-ras-mediated invasion is currently being investigated.

[PC1-43] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Expression of novel human angiotensin II/vasapressin like like gene during coculture of BMMC with swiss3T3 fibroblast

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Mast cells have been regarded as one of the most important effector cells in IgE-dependent allergic response. There are at least two distinct population of rodent mast cells. One is connective mast cells (CTMC) and the other is mucosal mast cells (MMC). CTMC contain heparin

proteoglycan, CTMC-specific proteases and large amounts of histamine, and generate the cyclooxygenase (COX) pathway product, prostaglandin (PG) D2, following FcεRI-dependent activation. MMC contain chondroitin sulfate proteoglycan, MMC-specific proteases, less histamine than CTMC and generate leukotriene (LT) C4, via the 5-lipoxygenase (5-LO) pathway in preference to PGD2 following FcεRI-dependent activation. Mouse bone marrow-derived mast cells (BMMC) developed in interleukin (IL)-3, a progenitor population of mast cells, resemble MMC in terms of their granule contents and preferred FcεRI-dependent LTC4 generation, but express mast cell proteases different from those expressed in CTMC and MMC. Coculture of BMMC with 3T3 fibroblasts in the presence of the stromal cytokine, c-kit ligand (KL) result in morphological and functional development toward a more mature CTMC-like phenotype. To characterize gene expression of cocultured BMMC, we examined the changes in genetic transcripts of BMMC and cocultured BMMC by the PCR-select cDNA subtraction method. In this study, we found that the expression of several genes were increased during coculture of BMMC with 3T3 fibroblast. Included among these were the known genes for MMCP (mouse mast cell protease)-1, MMCP-4, granzyme B and the novel gene AVRL. AVRL has high homology to human angiotensin II/vasopressin receptor like gene. We found that AVRL was at least 3 different form.

[PC1-44] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Conformations and activities of linear RGDX tetrapeptides

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The conformational study on Arg-Gly-Asp (RGD)-containing tetrapeptides in the unhydrated and hydrated states has been carried out using the force field ECEPP/3 and the hydration shell model. The tetrapeptides studied here are NH_2-RGDX-OH (X = Phe, Val, Cys, Gln, Ser, Tyr, and Leu), which show various activities against fibrinogen binding to platelets in the order of RGDF > RGDV > RGDC > RGDQ > RGDS ≒RGDY ≒RGDL.
In the unhydrated state, type I β-bends are found to be essential at the Gly-Asp sequence for all RGDX tetrapeptides except for RGDF and RGDY. In particular, type V'β-bends appear to be dominant for RGDF. In addition, type IV β-bends are significant at the Asp-Xaa sequence of almost tetrapeptides, followed by types I, VII, and II β-bends. On the other hand, in the hydrated state all RGDX tetrapeptides have type V'β-bends at the Gly-Asp sequence except for RGDQ, which has type I β-bends at the Gly-Asp sequence. Type IV β-bends are found to be dominant at the Asp-Xaa sequence for all RGDX tetrapeptides.
We can conclude that type V' β-bends at the Gly-Asp sequence and type IV β-bends at the Asp-Xaa sequence are necessary conditions not sufficient conditions for biological activity of fibrinogen binding to platelets.

[PC2-1] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Inhibitory Component of Mori Cortex Radicis on Alcohol Dehydrogenase Activity

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Mori Cortex Radicis is one of the medicinal plants used in oriental medicine for diabetes mellitus. But we found out that the methanolic extract of Mori Cortex Radicis inhibited horse liver alcohol dehydrogenase. In connection with Mori Cortex Radicis inhibitory effects, a bioactivity-guided purification of active substance on alcohol dehydrogenase(ADH) was carried-out. The most active