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