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Mini rat is a transgenic rat strain carrying antisense gene for rat growth hormone (GH), resulting in retarded growth. Mini rats have been used by several investigators as a GH deficiency model. In the present study, we assessed the redox status of mini rat liver to elucidate the effect of aging and calorie restriction (CR). Liver homogenates from mini rats at 31 and 100 weeks of age which were fed ad libitum (AL) and CR were used in the study. Total reactive oxygen species (ROS) generation was determined by dichlorofluorescin diacetate (DCFH-DA) method. We also investigated malonaldehyde (MDA) amounts using thiobarbituric acid (TBA) positive material assay. In addition, the mitochondrial membrane fluidity was measured by fluorescence polarization method. Results showed that total ROS generation of liver increased with age and was reduced by CR. Increased MDA levels might be due to increased ROS generation, which could cause a decrease of mitochondrial membrane fluidity. Moreover, other redox markers such as GSH/GSSG and total SH levels decreased during aging and was maintained by CR. The present findings are in agreement with our previous report showing age-dependent loss of the antioxidant potential and its modulation by CR.

[PC1-34] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

A Role of p38 MAPK on H-ras-Induced Invasion and Motility in MCF10A Human Breast Epithelial Cells

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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 and motility in human breast epithelial cells (MCF10A), while both H-ras and N-ras induce transformed phenotype. Since migration plays a crucial role in invasive, we examined motility of MCF10A cells transformed with H-ras or N-ras. We show that cell motility was increased by H-ras, but 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. To assess the functional significance of H-ras-activated p38 in invasion and migration, we examined the effect of SB203580 and dominant-negative p38(DN p38). Treatment of SB203580, an inhibitor of p38, reduced invasive activity and motility of H-ras MCF10A cells. H-ras MCF10A cells were transfection with dominant-negative p38 but not dominant-negative JNK-1 inhibited cell migration. These results suggest a possible involvement of p38 in H-ras-induced invasiveness/motility.

[PC1-35] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

A Role of Phosphatidylinositol 3-kinase (PI3K) on H-ras-Induced Invasive phenotype

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We have previously shown that H-ras, but N-ras, induces an invasiveness and cell motility in human