concentration was increased in a concentration-dependent manner of chitosan. These results suggest that RDPase release by chitosan may not relate to nitric oxide signal pathway.

[PC1-30] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Roles of Phosphatidylinositol 3-Kinase(PI3K) and Rac1

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Many studies have identified the phosphatidylinositol 3-kinase (PI3K) as a key regulator for various cellular functions including cell survival, growth and motility. We have previously shown that H-ras, but not N-ras, induces invasiveness and motility in human breast epithelial cells (MCF10A), while both H-ras and N-ras induce transformed phenotype. In the present study, we wished to investigate the functional role of PI3K pathway in H-ras-induced invasive phenotype and motility of MCF10A cells. Activation of PI3K in the parental, H-ras- and N-ras MCF10A cells was examined by detecting phosphorylation of Akt, a downstream molecule of PI3K. Marked activation of Akt was detected not only in H-ras MCF10A cells but also in non-invasive/non-motile N-ras MCF10A cells at comparable levels. We then further investigated the functional significance of PI3K activation in invasion and motility by using known PI3K inhibitors, LY294002 and wortmannin. Treatment of LY294002 and wortmannin significantly inhibited invasive phenotype and motility of H-ras MCF10A cells, suggesting that the activation of PI3K pathway is not sufficient, but may be required for H-ras-induced invasion and motility. Prominent downregulation of MMP-2 and MMP-9 were observed in H-ras MCF10A cells treated with LY294002 in a dose-dependent manner. The results provide evidence that PI3K pathway is critical for H-ras-mediated upregulation of MMPs in MCF10A cells, resulting in phenotypic conversion of non-invasive MCF10A cells to an invasive phenotype. In order to study the molecular mechanisms under PI3K effects cell invasion and migration, we investigated activation of ras downstream effector molecules, MAPKs, treated with PI3K inhibitors. Phospharylation of ERK and p38 level is slightly downregulated in H-ras MCF10A cells treated with LY294002. And many studies have identified relation PI3K and Rac with invasion and migration. In order to correlation of PI3K and Rac, we investigated Rac activity in parental, H-ras and N-ras MCF10A cells. Activation of Rac was detected in H-ras MCF10A cells. We then further studied the role of Rac activation in invasion and migration using dominant negative construct of Rac1. H-ras induced invasion and migration was significantly inhibited in DN-Rac1 transfectants. We further investigate the activation of MAPKs in DN-Rac1 transfectants in order to study the molecular mechanisms under Rac effects cell invasion and migration.

[PC1-31] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Involvement of MAPKs in GDNF-induced Proliferation and Migration in Hs683 Glioma Cells

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Glial cell-derived neurotrophic factor (GDNF) is a potent neurotrophic factor that enhances survival of midbrain doparminergic neuron. GDNF and its receptors are widely distributed in brain and are believed to be involved in the control of neuron survival and differentiation. GDNF