Sphingosine-1-phosphate Promotes the Survival of Mel-Ab Cells via ERK and Akt activation

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Sphingolipids have been emerged as bioactive lipid modulators that mediate a variety of cell functions. However, the effects of sphingolipids on the cell growth and survival of melanocytes are not yet known. In the present study, we investigated the actions of sphingolipids in Mel-Ab melanocytes. We observed the cytoprotective effect of sphingosine-1-phosphate (SPP) on UVB-induced cell death. Since SPP is well known as a mitogenic agent, it is possible that the mitogenic effect of SPP may contribute to cell survival. Surprisingly, we found that SPP inhibited DNA-synthesis significantly. We were next interested in the regulation of three subfamilies of MAPKs and the Akt pathway by SPP against UVB-induced cell death. UVB irradiation resulted in the remarkable and sustained activation of c-Jun N-terminal kinase (JNK), while p38 MAP kinase was activated transiently. The basal level of extracellular signal-regulated protein kinase (ERK) phosphorylation decreased 30 min after UVB irradiation, whereas that of Akt phosphorylation was not affected by UVB. These results suggest that JNK and p38 activation and ERK inactivation may be responsible for UVB-induced apoptosis. Therefore, we investigated whether SPP could inhibit UVB-induced JNK and p38 activation to explain its cytoprotective effect. However, SPP had no effect on UVB-stimulated JNK and p38 activity. In contrast, we clearly observed that SPP potently stimulated the phosphorylation of both ERK and Akt, which are involved in cell survival signaling cascade. Furthermore, the specific inhibition of the ERK and Akt pathways by PD98059 and LY294002, respectively, restored the cytoprotective effect induced by SPP.

[PA1-69] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Analysis of vasopressin-induced Ca2+ influx in rat hepatocytes

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To analyze vasopressin-induced Ca^{2+} influx in liver cells, rat hepatocytes were isolated and attached to collagen-coated cover slips. Using fura-2, a Ca^{2+}-sensing dye, changes in intracellular Ca^{2+} concentration by vasopressin were monitored. Results in this communication suggested that vasopressin-induced Ca^{2+} influx consists of two distinguishable components. One was present for a short time and the other was for a long time until it happened. The former influx was blocked by SK&F96365 in a dose-dependent manner. Vasopressin-induced Ca^{2+} release from internal stores diminished in a primary culture of hepatocytes according to the culture time. However, changes in vasopressin-induced Ca^{2+} influx across the plasma membrane differed from changes in the Ca^{2+} release from internal stores.

[PA1-70] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Sphingosine-1-Phosphate Decreases Melanin Synthesis via Sustained ERK Activation and Subsequent MITF Degradation

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