the secretory alkaline phosphatase (SEAP) as a transcription reporter in response to the NF-kB activity and contain the neomycin phosphotransferase (NPT) gene for the dominant selection marker for geneticin resistance. Melanogenic inhibitors (niacinamide, kojic acid, hydroquinone, resorcinol. arbutin, and glycolic acid) were preincubated with transfectant HaCaT cells for 3 hrs and then UV was radiated. NF-kB activation was measured with the SEAP reporter gene assay using a fluorescence detection method. Of the melanogenic inhibitors, niacinamide, hydroquinone and kojic acid were the most potent inhibitors of NF-kB activation by UVR. Especially, the preincubation of niacinamide and kojic acid displayed that cell morphology have few damage in the dangerous UV-induced environment. These observations suggest that NF-kB plays an important role in the paracrine mediation of UV-induced melanogenesis and skin-whitening effect may be involved in NF-kB activation in the genetic molecular basis.

[PC3-2] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

P-glycoprotein is not functionally overexpressed, and bcr/abl and bax is down regulated in cisplatin resistant human chronic myelogenous leukemia K562 cells

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Human chronic myelogenous leukemia K562 cell lines were used in our laboratory to study the mechanism in the development of cisplatin resistance in cancer. Several reports have suggested that expression of bcr/abl tyrosine kinase renders chronic myelogenous leukemia cell lines such as K562 cell lines resistant to the induction of apoptosis by a variety of treatments. As assessed by WST-1 cytotoxicity assay, the K562/CDDP cell lines were 4.87-fold more resistant to cisplatin than the parent cell lines. Both cell lines were treated with cisplatin, for the purpose of studying drug accumulation and efflux. Drug accumulation and efflux were not showed significantly differentiation. Also, we have found that K562/CDDP has a no differentiation of expression pattern of p-glycoprotein with compared parental cell lines by immunoblotting. Further, DNA fragmentation analysis showed that K562/CDDP cell lines had significantly more resistant. This result suggests that the antiapoptotic functions may be responsible for cisplatin resistance. Additionally, expression pattern of apoptosis-regulating proteins analysis showed that K562/CDDP cell lines had reduction of bax expression. This result indicates that there may cause resistant to apoptosis through reduction of bax expression in CML cells having a drug resistance. On the other hand, the expression of bcr/abl had reduction in the K562/CDDP cell lines. Our studies did not establish whether the down-regulation of bcr/abl is transcriptionally or *posttranscriptionally regulated. If cisplatin resistance affects the transcription of the bcr/abl fusion* gene, this may also be mediated directly or indirectly by altered gene-transcription and expression brought about by p53.

[PC3-3] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Absorption Enhancement of Heparin Disaccharide through Intracellular Regulation of Paracellular Permeability by Phytolaccosides from Phytolacca americana

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The effect of phytolaccosides on the intestinal absorption of heparin disaccharides was studied using Caco-2 cells. The absorption enhancing activity of these compounds (phytolaccoside B, D_2, E, F, G, I) was determined by changes in transepithelial electrical resistance (TEER) and the transport amount of heparin disaccharides across Caco-2 cell monolayers. With an exception of phytolaccoside G, all

of them decreased TEER value and increased the permeability of heparin disaccharides in a dose-dependent and time-dependent manner. Furthermore, there was difference among these compounds with respect to absorption enhancing activity and cytotoxicity. Phytolaccoside B and E showed both drastical enhancing activity and severe cytotoxicity. In case of phytolaccoside G, it had no significant enhancing effect and cytotoxicity as compared to the control. Phytolaccoside F and I had mild enhancing effects and cytotoxicity. Phytolaccoside D_2 had an absorption enhancing effect without severe cytotoxicity. In considering the mechanisms, Phytolaccoside F and I seemed to regulate the tight junction permeability via both IP_3- and DAG-pathways. On the other hand, phytolaccoside B and D_2 showed the effects by IP_3-pathway and the absorption enhancing effect of phytolaccoside E was not affected by inhibitors except BAPTA. It may increase the intracellular Ca^{2+} level by other mechanisms in modulating the paracellular permeability. Our results indicate that a series of phytolaccosides from *Phytolacca americana* may be applied as absorption enhancers which can increase the paracellular transport of hydrophilic compounds such as glycosaminoglycans and protein/peptide drugs.

[PC3-4] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Induction of p21WAF1/Cip1 expression via Sp1 sites by apicidin is mediated by Sp3

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We previously reported that apicidin, a novel histone deacetylase inhibitor, inhibits proliferation of tumor cells via induction of $p21^{WAF1/Cip1}$ and gelsolin. In this study, we tried to determine the molecular mechanisms by which apicidin induce $p21^{WAF1/Cip1}$ gene activation in HeLa cells. Apicidin treatment induced $p21^{WAF1/Cip1}$ mRNA independently of de novo protein synthesis and activated the $p21^{WAF1/Cip1}$ promoter through two Sp1 sites located at -82 and -69 relative to the transcription start site. Although, Sp1 and Sp3 have been shown to be the major factors binding to the Sp1 site of $p21^{WAF1/Cip1}$ promoter as measured by EMSA, apicidin did not alter their DNA binding activities. Moreover, Sp3, but not Sp1, mediated apicidin-mediated transcriptional activation of $p21^{WAF1/Cip1}$ gene promoter, whereas both Sp1 and Sp3 were suppressive in the absence of apicidin treatment. Taken together, these results demonstrate that Sp3 mediates the transcriptional activation of the $p21^{WAF1/Cip1}$ gene promoter by apicidin via Sp1 site in HeLa cells.

Poster Presentations - Field D1. Medicinal Chemistry

[PD1-1] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synthesis and Application of Dimeric Cinchona Alkaloid Phase-Transfer Catalysts: a,a'-Bis[O(9)-allylcinchonidinium]-o, m, or p-xylene dibromide

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