immune responses in the cases of various autoimmune diseases.

[PC1-1] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Apoptotic potential of Apicidin and its derivatives

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We previously reported that apicidin, a histone deacetylase (HDAC) inhibitor, arrests human cancer cell growth through selective induction of $p21^{WAF1/Cip1}$. In this study, the ability of apicidin and its derivative to induce apoptosis was evaluated. HL60 cell growth was completely arrested at G_2/M phase by treatment with apicidin and its derivative, which was correlated with marked induction of $p21^{WAF1/Cip}$ protein. These effects were paralleled by increase in cell death, nuclear morphological change, DNA ladder and apoptotic body formation. Furthermore, this apoptotic cell death was accompanied by conversion of the proenzyme form of caspase-3 to the catalytically active effector protease and subsequent cleavage of poly(ADP-ribose)polymerase and DFF45 (DNA fragmentation factor), one of the caspase-3 target. Taken together, these results suggest that apicidin and its derivative-induced apoptosis might be, in part, due to the activation of caspase-3

[PC1-2] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Effects of histone deacetylase inhibitor, apicidin, on the p21WAF1/Cip1 gene promoter

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We previously reported that apicidin, a histone deacetylase inhibitor, showed a broad spectrum of antiproliferative activity against various cancer cell lines through selective induction of $p21^{WAF1/Cip1}$, which plays important roles in the cell cycle. In this study, we examined the effects of apicidin on $p21^{WAF1/Cip1}$ gene promoter in a p53-mutated HeLa cells. $p21^{WAF1/Cip1}$ mRNA was markedly induced by treatment with 0.01μM apicidn, and dramatic $p21^{WAF1/Cip1}$ protein induction was detected. Using human wild-type $p21^{WAF1/Cip1}$ promoter, we found that apicidin strongly activates the $p21^{WAF1/Cip1}$ promoter in a dose and time dependent manner. Futhermore, the Sp1-luc plasmid containing SV40 promoter-derived three consensus Sp1 binding sites was markedly activated by apicidin. Theses results suggest that apicidin arrests the growth of HeLa by activating the $p21^{WAF1/Cip1}$ promoter through specific Sp1 sites in a p53-independent fashion.

[PC1-3] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Chemopreventive potential of the synthetic allylthiopyridazine derivatives on hepatocellular carcinoma cells

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