oxovalerate aldolase and 4-oxalocrotonate decarboxylase were determined. The 4-hydroxy-2-oxovalerate aldolase gene (tomF) was consisted of 1047 bases. Amino acid sequence of the tomF gene product exhibited 84% identity with those of 4-hydroxy-2-oxovalerate aldolase from Comamonas testosteroni and P. putida. The 4-oxalocrotonate decarboxylase gene (tomD) was consisted of 687 bases. Amino acid sequence of the tomD gene product exhibited 75% identity with that of 4-oxalocrotonate decarboxylase from P. putida.

[PC1-25] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Activation of $p21^{WAF1/Cip1}$ transcription through Sp1 sites by histone deacetylase inhibitor apicidin: Involvement of protein kinase C

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We previously reported that apicidin, a novel histone deacetylase (HDAC) inhibitor, inhibited the proliferation of tumor cells via induction of $p21^{WAF1/Cip1}$. In this study, we determined the molecular mechanisms by which apicidin induced the $p21^{WAF1/Cip1}$ gene expression in HeLa cells. Apicidin induced $p21^{WAF1/Cip1}$ mRNA independent of the de novo protein synthesis and activated the $p21^{WAF1/Cip1}$ promoter through Sp1-3 site located at -, 82 and -, 77 relative to the transcription start site. Calphostin C, a protein kinase C (PKC) inhibitor, significantly attenuated the activation of $p21^{WAF1/Cip1}$ promoter via Sp1 sites, which was accompanied by a marked suppression of $p21^{WAF1/Cip1}$ mRNA and protein expression induced by apicidin. Consistent with the transcriptional activation of $p21^{WAF1/Cip1}$ promoter by apicidin, apicidin treatment led to the translocation of PKCε from cytosolic to particulate fraction, which was reversed by pretreatment with calphostin C, indicating the involvement of PKC in the transcriptional activation of $p21^{WAF1/Cip1}$ via Sp1 sites by apicidin. However, the PKC-mediated transcriptional activation of $p21^{WAF1/Cip1}$ by apicidin appears to be independent of the histone hyperacetylation, since apicidin-induced histone hyperacetylation was not affected by calphostin C. Furthermore, a PKC activator, PDBu alone induced the transcriptional activation of $p21^{WAF1/Cip1}$ promoter, $p21^{WAF1/Cip1}$ mRNA and protein expression, without induction of the histone hyperacetylation, suggesting that the transcriptional activation of $p21^{WAF1/Cip1}$ by apicidin might have been mediated by a mechanism other than chromatin remodeling through the histone hyperacetylation. Taken together, these results suggest that the PKC signaling pathway plays a pivotal role in the transcriptional activation of the $p21^{WAF1/Cip1}$ gene by apicidin.

[PC1-26] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

2D/MALDI-TOF MS Analysis of Age-dependent Rat Proteome in Rat Liver Mitochondria

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Mitochondria is called power plant of the cell because they product biological energy, ATP, using electron transport system and proton pump. This system is very toxic to living cells because these systems generate the superoxide anion radical and hydroxyl radical, which induce apoptosis via