pylori-infected mice were sacrificed 4, 8, 16, 24, 36, 50 and 80 weeks after the bacterial infection. After 80 weeks of infection, almost all *H. pylori*-infected mice developed hyperplastic or atrophic gastritis, but did not show any evidence of adenoma, dysplasia or carcinoma. PCNA positive cells were the most abundant 50 weeks after the *H. pylori* infection, but their number decreased thereafter up to 80 weeks. Apoptotic cell death became evident 8 weeks after *H. pylori* infection, with 7-8 apoptotic cells/high power field, and increased thereafter. Production of normally observed neutral muscin was decreased gradually, with maximal reduction observed 50 weeks after *H. pylori* infection, which was accompanied by acid chracterization thereafter. The SS1 infected mouse seems to be a suitable animal model for *H. pylori*-related research, although *H. pylori* infection itself does not induce gastric cancer in a long-term normal wild-type mouse model, which could be explained by the balance between cell proliferation and apoptosis.

[PC1-24] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Effects of chitosan on renal dipeptidase in vivo

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Urinary dipeptidase (Udpase) which was detected in urine of various animals including rat, rabbit, pig and human is a released form of renal dipeptidase (RDPase, EC 3.4.13.19), a glycosylphosphatidylinositol (GPI) linked ectoenzyme of renal proximal tubules. Udpase activity was decreased in urine samples of acute and chronic renal failure patients. This study was undertaken to examine the effect of chitosan, a deacetylated derivative of chitin, on RDPase from rat kidney in vivo. Rats were fed with chitosan (0.1% in distilled water) for 3, 8 and 15 months and the urine samples were collected followed by ammonium sulfate precipitation (50~75% saturation). The activity of Udpase was measured with the modified fluorometric method of Ito et al (1984) and the protein was related with band intensity of SDS-electrophoresis. Approximately 4-folds Increase of Udpase was observed in the chitosan fed rats for 3 months and such increase was less prominent in rats of 12 months or older. These results suggest that chitosan may elevate the renal function and speed up the recovery from renal failure, or even prevent the renal diseases.

[PC1-25] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Genetic structure responsible for catechol catabolism in P.cepacia G4

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The meta-cleavage pathway for catechol is one of the major routes for the microbial degradation of aromatic compounds. Pseudomonas cepacia G4 grows efficiently on toluene, cresol, or phenol via a plasmid-encoded catechol 2,3-dioxygenase and a subsequent meta-cleavage pathway. A recombinant plasmid pCNU 301 is a 23.0-kb BamHI restriction endonuclease-cleaved DNA fragment cloned from the chromosome of Pseudomonas cepacia G4. The pCNU 301 contains tomBCEGFD gene cluster which can encode six enzymes catabolizing catechol to acetyl CoA. In this study nucleotide sequences of tomBCEGFD gene encoding catechol-2,3-dioxygenase(C23O), 2-hydroxymuconic semialdehyde dehydrogenase (HMSD), 2-hydroxypenta 2,4-dienoate hydratase(HPDH), acetaldehyde dehydrogenase(ADH), 4-hydroxy-2-oxovalerate aldolase, and 4-oxalocrotonate decarboxylase were determined. The catechol 2,3-dioxygenase gene(tomB) was consisted of 945 bases. Amino acid sequence of the tomB gene product exhibited 82% identity with that of catechol 2,3-dioxygenase from P. putida UCC2. The 2-hydroxymuconic semialdehyde dehydrogenase gene(tomC) was consisted of 1458 bases. Amino acid sequence of the tomC gene product exhibited 78% identity with that of 2-hydroxymuconic semialdehyde dehydrogenase from P. putida CF600. The 2-hydroxypenta 2,4-dienoate hydratase gene(tomE) was consisted of 783 bases. Amino acid sequence of the tomE gene product exhibited 81% identity with those of 2-hydroxypenta 2,4-dienoate hydratase from Pseudomonas sp. LB400 and P. pseudoalcaligens KF707. The acetaldehyde dehydrogenase gene(tomG) was consisted of 912 bases. Amino acid sequence of the tomG gene product exhibited 88% identity with those of acetaldehyde dehydrogenase from Pseudomonas sp. LB400 and P. pseudoalcaligens KF707. The 4-hydroxy-2-oxovalerate aldolase gene(tomF) was consisted of 1047 bases. Amino acid sequence of the tomF gene product exhibited 87% identity with that of 4-hydroxy-2-oxovalerate aldolase from Comamonas testosteroni TA441. The 4-oxalocrotonate decarboxylase gene(tomD) was consisted of

687 bases. Amino acid sequence of the tomD gene product exhibited 71.1% identity with that of 4-*oxalocrotonate decarboxylase from C. testosteroni* TA441.

[PC1-26] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

PI3K-PKCε signaling pathway is essential for the p21WAF1/Cip1 expression by apicidin

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We previously reported that PKC signaling event was closely involved in the expression of $p21^{WAF1/Cip1}$ by apicidin, a novel histone deacetylase inhibitor. In this study, we extended our study to elucidate the upstream signaling pathway for the expression of $p21^{WAF1/Cip1}$ by apicidin. The expression of $p21^{WAF1/Cip1}$ by apicidin appears to be mediated by PKCε, because the expression of dominant negative PKCε significantly attenuated the activation of $p21^{WAF1/Cip1}$ promoter via Sp1 sites and also inhibited the protein level of $p21^{WAF1/Cip1}$. And antisense oligonucleotide against PKCε decreased PKCε expression and inhibited the expression of $p21^{WAF1/Cip1}$, indicating that PKCε signaling event is essential for the expression of $p21^{WAF1/Cip1}$ by apicidin. Next, we examined the involvement of PI3K signaling pathway, a possible candidate upstream molecule of PKCε. LY294002 and wortmannin, a well known PI3K inhibitors, attenuated the activation of $p21^{WAF1/Cip1}$ promoter via Sp1 sites and also inhibited the protein level of $p21^{WAF1/Cip1}$. The expression of dominant negative PI3K abrogated the activation of $p21^{WAF1/Cip1}$ promoter, suggesting that the PI3K signaling event was deeply involved in the apicidin-induced $p21^{WAF1/Cip1}$ expression. And apicidin-mediated PKCε signaling event might be regulated by PI3K signaling pathway, since the expression of $p21^{WAF1/Cip1}$ by PDBu, a PKC activator, was not inhibited by the PI3K inhibitors and membrane translocation of PKCε in response to apicidin was blocked by the PI3K inhibitor. However, the $p21^{WAF1/Cip1}$ expression by apicidin appears to be independent of the histone hyperacetylation, since apicidin-induced histone hyperacetylation was not affected by PI3K inhibitors, suggesting that the expression 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 PI3K-PKCε signaling pathway plays a pivotal role in the expression of the $p21^{WAF1/Cip1}$ by apicidin.

[PC1-27] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

MALDI-TOF MS Approach to Identify the E6AP-interacting factors in HeLa cervical cancer cells

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Cervical cancer is one of the leading causes of female death. Human papillomaviruses have been recognized as the primary cause of cervical cancer. Viral oncoproteins are selectively retained and expressed in carcinoma cells infected with human papillomavirus and cooperated in immortalization and transformation of primary keratinocytes. E6 associated protein (E6AP) is a 100 kDa cellular protein which mediates the stable association of the high-risk HPV E6 oncoprotein with tumor suppressor protein p53, resulting in the degradation of p53. E6AP was known as E3 ubiquitin-protein ligase, which has been proposed to play a role in defining the substrate specificity of the ubiquitin-proteasome degradation. In order to identify the E6AP-interacting molecules, HeLa cervical carcinoma cells having HPV type 18 genome, was used. We have produced his tagged E6AP and E6AP-Ni2+-NTA-affinity column was prepared to obtain E6AP-interacting proteins. The E6AP-interacting proteins were resolved in 2D-gel and analysed by matrix-assisted laser desorption/ionization (MALDI/TOF). Among 17 proteins identified in 2D patterns of