fragmentation. SNP treatment also led to the depletion of intracellular GSH and lipid peroxidation. In addition, SNP caused elevated COX-2 expression and PGE2 production, which was accompanied by AP-1 activation. Pretreatment with celecoxib rescued PC12 cells from apoptotic death, nitrosative stress and repressed COX-2 expression and subsequent PGE2 production. Interestingly, both DNA binding and transcriptional activities of AP-1 induced by SNP were blocked by celecoxib. These results suggest that activated AP-1 mediates SNP- induced COX-2 expression, subsequent PGE2 production, and apoptosis. Additional studies are in progress to determine whether attenuation of SNP-induced nitrosative PC12 cell death by celecoxib is associated with its inhibition of AP-1 activation and COX-2 expression.

[PC1-8] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Requirement of PI3K-PKCε Signaling Pathway for Apicidin Induction of $p21^{WAF1/Cip1}$

Kim Yong Kee°, Cho Eun-Jung, Lee Hoi Young, Han Jeung-Whan, Lee Hyang Woo
Dept of Pharmacology, College of Medicine, Kwandong University, Dept of Biochem & Mol Biol, College of Pharmacy, Sungkyunkwan University, Dept of Pharmacology, College of Medicine, Konyang University

We previously reported that the activation of $p21^{WAF1/Cip1}$ transcription by histone deacetylase inhibitor apicidin was mediated through Sp1 sites and pointed to the possible participation of protein kinase C (PKC). In this study, we investigated the role and identity of the specific isoforms of PKC involved and identified phosphatidylinositol 3-kinase (PI 3-kinase) as an upstream effector in HeLa cells. Using an isoform-specific pharmacological inhibitor of PKC, a PKCε dominant-negative mutant, and antisense oligonucleotide to inhibit PKCε specifically, we found that among PKC isoforms, PKCε was required for the $p21^{WAF1/Cip1}$ expression by apicidin. In addition to PKCε, PI 3-kinase appeared to participate in the activation of $p21^{WAF1/Cip1}$ promoter by apicidin, since inactivation of PI 3-kinase either by transient expression of dominant negative mutant of PI 3-kinase or its specific inhibitors, LY294002 and wortmannin, attenuated the activation of $p21^{WAF1/Cip1}$ promoter and $p21^{WAF1/Cip1}$ protein expression by apicidin. Furthermore, membrane translocation of PKCε in response to apicidin was blocked by the PI 3-kinase inhibitor, indicating the role of PI 3-kinase as an upstream molecule of PKCε in the $p21^{WAF1/Cip1}$ promoter activation by apicidin. However, the $p21^{WAF1/Cip1}$ expression by apicidin appeared to be independent of the histone hyperacetylation, since apicidin-induced histone hyperacetylation of $p21^{WAF1/Cip1}$ promoter region was not affected by inhibition of PI 3-kinase and PKC, suggesting that the chromatin remodeling through the histone hyperacetylation alone might not be sufficient for the expression of $p21^{WAF1/Cip1}$ by apicidin. Taken together, these results suggest that the PI 3-kinase–PKCε signaling pathway plays a pivotal role in the expression of the $p21^{WAF1/Cip1}$ by apicidin.

[PC1-9] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Antioxidant effect of flavonoid, myricetin with GSH, vitamin E, vitamin C on B16F10, murine melanoma cell

Ji-sun Yu°, An-Keun Kim
sookmyung wonen's uiversity

Reactive Oxygen Species (ROS) are produced during normal cellular function. ROS are very transient species due to their high chemical reactivity that leads to lipid peroxidation and oxidation of some enzyme, massive protein oxidation and degradation. Under normal conditions, antioxidant are substances that either directly or indirectly protect cells against adverse effects of ROS. Several biologically important compounds have been reported to have antioxidant functions. These incluce vitamin C, vitamin E, GSH, flavonoids. superoxidee dismutase(SOD), glutathione peroxidase(GPX) and catalase(CAT). The various antioxidant either scavange superoxide and free radicals or stimulate the detoxification mechanisms within cells resulting in increased detoxification of free radicals formation and thus in prevention of many pathophysiologic processes. This study carried out to investigate the antioxidant activity of flavonoids, myricetin and (+)-catechin with other antioxidants, GSH, vitamin E and vitamin C on B16F10. In order to investigate the efficacy of antioxidant activity, we mesured antioxidant enzyme activity(SOD, GPX, CAT), RT-PCR and intracellular reactive oxygen intermediate. In this