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The major hurdle of conventional chemotherapeutics is the toxicity to normal tissue. The possible therapeutic advantage(s) of nano-particle encapsulated chemotherapeutics (nano-molecules) may be the enhanced permeability and retention (EPR) effect. Nano-molecules with increase volume may incorporated into the tumor tissue selectively, which is composed of rather sparse structure. EPR effect may cause of increased effectiveness with lower toxicity to normal tissue of nano-chemotherapeutics. In this study, Doxorubicin was encapsulated (nano-Dox) with 50~200nm PLE nano particle (poly (lactic acid)-poly(ethyleneglycol) copolymer) to treat the renal cell carcinoma in mice. In the Balb/c mice having subcutaneous grown RENCA tumor for 3 weeks, nano-Dox was i.v. injected (8 mg/kg) once. Three weeks after the injection, mice were sacrificed to observe the systemic immunity. The growth of tumor burden was measured from the beginning of the experiment, periodically. Electron microscopy indicated the existence of injected nono-Dox in the late stage tumor tissue. The growth of s.c. tumor was inhibited by the treament of nano-Dox as well as naked-Doxorubicin(naked-Dox). No toxicity specific for nano-Dox was observed. Modulation of T and B cell proliferations, lymphocyte phenotypes and cytokine (IL-2, TNF-a) productions was observed in similar way for both nano and naked-Dox treatment. The data suggest the effectiveness of nano-Dox as an anti-tumor chemotherapeutics without specific toxicity. This study is supported by the "IMT 2000-Minstry of Health and Wealfare" in Korea

[PB4-13] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Ginsenoside Rg3 reduces the risk of neuronal cell death by attenuating reactive oxygen species and neurotrophins

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In regard to Aβ toxicity and AD, reactive oxygen species (ROS) are produced by macrophage families in response to Aβ stimulation. In addition to this, neurotrophins (NTs) regulate the neuronal function as well as cell survival and the growth of various types of neurons in both the peripheral nervous system (PNS) and central nervous system (CNS). As high expressions of the ROS and NTs are a routine findings in neuronal cell damage, we wanted to investigate whether Rg3 can inhibit the production of ROS and NTs in primary cell cultures. Results showed that 100㎍/㎖ Rg3 effectively inhibited the production of hydrogen peroxide around 12h to 24h, and NTs were not produced when Rg3 was pre-treated up to 24h from 6h. In conclusion, those results suggests that Rg3 diminish the risk of cell death induced by high concentration of ROS and NTs from the activated microglia.

[PB4-14] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Determination of the minimal sequence of bovine lactoferricin responsible for apoptosis induction

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We examined the minimal amino acid sequence of bovine lactoferricin (Lfcin-B), a cationic peptide corresponding to residues 17-41 near the N-terminus of bovine lactoferrin, to induce apoptosis in THP-1 human monocytic leukemic cells using synthetic peptides. A synthetic peptide (Lfc-17/29, amino acid sequence; FKCRRWQWRMKKL) which is consist of 13 amino acids near the N-terminus of Lfcin-B induced cell death in THP-1 cells in a dose-dependent manner, showing apparent apoptotic changes such as hypodiploid forms of genomic DNA and apoptotic DNA fragmentation. However, another synthetic peptide (Lfc-30/41, amino acid sequence; GAPSITCVRRAF) consist of 12 amino acids near the C-terminus of Lfcin-B was inactive. The characteristics of Lfc-17/29-induced apoptosis was entirely identical with that of Lfcin-B-induced apoptosis, with regard to increased apoptosis with reduction of serum concentration, and inhibition of apoptosis by addition of Ca^{2+}/Mg^{2+}-dependent endonuclease inhibitor or antioxidants. In an analysis using various synthetic peptides having the partial sequences of Lfc-17/29, we found that a peptide consist of 10 amino acids (Lfc-17/26,

FKCRRWQWRM), corresponding to residues 17-26 near the N-terminus of Lfcin-B, was the minimal sequence of Lfc-17/29 responsible for apoptosis induction in tumor cells.

[PB4-15] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Phospholipases D1 and D2 Regulate Different Phases of Exocytosis in Mast Cells

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The rat mast cell line RBL-2H3 contains both phospholipase D (PLD)1 and PLD2. Previous studies with this cell line indicated that expressed PLD1 and PLD2 are both strongly activated by stimulants of secretion. We now show by use of PLDs tagged with enhanced green fluorescent protein that PLD1, which is largely associated with secretory granules, redistributes to the plasma membrane in stimulated cells by processes reminiscent of exocytosis and fusion of granules with the plasma membrane. These processes and secretion of granules are suppressed by expression of a catalytically inactive mutant of PLD1 or by the presence of 50 mM 1-butanol but not tert-butanol, an indication that these events are dependent on the catalytic activity of PLD1. Of note, cholera toxin induces translocation of PLD1-labeled granules to the plasma membrane but not fusion of granules with plasma membrane or secretion. Subsequent stimulation of calcium influx with Ag or thapsigargin leads to rapid redistribution of PLD1 to the plasma membrane and accelerated secretion. Also of note, PLD1 is recycled from plasma membrane back to granules within 4 h of stimulation. PLD2, in contrast, is largely confined to the plasma membrane, but it too participates in the secretory process, because expression of catalytically inactive PLD2 also blocks secretion. These data indicate a two-step process: translocation of granules to the cell periphery, regulated by granule-associated PLD1, and a calcium-dependent fusion of granules with the plasma membrane, regulated by plasma membrane-associated PLD2 and possibly PLD1.

[PB4-16] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Inhibition of tyrosine phosphatases blocks plasma membrane blebbing during Fas-induced apoptosis of Jurkat T cells without affecting the cytotoxicity of Fas-ligation

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Plasma membrane blebs are observed in many types of apoptotic cells, but their processes of formation remain to be clarified. In the present study, we investigated whether there is a relationship between change of intracellular phosphotyrosine levels and biochemical apoptotic events in Jurkat T cells undergoing apoptosis by agonistic anti-Fas antibody. When Jurkat cells were treated with Fas-antibody in the presence or absence of pretreatment with sodium orthovanadate (Na_3VO_4), a phosphotyrosine phosphatase (PTPase) inhibitor, membrane blebs disappeared in orthovanadate-treated cells. In contrast, DNA fragmentation and externalization of the membrane phosphatidylserine after the induction of apoptosis were not affected by the pretreatment of the phosphatase inhibitor. In addition, Fas-induced activation of caspases cascade also remained unaffected. Theses results suggest that orthovanadate has inhibitory effect on the formation of the plasma membrane blebbing and that blebbing of the plama membrane may occur independently from other apoptotic changes.

[PB4-17] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Immunogenicity and protective effects of a novel reassortant influenza live virus, NC-22-8

Chung Young Mee°, Kim Seong Woo, Chun Hyung Ok, Kim Young Gi, Kim Hyun Ah, Kim Yeon Hee, Ha Suk-Hoon, Chae Myeong Yun, Park Wan Je