

had been prepared in the normal laboratory condition resulted in release of glycosylphosphatidylinositol (GPI)-anchored enzymes, renal dipeptidase (RDPase, EC 3. 4. 13. 19) and alkaline phosphatase (APase, EC 3. 1. 3. 1), from the membrane. This spontaneous release of membrane bound enzymes was inhibited by ampicillin, kanamycin and gentamicin. The release pattern of these GPI-anchored enzymes from the PTs and the inhibition by gentamicin were abolished in the presence of the long term incubation supernatant of PTs. The ammonium sulfate fraction (50 % saturation) of porcine 9h incubation supernatant, but not the 2h, caused time- and concentration-dependent release of RDPase and APase from the rabbit PTs suggesting the presence of transferable GPI-anchored protein hydrolyzing entity which is not limited to its own species. We identified *Bacillus cereus*, not identified its original source yet, as the causative factor. The porcine PTs were the better source of these GPI-anchored enzymes compared with the rabbit because of their availability in larger quantities. We report this simple and inexpensive method which may be applied for the solubilization of other GPI-anchored proteins as well.

[PC1-16] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Berberine induces interleukin-12 p40 production in mouse macrophages by promoting p38 mitogen-activated protein kinase pathway

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Interleukin-12 (IL-12) plays a pivotal role in the development of T helper type 1 (Th1) immune response, which may have potential therapeutic effects on diseases associated with pathologic Th2 responses such as allergic disorders and asthma. In this study we investigated the effects of berberine on IL-12 production in mouse macrophages. Berberine, known as an antimicrobial and antitumor alkaloid, significantly increased IL-12 p40 production from mouse macrophages in a dose-dependent manner. The IL-12 production induced with berberine was significantly inhibited by p38 mitogen-activated protein (MAP) kinase inhibitors. Moreover, phosphorylated p38 MAP kinase was increased in the presence of berberine, implying the involvement of p38 MAP kinase in the induction of IL-12 p40 by berberine. Furthermore, berberine synergistically increased IL-12 production when combined with lipopolysaccharide. This immunomodulatory effect may explain some of the known biological effects of berberine and suggest berberine as an immunotherapeutic compound for induction of IL-12, which is potentially applicable for tumors, infectious disease, and airway inflammation.

[PC1-17] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Effects of aging and dietary restriction on the apoptosis related genes of rat testis

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The purpose of this study was to determine whether the apoptosis related genes in rat testis alters with aging and dietary restriction. It was reported that apoptotic cell death of rat testicular germ cell increases with age. In this study, we investigated the changes of the apoptosis related genes such as p53, p21, bcl-2/bax, fas and caspase-3 in 6-, 12-, 18-, and 24-month old Fischer 344 rats which were fed ad libitum and diet-restricted. The protein level of p53 increased with aging. In 18 months, the protein level of p53 increased 5 times more than that of 6 month and in dietary restriction group, this increase was also modulated. P21 protein level was also increased with aging. In 18 months, the protein level of p21 increased 40 times more than that of 6 month and it was modulated in dietary restriction group. The bcl-2, bax ratio was decreased after increase in 12 month. But dietary

restriction had no effect on it. The fas protein level increased in 24 months of age more than 2 times, and dietary restriction had no effect on it. The active form of caspase-3 did not increase with aging but the proform of it was increased 3 times more than that of 6 months. And the increase was modulated in dietary restriction group. According to the above results, the increase of apoptotic cell death in rat testis cells is p53 and p21 dependent and fas protein will be related to the apoptotic death. It should be more investigated to confirm that dietary restriction has some effects on it.

[PC1-18] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Expression of HIF-1 inducible genes in the aged rat liver

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Some ROS have been suggested to play important roles as a second messenger in normal and diseases conditions. Recent findings on hypoxia established the induction of a DNA binding protein synthesis called hypoxia inducible factor-1 (HIF-1), which promotes transcription of multiple genes. HIF-1 plays a major role in adaptive responses essential to hypoxia as the case in angiogenesis to maintain O₂ homeostasis. HIF-1 has also been shown to activate transcription of genes encoding inducible nitric oxide synthase (iNOS) and heme oxygenase 1 (HO-1) which are important for the regulation of blood flow by synthesizing NO and CO, respectively. At present, there is no information on the HIF-1 inducible genes expression and DNA binding activity in aged tissues. We investigated expression of HIF-1 inducible genes in liver isolated from Fischer 344 rats at 6, 12, 18, and 24 months of age. We quantified the age-related changes in four genes, vascular endothelial growth factor (VEGF), HO-1, iNOS, and HIF-1a in rat whole liver. Quantitation of DNA binding activity was carried out by EMSA. Results showed that the protein levels of VEGF, HO-1, iNOS, and HIF-1a were increased with age. These changes are attributed to the age-related increase in HIF-1 DNA binding activity. Significances of our findings are the hypoxic induction of HIF-1 inducible genes may be critical factors in the maintenance of cerebral O₂ homeostasis and angiogenesis during aging. Our results warrant further investigation on molecular mechanisms underpinning hepatic aging and blood circulation under hypoxic conditions occurring during aging.

[PC1-19] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Effects of bisphenol A and 4-nonylphenol for development of cultured mammary gland

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The prevalence of synthetic chemicals in our environment that capable of mimicking the female hormone estrogen is a growing concern. One such chemical, bisphenol-A (BPA), has been shown to leach from a variety of resin-based and plastic products, including dental sealants food and beverage containers, in concentrations that are sufficient to induce cell proliferation in vitro. In order to development, mice on mammary determine if above endocrine disruptors (EDs) affect lobulo-alveolar development, and to determine if whole organ culture of mouse mammary glands is an appropriate model of estrogen effects on mammary development, mouse mammary glands were cultured in the presence or absence of EDs. Test chemicals selected for these studies included 17beta-estradiol, 4-nonylphenol and BPA. We also performed RT-PCR method. The RNA was prepared from mouse mammary tissues. These results