inflammatory activities in several animal models and in a clinical study on patients with OA, JOINS was revealed to have a good analgesic efficacy and safety profile.
In this study, we tried to evaluate the possibility of JOINS as a curative therapeutics of rheumatoid arthritis using several in vitro and in vivo models. JOINS inhibited adjuvant-induced arthritis in rats and reduced inflammatory pouch volume and capillary permeability. JOINS also attenuated the PMA-stimulated chemilunminescence in neutrophils and degradation of articular cartilage by oxygen radicals. JOINS decreased conA-stimulated T cell proliferation and LPS-stimulated B cell proliferation. In conclusion, JOINS has a strong potentiality to be developed as a safe drug for rheumatoid arthritis.

[PA1-61] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## Mucogen Ameliorates the Fibrosis and Inflammation of Chronic Pancreatitis in Mice

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In the present study, we established experimental chronic pancreatitis model in mice through repetitive induction of acute pancreatitis with intraperitoneal injections of cerulein (40 mcg/kg, 6 times every hours twice per week for 5 or 10 weeks), which led to chronic pancreatitis with fibrosis. Severe pancreatic acinar atrophy, trans-differentiation of acinar to duct like tubular complexes, islets hyperplasia, and dilatation of intraacinar lumina developed. Masson-Trichrome staining demonstrated progressive accumulation of extracellular matrix in interlobar and interacinar spaces. The extents of pancreatic fibrosis were statistically significantly decreased in accordance with lessened pancreatic inflammations after treatment of Mucogen (DA-9601), phytopharmaceutical showing antioxidative and cytoprotective actions. Using nuclear extracts from pancreas and radiolabeled NF-kappaB probe, EMSA was done, which showed the increased NF-kappaB binding in chronic pancretitis and significantly attenuated NF-kappaB binding activities after mucogen treatment. The levels of myeloperoxidase and iNOS activities were also significantly decreased in mucogen treated group compared to pancreatitis control group. Cytoprotective proteins such as heat shock protein-70 and metalotheionine were siginificantly increased in mucogen-treated group. Mucogen decreased the expressions of alpha-SMA and type I collagen in cultured pancreatic stellate cells. Conclusively, we could establish the mouse model of chronic pancreatitis and mucogen might be considered as therapeutics in the prevention and treatment of chronic pancreatitis with fibrosis.

[PA1-62] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## G protein-coupled phosphoinositide 3-kinase γ is required for autotaxin-mediated tumor cell motility

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Cell motility is a fundamental process required during normal embryonic development, inflammatory responses, wound healing, and tumor metastasis. Autotaxin (ATX) is a 125-kDa glycoprotein secreted by the human melanoma cell line A2058. This autocrine motility factor has been shown to stimulate random and directed motility of human tumor cells at high picomolar to low nanomolar concentrations (ED50 = ~300-500 pM). In the present study, we have shown that G protein-coupled phosphoinositide 3-kinase (PI-3 kinase) γis involved in the signal transduction of Autotaxin (ATX), a novel tumor cell motility-stimulating factor. Pretreatment of the cells with PI-3 kinase inhibitors, wortmannin or LY294002 inhibits ATX-induced motility. Reverse transcriptase PCR and Western blot analysis showed that human melanoma cells have PI-3 kinase, p110γ. ATX increased the PI3-kinase activity in p110γ, but not p85, immunoprecipitates, which can be abolished by pretreatment of PI-3 kinase inhibitors (wortmannin, LY294002) or pertussis toxin. Collectively these results strongly suggest that PI-3 kinase p110γ is