not blocked by βARKct that inhibits Gβγ-mediated signaling, and not by βarrestin1-V53D, a dominant negative mutant of βarrestin 1. We also tested several kinase inhibitors (wortmannin, genistein, and PKC inhibitors) and dominant negative mutants for c-Src, PI3-Kinase, mSOS, Ras, and Raf to see whether they follow the same signaling pathways. It was generally concluded that they show the similar time-dependency and dose-dependency, but D2 receptors are more potent than D3 receptor for the activation of MAPK. So far we have tested, D2 and D3 receptors seem to employ the same signaling components for the regulation of MAPK.

[PA1-7] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Effects of dopamine agonists and antagonists on the degranulation of mast cells and LPS-induced nitric oxide production in macrophage cells

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Generally dopamine agonists or antagonists for the treatment of Parkinson's disease or Schizophrenia are used on the long-term basis. It would be important to see whether they have any effect on physiological functions, such as hormonal or immune functions. In this study, we tested whether they have any effects on the degranulation of mast cell (RBL-2H3) and nitric oxide production from macrophage cells (RAW 264.7), which presumably represent the allergic and inflammation, respectively. Among dopamine agonists (dopamine, bromocriptine, 7-OH-DPAT) and antagonists (Sulpiride, U99194A) tested, bromocriptine and 7-OH-DPAT showed potent inhibitions of mast cell degranualtion (IC50 value, 10μM). On the other hand, nitric oxide induction from RAW 264.7 cell was markedly reduced by bromocriptine and dopamine (IC50 value, 10μM). When bromocriptine was tested for the effects on LPS-induced iNOS expression, bromocriptine showed a time-dependent and concentration-dependent inhibtion of iNOS expression. These results suggest that some of dopamine agonists, like bromocriptine, could have some effects on immune functions, and it would be necessary to be more careful for some patients depending on the their immunological status.

[PA1-8] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Reversal of multidrug-resistance by synthetic alkaloids in cancer cells

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The occurrence of resistance to chemotherapeutic drugs is a major problem for successful cancer treatment. Frequently, this resistant phenotype of cancer cell reveals a broad spectrum to structurally and/or functionally unrelated anticancer drugs, termed multidrug resistance (MDR). Overexpression of P-glycoprotein (Pgp), a transmembrane drug efflux pump, is a major mechanism of MDR. The MDR associated with Pgp-overexpression can be reversed or modulated by inhibition of Pgp-mediated transport, via increasing cellular accumulation of anticancer drugs with various agents such as calcium channel blockers, calmodulin inhibitors, antiarrythmics, steroids, antiestrogens cyclic peptide antibiotics and etc. To date, however, the usefulness of MDR-reversal agents has been limited since the undesired side effects such as cardiac toxicity or immunosuppression. The present study was performed to evaluate the ability of some synthetic alkaloids to overcome multidrug resistance by measuring the cytotoxicity of paclitaxel, a well-known Pgp substrate. Among the compounds tested, 2-(2-ethoxy-ethyl)-N,N'-bis-(2-methoxy-phenyl)-malonamide and [1-(N'-benzyl-hydrazinocarbonyl)-2-phenyl-ethyl]-carbamic acid benzyl ester revealed significantly inhancing of paclitaxel induced cytotoxicity to Pgp-positive cancer cells but not to Pgp-negative cancer cells in