MMP-2. In present study suggests that H-ras-induced activation of both p38 and ERK results in more invasive and motile phenotypes of human breast epithelial cells, whereas N-ras activation of ERKs is not sufficient for these phenotypic changes.

## Oral Presentations - Field D

[D1. Medicinal Chemistry] [D2. Pharmacognosy] [D3. Oriental Medicine] [D4. Analytical Chemistry]

[OD-1] [ 04/18/2003 (Fri) 14:45 - 15:00 / Orchid ]

### *ent*-Kaurane Diterpenoids from *Croton tonkinensis* Inhibit LPS-induced Transcription Factor NF-κB Activation and NO Production

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Nuclear factor-κB (NF-κB) belongs to a group of homodimers and heterodimers of Rel/NF-κB proteins that bind to DNA target sites, where they directly regulate gene transcription. The activation of NF-κB has been shown to mediate inflammation and suppress apoptosis. Activated NF-κB has been found in various inflammatory diseases such as rheumatoid arthritis, atherosclerosis, asthma, inflammatory bowel disease, and *Helicobacter pylori*-associated gastritis and associated with cancer, cachexia, diabetes, euthyroid sick syndrome, and AIDS. With its apparent involvement in a variety of human diseases, NF-κB has been an attractive target in the discovery of anti-inflammatory and cancer chemopreventive drugs. *Croton tonkinensis* Gagnep. (Euphorbiaceae), commonly named in Vietnamese as "Kho sam Bac Bo", is a tropical shrub native to the Northern Vietnam. Its dried leaves have been used in Vietnamese traditional medicine to treat burn (boil), abscesses, impetigo, abdominal pain, dyspepsia, gastric and duodenal ulcers. Bioactivity-guided fractionation of MeOH extract from leaves of *C. tonkinensis* toward NF-κB inhibitory activity led to the isolation of four active *ent*-kaurane-type diterpenoids including two new *ent*-1$\beta$-acetoxy-7$\alpha$,14$\beta$-dihydroxykaur-16-en-15-one and *ent*-18-acetoxy-7$\alpha$,14$\beta$-dihydroxykaur-16-en-15-one together with two known *ent*-7$\alpha$,14$\beta$-dihydroxykaur-16-en-15-one and *ent*-18-acetoxy-7$\alpha$-hydroxykaur-16-en-5-one. These *ent*-kauranoids were demonstrated to strongly inhibit NF-κB activation in LPS-induced murine macrophage RAW264.7 at $IC_{50}$ from 0.07 μM to 0.42 μM. Consistently, the *ent*-kauranoids markedly reduced LPS-stimulated NO production in a comparable concentration-dependent manner, thus appeared to inhibit iNOS gene expression by preventing the activation of NF-κB.

[OD-2] [ 04/18/2003 (Fri) 15:00 - 15:15 / Orchid ]

### Sensitive Determination of Alkylphenols, Chlorophenols, and Bisphenol A using GC/MS-SIM in Papers Materials

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The alkylphenols, chlorophenols and bisphenol A were determined by gas chromatography/mass spectrometry-selected ion monitoring (GC/MS-SIM) mode followed by two work-up methods for comparison; isoBOC derivatization method and TBDMS derivatization method. Eleven phenols in paper samples were extracted with acetonitrile. Also, solid-phase extraction (SPE) with XAD-4 and subsequent conversion to isobutoxycarbonyl derivatives or tert.-butyldimethylsilyl derivatives for sensitive analysis with the selected ion-monitoring (SIM) mode. The SIM responses were linear with the correlation coefficient varying 0.9717~0.9995 (isoBOC derivatization), and 0.9842~0.9980 (TBDMS derivatization). The recoveries were 82.4~108.8 % by area ratio of pheranthrene-d10 vs bisphenol A d16. (isoBOC derivatization and TBDMS derivatization) The range of concentrations was respectively, 0.95~1.44 ng/g in 2,4-dichlorophenol, 1.01~1.17 ng/g in t-butylphenol, 2.17~5.84 ng/g in pentachlorophenol, 12.68~14.88 ng/g in nonylphenol and 30.84 ~153.72 ng/g in bisphenol A.

## Oral Presentations - Field E

[E1. Pharmaceutics] [E2. Pharmacokinetics] [E3. Physical Pharmacy]

[OE-1] [ 04/18/2003 (Fri) 15:15 - 15:30 / Orchid ]

### Enhanced mucosal and systemic immune responses by mucosally administered hepatitis B surface antigen: effects of vaccine delivery vehicles and adjuvants

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The purpose of this study is to investigate the effect of mucosal vaccine delivery vehicles and adjuvants on the local and systemic antibody responses following mucosal immunization of mice with hepatitis B surface antigen (HBsAg). Mice were immunized on days 0 and 21 by administration of hepatitis B surface antigen B (HBsAg) into the vagina. HBsAg was delivered in saline or poloxamer(Pol)-based vehicle containing mucoadhesive polycarbophil (PC). In some cases, HBsAg was coadministered with plasmid pVAX/Rantes as an adjuvant. At various time points after immunization, the saliva and the blood were sampled. Vaginal secretion was obtained after flushing of the contents. Anti-HBsAg immunoglobulin A (IgA), IgG, IgG1, IgG2a were measured by enzyme-linked immunosorbent assay. Vaginal IgA levels were higher in Pol/PC vehicle as compared to saline vehicle. The coadministration of pRantes was more effective for induction of IgA in vagina. Salivary IgA levels, however, were not influenced by the vehicle or the adjuvant. Vaginal administration of HBsAg induced IgG in the serum. The coadministration of pRantes significantly increased the induction of IgG1, but not IgG2a in the serum. These results suggest that the use of mucoadhesive delivery vehicle would be advantageous for more effective induction of local immune response in vagina. Moreover, the use of a chemokine gene, pRantes, might have a potential to enhance the local immune response at the administered mucosal sites.