**[PD1-8] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Design and Synthesis of N-Aryl 8,9-Dihydro-7H-isoindolo[5,6-g]quinoxaline-7,9-dione Derivatives as Potential Antitumor Agent

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We have previously reported the synthesis and cytotoxic activities of a series of azaanthraquinone derivatives using doxorubicin as a lead compound. Doxorubicin is known to intercalate into DNA and to inhibit topoisomerase II activity. But in the case of quinone compounds like Dox, its use is limited because of systemic toxicities, primarily cardiotoxicity and myelosuppression. In this study, we discuss the synthesis of isoindolobenzoquinoxaline derivatives. The quinone group of the azaanthraquinone derivatives were removed in the target compounds. The removal of the quinone group was intended to lessen the cardiotoxicity of the doxorubicin. The target compounds were designed based on the structural features of acridine-4-carboxamide DACA and amonafide. DACA has a neutral chromophore and acridine moiety and poisons both topoisomerases I and II with DNA intercalating activity. In order to delineate the SAR of isoindolobenzoquinoxaline derivatives, various aryl substituents were introduced to the nitrogen of the target compounds. The synthesis of the target compounds used Diels-Alder rout as a key step.

**[PD1-9] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## AHL inhibition of Beckerelide and Fimbrolide

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Quorum sensing, a gene expression in response to population density, is regulated by chemical signals, most of which are acylated homoserine lactones (AHLs). The AHL derivatives have been reported to regulate bioluminescence, virulence factors and / or swarming motility in bacteria. It is hypothesized that higher organisms may have evolved specific means to interfere with bacterial communication as exemplified in the AHL-antagonistic activity of halogenated furanones isolated from the Australian macroalga Delisea pulchra. In order to explore the structure-activity relationship of these furanones, analogues were synthesized as described by Manny et. al. while the AHL inhibition activity was tested in a convenient colorimetric liquid culture assay system using the AHL-responsive recombinant Agrobacterium tumefaciens strain. Among the furanone analogues tested, (5Z)-4-bromo-5-(bromoethylene)-3-butyl-2(5H)-furanone, a fimbrolide analogue showed moderate AHL-antagonistic activity while 3-butyl-4-bromo-5-dibromomethyl-5-hydroxy-2(5H)-furanone, a beckerelide showed a more potent AHL-antagonistic activity.

**[PD1-10] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Detection, Identification and Characterization of In vitro GSH Metabolites Formed by 1- and 2-Bromopropane

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1- and 2-Bromopropane were reported as the causative agents for reproductive toxicity and immunotoxicity. The glutathione (GSH) metabolites resulting from in vitro treatment of 1- and 2-bromopropane were detected, identified and characterized. For the facile identification, expected GSH metabolites formed by 1- and 2-bromopropane were chemically synthesized as reference materials (positive controls) and characterized by $^{1}$H-

NMR, $^{13}$C-NMR, HPLC and LC/MS/MS. The treatment of GSH and S-9 fraction with 1- or 2-bromopropane at a physiological condition (pH 7.4, 37℃) for 1hr produced GSH metabolites, which were identified by UV, HPLC and ESI LC/MS/MS analyses. In addition, time-response and dose-response effects of formation of GSH metabolites were investigated. The present results suggest that 1- and 2-bromopropane might form GSH metabolites at in vivo condition. Detection of GSH metabolites formed by 1- and 2-bromopropane at in vivo experimental models is on progress.

**[PD1-11] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Practical Synthesis of α-Galactosyl Ceramide, KRN 7000.

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Galactosyl ceramides paly important roles in biological system as immunomodulator and essential constituents of membranes and cell walls. An efficient synthesis of α-galactosyl ceramide, KRN 7000, derived from marine sponge Agelas mauritianus as accomplished via a short reaction involving the coupling ceramide moiety and trichloroacetimidate as glycosylation donor. We could synthesize α-galactosyl ceramide stereoselectivity without β-anomer formation on a multigram scale.

**[PD1-12] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Design of Novel Ras Farnesyltransferase Inhibitors Based on Virtual Screening and Docking Studies

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Inhibition of the protein-modifying enzyme farnesyltransferase is considered as a major emerging strategy in cancer therapy because of the involvement of farnesylated proteins in oncogensis. We studied the structure-activity relationship of a novel class of CAAX-peptidomimetic farnesyltransferase inhibitors based on the benzophenone scaffold. FlexX docking of inhibitors confirmed reasonable fit of the molecule into the peptide binding site of farnesyltransferase. We also performed a virtual screening with LeadQuest chemical library databases to identify novel inhibitors of farnesyltransferase. Finally, detail docking studies were performed using these compounds which showed high scoring from the virtual screening experiment.

**[PD1-13] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Synthesis of 2-phenyl-1,8-naphthyridin-4-ones

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2-Phenyl-1,8-naphthyridin-4-ones had been synthesized for their cytotoxic activity. Substituted acetophenone was treated with NaH and diethyl carbonate to give ethyl benzoylacetates, which was reacted with substituted 2-aminopyridine and PPA to yield 2-phenylpyridopyrimidine-4-ones. These compounds was heated at 350℃ in liquid paraffin to afford final compounds, 2-phenyl-1,8-naphthyridin-4-ones.

**[PD1-14] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Wogonin and Its Analogs

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