K6(methoxy-), K8(chloro-), K16(ethoxy-) and K17(n-propoxy), induced elevated hepatic GSH levels. Four kinds of 3-alkoxy-6-allylthiopyridazine derivatives investigated were effective against aflatoxin B_1-induced hepatotoxicity.

[PD1-5] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Natural TACE (TNF-α Convertase) Inhibitor, Gelastatin Hydroxamate: Biological Evaluation and Target Validation

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One of attractive target for Rheumatoid Arthritis (RA) therapy is the cytokine, tumor necrosis factor –alpha (TNF-α), which has been shown to be overproduced in the joint of RA patients. The clinical success of anti-TNFR biologics has validated TNF-α as a drug discovery target. Thus, inhibiting of formation of TNF-α has been emerged to an intriguing approach for RA therapy. TNF-α is processed from its membrane bound precursor by the metalloprotease TNF-α converting enzyme (TACE), Here, biological evaluation, mode of action of natural TACE inhibitor, Gelastatin hydroxamate, are addressed. The correlation of α-secetase and TACE is evaluated based on cellular APP-α inhibition assay

[PD1-6] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

N-4-Substituted-benzyl-N'-tert-butylbenzyl Thioureas as Vanilloid Receptor Ligands: Investigation on the Role of Methanesulfonamido group in Antagonistic Activity

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Vanilloid receptor 1 (VR1) is a nonselective cation ion channel placed in the plasma membrane of peripheral sensory neurons that is potential target for analgesia. A series of N-4-substituted-benzyl-N'-tert-butylbenzyl thioureas were prepared for the study of their agonistic/antagonistic activities to the vanilloid receptor in rat DRG. Their structure-activity relationship in reveals that not only the two oxygens and amide hydrogen of sulfonamido group but also the optimal size of methyl in methanesulfonamido group play an integral role for the antagonistic activity on vanilloid receptor.

[PD1-7] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Efficient Synthesis of Nucleoside Phosphonates using Olefin Cross-Metathesis

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In recent years, olefin cross-metathesis (CM) has emerged as a powerful and convenient synthetic technique in organic chemistry; however, as a general synthetic method, CM has been limited by the lack of predictability in product selectivity and stereoselectivity. A number of excellent studies have recently appeared in the literature which have shown that with the correct catalyst and reaction conditions CM can be used to access a variety of di- and trisubstituted olefinic products in moderate to high yield with good E/Z ratios. Grubbs et al have recently published a method for the synthesis of vinylphosphonates via an olefin cross-metathesis reaction. As part of our ongoing research program examining the synthesis and biological application of backbone-modified nucleic acids, we had reason to examine a novel synthetic approach to nucleoside phosphonates, and we now wish to report our results in this area, which led to the formation of nucleoside phosphonates using olefin cross-metathesis reaction.