



Sigma Xi Student Research Paper Competition, University of Kansas, March 14, 2007

Undergraduates, <u>Malott Room</u> , Kansas Union Judges: K. Audus, G. Burg, L. Burmeister			Early Graduate Students, <u>Malott Room</u> , Kansas Union Judges: J. Gleason, G. Burg, L. Burmeister						
1:10 pm	1:30 pm	1:50 pm	2:20 pm	2:40 pm	3:00 pm	3:30 pm	3:50 pm	4:10 pm	4:30 pm
Umar Firman	Nicholas Philipp	Taras Zelenchuk	Andrea Crowther	Steve Davis	Patrick Johnson	Vitaly Kheyfets	Jason Palikij	Yelena Wu	Ezra Kulczycki
"Dynamic Light Scattering to Measure Diameters of Nano-size Particles," Mechanical Engineering, cari_gua@yahoo.com	"Two New Species of Zoanths from Southern Australia and Southern California," Ecology and Evolutionary Biology, nickphil@ku.edu	"Nomenclature in Sea Anemones," Ecology and Evolutionary Biology, taras@ku.edu	"A New Species of Shell-Forming Sea Anemone from Australia," Ecology and Evolutionary Biology, andreac@ku.edu	"Weevil diversity in Miocene Dominican amber: A preliminary overview (Coleoptera: Curculionidae)," Ecology and Evolutionary Biology, steved@ku.edu	"Self-control choice in Lewis and Fischer 344 rats: Manipulating delay between rather than within sessions," Applied Behavioral Science, circadia@ku.edu	"Free-Surface Coating Flows of Non-Newtonian Gels: 3-D Numerical Simulation of Gravity-Induced Flow," Mechanical Engineering, vok@ku.edu	"When Do Bees Make a Beeline?," Biological Sciences, jatku@ku.edu	"Psychosocial Functioning of Pediatric Renal and Liver Transplant Recipients," Clinical Child Psychology yelenawu@ku.edu	"Methanobacteria-promoted dissolution of Cu-substituted borosilicate glass," Geology, ezra55@ku.edu
Dr. Ronald L. Dougherty	Dr. Daphne G. Fautin	Dr. Daphne G. Fautin	Dr. Daphne G. Fautin	Dr. Michael S. Engel	Dr. Gregory J. Madden	Dr. Sarah L. Kieweg	Dr. Rudolf Jander	Dr. Ric G. Steele	Drs. David A. Fowle & Jennifer A. Roberts

Advanced Graduate Students, <u>Pine Room</u> , Kansas Union Judges: E. Morris, S. Macdonald, G. de Boer									
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Jeffrey Cole	Ginger Miller	Kendra J. Pittman	Patricia Ryberg	Kelly Desino	Pallabi Mitra	Daniel Mudra			
"Flumoxing female preference: discrepancy between preference and song in shield-back katydids," Ecology and Evolutionary Biology, jeffcole@ku.edu	"Position around a tree: consequences for pheromone detection," Ecology and Evolutionary Biology, glmiller@ku.edu	"Exploring species boundaries with phylogeography and morphometrics using the polytypic minnow <i>Notropis stramineus</i> ," Ecology and Evolutionary Biology, kjpi@ku.edu	"Permian and Triassic Trees as High-Latitude Paleoclimate Indicators," Ecology and Evolutionary Biology, rybergp@ku.edu	"Structural Modification of Paclitaxel to Reduce Interaction with P-Glycoprotein," Pharmaceutical Chemistry, kdesino@ku.edu	"Effects of acute and chronic exposure to bisphenol A on SULT1A1 activity in the human placental choriocarcinoma cell line BeWo," Pharmaceutical Chemistry, pmitra77@ku.edu	"An <i>in situ</i> model system for the simultaneous assessment of physical and biological barriers to drug absorption in the rat intestinal mucosa," Pharmaceutical Chemistry, dmudra@ku.edu			
Dr. Jennifer M. Gleason	Dr. Jennifer M. Gleason	Dr. Jennifer M. Gleason	Dr. Edith L. Taylor	Dr. Kenneth L. Audus	Dr. Kenneth L. Audus	Dr. Ronald T. Borchardt			



**Sigma Xi Student Research Paper Competition
University of Kansas
March 14, 2007**

Abstracts

Undergraduate Students

**Judges: K. Audus, G. Burg, L. Burmeister
(Malott Room, Kansas Union)**

1:10 pm “Dynamic Light Scattering to Measure Diameters of Nano-size Particles”
Umar Firman, cari_gua@yahoo.com
Mechanical Engineering
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Ronald L. Dougherty

Dynamic Light Scattering (DLS) is a technique to measure the hydrodynamic size of a nano-size particle suspended in fluid. This technique is a non-destructive product evaluation. The technique is executed by a laser source that penetrates through the particles ultimately measuring the change of scattered laser intensity due to the random movement of the suspended particles. The range of particles diameters examined is from 60 to 93 nm. Previous technology using single scattering allows the laser to study samples that are clear (up to approximately 0.01% volume fraction). Single scattering technique provides accurate data about the physical properties of the particles. Multiple scattering occurs when the selected sample is more dense having approximately 1% to 10% volume fraction. Multiple scattering particles intercept by the laser beam will reflect the beams intensity onto other particles around them and provide false fluctuations in data if compared to single scattering results. The objective of the research is to use suppression of the multiple scattering signals to analyze only the single scattered signal to measure the particles' diameters. To do this, software which correlates the fluctuation of the signal with respect with time is used. In application, DLS is used in many fields. Two possible fields are in pharmaceuticals and air pollution studies. In the pharmaceutical field, determining the properties of a protein solution without altering or contaminating the solution in some way is important due to sensitivity of the protein solution to the environment. DLS is also use to measure the size distribution of particulate in air. Accurate studies can be performed for both testing and regulating federal environment standards.

1:30 pm “Two New Species of Zoanthids from Southern Australia and Southern California”
Nicholas Philipp, nickphil@ku.edu
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University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Daphne G. Fautin

The phylum Cnidaria includes such diverse organisms as jellyfish, corals, and hydrozoans. They are characterized by possessing microscopic stinging cells called



nematocysts and being radially symmetrical. Zoanthidea (Class Anthozoa) is one of the least studied cnidarian orders. The “mat anemones,” as they are sometimes called, are closely related to sea anemones and corals in that they have mesenteries that divide their body cavity and an actinopharynx (a “throat”) that connects their oral opening to their digestive cavity (unlike the cnidarians not included in class Anthozoa). The major defining characteristics of zoanthids are a single cycle of short tentacles around the oral disc, unpaired mesenteries added in couples, and weak retractor muscles. Zoanthids are found all over the world and at all depths. Most species are colonial, and many live on other invertebrates like hermit crabs and octocorals. In both southern California and southern Australia a species has been referred to as “Yellow Zoanthids” but neither has been scientifically described. Much of the identification of these animals is based on their internal anatomy, their histology and the nematocysts that they possess. I will examine the external characteristics as well as use microscopic techniques to examine the morphology and location of the sphincter muscle, the arrangement of mesenteries, and the arrangement of nematocysts to describe these two species.

1:50 pm “Nomenclature in Sea Anemones”
Taras Zelenchuk, taras@ku.edu
Ecology and Evolutionary Biology
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Daphne G. Fautin

I am determining the type species of every genus of sea anemones, marine animals that belong to taxonomic order Actiniaria of phylum Cnidaria. According to the International Code of Zoological Nomenclature (ICZN), every genus of animal must contain at least one species, and one species of a genus must be designated the type species. Ideally, one scientific name refers to only one kind of organism. However, in some cases more than one name has been used for an organism; these are termed synonyms and are the province of taxonomy, beyond the scope of my project. I am working on problems of nomenclature, mostly application of one name to multiple types of organisms; these are termed homonyms. Three hundred eighty-two genera of sea anemones have been described; of them, 80% (305) have a clear type species, according to the rules of the ICZN. Of the remaining 77, 41 are homonyms. According to the ICZN “Principle of Priority,” the name belongs to the first type of organism to which the homonymous name was applied. In 13 of the 41 cases, the anemone name is senior and there is no problem, but in the other 28 cases, a junior homonym is being used and I may have to change it to the oldest alternative name that is not, itself, a junior homonym. In addition, 18 genera do not have a type designated and 18 have validity problems.

2:10 pm Break



Early Graduate Students

**Judges: J. Gleason, G. Burg, L. Burmeister
(Malott Room, Kansas Union)**

2:20 pm “A New Species of Shell-Forming Sea Anemone from Australia”
Andrea Crowther, andreac@ku.edu
Ecology and Evolutionary Biology
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Daphne G. Fautin

Sea anemones of the genus *Stylobates* (Cnidaria: Anthozoa: Actiniaria) form obligate symbioses with hermit crabs. This exclusively deep sea genus of anemone possesses the ability to produce a carcinoecium, a chitinous secretion that coats and extends the hermit crab's shell. Most hermit crabs live in abandoned snail shells; as a crab grows, it must relocate to a larger shell. In the deep sea, large snail shells are few. *Stylobates* can extend its carcinoecium as rapidly as the crab grows; thus its crab need not change shells. As well as providing a place for the crab to live, the anemone protects the crab from predators: the tentacles of anemones possess nematocysts (microscopic stinging capsules) that, when stimulated, will evert a spined tubule like a harpoon. Nematocysts are used to capture food for the anemone as well as deter enemies. The anemone benefits from this association by being carried to food; as the crab feeds the anemone eats the food scraps. Three species of *Stylobates* have been described: *S. cancrisocia* from east Africa, *S. aeneus* from near Hawaii and Guam, and *S. loisetteae* from north-west Australia. The known distribution of *Stylobates* is increased with the collection of this new species from north-eastern Australia in the Coral Sea. The new species of *Stylobates* differs from the others in the nature of the marginal sphincter muscle, size/distribution of cnidae, and size/arrangement of tentacles. A complete species description is currently being prepared.

2:40 pm “Weevil diversity in Miocene Dominican amber: A preliminary overview
(Coleoptera: Curculionidae)”
Steve Davis, steved@ku.edu
Ecology and Evolutionary Biology
Division of Entomology, Natural History Museum
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Michael S. Engel

While numerous lineages of weevils have been recorded from Tertiary ambers of the New World, only a few species have been hitherto described from these deposits. This is remarkable given the relatively considerable attention focused on weevils in other amber deposits or as compressions. Admittedly, the faunas of Dominican and Mexican amber are too young to provide insight into the diversification of a lineage as old as the Curculionidae but these species do give perspective on localized extinctions and biogeographic patterns among and within genera of particular New World weevil clades. As such these fossils are deserving of our attention. Herein are provided brief descriptions of a recently identified and remarkable zygotine weevil (Conoderinae), the first fossil *Caulophilus* (Cossoninae), as well as many other new cossonines, the first two species of Dryophthorinae recorded in amber, a new species of *Cenocephalus*



(Platypodinae), and a brief review of other weevils in Early Miocene (Burdigalian, ca. 19 million years) amber from the Dominican Republic.

3:00 pm “Self-control choice in Lewis and Fischer 344 rats: Manipulating delay between rather than within sessions”

Patrick Johnson, circadia@ku.edu
Applied Behavioral Science
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Gregory J. Madden

Fischer 344 and Lewis rats chose between one pellet immediately and three pellets after a series of delays (10 s, 5 s, 0 s). Anderson and Woolverton (2005) reported that Lewis rats were more impulsive than Fischer 344 rats when delays were adjusted within sessions. Cardinal et al. (2002) reported problems with adjusting delay values within sessions. Thus, we sought to systematically replicate these strain differences when delays were manipulated across conditions. Sessions consisted of 42 trials in which two-thirds of all trials were forced-choice (4 forced-choice trials were followed by 2 free-choice trials). Comparisons across strains replicated Anderson and Woolverton's findings. Analyses of individual rats' choices revealed frequent side biases and more gradual emergence of stable behavior in the Fischer 344 strain.

3:20 pm Break

3:30 pm “Free-Surface Coating Flows of Non-Newtonian Gels: 3-D Numerical Simulation of Gravity-Induced Flow”

Vitaly Kheyfets, vok@ku.edu
Mechanical Engineering
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Sarah L. Kieweg

Topical drug delivery vehicles must be properly formulated and analyzed to ensure they are serving their purpose during application. A finite bolus of gel carrying a microbicidal pharmaceutical agent, applied to the vaginal epithelium, is expected to serve as a physical and/or chemical barrier to HIV transmission during sexual intercourse. The gel must coat the entire epithelial surface and maintain its shape under the influence of gravity and squeezing forces.

We have formulated a mathematical model which simulates a finite bolus of gel coating the vaginal epithelium as a power-law fluid spreading down an incline. It describes flow spreading in both the x and y -directions, providing a differential evolution equation for the height of the gel as a function of space and time, $h(x,y,t)$. The new 3-D evolution equation will allow us to numerically compute the propagation of the gel using an implicit finite difference method. The resulting system of equations will be solved using Newton's method with time-adaptation, following the scheme of our prior 2-D model. In on-going work, the numerical simulation will be compared to bench-top fluid flow experiments to check if the evolution equation accurately accounts for the mass propagating in both the x - and y -directions. Initial and environmental conditions will be considered. Developing a reliable math model will allow us to choose the most optimal gel formulation based on its performance. Future versions of the math model will also be improved to account for additional perturbation forces like squeezing and slip.



3:50 pm

“When Do Bees Make a Beeline?”

Jason Palikij, jatku@ku.edu

Biological Sciences

University of Kansas, Lawrence, KS 66045

Faculty Sponsor: Dr. Rudolf Jander

Foraging honeybees, about to head home, were artificially displaced perpendicular to their home direction. Do the bees correct their homing direction appropriately after such as displacement? The result showed that bees displaced at a location close to the hive would depart in a direction towards the hive. This is in contrast to previously published experiments in which the bees were displaced at great distances (100 meters or more) from the hive will depart in a parallel path to their initial outward path. Next, the foraging bees were trained to increasingly longer distances, again displaced, and their departure bearings were measured. Eventually at 20 meters and 60 meters the result is that the change of departure orientation was observed- the perpendicularly displaced bees ignored the displacement and departing in the same, now wrong, compass direction, as if they had not been displaced. This suggests a changeover from peripheral (near the hive) to distal (distantly form the hive) orientation.

4:10 pm

“Psychosocial Functioning of Pediatric Renal and Liver Transplant Recipients”

Yelena Wu, yelenawu@ku.edu

Clinical Child Psychology

University of Kansas, Lawrence, KS 66045

Faculty Sponsor: Dr. Ric G. Steele

In recent decades, liver and kidney transplantations have been increasingly used as a treatment for children with end-stage liver and renal disease. While important medical advances have extended the life expectancy of children with these chronic illnesses, the transplant experience, in addition to the experience of having a chronic illness, places a considerable amount of stress on children and their caregivers. A better understanding of the psychosocial functioning of these children may improve adherence to post-transplant medical regimens and ultimately long-term health outcomes.

The current body of research is inconclusive with regard to psychosocial problems that pediatric transplant recipients may experience. The purpose of the present investigation is to further examine parent- and child-reported child psychosocial functioning post-transplantation on a widely used measure of psychosocial functioning, and to extend previous research using a larger sample size. Participants included 65 children who received kidney or liver transplantation and 72 parents who completed a standardized measure of children’s psychosocial functioning.

Although post-transplant children reported significantly fewer psychosocial difficulties than the normative average, parents reported that children had some psychosocial difficulties, with a higher than expected percentage of children receiving scores within a ‘clinically significant’ range. There were few differences in psychosocial functioning between boys and girls, liver and kidney recipients, and no differences between cadaveric organ and living donor organ recipients. Given the discrepancy between parent and child report, the results suggest that children may underreport psychosocial difficulties following transplantation.



4:30 pm

“Methanobactin-promoted dissolution of Cu-substituted borosilicate glass”

Ezra Kulczycki, ezra55@ku.edu

Geology

University of Kansas, Lawrence, KS 66045

Faculty Sponsors: Drs. David A. Fowle and Jennifer A. Roberts

Mineral weathering plays an important role in the global cycling of carbon and metals and there is an increasing realization that subsurface microbial activity may be a key factor controlling specific biogeochemical reactions and their rates. Methanobactin (mb) is an extracellular copper-binding compound excreted by methanotrophs to acquire copper for the regulation of methane oxidation. Bioavailable Cu regulates the expression and activity of pMMO versus sMMO (particulate versus soluble methane monooxygenase, respectively), key enzymes responsible for bacterial methane oxidation. In this study, we investigate the effect of methanobactin on the dissolution of Cu-substituted borosilicate glass at low temperature and near neutral pH conditions, using batch dissolution experiments. Methanobactin promotes the dissolution of Cu-substituted glasses at rates faster than control experiments. Glasses with lower concentrations of copper (80 p.p.m.) or no copper are dissolved more rapidly by methanobactin than those with more abundant copper (800 p.p.m.). Within the first 2 hours of reaction, methanobactin sorption onto glass surfaces limits mass transfer of Cu into solution, and at higher concentrations (100 μ molal) of the ligand, inhibits dissolution rates of all glass formulations. These results suggest that both the concentration of methanobactin in solution and the solid phase Cu concentration impact silicate weathering rates and related cycling of carbon in near-surface geologic settings.



Advanced Graduate Students

**Judges: E. Morris, S. Macdonald, G. de Boer
(Pine Room, Kansas Union)**

1:10 pm “Flummoxing female preference: discrepancy between preference and song in shield-back katydids”

Jeffrey Cole, jeffcole@ku.edu
Ecology and Evolutionary Biology
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Jennifer M. Gleason

Sexual selection theory predicts male mating traits evolve to match female preferences, because males possessing traits that satisfy female preferences enjoy high reproductive success. Male mating traits may therefore diverge in population isolates incorporating distinct female preferences. Over time, incompatible mating systems may result, forming new species. If sexual selection is producing an interpopulation difference in a male mating trait, mean trait and preference are expected to coincide in all populations. This prediction was tested in two closely related species of shield-back katydids (genus *Aglaothorax*) with statistically significant distributions of the number of pulse trains per chirp in male songs. Female preference functions were measured using choice tests, during which randomized stereo pairs differing in pulse train number were broadcast to females. The binary responses were analyzed with logistic regression. Data from *A. morsei* support the prediction, showing a stabilizing preference peak at 10 pulse trains per chirp, close to the population mean of 8 ± 2 (logistic regression, $p < 0.0001$). Trait and preference distributions are mismatched in *A. longipennis*, where males call with 4 ± 2 pulse trains per chirp, but female preference is a broad plateau centered at 12 pt/chirp (logistic regression, $p < 0.0001$). I suspect strong natural selection pressures within the *A. longipennis* population lie behind the pronounced mismatch between trait and preference.

1:30 pm “Position around a tree: consequences for pheromone detection”

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Faculty Sponsor: Dr. Jennifer M. Gleason

The air flow pattern expected around a cylindrical object such as a tree in slow wind is predicted from fluid mechanics to have areas of faster flow (upwind) and slower recirculating flow with eddies (downwind). An organism located on the surface of a tree would therefore experience different flow depending on its circumferential position. If that organism was searching for a chemical signal, such as a pheromone plume, it might maximize its probability of chemodetection by placing itself in areas of greatest flow speed (the upwind surface of the cylinder, i.e. in front of the separation points). We tested whether wood cockroaches in the genus *Parcoblatta* exhibit such upwind positioning; they live in forests, and males actively fly from tree to tree while searching for females releasing sex pheromone. In contrast to an expectation of upwind preference, male cockroaches were evenly distributed around trees relative to upwind (measured with a novel “feather boa” flow visualization technique), even though the wind direction was relatively steady. We investigated whether sex pheromone could be



detected at any location around a cylindrical surface in a laboratory flow chamber using *Bombyx mori* wing fanning as a bioassay. Although upwind moths arrayed on the surface detected pheromone more rapidly, pheromone detection occurred at least a third of the time at any position, which could explain the even distribution of *Parcoblatta* males around trees.

1:50 pm “Exploring species boundaries with phylogeography and morphometrics using the polytypic minnow *Notropis stramineus*”

Kendra J. Pittman, kjpi@ku.edu
Ecology and Evolutionary Biology
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Faculty Sponsor: Dr. Jennifer M. Gleason

Understanding the origins of biodiversity is central to the study of speciation. To accurately document biodiversity, we must be able to account for both morphological and genetic aspects of diversity. Unfortunately, patterns of genetic diversity are often hidden by patterns of morphological diversity. The field of phylogeography uses various methods to explore the genetic diversity of species across geography and to test whether descriptions of morphological variation correctly depict diversity coded in DNA.

The cyprinid fish *Notropis stramineus*, commonly known as the Sand Shiner, provides a unique opportunity to investigate the genetic diversity of a species in comparison to its morphological diversity. The Sand Shiner is a minnow with a widespread distribution across eastern North America. Across this range, this species shows great morphological variation that many authors have partitioned into two subspecies, one eastern (*N. s. stramineus*) and one western (*N. s. missouriensis*). I will present work on both the morphological and genetic divergence of the Sand Shiner across its distribution and compare and contrast the morphological and genetic variation for concordance. Specifically, I will examine the hypothesis that the subspecies are actually cryptic species needing new names and descriptions.

2:10 pm Break

2:20 pm “Permian and Triassic Trees as High-Latitude Paleoclimate Indicators”

Patricia Ryberg, rybergp@ku.edu
Ecology and Evolutionary Biology
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Edith L. Taylor

Permineralized logs and wood specimens have been found in the central Transantarctic Mountains, Antarctica. The Permian of Antarctica was dominated by the *Glossopteris* flora with a complete floral turnover in the Triassic to the *Dicroidium* flora. Antarctica during both the Permian and Triassic was at high latitudes, much like today, indicating that these wood specimens represent high latitude growth. Ring and cell analysis on the specimens using both modern dendrochronological techniques and those tailored for fossil wood specimens indicates an equitable climate for both periods. The presence of tree rings are believed to represent annual growth since Antarctica was in darkness for several months of the year, thus preventing photosynthesis during the winter. The presence of a large amount of earlywood (14-234 cells) and little latewood



(1-5 cells) indicates a rapid transition to dormancy, suggesting that tree growth occurred up until inadequate light levels prevented growth. With no forest growth at high latitudes today, a modern-day comparison can not be performed. These unique specimens represent a time of global change from the presumably cooler Permian to the greenhouse Triassic. These climatic differences are not represented in tree growth, presenting problems in paleoclimate reconstruction. Paleoclimate models conflict with paleoflora data at high latitudes suggesting that physical parameters in modeling need to be reanalyzed.

2:40 pm “Structural Modification of Paclitaxel to Reduce Interaction with P-Glycoprotein”

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Pharmaceutical Chemistry
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Kenneth L. Audus

Paclitaxel is a chemotherapeutic that was approved in the early 1990's and is effective against a wide variety of cancers but is not effective against cancer of the CNS. Although paclitaxel is lipophilic, it does not cross the blood-brain barrier (BBB) because it undergoes active efflux by P-glycoprotein (P-gp), a membrane transporter expressed at the brain endothelium. Paclitaxel analogues capable of evading P-gp while retaining potency are of interest as possible treatments for CNS localized tumors for which there are currently limited treatment options. One approach to reducing P-gp interaction is the development of paclitaxel analogues which due to structural modification are no longer substrates for P-gp, but maintain their chemotherapeutic effect.

In collaboration with the KU Department of Medicinal Chemistry, a variety of structural modifications of paclitaxel were examined including epimerization at the C10 position, addition of nutrient-like groups at the C7 or C10 positions as well as structural modifications within the C13 side-chain. *In vitro* assays such as Rhodamine-123 uptake by bovine brain microvessel endothelial cells (BBMECs) were used to detect potential P-gp interactions. Current data suggest that paclitaxel can in fact be structurally modified to reduce interaction with P-gp and application of this result could lead to paclitaxel analogues that are useful in the treatment of CNS localized tumors.

3:00 pm “Effects of acute and chronic exposure to bisphenol A on SULT1A1 activity in the human placental choriocarcinoma cell line BeWo”

Pallabi Mitra, pmitra77@ku.edu
Pharmaceutical Chemistry
University of Kansas, Lawrence, KS 66045
Faculty Sponsor: Dr. Kenneth L. Audus

Purpose: The sulfotransferase enzyme SULT1A1 is expressed in the human placenta but little is known about its placental function or regulation. Bisphenol A exhibits estrogenic properties and regulates the expression of many estrogen-responsive genes. Since its placental concentrations are five fold higher than maternal plasma concentrations, and estrogenic compounds have been shown to inhibit sulfotransferase activity, the objective of this study was to evaluate the effect of bisphenol A on SULT1A1 activity.



Methods: BeWo cells (trophoblast cells of placental choriocarcinoma origin) were utilized as a model of the human placenta. mRNA expression was determined with RT-PCR while enzyme activity was determined with SULT1A1 marker substrate 4 μ M 4-nitrophenol. For chronic exposure studies, BeWo cultures were exposed to bisphenol A for 48 hours.

Results: In the tested concentration range of 500nM-50 μ M, bisphenol A acutely inhibited SULT1A1 only at 50 μ M. Chronic exposure to bisphenol A showed that at concentrations above 100pM, there was a significant decrease in enzyme activity although there was a lack of dose dependency observed in this range. At these concentrations, bisphenol A was not cytotoxic to the BeWo cells. RT-PCR did not indicate any change in SULT1A1 mRNA levels in the treated cells relative to the control.

Conclusion: Chronic exposure of BeWo cells to bisphenol A produced a significant decrease in enzyme activity. The lack of any effect on the mRNA levels seems to indicate that the regulatory effect is post-transcriptional in nature. Future studies will examine the effects of 17 β -estradiol and selected phytoestrogens on placental SULT1A1.

3:20 pm Break

3:30 pm “An *in situ* model system for the simultaneous assessment of physical and biological barriers to drug absorption in the rat intestinal mucosa”

Daniel Mudra, dmudra@ku.edu

Pharmaceutical Chemistry

University of Kansas, Lawrence, KS 66045

Faculty Sponsor: Dr. Ronald T. Borchardt

The absorption of drug molecules across the intestinal mucosa is limited by physical and biological barriers including paracellular tight-junctions, efflux transporters (e.g., P-glycoprotein; P-gp) and metabolizing enzymes (e.g., cytochrome P450; CYP). These well characterized barriers are often modulated by concomitantly administered drugs and possibly by components of the drug formulation. Recent *in vitro* studies suggest that drug-solubilizing agents commonly used in dosing pre-clinical lab animals, may inhibit these clearance mechanisms thereby increasing the amount of investigative drug reaching the blood supply. Therefore, it is worthwhile to develop an *in situ* model to simultaneously assess modulation of these barriers in the intestinal mucosa. In this study, segments of rat intestine were perfused with atenolol (paracellular permeant) and verapamil (transcellular permeant subject to CYP- and P-gp-mediated clearance). Levels of unchanged drug and the CYP-mediated metabolite, norverapamil, were measured in the intestinal lumen and mesenteric blood. Changes in verapamil concentration had little effect on the permeability of atenolol or verapamil. However, there were concentration-dependent increases in the rate of norverapamil formation and the fraction of norverapamil appearing in the plasma ($p < 0.05$), consistent with the selective modulation of CYP- and P-gp mediated processes. Similarly, known modulators of CYP and P-gp selectively inhibited metabolic- and transport-mediated clearance of verapamil ($p < 0.05$) without any effect on physical absorptive barriers. Based on these data, it appears this *in situ* model will allow for the simultaneous assessment of the modulation of physical and biological barriers to drug absorption in the rat intestinal mucosa.