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## Michigan Regional Chapter of the Society of Toxicology



## NEWSLETTER

*Volume 22*

*Number 3*

October, 2004

Editor: Lawrence H. Lash

Associate Editor: Randall J. Ruch

### *MESSAGE FROM THE PRESIDENT*

(submitted by Stephen Frantz)

Greetings to all members of the Michigan Regional Chapter of the Society of Toxicology. I want to first thank our outgoing President, Bob Meeks, for his contributions and leadership during my first year as President-Elect and in helping me to have a smooth transition to the President's role this year. I am excited to continue working with the MISOT Council and its newly-elected officers, including our new President-Elect, Jim McKim, new Treasurer, Paul Stemmer, and new Councilor, Yvonne Frater. We will continue to have Councilor contributions from Bob Meeks (as Past President) and John LaPres (our outgoing Treasurer), and Paul Jean will return for his second year on the Council. Please join me in welcoming your new officers for the coming year.

Your Council has been busy during the early weeks of this Fall planning what we hope will be another excellent Fall Symposium for Friday, November 12, 2004. We have once again selected the Kellogg Center on the campus of Michigan State University in East

Lansing, based on the very positive feedback received last year. Through the hard work of your new officers and returning Councilors, led by our President-Elect Jim McKim, we have been able to assemble an excellent slate of speakers from both academic and industry backgrounds for the topic of “Mechanisms of Idiosyncratic Toxicity.” We invite all students, research staff and post-docs to consider submitting abstracts for the poster presentation portion of this meeting. We will again be awarding travel grants for the poster presentations, with a \$500 prize for the best student poster, a \$500 prize for the best poster from research staff, and a \$500 prize and an invitation to speak at the Spring MISOT meeting for the best poster presented by the postdoctoral winner. These prizes are intended to be applied toward travel to the Society of Toxicology meeting in New Orleans next Spring. Please help us to encourage participation in these categories.

The student liaison for our Chapter will be led this year by Tracy Pickering, who is a graduate student at Western Michigan University. Tracy replaces Jim Luyendyk from Michigan State in this role and she will also serve as a Co-Chair of the Student Advisory Committee to the national Society of Toxicology. Please join me in welcoming Tracy to her important new responsibility and in giving your support and help to our efforts to recruit new student members. Special thanks from the Chapter Council to Jim Luyendyk for his outstanding contributions and enthusiasm last year for recruiting student participation and contributions to the Chapter’s activities. As always, your ideas and suggestions on how to improve Chapter activities and increase our membership can be extended to any Chapter officer.

We have already had an excellent start with the early efforts of the Chapter’s leadership and I am looking forward to seeing as many of you as possible next month in East Lansing.

***The Michigan Chapter of SOT  
Fall 2004 Meeting***

**“Mechanisms of Idiosyncratic Toxicity”**

- 8:00 a.m. Registration
- 8:30 a.m. Continental Breakfast
- 8:45 a.m. Welcome – Stephen W. Frantz, Ph.D., D.A.B.T., MPI Research  
  
Remarks – James M. McKim, Ph.D., D.A.B.T., CeeTox, Inc.
- 9:00 a.m. Robert A. Roth, Ph.D., D.A.B.T., Michigan State University  
*“Inflammation as a Susceptibility Factor for Hepatotoxicity: A Connection to Drug Idiosyncrasy?”*
- 9:45 a.m. Mark J. Reasor, Ph.D., D.A.B.T., West Virginia University  
*“Drug-Induced Phospholipidosis: Characteristics and Consequences”*
- 10:30 a.m. Break
- 10:45 a.m. Neal Goodwin, Ph.D. ProNAi Therapeutics, Kalamazoo, MI  
*“The Humanized Mouse Model as a Tool for Evaluating Idiosyncratic Toxicity”*
- 11:30 a.m. Lunch and Posters
- 1:00 p.m. Michael Reily, Ph.D. Pfizer Inc./Ann Arbor  
*“Metabonomics as a Tool For Investigating Idiosyncratic Toxicity”*

1:45 p.m. Craig Harris, Ph.D.  
University of Michigan  
"Oxidative Stress: Intrinsic  
Factors That Can Tip the  
Balance Between  
Hypersensitivity and Resistance  
in the Developing Conceptus"

2:30 p.m. Chapter Business

3:00 p.m. Adjournment

## MISOT Registration Form

Deadline for registration and abstract submission  
is November 1, 2004

Name: \_\_\_\_\_

Affiliation (Company, University, etc):  
\_\_\_\_\_

Address: \_\_\_\_\_

City, State, Zip:  
\_\_\_\_\_

E mail: \_\_\_\_\_

Poster Presentation: Yes  No

*If yes: Please provide an abstract of no more than 250 words including, title of poster, authors and affiliations. These abstracts should be sent via email to: [pmstemmer@wayne.edu](mailto:pmstemmer@wayne.edu). Please include in the body of the message whether you are a student, technical staff or Post-Doc.*

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### WHAT IS MISMR?

The Michigan Society of Medical Research (MISMR) is an organization whose major objective is to advance and expedite research in the biological sciences, particularly that which promotes human and animal welfare and survival through the prevention, control, and cure of disease. Of special concern to MISMR is the public understanding of the methods, needs, and accomplishments of biomedical research and testing. The organization has a speaker's bureau available to Michigan schools and each year MISMR sponsors an essay and scholarship contest on animal research for secondary school students. **Look for an announcement for the 2005 essay competition in the near future!**

MISMR is, therefore, an important educational resource in Michigan and provides the means of counteracting animal activist measures aimed at institutions and research facilities. MISMR is consequently an organization that members of the Michigan Regional Chapter of the Society of Toxicology should also support. Please see the MISMR website ([www.mismr.org](http://www.mismr.org)) for how you can: (1) support MISMR through individual or corporate memberships, (2) find information on how you can actively participate, and (3) learn how to make use of the resources available.

Paul E. Newton, Ph.D., D.A.B.T.  
MPI Research, Inc.  
MISMR Board of Directors

#### Registration Fee:

- Member (\$50.00)  
 Student (member or non-member)(\$25.00)  
 Non-member (\$75.00)

Membership applications can be obtained at:

**Michigan Chapter:**

<http://www.toxicology.org/memberservices/regionalchapter/michigan/MichiganChaptDues.pdf>

*Please make registration checks payable to: The Society of Toxicology*

*Please send registration form to:*

*Paul Stemmer*

Wayne State University  
Institute of Environmental Health Sciences  
2727 Second Ave., Suite 4000  
Detroit, MI 48201

If you have questions: [pmstemmer@wayne.edu](mailto:pmstemmer@wayne.edu)

If you require Hotel accommodations contact The Kellogg Center: (800) 407-8486

When making reservations please say you are attending the Michigan SOT meeting and they will give you a discount rate of \$85.00 (single occupancy). These rooms are only available for Thursday November 11th.

## CALL FOR ENTRIES:

The **Michigan Society for Medical Research (MISMR)** annually sponsors an essay contest open to all Michigan middle school students. It is part of MISMR's educational outreach program to promote awareness of the benefits and the process of biomedical research, and increase awareness and interest in science. Entries will be judged on originality, creativity (**including a creative title**), command of the English language, and the demonstration that an extra effort was made to learn about biomedical research and why animals are used. Students are asked to describe one specific example of a situation in which animals help people. You can use an example from your own life or from the lives of your relatives or friends. Give as much detail as possible; for example, what kind of animal (or animals) is involved, why that animal was chosen, and what kind of people benefit the most. Creative answers will be rated the highest.

Students are encouraged to research some or all of the following ideas:

- **Why** animal research is necessary and the limitations of other alternatives (e.g., cell culture, computer simulations).
- **How** biomedical research has helped in the treatment of diseases for both humans and animals.
- **How** biomedical research helped a friend, family member, pet, livestock, or endangered species.
- **How** animal research helps with environmental protection (e.g., toxicity testing of pesticides).
- **What** the laws and regulations governing the use of animals in research are.

### AWARDS...

- The **STUDENT FINALIST** will be awarded a **\$500 cash prize and plaque**.
- The **TEACHER** of the student finalist will be awarded a **cash prize of \$100**.
- **HONORABLE MENTIONS** will be awarded a **\$50 cash prize and merit certificate**.
- **ALL STUDENTS** who enter receive a merit certificate.

*Winning essays will be published in a special booklet and the first place winners will be invited to the Michigan Society for Medical Research*

*annual meeting in 2005. Entries become the property of MISMR and may be reprinted, published, or distributed for educational purposes.*

**WINNERS ONLY** will be notified by the end of March, 2005.

All Michigan middle school students grades 6–8 are eligible to enter.

Submit essays in standard English with a bibliography that **must cite several different references** (may include documented oral sources). Essays should be typed on 8½" x 11" white paper, double-spaced, and 500–750 words.

Essay should be the original work of the student who enters.

Submit one coversheet followed by two copies of the essay. There should be **NO** identifying information on the essays **except for the title**. The coversheet needs the following information:

Title of Essay	School Address
Student's Name	School Phone Number
Home Address	Teacher's Full Name
Home Phone Number	Teacher's Email address
Grade Level	Class Title
Name of School	Small Student Photo

Entries accepted any time prior to deadline but must be postmarked by **December 15, 2004**.

Send entries to:

MISMR Essay Contest  
P.O. Box 3237  
Ann Arbor, MI 48106-3237

### **Other MISMR Awards:**

Nominations for the 2005 Bennett J. Cohen Education Leadership or the Science Education award should be postmarked by **January 26, 2005** and sent to:

Chair, Advocacy Awards  
MISMR, P.O. Box 3237  
Ann Arbor, MI 48106-3237

Tel: 734-763-8029; Fax: 734-930-1568

Email: [mismr@umich.edu](mailto:mismr@umich.edu)

Web: [www.mismr.org](http://www.mismr.org)

## STUDENT/POST-DOC NEWS

For those of you who do not know me, my name is Tracy Pickering. I represent the Michigan Regional Chapter on the SOT Student Advisory Committee. I hope to see everyone at the Fall meeting. The topic for this year's meeting is "Mechanisms of Idiosyncratic Toxicity." The Fall meeting is a great opportunity to talk with some of the experts in the field. Make sure to submit your abstract! The deadline for abstract submission is November 1<sup>st</sup>. The following awards will be presented:

- \$500 award for the best student poster
- \$500 award for best poster from research staff
- \$500 award plus an invitation to present a 20 minute talk at the Spring meeting for best poster from a postdoctoral fellow

Remember, unless you are a member of MISOT, you are not eligible for the awards described above. Applications for Regional Chapter membership will be reviewed if they accompany abstract submission paperwork for the Fall meeting. Also, make sure to join National SOT before the annual meeting to receive discounted registration rates.

Visit the following website for more information:  
<http://www.toxicology.org/MemberServices/StudentServices/studentServices.html>

Any questions on membership can be forwarded to [pmstemmer@wayne.edu](mailto:pmstemmer@wayne.edu) or [tracy.pickering@mpiresearch.com](mailto:tracy.pickering@mpiresearch.com)

See everyone on November 12<sup>th</sup>!

Tracy

## MEMBERSHIP NEWS

*News items about activities involving our members are invited for this section.*

## MEMBER ABSTRACTS OF RECENTLY PUBLISHED PAPERS

*Recent publications from the laboratory of Patti Ganey, Bob Roth, and Jane Maddox:*

Kinsler, S., Sneed, R.A., Roth, R.A., and Ganey, P.E.: Neutrophils Contribute to Endotoxin Enhancement of Allyl Alcohol Hepatotoxicity. *J. Toxicol. Environ. Health* 67: 911-928, 2004.

Maddox, J.F., Domzalski, A. C., Roth, R.A., and Ganey, P.E.: 15-Deoxy Prostaglandin J2 enhances allyl alcohol-induced toxicity in rat hepatocytes. *Toxicol. Sci.* 77: 290-298, 2004.

Allyl alcohol causes hepatotoxicity that is potentiated by small doses of bacterial lipopolysaccharide (LPS) through a cyclooxygenase-2 (COX-2)-dependent mechanism. The COX-2 product prostaglandin D(2) (PGD(2)) increases hepatocyte killing by allyl alcohol in vitro. In the present study the ability of the nonenzymatic product of PGD(2), 15-deoxy-Delta12,14-prostaglandin J(2) (15d-PGJ(2)), to increase the cytotoxicity of allyl alcohol was evaluated. In a concentration-dependent manner, 15d-PGJ(2) significantly augmented cell death caused by allyl alcohol in isolated rat hepatocytes. 15d-PGJ(2) also increased the cytotoxicity of acrolein, the active metabolite of allyl alcohol. An agonist for the PGD(2) receptor neither reproduced the increase in allyl alcohol-mediated cytotoxicity nor altered the response to 15d-PGJ(2). Similarly, these responses were not affected by either an agonist or an antagonist for the peroxisome proliferator-activated receptor-gamma. The enhancement by 15d-PGJ(2) of allyl alcohol-mediated cell killing was unaffected by augmentation or inhibition of cAMP. Protein synthesis was markedly decreased by 15d-PGJ(2), but inhibition of protein synthesis alone with cycloheximide did not increase allyl alcohol-mediated cell killing. Allyl alcohol at subtoxic concentrations increased translocation of nuclear factor kappa B (NF-kappaB), whereas at cytotoxic concentrations no translocation occurred. 15d-PGJ(2) inhibited translocation of NF-kappaB from the cytosol to the nucleus both in the presence and absence of allyl alcohol. Like 15d-PGJ(2), MG132, an inhibitor of NF-kappaB activation, enhanced allyl alcohol-induced hepatocyte death. Together these results indicate that 15d-PGJ(2) augments hepatocyte killing by allyl alcohol, and the mechanism may be related to the inhibition of NF-kappaB activation.

Luyendyk, J.P., Maddox, J.F., Green, C.D., Ganey, P.E., and Roth, R.A.: Role of hepatic fibrin in idiosyncrasy-like liver injury from lipopolysaccharide-ranitidine coexposure in rats. Accepted, *Hepatology*, 2004.

Luyendyk, J.P., Mattes, W.B., Burgoon, L.D., Zacharewski, T.R., Maddox, J.F., Cosma, G.N., Ganey, P.E., and Roth, R.A.: Gene expression analysis points to hemostasis in livers of rats cotreated with lipopolysaccharide and ranitidine. *Toxicol. Sci.* 80: 203-213, 2004.

Harrigan, G.G., Laplante, R.H., Cosma, G.N., Cockerell, G., Goodacre, R., Maddox, J.F., Luyendyk, J.P., Ganey, P.E., and Roth, R.A.: Application of high-throughput Fourier-transform infrared spectroscopy in toxicology studies: contribution to a study on the development of an animal model for idiosyncratic toxicity. *Toxicol. Letters* 146:197-205, 2004.

Copple, B.L., Rondelli, C.M., Maddox, J.F., Hoglen, N.C., Ganey, P.E. and Roth, R.A.: Modes of cell death in rat liver after monocrotaline exposure. *Toxicol. Sci.* 77: 172-182, 2004.

**Recent publications from the laboratories of B.L. Upham and J.E. Trosko:**

Nakamura, Y., J.E. Trosko, C-C Chang, **B.L. Upham** (2004). Psyllium extracts decreased the neoplastic phenotypes induced by the Ha-Ras oncogene transfected into a rat liver oval cell line. *Cancer Lett.* **203**:13-24.

Inhibition of gap junctional intercellular communication (GJIC) by tumor promoters and oncogenes has been implicated in the removal of initiated cells from the suppression of growth by neighboring cells in the tumor promoting step of carcinogenesis. The GJIC of WB-*Ha-ras* cell line is GJIC-deficient and they are capable of anchorage independent growth (AIG). The ethanol extract of Psyllium increased GJIC 1.65-times and decreased AIG in both number and size of colonies in WB-WB-*Ha-ras* cells. Histochemical staining of the gap junction protein, connexin43, showed that psyllium restored gap junction plaques on the plasma membrane of the *Ha-ras*-WB cells. In conclusion, the ethanol extract of psyllium reversed two tumor cell phenotypes, namely reduced GJIC and AIG, induced by the *Ha-ras* oncogene.

Machala, M, L. Bláha, J. Vondráček, J.E. Trosko, J. Scott, **B.L. Upham**, (2004). Inhibition of gap junctional intercellular communication by polychlorinated biphenyls: inhibitory potencies and screening for potential mode(s) of action. *Toxicol. Sci.* **76**:102-111.

Polychlorinated biphenyls (PCBs), a structurally diverse group of environmental pollutants, are effective promoters in two stage cancer models, which implies that epigenetic mechanisms are involved. Inhibition of gap junctional intercellular communication (GJIC) belongs among critical epigenetic events of tumor promotion. We determined the relative potencies of a series of environmentally

relevant PCB congeners to inhibit GJIC *in vitro* in a rat liver epithelial cell line with pluripotent-oval cell characteristics. The nonplanar PCBs were potent inhibitors of GJIC, whereas the coplanar PCBs did not inhibit GJIC. We then compared the effects of the coplanar PCB 126 (3,3',4,4',5-pentachlorobiphenyl) and the noncoplanar PCB 153 (2,2',4,4',5,5'-hexachlorobiphenyl) with effects of two model GJIC inhibitors, a tumor promoter 12-*O*-tetradecanoyl-phorbol-13-acetate (TPA) and epidermal growth factor (EGF). In contrast to TPA or EGF, PCB 153 elicited a long-term down-regulation of GJIC (up to 48 h). Using Western blot analysis with phospho-specific antibodies it was found that PCB153 and not PCB126 activated mitogen-activated protein kinases ERK1/2, however in contrast to TPA and EGF, this activation was observed at the time points subsequent to GJIC inhibition. Moreover, blocking of ERK1/2 activation did not prevent the GJIC inhibition induced by PCB153. Therefore, additional intracellular signaling pathways potentially involved in the down-regulation of GJIC by PCBs were screened by using specific chemical probes inhibiting serine/threonine kinases, tyrosine kinases and phospholipases. The selective inhibition of diacylglycerol lipase partially blocked and the selective inhibition of Src kinases and phosphatidylcholine-selective phospholipase C (PC-PLC) completely blocked the inhibitory effects of the noncoplanar PCB on GJIC, indicating that PC-PLC and Src might be upstream regulators of PCB-induced inhibition of GJIC.

Trosko, J.E., C.C. Chang, **B.L. Upham**, M.H. Tai (2004). Ignored hallmarks of carcinogenesis: Stem cells and cell-cell communication. *Ann. N.Y. Acad. Sci.* **1028**:1-10.

Since carcinogenesis is a multi-stage, multi-mechanism process, involving mutagenic, cell death and epigenetic mechanisms, during the "initiation/promotion/and progression" phases, chemoprevention must be based on understanding the underlying mechanism(s) of each phase. In principle, prevention of each of these phases could reduce the risk to cancer. However, because reducing the mutagenic/initiation phase to a zero level is impossible, the most efficacious intervention would be at the promotion phase that requires a sustained exposure to promoting conditions/agents. In addition, assuming the "target" cells for carcinogenesis are the pluri-potent stem cells and their early progenitor or transit cells, chemoprevention strategies for inhibiting the promotion of these two types of pre-malignant "initiated" cells will require different kinds of agents. An hypothesis will be proposed that involves adult stem cells, which express Oct4 gene and lack gap junctional intercellular communication (GJIC-) or the early progenitor cells which express GJIC+ and are partially-differentiated, if initiated, will be promoted by agents that either inhibit secreted negative growth

regulators or by inhibitors of GJIC. Consequently, anti-tumor promoting chemopreventing agents to each of these two types of initiated cells must have different mechanisms of action and work on different target cells. Assuming stem cells are target cells for carcinogenesis, an alternative method of chemoprevention would be to reduce the stem cell pool. Examples of many classes of anti-tumor promoter chemopreventive agents, such as green tea components, resveratrol, caffeic acid phenethyl ester, that either up-regulate GJIC in stem cells or prevent the down regulation of GJIC by tumor promoters in early progenitor cells will be provided. In addition, the use of human pluripotent stem cell systems, that can be induced to form 3-dimensional "organoid" structures, will be discussed as a more realistic model system to screen for relevant chemopreventive agents.

#### **2005 SOT Abstract from L.A. Obert et al.:**

In situ Quantitative Evaluation of Peroxisomal Proliferation in the Non-human Primate Liver via Laser Scanning Cytometry (LSC). Obert LA, Kostrubsky S, Okerberg C, Wijsman J, Urda E, Hanson J, Toy K, Collard W, Maier WE, Bell R, Zwick L, Frantz S, Dunstan R, Adler R.

Laser scanning cytometry (LSC) and biochemical markers were employed to evaluate the effect of a peroxisome proliferator-activated receptor (PPAR) mixed beta/alpha agonist under development for the treatment of dyslipidemia. Two- to 3.5-year old male cynomolgus monkeys received test compound at 0, 0.1, 0.3, 1, 3, or 10 mg/kg by oral gavage for 28 consecutive days. At necropsy, there were no drug-related gross pathologic findings. Immunohistochemical staining for the peroxisomal membrane protein (PMP70) within the hepatocytes was qualitatively increased in drug-treated monkeys compared to controls. Quantitative evaluation of the immunohistochemical labeling of peroxisomes via LSC confirmed an increase in peroxisomal labeling in all dose groups, which plateaued at drug levels  $\geq 0.3$  mg/kg. Similarly, liver biochemical analyses revealed increased peroxisomal beta-oxidation and acyl CoA oxidase activities in all dose groups, which also plateaued at  $\geq 0.3$  mg/kg. These changes correlated with increases in absolute and relative liver weights. The liver weight changes corroborated the histopathologic findings (hepatocellular hypertrophy) at  $\geq 0.3$  mg/kg. The hepatocellular hypertrophy was characterized by an increase in cell size due to increased quantities of granular eosinophilic cytoplasm. Interestingly, the plasma and liver concentrations of the test compound increased with increasing dosage. However, the above data suggests that maximal peroxisomal activity was achieved at 0.3 mg/kg indicating a saturation effect. In conclusion, quantitative evaluation of hepatocellular peroxisome levels was achieved in situ via LSC, which correlated

well with biochemical activities, organ weight changes, and histopathology.

#### **Rodent Subchronic Toxicity Studies with the Peptide Antibiotic XMP.629**

Roger J. Hawks<sup>1</sup>, Stephen W. Frantz<sup>2</sup>, James T. Secrest<sup>2</sup>, Kathleen E. Meyer<sup>1</sup>, XOMA (US) LLC., Berkeley, CA.,<sup>2</sup> MPI Research, Mattawan, MI.

XMP.629 is a novel D-linked 9-amino acid peptide based on a natural antimicrobial protein, and has been tested in Phase I/II trials as a topical treatment for acne. Subchronic 30- and 90-day studies have been performed in the rat. Due to low oral bioavailability, these studies used subcutaneous administration to maximize systemic exposure. In both studies, injection site lesions were noted at gross necropsy and histopathology. These findings included thickened skin, hemorrhage, necrosis and inflammation. Test article deposition at the site of injection was seen in the 30-day study. In both studies, systemic effects were seen that appeared to be indirect, secondary reactions to the injection site inflammation. These systemic effects in the 30-day study included  $\uparrow$  neutrophil and monocyte counts,  $\uparrow$  spleen weights,  $\downarrow$  Hgb, Hct and RBCs, and  $\uparrow$  reticulocyte counts. The 90-day study showed these alterations plus  $\uparrow$  liver weight,  $\uparrow$  lymphocyte, basophil and leukocyte counts, as well as histopathology findings of injection site fibrosis, granulation tissue, macrophage infiltration, Kupffer cell hypertrophy, mesenteric lymph node (LN) histiocytosis and splenic monocyte/macrophage hyperplasia. The  $\uparrow$  spleen weight and hematology alterations in both studies may indicate mild RBC hemolysis mediated by the strong inflammatory response. Some of the 90-day findings (such as injection site fibrosis and granulation tissue) illustrate a transition from acute to chronic inflammation. The 90-day findings of macrophage infiltration, Kupffer cell hypertrophy, and mesenteric LN histiocytosis likely indicate macrophage-mediated clearance of test article. PK data revealed that the mean high dose AUC<sub>0-24</sub> seen in the 90-day study was 2110 hr\*ng/mL. By comparison, all patient serum samples from a Phase I trial were below the LOQ of 1 ng/mL. The results from these studies demonstrate a high safety margin and support the use of this novel compound in clinical trials.

***Drug Metabolism and Transport:  
Molecular Methods and Mechanisms***

Edited by Lawrence H. Lash

Published by Humana Press (2005) as part of the *Methods in Pharmacology and Toxicology* series.

“This volume presents a collection of chapters on selected aspects of metabolism and transport. The general approach of the chapters is to first present background on the topic to define the state of the science, to summarize key experimental models and methods that are used in the study of the process, and then to evaluate the utility of the various approaches and methods” — from the preface.

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***JANUARY ISSUE PREVIEW***

The January, 2005 Issue of the Newsletter will feature a review of the Fall meeting, the annual report of the chapter, and other items of interest to our members.

Please submit any member news or ideas for the newsletter to your local contact person or directly to the editors. Material for the January newsletter should be submitted no later than January 10, 2005.

***BENEFITS OF MEMBERSHIP***

Don't forget that your membership to the Michigan Regional Chapter of the SOT includes:

- Discounted registration fees for chapter meetings
- Newsletter with chapter and regional news
- Free listing in the newsletter of training and employment opportunities
- Free listing in the newsletter of positions desired

**POSITIONS AVAILABLE**

*Postdoctoral fellowships, research assistantships, government positions, and industrial positions can be advertised in this space. Submissions to the editor should include a brief description of the position and contact information. This service is free to members!*

MPI Research exists to provide comprehensive nonclinical research that meets the requirements of pharmaceutical, medical device, animal health and chemical companies as well as governmental agencies as we partner to bring safer, healthier products to the world.

Due to extreme growth, MPI Research is recruiting for positions in the following departments:

**DEPARTMENT OF SURGERY**

- **SURGICAL STUDY DIRECTOR** – The successful candidate will have overall responsibility for proposal preparation and for the scheduling, performance, monitoring, evaluation, reporting, as well as financial oversight of studies performed in the Department of Surgery. The Surgical Study Director ensures high-level performance of contracted surgical efficacy and safety studies, in a GLP environment, for both regulatory and non-regulatory needs of Sponsors in accordance with international harmonized guidelines and generally accepted procedures for testing of pharmaceuticals, devices or other compounds intended for market. Conduct of these studies would require interaction between the Surgical Study Director and multiple departments within MPI Research including Quality Assurance, Reporting, In-Life and Pathology. He or she also would be responsible for training and professional development of staff, project leaders and technical personnel, as well as marketing and business development of the surgical line.

**Qualifications:** Doctor of Veterinary Medicine with Specialty Board Certification in Veterinary Surgery and surgical research experience, especially in the medical device or pharmaceutical industry. Alternatively, a D.V.M. or V.M.D. with research training and experience at the M.S. or Ph.D. level. Familiarity with animal modeling in a variety of domestic and laboratory animal species is a plus.

#### ADME

- **DIRECTOR OF ADME/SENIOR STUDY DIRECTOR** – This position is responsible for the overall proposal preparation and for the scheduling, performance, monitoring, evaluating and the reporting of studies performed in the ADME product line. Candidates must have 10 - 15 years of required experience in a contract laboratory setting or pharmaceutical industry. GLP experience and general toxicology or specialty areas required. Must have excellent communication skills both written and verbal. Board certified toxicologist preferred.

#### TOXICOLOGY SERVICES

- **Research Associate** – As part of a research team, you will be responsible for administering test materials via various routes (oral, dermal, IV, subcu, IP, IM), measuring body weights, collecting blood samples, and performing detailed observations with a variety of animal species varying from mice to non-human primates.

#### PATHOLOGY SERVICES

- **Research Associate** – As part of a research team, you will be responsible for performing tissue trimming, embedding, microtomy, staining, cover slipping, performing dissections, weighing and measuring internal organs, and following other protocols as instructed with a variety of animal species varying from mice to non-human primates.

For a complete listing of current employment opportunities please visit [www.mpiresearch.com](http://www.mpiresearch.com). If you are interested in joining an organization committed to providing high quality, on-time research that aids in the discovery, development and enhancement of human and animal health and the environment please complete an on-line application @ [www.mpiresearch.com](http://www.mpiresearch.com) or email [HR@mpiresearch.com](mailto:HR@mpiresearch.com).

#### **PK/Metabolism Postdoctoral Position At The Dow Chemical Company**

An industrial postdoctoral position is now available in the Biotransformation Group of the Toxicology and Environmental Research & Consulting Laboratory of The Dow Chemical Company in Midland, Michigan.

The successful candidate will actively participate in the design and implementation of mechanistic and research-based pharmacokinetic/ metabolism studies and in the development of physiologically-based pharmacokinetic models to support various toxicology issues. The candidates are encouraged to publish their research in peer reviewed journals. Postdoctoral positions are one-year contracts renewable up to two years. The ideal applicant will have experience in one or more of the following areas: *in vivo* PK/metabolism studies, *in vitro* metabolism or enzyme kinetic experiments, PK and/or PBPK modeling.

Please contact Dr. Michael Bartels (989-636-9057; [mjbartels@dow.com](mailto:mjbartels@dow.com)), if interested.

*Dow is an equal opportunity employer and offers a competitive compensation and benefits package including 401k, stock purchase, tuition reimbursement and performance incentives.*

#### **POSITION DESIRED**

*Individuals seeking positions in the region can advertise in this section. Submissions to the editor should include a brief description of research interests, experience, education, type of position desired, and geographical location desired. **This service is free to members!***

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