1 USE OF LASER CAPTURE MICRODISSECTION (LCM) IN MOLECULAR TOXICOLOGY RESEARCH.

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Laser capture microdissection (LCM) is a recently developed technique that allows one to rapidly procure morphologically defined cell populations from sections of heterogenous tissues using direct visualization. This technique has greatly expanded the ability of the toxicologist to conduct molecular analyses on a wide array of specific target cells and tissues of interest. Cells obtained by microdissection have been used as a source of genomic DNA, the isolation of mRNA amenable to reverse transcription polymerase chain reaction (RT-PCR), and the generation of expression libraries. LCM has been combined with cDNA microarray hybridization techniques and proteomic methods to provide new and exciting approaches for combining gene expression with traditional morphological methods. This seminar will review microdissection methods and equipment and discuss the utility of LCM in toxicology studies.

2 A PRACTICAL APPROACH TO BLOOD AND LYMPHOID TISSUE (BLT) IN TOXICOLOGY ASSESSMENTS.

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Blood, bone marrow, thymus, spleen, lymph nodes and mucosa-associated lymphoid tissue are a complicated but important interactive system of tissues and cells modulated directly and indirectly by xenobiotics. Evaluation of blood and lymphoid tissues (BLT) has always been part of a standard histopathology and toxicology screen but advanced evaluations of BLT are becoming increasingly important to the rapidly changing fields of immunotoxicology and immunotherapeutic development. The objective of this basic course is to provide contemporary information on the pathophysiology of BLT useful to individuals in regulatory and research areas of toxicology. This course will review important features of i) basic anatomy, function, and evaluation of blood and blood forming organs, ii) anatomy and function of lymphoid tissues and their component parts, iii) terminology, iv) general and toxic immunomodulation, and v) pathophysiology (neoplastic and non-neoplastic responses). Species, sex and age specific differences that may affect the design and outcome of studies, and techniques used to evaluate BLT will be discussed. A practical understanding of the anatomy, terminology, and toxicologic pathology associated with BLT, will aid toxicologists in making proper interpretation of treatment-related changes in safety and efficacy studies, and in communicating this information between disciplines, within teams and to regulatory agencies.

3 ALTERATIONS IN GENE EXPRESSION AS A MECHANISM OF TOXICANT ACTION.

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Over the last several years, it has become apparent that many environmental toxicants exert their effects by the activation or disruption of specific signaling pathways, ultimately resulting in alterations in gene expression. With the completion of the human genome project and the advent of many powerful new technologies, there has been a revolution in our understanding of these mechanisms on the molecular level. The proposed continuing education course is designed to review our current state of knowledge regarding toxicant-induced alterations in gene expression and also identify future directions and research opportunities. The first speaker will focus on our current understanding of the mechanism(s) whereby four receptors, i.e., the Ah receptor (AhR), the Constitutive Androstane Receptor (CAR), the Pregnane X Receptor (PXR), and the Peroxisome Proliferator Activated Receptor (PPAR), mediate the toxicity of four broad classes of chemicals. In contrast to these specific receptor mechanisms, metals exert their toxicity through both stress-response pathways, as well as specific metal-responsive transcription factors. The second speaker will focus on our current understanding of these pathways of toxicant action. The third speaker will review the many exciting discoveries in our understanding of how toxicants alter gene expression during specific windows of development and thereby exert their teratogenic effects. Finally, the fourth speaker will discuss the role of tissue-selective transcription factors on the expression of xenobiotic metabolizing enzymes and how this process impacts toxicant susceptibility. As an advanced course, this curriculum should appeal to toxicologists whose research is in or immediately peripheral to this focus area, but who are interested in gaining a better understanding of the overall subject and its future direction.

4 INTEGRATING TOXICOLOGIC PATHOLOGY INTO COMPOUND EVALUATION AND RISK ASSESSMENT.

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Pathology endpoints are the central response around which human health risk assessment is determined. This course is designed for the general toxicology community to gain an understanding of the basics of toxicologic pathology. Toxicologic pathology encompasses the study of changes in tissue morphology that help define the risk of exposure to xenobiotics. The first presentation will review the basics of pathology studies including tissue processing, pathology review, standard techniques, and efforts being made to standardize the conduct, review, and reporting of pathology studies which are important for appropriate interpretation of data. Other speakers will discuss the structural and functional aspects of the liver and kidney and the general concepts of mechanisms of injury, species and sex differences, background and induced lesions, which are necessary for appropriate risk characterization. The liver is the most common target for xenobiotic-induced adverse effects and the kidney has a central role in filtration, metabolism, and excretion and is frequently a site of toxic injury. Correlating clinicopathology with morphologic and functional alterations is necessary for full understanding of adverse effects. Finally, diagnostic terminology, study data relative to cancer bioassay findings, the steps in tumor development, and their relevance to human health risk will be presented.

5 BASIC PRINCIPLES AND PROTOCOLS IN MOLECULAR TOXICOLOGY.

W. B. Mattes[1], J. W. Davis, II[2], M. K. Walker[3], J. P. Vanden Heuvel[4], M. S. Denison[5] and C. B. Marcus[3]. *[1]Pharmacia, Kalamazoo, MI, [2]Schering Plough Institute, Lafayette, NJ, [3]University of New Mexico, Albuquerque, NM, [4]Pennsylvania State University, University Park, PA and [5]University of California- Davis, Davis, CA.*

Many of the mechanisms through which xenobiotics affect tissues or cells occur at the molecular level. Over the past ten or fifteen years the use of molecular techniques to dissect mechanisms of toxicity has grown greatly. These techniques are used to identify growth regulatory pathways, alterations in gene and/or protein expression, as well as protein:DNA and protein:protein interactions. Accordingly, there has been an explosion in the number of reagents and kits that are commercially available. While these kits and reagents have facilitated the detection of mechanisms of toxicity, a basic understanding of the methods used is just as important. This course will detail a number of basic techniques currently in use in an attempt to give a researcher new to this area information as to which tools may be most relevant with regards to their specific research area. Presentations will include the practical considerations when setting up a given technique as well as references that will help the investigator trouble shoot these systems. Finally, actual data will be shown in an effort to demonstrate the kinds of information that can be obtained by these experiments and the ways in which this information can be interpreted and used to develop hypothesis-driven research. This is a basic level course intended to introduce to the researcher the tools and references that are available to him or her.

6 TWO-STEPPING THROUGH TOXICOGENOMICS: A BASIC PRIMER.

M. J. Cunningham[1], T. Zacharewski[2], R. Somogyi[1] and B. A. Merrick[3]. *[1]Molecular Mining Corporation, Kingston, ON, Canada, [2]Michigan State University, East Lansing, MI and [3]NIEHS, Research Triangle Park, NC.*

Toxicogenomics as used here is broadly defined as gene and protein expression technologies and their application to addressing pertinent issues of toxicology. This basic course will start with an overview of how genomics and proteomics came into existence. Different microarray formats will be covered including cDNA, oligonucleotide, fiber optic, and high-throughput versions of gene expression microarrays as well as a broad overview on proteomics and data analysis. Several landmark papers will be discussed showing how genomics and proteomics can be applied. An in-depth presentation will follow detailing how to set up and run your own microarrays and will cover array manufacture, sample preparation, array hybridization and scanning, and image analysis. In addition, setting up and running 2D protein gels will be discussed as well as their interpretation using mass spectroscopy. With all of these technologies, complex data sets are generated and the final presentation will discuss alternative statistical and bioinformatic methods which can be used to analyze the data.

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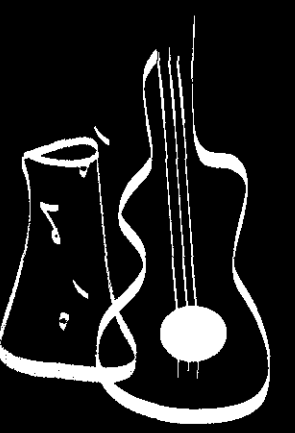

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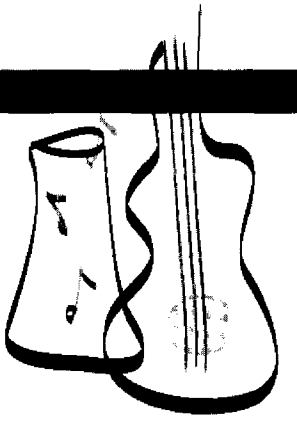

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, roundtable, and poster sessions of the 41st Annual Meeting of the Society of Toxicology, held at the Opryland Hotel and Convention Center, Nashville, Tennessee, March 17–21, 2002.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 385.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 411.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

Additional Late-Breaking Abstracts are issued in a supplement to this publication and are available at the 41st Annual Meeting and through the Society of Toxicology Headquarters office.

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