1 HERBALS AND DIETARY SUPPLEMENTS IN ATHLETIC PERFORMANCE ENHANCEMENT: FACT VS. FICTION.

T. S. Tracy. *University of Minnesota, Minneapolis, MN.* Sponsor: A. Fuciarelli.

Herbal products and dietary supplements have been used for years in an attempt to enhance athletic performances. However, this usage has not always been based on scientific data. Recent tragic cases, such as those involving ephedra supplements, have highlighted the need for an unbiased assessment of available data and additional research into their actions and effects. This presentation will discuss the various products used for athletic performance enhancement such as ephedra, androstenedione and androgens, creatine, gamma hydroxybutyrate, dimethylglycine, and others. Their promoted uses, purported mechanism of action, adverse effects/toxicities, and available clinical data will be presented to provide a perspective of what is known and areas in need of additional research. Additionally, the current regulatory status will be discussed and what factors may impact upon changes in this status.

2 BASIC NEUROTOXICOLOGY.

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Neurotoxicity may be defined as any adverse effect on the structure or function of the central and/or peripheral nervous system by a biological, chemical, or physical agent. Adverse effects can include both unwanted effects and any alteration from baseline that diminishes the ability of an organism to survive, reproduce or adapt to its environment. Neurotoxic effects may be permanent or reversible, and may result from direct or indirect actions on the nervous system. A multidisciplinary approach is necessary to assess neurotoxicity due to the complex and diverse functions of the nervous system. Many of the relevant effects can be measured by neurobiological, neurophysiological, neuropathological or behavioral techniques, as well as epidemiological approaches. After a general overview of neurotoxicity assessment from genes to human response, this basic course will present in greater depth the methods used to study populations, individual animals, cells, and genomes. Each speaker will review the basic concepts underlying the methodological approach presented. Selected neurotoxicants, including heavy metals, polyaromatic hydrocarbons, and drugs of abuse, will be used to illustrate principles. The first two lectures will address neurotoxic effects as studied by epidemiology in human populations and behavioral assessment in animal models, respectively. The next lecture will address the cellular responses of neurons, astrocytes, and oligodendrocytes to neurotoxicants. The course will be concluded with a description of a molecular approach to neurotoxicology including genomics. This course will be of interest to a broad range of scientists including drug developers, pharmacologists, neuroscientists, psychologists, regulators, and toxicologists.

3 TOOLS FOR FUNCTIONAL GENOMICS (PM10 REPEATED).

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The goal of this course is to discuss cutting-edge tools and techniques that may be used in ascribing hierarchical, functional analyses of gene products following DNA microarray experiments. First, we will discuss the advantages and disadvantages of a variety of pharmacological and molecular tools (i.e., antagonists, dominant negative approaches, siRNA). We will also discuss the means by which the molecular tools may be introduced into the cell or animal model, including the use of retro- and adenoviruses. Our second presentation will use data obtained in the laboratory to demonstrate the approaches that are typically used for determining whether the observed changes in mRNA of the gene product of interest occurs at the transcriptional or post-transcriptional levels. The third presentation will focus on use of the chromatin immunoprecipitation (CHIP) assay to demonstrate whether candidate transcription factors are involved in the regulation of the gene product of interest. Finally, our last presentation will introduce a novel approach, chemical genetics, that may be used to either activate or inactivate target gene products in able to discern their functional role(s) either the toxic or disease-related events.

4 OF MICE AND MAGNETS: METABONOMICS TECHNOLOGY IN SAFETY ASSESSMENT.

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Although metabonomics as a technology has been in the literature for over a decade, it is only in the past 3 to 4 years that the technology has gained widespread attention within the industrial sector. Metabonomics as a topic was introduced to the Society in a well-received sunrise mini-course in 2000. This was followed by a highly attended IAT symposium and poster session on metabonomics at the 2002 meeting. The technology has reached the level of maturity such that a full CE course is called for. The objectives of this basic level course will be to introduce the technology to SOT members unfamiliar with it, emphasizing the strengths and weaknesses of the technology in a practical way. The presentations will be from a toxicologist's perspective - communicating essential principles, but will avoid NMR and statistical jargon. The course will be primarily from a pharmaceutical development point of view, but will be broad enough to provide useful information for anyone interested in the technology.

5 FUNCTIONAL FLOW CYTOMETRY: APPLICATIONS IN TOXICOLOGY (PM12 REPEATED).

C. D. Bortner[1], D. Laskin[2], N. I. Kerkvliet[3] and S. W. Burchiel[4]. *[1]NIEHS, Research Triangle Park, NC, [2]Rutgers University, Piscataway, NJ, [3]Oregon State University, Corvallis, OR and [4]University of New Mexico, Albuquerque, NM.*

Flow cytometry provides a powerful tool for analyzing multiple characteristics of individual cells in a complex mixture of cell types without having to physically separate the cells. Yet, even though each cell is examined individually, the flow cytometer can process thousands of cells within a few seconds, allowing superior sampling of the population as compared to microscopic counting. The myriad of phenotypic and functional characteristics of cells that can be measured by flow cytometry continues to expand with the development of novel fluorescent probes to a variety of cellular components. The field of immunotoxicology has been greatly influenced by the use of flow cytometry with applications ranging from screening for toxic effects on immune cells to elucidating the mechanisms of toxic action on specific subpopulations of cells. However, other areas of toxicology are beginning to recognize the value of flow cytometry for mechanistic investigations as well. To address this growing interest, the intent of this course is to introduce the audience to novel applications of flow cytometry that have been used to assess tissue injury and mechanisms of toxicity at the whole animal, cellular, and biochemical levels. Although the context of many of the examples will emanate from immunotoxicology studies, each speaker will focus less on the immunology and more on the methods used in their studies that are broadly applicable to other areas of toxicology. Examples of methods to be covered include: apoptosis, oxidative stress, membrane integrity and fluidity, cell cycling using carboxyfluorescein (CFSE), and cell signaling.

6 UNDERSTANDING LIFESPAN CHANGES IN FORM AND FUNCTION OF THE FEMALE REPRODUCTIVE SYSTEM TO ASSESS AND INTERPRET TOXICITY.

P. M. Iannaccone[1], P. E. Blackshear[2], J. M. Cline[3] and P. J. Wier[4]. *[1]Northwestern University, Chicago, IL, [2]Integrated Laboratory Systems, Inc., Research Triangle Park, NC, [3]Wake Forest University School of Medicine, Winston-Salem, NC and [4]GlaxoSmithKline, King of Prussia, PA.*

This course reviews the basic morphology and endocrinology of the female reproductive system in rodents and primates as a basis for interpreting toxicity. Each of the 4 lectures will emphasize fundamental changes and vulnerabilities of the reproductive tract over the lifespan of the female. Both rodent and non-human primates will be discussed with respect to relevance to humans. The first lecture covers embryological development of the female reproductive system and will include key developmental and molecular events with an emphasis on timing of events in rodents and primates and potential periods of susceptibility to toxicity. The second lecture details the morphology and endocrinology of the female reproductive tract in rodents and will relate hormones and histology of the adult rodent reproductive tract from the onset of puberty to reproductive senescence and important sites of toxicity. The third lecture details the morphology and endocrinology of the female reproductive tract in nonhuman primates with emphasis on similarities and differences to rodents. The final lecture will combine the information of the first lectures and analyze issues of study design, endpoints to examine and interpretation of results in assessing female reproductive toxicity data.

Society of Toxicology
43rd Annual Meeting
Baltimore, Maryland

THE TOXICOLOGIST

a supplement to
TOXICOLOGICAL SCIENCES

An Official Journal of the Society of Toxicology

Volume 78, Number S-1, March 2004