FDA / NCTR Quarter Page

Research Highlights, Activities, and Publications (Vol. 15, Issue 1: October-March 2016)

Foretelling Toxicity

Read about NCTR research to predict risk of liver toxicity from drugs.

Size- and Dose-Dependent Antiviral Effects of Silver Nanoparticles

NCTR scientists have demonstrated both size- and dose-dependent antiviral effects of silver nanoparticles (AgNPs) in *in vitro* assays using feline calicivirus (FCV) as a surrogate for human norovirus. Whereas no effect was observed with 75 and 110 nm-sized AgNPs, treatment of cultures with 10 nanometer (nm)-sized AgNPs (at doses of 50 and 100 micrograms per milliliter [µg/mL]) completely inactivated FCV within 2-4 hours of exposure, resulting in:

- decrease in the viral titer
- absence of cytopathic effects in Crandell-Rees Feline Kidney cells
- reduction in viral capsid protein levels.

The use of AgNPs as antibacterial agents has increased in consumer-use products; however, its use as an antiviral agent is still an area of active research. This study is now available online at *Foodborne Pathogens and Disease*.

For additional information, please contact Sangeeta Khare, Ph.D., Division of Microbiology, FDA/NCTR.

Pediatric Anesthetic NeuroDevelopment Assessment (PANDA) Symposium

Dr. Merle Paule, Director of the Division of Neurotoxicology, NCTR, gave a presentation at the 5th PANDA Symposium held in New York, NY, on April 16-17, 2016. The presentation focused on NCTR's nonhuman primate studies on the long-lasting cognitive deficits associated with neonatal general anesthesia and summarized data from several recent publications. The symposium, sponsored in part by the SmartTots public-private partnership between FDA and the International Anesthesia Research Society, provides a forum for presentation and discussion of clinical and preclinical anesthesia studies being conducted at multiple U.S. institutions.

For additional information please contact Merle Paule, Ph.D., Director, Division of Neurotoxicology, FDA/NCTR.

Analyzing NGS Data With An Unusual Approach

NCTR scientists have developed a method, using concepts normally applied to computerized text analysis of publications, to identify gene-phenotype relationships and biomarkers from next generation sequencing (NGS) data. The prototype analysis successfully classified *Salmonella enterica* strains into serotypes utilizing fliC — one of the serotype-

determinant genes. The process can be modified to analyze other organisms.

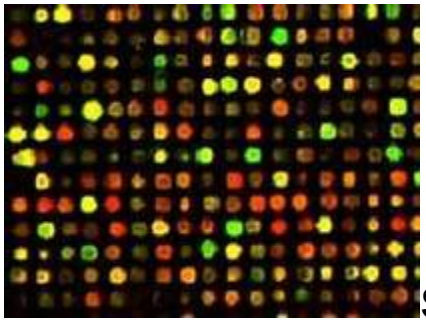
Similar to how computerized text mining detects the relevant content- of-interest in a publication by looking at word relationships, the:

- sequence is considered the "document"
- *Salmonella* sequence-SNPs are considered the "words."

The serotype (or other biomarkers of interest) can be deduced by analyzing the *Salmonella* sequence-SNP relationships in the NGS data of different *Salmonella* strains, mirroring document-word relationships in text mining.

The method provides a new approach to perform large-scale comparative and evolutional studies from NGS data for understanding and decoding hidden genetic information that is contained in big data sets of biological and medical information.

For additional information, please contact Wen Zou, Ph.D., Division of Bioinformatics and Biostatistics, FDA/NCTR.



Sequencing Quality Control (SEQC2) Workshop on September 13-14, 2016

SEQC2 is an FDA-led community-wide Sequencing Quality Control consortium. The consortium aims to develop best practices with recommended standard-analysis protocols and quality-control metrics for whole-genome sequencing and target-gene sequencing technologies that will support regulatory science research and precision medicine.

Find out more information and how to participate.

DATE:

September 7-9, 2016

THEME:

Nanotechnology Standards and Applications

The Global Summit on Regulatory Science 2016 (GSRS16) meeting on "Nanotechnology Standards and Applications" is scheduled from **September 7-9, 2016, at Natcher Auditorium, National Institute of Health (NIH) Campus, Bethesda, Maryland.** The GSRS16 workshop participation extends beyond global regulatory-, research-, and standards-agency researchers, to academic and industry participants.

The meeting focus is to learn about cutting-edge science and technologies that are being developed, and build upon this knowledge to develop appropriate standards for regulatory consideration. To facilitate regulatory review to enable commercialization, the GSRS16 topics include:

- a review of current standards in nanotechnology
- innovative science in drugs, devices, food, feed, and cosmetics
- panel discussions on standard research methodologies, consensus standards, and reference materials needs.

The goal of this summit is to establish practical approaches and requisite teams to facilitate development of such standards. Poster sessions are also scheduled as part of this meeting.

There is no registration fee; however, registration is required to attend the conference. If you have any questions, please contact: Roben Brooks.

Progress on FDA Studies Reviewed

The 46th meeting of the Toxicology Study Selection and Review Committee (TSSRC) was held at FDA's White Oak facility, May 4-5, 2016, to discuss ongoing studies that are part of the Interagency Agreement between FDA/NCTR and the National Institute of Environmental Health Sciences/National Toxicology Program (NIEHS/NTP) that supports toxicology studies providing data for the FDA risk-assessment process.

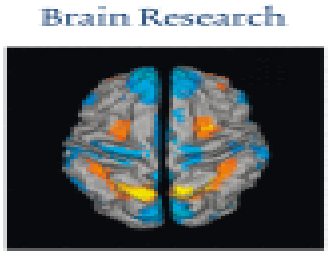
Ongoing studies at NCTR in the following areas were discussed:

- food constituents or contaminants (bisphenol A; arsenic; melamine + cyanuric acid; brominated vegetable oil)
- antibacterial chemicals (triclosan)
- dietary supplement component (aloin)

NIEHS/NTP presented updates on compounds under study at NTP that are of interest to FDA.

The TSSRC is comprised of regulatory scientists and subject-matter experts from each of the FDA Product Centers, NIEHS/NTP, and the National Institutes of Health. The committee meets twice each year and is responsible for scientific oversight of study design and progress of ongoing work under this Interagency Agreement. The next meeting of the TSSRC will be held November 9-10, 2016, at NCTR.

For additional information, please contact Paul Howard, Ph.D., Director, Office of Scientific Coordination, FDA/NCTR.



Commemorating Neurohistochemical Tracer Development

Dr. Larry Schmued outlined two of his inventions of novel histochemical tracers for the 50th Anniversary Issue of Brain Research. This issue of *Brain Research* features the most cited articles from their first 50 years of publishing. The manuscript describes two such tracers, specifically Fluoro-Gold and Fluoro-Jade C.

The Fluroro-Jade family of dyes represents several technical advancements for histochemical tracers significantly improving neuronal-detection sensitivity and selectivity that are used to detect axonal, dendritic and somatic degeneration/death axonal activity. The dyes are easy to use in practice and feature non-destructive, stable chemistry that provides opportunity for uses with other histochemical techniques to characterize neuroinflammation and neurotoxicity on the same slide.

Fluoro-Jade dyes have become an indispensable tool for academic scientists investigating neurotoxic mechanisms, and a well-accepted technology by industry often appearing in submissions as part of the Investigational New Drug application process.

For additional information, please contact Larry Schmued, Ph.D., Senior Research Scientist Head, Neurohistochemistry Laboratory, Division of Neurotoxicology, FDA/NCTR.

Assembly of Personal Genomes for Precision Medicine

Scientists from FDA's NCTR and Center for Biologics Evaluation and Research published a review article in *Pharmaceutics* that discusses issues surrounding the assembly of personal genomes to support precision medicine.

The review article provides an overview of human-genome sequencing technologies, genome-assembly software packages, and IT requirements. The article also proposes metrics and parameters for quality assessment of the assembled genomes. Finally, the authors discuss the potential benefits of using personal genomes as references in precision-medicine applications rather than the current public-reference genome derived from multiple individuals.

For additional information, please contact Wenming Xiao, Staff Fellow, Division of Bioinformatics and Biostatistics, FDA/NCTR.

Evaluation of Bisphenol A (BPA)

Internal Dose in "High Risk" Populations

Investigators from Pacific Northwest National Laboratory, Oregon State University, and NCTR evaluated a group of pregnant women under closely controlled clinical conditions, including some with the potential for high exposure to BPA. No differences in internal dose were found when comparing either women handling cash-register receipts or women reporting above-average consumption of canned foods (canned food liners contain BPA) with other groups.

The investigators concluded from the controlled collection and the analysis protocols used, that internal BPA exposures in typical pregnant women from both home and clinical settings reflect exposures representative of the general population — (i.e., picomolar or below limits of detection) as previously determined in large national surveys. A manuscript describing this study is now available online at *Food and Chemical Toxicology*.

For additional information, please contact, Daniel Doerge, Ph.D., Division of Biochemical Toxicology, FDA/NCTR.

National Institutes of Health (NIH) Tobacco Regulatory Science Conference

NCTR scientists presented results from tobacco research projects at the NIH Tobacco Regulatory Science Conference held on the NIH Campus in Bethesda, MD on May 16-18, 2016. The topics of the presentations included:

- predictive models for abuse liability
- tobacco-induced toxicity in *in vitro* cardiomyocytes and in 3D human-airway culture models
- bacterial populations and tobacco-specific nitrosamines in smokeless tobacco products
- impacts of smokeless tobacco products on the oral microbiome.

These research projects were developed in collaboration with and funded by FDA's Center for Tobacco Products.

For additional information, please contact Bradley Schnackenberg, Ph.D., Office of Research, FDA/NCTR.

View NCTR's Recent Scientific Publications

For more information about NCTR contact Dr. William Slikker, Jr., NCTR Director at William.Slikker@fda.hhs.gov or (870) 543-7517.

Links within documents:

NCTR research to predict risk of liver toxicity from drugs. - http://www.nature.com/nm/journal/v22/n5/full/nm0516-450.html?source=govdelivery&utm_medium=email&utm_source=govdelivery

Size- and Dose-Dependent Antiviral Effects of Silver Nanoparticles “Foodborne Pathogens and Disease” - https://www.ncbi.nlm.nih.gov/pubmed/26938256?source=govdelivery&utm_medium=email&utm_source=govdelivery

Link to “Smart Tots” - http://smarttots.org/?source=govdelivery&utm_medium=email&utm_source=govdelivery

For More information about Sequencing Quality Control (SEQC2) Workshop – http://www.fda.gov/ScienceResearch/BioinformaticsTools/MicroarrayQualityControlProject/ucm507935.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Commemorating Neurohistochemical Tracer Development “Brain Research” - http://www.sciencedirect.com/science/article/pii/S0006899316301925

Assembly of Personal Genomes for Precision Medicine “Pharmaceutics” –

http://www.mdpi.com/1999-4923/8/2/15?source=govdelivery&utm_medium=email&utm_source=govdelivery

Internal Dose in "High Risk" Populations “Food and Chemical Toxicology” - http://www.sciencedirect.com/science/article/pii/S0278691516300886

NCTR Recent Scientific Publications - http://www.accessdata.fda.gov/scripts/publications/more.cfm?center=NCTR&center_name=Toxicological&source=govdelivery&utm_medium=email&utm_source=govdelivery