3rd Annual Meeting of the Arkansas Bioinformatics Consortium
AR-BIC 2017

We are an Arkansas Collaborative Community in Bioinformatics Research

Microbiome and Biomedical Informatics

Embassy Suites Hotel
Little Rock, AR

April 24-25th, 2017

http://www.arkansasbioinformatics.org/

Organized by:

FDA U.S. FOOD & DRUG ADMINISTRATION
NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

Arkansas Bioinformatics AR BIC Consortium

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ARKANSAS STATE UNIVERSITY

UAPB University of Arkansas at Pine Bluff

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Research & Economic Development

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About the Arkansas Bioinformatics Consortium (AR-BIC)

Mission:

The Arkansas Bioinformatics Consortium (AR-BIC) is a virtual Arkansas-centric bioinformatics community aimed at developing, leveraging and enhancing state-wide collaboration, thus forming a stable environment available to support the AR-wide research, education, training and entrepreneurial/industrial activities in life sciences-related computing. AR-BIC activities are within the general area of life sciences computing in AR. The goals of AR-BIC are to (1) strengthen Arkansas' ability to compete at national and international levels for research funding, (2) enable and facilitate collaboration in research where synergy is identified, (3) enhance education, training and university curricula, and (4) expand AR economic growth and job opportunities. AR-BIC is founded on the belief that we can be more than the sum of our parts, and that in our unity; we can draw strength from our diversity. Through synergy, a true critical mass of capability can be assembled to take on large challenges in public health.

(AR-BIC homepage: www.arkansasbioinformatics.org)

AR-BIC Steering Committee:

- **Arkansas Research Alliance (ARA):** Jerry Adams, Art Norris, Julie LaRue, Roger Buchanan, Bryan Barnhouse
- **National Center for Toxicological Research (NCTR):** Weida Tong, Shraddha Thakkar, Roger Perkins, Steven Foley
- **University of Arkansas at Fayetteville (UAF):** Douglas Rhoads
- **University of Arkansas at Little Rock (UALR):** Mary Yang
- **University of Arkansas Medical Sciences (UAMS):**, Fred Prior, Meredith Zozus, Cesar Compadre
- **Arkansas State University (ASU):** Malathi Srivatsan

- Venue:

  Ambassador I - III
  Embassy Suites
  11301 Financial Centre Pkwy
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Conference sponsors and acknowledgement:

* Arkansas Research Alliance (ARA)
* University of Arkansas (UA)
* University of Arkansas at Little Rock (UALR)
* Arkansas State University (ASU)
* Arkansas Biosciences Institute (ABI)
* University of AR for Medical Sciences (UAMS)
*University of Arkansas at Pine Bluff (UAPB)

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Arkansas Bioinformatics Consortium (AR-BIC) 2017
3rd Annual Conference
Microbiome and Biomedical Informatics

Embassy Suites, Little Rock – Ambassador I - III

Agenda

Monday, April 24th 2017

01:00 pm - 02:00 pm	Registration and Poster Setup
02:00 pm - 02:25 pm	**Welcome Remarks and Opening** • Jerry B. Adams, *President and CEO, Arkansas Research Alliance, Conway, AR* • Pope L. Moseley, *M.D. Executive Vice Chancellor, Dean, College of Medicine , University of Arkansas for Medical Sciences, Little Rock, AR*
02:25 pm – 02:30 pm	**Education and Cross Training** Theme Introduction and vision Weida Tong, Ph.D., *Director, Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, US FDA, Jefferson, AR*
02:30 pm - 05:15 pm	**Establishing statewide bioinformatics education and training curriculum** Session Co-Chairs: • Cesar M. Compadre, Ph.D., *Professor, University of Arkansas for Medical Sciences, Little Rock, AR* • Mary Yang, Ph.D., *Associate Professor, University of Arkansas at Little Rock, Little Rock, AR*
02:30 pm - 02:50 pm	**Bioinformatics in drug discovery: educational and training opportunities** Cesar M. Compadre, Ph.D., *Professor, University of Arkansas for Medical Sciences, Little Rock, AR*
02:50 pm - 03:10 pm	**Bioinformatics education and training at UALR** Mary Yang, Ph.D., *Associate Professor, University of Arkansas at Little Rock, Little Rock, AR*
03:10 pm – 03:30 pm	**Bioinformatics societies and NCTR contribution** Shraddha Thakkar, Ph.D., *Visiting Scientist, National Center for Toxicological Research, Jefferson, AR*
03:30 pm – 03:45 pm	**Break**

03:45 pm – 04:05 pm	**Bioinformatics education and training at ASU** Xiuzhen Huang, Ph.D., *Professor, Arkansas State University, Jonesboro, AR*
04:05 pm – 04:25 pm	**BioMedical -informatics education and training at UAMS** Meredith Zozus, Ph.D., *Associate Professor, University of Arkansas for Medical Sciences, Little Rock, AR*
04:25 pm – 04:45 pm	**Bioinformatics education and training at UAF** Mark Arnold, Ph.D., *Director, Statistics and Analytics Program, Graduate School, Co-Director for the Institute for Advanced Data Analytics, University of Arkansas, Fayetteville*
04:45 pm – 05:00 pm	**Break**
05:00 pm – 05:30 pm	**Panel Discussion:** Moderator: Cesar M. Compadre, Ph.D., *Professor, University of Arkansas for Medical Sciences, Little Rock, AR* **Panelist:** • Meredith Zozus, Ph.D., *Associate Professor, University of Arkansas for Medical Sciences, Little Rock, AR* • Mark Arnold, Ph.D., *Director, Statistics and Analytics Program, Graduate School, Co-Director for the Institute for Advanced Data Analytics, University of Arkansas, Fayetteville* • Mary Yang, Ph.D., *Associate Professor, University of Arkansas at Little Rock, Little Rock, AR* • Xiuzhen Huang, Ph.D., *Professor, Arkansas State University, Jonesboro, AR* • Shraddha Thakkar, Ph.D., *Visiting Scientist, Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, Jefferson, AR*
05:30 pm - 08:30 pm	**Poster Session** Session Chair: Shraddha Thakkar, Ph.D., *Visiting Scientist, Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, Jefferson, AR*
06:30 pm - 09:00 pm	Reception (Sponsored by Arkansas Research Alliance)

Tuesday, April 25th 2017

07:45 am – 08:15 am	Light Breakfast
08:15 am – 08:30 am	**Microbiome and Biomedical Informatics** Theme Introduction and Vision Weida Tong, Ph.D., *Director, Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, Jefferson, AR*
08:30 am – 11:45 pm	**Session 1: Microbiome** Session Co-Chairs: • Douglas Rhoads, Ph.D., *Professor, University of Arkansas, Fayetteville, AR* • Steven Foley, Ph.D., *Research Microbiologist, Division of Microbiology, National Center for Toxicological Research, Jefferson, AR*
08:30 am – 09:00 am	**The respiratory and GI-tract microbiome in healthy aging, pulmonary disease and animal growth performance** Jiangchao Zhao, Ph.D., *Assistant Professor, University of Arkansas, Fayetteville, AR*
09:00am – 09:30 am	**Rodents as translational model to study the effects of xenobiotics on the development of microbiome from gestation to adult** Sangeeta Khare, Ph.D., *Research Microbiologist, Division of Microbiology, National Center for Toxicological Research, Jefferson, AR*
09:30 am – 10:00 am	**Microbiome changes associated with lung cancer** Mohammed Orloff, Ph.D., *Associate Professor, Department of Epidemiology , University of Arkansas for Medical Sciences, Little Rock, AR*
10:00 am – 10:15 am	**Break**
10:15 am – 10:45 am	**Human Microbiome: Integrated Systems Biology Approaches Used to Assess the Impact of Toxicants on the Microbiome** Carl Cerniglia, Ph.D., *Director, Division of Microbiology, National Center for Toxicological Research, Jefferson, AR*
10:45 am – 11:15 am	**Metapeptidomics Data Processing Pipe-Line: Application to the Study of Function of Gut Microbiome in Chronic Kidney Disease** Boris Zybalov, Ph.D., *Assistant Professor , University of Arkansas for Medical Sciences, Little Rock, AR*
11:15 am – 11:45 am	**Microbiome metabolites and their effects on mitochondrial function** Richard Frye, MD, Ph.D., *Associate Professor, College of Medicine, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR*
11:45 am – 12:00 pm	**Panel Discussion:** Moderator: Steven Foley, Ph.D., *Research Microbiologist, Division of Microbiology, National Center for Toxicological Research, Jefferson, AR*

	Douglas Rhoads, Ph.D., *Professor, University of Arkansas, Fayetteville, AR* **Panelist:** • Jiangchao Zhao, Ph.D., *Assistant Professor, University of Arkansas, Fayetteville, AR* • Sangeeta Khare, Ph.D., *Research Microbiologist, Division of Microbiology, National Center for Toxicological Research, Jefferson, AR* • Mohammed Orloff, Ph.D., *Associate Professor, Department of Epidemiology , University of Arkansas for Medical Sciences, Little Rock, AR* • Carl Cerniglia, Ph.D., *Director, Division of Microbiology, National Center for Toxicological Research, Jefferson, AR* • Boris Zybalov, Ph.D., *Assistant Professor , University of Arkansas for Medical Sciences, Little Rock, AR* • Richard Frye, MD, Ph.D., *Associate Professor, College of Medicine, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR*
12:00 pm – 01:00 pm	**Lunch break**
	Session 2: Biomedical Informatics Session Co-Chairs : • Fred Prior, Ph.D., *Chair - Biomedical Informatics, University of Arkansas for Medical Sciences, Little Rock, AR* • Meredith Zozus, Ph.D., *Associate Professor, University of Arkansas for Medical Sciences, Little Rock, AR*
01:00pm – 01:10pm	**Introduction** **DBMI and UAMS programs of research across the spectrum of Biomedical Informatics** Fred Prior, Ph.D., *Chair - Biomedical Informatics, University of Arkansas for Medical Sciences, Little Rock, AR*
01:10pm – 01:40 pm	**Keynote: Thoughts from 30 years of running a Contract Research Organization Specializing in Data Management** Anthony Goudie, Ph.D., *Assistant Professor, Center for Applied Research and Evaluation, Department of Pediatrics, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR*
01:40 pm – 02:00 pm	**Clinical Research Informatics at work: Data Collection and Management Infrastructure for the New IDeA State Pediatric Clinical Trials Network (ISPCTN)** Anita Walden, BS, Instructor, *Department of Biomedical Informatics, University of Arkansas for Medical Sciences, Little Rock, AR*
02:00 pm – 02:30 pm	**What it takes for an epic new install and upgrade** Thomas Powell, M.D., M.S., *Chief Medical Information Officer (CMIO),*

	Associate Vice Chancellor , University of Arkansas for Medical Sciences, Little Rock, AR Feliciano B. Yu, MD, MSPH,MSHI*, Professor, College of Medicine, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR*
02:30 pm – 03:00 pm	**Break**
03:00 pm – 03:30 pm	**Metagenomics for Population Health in Arkansas** David Ussery, Ph.D*., Professor, Biomedical Informatics, University of Arkansas for Medical Sciences, Little Rock, AR*
03:30 pm – 04:00 pm	**Informatics supporting Liquid Biopsy research** Donald Johann Jr., MD, *Associate Professor, Biomedical Informatics, , University of Arkansas for Medical Sciences, Little Rock, AR*
04:00 pm – 04:20 pm	**Imaging Informatics of a Large- Scale Public Information Repository (TCIA)** Lawrence Tarbox, Ph.D., *Assistant Professor, University of Arkansas for Medical Sciences., Biomedical Informatics, College of Medicine University of Arkansas for Medical Sciences, Little Rock, AR*
04:20 pm – 04:40 pm	**Venous Pressure Monitoring and Prediction in ICU settings: ongoing Research at UAMS and Vandy** Kevin Sexton, MD, *University of Arkansas for Medical Sciences., Biomedical Informatics, College of Medicine University of Arkansas for Medical Sciences, Little Rock, AR*
04:40pm – 05:00 pm	**Closing Remarks** • William Slikker, Jr., Ph.D*., Director, National Center for Toxicological Research, US Food and Drug Administration, Jefferson, AR* • Jerry B. Adams, *President and CEO, Arkansas Research Alliance, Conway, AR*

Jerry B. Adams

President/CEO
Arkansas Research Alliance
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Jerry Adams is the President/CEO of the **Arkansas Research Alliance**, an economic development non-profit modeled on the very successful Georgia Research Alliance. Its primary focus is to leverage university-based job-creating research in Arkansas. The ARA Board of Trustees consists of the five chancellors of the Arkansas research universities and sixteen Arkansas based CEOs. (www.aralliance.org). Jerry retired from **Acxiom Corporation** in October, 2007 after 34 years serving a variety of senior leadership roles and started the Arkansas Research Alliance in April 2008. Jerry served as the chair of **Accelerate Arkansas**, a statewide volunteer group of leaders focused on building a knowledge-based economy in Arkansas. He continues to serve on Accelerate Arkansas' executive committee.

Active in the start up community, Jerry serves on the Management Committee of **Funds for Arkansas' Future**, the state's first angel fund. Jerry also serves on the advisory board of the **Arkansas Regional Innovation Hub**, chairs the board of **BioVentures**, the incubator at UAMS and serves on the Board of **VIC Technology Venture Development**, a Fayetteville based for profit incubator. Jerry is involved with education reform having served on the **Governor's Blue Ribbon Committee for Higher Education**. He is currently serving on the **Board of Visitors** at the University of Arkansas at Little Rock, past board member of the **Dean's Advisory Board** at the University of Arkansas' Walton School of Business, the University of Central Arkansas **Advisory Board** for the College of Mathematics and Natural Sciences and the University of Central Arkansas **Regional Advisory Board** for the College of Fine Arts & Communication. Jerry was a founding member of the **STEM Coalition** and served as chair of the **EAST Initiative**, a secondary school technology based project learning initiative active in over 200 schools in Arkansas and six other states. Jerry also serves board chair of the **Arkansas Initiative for Math & Science (AAIMS)** focused on advanced placement of math and science in Arkansas high schools. Jerry also serves on the Board of the **Arkansas Center for Health Improvement (ACHI)**. Jerry is the founding board chair for the **Conway Interfaith Clinic**, a clinic focused on providing medical and dental services to segments of the community who are underserved. Jerry was the founding board chair for the **Faulkner County Community Foundation** and served as chair of the state board of the **Arkansas Community Foundation.** Jerry also serves as the vice-chair of the **Conway Development Corporation**, Conway's economic development organization. Jerry also serves on the Board of Directors of the **Winthrop Rockefeller Foundation**.

Pope L. Moseley, M.D.
Executive Vice Chancellor
UAMS
Dean, College of Medicine
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Dr. Pope L. Moseley, a leader in internal medicine and internationally recognized physician-scientist, has served as executive vice chancellor at the University of Arkansas for Medical Sciences (UAMS) and dean of the UAMS College of Medicine since July 2015.

Dr. Moseley oversees the college's interrelated missions to train the next generation of Arkansas' physicians, develop new knowledge that leads to better health, and deliver world-class, patient-centered care.

Dr. Moseley came to UAMS from the University of New Mexico (UNM) School of Medicine, where he was a Distinguished Professor and led the Department of Internal Medicine as its Chair for 14 years.

He is highly regarded both for his laboratory research focusing on cellular adaptations to exercise and for his expertise in disease systems biology. As an associate director of UNM's National Institutes of Health-funded Clinical Translational Science Center, Dr. Moseley led comparative effectiveness research initiatives and oversaw development of the UNM Health Sciences Center informatics platform.

In addition, Dr. Moseley continues to oversee graduate students at the University of Copenhagen, in the Systems Biology Group of the Center for Protein Research, where they are developing an informatics approach to uncovering disease associations using the Danish National Health Registry.

Dr. Moseley received his undergraduate degree from Davidson College, his medical degree from the University of Illinois College of Medicine and a master's degree in preventive medicine and environmental health at the University of Iowa.

He completed a residency in internal medicine and occupational medicine and a fellowship in pulmonary and critical care medicine at the University of Iowa. He is certified by the American Board of Internal Medicine, the American Board of Preventive Medicine (specialty in Occupational Medicine), and by the subspecialty board in pulmonary diseases.

Dr. Moseley was recruited to New Mexico in 1995 and served as Chief of Pulmonary/Critical Care and as Senior Associate Dean for Research prior to his appointment as Chair of Internal Medicine. He also held the Reva S. Skelton Research Endowment and was a Regents' Professor of the University.

William (Bill) Slikker, Jr., Ph.D.

Director
National Center for Toxicological Research/FDA
E Mail: william.slikker@fda.hhs.gov

Dr. William Slikker, Jr. is the Director of FDA's National Center for Toxicological Research (NCTR). He received his Ph.D. in Pharmacology and Toxicology from the University of California at Davis in 1978. Dr. Slikker holds Adjunct Professorships in the Departments of Pediatrics, and Pharmacology and Toxicology at the University of Arkansas for Medical Sciences. He has held committee chairmanships or elected offices in several scientific societies, including the Teratology Society (serving as President) and the American Society for Pharmacology and Experimental Therapeutics (Chair, Developmental Pharmacology Section and member of the Program Committee) and co-founder and past President of the MidSouth Computational Biology and Bioinformatics Society. He is currently Associate Editor for *NeuroToxicology* and *Toxicological Sciences*. He is the past President of The Academy of Toxicological Sciences, the Society of Toxicology (Presidential term ended 2013), and the recipient of the 2014 George H. Scott Memorial Award from The Toxicology Forum.

Dr. Slikker has authored or co-authored over 300 publications in the areas of transplacental pharmacokinetics, developmental neurotoxicology, neuroprotection, systems biology, and risk assessment. He has also served on several national/international advisory panels for the International Life Sciences Institute (ILSI)/Health and Environmental Sciences Institute (HESI), Chemical Industry Institute of Toxicology (CIIT) Centers for Health Research, Environmental Protection Agency (EPA), National Institute of Environmental Health Sciences (NIEHS), National Academy of Sciences (NAS), National Institutes of Health (NIH) and World Health Organization (WHO).

Weida Tong, Ph.D.

Director
Division of Bioinformatics and Biostatistics
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Dr. Tong is Director of Division of Bioinformatics and Biostatistics at FDA's National Center for Toxicological Research (NCTR/FDA). He has served a science advisory board member for several large projects involving multiple institutes in Europe and USA. He also holds several adjunct positions at universities in US and China. His division at FDA works to develop bioinformatic methodologies and standards to support FDA research and regulation and to advance regulatory science and personalized medicine. The most visible projects of his group are (1) leading the Microarray Quality Control (MAQC) consortium to develop standard analysis protocols and quality control metrics for emerging technologies to support regulatory science and precision medicine; (2) development of liver toxicity knowledge base (LTKB) for drug safety; (4) in silico drug repositioning for the enhanced treatment of rare diseases; and (4) development of the FDA bioinformatics system, ArrayTrack^{TM} suite, to support FDA review and research on pharmacogenomics. In addition, his group also specializes in molecular modeling and QSARs with specific interest in estrogen, androgen, and endocrine disruptor. Dr. Tong has published more than 230 papers and book chapters.

Cesar M. Compadre, Ph.D.

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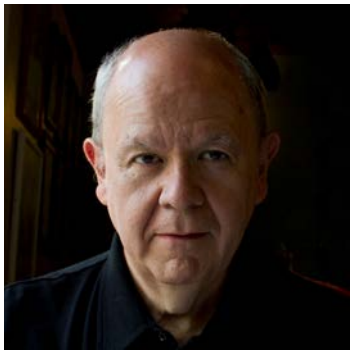

Dr. Compadre is a professor at the Department of Pharmaceutical Sciences, of the University of Arkansas for Medical Sciences. He has extensive research experience on the development of bioactive compounds based on naturally occurring compounds, and on the use of molecular modeling in drug design and structure-activity studies. He has published over 90 papers and co-authored more than 70 patents related to the development of bioactive compounds.

He is also the developer of one FDA approved antimicrobial technology, which is commercially used, and he is also co-founder of Tocol Pharmaceuticals, a company focused on the development of enhanced vitamin-E analogues. Dr. Compadre has extensive International research collaborations in Drug Discovery, Global Health and Phytopharmaceuticals. Dr. Compadre has a BSPharm degree, and obtained his Ph.D. degree in medicinal chemistry and pharmacognosy, from the University of Illinois at Chicago. He conducted postdoctoral research on structure-activity relationships studies using molecular modeling at the University of Illinois working with Dr. John M. Pezzuto and at Pomona College working with Professor Corwin Hansch. Additionally, he had a sabbatical experience at NASA Ames Research Center in computer modeling.

Mary Yang, Ph.D.

Associate Professor and Director
UALR-UAMS Joint Bioinformatics Graduate Programs
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Dr. Mary Yang is a tenured faculty at UALR and Director of the MidSouth Bioinformatics Center and the UALR-UAMS Joint Bioinformatics MS/Ph.D. Program. After completing MSECE, M.S., and a Ph.D. degree supported by a Bilsland Dissertation Fellowship at Purdue University, she joined the National Human Genome Research Institute at the NIH. During her tenure there, she made contributions to large-scale genomics and systems biology research projects, and was Founding Editor-in-Chief of International Journal of Computational Biology and Drug Design, a NIH PubMed indexed journal. She is on the editorial broads of The Journal of Supercomputing and International Journal of Pattern Recognition and Artificial Intelligence. She has published over 50 PubMed-indexed articles and 70 DBLP-indexed computer science papers. Dr. Yang's main research interest is in developing functional genomics and systems biology-based approaches that render a better understanding of the molecular mechanisms underlying complex diseases such as cancer.

Shraddha Thakkar, Ph.D.

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She received her MSc. degree in Biotechnology from Bangalore University, India and her MS, and Ph.D. degrees in Bioinformatics from the University of Arkansas at Little Rock (UALR)/University of Arkansas for Medical Sciences (UAMS) Joint bioinformatics program. She received her postdoctoral training at the FDA'S National Center for Toxicological Research. Dr. Thakkar is Adjunct Assistant Professor at UAMS College of Pharmacy and Graduate Faculty at UALR. Dr. Thakkar's research interests are on the use of structural and computational techniques for the elucidation of macromolecular mechanisms relevant for drug discovery and toxicity. Along with her expertise in crystallography, Dr. Thakkar has developed strong expertise in macromolecular cloning and expression, and on the use of molecular modeling, QSAR and virtual screening. She has ten research publications, two USA patent applications and many research presentations at national and international meetings. Dr. Thakkar has received multiple research and leadership awards regionally and nationally, including 2012 Genentech Innovation in Biotechnology Award from American Association of Pharmaceutical Scientist (AAPS) and Margret C. Etter Student lecturer award from American Crystallography Association. She is the Vice Chair of Pharmacogenomics Focus group from AAPS and Chair of AAPS Biotech Section Awards Committee. She is the founding president of the Regional Student Group – MidSouthernUS the MCBIOS student group. Dr. Thakkar was elected as Board member of the MCBIOS in 2014 and served as President in 2016-17.

Xiuzhen Huang, Ph.D.

Professor
Arkansas State University,
Jonesboro, AR

Dr. Xiuzhen Huang is a Professor in Department of Computer Science at Arkansas State University. She received the PhD degree in computer science from Texas A&M University in 2004. Her research in bioinformatics and computational biology focuses on effective modeling of biological objects and systems, development of non-trivial computational approaches and algorithms, including novel discrete and continuous mathematical approaches, which are related to high-dimensional data, next-generation sequencing, genomics data and imaging data analysis for studying stress reactions, genetic diseases, and human cancer study. Her interest in theoretical computer science is algorithm design and development, parameterized computation and complexity, and theory of computation. While many approaches in the current bioinformatics area are being developed for data analysis, her interest also lies in the seamless integration of approach development with wet-lab experiments and clinical practices in order to address biological and biomedical real challenges. Dr. Huang conceived the concept of No-Boundary Thinking (NBT) in bioinformatics and has initiated an NBT national network supported by NSF..

Meredith Nahm Zozus, Ph.D.

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Dr. Zozus' program of research focuses on Information Quality in Healthcare and Health Related Research. She has multiple publications and several ongoing federally funded research projects in the area. She recently moved from Duke University to join the Faculty of the University of Arkansas for Medical Sciences College of Medicine in the Department of Biomedical Informatics and serves as the Vice Chair for Academic Programs.

Prior to joining UAMS, Dr. Zozus served as the Director of the Clinical Data Integration department at the Duke Clinical Research Institute (DCRI), the Associate Director of Clinical Research Informatics for the Duke Translational Medicine Institute and the Associate Director for Academic Programs at the Duke Center for Health Informatics. She served as the Co-Investigator of a Clinical and Translational Science Award supplement to develop curriculum for Duke's two Master's degree programs in health informatics, served as the Co-Investigator for one of five ONC-funded Curriculum Development centers for the National Health IT Workforce Development program (1U24-OC000024, and served as the Program Director for Duke's ONC Workforce Development T15 titled Consortia for University-based Training of Health IT Professionals in Health Care. Dr. Zozus has developed and taught graduate level informatics courses for the last ten years and has developed curricula across the training and education spectrum. She is currently leading efforts with the Society for Clinical Data Management to align the international practice standard and professional certification exam for the management of data for clinical studies.

Dr. Zozus did her undergraduate and masters work in Nuclear Engineering at North Carolina State University and her doctoral work in Health Informatics at the University of Texas at Houston.

Mark Arnold, Ph.D.

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Mark Arnold, PhD, Associate Professor of Mathematical Sciences; Director, Statistics & Analytics program, Graduate School; Co-director, Institute for Advanced Data Analytics, University of Arkansas Fayetteville: After earning a PhD in Mathematics with an concentration in Computational Mathematics at Northern Illinois University, working for Allied Signal in chemical graph theory, and a post-doc at USDOE Ames Laboratory, Arnold joined the faculty of Mathematical Sciences at the University of Arkansas. His research is in Scientific Computation, primarily numerical linear algebra in statistics, control and signal processing. Current research projects are in graph theory and matrix QR factorizations. Arnold is a member of the University of Arkansas Teaching Academy, and has served as undergraduate coordinator, graduate coordinator and vice-chair for the Department of Mathematical Sciences, and on several departmental, college and university committees

Douglas Rhoads, Ph.D.

Director Graduate Program in Cell and Molecular Biology
University Professor of Biological Sciences
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Dr. Rhoads is Director of the interdisciplinary graduate program in Cell and Molecular Biology, and University Professor in Biological Sciences, at the University of Arkansas. His research has focused on genomic analyses in a variety of species including human, chicken, tomato, bear, scorpion, yeast and bacteria. His primary research is in metabolic diseases affecting meat type chickens, and he is an affiliated faculty in the Center of Excellence for Poultry Science at the University of Arkansas. Currently funded projects are working on genomic mapping of genes affecting pulmonary hypertension, and etiology and epidemiology of bacterial chondronecrosis with osteomyelitis leading to lameness. Dr. Rhoads teaches a course in Genomics and Bioinformatics. Dr. Rhoads was a founding member of the Cell and Molecular Biology program, and has served as the Director for the past 12 years. Dr. Rhoads research has produced more 53 journal articles, 8 industry technical reports, and 146 presentations.

Steven Foley, Ph.D.

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Dr. Steven Foley is the Deputy Director of the Division of Microbiology at the Food and Drug Administration (FDA)'s National Center for Toxicological Research (NCTR) in Jefferson, Arkansas. Dr. Foley earned his Bachelor of Science in Zoology and his Ph.D. in Cellular and Molecular Biology/Infectious Diseases from North Dakota State University in Fargo. He completed a postdoctoral fellowship with the FDA Center for Veterinary Medicine, where the focus of his research was developing methods for source tracking of *Salmonella* from food animal species. Following his postdoctoral fellowship, Dr. Foley served as an Assistant Professor at the University of Central Arkansas (UCA) where he taught courses in biology and microbiology and conducted research related antimicrobial resistance in *Salmonella* and *E. coli*. During his time at UCA, Dr. Foley also served as a Science Advisor for the FDA Office of Regulatory Affairs, where he provided technical advice on research needs and methodologies. He continued as a Science Advisor after accepting a position as an Associate Research Scientist with the National Farm Medicine Center at the Marshfield Clinic Research Foundation (MCRF). At MCRF, Dr. Foley led a research program focused on antimicrobial resistance and virulence of foodborne and zoonotic pathogens. In 2009, Dr. Foley joined the NCTR and his research team has been focused in the fields of zoonotic diseases, food safety, antimicrobial resistance and tobacco-associated microbiology. In addition, Dr. Foley completed the Leadership Arkansas program and the Leadership in a Democratic Society program through the Federal Executive Institute and is serving at the co-chair of the NCTR Institutional Biosafety Committee and an Adjunct Professor in the Food Science Department at the University of Arkansas.

Jiangchao Zhao, Ph.D.

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Dr. Zhao is a new faculty in the Department of Animal Science, Division of Agriculture, University of Arkansas. After he obtained a PhD in Environmental Microbiology and a graduate certificate from the University of Wisconsin-Madison in 2009, Dr. Zhao worked on the lung microbiome in cystic fibrosis in the University of Michigan Medical School for his postdoctoral training. Dr. Zhao published several high-impact papers in this field before he joined the faculty in the Department of Animal Science at U of A in 2015. His current research focuses on the roles that human and animal microbiome plays in health and diseases. He uses interdisciplinary approaches such as multi-omics (e.g. metagenomics, metatranscriptomics, metabolomics), bioinformatics, statistics, big data and mixed culture to: i) characterize and engineer gastrointestinal microbiome to promote human healthy aging, increase animal nutrient utilization and efficiency, production and well-being; ii) identify and apply prebiotics and probiotics to increase human and animal health and reduce antibiotics use; and iii) identify airway microbiome biomarkers in human and animal respiratory diseases such as cystic fibrosis, COPD and bovine respiratory disease for early and targeted therapy. He has served on the editorial board of two top tier ASM journals: *Applied and Environmental Microbiology* and *Journal of Clinical Microbiology*. Dr. Zhao has published 17 human and/or animal microbiome papers on the lung microbiome in cystic fibrosis, gut microbiome in healthy aging and animal production.

Sangeeta Khare, Ms, Ph.D.

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Dr. Sangeeta Khare joined as a Research Microbiologist in the Division of Microbiology, the National Center for Toxicological Research (NCTR), Food and Drug Administration (FDA) in 2010. Dr. Sangeeta Khare leads an active team with a research emphasis on host-pathogen and host-microbiome interaction during perturbations with xenobiotic agents (nanoparticles, antibiotics and other drugs, natural products and additives). The main focus of Dr. Khare's research group is on 1) the gastrointestinal tract exposure using *in vivo, in vitro* and *ex vivo* models, and 2) the use of advanced technologies, such as next generation sequencing, omics and systems biology approaches, in establishing innovative parameters of host toxicity, gut-associated immune response, and the effects on the population of intestinal microflora. Dr. Khare's research team has several ongoing studies that contribute extensively to the FDA mission and public health. For example, in the area of nanotechnology derived products, her laboratory has provided data that can be used as additional endpoints in the risk assessments of products containing nanoparticles. This supplements the metabolism, toxicity, and tissue residue disposition information that is traditionally used in the safety evaluation of such products. Another ongoing project, in collaboration with the Center of Veterinary Medicine, evaluates the effect of residual amounts of antibiotics on the development of antibiotic resistance and gastrointestinal permeability. An additional element of Dr. Khare's group's research is to delineate the impact of xenobiotic agents during developmental exposure, as well as, chronic and acute exposure to adults using animal models. Under cooperative agreement with the National Toxicology Program (NTP), her research group is also investigating the effect of chronic exposure to xenobiotic compounds, which humans are exposed to daily. Dr. Khare is professional member of several scientific organizations and adjunct faculty at Texas A&M University. She serves as a member for FDA Microbiome working group. She is reviewer for several journals and served as grant reviewer for FDA, USDA, NIEHS and several other international grant organizations. Dr. Khare has been invited to share her research findings at other FDA Centers, several national and international conferences as well as medical institutes and universities with in the US and abroad. The outcomes of collaborative projects within the NCTR, FDA Centers, NTP and other academic institutions are in-line with the NCTR/FDA strategic plan on regulatory science to "Evaluate Innovative Emerging Technologies" and "Modernize Toxicology to Enhance Product Safety."

Mohammed Orloff, Ph.D.

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Dr. Orloff is an Associate Professor at the Department of Epidemiology Fay W. Boozman College of Public Health, University of Arkansas for Medical Sciences (UAMS). He is a member of the Winthrop P. Rockefeller Cancer Institute, an Adjunct at the University of Arkansas at Little Rock (UALR) and a Visiting Associate Professor at the School of Medicine, at the Aga Khan University, in Kenya. He graduated and trained as a genetic and molecular epidemiologist at Case Western Reserve University, then worked in the area of Genomic Medicine at the Cleveland Clinic Foundation, before joining UAMS. His lab at the UAMS focuses on bioinformatics, genomics, epigenetics and microbiome of lung diseases, specifically, COPD and lung cancer. He integrates these omics approaches to reveal factors that play a role in the development of lung cancer and identify biomarkers that distinguish lung cancer subtypes in individuals of different genetic backgrounds. The goal of his projects is to develop biomarkers that will inform personalized medicine.

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Dr. Carl E. Cerniglia is a Senior Biomedical Research Service (SBRS) Research Microbiologist, Director of the Division of Microbiology at the National Center for Toxicological Research (NCTR), US Food and Drug Administration (FDA) and elected member of the American Academy of Microbiology. He is also an adjunct Professor in the Department of Pharmacology and Toxicology at the University of Arkansas Medical Sciences, Little Rock, AR. Dr. Cerniglia leads a team at the NCTR that has impacted public health in a variety of research areas including food safety, antimicrobial resistance, environmental biotechnology, nanotechnology, women's health and human intestinal microbiome-host interactions. Dr. Cerniglia's research has resulted in over 400 scientific publications and numerous book chapters and review articles. His research has been frequently highlighted in the scientific and popular press. Dr. Cerniglia has made more than 400 invited presentations at national and international conferences and meetings and is also an ASM Foundation of Microbiology lecturer. The research achievements of Dr. Cerniglia has been recognized by national and international awards from the Food and Drug Administration, American Pharmaceutical Association, International Society of Toxicity Testing, American Society for Microbiology, and American Academy of Microbiology and U.S. Department of Health and Human Services. Dr. Cerniglia was recently awarded the Silver Medal by the World Health Organization for outstanding scientific contribution to the Joint Expert Committee on Food Additives (JECFA) in advancing science-based risk assessments on evaluating the effects of veterinary drug residues and other food contaminants on the human intestinal microbiome, the FDA Lifetime Achievement Award, the FDA Commissioner's Award Merit, the DHHS Outstanding Leader Award in providing mentoring, training and career advancement opportunities to employees in a diverse workforce and Distinguished Alumnus Award at North Carolina State University.

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Dr. Zybailov is Assistant Professor in the Department of Biochemistry and Molecular Biology at UAMS. His research is focused on human gut microbiota and its role in chronic kidney disease. His research group develops novel methods of microbial protein quantification, de novo protein sequencing, post-translational modification analysis, and biomarker discovery. He is an expert in mass spectrometry-based proteomics, computational proteomics, systems biology, and large-scale ('omics') data integration. He has published 37 scientific articles and 2 book chapters.

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Dr. Richard Frye is the Director of Autism Research at Arkansas Children's Hospital Research Institute, Director of the Autism Multispecialty Clinic and Co-Director of the Neurometabolic Clinic at Arkansas Children's Hospital and Associate Professor in Pediatrics at the University of Arkansas for Medical Sciences. He received his MD/PhD from Georgetown University in 1998. He completed a residency in Pediatrics at the University of Miami, Residency in Child Neurology and Fellowship in Behavioral Neurology and Learning Disabilities at Children's Hospital Boston and Fellowship in Psychology at Boston University. He holds board certifications in Pediatrics, and in Neurology with Special Competence in Child Neurology. Dr. Frye is a national leader in autism and metabolic research. His research at ACRI focuses on metabolic aspects of neurodevelopmental disorders, including abnormalities in mitochondrial, folate and cobalamin pathways, particularly how these pathways are influenced by environmental factors such as enteric microbiome metabolites. He has authored over 100 peer-reviewed publications and book chapters.

Fred Prior, Ph.D.

Chair
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Fred Prior has been named the inaugural chair of the University of Arkansas for Medical Sciences Department of Biomedical Informatics. Before coming to UAMS he was the Director of the Electronic Radiology Laboratory in the Mallinckrodt Institute of Radiology at Washington University School of Medicine in St. Louis, where he has served as director since 2003. He is also was the director of the Center for High Performance Computing, as well as associate director of the Center for Biomedical Informatics and a research professor of radiology. Prior is the principal investigator for the Cancer Imaging Archive, supported by the National Cancer Institute, which provides researchers, educators and the general public with a vast, freely accessible, open archive of cancer-specific medical images and metadata. Prior holds seven U.S. and international patents and is working with a consortium of investigators on the Human Connectome Project, which is mapping comprehensively the neural pathways of the human brain. Prior received a Master of Science in biomedical engineering at Case Western Reserve University in Cleveland in 1984 and a Ph.D. in computer science at the Illinois Institute of Technology in Chicago in 1992. He served as chief of the Section on Radiologic Computing and Imaging Science at the Pennsylvania State University College of Medicine from 1993 to 1997. Prior spent six years in in medical information management research and development, holding senior management positions at Philips Medical Systems and Eastman Kodak Co., as well as Silicon Valley startups.

Anthony Goudie, PhD

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Dr. Goudie is the Director of Research and Evaluation at the Arkansas Center for Health Improvement. He holds a primary academic appointment in the Center for Applied Research and Evaluation and a secondary appointment in the Birth Defects Research Section in the Division of Pediatrics, College of Medicine and secondary appointments in the Department of Health Policy and Management in the Fay W. Boozman College of Public Health at the University of Arkansas for Medical Sciences. His current focus is lead evaluator on the Arkansas Section 1115 Demonstration Waiver Evaluation for the Health Care Independence Program ("Private Option" since renamed to Arkansas Works). He is also co-PI on grant to study the spillover benefits of the Arkansas Private Option program to the national treasury. Other areas of actively funded work include creating population-level linked longitudinal databases. One database will be used to conduct life course analyses in a population of Arkansas children with birth defects, while another will study early life prescription medication exposure and their effect on the body mass index trajectory of Arkansas children between 2 and 17 years of age.

Anita Walden, B. S.

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Anita Walden has more than 20 years of experience in clinical research and 15 years in informatics related activities. She has managed data operations for domestic and large international trials conducted in over 25 countries and has supervised data integration and informatics teams. Her informatics background is diverse, with experience in data standards development, data integration, and mobile and electronic health technology development. She has worked in the international data standards space which includes leadership roles in Health Level Seven (HL7), the Critical Path Institute and a strong relationship with Clinical Data Interchange Consortium (CDISC). As an informatics project leader, she managed grants funded by the FDA, NIH and Gates Foundation and developed 9 therapeutic area standards in infectious disease, mental health, cardiology, anesthesiology preoperative assessment, emergency services, trauma and bio- banking.

She is also an industry educator and trainer in data management, clinical research informatics and mobile health technologies with the Society of Clinical Data Management (SCDM).

As a faculty member in the Department of Biomedical Informatics at the University of Arkansas for Medical Sciences, her research interests are in international data standards, EHR data integration for clinical studies, but primarily in eHealth and mHealth technologies for underserved and under-represented communities.

Thomas E Powell, M.D. M.S.

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Dr. Powell is the active full-time CMIO, Associate Vice Chancellor of Clinical Programs at UAMS. He is a licensed physician and executive who has completed one of the original NIH sponsored fellowships in Clinical Informatics in partnership with Duke University, leading to a Masters in Biomedical Engineering in 2001. He has over 16 years of experience applying technology, informatics, and analytics in private, academic, and research settings. He has over a decade of experience in healthcare academia, with research faculty appointments at both University of Miami and UAMS. He has successfully led multiple clinical sites through full library Epic and Cerner implementation, stabilization, optimization, training, and change management efforts. He is able to coordinate and guide the operational/clinical involvement and participation necessary to support this project. He remains engaged in all administrative, IT, and clinical decision making for these projects and will work with IT resources to assure that he builds support for biomedical informatics research and education. He has guided numerous research and operational efforts to define, measure, and extract metrics from electronic health records. He has worked closely with our simulation center to establish a realistic laboratory setting for numerous clinical environments. He also holds a primary academic appointment in the Division of Biomedical Informatics at UAMS.

Feliciano “Pele” Yu, Jr., MD

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Dr. Feliciano “Pele” Yu, Jr., is a pediatrician with expertise in health informatics and health services research. He is the Chief Medical Information Officer at Arkansas Children’s Hospital and Professor of Pediatrics and Biomedical Informatics at the University of Arkansas for Medical Sciences College of Medicine. He maintains clinical practice at Arkansas Children’s Hospital General Pediatric and Circle of Friends Clinics.

Dr. Yu received a Bachelor of Science degree in Biology at the University of the Philippines in 1987. He received his medical degree from the University of the East RMMC School of Medicine (Philippines) in 1991. He completed pediatric residency training at the Children’s Hospital of Wisconsin (Medical College of Wisconsin, Milwaukee) in 1996. After residency, he practiced primary care pediatrics

in South Carolina until 2001 and then he moved to Birmingham to practice pediatric urgent care medicine at The Children’s Hospital of Alabama. In 2005, he completed the NIH Ruth L. Kirschstein National Research Service Award (NRSA) postdoctoral fellowship in health services research at the University of Alabama at Birmingham (UAB) Center for Outcomes and Effectiveness Research and Education. By 2006, he received Masters of Science degrees in both Health Informatics and Public Health from the UAB. He is a Fellow of the American Academy of Pediatrics, Diplomate of the American Board of Pediatrics, and a Certified Professional in Healthcare Information and Management Systems (CPHIMS) as well as a Fellow of the Health Information Management Systems Society (FHIMSS). He is also board certified in both Pediatrics and Clinical Informatics.

Dr. Yu’s primary focus lies in the intersection of health informatics, outcomes research and quality of care. He has authored several peer-reviewed papers and abstracts on the subject. His recent publications examine the impact of technologically advanced healthcare institutions on measurable processes of care, analysis on hospitals with computerized order entry systems, and clinical decision support systems, among others. The common theme across Dr. Yu’s work relates to helping clinicians make better decisions, provide quality care, and improve healthcare processes through the use of health information and communications technology

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Professor David Ussery was born and raised in Springdale, Arkansas. He has been working with bioinformatic analysis of bacterial genomes since the first sequence was published in 1995, and published one of the first text books in the field of Comparative Genomics. He has published more than 200 papers, which have been cited more than 10,000 times, including two papers with more than a thousand citations. He has been a co-applicant on grants funded totaling more than $30 million, since 2010. His popular course on Comparative Microbial Genomics, taught at The Technical University of Denmark from 1997 - 2013, is currently running for the 19th year; one-week workshops based on this course have been held in North and South America, Europe, Asia, and Africa. Prof. Ussery has collaborative projects with groups in Belgium, Denmark, France, Germany, The Netherlands, Norway, Spain, Sweden, and the UK, as well as in the U.S.

Prior to joining UAMS, Dr. Ussery was the Comparative Genomics Group leader at Oak Ridge National Labs, in Oak Ridge, Tennessee (2013-2016). He led the Comparative Microbial Genomics group at The Technical University of Denmark from 1997 – 2013, where he has successfully supervised more than 20 Ph.D. students in bioinformatics.

Prof. Ussery received a doctorate in Molecular Biology in1993 from The University of Cincinnati College of Medicine and did a post-doctoral fellowship at Oxford University (1992-1996). He earned his master's degree in biophysical chemistry at the University of New Mexico in Albuquerque. He earned a bachelor's degree in chemistry from William Jewell College (Liberty, Missouri) in 1982, and graduated from Springdale High School (Springdale, Arkansas) in 1978.

Donald Johann Jr., MD

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Dr. Johann is a physician/scientist, Associate Professor at UAMS and Scientific Director of the UAMS Genomics Sequencing Facility. His scientific focus concerns the application of advanced molecular profiling and high-throughput technologies for the characterization of molecular alterations in cancer cells. Areas of emphasis include next-gen sequencing (NGS), high-resolution identity-based mass spectrometry (proteomics), laser capture microdissection (LCM), bioinformatics, and cancer biology. Previously, he was an assistant investigator at the National Cancer Institute (NCI), Center for Cancer Research (CCR), in the Medical Oncology Branch in Bethesda, MD. Prior to attending medical school he worked as an engineer for the Unisys Corporation for six years, where he directed a team of five engineers on projects involving avionic and systems level (OS, compilers) software design and instrumentation. During this time he also earned a graduate degree in computer science with distinction from Hofstra University. Dr. Johann received his M.D., from Case Western and received a graduate with distinction honors for Computer Applications in Medicine. Following residency he became a postdoctoral research fellow at the NIH/NCI Lab of Pathology, under the mentorship of Dr. Lance Liotta, with a focus on clinical proteomics. He was twice selected for AACR Scholar-in-Training Awards for research work involving novel bioinformatics. Medical Oncology/Hematology fellowships were completed at NIH in the NCI and NHLBI. He has authored ~40 publications and contributed to three patents.

Lawrence Tarbox, Ph.D.

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Dr. Tarbox is the lead architect for The Cancer Imaging Archive, a large, publically accessible archive of cancer images and related data. He is also the principal investigator for the Chest Imaging Archive for the CDC-NIOSH. He also directs high performance computing efforts for data analysis at the University of Arkansas for Medical Sciences, Department of Biomedical Informatics (DBMI). He came to DBMI with over thirty years' experience in both the commercial and academic research sectors, with responsibilities ranging from basic research to product development to business planning to deployment in real-world settings. The majority of his career has been focused on providing tools for the acquisition, processing, archiving, and management of medical data. This experience includes applying high performance computing resources, such as GPUs and parallel processing, both on custom-built and generic hardware, to enhance and speed up image and data processing algorithms. Dr. Tarbox is very active in standards development, co-chairing the DICOM working groups on security and application APIs.

Kevin W. Sexton, MD

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My goal in life is to decrease patient suffering. My research focuses on processing physiologic signals and electronic healthcare record data to improve clinical decision making at the patient level. I work clinically in the Division of Trauma, Critical Care, and Acute Care Surgery as an Assistant Professor in the Department of Surgery at the University of Arkansas for Medical Sciences. Previously, I helped create the decision support behind Midas + Live and Kinsa. I tweet @kwsexton.

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Impact of Varying Amounts of Dietary Maillard Products (Barley Melanoidians) on Healthy Mice Gut Microbiota and Associated Biomarker

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Maillard reaction products (MRPs) are protein-carbohydrates complexes commonly formed through heating of food. Conflicting reports of MRPs impacts on human health are probably due to the fact that bioconversion of these poorly digestible large molecules by the gut microbiota has been marginally taken into account. Melanoidins, the bigger and more complex MRPs, are found in foods such as coffee, roasted cocoa, roasted barley, bread crust, and other products. Previous in vitro studies have suggested potential antioxidant and prebiotic effects. In this study, we tested the potential prebiotic impact of melanoidins in vivo.

75 mice were divided into 5 groups receiving different amounts of dietary melanoidins, through combination of lightly and heavily toasted malts (from barley). The control group consumed a diet with 0% of melanoidin-rich malts, and other groups received melanoidin malts by increments of 25%, up to group 5 consuming only malanoidins malts. Mice were housed in metabolic cages 6 hours on sampling days to collect feces at day 0, 1, 2, 3, 7, 14 and 21. Microbial DNA was extracted from fecal samples and V4 bacterial 16S rRNA amplicon libraries set up for Illumina MiSeq sequencing. All sequences were analyzed by using software package MOTHUR.

Melanoidins consumption significantly influenced the gut microbiota composition, with three major phases. In the first 2 days, Lactobacillus and unclassified Bacteroidetes were significantly stimulated in mice consuming the highest melanoidins amounts. Between day 2 and 7, only the unclassified Bacteroidetes were significantly increased. Day 7 to 21 were characterized by a steady decline of unclassified Bacteroidetes, and an increase in Alistipes, Bifidobacterium and Akkermansia. These results illustrate the importance of studying long-term impact of consumption of melanoidins. Interestingly, two distinct prebiotic impact appear to be confirmed, short-term Lactobacillus bloom and long-term bifidogenic effect associated with Akkermansia which is increasingly considered as beneficial. Akkermansia are also well known for their unique ability of using mucin (glycated proteins, similar to MRPs) as carbon and nitrogen source, so it is likely they are able to perform the same metabolic pathway with melanoidins.

Identification of nitrogen cycling mutants in Arabidopsis using combined bioinformatics and nitrogen-13 radiotracer assays

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[6]Current Institution: Purdue Research Foundation, WestLafayette, IN

Nitrogen (N) is often the most limiting nutrient for terrestrial plants. Nitrogen uptake is well studied, but transport of N within the plant to growing tissues is also an important factor determining growth and survival. A major knowledge gap is our limited understanding of N transport mechanisms and how they are regulated. We used a combination of large-scale transcriptomic data mining and experimentation to identify relevant N transporters. Knockout mutants were identified for candidate N-related transporters of interest. Mutants were screened for leaf N export defects by administering the radioactive isotope nitrogen-13 (13N) as 13NH3 gas at sub-biological concentrations, and measuring export of 13N from the target leaf. We have identified several genes in Arabidopsis that appear to be necessary for N export from leaves under low but not high soil N availability. One mutant had lower total N export of bolting plants than non-bolting plants, indicating this gene is important for transporting N to the reproductive sink tissues. We are currently characterizing these genes to determine their precise biological role. The assembly of these and yet-to-be-identified components into a complete conceptual model of the whole-plant N transport system, and translation to crop species will aid in engineering enhanced NUE in agricultural plants and crop trees, and minimizing energy-intensive fertilizer inputs into crop production.

OWL2TL: an easy way to share bio-ontology information with bioinformatics domain experts

John Judkins, Joseph Utecht, **Mathias Brochhausen**

University of Arkansas for Medical Sciences, Little Rock, AR

Ontologies (for instance, the Gene Ontology) play an increasingly important role in annotating, sharing, and curating bioinformatics data. Semantically-rich, machine-interpretable ontologies, coded in the Web Ontology Language hold great promise to integrate data from heterogeneous resources, but communicating the content of such ontologies to users, consumers, or domain experts is still difficult because these groups typically do not have working experience with semantic web tools, e.g. Protégé. This often hinders quick dissemination of ontology content and its updates, especially when working with a collaborative group. This poster demonstrates how the linked data abilities of Semantic Web Technologies can be used to easily create research project-specific term lists that are updated automatically and can be accessed from a stable URI. We developed a novel web service, OWL to Term List (OWL2TL), which allows users, consumers, or domain experts to generate an up-to-date list of all terms and definitions from any OWL file, with a results page accessible via a shareable URL. In addition to a list of terms users have the option of displaying multiple annotation properties, e.g. 'comment' or 'superclass'. The web service is accessible at http://owl2tl.com. The development of this web service was triggered by an arising need in the NIH-funded project CAFÉ (Comparative Assessment Frameworks for Environments of trauma care) (R01GM111324). During the development of the ontology for this project we needed to share constantly evolving terms and definitions with a diverse group of domain experts to solicit input. Since the web service went online, it has already been used by multiple projects in the field of bioinformatics and biomedical informatics. Expanding the functionality of OWL2TL over the last few months has demonstrated the strength of using semantic web technologies to manage terminological information in a flexible manner.

Rapid Detection of Zika Genomes from Clinical Isolates

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The Zika virus is a growing problem, that recently entered the United States. Zika is a human-pathogenic flavivirus that can be transmitted to humans through multiple avenues. Most often the virus is transmitted from an infected mosquito to a human through a bite. The virus can then be spread from an infected human to its sexual partners, as well as from an infected pregnant mother to her fetus.

We are developing a method to use third generation sequencing machines to rapidly detect Zika from clinical isolates. We will be using clinical isolates from people who have tested positive for Zika within the state of Arkansas; provided by the Arkansas Department of Health. We will also collect clinical samples from people who do not have the Zika virus, to be used as a control group. Using new Nanopore third generation sequencing technology we will be able to sequence the full length Zika Genome within one read of one sample.

The Oxford Nonopore MinIon Sequencer is a new form of sequencing technology that has the ability to produce long sequences within the first fifteen minutes of the run, and can generate more than 5 million reads at time. Our preliminary results show that we generate sequences with an average of fifteen thousand base pairs within the first fifteen minutes. Since the Zika genome is ten thousand bases long, a single read can contain the full length viral genome.

Extract Pharmacogenomics Information from FDA Drug Labeling to Advance the Study of Precision Medicine

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Background: Pharmacogenomics (PGx) focuses on how genomics and genetic variants (inherited and acquired) affect drug response. A better understanding of the association between genetic markers and individual phenotypes may improve therapy by enhancing drug efficacy, safety, and advance precision medicine.

Result: The FDALabel database (https://rm2.scinet.fda.gov/druglabel/#simsearch-0) was developed from the FDA's Structured Product Labeling (SPL) repository to allow users to perform full-text and customizable searches of the labeling section {e.g. Boxed Warning, Warning and Precautions, Adverse Reaction (AR) sections}. In this study, 48 known biomarkers were used to query PGx relevant contents from the FDALabel database, including Indication, Clinical Pharmacology, Clinical Studies, and Use in Specific Populations. As a result, we identified 162 drugs out of 1129 small molecule drugs with PGx biomarker information. Furthermore, statistical analysis, pattern recognition, and network visualization were applied to investigate association of drug efficacy and severe ARs with PGx biomarkers and subpopulation. The results indicated that these drugs have a higher association with certain ARs in specific patient subpopulations (e.g., a higher association between CYP2D6 poor metabolizers and ARs caused by drugs for the treatment of psychiatric disoders), and cover a broad range of therapeutic classes (e.g., Psychiatry, Cardiology, Oncology, and Endocrinology).

Conclusion: FDALabel database (free publicly available) provides a convenient tool to navigate and extract PGx information from FDA-approved drug. The knowledge gained from these drugs and biomarkers in this study will enhance the understanding of PGx to advance precision medicine.

Impact of Storage on Fungal Populations in Moist Snuff Smokeless Tobacco Products (STPs)

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The use of smokeless tobacco products (STPs) is associated with an elevated risk of mouth and throat cancers. Few studies have examined the fungal population of STPs, which is a potential concern because fungi present in STPs may cause an infection or contribute to the development of carcinogens. Thus the current study evaluated methods to characterize fungal populations in STPs and determine their impact on STP characteristics. To conduct the studies, multiple containers of ten different moist snuff products were purchased in Little Rock, Arkansas, in December 2015 and April 2016 and stored at three different temperatures (4ºC, 25ºC and 40ºC) over a 12-week period. At 4-week intervals, tobacco from individual containers was analyzed. Fungal analyses included total mold and yeast counts and fungal population analyses, using next-generation sequencing approaches that utilized the amplification of the internal transcribed spacer (ITS) region of the fungal ribosome genes and comparison to an ITS database using QIIME. Over the 12-week sampling period, there was a general trend of reduction in fungal numbers within the samples, as determined by total mold and yeast counts. This general reduction in numbers occurred across all of the different storage conditions evaluated. There were pronounced differences in the predominant fungal taxa identified among the different products. In five of the products, the Saccharomycetes were the predominant fungal class that remained throughout the study period, regardless of the storage conditions. The other five STPs had more variable fungal populations detected at different time points. Each of these five products had an increased percentage of Tremellomycetes at week 12, which could have been due either to reduction of the other fungal populations or to an increase in the Tremellomycetes. A challenge with the ITS-based metagenomics approach was that a relatively high percentage of samples had reads that could not be deciphered at the class level, which highlights the need for improved fungal taxonomy databases. This project examined the methods to evaluate fungi in STPs and the impact of storage conditions on fungal populations in the products. Overall, the results shed light on the impact of product type and storage conditions on fungal populations and STP changes over time.

Nonclinical modeling and risk assessment of nanocrystal-drugs

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Currently, more than 750 clinical trials are in progress involving potential nano-medicine products. Of these, 38 are approved products/currently in use and 128 are investigative new drugs applications, of which 14% are drug-nanocrystals. Approximately 82% of drug-nanocrystal IND applications are for oral-administration. For FDA regulatory/reviewer guidance, the agency needs experimental data to assess the effect of drug-nanocrystals on the human gastrointestinal-tract (GIT). Two model drugs were selected: zileuton (BCS class II/IV) and spironolactone (BCS class II) for the preparation of nanocrystalline-formulation. A comprehensive quality by design (QbD) approach involving three design of experiments (DoE) models (milling, spray drying and formulation) was used for the identification and optimization of the critical quality attributes (CQAs) of spray dried zileuton to achieve a stable nanocrystalline formulation. The comprehensive QbD approach will minimize the errors in product optimization and formulation in DoE models. The nano-size range, reduced intensity of the diffraction peaks and minor birefringence in zetasizer, PXRD and PLM, respectively, indicated the nano-crystalline nature of the optimized formulation.

Since the parent drugs (zileuton and spironolactone) are associated with several GIT side effects, the GIT permeability assay was optimized by measuring transepithelial electrical resistance (TER) using polarized intestinal-epithelial cells (IEC) to determine nanodrug-crystals and intestinal cells interactions. The results showed an increase in TER in IEC incubated with spironolactone in a dose-dependent manner at 24 and 48h compared to controls. Whereas, zileuton increased TER value in cells treated with 0.1 µm and 1 µm concentrations but not with higher-dose levels. Furthermore, the expression of GIT permeability-associated genes involved in the maintenance of cell-cell junctions and tight-junctions were analyzed. In conclusion, these findings provide evidence that there is a significant effect of zileuton and spirinolactone on the IEC resistance and integrity of cell-cell junctions. In future experiments, the optimized nano-crystalline formulations will be analyzed for in vitro dissolution testing, in vivo oral bioavailability and ex vivo immune-toxicity studies.

A Bioinformatics Workflow for Low-frequency Mutation Detection Enabled by Unique Molecular Identifier (UMI) and Deep Targeted Sequencing

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Background: Genetic mutations in the focused genes have long been proposed as a key factor of cancer initiation and progression, as well as chemotherapy sensitivity and resistance. However, due to tumor heterogeneity, the mutation allele fraction may be no more than 1%, which cannot be detected by conventional sequencing approaches, due to the high background error rate of PCR and sequencing.
Data and Methods: Here we present a workflow for ultralow-frequency mutation detection. The pilot data was generated using 10 cancer cell lines provided by Agilent Technologies. The gDNA samples were fragmented to about 300 nts in length and then ligated with adaptors with random unique molecular identifiers (UMI). After PCR amplification, the targeted fragments were captured through hybridization by IDT xGen® Pan-Cancer Panel of 127 genes. Sequencing was performed by Illumina HiSeq platforms. We have developed a bioinformatics pipeline for data processing and analysis, which contains five major steps: (1) data pre-processing and tag marking, (2) read mapping, (3) consensus making, (4) re-mapping, and (5) variance calling.

Results and Conclusion: The workflow is ideal for small genomes and targeted genomic regions. Most sequencing and PCR errors can be removed by building consensus reads from original reads with the same UMI tag and mapping position to the reference genome. Improper mapping reads can also be removed during the consensus reads building process. The local re-alignment of the consensus reads is recommended for better call of indels. An optional end-trimming process can decrease the false positive rate which may be introduced during the library preparation. Early-round PCR errors may not be removed by this workflow and may be improved by increasing the sequencing depth or using more complex methods by ligating UMI to both end of DNA fragments.

Differential Coexpression: A new paradigm for identification of genes from expression data.

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Analysis of differential expression between experimental groups is already a prevalent method for selection of interesting genes related to a trait of interest. However, an estimation of differential expression fails to select genes that exhibit differences in their interaction patterns, underplaying the identification of several dysregulated metabolic pathways and molecular processes. Interactions between genes is the fundamental principle of metabolic pathways. How gene interactions are rewired in different biological contexts, and which of these interactions are functional, is not very well understood. This study explored the concept of differential coexpression, and formulated a network density based algorithm to identify affected genes and metabolic pathways that remain elusive in traditional differential expression analysis. Using large scale expression data of the crop model rice (Oryza Sativa) as an example, we showed that several well-known pathways already implicated in drought stress could not be identified on the basis of differential expression alone, but only resurfaced within the framework of differential coexpression. Several hypotheses regarding the 'emergent properties' of the rice drought gene network are presented, along with novel genes that have significantly rewired edges upon exposure to drought. Overall, the results indicate that differential coexpression should be employed to complement differential expression in order to gain insights into 'hidden' information from expression data.

Impact of Storage Conditions on Bacterial Populations and the Formation of Tobacco-Specific Nitrosamines (TSNAs) in Smokeless Tobacco Products (STPs)

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The use of smokeless tobacco products (STPs) is associated with an elevated risk of mouth and throat cancers. Tobacco-specific nitrosamines (TSNAs) are carcinogens in STPs associated with the development of cancer. Certain bacterial species present in STPs may contribute to the development of TSNAs by the biotransformation of precursors needed for the nitrosation of nicotine, which leads to TSNA production. As a first step to investigate the impact of bacterial populations on TSNA formation, multiple containers of ten moist snuff products were purchased in Little Rock, Arkansas, and stored at three different temperatures (4ºC, 25ºC and 40ºC) over a 12-week period. At 4-week intervals, tobacco from individual containers was analyzed. The analyses included total bacterial plate counts, bacterial population analyses using next-generation sequencing of the V3-V4 region of the 16S rRNA, sample pH, moisture and water activities, and the levels of nitrate, nitrite, nicotine and TSNAs [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N'-nitrosonornicotine (NNN)] in the samples. The results for total bacterial populations in the products, obtained through high-throughput sequencing of the V3-V4 region of the 16S rRNA, showed that the majority of bacteria identified to the class level were in the Bacilli. The results of the bacterial culturing did not show any major trends related to storage at different temperatures or for different times. These findings may be due to a preponderance of Bacillus species, which can form spores that are resistant to many environmental conditions. The pH also varied among the samples. There was a steady decline in the pH of all of the samples stored at elevated temperature, while the pH changes are more varied in samples stored under the other conditions. Most samples showed a decrease in the moisture level of the products, especially after two weeks of storage. However, the water activity of the samples remained relatively stable throughout the 12-week period across the different storage conditions. The levels of nicotine, nitrate, and nitrite detected in the samples did not appear to display any consistent tendencies related to storage time and conditions. The levels of NNN appeared to increase in several samples (especially after week 4), while the levels of NNK remained relatively stable in most samples. The experiments presented here examined the impact of storage conditions on microbial populations and TSNA production to gain a fuller understanding of the potential bacterial contribution to carcinogen formation in STPs. Overall, the results should aid in determining the factors that contribute to the development of TSNAs and the conditions that could minimize the impact of nitrosamines on user health.

Next Generation Sequencing: Analysis of Genomic Relatedness, Virulence Factors and Antimicrobial Resistance of Salmonella enterica Isolated from Food Sources

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Seven Salmonella enterica strains, six of which contained incompatibility group (Inc) FIB plasmid isolated from food sources were sequenced using the Illumina MiSeq platform. Whole genome sequences (WGS) of these seven S. enterica isolates were compared to genomes of S. enterica isolated from food, animal, and human sources. SeqSero analysis predicted that six strains were serovar Typhimurium and one was Heidelberg. The genome sequences of the isolates were compared to determine evolutionary relatedness to previously sequenced genomes (n=52) of S. enterica serovars using core genome single nucleotide polymorphism (SNP)-based phylogenetic analyses. A SNP-based phylogenetic tree showed each Salmonella serovar (Typhimurium, Heidelberg, Kentucky) joined distinct phylogenetic clades, irrespective of presence or absence of an IncFIB plasmid. Among the S. Typhimurium strains, phylogenetic analyses revealed that five of the IncFIB containing isolates clustered as a single monophyletic S. Typhimurium subclade, while one of the other strains branched with S. Typhimurium from a bovine source. Different WGS based bioinformatics tools, including PlasmidFinder, ResFinder and ISsaga were used to evaluate the plasmid contents, antimicrobial resistance and mobile genetic elements of these S. enterica isolates. Composite phylogenetic trees were developed by averaging pairwise-comparisons of DNA sequences of IncFIB plasmid–associated genes in the Sit and aerobactin operons of S. enterica isolated from different sources. DNA sequence based phylogenetic diversity analyses showed that IncFIB plasmid-encoded Sit and aerobactin iron acquisition systems are conserved among bacterial species including S. enterica. WGS using next generation sequencing technology along with various bioinformatics tools are useful to identify genetic relatedness of Salmonella strains isolated from different sources and their genotypic and phenotypic traits.

Computational Method for Discovering MicroRNA and Long Non Coding RNA Interactions

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Background:
The majority of the transcriptome (98%) is made up of non-protein coding genes (ncRNA). In this research we are interested in the interaction between long-non-coding-RNA (lncRNA) and microRNA (miRNA). LncRNAs are crucial in regulating gene expression at transcriptional, post-transcriptional and translation levels. Many protein coding genes are regulated by competing endogenous RNA (ceRNAs). CeRNAs are a type of lncRNA that contains miRNA targets. These ceRNAs compete for a common pool of miRNAs as natural decoys. LncRNA play a role in the development and pathophysiology of disease. Linc-MD1 acts as a sponges for miR-133b. When the levels of miR-133b increase to the point where they can no longer be sponged up they then target and silence the HuR mRNA. When the HuR protein is no longer produced linc-MD1 switches from sponge to precursor source for miR-133b. This controls myogenesis in mice.

Result:
The known interaction between linc-MD1 and miR-133b was used as a positive control. Our goal is to find previously undiscovered interactions between other miRNA and lncRNA pairs. LncRNA and miRNA datasets were downloaded from the respective databases. A predictor of miRNA was applied to the lncRNA. Known mature miRNA were found in these predicted precursors. These mature miRNAs have validated targets and these targets have GO Ontology.
Conclusion:
If gene ontologies show interesting pathways, the plan is to offer these findings back to the authors of the paper that discovered the relationship of the positive controls. We are doing similar analysis on C. elegans, Drosophila melanogaster and Saccharomyces cerevisiae to find lncRNA and miRNA interaction and offer those results to researchers at UALR and UAMS.

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A genome wide association study of water use efficiency and photosynthesis under water deficit conditions in rice

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Rice (Oryza sativa L.) is an important cereal crop that uses 30% of the global fresh water resources during its life cycle. Water deficit is a major constraint, affecting various physiological processes such as photosynthesis and water use efficiency (WUE) that are crucial processes for plant growth and production of assimilates reducing rice grain yield. However, the abundant diversity of rice has naturally evolved genetic variation for WUE and photosynthesis, from which favorable loci can be identified for improvement of rice productivity traits for superior biomass, economic yield, and WUE. For this study, the USDA rice mini-core collection (URMC) of 206 rice genotypes were screened for WUE, photosynthesis, and multiple productivity traits under drought stress. We performed a genome-wide association study (GWAS) with ~200,000 SNPs to identify the genetic resources and favorable loci for improving WUE and photosynthesis. In the GWAS analysis, we identified 33 SNPs for WUE and 12 SNPs for photosynthesis under well-watered conditions, as well as 24 SNPs for WUE and 12 SNPs for photosynthesis under drought stress, that were closely positioned to genes whose functions predict that they could contribute to WUE and photosynthesis in rice. This study of WUE and photosynthesis within the natural variation available will help to uncover diverse sources for the traits and characterize genetic loci for rice genetics and molecular breeding research. Improving productivity of the rice crop under drought and other abiotic stresses remains as one the most important current and future challenges in plant genomics, which can only be helped by a concerted analysis of the complex traits both within the plant and across the variation present in nature.

Keywords: Rice, Drought, Water use efficiency, Photosynthesis, Genome wide association

The Impact of Graphene on Rat Intestinal Microbiota

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The use of nanoparticles (NPs) in commercial, agriculture,,food safety,biomedical , and pharmaceutical applications has become the subject of extensive research in recent years. Specifically, carbon based nanomaterials, including graphene, are a unique type of NPs with high strength, relative biocompatibility and easy functionality. Moreover, due to its antimicrobial and barrier properties, graphene has been suggested for use in food packaging material. Therefore, it is important to understand the health risks associated with the exposure to graphene. This study was conducted to assess if graphene exposure in the digestive tract can impact the intestinal microbiota .Since the rat intestinal microbiome is functionally similar to its human counterpart we used an animal model in this investigation.

To study the interaction of graphene with intestinal microbiota, fresh fecal samples from laboratory rats were obtained and exposed to different concentrations (1, 10 and 100 μg/ml) of pristine graphene for 3, 6 and 24 hours in a Bioreactor-Rotary Cell Culture System which allowed a continuous interaction of intestinal microbiota with graphene. Both aerobic and anaerobic live bacterial counts were assessed at 3, 6 and 24 hours post-exposure. Fecal samples of untreated and graphene treated groups were also collected for DNA extraction and analyzed for microbial population shift using quantitative real-time PCR.

The results showed that graphene had minimal to no effect on the survival of total anaerobic bacterial counts at all selected concentrations and time points. . However, rat fecal samples exposure to graphene (all concentrations) showed a significant increase of the bacterial count of total aerobic bacteria during the first 3 hours of exposure. After 3 hours, live aerobic bacterial counts of graphene treated samples were equal to the untreated control. DNA was used to assess shift in the predominant bacterial phyla, genus and family present in the intestine by quantitative real time PCR. The results showed that the ratio of Firmicutes and Bacteriodetes phyla changed significantly after exposure to the highest concentration of graphene (100μg/ml). At the same concentration, the abundance of Enterobacteriaceae family (representing several members of pathogenic and nonpathogenic bacteria) was found to increase in comparison to the untreated control. These results clearly indicate that the high concentration of graphene exposure may cause a dysbiosis in the intestinal microbiome. Further analysis of the gut microbial population will be carried out by V3-V4 based 16S sequencing.

The increased potential use of graphene in consumer use products demands a thorough understanding of microbial and cellular toxicity. This study could advance our knowledge for the safety assessment of graphene interaction with commensal microbiome.

This study is a part of the Arkansas Research Consortium in Nanotoxicity.

Identification and Annotation Of Conserved Lncrnas In Human And Rat Brain

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Background: Long noncoding RNAs (lncRNAs) play important roles in diverse biological processes. Presently function and regulation of lncRNAs remains elusive. Many lncRNAs show poor evolutionary conservation. Thus, the conserved lncRNAs in different species could suggest their essential functional roles.

Results: Here, we performed orthologous analysis of lncRNAs in human and rat. Rat is the most useful model for chemical toxicities and drug mechanisms studies. We analyzed a RNA sequencing (RNA-seq) data set generated from 80 human and 66 rat samples. The dataset contains more than 2 billion reads. Our analysis revealed a total of 386 conserved lncRNAs. Among these lncRNAs, 246 transcripts presented in known lncRNA databases; however the majority of them were not functional annotated yet, the remaining 140 transcripts were novel ones. We constructed co-expression networks using the expression profile of conserved lncRNAs and protein-coding genes and obtained 79 co-expression modules. The modules consisted of lncRNAs and protein-coding genes. Gene ontology analysis of protein-coding genes in different modules suggested that the conserved lncRNAs in human and rat involved in various biological processes such as brain development (p=1.12E-2), nervous system development (p=1.26E-3), and cerebral cortex development (p=1.31E-2). Furthermore, we investigated the expression of the lncRNAs, which were predicted to function in brain development by our GO analysis, at different time points of rat brain growth. We found that the expression levels of these lncRNAs kept increasing from 2 weeks to 104 weeks, consisting with our functional annotation.

Conclusion: Our orthologous analysis of lncRNAs in human and rat reveal novel lncRNAs. Further co-expression analysis provides functional annotation of orthologous lncRNAs in human and rat. Our results provide targets for experiment design to study lncRNA function and molecular mechanisms.

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Biomarker discovery for kidney cancer diagnosis based on a unique signature of metabolic reprogramming

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Otto Warburg firstly proposed aerobic glycolysis as a key metabolic reprogramming of cancer cell in 1956 that became a famous hallmark of cancer. However, in the past years, many studies showed different metabolic reprogramming indirectly associated with proliferation processes believed to be additional hallmarks of cancer. Thanks to high-throughput technologies that have been used to generate a fruitful amount of -omics data, shared across the research community, enabling a powerful holistic comparison of cancer metabolism. To search for the signatures of metabolic reprogramming in the different cancer types within this study, high-dimensional datasets derived from many cancer types, including SNP analysis, RNA-seq, and protein profile, were obtained from The Cancer Genome Atlas (TGCA) and The Human Proteome Atlas (HPA). Human Metabolic Atlas (HMA), our well-curated, comprehensive collection of human metabolism, was used as the scaffold for multilevel omics data mapping and integration. Through our developed computational pipelines/tools (e.g., PIANO, INIT), we identified divergences of kidney cancer metabolism from other cancer types. Metabolism of kidney cancer correlated with loss of von Hippel-Lindau tumor suppressor (VHL) located on chromosome 3p. Strikingly, the GAG pathway was discovered to be associated strongly with coordinated regulation and progression only in kidney cancer, and could, therefore, be used as a biomarker for clinical diagnosis. The GAG profile measured in both plasma and urine samples was distinctively altered in the cancer patients relative to healthy controls in a discovery cohort with accuracy greater than 82%. Furthermore, the biomarker was successfully validated in another independent cohort, strongly indicating the robustness of the biomarker. Applying systems biology to dissect the biological problem enables high quality biomarker discovery that can be translated into clinical diagnosis in practice.

Development of novel tocotrienol analogs, the tocoflexols, as radioprotectors with enhanced bioavailability

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Purpose of the study: Naturally occurring vitamin E components, collectively known as tocols, include eight isoforms, four tocopherols (α, β, γ and δ) and four tocotrienols (α, β, γ and δ). The tocotrienols have been shown to be active as radioprotectors with potential applications in the case of radiation accidents or terrorism scenarios, as well as for use in patients undergoing radiotherapy. Unfortunately, despite their very significant radioprotectant activity, tocotrienols have very short circulation half-lives and would require multiple dosing or very high doses to achieve the necessary therapeutic levels. Tocotrienol's shorter circulation half-life is due to their low affinity for α-tocopherol transfer protein (ATTP), the liver protein that maintains the tocol's plasma levels by recycling them into the systemic circulation. Thus rather than being recycled into circulation the tocotrienols have a longer residence time in the liver, from where they get metabolized and eliminated by biliary excretion. The goal of our research is to develop tocotrienol analogues with enhanced bioavailability that can be used clinically as radioprotectors. Based on the structural analysis of the complex of ATTP with α-tocopherol we have determined that the flexibility in the tail of tocols is crucial for effective binding. Thus, by using in silico molecular dynamics (MD) screening procedure we identified the novel tocotrienol analogs, the tocoflexols, that have a long isoprenoid dienyl tail with a chromanol head, that has the potential to bind to ATTP while retaining their bioactivity.
Methods: To test the binding pattern of the tocoflexols to ATTP, MD simulations of the open conformation of ATTP (PDB ID: 1OIZ) in complex with δ-tocoflexol, α-tocopherol, or δ-tocotrienol positioned in a dodecahedral water box were performed using GROMACS 5.1.4 with GROMOS96 43a1 force field and a production run of 20 ns. Cellular uptake of tocoflexols was studied, using mouse NSC-34 cells, and measured by a sensitive GC/MS methodology. The bioactivity of the tocoflexols was evaluated by measuring their ability to inhibit lipid peroxidation in microsomes using a TBARS assay. Results: MD simulations showed that the complex of tocoflexol with ATTP behaved very similarly to that of the α-tocopherol and ATTP. Cell uptake measurements showed that tocoflexol have cell uptake levels comparable to those of the tocotrienols and significantly greater than those of the tocopherols. Similarly, the TBARS assay showed that tocoflexols inhibit lipid peroxidation at levels comparable to those of the tocotrienols.
Conclusions: The potential of the tocols, as clinically useful radioprotectants depends on three distinct factors: their intrinsic level of bioactivity, their ability to penetrate the cells and their bioavailability. Although, some of the current tocols have good levels of intrinsic bioactivity their very limited bioavailability has hampered their clinical usefulness. Using molecular dynamics simulations, we were able to design the tocoflexols that demonstrated comparable levels of bioactivity to those of the most potent compounds currently available, and also have the potential for much greater bioavailability. These results highlight the potential of the tocoflexols for radioprotection in radiological accidents or attacks and in patients undergoing radiotherapy.

Methionine Sulfoxide Formation by Cigarette Smoke is Associated with The Degradation of Plasma Proteins

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Background: High level of protein carbonyls have been found in plasma proteins in smokers compared to non-smokers. While oxidation may directly interfere with activity, the extent to which oxidation affects protein turnover is less clear.
Objectives: To determine levels of oxidized serum proteins cleared in the urine of smokers and non-smokers with focus on methionine sulfoxide (MSO) formation in Human Serum Albumin (HSA) and to determine the effect of methionine oxidation on the turnover of HSA.
Method: 100 mL of urine were obtained from smoker and non-smokers. proteins were concentrated by reducing the sample size to 1.5% of the original volume. 200 µL of the concentrate then were separated by SDS-page gel electrophoresis. The band with intact HSA was cut out and the remainder of the gel was cut into four different pieces. Gel sections then were digested with trypsin. Levels of MSO in the resulting peptides were assessed by LC-MS/MS and data analysis was performed using the Skyline software package.
Results: A group comparison between non-smokers (control) and smokers showed a slight increase in the levels of MSO found in intact HSA of smokers relative to non-smokers. Regions of gels with proteins of lower mass than intact HSA showed that degraded fragments of HSA in urine of both smokers and non-smokers have higher levels of MSO than are found in intact HSA.
Conclusions: HSA in smokers has statistically significant higher levels of MSO than HSA in non-smokers. However, the higher levels of oxidation in smokers are concentrated in partially degraded HSA. At the moment, it is not possible to say unequivocally whether oxidized HSA is more likely to be cleaved and cleared, if cleaved protein is more likely to be oxidized before clearance, or both.

Bioinformatics Project Collaborations for the Rhoads' Research Group at University of Arkansas

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The Rhoads' research group primarily focuses on genomic and transcriptomic analyses in metabolic diseases of chickens. Current projects include: Bacterial Chondronecrosis with Osteomyelitis (BCO) in broilers leading to lameness, and Pulmonary Hypertension Syndrome (PHS) leading to ascites in broilers. The BCO project is using bacterial phylogenomics through *de novo* genome assembly of short and long reads to understand hypo and hyper virulent bacterial strains and species. We seek to identify the genes responsible for macrophage evasion, epithelial penetration, and bone pathogenesis. The PHS project is using Genome Wide Association Studies (GWAS), transcriptomics, and genome resequencing to identify genes and gene networks that contribute to PHS leading to ascites. Both the BCO and PHS projects relate not only to important issues in the poultry industry, but also as models for analogous human diseases. Additional projects include: RNAseq analysis for identification of gender specific transcription in primoridial germ cells of broilers and layers, de novo assembly and annotation of the genome for the Timber Rattlesnake, *Crotalus horridus,* and *de* novo assembly and annotation of the genome for the striped bark scorpion, *Centruroides vittatus.*

Cecum Specific Mitochondrial Dysfunction in Children with Autistic Disorder and Gastrointestinal Symptoms

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Background: Gastrointestinal (GI) symptoms are prevalent in autism spectrum disorder (ASD) but the pathophysiology is poorly understood. Imbalances in the enteric microbiome have been associated with ASD and can cause GI dysfunction potentially through disruption of mitochondrial function. In this study we compared mitochondrial function in rectal and cecum biopsies under the assumption that microbiome metabolites are more abundant in the cecum as compared to the rectum.

Methods: This is a single blind case-control study of rectal and cecum mucosal biopsies collected at the Massachusetts General Hospital during elective diagnostic colonoscopy. Electron transport chain complex I and IV and citrate synthase activities and electron transport chain complex I-V protein quantity were measured in biopsies from 10 children with ASD, 10 children with Crohn's disease and 10 neurotypical children with nonspecific GI complaints in a blind fashion.

Results: The protein for all complexes, except complex II, in the cecum as compared to the rectum was significantly higher in ASD samples as compared to other groups. For both rectal and cecum biopsies, ASD samples demonstrated higher complex I activity, but not complex IV or citrate synthase activity, compared to other groups. These changes were not due to inflammation identified during endoscopy.

Conclusions: Mitochondrial function in the gut mucosa from children with ASD was found to be significantly different than other groups who manifested similar GI symptomatology suggesting a unique pathophysiology for GI symptoms in children with ASD. Abnormalities localized to the cecum suggest a role for imbalances in the microbiome causing GI symptoms in children with ASD.

Structural changes of androgen receptor ligand-binding domain due to antagonist binding elucidated by molecular docking and dynamic simulations

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Division of Bioinformatics and Biostatistics, National Center for Toxicology Research, U.S. Food and Drug Administration, Jefferson, AR 72079

Androgen receptor (AR) is a ligand-dependent transcription factor and a member of the nuclear receptor superfamily. It plays a vital role in the male sexual development and regulates genes expression in a variety of tissues. Ligands binding to AR induces the conformational changes in AR-LBD (ligand binding domain) which, subsequently, affects the binding of co-regulator proteins and to the DNA binding domain. Thus, three dimensional (3D) structures of AR-antagonist complexes are essential for androgenic activity of chemicals which can be studied using various computational techniques. Unfortunately, wild type (WT)-AR-LBD complex with an antagonist is not available in the protein data bank. Hence, we have applied molecular docking and molecular dynamics simulations to identify the important residues involved in the structural changes due to antagonist binding. Molecular docking was carried out to determine the binding orientation of the antagonist (Bicalutamide) in the ligand binding pocket (LBP) of AR-LBD. The complexes of WT-AR-LBD with Bicalutamide, WT-AR-LBD with agonist (R1881), and mutant-AR-LBD with antagonist (Bicalutamide) obtained from molecular docking were optimized through 100 nanoseconds (ns) molecular dynamics simulations to identify the conformational changes in the LBD and the activation function 2 (AF2) site. The results revealed that the binding of the antagonist in WT-AR-LBD moved the residues present in the H12 (Phe222, Met226, and Ile230) and Arg726 outward when compared with the WT-AR-LBD-agonist. The displacement of residues in the H12 pushed the helix outwards and the Arg726 distorted the AF2 site, which may play a major role in binding of co-regulators. The structural changes elucidated in this study could be helpful to gain a structural insight of WT-AR-LBD-antagonist, which are expected to facilitate the development of in silico predictive models for identification of potential AR antagonists.
Disclaimer: This presentation is not a formal dissemination of information by FDA and does not represent agency position or policy.

Microbial Populations and Tobacco-Specific Nitrosamines (Tsnas) In Moist Snuff Smokeless Tobacco Products Sampled Over A Sixteen-Month Period

Yasser M. Sanad, Jing Han, Kellie A. Woodling, Huizhong Chen, Jinshan Jin, Gonçalo Gamboa da Costa, John B. Sutherland, and Steven L. Foley

National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR 72079

Introduction: There is a growing concern about the presence of microorganisms in smokeless tobacco products (STPs) and the possible contribution of individual microbial species to increases in carcinogenic TSNAs. Previous work in our lab identified multiple microorganisms in a variety of STP samples that are known to reduce nitrate and nitrite, which contribute to the development of TSNAs. Therefore, understanding the potential microbiological risks associated with STP use as well as the contributions of specific microbial populations to the development of TSNAs will add to the science. This study identifies the microbial (bacterial and fungal) populations and TSNA levels in 15 moist snuff products that were aseptically sampled every other month over a period of sixteen months beginning in July 2015. Methods: Culturable aerobic and anaerobic bacteria along with fungi (molds and yeasts) were detected and enumerated in all products using different media. Representative colonies were collected and the bacterial 16S rRNA gene and the fungal ITS-based DNA were sequenced to determine their identities. Metagenomic analyses of total microbial populations were done to provide a culture-independent determination of the bacteria and fungi presence and their relative proportions within the products. Mass spectrometry and HPLC were used to determine the levels of TSNAs [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N'-nitrosonornicotine (NNN)] and nicotine in the STPs. Nitrate and nitrite levels were quantified utilizing a nitrate-ion specific probe and the Griess Reagent System, respectively. Results: Bacillus species represented the majority of bacterial isolates identified by conventional culturing. Other taxa identified included some potential opportunistic pathogens, such as Enterococcus faecalis, Streptococcus pneumoniae, and Staphylococcus epidermidis. The most commonly identified fungal taxa were Penicillium, the Agaricaceae and Coprinellus. Metagenomic analysis of the total bacterial populations shows that the predominant class was the Bacilli in each of the samples; however, some products had relatively high proportions of the phylum Actinobacteria. The Saccharomycetes, Dothideomycetes, and Tremellomycetes were the classes with the highest proportion of reads among the fungal populations in the samples. In nearly every sample, NNN levels were greater than 1.0 µg/g, while the NNK levels ranged from 0.29-1.55 µg/g. These data are informative to help define temporal changes related to microbial populations and TSNA formation in STPs.

Funded by: The Center for Tobacco Products, US Food and Drug Administration

R-loop Forming Structure Prediction in Viral Genomes

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Background: An R-loop is a triple-stranded nucleic acid structure comprising nascent RNA hybridized with its corresponding DNA template strand, while leaving the non-template DNA single-stranded. R-loop formation has been observed in a wide range of organisms, from bacteria to mammals. Possible roles of R-loops in transcription, telomere maintenance, genome instability, epigenetic regulation as well as disease involvement have been demonstrated. In viruses, R-loop detection is rare and their functional importance is poorly understood. Thus, we aim to investigate the prevalence and distribution of R-loop in the viral genomes.

Results: We use 6,153 viral complete genomes collected from NCBI as a reference set. R-loop prediction by QmRLFS-finder (http://rloop.bii.a-star.edu.sg/?pg=qmrlfs-finder) is performed on these genomes. A total of 1,586 out of 6,153 genomes contain at least one R-loop. The number of R-loops and the ratio of R-loop length per kb of the viral genome are presented. We find that herpesviruses are enriched with R-loops, especially human herpesvirus. In addition, the distribution of these R-loops throughout the genome is not uniform.

Conclusion: We report here the results of a search for the existence and prevalence of R-loops in viral genomes. The pervasiveness of R-loops, their enrichment at specific genomic locations suggest that these structural entities may represent a novel class of functional elements in herpesviruses. Future analysis will be focused on the R-loop-positive genes and regulatory elements of these viruses.

This work is funded in part from the Arkansas Research Alliance and the Helen Adams & Arkansas Research Alliance Professor & Chair

Mapping MedDRA In FDA Approved Drug Labeling To Facilitate Adverse Drug Reaction Study

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Background: Adverse Drug Reactions (ADR) are a public health concern. Adverse events, described in FDA-approved drug labeling, help promote the safe use of drug products and facilitate regulatory oversight. The Medical Dictionary for Regulatory Activities (MedDRA) is used as a reference for standard terminology in ADR coding and reporting. FDA approved drug labeling, which is largely based on natural language (free text), has not been subjected to coding with standard terminology. We describe the use of MedDRA to extract ADR related terms from FDA approved drug labeling in order to facilitate computer-aided ADR monitoring and drug safety evaluation.

Result: Structured Query Language (SQL) queries were performed on FDALabel (http://www.fda.gov/ScienceResearch/BioinformaticsTools/ucm289739.htm), a database developed and maintained by FDA/NCTR, to extract MedDRA terms based on the text of 1160 small molecule drug labeling. The systematical investigation focused on adverse events related labeling sections: BOXED WARNINGS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS. Results demonstrated that the ADVERSE REACTION section included the most MedDRA terms with 3,660 Preferred Terms (PTs) and BOXED WARNINGS included 663 PTs potentially associated with severe adverse events. The most common terms found in both BOXED WARNINGS and WARNINGS AND PRECAUTIONS were: Death, Pregnancy, Hemorrhage, Depression, Cardiac Failure, and Pain. Death appeared in 110 out of 345 drugs with BOXED WARNINGS. By mapping to the higher hierarchy level of the 22 disorder related System Organ Classes (SOCs) in MedDRA, we found that the most common PTs in BOXED WARNINGS are from SOCs of Nervous system disorders, General disorders and administration site conditions, and Psychiatric disorders

Conclusion: By studying adverse events in drug labeling using MedDRA terminology, we were able to obtain profiling and ranking frequency of the adverse events in FDA-approved drug labeling. This collection of information could be valuable to support robust ADR study, drug safety research, and advance pharmacovigilance.

Identification of Somatic Mutations In Pancreatic Cancer

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Background: Pancreatic cancer is one of most lethal malignancy in the United States. The five-year survival rate is approximately 6%. Cancer whole genome or whole-exome sequencing shed light in the field.
Results: Here we analyzed pancreatic cancer whole-exome sequencing data generated from five pancreatic tissue samples and five paired normal tissue samples, using our sequencing data processing pipeline. We identified a total of 145 genes that had significant somatic mutations in one or more patients. However very few of mutated genes are common between individual patients. Tumor cellularity of the samples ranged from 10% to 60% might contribute to the low concordant rate of mutated genes. The gene ontology analysis suggested that these genes were significantly enriched in reproduction (P=0.01) process and mesoderm development (P = 0.02) process. Moreover, we found 18 of TCGA project reported mutated gene in pancreatic cancer showed mutations in two or more patients in our study. Particularly four of five pancreatic cancer patients in our study harbored ZNF717 and MUC3A mutations.

Conclusion: Our study reveal two pathways that are significant enriched of genes mutated in pancreatic cancer. Our results consist with previous findings and highlight several common mutated genes. We will increase the sample size in the analysis to gain more insight into the mechanism of the disease.

We acknowledge the supports from NIH/1R15GM114739, ARA/FDA award and the Arkansas INBRE program with grants from NCRR (P20RR016460) and NIGMS (P20 GM 10342

Cyanobacteria Colonization in the Lung Exhibit Innate Inflammatory Response Leading To Lung Adenocarcinoma

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Background: The leading cause of cancer deaths worldwide is lung cancer. Non-small cell lung cancer (NSCLC) is the major form of lung cancer, with adenocarcinoma (LUAD) and squamous cell carcinoma (LUSC) being the major forms of NSCLC. Although smoking and genetic predisposition are established risk factors, majority of lung cancers have unknown etiology. We hypothesize that altered lung microbiome together with chronic inflammatory insults within the lung tissue contribute to the development of lung cancer.
Methods: We sequenced the 16s rRNA of the microbiota in FFPE lung tumor tissue and compared with normal adjacent tissue from the same patients. The sequence data was then used to identify microbe-specific pathways then integrated with host CD36-specific mRNA expression levels and associated pathways.
Results: Phylum *Cyanobacteria* was persistently observed only in the LUAD samples. The imbalance and increased levels of phyla *Proteobacteria, Bacteroidetes, Actinobacteria* and *Firmicutes* correlates with phylum *Cyanobacteria* in the LUAD compared to LUSC and the normal samples (p-value=0.058-0.0230). Pathways analyses revealed significant inflammatory related pathways important in lung cancer development. Integrating lung cancer specific *CD36*-mRNA data and *Cynobacteria*-specific pathways revealed CD36 associated pro-inflammatory mediators or genes that reside in lung tissues.
Conclusions: CD36 internalizes and processes *Cyanobacteria* and/or its toxin in the lung consequently producing pro-inflammatory mediators that influence carcinogenesis. These results will provide promise as potential targeted therapy and prevention of inflammation-associated lung carcinogenesis.

This study was supported by seeds of science grant
Translational Research Institute (TRI), grant UL1TR000039 through the NIH National Center for Research Resources and National Center for Advancing Translational Sciences supports the UAMS sequence core, where the sequencing was done for this project.

Characterizing the 'Unknown Unknowns' in the Gut Microbiome - A Possible New Bacterial Phylum?

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Background: The MetaHIT project has sequenced the genomic DNA and RNA from fecal samples of several hundred people, with multiple time points, producing an enormous amount of data that can be mined for reconstructing genome scaffolds for the microbial community.

Results: Out of several hundred 'metagenomic species' genome scaffolds extracted from the MetaHit gut microbiomes, we found 10 genome scaffolds with very low sequence identity for nearly all of the 2000 proteins in each genome. These 10 scaffolds likely represent a new major clade (perhaps phylum) for which little information is available in current databases. We have used Average Amino acid Identity (AAI) of a set of type strain genomes for the major known bacterial classes, and find that these set of 10 genomes form their own unique, deeply rooted branch. The nearest match is cyanobacteria, although this is distant. These bacteria likely require an anaerobic community structure for growth and survival, and are likely difficult to characterize in the lab, which would explain why they have not been characterized to date.

Conclusion: We find a distinct set of 10 'metagenomic scaffolds' that belong to a different phyla than currently found in more than a hundred-thousand currently available prokaryotic genomes.

dBBQs : dataBase of Bacterial Quality scores

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Background: It is well-known that genome sequencing technologies are becoming significantly cheaper and faster. As a result of this, the exponential growth in sequencing data in public databases allows us to explore ever growing large collections of genome sequences. However, it is less known that the majority of available sequenced genome sequences in public databases are not complete, drafts of varying qualities. We have calculated quality scores for more than 100,000 bacterial genomes from all major genome repositories and put them in a fast and easy-to-use database.

Results: Prokaryotic genomic data from all sources were collected and combined to make a non-redundant set of bacterial and archaeal genomes. The genome quality score for each was calculated by four different measurements: assembly quality, number of rRNA and tRNA genes, and the occurrence of conserved functional domains. The dataBase of Bacterial Quality scores (dBBQs) was designed to store and retrieve quality scores. It offers searching function with Elasticsearch, a fast and scalable search and analytics engine for large scale database. In addition, the search results are shown in interactive JavaScript charts using dc.js. The analysis of quality scores across major public genome databases find that most (perhaps 80% or more) of the genomes are of acceptable quality for many uses. However, some genome sequences are of very quality, in a few cases even for 'complete' genomes.

Conclusion: dBBQs (available at http://arc-gem.uams.edu/dbbqs) provides genome quality scores for all available prokaryotic genome sequences with a user-friendly Web- interface. These scores can be used as cut-offs to get a high-quality set of genomes for testing bioinformatics tools or improving the analysis. Moreover, all data of the four measurements that were combined to make the quality score for each genome, which can potentially be used for further analysis. dBBQs will be updated regularly and is freely use for non-commercial purpose. This work is funded in part from the Arkansas Research Alliance and the Helen Adams & Arkansas Research Alliance Professor & Chair.

Enteric Ecosystem Disruption in Autism Spectrum Disorder: Can the Microbiota and Macrobiota be Restored?

John C Slattery

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Background: Many lines of scientific research suggest that Autism Spectrum Disorders (ASDs) may be associated with alterations in the enteric ecosystem, including alterations of the enteric macrobiome (i.e. helminthes and fauna) and changes in predominant microbiome species, particularly a reduction in microbiome species diversity.

Methods: We performed a comprehensive review of the literature and summarized the major findings.

Results: Alterations in the enteric ecosystem are believed to be due to a variety of factors including changes in the post-industrial society related to decreased exposure to symbiotic organisms, increased human migration, overuse of antibiotics and changes in dietary habits. Changes in the enteric ecosystem are believed to alter metabolic and immune system function and epigenetic regulation. If these changes occur during critical developmental windows, the trajectory of brain development, as well as brain function, can be altered. This paper reviews theoretical models that explain how these perturbations may in isolation or in combination be causative for ASDs as well as the preclinical and clinical studies that support these models. We discuss how these alterations may converge to trigger or exacerbate the formation of an ASD phenotype. We focus on possible preconception, prenatal, perinatal and postnatal factors that may alter the enteric ecosystem leading to physiological disruptions, potentially through triggering events.

Conclusion: If these theoretical models prove to be valid, they may lead to the development of practical interventions which could decrease ASD prevalence and/or morbidity.

Bioinformatics Education for Molecular Biosciences and Biotechnology students at ASU

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[1] Director, Molecular Biosciences Graduate Program, [2] Director Biotechnology undergraduate and graduate program, College of Sciences and Mathematics, Arkansas State University, Jonesboro, AR 72401

Bioinformatics is a rapidly growing application oriented interdisciplinary science at the interface of biology and computer science. It enables development of tools based on computational approaches to studies of life processes. Now that the genome of a number of model organisms including human are known, Bioinformatics has become even more important to basic, medical and applied sciences in academia as well as industry. Therefore teaching the basics and application aspects of Bioinformatics has been the focus of graduate programs in Molecular Biosciences and undergraduate as well as graduate programs in Biotechnology at Arkansas State University. The courses are taught as interwoven lecture-discussions and hands on computer lab practices. At the beginning, the students choose a protein associated with a disease or functional significance, access data bases, construct queries and apply different bioinformatic analyses for that protein such as sequence/functional domain analyses, protein structure prediction, phylogenetics, metabolism and networks, molecular genetics, and genomics. The collection of all their assignments help them to form a complete profile on that chosen molecule resulting in a review which is worthy of publication. We are planning to dual list the course so that computer science students will also take this course so that biology and computer science students can perform team work and learn from each other as they will be bringing different background and strengths to this course.

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The respiratory and GI-tract microbiome in pulmonary disease, healthy aging and animal growth performance

Jiangchao Zhao. Department of Animal Science, University of Arkansas

Human microbiome plays critical roles in different aspects of health and diseases. My talk will cover the following topics:

i) The gut microbiome in cystic fibrosis (CF). CF is the most common inherited disease in Caucasians. Bacterial infection and inflammation are the leading causes of morbidities and mortalities. Recent studies show that the lung microbiome in CF is more complicated than previously appreciated, however, there is still a large knowledge gap of the correlation between the lung microbiome and disease progression. By characterizing 818 sputum microbiomes, we categorized the lung microbiomes into 8 pulmotypes, which are highly correlated with different clinical outcomes.

ii) The gut microbiome in healthy aging. An aging global population poses substantial challenges to the economy, society and healthcare system. Thus, new solutions are needed to mitigate age related health problems. Centenarians are a model for healthy aging due to their ability to reach the extreme limit of life by escaping, surviving or delaying chronic diseases. The genetics of centenarians has been extensively examined, but much remains unknown about their gut microbiomes. We recently characterized the gut microbiomes in healthy aging people (≥90 years of age) in Dujiangyan, Sichuan, China. We found that the gut microbiome diversity in this cohort is greater than that in younger adults. Several potential probiotics (e.g. members of Akkermansia, Clostridium XIVa) are enriched in the long-living group. We validated these discoveries by an independent Italian dataset. Our study identified gut microbiome signatures for healthy aging and suggests that gut microbiome opens a new avenue in healthy aging studies.

iii) The development of early-life gut microbiome in swine growth performance. The development of gut microbiome in early life is critical and dysbiosis at this stage has been linked to different diseases. Many factors could affect the development of the gut microbiomes in children. Here we use piglets as a model showing how the environment affect the early-life gut microbiome establishment. We assigned piglets into two groups, with one group raised in conventional farrowing crates and the other group exposed daily to topsoil during lactation stage. At the end of the finishing stage, the topsoil treated group gained an average of 4.6 Kg more weight than the control group. We observed a greater gut microbiome diversity and enrichment of potential probiotics during the lactation stage during topsoil exposure in the treatment group. This data suggests that the environment plays an important role in shaping the development of the early-life gut microbiome, which could be translated to increase swine production. This study also indicates that the piglets could be used as a model to study the establishment of gut microbiota in early-life stage and how such establishment correlates with childhood diseases such as asthma and obesity.

Rodents as translational model to study the effects of xenobiotics on the development of microbiome from gestation to adult

Sangeeta Khare, Division of Microbiology, National Center for Toxicological Research, US-Food and Drug Administration, Jefferson, AR, 72079

Several xenobiotic compounds are associated with gastrointestinal disturbance and adverse effects related to enteric flora imbalance. Human exposure to xenobiotic substances, like arsenic, occurs mainly via drinking water or consumption of produce/products grown in contaminated soils. Available epidemiologic data suggests that if mother is exposed to arsenic during the gestational stage, newborns are more prone to metabolic diseases, cardiovascular irregularities and behavioral, cognitive and motor disabilities. Independent studies propose that these disorders are correlated with the alterations in the gastrointestinal microbiome. Thus it is pertinent to study the effect of arsenic exposure during microbiome establishment and development. In collaboration with the NCTR/ NTP-NIEHS, we have used rodents as translational model to study the effects of xenobiotics on the development of microbiome from gestation to adult. Toxicity caused by exposure of inorganic arsenic to the gastrointestinal microbiome was evaluated by assessing the development of microbial population during entire period of developmental stages. Plug positive females were placed on dosed water (~1mg/L). Pregnant animals were sacrificed at gestational day 17 and microbiome was analyzed in samples collected from dam and fetus. Furthermore neonatal animals (PND 3, 10 and 21) were exposed to single dose of arsenic (oral gavage 0.05mg/kg bw) and microbiome was analyzed in the samples collected 24 hr and 48 hr post-exposure. Results revealed that the single gavage of arsenic to neonatal animal leads to development of distinct bacterial population. The correlation of the distinct bacterial population with host gene expression will be also discussed. This presentation will focus on the importance of evaluating gastrointestinal toxicity of xenobiotic compounds to the microbiome for safety assessments.

Microbiome changes associated with lung cancer

Patrick L. Apopa, Lisa Alley, Rosalind B. Penney, Konstantinos Arnaoutakis, Mathew A. Steliga, Susan Jeffus, Emine Bircan, Banu Gopalan, Jing Jin, Nishi Shah, Gurkan Bebek and **Mohammed S. Orloff** *

Background: The leading cause of cancer deaths worldwide is lung cancer. Non-small cell lung cancer (NSCLC) is the major form of lung cancer, with adenocarcinoma (LUAD) and squamous cell carcinoma (LUSC) being the major forms of NSCLC. Although smoking and genetic predisposition are established risk factors, majority of lung cancers have unknown etiology. We hypothesize that altered lung microbiome together with chronic inflammatory insults within the lung tissue contribute to the development of lung cancer.

Methods: Extraction of microbiome DNA in FFPE lung tumor and normal adjacent tissues was done meticulously and using aseptic conditions. The 16s rRNA product from the isolated microbiota was then subjected to Metagenomic sequencing using the Illumina MiSeq. The host CD36-specific mRNA expression levels were analyzed and integrated with altered NSCLC subtype-specific microbe sequence data.

Results: Phylum Cyanobacteria was persistently observed only in the LUAD samples. The imbalance and increased levels of phyla Proteobacteria, Bacteroidetes, Actinobacteria and Firmicutes correlates with phylum Cyanobacteria in the LUAD compared to LUSC and the normal samples (p-value=0.058-0.0230). Pathways analyses revealed significant inflammatory related pathways important in lung cancer development. Integrating lung cancer specific CD36-mRNA data and Cynobacteria-specific pathways revealed CD36 associated pro-inflammatory mediators or genes that reside in lung tissues.

Conclusions: CD36 internalises and processes Cyanobacteria and/or its toxin in the lung consequently producing pro-inflammatory mediators that influence carcinogenesis. These results will provide promise as potential targeted therapy and prevention of inflammation-associated lung carcinogenesis

Human Microbiome: Integrated Systems Biology Approaches Used to Assess the Impact of Toxicants on the Microbiome

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The importance of the human microbiome in health, including the ways that environmental stressors affect the composition and functions of the oral, nasal, skin, urogenital and intestinal microbiota and thus contribute to disease, has recently been recognized as a major topic of research. Large-scale research endeavors from the NIH Human Microbiome and International Human Microbiome Projects using next-generation sequencing have increased our understanding of the important role that the microbiome plays in human health and disease. Effective metagenomics, functional genomics technologies and bioinformatics tools that are now available and affordable have expanded our knowledge on microbial community composition, functions and metabolic activities to help understand microbiome-host interactions. Acute or chronic exposure of the microbiome to toxicants has the potential to disrupt the colonization barrier and alter important functions of the microbiota. Therefore, the microbiome has emerged as an important area to consider in toxicology testing for human health risk assessments. This presentation will highlight an integrated systems biology approach for the safety evaluation and risk assessment of toxicants and their effect on the intestinal microbiome with the goal of insuring safety of the human food supply. Critical issues and knowledge gaps associated with the impacts of toxicants in foods on the intestinal microbial community and hazard analysis of potential toxicants in support of public health will be discussed.

Metaproteomics: Study of Function of Gut Microbiome in Chronic Kidney Disease

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Metaproteomics aims to characterize complex protein mixtures derived from diverse environments, such as human gut. Recent evidence suggests strong correlation between gut dysbiosis and disease. Metaproteomics methods have potential to provide information on both organismal diversity and function, and provide unique insight into the host-microbiome interactions.

Chronic kidney disease (CKD), a progressive decline in kidney function, is a growing health problem: 13% of adults in the US have CKD. In 40% of cases, CKD leads to irreversible loss of kidney function, end-stage renal disease. As urea increases in the gut, urease-containing bacteria is favored and results in the dysbiosis. Resistant starch (RS) is a type of pre-biotic that is not fully broken down and absorbed, but rather turned into short-chain fatty acids by intestinal bacteria. A diet rich in RS was shown to reduce dysbiosis in a CKD-rat model. We used mass-spectrometry based metaproteomics approach to assess changes in microbial diversity and function during the RS dietary supplementation.

Here, we report our preliminary results on the RS-diet effect using a rat model of chemically-induced CKD. After the two weeks of RS diet, cecal samples were collected, followed by protein extraction. Nine-vs-nine comparison of treatment-vs-control was performed. LC-Orbitrap-Tribrid-Fusion mass-spectrometry was used to identify proteins. Label-free quantification based on spectral counts was use. PEAKS Software was used to identify peptides via de novo sequencing. The filtered peptide lists were used to estimate organismal diversity using online tools (UniPept and MetaCoMET). A set of R/Bioconductor packages and in house written scripts was further used to perform statistical analysis and hierarchical clustering.

In total, we identified 116,317 high-confidence de novo peptide-to-spectrum yielding 8,427 unique de novo peptide sequences. UniPept matched 25% and 10% of these peptide sequences to taxonomic levels at phylum or species, respectively. Hierarchical clustering of this peptide-level data clearly separated the two phenotypes. Using PEAKS database and homology searches, de novo peptides were assembled into proteins. Label-free and quantitative results were combined, cross-referenced and checked for consistency. Our methodology results in data on both host and bacterial proteins and yields both peptide-level and protein-level information. Our studies provide foundation for identification of peptide-level, protein-level, and organism-level biomarkers of advanced kidney disease and suggest novel therapeutic targets.

Microbiome metabolites and their effects on mitochondrial function

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The human gut houses a diverse ecosystem of microbes collectively referred to as the enteric microbiome. It is becoming clear that the enteric microbiome can modulate host physiology through production of metabolic mediators, particularly short chain fatty acids (SCFAs). SCFAs, specifically propionic acid (PPA) and butyric acid (BUT), modulate energy metabolism through both alterations in gene expression and as mitochondrial substrates for energy production. Interestingly autism spectrum disorder (ASD) has been linked to microbiome alterations favoring the production of PPA and BUT and these SCFAs have been shown to modulate ASD behavior in animal models. This presentation will review the physiological effects of SCFAs on energy metabolism as well as present original data demonstrating that these SCFAs differentially modulate mitochondrial function in ASD and control cell lines. The implication for health and disease in the context of microbiome alteration will be discussed.