AACC
Better health through laboratory medicine.

The Best of AACC

December 3, 2016 | Intercontinental Hotel | Shenzhen | China

PROGRAM BOOK

AACC
Better health through laboratory medicine.

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Welcome

Dear colleagues:

Welcome to **The Best of AACC**, a one-day conference featuring a selection of timely topics in laboratory medicine presented by internationally recognized speakers.

AACC is a global scientific and medical professional organization dedicated to clinical laboratory science and its application to healthcare. **AACC** provides essential content, conducts advocacy and outreach, and stimulates collaboration to help lab professionals adapt to change and provide vital clinical insight and guidance so patients get the care they need. Delivering high quality education and knowledge resources is integral to this mission. **AACC** offers more than 60 educational programs annually, including the **AACC Annual Scientific Meeting & Clinical Lab Expo**, which is attended by 20,000 laboratory medicine professionals and healthcare leaders, and features more than 730 exhibitors, 200 educational sessions, and nearly 800 scientific abstracts.

Today's edition of **The Best of AACC** is sponsored by Mindray, and highlights **AACC**'s latest content in areas ranging from HIV testing to vitamin D analysis. The agenda features presentations by:

Mark A. Marzinke, PhD, DABCC
Assistant Professor, Pathology and Medicine
Johns Hopkins University School of Medicine
Director, Preanalytics and the General Chemistry Laboratory
Director, Clinical Pharmacology Analytical Laboratory, Division of Clinical Pharmacology
Johns Hopkins Hospital
Baltimore, Maryland

James C. Ritchie, PhD, DABCC, FACB
Director, Emory Core Laboratory, Special Chemistry, and Point-of-Care Testing
Medical Director, Emory Medical Laboratory
Atlanta, Georgia

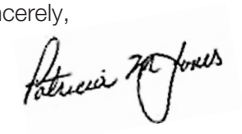
Yusheng Zhu, PhD, DABCC, FACB
Professor and Medical Director, Clinical Chemistry and Toxicology
Director, Postdoctoral Clinical Chemistry Fellowship Program
Medical University of South Carolina
Charleston, South Carolina

Prof. Guobin Xu
Peking University Cancer Hospital
Beijing Cancer Hospital
Beijing Institute for Cancer Research

The subjects they will discuss include Current Recommendations for HIV Screening and Confirmation, Recommendations and Controversies in Cancer Detection, Validation of Laboratory Developed Tests, and Testing for 25-hydroxyvitamin D and The Clinical Application of Serum Tumor Marker, CTC and ctDNA in Patients with Advanced Lung Cancer.

Thank you for joining us at **The Best of AACC**. We hope you find value in today's talks and we look forward to seeing you at future **AACC** education programs.

Sincerely,



Patricia M. Jones, PhD, DABCC, FACB
2016 AACC President

Scientific Agenda

Scientific Agenda

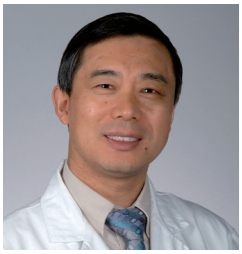
Saturday, December 3, 2016

Time	Topic	*Speaker*
9:00-9:30	Opening and Welcome Remarks from AACC and Mindray	AACC VP: *Bradley R. Pine* Mindray VP: *Wenjing Chen*
Session One		
9:30-10:30	HIV Testing: Current Recommendations on Screening and Confirmation	*Dr. Mark Marzinke*
10:30-10:40	Panel Discussion - Q&A	
10:40-11:00	Break	
Session Two		
11:00-11:30	25-Hydroxyvitamin D: Analysis and Clinical Applications	*Dr. Yusheng Zhu*
11:30-12:00	The Recognition of 25-hydroxyvitamin D2 and D3 by Different Assays	*Dr. Yusheng Zhu*
12:00-12:10	Panel Discussion - Q&A	
12:15-13:30	Lunch	
Session Three		
13:40-14:10	Cancer Screening: Recommendations and Controversies, including Tumor Marker Testing using Chemiluminescence	*Dr. James Ritchie*
14:10-14:40	FDA/CLIA Requirements for Validation of Laboratory Developed Tests	*Dr. James Ritchie*
14:40-14:50	Panel Discussion - Q&A	
14:50-15:10	Break	
Session Four		
15:10-15:40	The Clinical Application of Serum Tumor Marker, CTC and ctDNA in Patients with Advanced Lung Cancer	*Prof. Guobin Xu*
15:40-15:50	Panel Discussion - Q&A	
15:50-16:10	Closing	

Faculty

Mark Marzinke, PhD, DABCC

Dr. Marzinke is an Assistant Professor of Pathology and Medicine in the Johns Hopkins University School of Medicine. He is the Director of Preanalytics and the General Chemistry Laboratory in the Johns Hopkins Hospital and the Director of the Clinical Pharmacology Analytical Laboratory in the Division of Clinical Pharmacology. Dr. Marzinke received his Ph.D. in Biochemistry from the University of Wisconsin-Madison, followed by a post-doctoral fellowship in Clinical Chemistry at the Johns Hopkins University School of Medicine. Dr. Marzinke is board certified in Clinical Chemistry by the American Board of Clinical Chemistry and is a fellow of the National Academy of Clinical Biochemistry. His primary research interests are in the areas of antiretroviral pharmacology and precision medicine. Dr. Marzinke is a principal investigator or co-investigator on several NIH-funded grants, and has co-authored more than 50 peer-reviewed manuscripts.



Yusheng Zhu, PhD, DABCC, FACB

Dr. Zhu is a tenured Professor and Medical Director of Clinical Chemistry and Toxicology, Director of Postdoctoral Clinical Chemistry Fellowship Program at the Medical University of South Carolina. He is board certified by the American Board of Clinical Chemistry (ABCC) in Clinical Chemistry, Toxicological Chemistry, and Molecular Diagnostics and a Fellow of the National Academy of Clinical Biochemistry (NACB). Yusheng had worked in clinical laboratories in China for over ten years before he moved to the United States in 2000. He completed postdoctoral fellowship in biochemistry and molecular biology at the University of Georgia and clinical chemistry and pharmacogenetics at the University of Louisville. Yusheng joined the American Association for Clinical Chemistry (AACC) in 2003 and served as the Chair of AACC Ohio Valley Section Awards Committee (2006) and Alternate Delegate of AACC Southeast Section (2007-2009). He served as the President of the North American Chinese Clinical Chemists Association (2012), President of the Commission on Accreditation in Clinical Chemistry (ComACC) and Chair of Southeast Section in 2015, and Secretary of Proteomics & Metabolomics Division (2013-15). Currently, he is the Director of ABCC, Chair of Clinical Translational Science Division and, Treasurer of Mass Spectrometry & Separation Science Division of AACC, Member of the AACC Asia-Pacific Working Group, Contributor of two CLSI documents. He is also a member of the Organizing Committee of the AACC Mass Spectrometry & Separation Science Conference. Yusheng serves on the Editorial Boards of three medical journals. Yusheng is an invited reviewer of seven international medical journals. He has given many presentations at national and international conferences. He is interested in clinical and translational research in clinical chemistry, toxicology, hemoglobinopathy, pharmacogenetics, proteomics, and clinical application of mass spectrometry and has received funding for research from NIH, AHA, and IVD industry. He has over 100 publications including peer-reviewed papers, editorials, book chapters, and abstracts. He has received 31 awards from AACC, NACB, and other organizations.

James C. Ritchie, PH.D., DABCC, FACB

Professor Ritchie received his BS Zoology in 1970, a Masters in Public Health Epidemiology in 1976 both from the University of Michigan and his Ph.D. in Pharmacology from Duke University in 1995. He has been continuously involved in clinical laboratory work since 1972. Currently he is the Medical Director of the Emory Medical Laboratory (EML), Director of the Emory Core Laboratory, Special Chemistry, and Point of Care Testing

His specific areas of research interest are laboratory utilization, the clinical use of LC-MSMS in proteomics, therapeutic drug monitoring, and neuropharmacology of mental illness including the pharmacology of antidepressants, antipsychotics, and antiepileptics during pregnancy.

Prof. Guobin Xu

Peking University Cancer Hospital
Beijing Cancer Hospital
Beijing Institute for Cancer Research

In 1984, Prof. Xu was graduated from Shanghai Medical University (now Shanghai Medical College of Fudan University), then worked at No.1 Hospital of Peking University until August. 2012. From September, 2012, he started to work at Peking University Cancer Hospital until now.

From 2000, Prof. Xu worked on the standardization of CKD laboratory diagnosis, epidemiology survey and prognosis factors research. Cooperating with nephrologists, he reported CKD prevalence rate of Chinese and CKD high risk factors. He had done serum creatinine and urine micro albumin standardization and established the reference range, making the standard on CKD screening and diagnosis. As a main member, he was involved in AKI prevalence rate and death rate survey project. He found that ICU AKI prevalence rate in general hospitals is as high as 30%. Although AKI prevalence rate cancer hospitals is lower as 10%, the death rate is even higher as 50%. He suggested every medical facility must be aware of AKI prevalence. He is preparing to serum creatinine critical value report strategy, as a reference on AKI laboratory diagnosis.

From 2003, Prof. Xu worked on clinical chemistry quantitative test standardization, and founded the serum test reference laboratory. Then he had made urine, blood glucose, urine acid and icon test reference method and serum standard material, helping the IVD company to assign calibrator value, make laboratory capability accreditation and reagent evaluation.

From 2012, Prof. Xu has been working on tumor marker research, evaluation serum tumor marker usefulness in different tumor therapy prediction. 2013, Prof. Xu starts to build the high throughput sequencing platform, from then he is focusing on detection, diagnosis and quality control on tumor genetic risk gene and tumor molecularly targeted therapies.

Executive Summary

Mark Marzinke, PhD, DABCC

HIV Testing: Current Recommendations on Screening and Confirmation

It is currently estimated there are 34 million individuals living worldwide with HIV/AIDS, with approximately 1.5 million new infections occurring annually. The major treatment modality for infected individuals is the implementation of antiretroviral therapies (ART), which involve the combinatorial administration of several antiretroviral agents. Early identification of an infected individual is important, as the virus is more infectious in the early stages post-seroconversion. Further, early screening and confirmation of infection can facilitate earlier implementation of ART, which has been shown to improve morbidity and mortality and decrease disease progression to AIDS. Therefore, diagnostic laboratory tests must be sufficiently sensitive and specific to identify individuals in the early stages post-infection.

Laboratory tests for HIV screening have been available since 1985; 1st generation immunoassay-based methods screened for the presence of antibodies to the HIV virus. However, there were limitations in assay performance, thus creating a need for confirmatory Western blot analysis. Over the subsequent two decades, iterative generations of immunoassays became available, including 3rd generation laboratory tests that detected both HIV IgG and IgM antibodies. Third generation assays resulted in a detection window of approximately 3 weeks' post-seroconversion and improved sensitivity and specificity over 1st generation assays. In the late 2000s, the availability of 4th generation assays resulted in the simultaneous identification of not only HIV antibodies, but also the HIV-1 p24 antigen, further improving the clinical sensitivity of HIV laboratory screening to two weeks' post-infection. Thus, such testing platforms further shortened the detection window post-seroconversion.

More recently, the improved performance of 4th generation assays resulted in drastic modifications of HIV serology testing algorithms. Currently, the Center for Diseases Control and Prevention recommends the use of a 4th generation assay as the first step in screening for an HIV infection. Based on the superior performance to both previous generations of immunoassays and the Western blot confirmatory analysis, positive results by 4th generation assays would be reflexed to HIV-1/2 discrimination testing or nucleic acid testing for HIV-1 RNA for downstream analysis.

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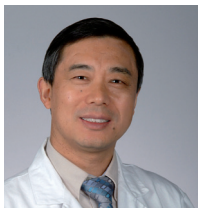

Yusheng Zhu, PhD, DABCC, FACB

25-Hydroxyvitamin D: Analysis and Clinical Applications

25-Hydroxyvitamin D (25-OHD) is one of the most popular tests requested by clinicians nowadays because in addition to bone diseases, many non-skeletal disorders have been suggested to be linked to vitamin D deficiency or insufficiency. Methodologies used in clinical laboratories include competitive vitamin D protein binding assays (CPBA), immunoassays, high performance liquid chromatography (HPLC), and liquid chromatography–tandem mass spectrometry (LC–MS/MS). In this session, I will introduce the basic metabolism and physiology of vitamin D, key issues in the methods for 25-OHD measurement currently used in most clinical laboratories, and clinical applications of 25-OHD testing. We conclude that although the methodologies for 25-OHD testing have improved significantly, considerable bias between different methods and laboratories still exists. Therefore, standardization of the method is critical. The optimal 25-OHD levels should be determined based on the standardized method. Also, more studies are needed to further determine the relationship between vitamin D deficiency or insufficiency and non-skeletal diseases as well as daily vitamin D dose requirement for reducing the risk of non-skeletal diseases.

The Recognition of 25-hydroxyvitamin D2 and D3 by Different Assays

The circulating form of vitamin D, 25-Hydroxyvitamin D (25-OHD), is commonly measured in clinical labs to evaluate vitamin D status of an individual. Vitamin D exists in 2 major forms: vitamin D3 and D2. Current methodologies for 25-OHD testing include antibody or vitamin D binding protein based assays, HPLC, and LC-MS/MS. Although most current antibody or vitamin D binding protein based assays claim that they measure 25-OHD3 and 25-OHD2 equally, bias may still exist in the measurement of total 25-OHD when high concentration of 25-OHD2 is present. HPLC and LC-MS/MS can measure 25-OHD3 and 25-OHD2 separately. Previous studies have shown that certain antibody and DBP based assays do not recognize 25-OHD2 and 25-OHD3 equally. LC-MS/MS and HPLC methods are preferred for patients taking vitamin D2 supplement.

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James C. Ritchie, PH.D., DABCC, FACB

FDA/CLIA Requirements for Validation of Laboratory Developed Tests

Recently the United States Food and Drug Administration (FDA) has issued two guidance drafts regarding a proposed system for regulating Laboratory Developed Tests (LDTs). In these documents the Administration outlines the legislation giving it the power to regulate these tests as well as the reasons they believe regulation has become necessary.

Until recently FDA had exercise its enforcement discretion regarding these "homebrew" tests. FDA has determined that modern LDTs are not the same as the LDTs offered in 1976 (when the legislation giving them the mandate to regulate these test was enacted), and now represent an increased risk for patients.

Many modern LDTs are; manufactured with components that are not legally marketed for clinical use; offered beyond local populations and manufactured in high volume; used widely to screen for common diseases rather than rare diseases; used to direct critical treatment decisions (e.g., prediction of drug response); highly complex (e.g., automated interpretation, multi-signal devices, use nontransparent algorithms and/or complex software to generate device results). They estimate there are >100,000 LDTs in use throughout the U.S.

The issuance of the draft guidelines has caused much controversy among clinical laboratorians and the FDA received more than 300 comments regarding them in the comment period (required before the final rules can be put in place). Initially the reaction of the laboratory community was that this change in enforcement policy was illegal and that FDA should be following the more protracted federal rule making procedure. This idea may still eventually be tested in the courts. For now most laboratory associations in the U.S. have accepted the notion that some regulation of LDTs will happen.

In the Guidances the FDA proposes a risk based system with 3 tiers (Low, Moderate, and High) complexity) to categorize LDTs and sets different requirements for each tier. It states it will not disrupt current testing and will continue discretionary enforcement for "traditional LDTs". LDTs with the highest patient risk will be evaluated first and all high risk LDTs will fall under enforcement within 5 years of finalization of the Guidances.

The new rules essentially make laboratories developing LDTs into manufacturers who will fall under the FDA Quality Systems Management rules. Most LDTs will require the filing of a Premarket Approval Application (PMA) and that process requires that the test evaluate both the analytical validity and well as the **clinical validity** of the test. This is not a process that labs have had to do previously and can be very time-consuming and expensive. FDA has signaled that it will consider published research findings in some instances to validate clinical utility.

The FDA has said it will issue finalized versions of the Guidances by the end of 2016.

Laboratories must submit a list of their LDTs to FDA within 6 months of the issuance. FDA will then have 6 months to categorize the LDTs on the list and the laboratory must file a PMA for their high risk LDTs within one year or cease and desist performance of this testing. Other categories of testing will follow and the whole process (all 3 levels) will be completed within 9 years of enactment of the final Guidances.

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James C. Ritchie, PH.D., DABCC, FACB

Cancer Screening: Recommendations and Controversies, including Tumor Marker Testing using Chemiluminescence

Tumor markers are defined as molecules produced by tumor or other cells of the body in response to cáncer. Most tumor markers in use today are secreted into blood, urine or tissues. They are used for diagnosis, staging, monitoring, prognosis, and re-occurence. The ideal tumor marker should have high sensitivity and specificity for a particular cancer type, and can be measured by immunoassay, immunohistochemistry, molecular, proteomic, or metabolomic techniques. In the United States,"Intended Use" is a key determinant of the class of a medical device. The U.S. Food and Drug Administration (FDA) regulations require a higher level of evidence of clinical utility for approval of diagnostic and screening tumor markers (Class III) than for staging and monitoring (Class II). Only three plasma tumor markers are cleared by the FDA to be used clinically for early detection/diagnosis:(PSA, CA-125 and AFP). Many more tumor markers have been approved for monitoring re-occurrence.

Chemiluminescence immunoassay techniques are now the dominant test methods used in the clinical quantitative detection of tumor markers, due to their high specificity, high sensitivity (10^{-6} to 10^{-12} g/L), and high signal to noise ratio. Additionally they are easily automated and often commercially available. However there are concerns with the use of immunoassay to measure these important biomarkers. Most lack enough sensitivity for very early detection, are present in other (healthy or benign) conditions, suffer from heterophile antibody interferences, and generally are not standardized (neither Abs or Epitopes) among manufacturers.

Three new tumor markers have recently been cleared by FDA, [-2]proPSA, ProGRP, and HE4, for monitoring of prostate cancer, small cell lung cancer and epithelial ovarian cancer, respectively. Two of these ([-2] proPSA and HE4) are part of an ongoing trend to improve tumor diagnosis by employing several biomarkers in an algorithm to increase the sensitivity and specificity of the tests.

Several other new biomarkers have shown promise of improved diagnosis, screening or monitoring. These are PG I and PGII for gastric cancer, SCCA for squamous cell cancer, CA 242 for pancreatic and gall bladder cancer, and CA 50 for pancreatic and colorectal cancer. Whether these biomarkers find wide acceptance is hard to predict and is dependent on more clinical research.

Since the advent of immunoassay several new techniques have been developed (proteomics, metabolomics, multiplex assays utilizing large data sets, etc.) and many of these offer increased specificity and sensitivity over two site immunoassays. Of course this comes with increased costs. However, cancer is a worldwide major public health problem which is responsible for 25% of the deaths per year in the United States alone. Thus the search for the perfect tumor marker will continue.

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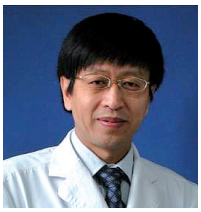

Prof. Guobin Xu

The Clinical Application of Serum Tumor Marker, CTC and ctDNA in Patients with Advanced Lung Cancer

Lung cancer incidence and mortality have been increasing in China, making it the one of the major cause of death and a major public health problem in the country. There are two main types of lung cancer: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Using tumor marker can give quick and accurate discrimination between SCLC and NSCLC for a faster decision on patient treatment. ProGRP a novel tumor marker with benefits for lung cancer patient management, while NSE is less sensitive, but ProGRP has utility in conjunction with NSE in monitoring the therapy of established SCLC. Another biomarker Cyfra 21-1is useful in stratifying populations with advanced NSCLC. China has established the practice guidelines and recommendations for use of tumor markers in the clinic lung cancer.

The advanced noninvasive diagnostic such as CTC and ctDNA through noninvasive sampling of blood is one of the most exciting and rapidly advancing fields in cancer diagnostics, it may change the ways in which we select and monitor lung cancer treatments. Circulating tumor cell (CTC) count is widely recognized in determining tumor stage, assessing prognosis, monitoring therapy response. Circulating tumor DNA (ctDNA) has offered a minimally invasive and feasible approach for detection of EGFR muation for NSCLC. I will talk about the clinical applications of CTC and ctDNA analyses, also compare the technologies on analysis of ctDNA. For one lung cancer patient, I will try to reveal the clinical significance of the tumor marker from body fluid, molecular and circulating tumor cell, at different stage of disease.

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About AACC:

AACC is a global scientific and medical professional organization dedicated to clinical laboratory science and its application to healthcare. Our leadership in education, advocacy and collaboration helps lab professionals adapt to change and do what they do best: provide vital insight and guidance so patients get the care they need.

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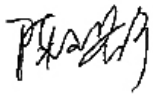
Mindray is pleased to support "**The Best of AACC**" in Shenzhen.



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