

MS3 at the AACC Annual Meeting in Atlanta

Dear Friends and Colleagues,

I hope that you are all ready for the American Association for Clinical Chemistry (AACC) meeting in Atlanta, which we are excited to attend at the end of July.

As your Chair, it is my pleasure to inform you that our Mass Spectrometry and Separation Sciences (MS3) Division has grown tremendously to serve over 200 members since January, when MS3 first achieved official Provisional status as an AACC Division. I would like to personally thank every one of our supporters for helping us to grow at such an impressive speed.

Even though we consider MS3 to still be in its infancy, we are proud to revel in its accomplishments over the past few months. MS3 has been an active participant in all aspects of AACC activities. Many of the mini-track programs that were co-developed with our division have been incorporated into the AACC annual meeting. MS3 selected two outstanding abstracts from over 50 equally impressive submissions. Thirteen posters are selected to represent MS3 at the Poster Walk event and showcase the talent that we bring to the larger organization. Furthermore, we continue to provide robust programming and will host our division member meeting on Sunday, July 26, 2015, where Dr. Graham Cooks will present Miniaturization of Mass Spectrometry.

The MS3 division continues to reach out to other organizations such as ASMS, CLMA, MSACL, and international groups such as Chinese Society for Laboratory Medicine for further growth and to increase our impact in the community. We have been also working with other divisions in AACC and have been invited by the Division of Animal Clinical Chemistry; Dr. Steven Cotten and I will present at their Lunch and Learn Session in AACC. As we grow, we see greater opportunity to contribute to our community and society.

I would also like to draw attention to a new section in our newsletter entitled Meet the Experts, which has arisen out of suggestions from our members and their desire to hear from the groundbreaking thinkers in our field. Meet the Experts provides our newsletter readers with a unique perspective into the lives and ideas of our interviewees, to hear the stories that were instrumental in shaping careers and industries. Drs. Steven Soldin and Graham Cooks are featured in this issue.

MS3 Activities at the 2015 Annual Meeting in Atlanta

MS3 Division Meeting Speaker: Dr. Graham Cooks Abstract Awards Division Member Networking	Sunday July 26, 2:30-4:30 pm "Miniaturization in Mass Spec" Hyatt Regency, Hanover CDE
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Poster Walk	Tuesday July 28 th 12:30-1:30pm
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MS3 Business Meeting	Wednesday July 29 th 9:00-10:30 pm
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Looking forward, MS3 and AACC have finished putting together an outstanding two-day conference, AACC/MSSS: Mass Spectrometry and Separation Sciences in Laboratory Medicine, in Chicago on October 1-2, 2015. This conference will showcase experts in the sciences who will have the opportunity to share their views on numerous hot topics, ranging from daily operations of mass spectrometry to FDA regulations on laboratory-developed tests. A roundtable discussion is also in the works, entitled Envisioning "Next Generation" Mass Spec Diagnostics in 2020, which will collect input from our MS3 community on the future of clinical mass spectrometry. Registration is now open on the AACC website.

There are also numerous other programs that MS3 is developing to further strengthen our interactions with the scientific community and benefit our division members. I am proud to say that we are in the final stages of bringing to you both an invaluable expert panel that will present at local AACC section meetings and multiple travel awards that will provide opportunities for select MS3 students and members to attend our conferences. Being a part of AACC allows us to take advantage of the AACC artery, which has untapped potential to enhance communication and discussions among members, facilitate collaboration with other divisions in developing future AACC events, and establish a range of educational programming within the next few months. I will keep our members informed as plans begin to unfold.

I would like to take this opportunity to thank the many colleagues who have reached out to MS3 with suggestions that have nourished the growth of our division and the Executive Board for its strategic thinking and impeccable implementation that have ensured the success of division initiatives. Last but certainly not least, I would like to thank our industry sponsors who have provided tremendous support and have made many of our events possible.

I look forward to seeing all of you in Atlanta!

Best regards,



Y. Victoria Zhang, Ph.D., DABCC
Chair, MSSS division

MS3 Poster Awards and Poster Walk

2015 was the first year that AACC members could submit abstracts for consideration for the MS3 poster awards. Beginning this year, the division will award 2 posters that show outstanding applications or contributions of mass spectrometry and separations sciences in the field of laboratory medicine. Each award winner receives \$250. This year the division received 50 abstracts for consideration. Each abstract was evaluated for innovation, novelty, research-depth, feasibility, and clarity of the topic. This year's first place winner was Dr. John Mills, a second-year clinical chemistry fellow at the Mayo Clinic with his abstract on "Combining

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Nanobody Immunoenrichment and MALDI-TOF Mass Spectrometry to Detect and Isotype Monoclonal Immunoglobulins.” The second place winner was from Dr. Bruna Andreguetto, a research trainee in Immunology at the Mayo Clinic which described “Alternatives to Oligoclonal Banding Electrophoresis in CSF: Method Comparison with Quantitative Free Light Chains and Accurate Molecular Mass Measurements of Immunoglobulins.” Congratulations to both winners and everyone who submitted abstracts. We look forward to another fantastic set of abstracts next year for 2016.

Expanding upon the success of poster walks at AACC, the MS3 Division will be hosting a poster walk at the annual meeting to highlight other exceptional posters. The MS3 Poster walk is Tuesday July 28th from 12:30-1:30pm and is lead by Dr. Brent Dixon. Below is a list of the posters included on the 2015 walk

Abstract Number	Title
15-A-1065	Combining Nanobody Immunoenrichment and MALDI-TOF Mass Spectrometry to Detect and Isotype Monoclonal Immunoglobulins
15-A-588	Alternatives to Oligoclonal Banding Electrophoresis in CSF: Method Comparison with Quantitative Free Light Chains and Accurate Molecular Mass Measurement of Immunoglobulins
15-A-1069	Rapid Detection of Microbial Resistance to Lactam Antibiotics by LC-MS/MS
15-A-1114	Improved Sensitivity and Throughput for the Quantification of Buprenorphine, Norbuprenorphine and Naloxone in Human Oral Fluid by LC-MS/MS.
15-A-465	Magnetic bead-based serum peptidome profiling for identifying circulating biomarkers in esophageal squamous cell carcinoma
15-A-480	Development of a LC-MS/MS assay for the detection of sulfonylurea drugs, and application of the assay in emergent hypoglycemia cases.
15-A-663	Development of a Reference Measurement System for Urine Albumin
15-A-690	Determination of Monosialogangliosides in Human Plasma by a Novel UPLC/MS/MS Assay Coupled with Chemical Derivatization
15-A-748	Simultaneous Sensitive Quantitation of Testosterone and Estradiol in Serum by LC-MS/MS Without Derivatization
15-A-752	Tandem mass spectrometry-based molecular networking to detect drugs of abuse and analogues
15-A-766	Screen and Identification of Four Biomarkers for Discriminating Non-small Cell Lung Carcinomas and Pulmonary Nodules by MALDI-TOF MS
15-A-957	High Resolution Accurate-mass Mass Spectrometry (HRAMS) Offers Superior Accuracy For Quantitation of Steroids and Proteins
15-A-961	Analysis of Bile Acid Profiles by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

Meet the Experts: Drs. Steve Soldin and Graham Cooks

The MS3 Division reached out to Dr. Graham Cooks and Dr. Steven Soldin to learn a little about their career paths, the impact of mass spectrometry in laboratory medicine and the some challenges our field will face as it matures.

Please briefly describe your career progression?

Cooks: I received my PhD.s from University of Natal (South Africa) and the University of Cambridge. I began as an Assistant Professor in Chemistry at Kansas State University from 1968-1971. I moved Purdue in 1971 and over the years moved to Associate Professor, Professor, and am now a Henry Bohn Hass Distinguished Professor of Chemistry at Purdue. During my time at Purdue I have been Director Mass Spectrometry Center, Head of the Analytical Division and am now the co-Director of the Center for Analytical Instrumentation Development.

Soldin: I completed my undergraduate (BSc.Hons Chemistry) and graduate (MS Organic Chemistry, PhD Biochemistry, 1968) training at the University of the Witwatersrand, Johannesburg South Africa. This was followed by postdoctoral training in Clinical Biochemistry at the University of Toronto (1972- 1975).

What inspired you to pursue a career in clinical mass spectrometry?

Cooks: I was inspired by my early experience with characterization of natural products using mass spectrometry. Mass spectrometry was relatively new to chemistry at the time and the alkaloid structure I had been trying for months to determine by IR and UV spectroscopy was solved in less than a week by mass spec.

Soldin: It was apparent that while immunoassay tests were very precise, several of them lacked specificity and provided *precisely* the wrong answer.

Can you tell us how you apply mass spectrometry to solve clinical problems?

Cooks: Our lab uses paper spray - one of the ambient ionization methods. This method minimizes sample work up and avoids chromatography while still allowing for quantitative analysis of complex biological samples through judicious use of MS/MS and – sometimes - derivatization during ionization.

Soldin: One major focus is the application of mass spectrometry to patients suffering from hypothyroidism. The first clue that an immunoassay test is not functioning well is when it fails to help clinicians diagnostically or when despite treatment, the patient insists that she/he is not feeling better. The results of the immunoassay test may lead to either an incorrect diagnosis or suboptimal treatment. This occurs frequently in hypothyroid patients treated with T4 alone and approximately 20-30% of these patients feel better with an additional small dose of T3. Mass spectrometry provides us much greater fidelity to accurately diagnosis and treat this patient population.

How would you describe the current state of mass spectrometry in medicine?

Cooks: I think we are still in a very early stage. There are many areas where more could be done, especially *in situ* analysis of therapeutic drug levels.

Soldin: I believe mass spectrometry in medicine is in its infancy. Specific fields that need to be explored include measurement of neurosteroids in depressive diseases, epilepsy, and mood disorders such as PMS. Another important new horizon is the role of free hormones (estradiol, testosterone, vitamin D3) in malignant diseases.

What has been the biggest surprise (positive or negative) related to clinical mass spectrometry development?

Cooks: The power of lipid profiles as a diagnostic of disease state in tissue has been surprising. This experiment does not require identification of particular compounds; it simply requires reproducible low-resolution mass spectra and automated comparison with libraries of samples of known disease state.

Soldin: The performance of mass spectrometry compared to immunoassays for the diagnosis of 4–6 million (of the 20 million) Americans with hypothyroidism has been impressive. The improved accuracy and reliability of FT4, FT3 and TT3 is a testament to the power of mass spectrometry. The assessment also permits accurate evaluation of T3 needs in these patients. Immunoassays for these 3 analytes do not correlate well with TSH, but LCMSMS ultrafiltration or equilibrium dialysis methods correlate excellently with TSH or log TSH. This then leads to correct diagnosis and better treatment.

On the negative side LCMSMS requires skilled technologists, is less automated and more expensive.

What factors and decisions (intentional or otherwise) were essential to your career development? Were there any lucky accidents?

Cooks: Staying with mass spectrometry was the key to my success. The field has accelerated in importance over the decades. Mass spectrometry is not a type of spectroscopy – it is the science and technology of ions. So it deals with a state of matter and as such embraces ion reactivity, ion thermochemistry, ionic structure, and much more. One of the most interesting areas of mass spectrometry now is preparative and synthetic MS. This is done by depositing ions on surfaces to create modified structures through a process known as ion soft landing. It is also done in solution droplets where ordinary reactions can be accelerated so that reactions taking minutes occur in milliseconds.

Soldin: Listening to problems brought to me by clinicians and addressing them has been the key to my success. Listening to the concerns of hypothyroid patients who despite treatment did not feel better reinforced the need to improve testing. This led to studies demonstrating the shortcomings of approved immunoassays for FT4, FT3 and TT3.

How do you achieve your work-life balance and what are your hobbies outside of your work?

Cooks: I might try for that balance but don't achieve it often. I like gardening, reading novels,

and music.

Soldin: Work is an enormous part of my life and I have loved my professional career immensely. I also enjoy my family and the arts in general.

What are the major challenges or roadblocks in the translation of mass spectrometry into new fields of medicine? How do you think should we address them?

Cooks: The regulatory environment is the main roadblock. We published the first tumor margin studies on MS in 2005. It took another 5 years to set up collaborations and go through IRB's to allow research studies on tissue taken during surgery. It will probably be another 5 years from now before the information from these experiments can be used in the practice of medicine.

Soldin: Some FDA approved immunoassays (FT4, FT3, TT3) have led to incorrect values being provided to clinicians and resulted in suboptimal diagnosis and treatment. Nothing endures but change. This provides a great opportunity for clinical mass spectrometry to make a difference. My daughter is about to start her training to be a physician at Tulane and I emphasize to her that much of what she will be taught will be wrong. She needs to keep an open mind. She also needs to understand " [the wisdom of insecurity](#)"! The latter is the title of a book written by Alan Watts that I can strongly recommend to your readers.

Where do you see mass spectrometry going in the next 5 or 10 years?

Cooks: I see mass spectrometry expanding into the clinics and operating rooms especially in the form of miniature mass spectrometers. Additionally I also see mass spectrometers being used as devices for the synthesis of small (mg) amounts of key compounds by harnessing their ability to accelerate chemical reactions.

Soldin: I believe we are at the early stages in the application of mass spectrometry and that eventually teaching hospitals and research institutes will have large sections of their laboratories dedicated to help physicians develop tests to improve diagnosis and treatment of many human diseases.

What advice would you give to young investigators to help them achieve their career goals?

Cooks: Eschew obfuscation.

Soldin: Listen to yourself. Believe in yourself. Believe in your ideas.

Mass Spectrometry Mini-Track at the Annual Meeting

This year the annual meeting organizers have created Mini-Tracks focusing on special topics. Below are the sessions for the mass spectrometry Mini-Track for the annual meeting in Atlanta.

[35203 Targeted Mass Spectrometry as an Enabling Technology in the Clinical Laboratory](#)

Multiplexed, targeted mass spectrometry based protein assays present several advantages over conventional clinical tests. However, establishing and validating the performance of these tests to make informed clinical and public health decisions pose significant scientific challenges. This symposium will present recommendations for studies designed to establish the analytical and clinical performance of these mass spectrometry based in vitro diagnostic tests to advance their adoption into routine clinical practice.

[33105 The Marriage of Clinical Microbiology and Clinical Chemistry: A Technological Exchange of Vows and Partnership](#)

The disciplines of clinical microbiology and clinical chemistry intersect now more than ever before. This symposium will explore specific areas of overlap, including technology and clinical utilization of methods from the perspective of both a microbiologist and a clinical chemist.

[72420 Mass Spectrometry as an Immunoassay Complement: Best of Both Worlds](#)

In recent years the diagnostics community witnessed a paradigm shift in migration of analytes traditionally done by immunoassays to mass spectrometry. This session will compare the two technologies and provide a tool-set for development of practice-specific testing algorithms focusing on mass spectrometry as a complementary technique to immunoassay.

[191002 Is LC-MS/MS Right for Your Clinical Laboratories? What You Need to Know About the Technology and Finance Before Bringing it to Your Lab](#)

This short course will introduce the fundamental principles of LC-MS/MS and its evolving applications in clinical laboratories. We will discuss considerations such as staffing, space and budgeting related to this introducing this technology. Suggestions and considerations for choosing the right LC-MS/MS system and obtaining financial capital equipment approval will be discussed.

[192009 Troubleshooting for Clinical LC-Tandem MS - Interactive Case Histories](#)

In this short course, get practical advice and the theory supporting that advice for detecting, identifying the root cause, and preventing further occurrences of common problems with clinical LC-MS/MS assays and instruments. Examples that might present a risk to patient safety will be included.

[42125 Fundamentals of Chromatography and Mass Spectrometry \(LC-MS\) Applications in the Clinical Laboratory \(Repeats as 52225\)](#)

This brown bag will cover a basic overview of chromatographic and mass spectrometric concepts. The different chromatography and mass spectrometry methods available in the clinical laboratory will also be discussed along with the types of analytes that can be measured.

[42119 Breaking it Down: Immunoassay vs Mass Spectrometry, What You Need to Know \(Repeats as 52219\)](#)

The goal of this brown bag is to enable participants to make an informed decision when deciding between using mass spectrometry-based methods or immunoassays for specific analytes. Case studies

will be included, along with data from the literature and recommendations from national societies (when appropriate).

[43123 Mass Spectrometry in the Clinical Lab: Developing a Qualitative Comprehensive Drug Screening Method \(Repeats as 53223\)](#)

Comprehensive drug screening is useful in identifying overdoses and poisonings as well as for routine monitoring of patient compliance with prescription medications. This brown bag will explore how to develop a comprehensive drug screening method using two different techniques, liquid chromatography tandem mass spectrometry and high resolution mass spectrometry.

[44104 Method Development and Validation of LC-MS/MS Assays in the Clinical Lab: Tips for the First-Time Users \(Repeats as 54204\)](#)

The introduction of the LC-MS/MS analyzer to the clinical laboratory has seen exponential growth in the last decade. This technology offers superior sensitivity and specificity over other methods currently being offered in the clinical laboratory. This brown bag will cover the basics of LC-MS/MS instrumentation and describe procedures for regulatory compliant method validations.

[44119 The Proteomics Revolution in Clinical Microbiology: Understanding MALDI-TOF Mass Spectrometry](#)

The routine use of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has revolutionized microorganism identification in the clinical microbiology laboratory. This brown bag will explore the basics of MALDI-TOF MS instrumentation, how microorganisms are identified from their proteomic fingerprint, and future applications of this technology in Clinical Microbiology: Understanding MALDI-TOF Mass Spectrometry (Repeats as 54219)

Calendar of Events

Location

July 26 th 2:30-4:30	MS3 Division Meeting	Hyatt Regency
	Dr. Graham Cooks	Hanover CDE
	Poster Awards	
	Division Networking	
July 28 th 12:30-1:30	MS3 Poster Walk	Poster Hall
October 1-2, 2015	<u>Mass Spectrometry and Separation Sciences for Laboratory Medicine</u> (see program summary on the next page)	Chicago, IL

**AACC/MSSS: Mass Spectrometry and Separation Sciences for Laboratory Medicine
5th Annual Conference**

October 1-2, 2015 * Doubletree Hotel - Miracle Mile * Chicago, IL

DAY 1: Thursday, October 1

SESSION I – SCOPE OF MASS SPEC TESTING FOR LABORATORY MEDICINE/PATHOLOGY

Welcome and Program Open

*AACC President David D. Koch, PhD
Emory University School of Medicine (Atlanta, GA)*

Program Overview

*Steven H. Wong, PhD
Wake Forest University School of Medicine (Winston-Salem, NC)*

KEYNOTE ADDRESS

High Resolution Mass Spectrometry for Laboratory Medicine – Current Status and Perspectives in TDM-Tox

Professor Dr. Hans Maurer, Saarland University (Homburg, Germany)

Panel Discussion: Navigating Development and Implementation of Mass Spec-based LDTs

*Saeed A. Jortani, PhD – Moderator, University of Louisville (Louisville, KY)
Henry Rodriguez, PhD, MBA, National Institutes of Health/National Cancer Institute (Bethesda, MD)
Alberto Gutierrez, PhD, U.S. Food and Drug Administration (Silver Spring, MD)
Steven J. Soldin, PhD, National Institutes of Health Clinical Center (Bethesda, MD)
Charles Root, PhD, CodeMap, LLC (Schaumburg, IL)*

SESSION II – ESSENTIAL CONCEPTS IN CLINICAL MASS SPEC

Common Mistakes in LC-MS/MS Assay Development - What They Are and How to Avoid Them

Daniel T. Holmes, MD, St. Paul's Hospital Providence Health Care (Vancouver, British Columbia)

Sample Preparation – A Practical Approach for Robust Analyses

R. Brent Dixon, PhD, Physicians' Choice Laboratory Services (Rock Hill, SC)

Bringing Mass Spectrometry to Clinical Practices: Finance, Personnel and Interface Considerations

Y. Victoria Zhang, PhD, University of Rochester Medical Center (Rochester, NY)

Method Development and Validation for Certification in Accordance with CLSI C62-A and CAP Guidelines

Steven W. Cotten, PhD, The Ohio State University Wexner Medical Center (Columbus, OH)

Antifungals, TDM, and DAU Chiral Analysis by LC-MS/MS

Steven H. Wong, PhD, Wake Forest University School of Medicine (Winston-Salem, NC)

Complementary Role of GC/MS in the Clinical Laboratory and Beyond

Uttam Garg, PhD, Children's Mercy Hospitals and Clinics (Kansas City, MO)

SESSION III – INDUSTRY PERSPECTIVES

SESSION IV – **Open Forum: “Clinics in Mass Spec Analyses”**

DAY 2 Friday, October 2

SESSION V – *Translating Mass Spectrometry Tools to Clinical Practice*

PLENARY LECTURE

The Role of Assay Specificity in Improving Diagnosis and Treatment of Endocrine Disorders

Steven J. Soldin, PhD, National Institutes of Health Clinical Center (Bethesda, MD)

Measurement of Water Soluble Vitamins by UPLC-MS/MS

Yusheng Zhu, PhD, Medical University of South Carolina (Charleston, SC)

PLENARY LECTURE

Metabolomic Analysis for Newborn Screening and Diagnosis of Metabolic Disorders

Michael J. Bennett, PhD, Children's Hospital of Philadelphia (Philadelphia, PA)

Advanced Pain Management – Pharmacogenomics Data to Complement Oral Fluid Compliance Testing

R. Brent Dixon, PhD, Physicians' Choice Laboratory Services (Rock Hill, SC)

The Future of Reimbursement for Mass Spec-based LDTs

Charles Root, PhD, CodeMap, LLC (Schaumburg, IL)

SESSION VI – “NEXT GENERATION” MASS SPEC ANALYSES FOR 2020

SPECIAL LECTURE

Emerging Mass Spec Applications in Anatomic Pathology: Tissue Imaging

Richard M. Caprioli, PhD, Vanderbilt University (Nashville, TN)

Translating “-Omics” Biomarkers from Bench to Bedside

Y. Victoria Zhang, PhD, University of Rochester Medical Center (Rochester, NY)

Linking Massive DNA Sequencing with Mass Spec Proteomics for Advancing Cancer Research and Precision Medicine

Henry Rodriguez, PhD, MBA, National Institutes of Health/National Cancer Institute (Bethesda, MD)

Mass Spectrometry-based Single Cell Measurement

Sean C. Bendall, PhD, Stanford University School of Medicine (Stanford, CA)

Roundtable: Envisioning “Next Generation” Mass Spec Diagnostics in 2020