Sponsored by ASMS, the 2007 Asilomar conference "Mass Spectrometry in Clinical Chemistry and Molecular Diagnostics" included 120 participants from backgrounds as diverse as industry, instrumentation companies, hospitals, governmental laboratories, reference laboratories, medical schools, and other academic institutions. The American Association for Clinical Chemistry accredited this conference for ACCENT continuing education credits.

Following opening comments by organizers Alan Rockwood and Ravinder Singh, Jack Henion from Advion Biosciences presented “Can Mass Spectrometry Add Value to Modern Clinical Chemistry?” which overviewed the merits and issues pertaining to implementing mass spectrometry (especially LC/MS) into the modern clinical laboratory. Strengths and limitations of mass spectrometry were described, emphasizing the value provided by LC/MS in clinical tests that have historically employed immunoassay techniques. Ambient ionization techniques, ion mobility, chip-based nanospray, and others were also discussed.

Charles Cantor from SEQUENOM, Inc. and Boston University School of Medicine then presented “SNP Detection by Mass Spectrometry,” focusing on genetic applications of mass spectrometry.

The session on Biomarker Applications and Genetic Testing, chaired by Leigh Anderson, Plasma Proteome Institute, led off with Anderson’s lecture, “Specific MS Assays for Peptides and Proteins Using Selected Reaction Monitoring and SISCAPA.” This described the technique of “Standards and Capture by Anti-Peptide Antibodies” (SISCAPA), essentially an immunoassay with a mass spectrometer replacing the second (capture) antibody of a conventional immunoassay. Robert Plumb from Imperial College, London, described “The Application of High Resolution Liquid Chromatography and High Resolution Exact Mass Spectrometry to Investigate the Effects of Gut Microflora on Metabolism and Toxicity.”

Andrew Hoofnagle from the Department of Laboratory Medicine, University of Washington, described in “Clinical Tumor Marker Quantitation with LC/MS/MS: Is There Hope?” thyroglobulin (an important tumor marker) as a model of immunoassay imperfection. Immunoassays are unreliable in some patients due to the presence of auto-antibodies that interfere with the test. Hoofnagle’s approach solves the problems of endogenous interfering antibodies (digest the sample into peptides) and the lack of standardization between different commercial immunoassays (include an internal standard peptide).

Christie Hunter from Applied Biosystems described in “Peptide MRM-Based Assays in Plasma for Biomarker Verification Studies,” the use of a triple quadrupole linear ion trap mass spectrometer to create more than 1000 high quality, specific MRM transitions for multiple peptides to many human plasma proteins. A non-isobaric chemical labeling strategy was employed to create global reference standards to enable quantitative analysis. The session concluded with “Automated Nucleic Acid Based Signature Sequence Analysis by MALDI-TOF Mass Spectrometry—a Comparative Sequence Analysis Tool” by Christiane Honisch, Ph.D., SEQUENOM, Inc.

Russell Grant from Labcorp, Inc./Esoterix, chair of the session “Instrumentation and Automation,” presented “Application of Automation Tools in LC-MS/MS Assays for Clinical Diagnostics.” He discussed a number of automation tools employed at LabCorp in development and application of LC-MS/MS workflows, including smart automation tools in optimization of method development. The application of automation in the various components of sample analysis were also discussed, including staggered parallel multidimension LC systems. The goal of automation in clinical testing was highlighted by comparison to the existing autoanalyzer workflows utilized in modern clinical diagnostics. Scott Kuzdzal from Perkin Elmer, Life and Analytical Sciences, then presented “Better Biomarkers by Bacon’s Bees.”

Donald H. Chace from Pediatrix Analytical chaired the evening session “Metabolic Disorders” and presented “Beyond Newborn Screening: Clinical Mass Spectrometry Application Expansion in the Next Ten Years.” Newborn screening by mass spectrometry may serve as a model for overall expansion of MS in the clinical lab. The use of MS/MS in newborn screening

© 2008 American Society for Mass Spectrometry. Published by Elsevier Inc.
1044-0305/08/$32.00
doi:10.1016/j.jasms.2008.04.022
increased from a few hundreds of samples in the early 1990s to several million specimens analyzed in year 2008. The success was based on several factors, one of which is that tandem mass spectrometers have the ability to measure complex profiles from a single small sample.

Michael Morris, Clinical Operations Group, Waters Corporation, presented “The Role of Time-of-Flight Technology in Routine Clinical Applications.” Morris reviewed clinical screening applications, including aspects of neonatal screening for inborn errors of metabolism. The criteria for identification of compounds by mass spectrometry from a number of agencies (FDA, EU, CAP, CLSI) were also reviewed, and ways of meeting the criteria were discussed, including multiple MRM transitions and exact mass measurement, and theoretical versus experimental isotope ratio comparisons. The application of LC-TOF to the screening of a panel of drugs implicated in drug-facilitated crime was presented. The session concluded with “Tandem Mass Spectrometry in Biochemical Genetics” by Dietrich Matern from Mayo Clinic College of Medicine.

Shalender Bhasin, Boston Medical Center, chaired Sunday morning’s session “Quality, Clinical and Client Perspectives, and Unmet Needs,” which highlighted the challenges of making accurate sex steroid measurements with the existing methodologies, and how mass spectrometry can address current problems in patient care. Also presented were perspectives on standardization of test results and a summary of approaches for rigorous method validation. William Rosner, St. Luke’s-Roosevelt Hospital Center and College of Physicians and Surgeons, Columbia University, presented “Assays for Plasma Testosterone: What’s the Problem?” Maria Ospina, Centers for Disease Control and Prevention discussed “Harmonizing Testosterone Measurements—CDC Perspective a.k.a. the CDC Sex Steroid Harmonization Project.” Steroid hormones measurements, especially of testosterone and estradiol, are increasingly used in patient care at research. However, there are problems with comparability and reliability of these measurements. CDC’s steroid hormone standardization project includes preanalytical, analytical, and postanalytical issues. Bhasin’s talk described “Population-Based Reference Ranges for Sex Steroid Assays: The Impact of Assay CV and Quality on Clinical Decision Making.”

Russell Grant’s talk “Validation of Endogenous Quantitative Assays with LC-MS/MS Technologies” discussed a step-wise process flow to analytically validate LC-MS/MS for utility in endogenous analyte measurement in clinical diagnostics. The presentation highlighted experimental designs and failure analysis when key components of assay validation were undertaken. The talk also described streamlined workflows to establish assay stability.

The Sunday evening session, chaired by Pierre Chaurand, Vanderbilt University, covered Imaging and Emerging Technologies. Gilbert S. Omenn, University of Michigan Medical School, described “Biomarker Discovery from Tumor Tissues and Plasma” and demonstrated the strategy of starting with evidence for tumorigenic pathway mechanisms in the tumor and tracking the corresponding protein biomarker candidates through proximal biofluids to the plasma, using the Her2/neu mouse model of human breast cancers and the androgen-driven fusion gene TMPRSS2/ETS in human prostate cancers. He also discussed the detection of autoantibodies. This was followed by lecture by Dean Hafeman, Protein Discovery Inc., “High Throughput Biomarker Discovery and Small Molecule Quantification in Biological Tissues using Parallel Electrochromatographic Preparation.”

Pierre Chaurand in “Molecular Imaging of Tissue Sections by MALDI Mass Spectrometry” described a relatively new technology that can be used to locate drugs, lipids, peptides, and proteins directly from the surface of fresh frozen tissue sections. When analyzing tissue sections for proteins, the profiles recovered typically contain about 500 distinct signals in the m/z range up to 100,000. Thousands of proteomic profiles of tissue sections can now be acquired from large sample sets in very short periods of time.

The Monday morning session chaired by Steven Soldin, Georgetown University, focused on Endocrine, Drugs, and Toxicology. Soldin described “Tandem Mass Spectrometry for Thyroid and Steroid Hormone Replacement.” Following were Mary F. Lopez, Thermo Fisher Scientific, “Targeted MS Quantitation of the Anti-aging Hormone Klotho,” and Robert A. Middleberg, NMS Laboratories, “The Role of Mass Spectrometry in TDM/Toxicology.”

In his talk “Toxic Trace Elements and the Role of ICPMS,” Sum Chan, Quest Diagnostics, discussed symptoms, and the physiological and molecular basis of trace element toxicity, illustrating this with arsenic, cadmium, lead, and mercury examples using inductively coupled plasma-mass spectrometry (ICP-MS). The principles and the variations of available hardware such as nebulizers, RF generators, and collision/reaction cells were given, as well as various strategies to deal with interferences.

Steven Hofstadler, Ibis Biosciences, chaired the Monday afternoon “Infectious Disease” session. In his talk “High Throughput Analysis of Nucleic Acids for the Identification and High Resolution Strain Typing of Bacterial and Viral Pathogen,” Hofstadler described using mass spectrometry, signal processing, and base composition analysis of PCR amplification products to identify microorganisms without the need for culture. This is applicable to bacteria and viruses and has recently been applied to mtDNA-associated mitochondrial diseases.

In his talk “Identification of Clinical Isolates of Campylobacter (and Other Human Pathogens) by MALDI-TOF-MS and Proteomics Identification of Their Protein Biomarkers,” Clifton K. Fagerquist, Western Regional Research Center, U.S. Department of Agriculture,
presented results on cell lysates of bacterial clinical isolates of foodborne bacteria analyzed by MALDI-TOF-MS. Protein biomarkers (m.w. range 4–16 kDa) constitute a MS profile or “fingerprint” allowing taxonomic classification of an unknown isolate when compared with a database MS spectra of known microbial isolates. Using software tools, isolates were successfully “grouped” and separated two distinct sub-species of *Campylobacter jejuni*: *C. j. jejuni* and *C. j. doylei*. Finally, proteomics techniques were used to detect amino acid substitutions caused by mutations.

Randall W. Nelson, Intrinsic Bioprobes, Inc. and Biodesign Institute at Arizona State University, presented the talk “The Use of Mass Spectrometric Immunoassay in the Study of Disease,” which described the use of targeted mass spectrometric approaches to investigate microheterogeneity in human plasma proteins. By understanding the breadth of protein diversity in the “healthy” population, one can establish a baseline for further investigations related to disease. Nelson also discussed the potential of multiplexed mass spectrometric immunoassays to accurately detect and monitor myocardial infarction and Type 2 diabetes.

Each of seventeen poster presenters gave five-minute oral introductions to their posters:

5. Stephanie Marin, ARUP Laboratories. Confirmation of Benzodiazepines in Urine, Serum, Plasma, and Meconium by LC/MS/MS.
9. Ivana Bobeldijk, TNO.NL. Comparison of Lipid Profiling Methods: LC-MS Versus Direct Infusion MS.


12. Hasmik Keshishnian, Broad Institute. Limits of Quantitation for Low Abundance Proteins in Plasma by Targeted MS.


15. Elizabeth Pattison, ARUP Laboratories. LC/MS/MS Analysis of Urine Cortisol and Cortisone by utilizing high-Field Asymmetric waveform Ion Mobility Spectrometry (FAIMS).


David Herold, University of California, San Diego Medical School and the Veterans Hospital, announced the first annual “Mass Spectrometry Applications in the Clinical Laboratory” conference, to be held November 1–5, 2008 at the Hilton, Mission Bay, San Diego, CA. It will include a scientific program, posters, short courses, exhibits, and industrial sponsored lunch presentations. For additional information see http://www.msacl.org or contact Dave at dherold@ucsd.edu or 858-552-8585 ext. 7758.

The authors thank ASMS for selecting this topic for an Asilomar conference, and acknowledge support from our institutions (ARUP Laboratories, University of Utah School of Medicine, Mayo Clinic and Mayo Medical School).