Focus in Honor of Dr. Robert J. Cotter, Recipient of the 2011 ASMS Award for a Distinguished Contribution in Mass Spectrometry

This special focus issue of the *Journal of the American Society for Mass Spectrometry* celebrates the accomplishments of the recipient of the 2011 ASMS Award for a Distinguished Contribution in Mass Spectrometry, Professor Robert J. Cotter. Bob was Professor of Pharmacology and Molecular Sciences, Professor of Biophysics and Biophysical Chemistry, and Director of the Middle Atlantic Mass Spectrometry Laboratory at Johns Hopkins University School of Medicine. He served as President of ASMS from 1998 to 2000.

Tandem mass spectrometry (MS/MS) is a key enabling tool for molecular structure elucidation. Many instrument configurations are feasible for accomplishing gas-phase analyte selection followed by activation and molecule-specific dissociation. Bob Cotter was recognized for his invention and development of tandem time-of-flight (TOF/TOF) mass spectrometry that utilizes high-energy collisions (up to 20 keV) for collision-induced dissociation (CID).

Bob's first instrument design incorporated two dual-stage reflectrons (rTOF/rTOF), which were later replaced by single-stage reflectrons for improved focusing of product ions over a wider mass range. This work was followed by the development of the curved-field reflectron to enable simultaneous focusing of the entire product ion mass range. Kratos Analytical, and later Shimadzu, incorporated Bob's designs of the curve-field reflection into their commercial systems, and hundreds of curved-field reflectron instruments have been manufactured and sold worldwide.

Combining the virtues of high-energy collisions with matrix-assisted laser desorption ionization (MALDI) TOF/TOF mass spectrometry makes possible "top-down" or "middle-down" protein characterization. Another opportunity for high-energy collisions is to allow charge-remote fragmentation to be utilized again (i.e., without the need for high-energy sector instruments), which is useful for analysis of lipids, steroids, and even peptides. Bob's research demonstrated how well tandem mass spectrometry could address a wide range of areas, from characterizing proteins involved in human diseases, detection of biological threat agents, to searching for signs of life on Mars.

On June 6, 2011, Bob was presented the Award by then-ASMS President Scott McLuckey at the 59th ASMS

Bob Cotter (left) and ASMS President Scott McLuckey at the 2011 ASMS Conference (Denver, Colorado).

Conference on Mass Spectrometry and Allied Topics in Denver, Colorado. As remarked by Scott McLuckey: "Significant contributions come from insight—really understanding the problem, creativity, coming up with novel solutions to approach the problem, and diligence, making that solution work. Those of you who build instruments know that....it takes a lot of work to make them work. Bob has epitomized all of those characteristics...It took pioneers like Bob to bring us to where we are (today)."

This special focus issue was in preparation before Bob's untimely passing on November 12, 2012. The focus contains papers devoted to the development and application of TOF mass spectrometry and reflects Bob's interests and accomplishments. The contributing authors were selected and invited by *JASMS* Associate Editors Joseph Loo and Carol Robinson, and many of the authors were suggested by Bob himself. A paper contributed by Jim Reilly's group (Indiana University) describes the generation of abundant high-energy product ions from 157 nm vacuum ultraviolet light with MALDI-TOF/TOF MS to fragment peptides. Chip Cody and colleagues from JEOL report the high-energy CID analysis of triacylglycerols with a MALDI-TOF/TOF system that uses multi-turn and "perfect focusing" ion optics to achieve monoisotopic precursor selectivity. Gary Hieftje's group (Indiana University), Chris Enke (University of New Mexico), and a team from Pacific Northwest National Laboratory (Richland, Washington) describe how decoupling energy and space focusing in TOF and distance-of-flight systems can be used to provide improvement in resolution. Günter Allmaier's group (Vienna University of

Technology) used high-energy CID and MALDI-TOF/TOF MS to identify an impurity commonly found in MALDI matrix, α -cyano-4-hydroxy-cinnamic acid (CHCA), that negatively impacts the quality of peptide mass spectra. The application of MALDI-MS for tissue imaging is growing in popularity, and Ron Heeren and colleagues from the FOM Institute AMOLF (Amsterdam, The Netherlands), the Netherlands Proteomics Centre (Utrecht, The Netherlands), and the Johns Hopkins University School of Medicine demonstrate the potential of MS imaging for medical research in their report of MALDI quadrupole-TOF imaging of a protein in breast tumor xenografts. The focus issue's

lead paper, "High Energy Collisions on Tandem Time-of-Flight Mass Spectrometers," is an Account and Perspective by Bob, and it thoroughly details the history of TOF and tandem TOF. It will be a "must read" tutorial on the development of TOF mass spectrometry. The paper is both insightful and educational—as was our friend, Bob.

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