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FOCUS: MS/MS PEPTIDE IDENTIFICATION: CONFERENCE REVIEW

23rd Sanibel Conference on Mass Spectrometry: From Fragmentation Mechanisms to Sequencing: Tandem Mass Spectrometry Based Peptide and Protein Identification

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The 23rd Sanibel Conference, sponsored by the American Society for Mass Spectrometry, was held January 21–24, 2011, at the TradeWinds Island Grand Hotel, St. Pete Beach, Florida. The topic of this year was "From Fragmentation Mechanisms to Sequencing: Tandem Mass Spectrometry-Based Peptide and Protein Identification." The conference was co-organized by Béla Paizs, German Cancer Research Center, Heidelberg, Germany, and Matthias Mann, Max-Planck Institute of Biochemistry, Martinsried, Germany.

A key information unit in the use of tandem mass spectrometry (MS/MS) in proteomics is the product-ion spectrum of peptides or intact proteins. Most of the basic biological and clinical investigations in proteomics face the problem of peptide or protein sequencing by using raw MS/MS data. The current data-processing strategies apply both fragmentation models that describe how peptides or proteins fragment in mass spectrometers and various bioinformatics strategies that attempt to derive the sequences from the raw spectral data based on these fragmentation models. It is widely accepted in the proteomics community that robust peptide and protein sequencing requires further improvement in fragmentation models and bioinformatics tools.

Historically, peptide fragmentation chemistry and bioinformatics approaches to sequencing have been developed by their respective, distinct communities, with limited interaction between them. This is despite both communities working towards the same goal; the development and implementation of an accurate peptide and protein sequencing strategy. As a direct result of this parallel and independent development, recent mechanistic insights into peptide fragmentation are seldom incorporated into the most popular peptide identification or sequencing algorithms. These software packages are mainly based on peptide fragmentation models developed in the mid 1990s.

The purpose of the 23rd Sanibel conference was to bring the peptide fragmentation and bioinformatics communities closer to each other by offering a forum to create a common language, exchange ideas, and establish joint research projects. This initiative was well-appreciated by the community, and the conference attracted a record attendance in the history of Sanibel meetings with 200 participants presenting 27 invited lectures and submitting 77 poster abstracts. The conference opened with a general introductory talk by Matthias Mann (Max-Planck Institute of Biochemistry, Martinsried) on Friday evening, followed by a reception. This overview demonstrated that MS-based proteomics has become an extremely powerful tool for biological and medical research, with applications ranging from deep protein expression studies, modification analysis, interaction mapping, to even clinical applications.

Saturday started with an overview of basic fragmentation chemistry and sequencing strategies given by Béla Paizs (German Cancer Research Center, Heidelberg), attempting to bridge the two communities and to define a common language. Sessions discussing the chemistries of collision-induced dissociation and electron capture/transfer dissociation made up the rest of the day, with presentations by Simon Gaskell (Queen Mary University of London, London, UK), Gary Glish (University of North Carolina, Chapel Hill), Gavin Reid (Michigan State University, East Lansing),

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Stephen Stein (NIST, Gaithersburg), Roman Zubarev (Karolinska Institutet, Stockholm), Frank Tureček (University of Washington, Seattle), Helen Cooper (University of Birmingham), Kristina Håkansson (University of Michigan), Vicki Wysocki (University of Arizona, Tucson), and Joshua Coon (University of Wisconsin, Madison). Topics covered included primary dissociation of peptide ions, structures, and reactions of fragments, experimental and computational strategies to investigate gas-phase peptide chemistry, statistical studies, ion mobility spectrometry of fragments, proton and electron driven chemistries, and many others, giving a general overview of current research interest in peptide fragmentation. A common theme was rearrangement reactions of N-terminal CID fragments and phosphopeptides and the extent of difficulties these chemistries can cause in large-scale proteomics applications. Another intensely discussed issue was proper adaptation of the amazingly rich world of radical ion chemistry for peptide sequencing.

Saturday was concluded by a Hot Topics session featuring lectures based on selected poster presentations by Peter Armentrout (University of Utah, Salt Lake City), Benjamin Bythell (National High Magnetic Field Laboratory, Tallahassee), Shabaz Mohammed (Utrecht University, Utrecht), Ann Westman-Brinkmalm (Sahlgrenska University Hospital, Molndal), Roman Zubarev (Karolinska Institutet, Stockholm), Meng-Qiu Dong (National Institute of Biological Sciences, Beijing), and Weidong Cui (Washington University, St. Louis), and a vivid poster session.

Morning sessions on Sunday were devoted to peptide sequencing and bioinformatics. The session on de novo sequencing featured Pavel Pevzner (University of California, San Diego), Bernhard Spengler (Justus Liebig University, Giessen), Annette Michalski (Max-Planck Institute of Biochemistry, Martinsried), and Bin Ma (University of Waterloo, Waterloo). They gave a great overview of the related algorithmic strategies, possibilities, and limits of de novo sequencing, the advantages dealing with high resolution–high accuracy data, and proper utilization of de novo sequencing information. A lively discussion ensued as to whether or not these high resolution and high accuracy data would finally be sufficient to allow high-confidence de novo sequencing on a large scale. Database search-related issues were discussed by Marshall Bern (Palo Alto Research Center, Palo Alto), William Stafford Noble (University of Washington, Seattle), Ronald Beavis (The University of British Columbia, Vancouver), and Alexey Nesvizhskii (University of Michigan, Ann Arbor). This session reviewed advanced algorithmic strategies, analysis of large datasets, creation and search of spectral libraries, and proper exploitation of search results.

Sunday was concluded by a Vendor Workshop and Hot Topics session and a poster session. The Vendor Workshop featured new instrumental and software developments and advanced applications, presented by Shannon Cornett (Bruker Daltonics, Fairview), John Cottrell (Matrix Science Ltd., London), Martha Stapels (Waters Corporation, Milford), and Robert B. Cody (JEOL USA, Inc., Peabody). The closing Hot Topics session included talks by Peng Zhao (University of Georgia, Athens), Helene Cardasis (Merck Research Labs, Rahway), Katharina Kramer (Max Planck Institute for Biophysical Chemistry, Göttingen), and Bruce Southey (University of Illinois at Urbana Champaign, Urbana) discussing sequencing applications of ETD and HCD, modifications, neuropeptides, and protein-RNA cross-linking. General take-home message of this session is that not only academics but also vendors manufacturing MS instrumentation and software are devoting substantial efforts to improve the current sequencing technologies, not just refining the existing technologies but also paving the road by introducing new strategies or reanimating once mainstream techniques. The various sequencing applications discussed in the Hot Topics session provided great examples of the role peptide sequencing can play in applications in neuroscience and other basic biology studies.

The last day of the conference began with a session on sequencing of post-translationally modified peptides. Discussing more and less frequent modifications were Ole Jensen (University of Southern Denmark, Odense) and Kati Medzihradszky (University of California, San Francisco), while Nathalie Ahn (University of Colorado at Boulder, Boulder) discussed how to evaluate spectrum–peptide matches. This presentation gave a nice example of utilizing advanced fragmentation chemistry for validating sequence hits from large-scale database searches, demonstrating that peptide fragmentation chemistry and bioinformatics approaches can indeed converge. As a long-standing Sanibel tradition, the conference was concluded with a session on Perspectives and New Directions. Topics discussed included advanced ion chemistry for sequencing, protein sequencing, IR spectroscopy, and advanced bioinformatics, presented by Scott McLuckey (Purdue University, West Lafayette), Neil Kelleher (University of Illinois at Urbana-Champaign, Urbana), Philippe Maitre (Université Paris-Sud 11, Paris), and Jürgen Cox (Max-Planck Institute of Biochemistry, Martinsried). These talks clearly showed that there are developments in basic ion chemistry that need to be completed and offer promise to fuel advances of the field for decades to come!

Selected papers covering mainly the first day of the meeting are presented in this issue of *JASMS* as a Focus on MS/MS Identification, honoring one of the authors of this review who was awarded the 2011 Biemann Medal. These papers are discussed in detail in the accompanying Editorial by Michael L. Gross, Veronica M. Bierbaum, and Richard O'Hair.

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