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Meeting Report on the 2nd Chinese American Society for Mass Spectrometry Conference: Advancing Biological and Pharmaceutical Mass Spectrometry

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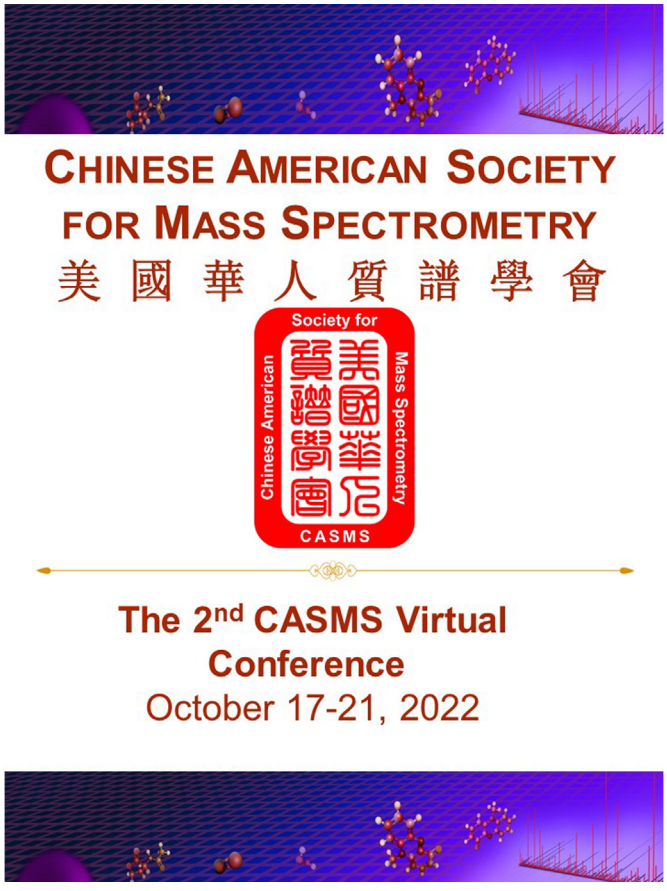
In Brief

The Chinese American Society for Mass Spectrometry (CASMS) was formed in 1981 and currently has ~1500 active members. The mission of CASMS is to promote academic and social interactions among the mass spectrometrists within the Chinese community and beyond. To better serve our community, CASMS organized the second CASMS conference virtually on October 17 to 21, 2022 using the Gather.Town platform to bring together a diverse group of prominent scientists and young rising stars worldwide in the mass spectrometry field.

Graphical Abstract



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Highlights

- Two scientific themes on biological and pharmaceutical mass spectrometry.
- 115 invited speakers and panelists for 20 oral sessions and 5 workshops.
- One MCP lectureship and 5 young investigator awards.
- 144 posters and 54 lightning talks, from which 28 presentation awards were selected.
- Integration of academic and industrial research and development.

Meeting Report on the 2nd Chinese American Society for Mass Spectrometry Conference: Advancing Biological and Pharmaceutical Mass Spectrometry

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The 2nd CASMS conference was held virtually through Gather. Town platform from October 17 to 21, 2022, with a total of 363 registrants including an outstanding and diverse group of scientists at the forefront of their research fields from both academia and industry worldwide, especially in the United States and China. The conference offered a 5-day agenda with an exciting scientific program consisting of two plenary lectures, 14 parallel symposia, and 4 special sessions in which a total of 97 invited speakers presented technological innovations and their applications in proteomics & biological mass spectrometry and metabo-lipidomics & pharmaceutical mass spectrometry. In addition, 18 invited speakers/panelists presented at 3 research-focused and 2 career development workshops. Moreover, 144 posters, 54 lightning talks, 5 sponsored workshops, and 14 exhibitions were presented, from which 20 posters and 8 lightning talks received presentation awards. Furthermore, the conference featured 1 MCP lectureship and 5 young investigator awardees for the first time to highlight outstanding mid-career and early-career rising stars in mass spectrometry from our society. The conference provided a unique scientific platform for young scientists (*i.e.*, graduate students, postdocs and junior faculty/investigators) to present their research, meet with prominent scientists, and learn about career development and job opportunities (http://casms.org).

The Chinese American Society for Mass Spectrometry (CASMS) was formed in 1981. After 42 years of growth, we have more than 1500 active members. The mission of CASMS is to promote academic and social interactions among the mass spectrometrists within the Chinese community and beyond. To better serve our members, the CASMS leadership team successfully organized the first scientific conference in 2021 to bring together an outstanding and diverse group of prominent and well-established scientists as well as promising young researchers at the forefront of their research fields. Built upon the success of the 1st CASMS conference, the 2nd CASMS conference was held virtually again on October 17 to 21, 2022, using the Gather. Town platform to replicate a real-life experience (Fig. 1). This conference was co-chaired by Drs

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Lan Huang (President of CASMS, University of California, Irvine) and Naidong Weng (President-Elect of CASMS, GSK), focusing on two main scientific themes: (1) Proteomics and Biological Mass Spectrometry, and (2) Metabolomics, Lipidomics & Pharmaceutical Mass Spectrometry. The 5-day conference was composed of a very exciting program, containing 2 plenary lectures, 14 parallel symposia, 3 special society sessions, and 1 young investigator award symposium, in which a total of 97 invited presentations were given. In addition, 5 CASMS and 5 sponsor workshops were organized to highlight specific topics. Moreover, 144 posters and 54 lighting talks were presented to further showcase recent research from our members on the two main themes.

The conference began with an Opening Plenary Lecture on October 17th delivered by Prof. Albert Heck (Utrecht University, Netherlands). Dr Heck presented new developments of high-resolution native MS for the mass analysis of intact proteins and protein assemblies at the level of single particles. The unique capability of detecting single molecules by charge detection MS has facilitated the detailed characterization of a diverse array of biomolecules including antibodies, naive viruses, and advanced biopharmaceuticals. Such technology will bring a broad impact of native MS to various disciplines of life sciences. The Closing Plenary Lecture was given on October 21st by Dr Kevin Bateman (Scientific Associate Vice President, Merck, USA). Dr Bateman's presentation focused on some of the recent efforts to improve the ability to perform MS-based analysis in the pharmaceutical industry. MS in the pharmaceutical industry has a long history of innovation and impact on our ability to discover and develop new therapeutics. The constant strive for improved sensitivity, speed of analysis, and better tools for structure elucidation have driven many of these innovations through partnerships with academia and instrument companies. The massive data generation capability from the improved MS is also an opportunity to consider how predictive models will impact the future of our analytical workflows and will drive future innovations.

SYMPOSIA ON PROTEOMICS AND BIOLOGICAL MS

The proteomics-focused symposia covered a wide range of research areas to highlight new technological advances and their biological/clinical applications to understand protein structures and functions at the systems level and to advance biomedical research for human health and medicine. In this conference, a total of seven symposia on specific proteomics topics were organized to reflect the diverse aspects of modern proteomics research, which were summarized below.

Technology Innovation for Biological Discovery

This symposium was co-chaired by Drs Lingjun Li (University of Wisconsin-Madison) and Liangliang Sun (Michigan State University), featuring six MS experts, who shared the most recent technological innovations in single-cell proteomics, glycoproteomics, ion mobility MS, and native MS. For single-cell analysis, Dr Ying Zhu (Genentech), a world expert of single-cell proteomics (SCP), introduced some exciting improvements in the NanoPOTS (nanodroplet processing in one pot for trace samples)-based SCP workflow to improve the proteome coverage, throughput, and spatial resolution for protein imaging across tissues. Discovery-based SCP still needs significant improvement to detect low-abundance protein biomarkers in mass-limited clinical human samples. Dr Yu Bai (Peking University) presented a highly sensitive MS-based immunoassay with zeptomole sensitivity for targeted analysis of protein biomarkers from a few or even single human cells and mass-limited serum/plasma samples. Another limitation of MS-based single-cell study is low throughput. Dr Tian Qiu (Michigan State University) demonstrated the potential of a MALDI-TOF-based technique for high-throughput chemical measurements of single neurons using a nematode model organism. Protein glycosylation affects protein function dramatically and is linked to various diseases. Dr Ronghu Wu (Georgia Institute of Technology) presented the most recent studies from his group regarding the development of MS-based chemical and enzymatic methods for the comprehensive characterization of protein *O*-GlcNAcylation and N-GalNAcylation. Ion mobility MS (IM-MS) has gained significant traction for high-throughput gas-phase separation and characterization of biological molecules. Dr Erin S. Baker (University of North Carolina at Chapel Hill) discussed the development of an IM-MS method for the high-resolution separation of opioids and their isomers. Her research group coupled Agilent LC to IM-MS for a rapid screen of opioids in urine samples. Native MS is a powerful technique for obtaining helpful information on protein–ligand interactions in a high-throughput manner, which provides us with valuable guidance to design drugs targeting specific protein biomarkers. Dr Mowei Zhou (Pacific Northwest National Laboratory) showed their recent efforts in coupling native MS and surface-induced dissociation to delineate interactions between small-molecule inhibitors and SARS-CoV-2 nonstructural proteins for structure-based drug design. Collectively, this symposium covered a range of MS-based technological developments and their applications to various biological systems and significant biomedical problems for an exciting discovery.

PTMs and Diseases

This symposium co-chaired by Drs W. Andy Tao (Purdue University) and Ronghu Wu (Georgia Institute of Technology) invited six world-renowned scientists to present their latest and exciting research on the specific topic. Dr Ileana Cristea (Princeton University) talked about protein posttranslational modifications and virus infection and discussed the mechanisms underlying organelle remodeling and protein modification changes during viral infections. Next, Dr Yue Chen (University of Minnesota at Twin Cities) shared their fabulous

work on quantitative proteomics analysis of hypoxia-mediated ubiquitination signaling. Using quantitative proteomics, affinity enrichment, and new E3 ligase activity profiling analysis, they explored the hypoxia-mediated dynamic changes of protein ubiquitination in cancer cells and identified new hypoxia-regulated pathways in protein homeostasis and DNA damage response. *O*-GlcNAcylation is a very unique type of protein glycosylation, the only known glycosylation occurring in the nucleus of human cells. Dr Junfeng Ma (Georgetown University Medical Center) presented his work on understanding the cross-talk between *O*-GlcNAc and other PTMs using proteomics approaches. As one of the most common and important modifications, protein phosphorylation regulates signal transduction and gene expression. Two speakers, Drs Tujin Shi (PNNL) and Zhiyong Wang (Carnegie Institution for Science, Stanford), talked about the analysis and biological significance of protein phosphorylation. While Dr Shi described a streamlined tandem tip-based workflow for sensitive nanoscale phosphoproteomics, Dr Wang discussed how to map the signaling network of a GSK3 kinase using TurboID-mediated biotin labeling and phosphoproteomics.

Finally, a special award lecture was delivered by Dr Yonghao Yu, the recipient of the MCP lectureship award, which was sponsored by *MCP* and presented virtually by Dr Anne-Claude Gingras (Deputy Editor of *MCP*) at this symposium. Dr Yu obtained his B.S. in 2001 from Fudan University in China and PhD in Chemistry from the University of California, Berkeley in 2006. After his postdoc training at Harvard Medical School, he joined the Department of Biochemistry, University of Texas Southwestern Medical Center as an Assistant Professor in 2012 and became a Full Professor with tenure at Columbia University Irving Medical Center in 2022. Through his independent career, Dr Yu has built an extremely successful research program focusing on developing novel proteomic methods to study protein PTMs and employing them to understand molecular mechanisms of signal transduction associated with cancer biology. He has co-authored more than 60 peer-reviewed articles with most of them published in prestigious and highly impactful journals including *Nature Methods, Science, Nature Chemical Biology, Nature Communications, and Cell Reports.* Due to his outstanding academic achievements, Dr Yu was selected by CASMS as the mid-career rising star in proteomics for this special recognition. During his award lecture, Dr Yu presented his groundbreaking work on identifying protein poly-ADP-ribosylation and characterizing its role in cancer biology. He highlighted his recent studies on global analyses of the PARylated proteome to uncover new molecular targets for improved cancer diagnostics and therapeutics.

Protein Structures and Proteoforms

This symposium was co-chaired by Drs Ying Ge (University of Wisconsin-Madison) and Si Wu (University of Oklahoma) to highlight breakthroughs in this area. Seven speakers presented their cutting-edge research on elucidating protein structures and characterizing proteoforms. With a heavy focus on method development, application, and data analysis for both bottom-up and top-down MS-based proteomics, attendees were treated with a selection of presentations that encapsulated the full range of breakthroughs in this area. First, Dr Ljiljana Pasa-Tolic (PNNL) presented her novel methods in the application of Fourier transform MS for spatially resolved omics. Next, Dr Liangliang Sun (Michigan State University) presented new developments in capillary electrophoresis coupled with MS (CE-MS) to enable the effective separation of intact proteoforms for top-down analysis. As RPLC is used most commonly for MS-based proteomics, the discussion of the advantages of CE for protein separation was fascinating. Dr Xiaowen Liu of Tulane University presented his recent work on the use of machine learning models to predict the retention/migration time of intact proteoforms for improved identification. Two speakers from China, Dr Guanbo Wang (Peking University) presented his work on improving the accuracy in analyzing intact heterogeneous proteins utilizing the universal benefits of charge reduction and alternative gas-phase reactions, and Dr Chenxi Jia (National Center for Protein Sciences) described his study of sORF-encoded peptides in bacteria. The session was wrapped up with presentations from two young researchers. David Roberts (University of Wisconsin-Madison), AHA predoctoral fellow in Dr Ying Ge's laboratory discussed the application of top-down proteomics in the study of low-abundance protein biomarkers. Finally, Dr Kellye A Cupp-Sutton (University of Oklahoma), postdoctoral researcher in Dr Si Wu's lab, presented her research on thermal proteome profiling using top-down proteomics approaches. Overall, the presentations gave impressive insights into the future directions for the use of MS-based proteomics to study protein and proteoform structure.

Proteomics in Precision Medicine

This symposium, co-chaired by Drs Junmin Peng (St Jude Children's Research Hospital) and Ling Hao (George Washington University), featured six speakers who focused on the applications of diverse proteomics technologies in biomedical research. Dr Michael J. MacCoss (University of Washington, Seattle) presented the quantitative analysis of hundreds of post-mortem human samples of Alzheimer's Disease, including different disease-affected brain regions. The collected data from well-characterized brain tissues provide important insights into therapeutic strategies for Alzheimer's disease. Dr Tiannan Guo (Westlake University, China) presented AI-empowered proteomics studies of diagnosing thyroid cancer from a nodule biopsy through a highly sensitive platform of pressure-cycling technology coupled with SWATH MS. The Guo group developed a panel of 19 protein biomarkers from more than one thousand tissue samples, achieving at least 85% diagnosis accuracy in multiple cohorts. Dr Ruibing Chen (Tianjin University, China) developed a high-

throughput affinity purification and MS strategy to analyze the RNA–protein interaction and identify the interactome of lncRNA-HULC (Highly Upregulated in Liver Cancer). The strategy was also employed to characterize the complex RNA–protein interactions in different subcellular localizations. Dr Tao Liu (PNNL) described the development of targeted proteomics with increased throughput and sensitivity for analyzing various cancer tissues and biofluids (*e.g.*, blood plasma, breast proximal fluids, and cerebrospinal fluid) as well as the integration of protein PTM studies. Dr Xiaofeng Wu (Pfizer Inc) described an efficient method to isolate extracellular vesicles (EVs) to monitor the activities of drug absorption, distribution, metabolism, and excretion (ADME). Numerous ADME proteins were measured by TMT-MS in liver EV and plasma EV samples, serving as potential indicators of drug response. Finally, Dr Ruben Y. Luo (Stanford University) introduced the utilization of the resolution power of CE-MS to precisely identify intact human hemoglobin variants during the clinical diagnosis of hemoglobinopathy. He also discussed an alternative career path in clinical chemistry to become a clinic-track faculty member for mass spectrometrists. These diverse proteomics strategies presented in this symposium shed light on the accurate diagnosis and treatment of human diseases such as neurodegenerative disease, cancers, blood disorders, drug response, and biomarker discovery, demonstrating the promise of proteomics techniques and their potential clinical applications in personalized medicine.

Frontier in Data Acquisition and Analysis

This symposium was co-chaired by Drs Yue Chen (University of Minnesota) and Xiaowen Liu (Tulane University), with a focus on new methods and applications in MS experiments and data analysis. It included six presentations on data-independent acquisition (DIA)-MS, MS library query, immunopeptide prediction, and RNA MS data analysis. Three invited speakers, Dr Alexey Nesvizhskii (University of Michigan), Dr Liang Qiao (Fudan University, China), and Mr Ronghui Lou (ShanghaiTech University, China), presented the latest DIA-MS data analysis tools developed in their labs. Dr Nesvizhskii introduced the recent development of FragPipe, a widely used pipeline for MS-based protein identification and quantification. A new DIA-MS data analysis function integrated into FragPipe enabled searching DIA-MS spectra directly against protein sequence databases for peptide identification, simplifying the pipeline for DIA-MS data analysis. With this improvement, FragPipe was extended to fully support DIA-MS data for both library-based and library-free peptide identification. Dr Qiao presented the recent progress on three research projects in DIA-MS data analysis: DeepDIA for in silico spectral library generation, GproDIA for DIA-MS-based glycopeptide identification and quantification, and an application of directDIA for DIA-MS metaproteomics data analysis. Mr Lou from Dr Wenqing Shui lab (iHuman Institute, ShanghaiTech University, China) gave a presentation on DeepPhospho, a new software tool for deep phosphoproteome profiling using DIA-MS, in which a deep learning model was employed to predict mass spectra of phosphopeptides and *in silico* spectral libraries generated by the model were used for phosphopeptide identification. Dr Ming Li (University of Waterloo) described a personalized deep learning method for identifying cancer neoantigens, in which a deep learning model was trained for each patient to learn patterns of the immunopeptidome from the MS data of the patient and to identify personalized peptide neoantigens using *de novo* peptide sequencing. Dr Mingxun Wang (University of California Riverside) described MassQL, a query language for spectral library searching and mining, which offers the MS community a flexible, scalable, and user-friendly language to facilitate MS-based discoveries. Dr Rui-Xiang Sun (National Institute of Biological Sciences (NIBS), China) presented his recent studies on fragmentation mechanisms and patterns of RNA oligos in collision-induced dissociation MS. Taken together, these presentations covered cutting-edge informatics tools and technologies with diverse applications and offered new insights to the future development of data analysis strategies and infrastructure in mass spectrometry-based omics studies.

Proteomics and Multi-Omics in Pharma and Biotech

This symposium was co-chaired by Drs Karen Wang (Novartis Institutes for BioMedical Research) and Yu Tian (Abbvie). Six presentations were given by leading experts in industry and academia focusing on multi-omics technology and applications with potential signification impact on the drug discovery efforts. Dr An Chi (Merck) presented chemo-proteomics method and application to drug mode of action studies in cells. Dr Jeff Xia (McGill University) described metabolomics and multi-omics data integration to address the big data challenges and multi-omics data integration and cross-functional collaboration in biomedical research. Dr Yu Tian (Abbvie) presented spatial multi-omics technology and applications to disease mode of action elucidation. Dr Junmin Peng (St Jude Children's Research Hospital) talked about his recent work on deep profiling proteomics of brain samples of patients with Alzheimer's disease for the discovery of novel therapeutic strategies. He also discussed how to increase the throughput of chemo-proteomics for compound screening by compound pooling. Dr Mingliang Ye (CAS Key Laboratory, China) presented the identification of drug targets by pH-dependent protein precipitation in cells. Mr Haorong Li from Dr Ling Hao's laboratory (George Washington University) presented multi-omics study of patient-derived fibroblasts leading to the identification of potential therapeutic targets for MELAS, a progressive neurodegenerative disease.

Systems Biology and Epigenetics

This symposium was co-chaired by Drs Yinsheng Wang, (University of California, Riverside) and Yansheng Liu (Yale

University). Histone modifications are essential molecular hubs linking epigenetic regulation and metabolism. This integrative session began with a lecture from Dr Yingming Zhao (University of Chicago), who described a family of lysine acylation modifications. Using a series of analytical, pharmaceutical, and immunological methods, the Zhao lab discovered different regulatory mechanisms between lysine L-lactylation (KL-la) and its two structural isomers, lysine D-lactylation (KD-La) and N-epsilon-(carboxyethyl)Lys (Kce), enhancing our understanding of L-lactate biology. DNA N6-methyladenine (6 mA) is one of the most prevalent epigenetic base modifications in prokaryotes and some multicellular eukaryotes. Dr Hailin Wang (Chinese Academy of Sciences, Research Center for Eco-Environmental Sciences) described a series of their work on misincorporated 6 mA in mammalian embryonic stem cells using isotope tracer and mass spectrometry. The mammalian proteome expression shapes the biodiversity on Earth. Dr Yansheng Liu (Yale University) presented the application of DIA-MS in quantifying proteins across the scales of cancer cell lines, human individuals, and 11 common mammalian species, revealing distinctive variability extent of different pathways in and across scales. The protein quantitative variability is driven by many factors including protein translation. Dr Kuan-lin Huang (Icahn School of Medicine at Mount Sinai) focused on the translation step in his talk. Using proteogenomic datasets, they identified thousands of translation regulators by devising a new algorithm that concurrently analyzes mRNA transcriptome and global protein expression profiles across six cancer cohorts. Dr Yue Andy Qi, (National Institute of Aging) shared their automatic FAIMS DIA-MS pipeline. This technique was applied in isogenic human induced pluripotent stem cell lines following CRISPR inhibition on 13 frontotemporal dementia-associated genes. Qi reported new dementia biomarkers and pathways. To define small open reading frames (sORF)–encoded microproteins or peptides, Dr Qian Zhao (Hong Kong Polytechnic University) delivered an optimized workflow of sample enrichment, MS data acquisition, and customized database searching based on ribosome profiling results. The integrated approach allowed the identification of hundreds of sORF peptides in mouse tissues. DNA polymerase η (Pol η) is known to catalyze bypass of ultraviolet light-induced cyclobutane pyrimidine dimers. To explore new functions of this polymerase, Dr Feng Tang (University of California Riverside), a postdoctoral researcher in Dr Yinsheng Wang's laboratory, presented unbiased proteome-wide profiling of Pol η-interacting proteins using proximity labeling and affinity pull-downs. A few Pol η interactors, such as helicases, were followed up. Overall, the "Systems Biology and Epigenetics" session embraced the discoveries of novel DNA and protein modifications, quantitative biology in basic and translational research, and molecular mechanisms in protein translation and epigenetics, all enabled by the development of state-of-the-art MS methods.

SYMPOSIA ON METABOLOMICS, LIPIDOMICS, AND PHARMACEUTICAL MS

Metabo-lipidomics & Pharmaceutical MS symposia consisted of seven topics covering frontiers of mass spectrometry applications in drug discovery and development to highlight current research directions in the pharmaceutical industry and academia.

Lipidomics in (Pre)translational Research

This symposium was chaired by Dr Xianlin Han (University of Texas Health Science Center at San Antonio), focusing on lipidomics applications for biomedical and biological research. The session was very dynamic on the selected topics presented by the six invited speakers, which began with the presentation of "Elucidate Postprandial Metabolic Excursions Following Dairy Interventions *via* Comparative Lipidomics" delivered by Dr Jiangjiang Zhu (The Ohio State University). It was followed by Dr Changfeng Hu (Zhejiang Chinese Medical University) who presented their recent discoveries by lipidomics on systemic lupus erythematosus entitled "Lipidomics Revealed Aberrant Lipid Metabolism in Systemic Lupus Erythematosus". Next, Miss Ziying Xu, a graduate student in Dr Xianlin Han's laboratory at the University of Texas Health Science Center at San Antonio, presented her novel findings on "Alterations of Brain Bioactive Lipids after Microglia Elimination in Alzheimer's Disease: A Functional Lipidomics Study". The fourth speaker, Dr Jun Yang (University of California-Davis), talked about his targeted lipidomics studies on inflammatory diseases entitled "Modulating Lipid Mediators in Diseases Guided by a Targeted Lipidomic Approach." Then, Dr Shuling Xu, a postdoctoral fellow from Dr Lingjun Li's laboratory (University of Wisconsin-Madison), presented her recent work on "Probing Aminophospholipids Alteration in Alzheimer's Disease Progression at *sn*-Position Level through Isotopic N, N-dimethyl Leucine Labeling *via* High-resolution Ion Mobility Mass Spectrometry." Finally, Dr Peter Meikle at Baker Heart and Diabetes Institute in Australia and an outstanding investigator in clinical lipidomics, delivered a talk on "Application of Clinical Lipidomics in Health and Disease." In summary, the speakers at the symposium presented their exciting and novel findings by using lipidomics for (pre)translation research, which well represents the advances and frontier of lipidomics research.

Multi-Omics Integration for Biomarker Discovery

This symposium was co-chaired by Drs Jianguo (Jeff) Xia (McGill University, Canada) and Yanping Lin (Johnson & Johnson). Six world-renowned scientists presented their latest and exciting research results about proteomics, metabolomics, and lipidomics applied in biomarker discovery. Dr Guodong Zhang (National University of Singapore) talked about using LC-MS/MS-based metabolomics to

systematically profile lipid signaling molecules to identify therapeutic targets and environmental risk factors of gut diseases, including but not limited to colonic inflammation (inflammatory bowel disease or IBD) and colon cancer. Using this powerful and novel strategy, Dr Zhang demonstrated that the previously unappreciated cytochrome P450 (CYP)/soluble epoxide hydrolase (she)-mediated lipid metabolism pathway plays critical roles in the pathogenesis of colonic inflammation, colon cancer, and colon barrier dysfunction. Next, Dr Zuo-Fei Yuan (St Jude Children's Research Hospital) shared the tips of their multiple computational pipelines to decode tandem mass tag (TMT) labeled two-dimensional LC-MS/MS–based whole proteome and phosphoproteome data. Dr Jessica Ewald (McGill University) followed to give some tips on using web-based tools to extract value from the multi-omics data. Multi-omics data promise to give more insights into biological processes than single omics data. When integrating details across omics layers, orthogonal information uncovers more processes and themes, offering a more holistic view, while redundant information reduces false positives/negatives, giving more robust results. Dr Ewald demonstrated two main approaches for multi-omics integration and presented one web-based tool for each: OmicsNet for knowledge-driven integration and OmicsAnalyst for data-driven integration. Dr Liang Jin (AbbVie Bioresearch Center in Worcester) shared how their team used transcriptomic and proteomic analysis for mucosa and wall layers separated from the same colon biopsies to investigate Crohn's Disease (CD), the most common type of inflammatory bowel disease (IBD). Their results suggested a strong correlation between transcriptomics and proteomics based on biological functions and a moderate correlation based on abundance and effect size. Differential isoform abundance was observed between different compartments of the colon, which may uncover new disease mechanisms. Dr Simone Sidoli (Albert Einstein College of Medicine) leads his lab in developing and utilizing biochemical methods to characterize anomalous changes in chromatin compaction in aging cells. Genomic instability during natural aging is currently indicated as a major cause of increased stochastic gene expression, tumorigenesis activation, and reduced DNA repair efficiency. His lab identified proteins that minimize anomalous RNA transcription and maintain compacted heterochromatin. To do so, they innovate biological models based on 3D cell cultures and optimize methods using MS. At the end, Dr Shuzhao Li (Jackson Laboratory for Genomic Medicine) demonstrated how his lab employs ultrahigh-resolution MS to measure the metabolome, lipidome, and small molecules of dietary, microbial, and environmental origins to investigate mammalian systems' immunology. Along the way, he and colleagues developed mummichog for pathway/network analysis, data processing, and multi-omics integration approaches.

Analytical Method Development in MS-Based Metabolomics

This symposium was chaired by Dr Tao Huan (University of British Columbia). Six leading scientists in metabolomics and mass spectrometry were invited and gave excellent talks on the recent analytical method developments in their labs. These speakers are from research institutes and universities worldwide, representing different academic stages with a good gender balance. Dr Boone M. Prentice (University of Florida) talked about the recent development of instrumentation and methods to enable gas-phase reactions (*e.g.*, ion/ion reactions) to facilitate lipid structural isomer differentiation and identification. The next speaker is Dr Zheng-Jiang Zhu (Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences), who presented their newly developed bioinformatics tools for unknown metabolite annotation. Dr Haiwei Gu (Florida International University) utilized complementary GC-LC-MS platforms to detect and monitor 2080 metabolites in 48 post-mortem tissue samples harvested from the superior frontal gyrus of male and female subjects. From this study, a 9-metabolite panel of disease markers (lauric acid, stearic acid, myristic acid, palmitic acid, palmitoleic acid, and four unidentified mass spectral features) was discovered. Next, Dr Dajana Vuckovic (Concordia University) talked about solid-phase microextraction in LC-MS-based lipidomics, followed by Dr Jane E. Hill (University of British Columbia)'s talk on breath metabolomics. Finally, Dr Guanshi Zhang (University of Texas Health Science Center at San Antonio) presented a mass spectrometry imaging study to reveal the accumulation of lysophosphatidic acid (LPA) in the diabetic kidney and the blockage of LPA receptor 1 that protects against diabetic kidney disease.

High-Throughput MS for Drug Discovery

This symposium was organized by Dr Hui Zhang (Entos), focusing on High-Throughput MS (HTMS) methodologies and applications for drug discovery. HTMS has seen expanded utility in drug discovery, including target validation, hit discovery, lead optimization, non-GLP analysis, and so on. Dr Xueyun Zheng (PNNL) presented the application of ion mobility spectrometry (IMS)-MS for high-throughput bioanalysis in isomer separation and collision cross-section database application enabled by informatics and hardware advancements. Dr Juncai Meng (Janssen) focused on developing HTMS-based methodologies for hit identification. His group identified covalent ligands as validated hits for an undisclosed kinase target. High-throughput data deconvolution was enabled by a commercial software (GeneData). Dr Meng also applied affinity selection MS (ASMS), a very HTMS methodology for noncovalent hit discovery, and successfully identified hits for several challenging targets, including ligases, transcription factors, and protein-protein-interaction targets.

Dr Xianshu Yang from Merck brought an exciting talk on applying ASMS for drug target deconvolution with Cytosolic Proteome & Affinity-based Target Identification (CPATI) approach. ASMS hits identified from cytosol protein fractions were aligned with quantitative proteomics results and matches of distribution profiles between protein and detected ligand to indicate interactions between them. Three distinctive ligand/target pairs were identified and verified with recombinant proteins afterwards. Dr Yang also provided insights into the critical comparisons of CPATI with Celluar Thermal Shift Assay methods. Dr Wenqing Shui (iHuman Institute, China) shared her recent research in G-protein coupled receptor (GPCR) targets identification for neurological disorders using a deep DIA phosphoproteome MS profiling methodology. Her group successfully characterized regional distributions and dynamics of the transmembrane proteome in brain tissue, from which a GPCR interaction network was built, and specific GPCRs were identified as potential targets to modulate depression and anxiety. Acoustic ejection mass spectrometry (AEMS) was recently developed and commercialized, and we had two presentations highlighting this technology. Dr Olive Wang from Cedars-Sinai Center applied AEMS to multiplex Stable Isotope Standards and Capture by Anti-Peptide Antibodies assay and demonstrated an impressive quantitation result with 10,000 plasma samples in 5 h. Second, Dr Tim T. Häbe from Boehringer Ingelheim Pharma shared their research that led to 6Hz-data-acquisition speed and enhanced instrument robustness. A 1.5 million-compound library was successfully screened in a short period of 33 working days. This screening outcome and other technology development shown in this session demonstrated the power of HTMS for drug discovery.

Recent Advances in Biotransformation Sciences for Small Molecules, Proteins, and New Modalities

This symposium was chaired by Dr Shuguang Ma (Amgen Inc). Biotransformation field is constantly evolving with new molecular structures, novel modalities, and discoveries of new metabolic pathways. Six leading scientists from pharmaceutical industry and academia presented their latest and exciting research in biotransformation sciences. Macrocyclic peptides are an emerging class of promising drug modalities that can be used to interrogate hard-to-drug ("undruggable") targets. Dr Dian Su (Mersana Therapeutics) discussed the strategies and toolkits for assessing the metabolic stability and biotransformation of Macrocyclic peptides in drug discovery. An integrated approach, including physiologically relevant matrices, high-resolution LC–MS, and WebMetabase-based semi-automatic data analysis, was established to facilitate macrocyclic peptides discovery. As complex biotherapeutic molecules continue to progress in biopharmaceutical pipelines, pre-clinical and clinical analysis strategies for assessing biotransformation will play an important role in drug development. Dr John F. Kellie (GSK) presented various LC-MS approaches for monitoring the biotransformation of biotherapeutics including intact mass monitoring, reduced subunit LC-MS, and peptide-mapping. Dr Pan Deng (Soochow University, China) presented her latest research to identify microbiota-driven polysaccharide biotransformation/degradation and associated biochemical interplays with host organs using stable isotope resolved metabolomics (SIRM). Dr Josh Yu of Gilead Sciences reported an improved acyl glucuronide stability assay, based on the rate of ^{18}O-incorporation from [^{18}O] water, which is compatible with high-throughput bioanalytical LC-MS workflows but requires no LC method development or AG reference standard. Dr Shuai Wang (Genentech Inc) discussed an unexpected cyanide release from imidazo[1,5-a]isoindole of GDC-0919 and species differences in glucuronidation in animals *versus* humans. The mechanism of the cyanide release was proposed and the species differences in glucuronidation were investigated. Finally, Mei Han (Amgen Inc) presented the development of a universal automated immunoaffinity purification CE-MS intact mass workflow for next-generation biologics (NGBs) biotransformation studies. CE-MS offered additional separation power to the detection and identification of comprehensive biotransformation assessment of NGBs. Automated IA workflow enabled high-throughput sample preparation from biologic matrices.

New Applications of MS in Drug Discovery

This symposium was chaired by Dr Wilson Shou (Bristol-Myers Squibb Company) and composed of a total of six presentations that were delivered by a diverse group of outstanding scientists from the biopharma industry to highlight the dynamic role mass spectrometry plays in drug discovery. Dr Bingming Chen (Merck) led off the symposium with an excellent presentation on using label-free mass spectrometry imaging (MSI) approaches to rapidly determine tissue distributions of drugs/metabolites/biomarkers. Several examples including renal toxicity elucidation, rapid on-tissue metabolite identification, and whole-body drug localization were given to demonstrate the high-impact MSI has had at Merck. Dr Tim Häbe (Boehringer Ingelheim) delivered a presentation on the development of a fully integrated sample preparation and bioanalysis system for discovery *in vivo* sample analysis. Extensive automation and a machine learning-enabled algorithm allowed discovery bioanalysis to be performed with a high success rate without any intervention from the end users. Next, Dr Long Yuan (Biogen) described a very systematic approach to determining the free fraction of antisense oligonucleotides (ASOs). Since ASO drugs are often designed to treat diseases in the central nervous system, it is critical to determine free drugs in not only plasma but also brain homogenate and cerebrospinal fluid. Dr Yifan Shi (Janssen) presented a workflow to determine protein resynthesis rate in tissue samples with deuterium labeling. Reproducible protein resynthesis results were demonstrated using a model protein with both a nano-LC Orbitrap system

and a micro-LC Zeno TOF system. The last two presentations of the symposium, both of which on innovative bioanalytical methods, were given by Drs Xue Dong (Amgen) and Karan Agrawal (Janssen), respectively. Dr Dong presented an innovative, antibody-free sample preparation method that used high-pH reversed-phase fractionation prior to LC-MS for the analysis of mitochondrial amidoxime-reducing component 1 (mARC1) in tissue or cell samples. The high-pH fractionation approach generated an impressive 20 times improvement over the traditional immunoprecipitation method. Dr Agrawal described a hybrid antisense capture and LC-MS/MS bioanalytical method for two short interfering RNAs (siRNAs). The sensitivity offered by hybrid ELISA and the specificity by LC-MS were combined to generate a highly sensitive and robust method for siRNA quantification. Overall, this symposium effectively demonstrated the cutting-edge applications of mass spectrometry in drug discovery and highlighted the significant impact mass spectrometry has on areas such as high-throughput screening, lead optimization, pharmacokinetic/pharmacodynamic (PK/PD) characterization, and drug/metabolite/biomarker quantifications.

Recent Issues in Regulated Bioanalysis

This symposium was co-chaired by Drs Xiaorong Liang (Genentech) and Wenkui Li (Novartis) and featured six world-renowned scientists. First, Dr Chongwoo Yu (FDA) highlighted the criticality of bioanalytical data and documentation from both method validation and clinical trials in supporting regulatory submissions such as new drug applications (NDAs) or biologics license applications (BLAs). Following the tradition established in the 1st CASMS conference, Dr Qin Ji (AbbVie) introduced the research work and accomplishments of the Chinese American scientists in the field of bioanalytical mass spectrometry along with their career path, which was an inspiration for those who just started scientific careers in the field. The scientists introduced here included Drs Zhenmin Liang (Vertex), Linzhi Chen (Boehringer Ingelheim), Allena J Ji (Chiesi), Wenying Jian (Janssen), Keyang Xu (Genentech), Wilson Shou (BMS), Guowen Liu (Disc Medicine), and Long Yuan (Biogen). Following Dr Ji's presentation, Dr Nevena Mollova (Gilead) elaborated in a case study the development and optimization of quantitative bioanalytical methods for the measurement of remdesivir and its metabolites in monkey plasma and peripheral blood mononuclear cells. Next, Dr Yuxiang Cui (Genentech) shared the strategies to conquer the complications of combo assays in regulated small molecule LC-MS bioanalysis. The complications arose from several areas, including but not limited to extraction, choice of internal standard, calibration curves and QCs, chromatography, interference between analytes and the internal standards, and stability of analytes in the presence of each other. Next, Ms Yunlin Fu (Novartis) highlighted the practical strategies to overcome the challenges in LC-MS/MS bioanalysis of radioligand therapy (RLT) drug candidate(s) in support of preclinical development, for which both unlabeled (*i.e.*, ligand-linker-chelator) and labeled molecules (*i.e.*, ligand-linker-chelator-metal) were formulated in a ratio mimicking the manufacturing conditions for the RLT drug to be used clinically in humans. Finally, Dr Allena Ji (Chiesi) presented the practical solution of cross-lab validation for the analysis of sphingolipid biomarkers that carry multiple isoforms. The multiple isoforms are associated with the difference in isoform distribution profiles in LC-MS/MS analysis between the reference standards extracted from animal samples and total sphingomyelins in human samples.

SPECIAL SESSIONS OF SISTER MS SOCIETIES IN ASIA

CASMS has a long history of scientific interactions and collaborations with sister MS societies in Asia. The dynamic interactions among these societies were unfortunately disrupted by the pandemic during the last 3 years. To reconnect with friends and colleagues in the field of mass spectrometry worldwide and to facilitate the exchange of scientific findings among MS societies, we invited three sister MS societies, including China Mass Spectrometry Society (CMSS), the Hong Kong Society for Mass Spectrometry (HKSMS), and the Taiwan Society for Mass Spectrometry (TSMS) to organize three special sessions. These sessions covered a wide range of frontier research on novel methods and applications of mass spectrometry presented by a total of nine leading experts in proteomics and lipid/metabolomics.

The CMSS Special Session

It was chaired by Dr Meng-Xia Xie (Vice President and Secretary of CMSS, Beijing Normal University), and featured three speakers, Drs Catherine C. L. Wong (Peking Union Medical College Hospital), Haojie Lu (Fudan University), and Guowang Xu (Dalian Institute of Chemical Physics, CAS). Dr Wong presented new developments and applications of Glass-Oil-Air-Droplet (GOAD) nano chip for single-cell proteomics. The new version of GOAD (v3.0) enabled the identification of stage-specific proteomes with great coverage at the single-cell level. The analysis of single oocytes yielded new insights into functional genomic changes across human pre-implantation embryo development and identified important functions during genome reprograming, stem cell proliferation, and cell fate commitment. Dr Lu presented novel approaches for glycoproteomics to enable comprehensive and quantitative MS analysis of *N*-glycoproteomes and *N*-glycomes of clinical samples. The integration of sialic acid derivatization and MCE (microcapillary electrophoresis)-MS facilitated the identification of N-glycan isomers. The combination of TMT and *N*,*N*-dimethylethylenediamine (DMEN) labeling with HILIC enrichment has significantly enhanced the identification of intact *N*-glycopeptides and multiplexed quantitation of site-specific glycoproteomes. These methods have been applied to

identify serum biomarkers from ovarian cancer and liver disease samples. Dr Xu talked about the development of new analytical tools to advance metabolomics research with better coverage, reliability, and accuracy. He presented new strategies to construct high-quality database containing rich metabolites with multidimensional information including retention time and high-resolution MS (HRMS) spectra (MS1, MS2, and modifier groups) to significantly improve the annotation and identification of metabolites for untargeted metabolomics studies.

The TSMS Special Session

It was chaired by Dr Yi-Sheng Wang (President of TSMS, Genomics Research Center, Academia Sinica), and the session began with a lecture given by Dr Jau-Song Yu (Chang Gung University, Taiwan). Since surface/membrane proteins are considered cellular markers and major targets for therapeutic drugs, Dr Yu's lab employed multiplexed quantitative mass spectrometry for comprehensive profiling of colorectal cancer (CRC)-derived EV membrane proteome to examine their potential usefulness as plasma biomarkers for early detection. The identified candidate proteins were validated and verified using targeted MS assays in plasma of CRC patients, resulting in a potential EV biomarker panel for the detection of CRC. Dr Ching-Hua Kuo (National Taiwan University) presented the development of MS-based strategies for metabolomics based on matrix-induced ion suppression (MIIS), postcolumn-infused internal standard (PCI-IS), and/or chemical derivatization to improve data integrity and enhance the detection of metabolites. These methods have been applied to identify metabolite biomarkers in clinical samples for evaluating therapeutic responses in breast cancer and distinguishing early- and late-stage patients of Parkinson's disease, indicating the great potential of clinical metabolomics for precision medicine. Dr Yet-Ran Chen (Agricultural Biotechnology Research Center, Academia Sinica) presented the development of MS-based omics approaches for global analysis of plant peptidome upon the activation of immune process to understand how peptide cytokines regulate the fundamental function of plant immunity. The identification of CAPE9 peptide (derived from pathogenesis-related protein 1) and its receptor (CAPER), as well as the verification of CAPER-CAPE9 interaction *in vivo*, illustrates the effectiveness of their approaches to study peptide cytokine signaling in plants. Their results suggest that CAPE9 can be a mobile signal to transmit immune signaling from the local infected site to the distal uninfected site and induce plant defense response upon pathogen infection.

The HKSMS Special Session

It was chaired by Dr Chi-Kit Andy Siu (President of HKSMS, City University of Hong Kong) and featured three speakers, including Drs Zhongping Yao (The Hong Kong Polytechnic University), Liang Zhang (City University of Hong Kong), and Terence Chuen Wai Poon (University of Macau). Dr Yao presented their exciting work on developing a novel method based on peptides for data storage and MS/MS peptide sequencing for data retrieval. This method couples data storage with peptide synthesis and proteomic analysis for the first time, generating new possibilities for future studies. In addition, he shared his work on investigating interactions between β-lactamases and β-lactamase inhibitory protein (BLIP) to understand antibiotics and drug resistance. Hydrogen/deuterium exchange MS analysis of the selected β-lactamases revealed their structural flexibility at free states and binding to BLIP induced significant changes in their conformational dynamics. In combination with the analyses using ion mobility MS, molecular dynamics simulation, and mutagenesis, new structural insights were obtained, which could be used to assist the design of enhanced inhibitors to β-lactamases in the future. Moreover, Dr Yao mentioned the recent development of an integrated approach by coupling quantitative proteomics with vesicle formation assay to understand how proteins are sorted into transport vesicles. Dr Zhang presented his recent development and application of CRISPR-Assisted RNA-Protein Interaction Detection method, by integrating CRISPR/CasRx-based RNA targeting with proximity labeling to investigate lncRNA-protein interactions in living cells. This method can systematically detect the lncRNA-binding proteome in native cellular states, establishing the groundwork for defining the landscape of RBP-lncRNA interactions in the future. Dr Poon discussed his strategies to effectively apply LC-HRMS-based untargeted metabolomic profiling to identify reliable biomarkers in blood with low false positives. During the biomarker study, he found that a significant portion of "the statistically significant" differential metabolomic features using untargeted metabolomic profiling could be fake. To resolve the problem, he performed a stringent study to identify biomarkers in serum and plasma for chronic kidney disease and developed equations to estimate glomerular filtration rate (kidney function) using linear regression. This strategy displayed satisfactory performance based on independent validation cases.

CASMS YOUNG INVESTIGATOR AWARD

For the first time, CASMS established the CASMS Young Investigator Award, aiming to recognize outstanding young researchers from our society in the field of mass spectrometry from all major sectors including academia, industry, and government laboratories. Current CASMS members who obtained their PhD within the last 10 years are eligible to apply. This year, we have received nomination packages from many deserving and qualified candidates. The selection process was highly competitive and was based on four criteria: (1) Academic and scientific accomplishments; (2) Original contributions to the field; (3) Significance, innovation, and impact of the work; and (4) Relevance to the mission of CASMS. With

careful consideration, the Young Investigator Award committee selected five promising scientists for the 2022 CASMS Young Investigator Award. The awardees are Drs Tao Huan (Assistant Professor since 2018, University of British Columbia), Xin Yan (Assistant Professor since 2018, University of Texas A&M), Ling Hao (Assistant Professor since 2019, George Washington University), Hui Ye (Professor, China Pharmaceutical University) and Dr Chang Liu (Staff Research Scientist, Sciex). These young investigators have been recognized as rising stars in their fields with an impressive record of achievements during their early careers.

To highlight the awardees' accomplishments, the inaugural Young Investigator Award symposium was co-chaired by Drs Lan Huang (President of CASMS, University of California, Irvine) and Dr Naidong Weng (President-Elect of CASMS, GSK) in this conference. The first speaker was Dr Tao Huan, an active member of the CASMS Executive Committee, who served as the chair for the symposium on "Analytical Method Development in MS-based Metabolomics" and the lightning talk session during the 1st and 2nd CASMS conferences. Dr Huan's research focuses on the synergistic development of analytical and bioinformatics methods for mass spectrometry-based metabolomics. He has published 68 peer-reviewed publications with many in high-impact journals, including *Nature Methods, Nature Protocols, and Analytical Chemistry*. Due to his outstanding academic achievement, he has been recognized with many awards including 2022 Early Career Rising Star Award from Metabolomics Association of North America, 2022 the Association of commonwealth universities fellowship, and 2021 Emerging Investigator by *JASMS*. Dr Huan delivered his award lecture entitled "Interrogating Tandem Mass Spectrometry Data for Chemical Compound Identification", highlighting the latest computational developments to better understand MS/MS spectral data and facilitate the identification of unknown metabolites. A novel core-structure-based spectral similarity algorithm was introduced, which had been demonstrated to better reveal chemical structural similarities using their spectral similarities. Next, the issue of chimeric MS/MS spectra and the solution to clean up them were discussed. Finally, a comprehensive computational platform that can perform accurate molecular formula prediction were presented.

Dr Xin Yan's research group centers on developing microdroplet chemistry and electrochemical reaction-based MS methods for lipid structural analysis and accelerating the discovery of transition metal catalysis. She has co-authored more than 40 peer-reviewed articles with many on high-impact journals including *J. Am. Chem. Soc., Angew. Chem. Int. Ed. Eng.* and filed five patents. She has received many awards including ASMS Research Award, NSF CAREER award, Emerging Investigator by *JASMS*, and NIH MIRA award. Dr Yan presented her award lecture on chemistry-driven in-depth structural and quantitative analysis for lipids. Dr Yan introduced derivatization-based methods capable of resolving different types of isomers commonly encountered in lipid samples and quantifying them using mass spectrometry. The methods include divergent cascaded electrochemical reactions of lipids in an interfacial microreactor followed by fragmentation of lipid epoxides in tandem MS, taking advantage of the voltage-controlled and dramatically accelerated electrochemical derivatization of multiple lipid isomers in microdroplets at different voltages to achieve structural elucidation. Applications of these methods in diseased sample analysis were also included.

Dr Ling Hao delivered the third award lecture, who is an active member of the CASMS Executive Committee and served as a co-chair of the symposium on "Proteomics in Precision Medicine". Dr Hao's research focuses on developing novel proteomics and metabolomics methods to study molecular interactions and organelle dynamics in living cells to decipher molecular mechanisms underlying brain diseases. She has co-authored 31 peer-reviewed articles. Since starting her independent career in 2019, Dr Hao has been very productive and secured multiple funding including an NIH R01 grant. She has been recognized by multiple awards, including Emerging Investigator by *JASMS*, Five of the Future Alumni Rising Stars (UW-Madison School of Pharmacy), and ORAU R.E. Powe Junior Faculty Enhancement Award. She presented her award lecture on "Capturing Organelle Dynamics with Multifaceted MS-Omics Strategies". Dr Hao described their recent efforts in developing proximity labeling proteomic methods and understanding neurodegenerative diseases in patient-derived fibroblasts and iPSC-derived neuron platforms. She also introduced their newly established universal and sample type-specific contaminant libraries that can benefit the broad proteomics community.

The fourth award lecture was given by an outstanding researcher from industry, Dr Chang Liu, an associate staff research scientist at Sciex. Dr Liu has been working on developing the front-end sample preparation and sample introduction technologies, including the invention of AEMS technology and its applications in high-throughput drug discovery. Dr Liu has published ~40 papers and received 12 granted patents. He was the editor of the book entitled "High-Throughput Mass Spectrometry in Drug Discovery" (Wiley) and the recipient of the 2021 Bioanalysis Outstanding Contribution Award (BOSCA). In his presentation, Dr Liu described an innovative AEMS platform based on the integration of acoustic droplet ejection (ADE) technology, an open-port interface (OPI), and electrospray ionization (ESI) MS, enabling high-speed sampling and label-free analysis.

Finally, Dr Hui Ye from China Pharmaceutical University delivered her award lecture on "Mining the dark proteome: cyclic immonium ion of lactyllysine reveals widespread lactylation in human". Dr Ye's research focuses on developing and implementing an array of innovative mass spectrometry-based tools to investigate the dysregulation of metabolism in human health and diseases. She has published over 30

research papers in journals including *Nature Methods, Redox Biology, Analytical Chemistry, and Molecular & Cellular Proteomics*. In her presentation, Dr Ye's team found that the cycIm ion formed during MS/MS accurately signifies lysine lactylation. With this diagnostic ion-based strategy, they confidently determined new lactylation sites in the human proteome. They partially demonstrated the functional importance of lactylation: site-specific engineering of lactylation into ALDOA caused enzyme inhibition, suggesting a lactylation-dependent feedback loop in glycolysis. Collectively, their study revealed lactylation as a widespread PTM in the human proteome and implied how lactate may inform a plethora of biological events in distinct cell populations and participate in pathophysiological activities through lactylation.

SCIENTIFIC WORKSHOPS

Three 1-h scientific workshops were organized, aiming to provide an interactive platform for both experienced and newcomers in specific research areas.

Frontiers in Metabolomics

This workshop was chaired by Dr Liang Li (University of Alberta, and Co-Director, the Metabolomics Innovation Centre (TMIC) of Canada), featuring three speakers. Dr Oliver Fiehn (University of California, Davis, and Director, West Coast Metabolomics Center) gave a presentation entitled "Confidence in MS-Based Metabolome Annotations". He discussed the current challenge of annotating the metabolite peaks detected in LC-MS-based metabolome analysis techniques. Many mass spectrometric features are often detected, but only a small fraction of them can be identified with high confidence. Dr Fiehn described methods for improving peak annotations such as the development of large MS/MS spectral libraries and better algorithms for MS/MS spectral matches. Dr Lloyd Sumner (Department of Biochemistry, and Director of the Metabolomics Center at the University of Missouri, Columbia) gave a presentation on "Addressing the Grand Challenges of Metabolomics with Advanced Instrumentation". He described the unmet need of analyzing a large number of metabolites with high specificity such as isomer differentiation in metabolomics. He presented an approach of using ion mobility, in combination with LC-MS, to improve metabolite separation and detection. Dr Sumner also discussed the possibility of using high-resolution electron microscopy (EM) to identify metabolites. EM is widely used for protein structure analysis. However, according to Professor Sumner, EM may become a powerful tool for small molecule identification, addressing the current limitation of performing definite structure analysis of unknown metabolites using MS alone. Dr Liang Li gave a presentation on "High-Coverage Metabolome Analysis of Samples of Limited Amounts". Many biological samples such as single-cell or few-cells, needle biopsies, etc., have a limited amount of starting materials. Dr Li described high-performance chemical isotope labeling (CIL) LC-MS to analyze the metabolome from samples of limited amounts. Using a proper reagent with rationally designed structures to label metabolites, the derivatized metabolites can be ionized with much higher efficiencies, significantly improving the detectability of metabolites in a small amount of samples. Using differential isotope labeling, accurate relative quantification of metabolites in comparative samples can be achieved.

Clinical Applications of Quantitative Glycoproteomics

This workshop was chaired by Dr Hui Zhang (Johns Hopkins University). Protein glycosylation is one of the most common protein modifications. Due to the complexity of protein glycosylation, large-scale quantitative glycoproteomic analysis has been challenging. However, recent technological advances in glycopeptide isolation, mass spectrometry, and data analysis tools have made the clinical applications of large-scale quantitative glycoproteomics possible. In this workshop, three speakers presented the clinical applications of their glycoproteomic workflows. Shisheng Sun (Northwest University, Xi'an) talked about the structural analyses of site-specific N-glycans using StrucGP software. Mingming Dong (Dalian University of Technology, Dalian) showed the glycan database-independent peptide matching and in-depth characterization of site-specific N-glycosylation enabled by Glyco-Decipher. Yingwei Hu (Johns Hopkins University, Baltimore) presented the proteogenomic characterization of ovarian and pancreatic tumors using MS-based glycoproteomic approaches and GPQuest. All three speakers started with a similar glycopeptide enrichment strategy by hydrophilic interaction chromatography. The enriched intact glycopeptides were then analyzed by tandem mass spectrometry using Higher-energy C-trap Dissociation. However, the three invited speakers developed different data analysis software tools to analyze the glycoproteomic data from mass spectrometry in assigning the glycopeptide spectra to glycans and the glycan-containing peptides. They showed that each software tool had unique features in terms of glycan structure assignments. The applications of the glycoproteomic pipelines in body fluids and tumor tissues further demonstrated the crucial roles of glycoproteomics in the identification of protein glycosylation associated with clinical outcomes of diseases.

Drug Metabolism and Pharmacokinetics

This workshop was chaired by Drs Naidong Weng (GSK) and Shuguang Ma (Amgen).

The purpose of biotransformation studies in drug development is to comprehensively characterize its ADME to support clinical progress. This usually includes: Estimate the fraction of the dose absorbed; Determine the fate of the total administered dose; Describe the complete metabolism; Know the routes of elimination; Measure the rates of clearance;

Determine major circulating metabolites; Determine if there are contributions of metabolites to pharmacological or toxicological outcomes; Metabolites that are more than 10% of total in human have sufficient safety coverage in animals (MIST); Inform need for DDI, liver or kidney impairment, and other clinical pharmacology studies. In this workshop, three important topics relevant to drug development were covered: (1) *Contribution of drug metabolizing enzymes to in vivo clearance of marketed drugs*-Metabolism is the major route of elimination for most drugs. P450 and UGT are the major enzymes. P450 enzymes metabolize diverse number of substrates. Major enzymes in human are: CYP3A4, 2C9, 2D6, 1A2, 2C19 followed by 2C8 and 2B6. Other enzymes can't be ignored specially as we work with new chemical scaffolds. (2) *Evolution of MS technologies and strategies for metabolite identification in drug discovery and development*-Recent advances in HRMS technologies, data acquisition, and processing approaches have dramatically improved the accuracy and throughput of metabolite identification. An overview of experimental metabolite ID including data acquisition and analysis was presented. (3)*Metabolite-in-safety testing (MIST) and chiral metabolites*-Generally, metabolites that were identified only in human plasma or detected at much higher levels in humans than animal test species should be considered for safety assessment. Such metabolites are called disproportionate drug metabolites. Human metabolites that are at greater than 10% of total drug-related exposure at steady state can raise a safety concern, which requires further studies in animals to determine the potential toxicity of those metabolites. Different approaches for assessing MIST were discussed in the workshop, including the mixed matrix method, biogeneration of stable isotope-labeled internal standards for absolute and relative quantitation of drug metabolites by LC-MS, analysis of polar metabolites by hydrophilic interaction chromatography LC-MS, and strategy of chiral bioanalysis for enantiomer metabolites.

CAREER DEVELOPMENT WORKSHOPS

Two professional development workshops were organized to help CASMS members excel at all stages of their scientific careers. The professional development workshop on job searching tips, and opening was chaired by Drs Ling Hao, Junming Peng, and Shuguang Ma. Drs Yansheng Liu (Yale),

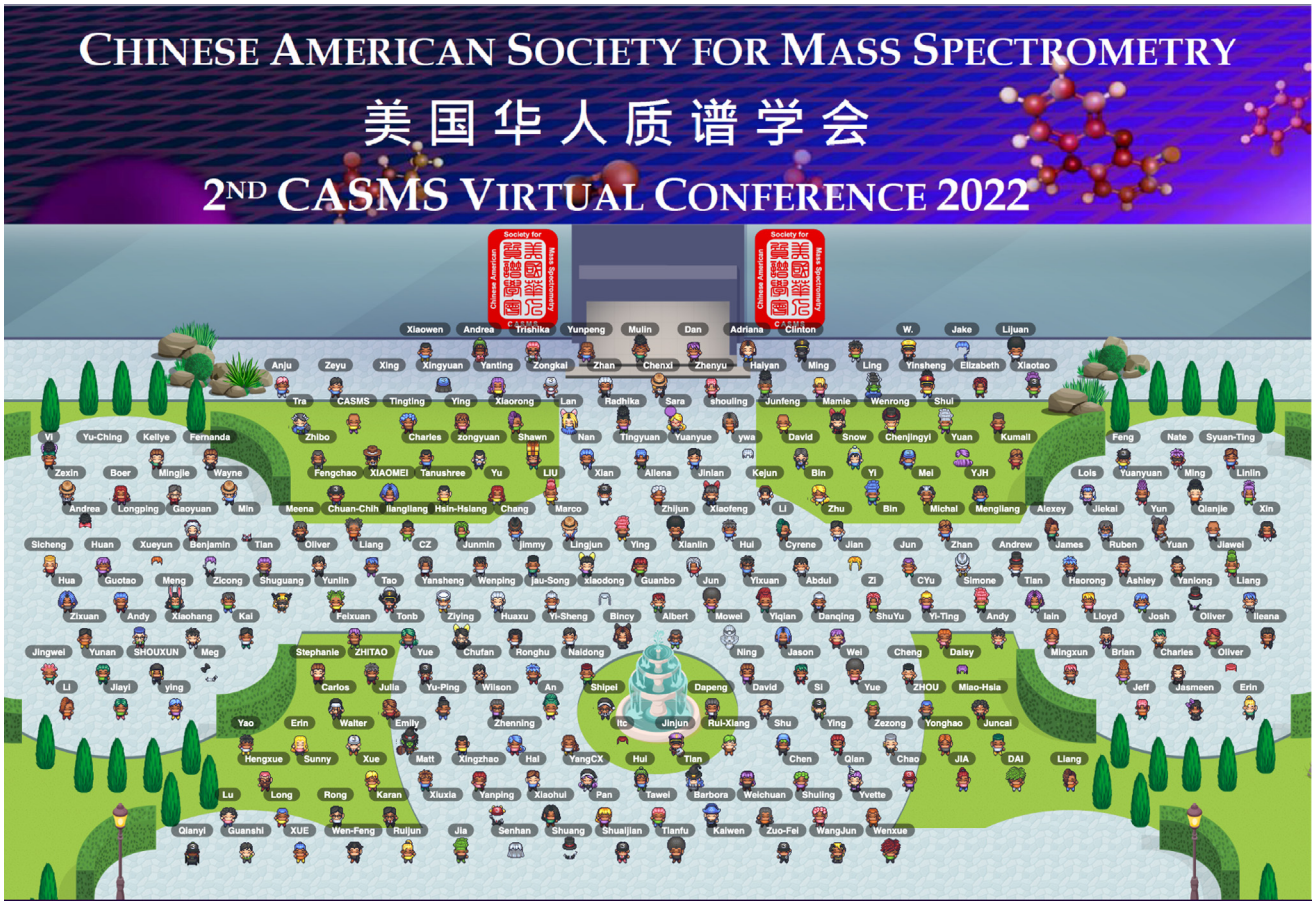

FIG. 1. **The 2nd CASMS virtual conference (October 17–21, 2022) at Gather.town.** CASMS, Chinese American Society for Mass Spectrometry.

Ruben Luo (Stanford), and Liuxi Chen (Genentech) were invited as panelists and shared insights on career paths and opportunities in academia, clinical chemistry, and industry, respectively. This workshop aims to help students and young scholars prepare for their career development during and after mass spectrometry training and help them to set up career goals in the field of mass spectrometry.

To help the next generation of CASMS scientists become successful in their future careers, the "meet 2022 CASMS Awardees" workshop was organized by Dr Lan Huang. All of the six 2022 CASMS awardees (1 MCP lectureship and 5 Young Investigator awards) shared personal experiences on their professional developments and provided valuable advice on how to succeed at early career stages. Six senior and well-established CASMS members (3 full professors and 3 industry directors) served as the panelists and talked about their experience on how to rise to the top in their selected career paths and stay successful. The unique stories presented by all awardees and panelists are truly inspiring.

Apart from symposia and workshops, we had a total of 144 poster presentations and 54 lightning talks, which were distributed evenly on the two conference themes. The lightning talk session was chaired by Dr Tao Huan (University of British Columbia), which provided young researchers the opportunity to showcase their science and interact with other attendees. Among these presentations, a panel of judges selected 20 Best Poster Awards and 8 Best Lightning Talk Awards.

SUMMARY

This 5-day conference has brought together an outstanding group of scientists from both academia and industry, from North America and other parts of the world, to discuss exciting work on proteomics, metabolomics, lipidomics, and other mass spectrometry studies. We have heard and learned exciting science through symposia, workshops, as well as lighting talks, and poster presentations. It has been a great meeting!

For the 2nd CASMS virtual conference, we had a total of 363 registrants. Many people attended the sessions, despite their busy schedules and time zone differences. To facilitate the interactions among the attendees, a social time was arranged each evening at the Recreation Park of the Gather.-Town conference site. Many attendees had very positive experiences in using the platform to interact with the speakers and poster presenters, meet old friends, and make new friends, during the evening social time. This conference was strongly supported by our sponsors. We had a total of 25 sponsors, including 5 diamond sponsors. In addition to a virtual exhibit hall with designated sponsor booths, there were five sponsor workshops organized at the conference. Each workshop had one keynote speaker to discuss science and technology related to new products or product development, as well as their applications.

We could not have organized and staged this conference without the strong support and assistance from many organizers, coordinators, IT support, and student volunteers. For this conference, the organization team was assembled by a group of talented and dedicated scientists composed of 19 professors and 11 industry directors/senior investigators, purely on a volunteer basis. All duties, including program planning, meeting logistics, webinar and zoom setup, and website management, were fulfilled and shared among our own conference organization team without any professional help. Everyone had put in an enormous amount of time and made tremendous efforts to work seamlessly together as one team, with a mission in mind, that is to better serve our community, bring our society together, and help our society grow to the next level! We thank our organization team, student volunteers, speakers and attendees as well as sponsors for making this event successful! We look forward to seeing you at the third CASMS annual virtual conference in August 2023 (http://CASMS.org)!

Author Contributions—All authors contributed to the meeting, planning, and organization. Their specific roles are described in the text. Drs Zhibo Yang (Secretary of CASMS) and Shouxun Zhao (Treasurer of CASMS) were in charge of bookkeeping for the event.

Conflict of interest—The authors declare no competing interests.

Abbreviations—The abbreviations used are: ADME, absorption, distribution, metabolism, and excretion; ASMS, affinity selection MS; BLIP, β-lactamase inhibitory protein; CASMS, Chinese American Society for Mass Spectrometry; CE-MS, capillary electrophoresis coupled with MS; CPATI, Cytosolic Proteome & Affinity-based Target Identification; CRC, colorectal cancer; DIA, data-independent acquisition; EM, electron microscopy; GPCR, G-protein coupled receptor; IM-MS, Ion mobility MS; NGB, next-generation biologics; SCP, single-cell proteomics; sORF, sORF, small open reading frames.

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