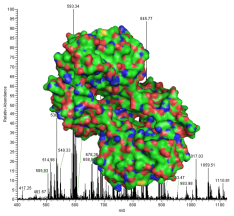
American Association for Clinical Chemistry

Proteomics and Metabolomics Division NEWSLETTER



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Message from the Chair: Regulatory Challenges Ahead

Stephen R. Master, MD, Ph.D., Chair, Proteomics and Metabolomics Division

2014 has been another eventful year for the Proteomics and Metabolomics Division, and we will have much to discuss over the coming months. Overall, the Division has made great progress on a number of fronts, and I want to take this opportunity to briefly update you on both the past successes and future possibilities within our Division and (more importantly) our field.

Since so much of the clinical and translational testing of particular interest to our Division is currently implemented as laboratory-developed tests, perhaps the most significant news for all of us this year came from the FDA. Specifically, a draft guidance document (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM416685.pdf) was sent to Congress in October and reflected FDA's intent to review and approve laboratory developed tests (currently the responsibility of individual CLIA laboratories), with a particular emphasis on tests considered to be in a high-risk category (for an overview, see http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407296.htm). This proposal will certainly affect many mass spectrometry-based assays in the clinical lab; additionally, the guidance lists interpretive software as one factor that may alter its regulatory priorities, suggesting that multiplex tests with a computational algorithm for interpretation (so-called IVDMIAs) may be singled out for particular scrutiny. As a Division, we want to ensure not only that we track this issue carefully but also that we--as a community--encourage and support best practices among our members as we navigate this emerging situation.

In this Issue:

Of course, the AACC National office has been very active on this issue, with specific efforts such as lobbying by Board members on Capital Hill in November, approval of a letter co-signed

by the AMA and others, and development of educational materials such as a webinar. Beyond the national office work on LDT regulation, some of our Division members are also involved in directly influencing the FDA with respect to the regulation of emerging proteomic assays. For example, the FDA public workshop "Proteomics in the Clinic", held in June, featured talks from Division Chair-Elect Andy Hoofnagle as well as other long-term participants in Divison-related symposia, such as Russ Grant and Leigh Anderson. Our goal as a Division will be to extend this engagement to ensure that proteomic and metabolomic test development continues at a rapid pace while maintaining high standards for test validation in the interest of patient safety.

Other Divisional activities this past year focused on communicating the need for translational researchers to involve clinical laboratorians early in the process of developing omics-based assays. As many of you will recall, an AACC workshop in 2012 brought together representative of 4 divisions (Proteomics [now P&M], Clinical Translational Science, Molecular Pathology, Immunology) in a working group to discuss a response to the IOM omics report (http://www.iom.edu/Reports/2012/Evolution-of-Translational-Omics.aspx). While this group identified several areas in which the clinical laboratory perspective provided important clarifications to the IOM report, we reopened the discussion this year to ensure that these perspectives are adequately communicated to the broader scientific community. In addition to representative of the 4 AACC Divisions, participants in these discussions have included Keith Baggerly (MD Anderson, bioinformatics), Henry Rodriguez (NCI), and Alberto Guttierez (FDA). The first summary of these discussions has been submitted as a letter for publication signed by Steve Wong in his capacity as AACC President, and a follow-up white paper and AACC position statement are also underway for 2015.

Our Division was also instrumental in the planning and execution of AACC's first virtual conference, Personalized Diagnostics Today, held in late October. I think this type of virtual meeting platform will provide significant flexibility for Divisions such as ours to hold regular conferences and benefit from high-quality speakers without being constrained by travel budgets. We will continue to support this and other technologies that allow our members to more efficiently communicate at a scientific and personal level. Outside of the AACC sphere, a number of our members also continue to participate in and benefit from the outstanding MSACL meeting in San Diego, organized by long-term colleague and AACC member Dave Herold (see announcement below for 2015 meeting details).

Of course, our primary opportunity for face-to-face meetings as a Division has traditionally come at the Annual Meeting, and this year we continued our practice (an emerging tradition?) of holding a lunch co-meeting with colleagues in the Molecular Pathology Division. The overlap of interests between our Divisions remains strong, and I believe that there is an opportunity for us to co-develop significant content in the future. During this year's lunch we were pleased to offer our annual Division poster award to Dr. John Mills (Mayo Clinic) for his abstract "High sensitivity detection of residual disease in multiple myeloma using mass spectrometry." As usual, the Division also sponsored or codeveloped a number of short courses and symposia at this year's annual meeting. One last highlight of particular interest to our Division was Dr.

Wong's presentation of an AACC Presidential Award to the NCI. This was gratifying and appropriate, as we have benefitted tremendously over the past few through our association with NCI and CPTAC, largely through ongoing collaborations with Henry Rodriguez and facilitated by the MOU between NCI and AACC that was championed by Henry along with then-Division Chair Saeed Jortani.

Perhaps the other news this year of greatest significance to our Division members is the AACC Board's recent approval of a new Division for Mass Spectrometry and Separation Sciences (MS3). The inaugural chair of this new Division will be Proteomics and Metabolomics executive committee member Victoria (Yan) Zhang. As a Division, we are excited both to see support for mass spectrometry continue to increase within the AACC as well as to identify ways in which we can work closely with this emerging group (and, as a special plug for Victoria, let me encourage you all to join the new Division as well!).

As I reflect on the state of our field at the end of 2014, I'm struck by two things. First, although our Division went through many years when it appeared that a groundswell of clinical assays was always just around the corner, I believe that we are truly poised to take that (long-awaited) next step. MRM-based assays in particular have been shown to be both robust and reproducible, and well-known examples using this technology (such as measurement of thyroglobulin) are in widespread use. Second, I've realized just how far ahead the metabolomics world has been on the clinical front for a number of years. The diagnosis of inborn errors of metabolism using mass spectrometry has long played an important role in clinical care, and current assays for, e.g., urinary organic acids are truly "metabolomic": large numbers of unselected analytes, identified by MS/MS, yielding complex signal patterns (due to a combination of normal physiological processes and possible pathophysiology), with a correspondingly complex interpretive task required to render a diagnosis. As we move forward toward the future of omics assays, I think that the success of this pediatric metabolomics (not always recognized as such!) provides a blueprint for success in other areas as well as a clear example of the power of multiplex clinical diagnostics.

I'd like to once again thank the Division officers for their tremendous service over the past year. Steve Wong has been our past Chair while simultaneously serving as President of AACC; we have friends in high places! Steve has been a strong supporter of AACC's role in the omics over the past year, and he has certainly worked to advance a number of Divisional priorities at the national level. Andy Hoofnagle served as chair elect, Yusheng Zhu as secretary, Pam Nakhle as treasurer, Victoria Zhang and Alex Rai as members at large, and Mark Marzinke and Jerry Yeo as the nominating committee. Alan Rockwood continues to serve the executive committee as membership chair, and Jim Ritchie continues to contribute as head of the awards committee (while continuing his day job of teaching us all how to do Ebola testing!). I'm turning the reins over to Andy as he assumes his role as Chair in 2015, and I believe that our Division is well-poised to address the challenges of the future. Thank you all for your help!

Happy Holidays!

Division co-Founder honored by HUPO

Proteomics and Metabolomics Division co-founder Dr. Daniel Chan (Johns Hopkins) received the 2014 Translational Proteomics Award from the Human Proteome Organization (HUPO) during their annual meeting held in October in Madrid, Spain. I've included an excerpt the press release below, with thanks to Dan for his ongoing support and mentorship for this Division. Congratulations!

Professor Daniel W. W. Chan, Ph.D, DABCC, FACB is a world leader in **Translational Proteomics**. He is Professor of Pathology, Oncology, Radiology and Urology, and the Director of the Center for Biomarker Discovery and Translation at the Johns Hopkins University, USA. He is a diplomat of the American Board of Clinical Chemistry and a fellow of the National Academy of Clinical Biochemistry. At the Johns Hopkins Hospital, he is the Director of Clinical Chemistry Division and the Co-Director of Pathology Core Laboratories.

Dr. Chan's research focuses on the translation of proteomics discovery into clinical diagnostics. He is the inventor of OVA1 test for ovarian cancer, the 1st FDA cleared proteomic IVDMIA. When he was the Chair of the prostate cancer group at the National Cancer Institute, Early Detection Research Network, he was instrumental in the development of public-private partnerships leading to the clinical study and FDA approval of two prostate cancer tests – proPSA (*phi*) and PCA3 (*PROGENSA*).

Dr. Chan is the Editor-in-Chief of *Clinical Proteomics,* a journal focusing on **Translational Proteomics**. He has written 5 books, 40 book chapters and >275 scientific articles. He was one of USHUPO founders and is serving on the Board of Directors. He was a pioneer of the HUPO plasma proteome project with Gil Omenn when he designed and conducted the 1st HUPO plasma proteomics comprehensive global study. Dr. Chan organized and chaired the Clinical Days for the HUPO annual world congress in 2006, 2009, 2011, 2012 and 2013 with the major emphases on **Translational Proteomics**

MSACL 2015

The MSACL (Mass Spectrometry Applications in the Clinical Laboratory) conference will be held in San Diego, CA from March 28-April 1, 2015. Abstracts are still being accepted, with the poster deadline set at February 11, 2015. As has been the case in this past, this highly successful conference has content planned that is of significant interest to both the metabolomics and proteomics communities. Planned topics include:

1. Fundamentals : General
2. Fundamentals : Metabolomics
3. Fundamentals : Microbiolgy
4. Fundamentals : Proteomics
5. ICP-MS
6. Inborn Errors of Metabolism
7. Metabolomics
8. Microbiology/Virology
9. Molecular Diagnostics
10. New Advances
11. Occupational and Environmental Health
12. Pain Management
13. Proficiency, Regulations, Standards
14. Proteomics
15. Sample Prep & Automation
16. Small Molecule Analytes
17. Tissue Imaging and Analysis
18. Toxicology
19. Translational Mass Spec
20. Various OTHER

As in past years, this promises to be an outstanding meeting, and we look forward to continuing the good relationship between MSACL and the AACC. For more information, including a registration link, please consult www.msacl.org.

Emerging Clinical and Laboratory Diagnostics

Keep your eye out for further information on the AACC Emerging Clinical and Laboratory Diagnostics Conference (formerly Oak Ridge Conference), with its continued emphasis on new technologies for the clinical laboratory. This year's conference is scheduled to occur in Fall 2015, with additional details to be released as to date and venue. Check out https://www.aacc.org/meetings-and-events for more information as it becomes available.

NCI/CPTC

As a reminder to those who may be new to our group, the AACC Proteomics Division has been engaged with the NCI in a long-term partnership that has been formalized through an memorandum of understanding between NCI and AACC. One tangible way in which this has moved forward has been in the integration of clinical chemistry expertise into NCI proteomic efforts, including the Proteome Characterization Centers funded by the NCI CPTAC program under the direction of Henry Rodriguez. For further information about work supported by CPTAC, including funding opportunities as they develop as well as links to publications reflecting CPTAC-supported work designed to rigorously evaluate emerging technologies for proteomic measurement, visit the web site at:

http://proteomics.cancer.gov

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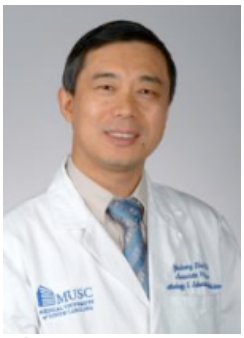

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