ASMS 2017 Fall Workshop Proposal – Top-down Proteomics

Organizers:

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Synopsis

A comprehensive analysis of all proteoforms that arise from genetic variations, alternative splicing, and post-translational modifications (PTMs), is essential to gain a transformative understanding of disease mechanisms and identify new therapeutic targets. Top-down mass spectrometry (MS)-based proteomics is arguably a disruptive technology for the comprehensive characterization of proteoforms by providing a "bird's eye" view of all proteoforms to decipher the PTM codes together with genetic variations that regulate cellular signaling in healthy and diseased states. In the top-down approach, intact proteins are analyzed without proteolytic digestion. Subsequently, specific proteins of interests can be isolated and modification sites could be mapped by tandem MS (MS/MS) strategies. In contrast, the traditional bottom-up approach has intrinsic limitations for the analysis of proteoforms as a result of protein digestion which includes dramatically increased complexity in examining an already complicated proteome as each protein is digested into many peptide components; incomplete sequence coverage since only a fraction of the digested peptides are recovered, loss of information of co-occurring PTMs and mutations, as well as the inability to distinguish between splicing variants with high sequence similarity.

Over the last decade we have made significant strides to advance top-down MS and bring it to the mainstream in a way that is accessible to the scientific community. As a result, interest in top-down MS has grown considerably and a number of studies have already showcased the potential of top-down proteomics for the unraveling of disease mechanisms and discovery of new biomarkers. Recently, the burgeoning top-down proteomics field has gained momentum through the creation of the Consortium for Top-down Proteomics (http://www.topdownproteomics.org/). Nevertheless, despite recent advances in MS hardware and software, top-down MS-based proteomics still faces challenges in sample preparation, and the separation and detection of intact proteins, as well as difficulties in analyzing complex top-down high-resolution mass spectra.

In this workshop, we will invite world-leading experts in top-down MS-based proteomics to present the most advanced technologies and approaches to overcome these challenges and help propel top-down MS into the high-throughput proteomics mainstream. The workshop will cover a wide range of topics, including sample preparation, intact protein separation, MS and MS/MS for intact proteins, bioinformatics and data analysis tools for top-down proteomics, as well as the biomedical applications. Each presentation will be a tutorial aimed at beginners/newcomers to the top-down proteomics field, and will conclude with a dynamic moderated discussion/quiz session, based on "seeded" questions solicited from the instructors prior to the workshop, as well as questions posted by the participants during the presentations, using an interactive real-time on-line forum (e.g., www.gosoapbox.com).

The timeliness of a workshop on this topic is clearly indicated by the rapid growth, attendance, and overall interests in top-down proteomics at prior ASMS meetings, including the 2013 Sanibel conference organized by Neil Kelleher and Ljiljana Paša-Tolić on Top-down Mass Spectrometry, which brought together 135 attendees from 16 different countries, and 2013 Inaugural ASMS Workshop of Consortium for Top Down Proteomics which was extremely well-attended. We anticipate broad participation from academic and industry researchers, and mass spectrometry vendor representatives. During our conversations with the with top MS vendors, top-down mass spectrometry will be their focus in the next couple of years and they are excited to be involved in the top-down consortium. So we expect that the workshop topic and program would ready attract additional sponsorship from industry and vendors, if needed, to cover the cost of the additional suggested instructors and the expert instructors coming from overseas.

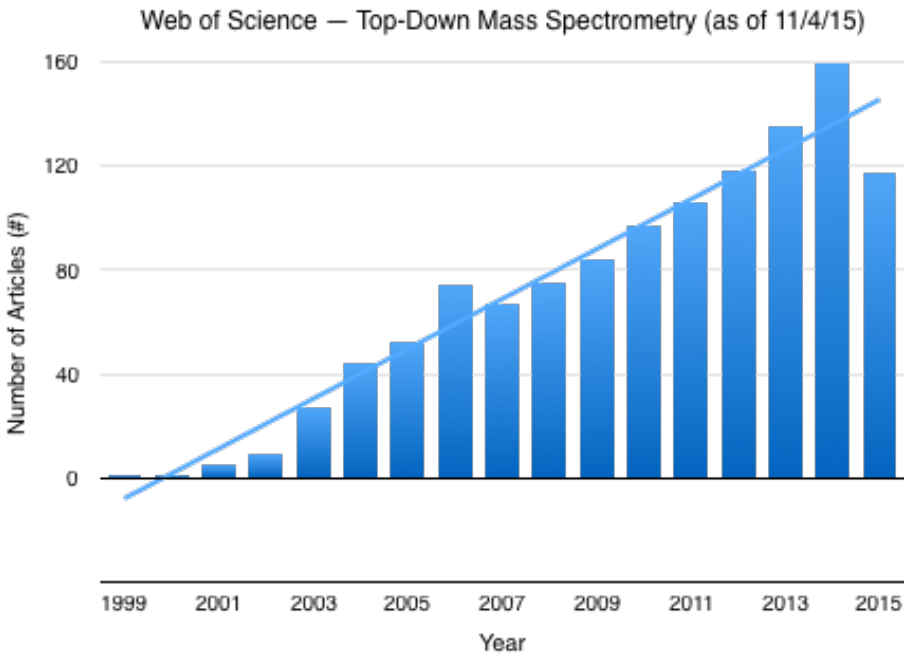

Figure. Sustained growth of top-down mass spectrometry as indicated by the number of articles published from 1999 to 2015 from Web of Science.

Potential Workshop Schedule, Topics and Instructors: (please note that the following list of instructors is preliminary, and that would have a broad range of well qualified alternate instructors to choose from if any of these declined or were unable to participate)

Day 1
7:30-8:20 Registration (and Breakfast)
8:20-8:30 Welcome

Session 1: 8:30-10:15 (includes discussion)

 Introduction to top-down mass spectrometry: Joseph Loo, UCLA
 I**nstrumentation for top-down mass spectrometry**: Ron Heeren, Maastricht University

10:15-10:30 Break

Session 2: 10:30-12:15 (includes discussion)

 Sample preparation for top-down mass spectrometry: Jeff Agar, Northeastern University
 Chromatographic separation strategies for top-down proteomics: Ying Ge, UW-Madison

12:15-1:15 Group Lunch

Session 3: 1:15-3:00 (includes discussion)
 Tandem mass spectrometry techniques for top-down proteomics: Jennifer Brodbelt, UT-Austin
 Quantitative strategies in top-down proteomics: Neil Kelleher, Northwestern University

3:00-3:15 Break

Session 4: 3:15-6:00 (includes discussion)
 How to interpret top-down high-resolution mass spectrometry data: Ying Ge, UW-Madison
 Bioinformatics for top-down proteomics: an overview Ljiljana Paša-Tolić, PNNL
 Demo of Top-down proteomics software for data processing, database searching, etc: (Freeware and commercial software demonstration – from both vendors and academic labs)

6:00-7:00 Happy Hour / Networking
7:00 - Dinner (on your own)

Day 2
8:00-8:30 (Breakfast)

Session 5: 8:30-10:15 (includes discussion)

 Top-down glycoproteomics: Cathy Costello, Boston University
 Top-down phosphoproteomics: Ying Ge, UW-Madison

10:15-10:30 Break

Session 6: 10:30-12:15 (includes discussion)

 Top-down proteomics applications in human disease: Jeff Agar, Northeastern University
 Top-down proteomics applications in microbiology: Ljiljana Paša-Tolić, PNNL

12:15-1:15 Group Lunch

Session 7: 1:15-3:00 (includes discussion)

 Top-down proteomics application in pharmaceutical industry/protein therapeutics: Jason Rouse, Pfizer, Inc.
 Top-down imaging mass spectrometry: Ron Heeren, Maastricht University

3:00-3:15 Break

Session 8: 3:15-4:45 (includes discussion)
 Native top-down proteomics of protein complexes: Joseph Loo, UCLA
 The future of top-down proteomics: Neil Kelleher, Northwestern University

4:45-5:00 Closing remarks