

Report: Top-Down Mass Spectrometry: Panel Discussion to Address the Community's Challenges

Date/Time: June 7th, 2022, 5:45 – 7 PM CST

Location: Minneapolis, MN

Presiding: Caroline DeHart, Frederick National Laboratory for Cancer Research (In-person); Mowei Zhou, Pacific Northwest National Laboratory (In-person)

Estimated Attendance: 60

List of Presenters/Panelists:

Lissa Anderson, PhD, National High Magnetic Field Laboratory

Philip Compton, PhD, Northwestern University & Integrated Protein Technologies, Inc.

James Fulcher, PhD, Pacific Northwest National Laboratory

Ying Ge, PhD, University of Wisconsin-Madison

Chen Li, PhD, ProtaGene

Jared Shaw, PhD, eMSion

Peter Verhaert, PhD, ProteoFormiX

Summary:

Following the introduction of the seven panelists and an overview of the results of the pre-conference survey, both the panelists and the audience were asked about challenges they were currently facing in performing research in or joining the top-down proteomics field. There was a consensus across non-academia participants for a need to move beyond simple intact mass measurements for more in-depth characterization, especially for complex samples. Multiple attendees wished for a simple, generic pipeline, but the panelists acknowledged the technical challenges due to the wide range of properties of intact protein samples that cannot be easily addressed with a “one size fits all” approach. A lively discussion ensued, covering topics ranging from the difficulty of obtaining and analyzing MS2 fragmentation data from higher-MW proteins, to the challenges of learning top-down data analysis (especially deconvolution), to the inaccessibility of high-quality training materials for top-down proteomics in general (and data analysis in particular). The panelists and audience were then asked what types of new resources or training materials would be most helpful to newcomers and current members of the field. A further lively discussion ensued, covering topics ranging from individual wish lists to a broad request for more involvement by the Consortium for Top-Down Proteomics (CTDP) to the pressing need for free, high-quality, and gold-standard top-down proteomic datasets for ease of learning and comparing between various instrument or software types across a broad MW range. Paul Danis, CEO of the CTDP, along with other CTDP Executive Board members, were then given the opportunity to respond to the points raised during the workshop discussions. Finally, several panelists and audience members volunteered their time and expertise to support future training and education initiatives to meet the clearly pressing needs of the top-down proteomics community.

The wish list for new training resources expressed by workshop participants is as follows:

- 1) A gold-standard, curated proteoform database representing a broad range of protein MW, instrument types, MS1/MS2 types, software types, and deconvolution algorithms. The database should comprise validated spectra and represent a field-wide standard for proteoform characterization. The database should also be freely accessible to all for training/benchmarking top-down software.
- 2) A centralized location for existing standard protocols, tutorials, videos, course materials, and publications to serve as a community resource for newcomers and experienced practitioners. This repository would ideally host a suggestion box where new materials could be requested.
- 3) A discussion forum wherein participants can ask questions regarding sample preparation, data acquisition, data analysis, data interpretation, or experiment troubleshooting. The forum would be moderated and the questions would be answered by volunteers willing to lend their expertise. The forum would be located on a private site, such as the CTDP website or a Google group, for which a simple email invitation would be required.
- 4) Increased transparency and visibility for opportunities to join and contribute to CTDP initiatives, as many workshop participants wished to get involved but felt they were unable to do so.
- 5) A collective effort by the CTDP and top-down proteomics community to generate new standard protocols, tutorial videos, training courses, and software demos to facilitate learning and collaboration.

Top-Down Interest Group members who would like to contribute to any of the resources listed above are encouraged to contact the workshop co-chairs (caroline.dehart@nih.gov, mowei.zhou@pnnl.gov) and the CTDP (<https://www.topdownproteomics.org/about-the-consortium/contact-us/>). The co-chairs would also like to thank the panelists and workshop attendees for their enthusiastic and helpful feedback.