Summary of Monday 5th June 2023 Workshop #10 in Houston, TX

Making Top-Down Mass Spectrometry Easier to Develop and Apply: Ways to Work Together and How Everyone Can Contribute

From the Top-Down Proteomics Interest Group

Presiding: Yuri van der Burgt and Mowei Zhou

Estimated in person attendance: ~60

The workshop started with a short update from the Consortium for Top-down Proteomics (CTDP), presented by Paul Danis (CTDP chief executive officer). The CTDP promotes "collaboration, education, and innovative research to accelerate the comprehensive analysis of all human proteoforms." CTDP hosts a monthly webinar called "Proteoform Thursdays" featuring presenters and participants from more than 50 different countries and various academic/industrial institutions. Finally, the audience was reminded to consider participation at the second international top-down proteomics symposium (TDP2023.org), this meeting will take place 3-5 October of this year at Northwestern University in Chicago.

Next, Ying Ge (University of Wisconsin) gave an introduction on the Early Career Researcher (ECR) committee (https://www.topdownproteomics.org/about-the-consortium/early-career-researcher-ecr-committee/) that aims to promote education and outreach, followed by updates of recent ECR-led activities from several ECR members. Mowei Zhou (Pacific Northwest National Laboratory) highlighted the newly opened CTDP LinkedIn group for barrier-free communication (https://www.linkedin.com/groups/14121000/). Luca Fornelli (University of Oklahoma) presented the plan to share and compile various workflows and present this in a protocol paper as a follow-up of the "Best practices and benchmarks for intact protein analysis for top-down mass spectrometry" published in 2019 in Nature Methods, with emphasis on MS2 rather than on MS1. Another pilot study plan was presented by Frederik Lermyte (Darmstadt Technical University) to create "golden datasets" with high-quality spectra and thorough assignments. The aim is to provide some ground truth and facilitate TDP software development.

The workshop was continued by an update about the CTDP initiative on an interlab study of capillary electrophoresis from Alexander Ivanov (Northeastern University, Boston). Also on behalf of Liangliang Sun and Kevin Jooss, the CE-MS TDP Initiative aims to highlight the potential and reproducibility of capillary electrophoresis-mass spectrometry (CE-MS) methods for top-down proteomics analysis. Currently, 12 different groups from 5 different countries join this initiative. These groups have measured three commercial samples: (a) intact protein standard mixture, (b) yeast cell lysate, (c) human HeLa lysate, and results were briefly presented and discussed.

For the panel discussion three panelists were introduced, namely Ruben Y. Luo (Stanford University), Guusje van Schaick and Constantin Blöchl (both Leiden University Medical Center).

The panelists also introduced themselves by answering the question “what is the biggest benefit TDP gives you in your research?” and “what is the most important change/development you want to see in the TDP field?”. Overall, the panelists agreed on the relative ease of applying TDP to targeted analysis in biomedical and biopharmaceutical applications. However, establishing standards into existing infrastructure and regulatory requirements of applications such as clinical testing may require more time and effort. In addition, the community needs to design ways to better evaluate the biological significance of the proteoforms detected.

Our online survey before the conference showed most people felt more resources are available for TDP compared to the past. However, most responders (both online and in person) identify their work as method development, suggesting TDP is likely not yet fully adopted in the applied field. A quick survey among the audience at the workshop indicated the remaining challenge in software and data analysis. The new activities and opportunities in CTDP and the ECR could hopefully fill these gaps soon and advance the TDP into wider practice.