Top-Down Analysis of Antibodies

University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)

Science Exchange and Conference Grants

June 20, 2014

On June 20, 2014 the University of Maryland School of Pharmacy welcomed researchers from academia, government, and industry to "Top-Down Analysis of Antibodies," a conference sponsored by the **University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)** and the Food and Drug Administration (FDA), in collaboration with the Waters Corporation. This conference spotlighted the use of top-down mass spectrometry to analyze antibodies for the development of new, targeted therapeutics. Top-down proteomics allows researchers to analyze intact proteins in close to native form using a mass spectrometer. Researchers can access the complete amino acid sequence from which the protein is formed, as well as locate and characterize post-translational modifications within the protein. Identifying and understanding these proteoforms and post-translational modifications is crucial to helping researchers develop new drugs to treat a wide range of illnesses.

John Schiel, PhD, research chemist in the biomolecular measurement division at the National Institute of Standards and Technology (NIST), kicked-off the conference with a presentation highlighting his organization's effort to develop a universal reference standard that researchers in government, academia, and industry could use to assess monoclonal antibodies (mAb) – a relatively new class of targeted drug therapies used to treat cancer.

Michael Boyne, PhD, research chemist in the Division of Pharmaceutical Analysis at the FDA, followed Schiel's presentation with an assessment of current top-down approaches in mass spectrometry to identify and characterize active pharmaceutical ingredients, perform chemical comparability or similarity assessments, conduct surveillance, and assist with process development.

Antibody-drug conjugates -- a new class of highly potent biopharmaceutical drugs used to treat patients with cancer -- were spotlighted in the lecture delivered by **Shawna Hengel, PhD**, and scientist at Seattle Genetics. She provided an overview of the conjugation process and discussed the wide range of mass spectrometry platforms currently used to analyze these molecules, explaining how the top-down approach, which is currently in the exploratory phase at her organization, could improve researchers' efficiency.

Yury Tsybin, PhD, assistant professor of physical and bioanalytical chemistry and director of the Mass Spectrometry Service Facility at École Polytechnique Fédérale de Lausanne in Switzerland, and **Christoph Borchers, PhD**, chief scientific officer for MRM Proteomics, Inc., and professor and director of the Genome British Columbia Proteomics Centre at the University of Victoria in Canada, offered additional insights on the use of top-down mass spectrometry to perform structural analysis and characterization of proteins.

Shifting the focus of the conference, **Michael Gross, PhD**, professor of chemistry, immunology, and internal medicine at the Washington University School of Medicine, highlighted how protein footprinting can be used to solve problems in the field of biophysics.

Jenny Brodbelt, PhD, the William H. Wade Endowed Professor and Chair of the Department of Chemistry at the University of Texas at Austin, brought the conversation back to top-down proteomics as she described the development of UV photodissociation (UVPD) for the analysis of biological molecules. She highlighted the need for fast, efficient, and robust ion activation methods and development of UVPD for studying intact proteins to achieve deeper fragmentation and, as a result, high sequence coverage.

To conclude the conference, **Vicki Winsock, PhD**, an Ohio Eminent Scholar, professor in the Department of Chemistry and Biochemistry at Ohio State University, and director of the University's Chemical Instrument Center, provided an overview of surface-induced dissociation (SID) and ion mobility, which can be used to characterize non-covalent complexes. She described how single-step SID activation can provide researchers with more access to different dissociation pathways, allowing them to avoid multiple sample preparation processes.