ASMS LC-MS & Related Topics Workshop and Interest Group Meeting Summary, 2013

Presiding: Helene L. Cardasis, Ph.D. (Scientist, R&D; Thermo Fisher Scientific)
Date: Tuesday, June 10, 2014 (5:45 pm)
Attendance: Approximately 250

Workshop Summary:
The agenda for the 2013 Workshop for the LC-MS & Related Topics Interest Group at ASMS in Minneapolis was as follows:

5:45-5:55 pm: Introduction/ Definitions
5:55-6:20 pm: Discussion: What is the ideal QC sample? Which metrics do you track?
6:20-6:30 pm: Perspective: QC requirements for a clinical lab (Brent Dixon)
6:30-7:00 pm: Live demo of open source, vendor neutral software for QC/platform performance tracking (Skyline, Michael Bereman)

Panelists:
Michael Bereman, Ph.D. (Assistant Professor, North Carolina State University)
Brent Dixon, Ph.D. (Chief Scientist, Physicians Choice Laboratory Services)
Gene Cicciamaro, Ph.D. (Research Investigator, Bristol Meyers Squibb)

Workshop Topic: "LC-MS platform performance tracking"

In past years, this workshop has aimed to provide some structure around the process of LC-MS troubleshooting. This year, we took a more preventative approach, and instead focused on platform performance tracking and quality control. We made a point to distinguish the platform QC (independent of upcoming experiment/ application, constant over time) vs the assay QC (dependent on up-coming experiment/ application, potentially variable over time), and tie the value of the platform QC to preventative maintenance and expedited troubleshooting.

The question "is there an ideal QC sample?" was posed to the audience, and discussion proceeded around the different samples audience members used for their QC, when they missed an instrument issue vs when their QC was diagnostic, and importance of the gradient length for diagnostic performance. We presented a representation of information one can extract from samples of varying complexity, ranging from a simple mix of synthetic peptides or analytes, to a single protein digest, to a cell lysate, to a reference standard composed of tissue or fluid homogenate. We suggested that simple mixtures could be used to effectively assess carry over and various LC and MS metrics via simple, visual assessment, or be spiked into a real sample or alternative complex matrix to track matrix effects and assess relative efficiency of sample preparation. Simple mixtures can also be infused directly to decouple LC and MS. Alternatively, a complex QC sample provides valuable statistics on a number of LC and MS metrics, can be taken through the sample prep process for process control, but requires software for data processing. Metrics of interest were also discussed, and classified with regard to their ability to detect a primary symptom (selective, points to potential source of problem; ex. peak tailing or spray instability) or secondary symptom (sensitive, but non-selective symptom of declining performance; ex. PSM count or protein coverage). Discussion revolved around how a combination sensitive/non-selective metrics and selective/non-sensitive metrics can be monitored to provide a broader view of system performance, and the audience provided feedback on what they track for given platforms. A distinction was again made between metrics monitored in a platform QC vs an assay QC.

To provide some insight on QC requirements for a clinical lab, Brent gave an overview of FDA and CLIA regulations with regard to the topic. Finally, Michael presented a variety of open source, vendor neutral software available for QC tracking. He provided some background on the QC node he developed in Skyline, SProCoP, which is open source and downloadable online (Beremen et al. "Implementation of Statistical Process Control for Proteomic Experiments via LC MS/MS." *J Am Soc Mass Spectrom.* 2014 April; 25(4)). SProCoP tracks five "ID-free" metrics; retention time reproducibility, peak symmetry, LC peak capacity/ resolution, targeted peptide ion intensity, and targeted peptide ion mass accuracy.

Thresholds can be established by the user based on a defined control data set, and Pareto analysis is used to monitor performance and identify metrics with high variance.

Overall the workshop was well received and we had a higher than usual degree of audience participation/ questions/ comments. Many came up to ask questions and discuss key points after the workshop, as well as suggest ideas for next year. A representative from Sciex recommended consultation with instrument vendors to help set up QCs. It is apparent that this is a subject of increasing importance in the field, as instruments get “easier” to use, but more complicated to troubleshoot.