**Clinical Chemistry Workshop Report**
**72nd ASMS Conference**

**Brian Rappold**
**Timothy Collier**

The Clinical Chemistry workshop for the 72nd ASMS Conference on Mass Spectrometry and Allied Topics was held on June 4th, 2024 from 5:45 to 7:00 PM in Room 304AB of the Anaheim Convention Center. This year's workshop was titled "Tales from Clinical Analysis – Discovery Translation", with Brian Rappold serving as lead and assisted by Timothy Collier, and was attended by more than 100 participants. Roughly 10% of attendees were familiar with the clinical chemistry field, with 90% or attendees having backgrounds in research laboratories involved in biomarker discovery.

The workshop was an interactive dialogue using discussion prompts arising from four focus areas based on translation of biomarkers discovered in research/core laboratories to clinical use in accredited clinical laboratories. These areas included analytical specificity, metrology/traceability, data fidelity, and machine learning validity.

Analytical specificity focused on the use of ion ratios (the ratio of chromatographic peak areas from multiple parent/product ion transitions in an LC-MS/MS method) to ensure specificity of analytical measurements. The metrology/traceability section of the workshop prompted discussion on the use of standards, quality control specimens, etc. that are traceable to a known absolute quantity to ensure consistency and accuracy of analytical measurements. A focus on the need to anchor to absolute known quantity rather than "relative" ratiometric quantitation of an experimental specimen relative to a control was a pronounced feature that attendees agreed was essential. Data fidelity focused on the use of proper figures of merit when characterizing a chromatographic peak. A series of noisy chromatograms with arbitrarily integrated peaks and overlayed signal-to-noise ratios were used as example data. Lively discussion ensued on whether the examples were, in fact, quantifiable peaks or just noise. A consensus of actionable data vs noise was, disappointingly, not reached. A discussion ensued on the use of signal-to-noise to establish limits of quantitation vs verifiable parameters such as the imprecision of measurements at the limit of quantitation; signal-to-noise being removed from best practice guidance for clinical analysis was shared. Finally, discussion of the verification of machine learning, specifically regarding data leakage leading to overfitting and overly optimisitic results, and contrasting with proper verification procedures.