Clinical Chemistry

December 2018 Audio Summary

This is the December 2018 issue of *Clinical Chemistry*, Volume 64, Issue 12.

ON THE COVER AACC Learning Lab authors. The AACC Learning Lab for Laboratory Medicine on NEJM Knowledge+ is currently considered the most ambitious cloud-based medical education program in world. Over 90 laboratory medicine physicians and scientists from around the globe have volunteered their time to author courses for this initiative. In recognition of their efforts and in appreciation for their commitment to this program, *Clinical Chemistry* wishes to honor the authors by displaying their photos on the cover of this issue and by highlighting this program and the authors' contributions to it in an editorial.

Padlock Probe Assay for Detection and Subtyping of Seasonal Influenza
By Felix Neumann, et al.

Influenza is a constant threat worldwide due to its continuous evolution that can lead to pandemics. Seasonal influenza especially affects elderly and persons with chronic medical conditions. The authors of this study developed an isothermal nucleic acid assay for the detection and subtyping of seasonal influenza that could help to classify patient infections accurately and perform global surveillance on the subtype level. The design of the assay aimed for increased robustness and tolerance towards mutations in the influenza genome segments. The assay was combined with a prototype cartridge read-out to allow for semi-quantitative analysis without the need for specialized instrumentation.

Misclassification of Calcium Status Based on Albumin-Adjusted Calcium: Studies in a Tertiary Hospital Setting
By Joel Smith, et al.

Clinical laboratories measure total calcium and adjust for albumin concentrations to more closely resemble ionized calcium. This can lead to overcorrection and false information regarding patients' calcium status. The authors of this study analyzed a large set of results, where adjusted calcium and ionized calcium were measured in close time proximity and found poor agreement for calcium status classification. Agreement worsened with decreased renal function and lower albumin concentrations. Restriction of the reporting of adjusted albumin to albumin concentrations >3.0g/dL improved the correct classification of calcium status. Based on these results the authors suggest that laboratories should limit their reporting of albumin adjusted calcium concentrations.

Brain Natriuretic Peptide in Plasma as Predictor of All-Cause Mortality in a Large Danish Primary Health Care Population Suspected of Heart Failure
By Julie L. Hejl, et al.

Only a few studies have examined the utility of B-type natriuretic peptide, abbreviated BNP, as a predictor of all-cause mortality in the primary health care sector, where BNP measurement may have its greatest potential. In the present study, the authors examined the prognostic value of BNP for all-cause mortality in a Danish primary care cohort of 61,665 individuals. Kaplan-Meier curves were plotted for overall survival probability and showed statistically significant increasing mortality with increasing BNP. The all-cause mortality was increased by 32.3% for each doubling of BNP. These results underscore that BNP measurement in plasma, even in a primary care population, predicts all-cause mortality.

Applying Standard Clinical Chemistry Assay Validation to Droplet Digital PCR Quantitative Liquid Biopsy Testing
By Dragana Milosevic, et al.

The liquid biopsy is increasingly used in cancer diagnosis and is starting to be applied to monitoring patients during and after treatment. However, most of the initial efforts have focused on qualitative and semi-quantitative testing. In this study the authors show that fully quantitative measurement of cell free DNA is possible and that its performance characteristics can be determined seamlessly by use of standard clinical chemistry assay validation approaches. This should facilitate and standardize development of quantitative cell free DNA assays, and should, based on the assay performance characteristics, allow differentiation of biologically significant changes in oncogene cell free DNA concentrations from assay variability.

Systematic Comparison of Bacterial Colonization of Endometrial Tissue and Fluid Samples in Recurrent Miscarriage Patients: Implications for Future Endometrial Microbiome Studies
By Yingyu Liu, et al.

The microbiota in endometrial fluid of patients receiving in vitro fertilization treatment has been shown to be useful for predicting pregnancy rates, but whether it reflects the microbiota in the endometrial tissue remains obscure. To address this question, the authors of this study profiled simultaneously the microbiomes in endometrial fluid and biopsy samples of in vitro fertilization patients using massively parallel sequencing. They identified bacterial taxa that were frequently detected only in endometrial biopsies but not in fluid samples, and taxa that were differentially abundant between these two sample types. Profiling both fluid and biopsy samples will reveal a more comprehensive view of the endometrial microbiome.

Multiplex Droplet Digital PCR Method Applicable to Newborn Screening, Carrier Status, and Assessment of Spinal Muscular Atrophy
By Noemi Vidal Folch, et al.

This manuscript is about the successful application of droplet digital PCR technology to the laboratory detection of Spinal Muscular Atrophy from dried-blood spots and other tissues. The purpose of this study is to investigate whether the droplet digital PCR platform can enhance testing for this inherited condition. The authors assessed over 1500 patient samples and determined that this technology can be successfully applied to high-throughput newborn screening as well as carrier determination from whole blood specimens.

Denaturation-Enhanced Droplet Digital PCR for Liquid Biopsies
By Mariana Fitarelli-Kiehl, et al.

While interest in digital-droplet PCR technology for circulating-DNA analysis is burgeoning, the paucity of starting DNA material often acts as a glass ceiling in the molecular analysis of liquid biopsies. Here the authors present a solution to this universal problem that enhances the information obtained from clinical samples with little change in established protocols. By appropriate denaturation of the sample prior to digital-droplet PCR technology the information obtained is doubled, also doubling the number of possible assays and improving digital-droplet PCR technology accuracy.

UPLC-MS/MS Analysis of Urinary Free Oligosaccharides for Lysosomal Storage Diseases: Diagnosis and Potential Treatment Monitoring
By Rongrong Huang, et al.

A group of lysosomal storage diseases, primarily the glycoproteinoses, are characterized by accumulation of free oligosaccharides as a result of impaired glycoprotein degradation. Upon initial clinical suspicions, the first-tier screening of these conditions is typically done by detecting the abnormal accumulation of urine oligosaccharides via thin-layer chromatography. To provide a more rapid, sensitive and objective test, the authors developed an ultra-performance liquid chromatography-tandem mass spectrometry assay for the analysis of disease-specific urine oligosaccharides from 110 unaffected controls and 51 affected patients with lysosomal storage diseases. The results show that the assay can be used for the diagnosis of eight different lysosomal storage diseases and is potentially useful for treatment monitoring.