Clinical Chemistry

July 2014 Audio Summary

This is the July 2014 issue of *Clinical Chemistry*, Volume 60, Issue 7.

On the cover this month: *"Chicago" Neon Sign*. Each year the July cover highlights the location of the AACC's Annual Meeting and Clinical Lab Expo. It does not take much effort to identify this year's host city. The Chicago Theatre, built in 1921, was originally known as the Balaban and Katz Chicago Theatre. The preeminent theatre for nearly 50 years, this ornate but obsolete movie house closed in 1985. But it did not die. After a meticulous renovation, this 3600-seat, 7-story high icon with its 29-rank Wurlitzer theatre pipe organ regained prominence and is as popular today as it was nearly 100 years ago. Of course, there is more to Chicago than this one theatre. There are dozens of art galleries, 26 miles of lakefront, and the Magnificent Mile. But most importantly, this year Chicago is the home of cutting-edge science and the world's largest Clinical Lab Expo, which will provide you with all you need to make informed decisions about the future of your laboratory. See you in Chicago!

Harmonization of Measurement Results of the Alcohol Biomarker Carbohydrate-Deficient Transferrin by Use of the Toolbox of Technical Procedures of the International Consortium for Harmonization of Clinical Laboratory Results
By Cas Weykamp, et al.

This paper describes the harmonization of measurement results for the alcohol marker carbohydrate-deficient transferrin. Current commercially available assays for carbohydrate-deficient transferrin have different results and different reference intervals. These differences create confusion and hamper the clinical use of carbohydrate-deficient transferrin as a long-term marker for chronic heavy drinking. Harmonization can overcome this limitation of the test. The authors followed the model proposed by the International Consortium for Harmonization of Clinical Laboratory Results called the "toolbox of technical procedures." Their results indicate that harmonization of carbohydrate-deficient transferrin is possible. This study will provide the basis for harmonization of the results of all carbohydrate-deficient transferrin tests, allowing for uniform clinical decision limits and thus a sound test for chronic abuse of alcohol.

Maternal Plasma RNA Sequencing for Genome-Wide Transcriptomic Profiling and Identification of Pregnancy-Associated Transcripts
By Nancy B.Y. Tsui, et al.

This paper describes the development of a technology for obtaining a global view of circulating RNA in the plasma of pregnant women using massively parallel sequencing. Despite the potential utilities of circulating RNAs as biomarkers, research in this field has been hampered by the low quantity and poor integrity of circulating RNA. As demonstrated in this paper, massively parallel sequencing, which is sensitive and quantitative, has enabled the detection, identification, and quantification of circulating RNA in the maternal plasma. These findings have laid the foundation for future research into circulating RNA, which could have important utilities in the clinical setting.

Early Detection of Fragile X Syndrome: Applications of a Novel Approach for Improved Quantitative Methylation Analysis in Venous Blood and Newborn Blood Spots
By Yoshimi Inaba, et al.

Fragile X Syndrome is the most common single gene cause of intellectual disability and comorbid autism and almost always results from epigenetic silencing of the FMR1 gene. Standard diagnostic tests can predict severity of the disease in males from birth, but not in females. The authors describe potential diagnostic and prognostic applications of a new low-cost method in Fragile X Syndrome for both sexes. It combines the unique features of high-resolution melt and the high-throughput, quantitative real-time PCR analysis to provide accurate quantification of FMR1 intron 1 methylation in a single assay. The authors have named this method Methylation Specific-Quantitative Melt Analysis.

Generation of a New Cystatin C–Based Estimating Equation for Glomerular Filtration Rate by Use of 7 Assays Standardized to the International Calibrator
By Anders Grubb, et al.

Knowledge of glomerular filtration rate (or GFR) is essential to detect renal disease and to allow administration of correct dosage of medicines cleared by the kidneys. To be able to estimate GFR, equations based upon cystatin C are used, but because of differences in the assays for cystatin C, several different equations have been described. By using an international reference material for cystatin C, the authors of this study adjusted 7 of the major commercial assays to achieve minimal interassay variation. By use of plasma samples from about 5,000 patients with known GFR, it was then possible to generate an assay-independent cystatin C-based equation for estimation of GFR.

Mass Spectrometry–Based Candidate Reference Measurement Procedure for Quantification of Amyloid-β in Cerebrospinal Fluid
By Andreas Leinenbach, et al.

Several immunoassays for amyloid-β 1-42 (or $A\beta_{42}$) exist but may suffer from matrix interference, hampering comparisons between laboratories and general cutoff levels. In this paper the authors present a reference measurement procedure for absolute quantification of $A\beta_{42}$ in human cerebrospinal fluid using mass spectrometry. The use of 2 different stable isotope-labeled variants of $A\beta_{42}$ enables calibration and quantification in human cerebrospinal fluid. The quantification is conducted as near as possible at real conditions using labeled peptides in human cerebrospinal fluid with high accuracy and precision. This represents an important step towards standardization and a more general use of cerebrospinal fluid $A\beta_{42}$ in clinical practice and trials.

Validation of DNA Methylation Biomarkers for Diagnosis of Acute Lymphoblastic Leukemia
By Zac Chatterton, et al.

This paper considers the development of a sensitive multiplex assay for detection of DNA methylation associated with disease in childhood acute lymphoblastic leukemia the authors call methylSABER. They compared their method to commercially available EpiTYPER chemistry and found their approach to be more sensitive. In addition, these DNA methylation biomarkers are found in all individuals with leukemia and can be used to track and monitor disease burden without the need to develop patient-specific genetic assays.

Molecular Profiling of Appendiceal Epithelial Tumors Using Massively Parallel Sequencing to Identify Somatic Mutations
By Xiaoying Liu, et al.

This study identified molecular profiles of tumors of the appendix which are rare but very challenging from a management perspective. The authors used next generation sequencing to identify somatic mutations in a panel of 50 cancer-related genes. They found several mutations in the *KRAS* and *GNAS* genes, as well as less common mutations in other genes. These findings demonstrate the degree of tumor heterogeneity and highlight the potential for some tumors to be targeted for the application of new therapeutic approaches.