Clinical Chemistry

July 2016 Audio Summary

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ON THE COVER *We the People*. These three words, which are among the most famous in American history, open the preamble to the United States Constitution, which was written during the Philadelphia Convention in 1787. Another notable gathering takes place in Philadelphia this month, the AACC Annual Meeting and Clinical Lab Expo. Among the many available scientific sessions, renowned plenary speakers will share their knowledge of programmable biochips, preventable causes of death, the epigenetic basis of human disease, direct mass spectrometric profiling of biological tissues, and the science and use of cannabis. Of course, if you want to take a break from the activities at the meeting, you can always climb the "Rocky Steps"—better known as the Philadelphia Art Museum steps, and pose with the Rocky Statue.

Selecting Statistical Procedures for Quality Control Planning Based on Risk Management
By Martin Yago and Silvia Alcover

This paper deals with the selection of appropriate statistical QC procedures to decrease the number of erroneous patient results reported by the laboratory to a level acceptable from the point of view of patient safety. The authors investigated the relationship between the probability of detection of error, a classical criterion used for QC planning, and the maximum expected increase in the number of unacceptable patient results reported during the presence of an undetected out-of-control error condition. The study found that the classical probability of error detection criterion was useful for estimating the probability of patient harm, allowing for the selection of appropriate QC procedures in QC planning based on risk management.

Iterative outlier removal: A method for identifying outliers in laboratory recalibration studies
Christina Parrinello, et al.

Extreme values that arise through non-laboratory measurement procedure-related processes lead to outliers and inflate errors in recalibration studies. This paper presents an approach termed iterative outlier removal for identifying such outliers. Data were derived from uric acid re-measurements undertaken to recalibrate previous measurements in 200 Atherosclerosis Risk In Communities participants. In conducting iterative outlier removal, data points greater than 3 standard deviations from the mean difference were excluded at each iteration until no outliers remained. In simulation studies iterative outlier removal was found to detect more outliers and yield better recalibration precision, even when the error rate was high. Iterative outlier removal was found useful for removal of extreme outliers irrelevant to recalibration and identified more extraneous outliers than the standard approach.

Bloodborne viral pathogen contamination in the era of laboratory automation
Andrew Bryan, et al.

Guidance from the Centers for Disease Control states that routine laboratory testing can be safely performed on persons under investigation for Ebola virus disease by adhering to bloodborne pathogen practices. The authors of this study assessed contamination of a total laboratory automation system by Hepatitis B and C viruses that occurred through routine clinical use and after processing high-titer Hepatitis C-positive specimens. Contamination was detected primarily in association with a decapper instrument, but was also found in other locations including exposed surfaces. These data suggest a need for more detailed guidance regarding the handling of specimens potentially positive for Ebola virus.

Growth Differentiation Factor 15, Its 12-Month Relative Change, and Risk of Cardiovascular Events and Total Mortality in Patients with Stable Coronary Heart Disease: 10-Year Follow-up of the KAROLA Study
Dhayana Dallmeier, et al.

Growth differentiation factor-15 or GDF-15 has been associated with mortality and disease progression in patients with acute coronary syndromes, angina pectoris, heart failure, and stroke. It is unclear whether high concentrations of GDF-15 might be only a response to biologic stress or might directly reflect a harmful pathway. The authors of this study evaluated the association between baseline concentrations and 12-month changes of GDF-15 with the onset of subsequent cardiovascular events and total mortality in patients with stable coronary heart disease during long-term follow-up. Their study shows an association between baseline GDF-15 as well as its 12-month changes with total mortality in patients with coronary heart disease, supporting further evaluation of GDF-15 as a prognostic biomarker.

Toward Worldwide Hepcidin Assay Harmonization: Identification of a Commutable Secondary Reference Material
Lisa N. van der Vorm, et al.

Absolute plasma hepcidin concentrations measured by various measurement procedures differ substantially. Therefore, the authors of this study aimed to identify a commutable secondary reference material to improve their equivalence. To this end, 12 measurement procedures were used to measure hepcidin in triplicate in 32 native plasma samples and 8 types of candidate reference materials. Native lyophilized plasma with cryolyoprotectant was commutable for all measurement procedures. Simulated calibration with this material could potentially reduce the inter-measurement procedure CV from 28.6% to 7.7%. This study is an important step towards harmonization of plasma hepcidin methods, which is pertinent for its implementation as a biomarker in clinical practice and research.

Direct Comparison of Metastasis-Related miRNAs Expression Levels in Circulating Tumor Cells, Corresponding Plasma, and Primary Tumors of Breast Cancer Patients
Athina N Markou, et al.

In the present prospective study the authors evaluated the expression levels of microRNA-21, microRNA-146a, microRNA-200c and microRNA-210 in circulating tumor cells of breast cancer patients with verified metastasis, and compared their expression levels in corresponding plasma and primary tumors. All peripheral blood samples were collected in a way that allowed circulating tumor cells and plasma to be isolated from the same blood draw, and all samples were analyzed in parallel with the same methodologies. The study results indicate that these microRNAs were differentially expressed between primary tumors and non-cancerous tissues, and microRNA-146a over-expression was significantly associated with the disease free interval. In peripheral blood, these microRNAs are over-expressed in circulating tumor cells and plasma.

Comparison of 3 Methodologies for Genotyping of Small Deletion and Insertion Polymorphisms
Su Kah Goh, et al.

Markers that can identify donor DNA in the blood of a transplant recipient are likely to be the best approach to monitor the health of a transplant to minimize the risk of acute organ rejection. In this study the authors compared three methodologies to determine which one best gave efficient and accurate genotyping to identify such donor-specific markers. A methodology called high resolution melting analysis was the preferred approach due to its simple workflows and its robustness. High resolution melting analysis can readily be adopted for genotyping since suitable equipment is readily available.

Comparison of the Predictive Value of GlycA and Other Biomarkers of Inflammation for Total Death, Incident Cardiovascular Events, Noncardiovascular and Noncancer Inflammatory-Related Events, and Total Cancer Events
Daniel A. Duprez, et al.

GlycA, a composite marker of inflammatory factors derived from nuclear magnetic resonance assay, was studied as a clinical variable which might help in prediction of diseases resulting from inflammation. Using 12 year followup data in 6523 participants in the Multi-Ethnic Study of Atherosclerosis, this study found that GlycA has substantial correlation with interleukin-6 and C-reactive protein. Higher GlycA values predict future cardiovascular disease, total cancer, chronic inflammatory related disease, and total death, in most cases above and beyond interleukin 6 and C-reactive protein. GlycA may assist laboratory pathologists in predicting a wide variety of chronic diseases.