Clinical Chemistry

April 2013 Audio Summary

This is the April 2013 issue of *Clinical Chemistry*: Volume 59, Issue 4.

On the cover this month, HIV – The faces of lives saved. Adapted from an original image entitled "South Africa – 99 Faces, Thousands of Lives Saved," this month's cover shows the faces of people who have received lifesaving treatment through the Siyaphila La (or 'We are living here') HIV-treatment program in South Africa. In addition to a shortage of lifesaving drugs, resource-limited countries also suffer from a lack of access to laboratory diagnostic equipment and patient health records. In this issue of *Clinical Chemistry*, a large group of collaborators from the United States, Rwanda, and The Netherlands describe a clinically proven, low-cost mobile device that can perform a blood-based HIV serodiagnostic test with laboratory-level accuracy and real-time synchronization of patient health record data. An accompanying editorial by George Whitesides discusses this remarkable example of what happens when one rethinks, both creatively and practically, how to collect diagnostic information in the developing world.

Mobile Device for Disease Diagnosis and Data Tracking in Resource-Limited Settings
By Curtis D. Chin, et al.

Collection of epidemiological data and care of patients are hampered by lack of access to laboratory diagnostics equipment and patients' health records in resource-limited settings. The authors engineered a low-cost mobile device that combines cell phone and satellite communication technologies with fluid miniaturization techniques for performing all essential functions of enzyme-linked immunosorbent assay, the gold standard test for detecting protein markers of many infectious diseases. HIV testing on 167 Rwandan patients evaluated for HIV, viral hepatitis, and sexually transmitted infections yielded diagnostic sensitivity and specificity of 100% and 99%, respectively. The mobile device also successfully transmitted all whole blood test results from a Rwandan clinic to a medical records database stored on the cloud.

Lateral Flow Assay with Near-Infrared Dye for Multiplex Detection
By Christina D. Swanson and Annalisa D'Andrea

In this study the authors developed a lateral flow assay platform using near-infrared dyes, which have less background than fluorescent dyes in the visible region. This allowed the measurement of interleukin-6 in a 10% plasma matrix with a limit of detection of 4 pg/mL and coefficient of variation less than 7%. Further, to show the flexibility of the platform, the authors built a duplex assay that could simultaneously measure interleukin-6 and C-reactive protein. The lateral flow assay results highly correlated with individual ELISA readouts. This assay could be useful in point-of-care settings where measurement of multiple biomarkers simultaneously is important.

Predicting the Cost and Pace of Pharmacogenomic Advances: An Evidence-Based Study
By Ramy Arnaout, et al.

Genomics will eventually affect every area of medicine and human health. But when will this happen, and what size research investment will be required? The answers to these questions are essential for setting expectations. This study used Monte Carlo modeling to project the time and cost required to develop pharmacogenomics-based drug dosing guidelines sufficient to cut the incidence of drug-related adverse outcomes in half. Based on this modeling, the authors estimate a cost of under $6 billion over 20 years. Such estimates make it possible to compare the relative merit of investments. The modeling also identified potential bottlenecks and workarounds for translating genomic research into the clinic more quickly and efficiently.

Increased Serum and Urinary MicroRNAs in Children with Idiopathic Nephrotic Syndrome
By Yang Luo, et al.

Childhood idiopathic nephrotic syndrome is the most frequent glomerular disease that presents during childhood and is associated with an increased risk of life-threatening complications if untreated. However, the molecular pathogenesis of nephrotic syndrome is unclear. The authors conducted a multiphase case-control study of 159 children with idiopathic nephrotic syndrome and 109 controls by performing TaqMan Low Density Array analysis followed by RT-qPCR confirmation. They found five serum microRNAs and urinary miR-30a-5p were significantly increased in the patients and markedly declined with clinical improvement of the patients. These cell-free miRNAs may represent potential diagnostic and prognostic biomarkers for idiopathic nephrotic syndrome.

Importance of the Efficiency of Double-Stranded DNA Formation in cDNA Synthesis for the Imprecision of Microarray Expression Analysis
By Hans Guttormur Thormar, et al.

This paper describes a novel method for measuring efficiency of cDNA synthesis. This method, called Two-Dimensional Strandness-Dependent Electrophoresis, allows separation and length distribution analysis of products of cDNA synthesis including single- and double-stranded DNA and RNA*DNA hybrids. The data in this article demonstrate that the amount of the double-stranded DNA products can be important in determining the precision of in-vitro testing-based microarray expression analysis.

Albuminuria Prevalence in First Morning Void Compared with Previous Random Urine from Adults in the National Health And Nutrition Examination Survey, 2009-2010
By Sharon Saydah, et al.

In February 2012, the National Health and Nutrition Examination Survey, a nationally representative survey, released data on two urine collections from participants with measured urine albumin and urine creatinine. This report presents measures of agreement, overall and by various population characteristics, between the two urine collections (a random sample and a first morning void), and highlights the related methodological issues. Based on these analyses the authors recommend caution when estimating the prevalence of albuminuria based on a single random specimen. They found that albumin to creatinine ratios measured on random urine specimens appear to overestimate the prevalence of albuminuria when compared to first void collections.

Collagen Binding Provides a Sensitive Screen for Variant von Willebrand Disease
by Veronica H. Flood, et al.

Von Willebrand disease is a common bleeding disorder, but laboratory testing for this condition is difficult owing to limitations of current diagnostic assays. This article uses data from a large multicenter study to validate the use of von Willebrand factor collagen binding as a diagnostic substitute for the more expensive and labor intensive multimer distribution. In this study, collagen binding was able to substitute for multimer distribution and provided a sensitive screen for variant von Willebrand disease, including types 2A and 2B. This finding suggests that collagen binding could substitute for multimer distribution, providing a more efficient and cost-effective diagnostic strategy.

Comparison and Evaluation of Cardiac Biomarkers in Patients with Intermittent Claudication: Results from the CAVASIC Study
By Barbara Kollerits, et al.

There is limited conclusive information regarding mid-regional pro-adrenomedullin, mid-regional pro-atrial natriuretic peptide, and C-terminal endothelin-1 precursor fragment concentrations in patients with symptomatic peripheral artery disease. Whether increases in the concentrations of these 3 peptides are independent from the established heart failure parameter N-terminal pro-B-type natriuretic peptide and persist in individuals free of prevalent cardiovascular disease is not known. The authors studied these 3 peptides as compared with N-terminal pro-B-type natriuretic peptide in patients with symptomatic peripheral artery disease from the CAVASIC Study. All three peptides were found to be significantly associated with symptomatic peripheral artery disease after adjustment for classical cardiac risk markers. Moreover, mid-regional pro-adrenomedullin and C-terminal endothelin-1 precursor fragment provided additive information in comparison to N-terminal pro-B-type natriuretic peptide and were significant predictors of peripheral artery disease in those patients and controls free from prevalent cardiovascular disease.