Clinical Chemistry

August 2013 Audio Summary

This is the August 2013 issue of *Clinical Chemistry*: Volume 59, Issue 8.

On the cover this month: *HIV Life Cycle* (detail)—Interaction of HIV-1 virions with host cell during the HIV life cycle. A substantial percentage of HIV-infected individuals experience a sharp decline in CD4+ T cell counts and progress to AIDS rapidly after primary infection. It is unclear what factors influence the susceptibility of these individuals to rapid disease progression. In this issue of *Clinical Chemistry*, collaborators from the United States and China provide novel insights to the pathogenesis of HIV infection by describing the mRNA and miRNA expression profiles in peripheral blood mononuclear cells in the first few months after infection and identifying a distinct transcriptomic signature in peripheral blood mononuclear cells of rapid progressors. An accompanying editorial discusses the contribution of this study to our understanding of HIV progression and prognosis.

Transcriptomic Analysis of Peripheral Blood Mononuclear Cells in Rapid Progressors in Early HIV Infection Identifies a Signature Closely Correlated with Disease Progression

By Zi-Ning Zhang, et al.

A substantial percentage of HIV-infected individuals become rapid progressors after primary infection, but the underlying mechanisms for the rapid disease progression remain unclear. In this manuscript, the authors have analyzed mRNA and miRNA expression profiles in rapid progressors and chronic progressors in early HIV infection. They identified a 5-miRNA signature closely correlated with disease progression and the effects of the signature miRNAs and mRNA expression in rapid progressors converged on the apoptosis pathway. These results provide a potential biomarker for HIV prognosis and novel insights to HIV pathogenesis.

Failure of Current Laboratory Protocols to Detect Lot-to-Lot Reagent Differences: Findings and Possible Solutions

By Alicia Algeciras-Schimnich, et al.

Differences between reagent lots may not be detected by commonly used lot verification protocols. An example is the Insulin Growth Factor 1 Immulite assay, where 32 lot-to-lot changes over 5 years, with 20 sample comparisons each, were found acceptable. However, retrospective analysis of patient data showed a doubling of the proportion of increased results and significant increases in result means and medians over time, and these measures also differed significantly for 11 lot-to-lot changes. Monitoring of these parameters might detect lot-to-lot changes otherwise missed. Such monitoring could be provided by centralized lot databases, fed in real-time via instruments uplinks installed by assay manufacturers.

Microfluidic Assay of Platelet Deposition on Collagen by Perfusion of Whole Blood from Healthy Individuals Taking Aspirin
By Ruizhi Li, et al.

Microfluidic devices can recreate the hemodynamic conditions needed for platelet assays. In this study an 8-channel device was validated in a study of inter-donor response to aspirin using whole blood from 28 healthy individuals. Ex-vivo addition of aspirin to blood drawn prior to aspirin ingestion caused a reduction in platelet deposition. Most individuals displayed insensitivity to ex vivo aspirin addition if they had ingested aspirin. Microfluidic devices provide a rapid, novel method for quantifying the effects of aspirin on platelet function under flow.

Association between Natriuretic Peptides and Mortality among Patients Admitted with Myocardial Infarction: A Report from the ACTION Registry®–GWTG™
By Benjamin M. Scirica, et al.

Natriuretic peptides have been proposed to improve the prognostic assessment of patients with acute coronary syndrome. The authors of this study evaluated the utilization of natriuretic peptides in almost 70,000 patients with myocardial infarction enrolled in a larger US-based myocardial infarction registry. Natriuretic peptides were measured in 47% of non-ST-elevation myocardial infarction and 33% of ST-elevation myocardial infarction patients. There was a stepwise increase in the risk of in-hospital mortality with increasing natriuretic peptide quartiles. The addition of natriuretic peptides significantly improved the discrimination and reclassification of a validated clinical model. Specific treatment strategies targeted towards patients with an increased concentration of natriuretic peptides should be a focus of future prospective studies.

Complex Biological Pattern of Fertility Hormones in Children and Adolescents: A Study of Healthy Children from the CALIPER Cohort and Establishment of Pediatric Reference Intervals
By Danijela Konforte, et al.

This comprehensive study was initiated to close critical gaps in pediatric reference values of fertility biomarkers allowing for improved diagnosis and monitoring of children with endocrine and fertility disorders. The study included a large cohort of children and adolescents and revealed marked changes in most of the sex hormones studied, both during the first year of life and during puberty. These changes required extensive partitioning of the reference intervals for most of the biomarkers studied. This database will be of global value when assessing children with developmental and fertility disorders.

High-Resolution Profiling of Fetal DNA Clearance from Maternal Plasma by Massively Parallel Sequencing
By Stephanie C.Y. Yu, et al.

In this study the authors investigated the clearance profile of circulating fetal DNA by massively parallel sequencing analysis of maternal plasma and urine samples collected serially after delivery. With massively parallel sequencing, DNA analysis could be performed in a genome-wide manner and with high precision. The authors demonstrated that fetal DNA clearance occurred in a biphasic manner and then they estimated the renal contribution to this clearance. They also explored the size profile of circulating DNA during the clearance process. These data represent the reference information upon which to build future studies of plasma DNA clearance and might have implications in pregnancy-associated disorders and other clinical contexts such as cancer and transplantation.

Genotyping of 25 Leukemia-Associated Genes in a Single Work Flow by Next-Generation Sequencing Technology with Low Amounts of Input Template DNA
By Jenny Rinke, et al.

Myeloid neoplasms are characterized by a variety of somatic gene mutations in different combinations. The authors of this study established a convenient sensitive next-generation sequencing method for genotyping of the 25 most commonly mutated leukemia-associated genes in a single workflow and without introducing bias optimized the method for low amounts of input template DNA (20 ng of genomic DNA) by combining next-generation sequencing and whole genome amplification.

Methods for Measuring Serum Activity Levels of the 192 Q and R Isoenzymes of Paraoxonase 1 in QR Heterozygous Individuals
By John F Teiber, et al.

This article describes two new methods which can be used to determine the serum activity levels of the 192 glutamine and arginine isoenzymes of paraoxonase 1 in heterozygous individuals. The methods are based on interpolation equations derived from the relationship of the ratio of Q to R isoenzyme activities of serum paraoxonase as determined with different substrates. The methods accurately quantified the paraoxonase isoenzyme activity levels in heterozygous individuals and demonstrate the ratio of Q to R isoenzymes can deviate substantially from 1 to 1. These methods will allow a more thorough comparison of the association of paraoxonase 1 and its isoenzymes with various disease measures.

Mitochondrial Coenzyme Q10 Determination by Isotope-Dilution Liquid Chromatography–Tandem Mass Spectrometry
By Outi M Itkonen, et al.

In this article the authors describe a liquid chromatography tandem mass spectrometry assay for mitochondrial Coenzyme Q10 that uses an isotopically labeled Coenzyme Q10 internal standard. Isolated muscle mitochondria were used to study preanalytical factors and establish a reference range for the ratio of mitochondrial Coenzyme Q10 to citrate synthase activity. The authors also compared the Coenzyme Q10 to citrate synthase ratio in fibroblast mitochondria from healthy individuals and a patient with known Coenzyme Q10 defect. A 5-fold decrease in the ratio of mitochondrial Coenzyme Q10 to citrate synthase was seen in the Coenzyme Q10-deficient patient. This assay is likely to improve the diagnosis and treatment of patients with Coenzyme Q10 deficiency.