Clinical Chemistry

June 2014 Audio Summary

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On the cover this month: Leonardo Da Vinci anatomy drawing: *Heart and Its Blood Vessels*. In addition to being a preeminent painter and sculptor, Leonardo Da Vinci was also an anatomist. His anatomical studies began with the postmortem dissection of an old man whose death Da Vinci had just witnessed. Da Vinci hypothesized that the man's death was due to heart failure brought about by a narrowing of the mesenteric vessels by a thick coating. There was likely a substance carried though the blood that bound to arteries and blocked blood flow. This substance, which we now know to be cholesterol, is routinely monitored as a risk factor for heart disease. This issue of *Clinical Chemistry* contains 2 articles and an accompanying editorial on the biomarker troponin, as well as a Q&A on microRNAs as biomarkers for acute myocardial infarction.

Weekly and 90-Minute Biological Variations in Cardiac Troponin T and Cardiac Troponin I in Hemodialysis Patients and Healthy Controls
By Kristin Moberg Aakre, et al.

Myocardial infarction is diagnosed by the finding of a single troponin result above the 99th percentile and a significant time-dependent troponin concentration change. This study aimed to determine the 90-minute and weekly biological variation, reference change values, and index of individuality for 2 high-sensitivity assays for cardiac troponin T and troponin I in patients receiving hemodialysis and in healthy individuals. The results indicated that a change of 20% to 50% may be applicable for the diagnosis of myocardial infarction when using the high-sensitivity troponin T assay , but not when using the high-sensitivity troponin I assay. The low index of individuality for both assays suggests that use of a diagnostic cutoff value can be abandoned.

Use of Observed Within-Person Variation of Cardiac Troponin in Emergency Department Patients for Determination of Biological Variation and Percentage and Absolute Reference Change Values
By Aaron J. Simpson, et al.

In the emergency department, there is a need to quickly assess and exclude patients who do not have the acute coronary syndrome. With the introduction of a high-sensitivity assay for cardiac troponin I into routine clinical practice, the authors of this study noticed that patients without the acute coronary syndrome had only small changes in cardiac troponin I concentration on repeat sampling. For patients in whom the acute coronary syndrome is excluded, these small changes in cardiac troponin I concentration are a result of analytical imprecision and biological variation. The authors used these data to calculate biological variation and to determine absolute delta changes in cardiac troponin I. This information will be useful in excluding patients who do not have the acute coronary syndrome.

Measurements for 8 Common Analytes in Native Sera Identifies Inadequate Standardization among 6 Routine Laboratory Assays
By Hedwig C.M. Stepman, et al.

This study used a panel of fresh-frozen single-donation sera to assess the quality and standardization status of 6 assays used in daily practice for measurement of 8 analytes. The considered quality indicators were within-run imprecision, combined imprecision (including sample-matrix interference), bias, and total error. The assessment was done at the peer group level and by comparison against the all-method trimmed mean or reference method values, where available. Most assays showed excellent peer performance attributes. However, the observation of considerable between-assay discrepancies owing to high biases of individual assays and laboratory effects was striking. Considered in aggregate, these effects jeopardize the interchangeability of measurement results.

Genotyping Accuracy of High-Resolution DNA Melting Instruments
By Mei Li, et al.

High-resolution DNA melting is a simple technique for genotyping and genetic scanning that is rapid and can be conducted in a closed tube. However, assay accuracy in different instruments has never been assessed. The authors of this study compared 10 different instruments with use of more than 6,000 samples to reveal factors important for accuracy, including melting rate, PCR product size, and method of fluorescence acquisition. Their findings raise cautions for users regarding limitations of the method and point to possible directions for instrument and assay improvement.

Genome-Wide Characterization of Circulating Tumor Cells Identifies Novel Prognostic Genomic Alterations in Systemic Melanoma Metastasis
By Connie G. Chiu, et al.

Circulating tumor cells are associated with advanced cancer stage and poor patient outcome and may be critical in the development of tumor metastasis. In this study a genome-wide SNP-based characterization of melanoma circulating tumor cells was conducted. The authors report 131 aberrant loci in circulating tumor cells with high concordance to paired tumor metastases and notable recurring loci across patients. The authors found that a biomarker gene panel conferred prognostic utility in subsequent exploratory studies. This report provides the first detailed genomic analysis of melanoma circulating tumor cells and illustrates how circulating tumor cells can be utilized as a novel approach for identification of pro-metastatic genes in cancer research.

Quantification of Integrated HIV DNA by Repetitive-Sampling *Alu*-HIV PCR on the Basis of Poisson Statistics

By Ward De Spiegelaere, et al.

Quantification of integrated HIV DNA is considered to be a marker for the size of the HIV reservoir in infected patients. Here, a new analysis method is described based on Poisson statistics to perform the *Alu*-HIV PCR with multiple replicates at limiting dilution to enable accurate quantification of low levels of integrated HIV DNA. A comparison of this method with the formerly used methodologies for data analysis revealed that the Poisson method is both accurate and less complex. This new methodology will facilitate a wider use of the *Alu*-HIV PCR as a tool to measure the HIV reservoir.