Clinical Chemistry

May 2018 Audio Summary

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ON THE COVER Mycobacterium tuberculosis bacilli secreting virulence antigens. The incidence of tuberculosis (TB) remains high globally, with more than 10 million new cases reported each year. At present, most methods for identifying active infection, such as sputum analysis, have lower clinical sensitivity when few bacilli are present (paucibacillary TB). One approach to enhancing the detection of active TB is the detection of antigens secreted by live bacilli. This issue of *Clinical Chemistry* contains a report of a signal-enhancing nanoparticle platform to detect peptides in serum derived from these antigens to diagnose tuberculosis cases and to monitor antimycobacterial therapy responses.

Clinical Evaluation of a Blood Assay to Diagnose Paucibacillary Tuberculosis Via Bacterial Antigens
By Chang Liu, et al.

Current frontline microbiologic and molecular assays used to diagnose active tuberculosis require Mycobacterium tuberculosis-rich sputum or invasive biopsy samples, which can be difficult to obtain in certain patient populations and have reduced clinical sensitivity in patients with paucibacillary disease. This study evaluates the diagnostic performance of a novel platform that can rapidly detect and quantify Mycobacterium tuberculosis antigens in peripheral blood samples and yields robust diagnostic performance with both pulmonary and extrapulmonary tuberculosis cases, irrespective of Mycobacterium tuberculosis culture status. This methodology represents a significant advancement over current tuberculosis diagnostic assays, especially in paucibacillary and extrapulmonary disease populations.

The Effect of Single Mismatches on Primer Extension
By Nicholas A. Rejali, et al.

This study investigates the effects of base-pair mismatches on primer extension using a fluorescence-based assay to monitor nucleotide incorporation under PCR conditions. The authors found that mismatches near the 3'-end of the primer inhibit extension rates by 40 to 20,000-fold dependent on mismatch type. 3'-mismatched primers exhibit lower temperature optimums for extension compared with non-mismatched oligonucleotides, and the rate of extension from mismatched primers relative to matched primers increases as temperatures decrease. These findings suggest allele-specific PCR assays should be utilized for certain types of single nucleotide variants, while detection of other variants may be better suited for other detection methods.

Quality Control of Serum and Plasma by Quantification of (4E,14Z)-Sphingadienine-C18-1-Phosphate Uncovers Common Preanalytical Errors During Handling of Whole Blood
By Xinyu Liu, et al.

Blood samples are one of the most frequently analyzed body fluids. However, no objective and reliable assessment of serum and plasma quality is currently in general use (beyond checking for hemolysis, icterus, and lipemia). In this study the authors identified and rigorously validated a novel biomarker, (4E,14Z)-sphingadienine-C18-1-phosphate, that reflected the adherence to standard operating procedure-dictated time for processing to plasma or serum and/or time-to-storage of whole blood at 4°C. This novel quality assessment step could enable clinical chemists and other scientists to identify serum and plasma samples that should be excluded from certain investigations, and control samples prior to expensive long-term storage in biobanks.

Evaluating Rapid Rule-out of Acute Myocardial Infarction Using a High-Sensitivity Cardiac Troponin I Assay at Presentation
By Jaimi H. Greenslade, et al.

The paper investigated whether troponin values, assessed on presentation to the emergency department, are diagnostic for acute myocardial infarction. The Beckman Coulter Access high sensitivity troponin I assay was used as there is limited research on its clinical performance. Troponin values were assessed for 1,871 emergency department patients. 99% of patients ultimately diagnosed with acute myocardial infarction had presentation values above the manufacturer specified limit of detection. Thus, a single baseline troponin below the limit of detection, measured with the Access high sensitivity troponin I assay, can be used to rule out acute myocardial infarction and reduce the number of patients undergoing lengthy chest pain assessment.

Liquid Profiling of Circulating Tumor DNA in Plasma of Melanoma Patients for Companion Diagnostics and Monitoring of BRAF Inhibitor Therapy
By Verena Haselmann, et al.

In this large-scale translational melanoma study the suitability of circulating cell-free DNA to assess BRAF V600E tumor mutational status in real-time compared to conventional tissue-based testing was evaluated. This represents the first study that includes all melanoma stages, with monitoring of disease course, and use of prospectively collected blood samples to facilitate adherence to all preanalytical requirements. The study revealed a high level of concordance between testing modalities and the superiority of plasma-based testing compared to imaging techniques and conventional serum biomarkers S100 and LDH for monitoring BRAF inhibitor therapy. These data should facilitate the fine-tuning of therapy administration, potentially enabling improved patient outcomes.

Establishment of Community-Based Reference Intervals for Fructosamine, Glycated Albumin, and 1,5-Anhydroglucitol
By Elizabeth Selvin, et al.

This study provides the first reference intervals or "normal values" for three important non-traditional measures of hyperglycemia: fructosamine, glycated albumin, and 1,5-anhydroglucitol. The authors conducted measurements of these assays in blood samples obtained from a community-based population of black and white adults in the U.S. Their results provide reference intervals for these measures of hyperglycemia in a general U.S. population and establish cut-points that could be used to identify hyperglycemia in clinical practice and research studies using these biomarkers.

Biological Variation of Creatinine, Cystatin C, and eGFR over 24 Hours
By Judith M. Hilderink, et al.

This study assessed the within-subject biological variation of different eGFR variations in two study groups: people with and people without chronic kidney disease. Hourly samples of creatinine and cystatin C were collected from 37 individuals over 24 hours. Glomerular filtration rate was estimated using the Modification of Diet in Renal Disease and the Chronic Kidney Disease Epidemiology Collaboration equations based on creatinine, cystatin C, and the combination of creatinine and cystatin C. Despite differences in the biological variation of creatinine between the study groups, reference change values of all derived eGFR equations were within the same range and relatively similar for people with or without chronic kidney disease.