Clinical Chemistry

October 2018 Audio Summary

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ON THE COVER Collecting blood for HIV testing in Kenya. With healthcare emphasis shifting towards precision medicine, population health, and chronic disease management, the potential global impact of point-of-care technology continues to grow and several prominent point-of-care technology trends have emerged in the last decade. In this month's issue of *Clinical Chemistry*, Wang and Kricka provide a timely overview of technologies in development (e.g., wearables, noninvasive testing, mass spectrometry and nuclear magnetic resonance, paper-based diagnostics, nanopore-based devices, and digital microfluidics), discuss their potential clinical applications, and provide perspectives on strategies beyond technological and analytical proof-of-concept. Important topics covered are point-of-care testing growth points and emerging trends, representative commercialized diagnostic devices and apps enabled by smart phones, smart watches and tablets, and checklist questions for different stakeholders during point-of-care technology development, optimization, and clinical adoption.

A "Culture" Shift: Broad Bacterial Detection, Identification, and Antimicrobial Susceptibility Testing Directly from Whole Blood
By Nadya Andini, et al.

The time required for current bloodstream pathogen detection, identification, and antimicrobial susceptibility testing does not satisfy the acute needs of disease management. Therefore, the authors of this study designed a combined real time PCR-based identification plus antimicrobial susceptibility testing assay with sequential detection, identification, and antimicrobial susceptibility testing of leading nosocomial bacterial pathogens. The assay detected 1 colony forming units/mL bacteria in blood, identified them by melting curves, and profiled drug susceptibility by cycle threshold differences. Using an RNA target allowed faster antimicrobial susceptibility testing, and rapid PCR reduced amplification time for an even faster assay. The identification plus antimicrobial susceptibility testing assay provides a complete solution for rapid diagnosis of bloodstream infections.

Development of a Highly Sensitive Device for Counting the Number of Disease-Specific Exosomes in Human Sera
By Yasuaki Kabe, et al.

This study presents the development of a novel type of exosome-counting system, named ExoCounter, which can determine the absolute number of specific exosomes in biological fluids without any pre-isolation procedure. The ExoCounter was found to detect exosomes with high sensitivity and high linearity as compared with conventional labeling-detection methods such as ELISA or flow cytometry analysis. Use of various antibodies against surface antigens of exosomes enabled disease-specific exosomes to be detected by the ExoCounter. Furthermore, HER2-positive exosome counts were found to be significantly higher in patients with breast cancer and ovarian cancer compared with sera from healthy donors or individuals with non-cancer diseases.

Proteomic Discovery and Validation of the Confounding Effect of Heparin Administration on the Analysis of Candidate Cardiovascular Biomarkers
By Hans C. Beck, et al.

This paper is about the possible confounding of heparin administration on the measurement of a variety of plasma proteins that in previous studies are identified as plasma biomarkers for cardiovascular events such as myocardial infarction. Using a proteomic approach, the authors analyzed plasma samples from two cohorts, from 9 patients before and after heparin administration, and samples from 500 patients with suspected myocardial infarction, 363 of whom were treated with heparin before hospitalization. When heparin was administrated, a large portion of the measured plasma proteome was found to change significantly in concentration. This finding demonstrates that medication may confound discovery of biomarkers and their clinical evaluation.

Comparability of Lipoprotein Particle Number Concentrations Across ES-DMA, NMR, LC-MS/MS, Immunonephelometry, and VAP: In Search of a Candidate Reference Measurement Procedure for apoB and non-HDL-P Standardization
By Vincent Delatour, et al.

Advanced lipoprotein testing methods separate and/or measure lipoproteins according to different characteristics, and equivalence of results across methods has not been demonstrated. Through a split-sample study, the comparability of non-HDL-particles and apoB-100 concentrations measured by electrospray differential mobility analysis, nuclear magnetic resonance, immunonephelometry, LC-MS/MS and vertical auto profile was assessed. This study demonstrates that advanced lipoprotein testing methods do not yet provide equivalent results and suggests that standardization of advanced lipoprotein testing methods by use of a common commutable calibrator will improve comparability. LC-MS/MS was also identified as the most suitable candidate reference measurement procedure to standardize apoB-100 as it would provide results with SI-traceability.

Circulating Adipocyte Fatty Acid–Binding Protein Concentrations Predict Multiple Mortality Outcomes among Men and Women with Diabetes
By Chi-Ho Lee, et al.

In 2006, the authors of this study reported the first demonstration that adipocyte fatty acid-binding protein, abbreviated AFABP, was a circulating biomarker of adiposity in humans. However, the relationship of serum AFABP levels with mortality outcomes has remained to be defined, despite the association between AFABP and various diseases. In this study involving men and women with type 2 diabetes, the authors found that increased serum AFABP concentrations significantly predicted all-cause mortality, infection-related death and cardiovascular mortality. These findings suggest a potential role for circulating AFABP as a biomarker for mortality risk stratification in diabetes.

Chromosomal Aberrations Associated with Sequential Steps of the Metastatic Cascade in Colorectal Cancer Patients
By Simon A. Joosse, et al.

This study describes the genomic aberrations that are associated with the different stages of systemic and lymphatic metastasis of colorectal cancer. The study results imply that invasive colorectal cancer accumulates specific chromosomal changes that enable its dissemination in the mesenteric vein, metastasis to the liver, dissemination beyond the liver in the peripheral blood circulation, and finally outgrowth in distant organs beyond the liver. This information might be helpful to identify patients with limited metastatic spread who could profit from liver metastasis resection. Further evaluation of these chromosomal aberrations might lead to the discovery of new therapeutic targets.

Discovery and Validation of Salivary Extracellular RNA Biomarkers for Noninvasive Detection of Gastric Cancer
By Feng Li, et al.

The aim of this study was to develop salivary extracellular RNA biomarkers for noninvasive screening and risk-assessment of gastric cancer. In this study with a prospective- specimen-collection and retrospective-blinded-evaluation design, the authors used a combination of microarray, Taqman microRNA array and RT-qPCR technologies to develop and validate a panel of salivary extracellular RNA biomarkers consisting of 3 messenger RNAs and 2 microRNAs for gastric cancer detection, yielding an area under the ROC curve performance of 0.81. When combined with demographic factors, the performance of the panel reached an area under the curve of 0.87. This study demonstrates the potential of salivary extracellular RNA biomarkers as potential screening and risk-assessment tools for gastric cancer.

Evaluation of Preanalytical Conditions and Implementation of Quality Control Steps for Reliable Gene Expression and DNA Methylation Analyses in Liquid Biopsies
By Martha Zavridou, et al.

Liquid biopsy provides important information on prognosis and treatment of cancer patients. The authors of this study evaluated pre-analytical conditions and implemented quality control steps for reliable gene expression and DNA methylation analyses in liquid biopsies. RNA-based circulating tumor cell-analysis was severely affected by the type of peripheral blood collection tubes and time to analysis. Plasma and sodium bisulfite-converted DNA samples were stable when kept at -80°C, while downstream whole genome analysis of sodium bisulfite-converted DNA was able to compensate for the limited amount of sample. Standardization of pre-analytical conditions and implementation of quality control steps are extremely important for reliable liquid biopsy analysis, and are a prerequisite for routine applications in the clinic.