Clinical Chemistry

September 2018 Audio Summary

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ON THE COVER Allan Jaffe. Although he is known as a world authority on the use of cardiac biomarkers, in particular troponin, Allan Jaffe is inspiring not only because of his successes but also because of his resilience in overcoming challenges in his life. His gravelly voice hides an individual whose internal voice is actually a soft one that reflects a passion for helping others, especially young people. For example, during his first year in medical school, he signed up with the Big Brother Foundation and was paired with a fatherless boy with whom he met weekly for the next four busy years. Who got the most direction in life from the experience? You will have to read this month's Inspiring Minds article to decide for yourself.

Detection and Quantification of Carbohydrate Deficient Transferrin by MALDI-Compatible Protein Chips Prepared by Ambient Ion Soft Landing
By Petra Darebna, et al.

In this study the authors prepared protein chips by functionalization of indium tin oxide glass using ambient ion landing of electrosprayed anti-transferrin antibody for the in situ detection and quantification of carbohydrate deficient transferrin. The transferrin molecule was detected by MALDI-TOF mass spectrometry and the peak intensities of each transferrin form were used to calculate total carbohydrate deficient transferrin. A cohort of samples from 186 patients was analyzed using functionalized MALDI chips and the results were compared with data obtained by capillary electrophoresis. The results obtained by chip-based MALDI mass spectrometry were in good agreement with the data obtained by capillary electrophoresis. The carbohydrate deficient transferrin values coincided in 95% of samples.

A Simple and Novel Fecal Biomarker for Colorectal Cancer: Ratio of Fusobacterium Nucleatum to Probiotics Populations Based on Their Antagonistic Effect
By Songhe Guo, et al.

There is a need to improve microbial indicators for colorectal cancer diagnosis. The authors of this study evaluated various fecal microbial ratios for clinical use in detecting colorectal cancer. They found that Fusobacterium nucleatum could play a role in microbiota dysbiosis via the secretion of antagonistic substances against probiotics. Moreover, the ratios of Fusobacterium nucleatum to the important probiotics Faecalibacterium prausnitzii and Bifidobacterium were identified as valuable markers for screening early colorectal cancer.

Genome-Wide Analysis of Circulating Cell-Free DNA Copy Number Detects Active Melanoma and Predicts Survival
By Shobha Silva, et al.

The prognosis of patients with advanced melanoma has improved with the emergence of immunotherapy and BRAF & MEK-targeted therapies. Early detection of metastatic relapse is crucial to maximize the benefit from these therapies. Circulating cell-free DNA is being increasingly investigated as a genomic biomarker. The authors of this study show how low-coverage next-generation sequencing can be utilized to create copy number profiles in cell-free DNA, and they demonstrate the utility of this cost-effective approach in detecting active melanoma and predicting survival. This approach has the potential to be applied to a wider population of cancer patients as an early marker of relapsed disease.

Clinical Validation of a Novel High-Sensitivity Cardiac Troponin I Assay for Early Diagnosis of Acute Myocardial Infarction
By Jasper Boeddinghaus, et al.

The performance of the novel high-sensitivity cardiac troponin I ADVIA Centaur assay in the early diagnosis of acute myocardial infarction is unknown. The authors of this study set out to validate its performance, to compare it with the established high-sensitivity cardiac troponin T and I assays performed respectively on the Roche Elecsys and Abbott Architect analyzers, and to derive and validate assay-specific 0/1h- and 0/2h-algorithms for rapid rule-out and rule-in of acute myocardial infarction. Patients presenting with symptoms suggestive of acute myocardial infarction to the emergency department were included. Final diagnoses were adjudicated by two independent cardiologists. The diagnostic accuracy of the high-sensitivity cardiac troponin I ADVIA Centaur assay was excellent and comparable to high-sensitivity cardiac troponin T and I assays performed, respectively, on the Roche Elecsys and Abbott Architect analyzers. Both newly developed algorithms safely ruled-out and accurately ruled-in acute myocardial infarction.

Circulating Proenkephalin, Acute Kidney Injury and Its Improvement in Patients with Severe Sepsis or Shock
By Pietro Caironi, et al.

The authors of this study examined whether a circulating peptide related to proenkephalin could predict incident acute kidney injury and its improvement in septic patients. The hypothesis was tested in 1000 patients with sepsis or septic shock from the multicenter trial ALBIOS. Day-1 and repeated measurements of proenkephalin independently predicted incident acute kidney injury, and future need for renal replacement therapy in intensive care units, showing added prognostic value to that of serum creatinine. Proenkephalin was also associated with improvements in renal function and 90-day mortality.

Cardiac Troponin T Concentrations, Reversible Myocardial Ischemia, and Indices of Left Ventricular Remodeling in Patients with Suspected Stable Angina Pectoris: a DOPPLER-CIP Substudy
By Peder L. Myhre, et al.

Cardiac troponins provide important prognostic information in patients with stable coronary artery disease. However, whether high sensitivity cardiac troponin T concentrations mainly reflect left ventricular remodeling or recurrent myocardial ischemia is not known. This study measured high sensitivity cardiac troponin T in 619 individuals with stable coronary artery disease and investigated associations with indices of left ventricular remodeling as assessed by cardiac MRI and echocardiography and evidence of myocardial ischemia as assessed by single positron emission computed tomography and perfusion-MRI. Higher concentrations of high sensitivity cardiac troponin T were associated with higher age, lower estimated glomerular filtration rate (eGFR), greater left ventricular mass, lower left ventricular ejection fraction and evidence of reversible myocardial ischemia including both perfusion defects and wall-motion abnormalities. The results were consistent with analysis using single positron emission computed tomography and perfusion-MRI.

The EuBIVAS: Within- and Between-Subject Biological Variation Data for Electrolytes, Lipids, Urea, Uric Acid, Total Protein, Total Bilirubin, Direct Bilirubin and Glucose
By Aasne K. Aarsand, et al.

The European Biological Variation Study (EuBIVAS) has been established to deliver rigorously determined data describing biological variation of clinically important measurands. This paper delivers biological variation estimates of serum electrolytes, lipids, urea, uric acid, total protein, total bilirubin, direct bilirubin, and glucose. The within-subject biological variation estimates of all measurands, with the exception of urea and LDL cholesterol, were lower than estimates available in an online biological variation database. These new reference data deliver revised and more exacting analytical performance specifications and reference change values, and thus, have direct relevance to diagnostics manufacturers, service providers, clinical users, and ultimately, patients.

Specifying a Gold-Standard for the Validation of Fetal Fraction Estimation in Prenatal Screening
By Nicholas J Wald, et al.

The percentage of fetal DNA in maternal plasma, the fetal fraction, is important in interpreting cell-free DNA tests in prenatal screening. Various methods are available for estimating fetal fraction, but there is no gold standard against which these can be evaluated in all pregnancies. In this studied the authors specify a gold standard based on the fixed relationship between fetal fraction and the percentage of cell-free DNA fragments from chromosome 21 in Down syndrome pregnancies and the observed median value in unaffected pregnancies. The gold standard was used to evaluate a published method of estimating fetal fraction.