Clinical Chemistry

October 2013 Audio Summary

This is the October 2013 issue of *Clinical Chemistry*: Volume 59, Issue 10.

On the cover this month: Ulf-Håkan Stenman. As a young man, Stenman, known to his friends as Uffen, loved to build model planes and draw sketches of cars. In fact, his dream was to be a car designer. Fortunately for us, he followed a career in clinical chemistry. He is best known for his work on tumor markers, especially his discoveries that prostate specific antigen (or PSA) forms a complex with the enzyme alpha 1-antichymotrypsin, and that the proportion of this PSA complex, relative to free PSA, is higher in men with prostate cancer. But there is more to Uffen than science, as readers of this month's Inspiring Minds article will find out.

Glycemic Control in the 12 Months following a Change to SI Hemoglobin A_{1c} Reporting Units
By Eric S. Kilpatrick, et al.

The change in hemoglobin A_{1c} units to SI has been a major event in many countries, with the concern that any subsequent confusion with the new units could be detrimental to patient care.

This study looked at hemoglobin A_{1c} before and after the change of units in a large United Kingdom center and found that a move to SI hemoglobin A_{1c} reporting did not lead to any marked short-term deterioration in glycemia or a different hemoglobin A_{1c} outcome in patients with initial poor glucose control. If replicated elsewhere these findings suggest that, with proper education, such a unit change can be safely made.

High-Throughput Immunoassay for the Biochemical Diagnosis of Friedreich Ataxia in Dried Blood Spots and Whole Blood
By Devin Oglesbee, et al.

This manuscript details the analytical and clinical validation of a high-throughput immunological assay for the detection of a progressive neurological disease, Friedreich ataxia, in dried blood spot or whole blood specimens. It is the first description of a high-throughput assay applicable to population screening of individuals with Friedreich ataxia. From the analysis of blood frataxin concentrations, the authors demonstrate that it is possible to diagnose this neurological disease from a sample type that is presently used for newborn screening for metabolic conditions. Thus, this study will open the door to future work on population screening presymptomatic newborns.

Single-Nucleotide Polymorphisms and Other Mismatches Reduce Performance of Quantitative PCR Assays
By Steve Lefever, et al.

The immense increase in number of known single nucleotide polymorphisms makes designing primers annealing to single nucleotide polymorphism-free regions challenging. Using an innovative approach combining both synthetic primers and templates, this study assesses the impact of mismatches in primer annealing sites on quantitative PCR performance. Results show the impact is most pronounced in relation to the number of mismatches or their distance to the 3'

primer end, with higher mismatch numbers (>3) completely blocking amplification. This, together with the concentration independent effect of single mismatches, can help chart mismatch behaviour in quantitative PCR reactions and increase primer design success rate for high density single nucleotide polymorphism regions.

A Comprehensive Assay for *CFTR* Mutational Analysis Using Next-Generation Sequencing
By Ahmad N. Abou Tayoun, et al.

This manuscript describes validation of a next generation sequencing assay to identify mutations in the *CFTR* gene. The authors utilized previously tested patient samples and cell lines with known mutations to validate this assay on the Ion Torrent PGM platform. This assay was found to be robust and adaptable to a busy clinical lab setting.

Deregulated Serum Concentrations of Circulating Cell–Free MicroRNAs miR-17, miR-34a, miR-155, and miR-373 in Human Breast Cancer Development and Progression
By Corinna Eichelser, et al.

The aim of this study was to evaluate whether changes in the levels of circulating microRNAs in the blood are associated with a particular breast cancer subtype. RT-qPCR was performed to quantify a panel of six microRNAs. Serum levels of miR-17, miR-34a, miR-155 and miR-373 were found associated with breast cancer development and progression. This is the first study showing that miR-10b, miR-17, miR-34a and miR-373 potentially may serve as novel blood-based molecular biomarkers for breast cancer.

Incremental Prognostic Value of Biomarkers beyond the GRACE (Global Registry of Acute Coronary Events) Score and High-Sensitivity Cardiac Troponin T in Non-ST-Elevation Acute Coronary Syndrome
By Christian Widera, et al.

Guidelines recommend using validated risk scores and a high-sensitivity cardiac troponin assay for risk stratification in non-ST-elevation acute coronary syndrome. The incremental prognostic value of biomarkers in this context is unknown. The authors of this study measured cardiac troponin T with a high-sensitivity assay and calculated the GRACE score in 1146 patients with non-ST-elevation acute coronary syndrome. They also measured the circulating concentrations of eight additional biomarkers. All biomarkers added prognostic information to GRACE and high-sensitivity cardiac troponin T. The incremental information offered by individual biomarkers varied considerably however. This study provides the first comparative analysis of the added value of biomarkers in non-ST-elevation acute coronary syndrome in the current clinical environment.

Simple Paper-Based Test for Measuring Blood Hemoglobin Concentration in Resource-Limited Settings
By Xiaoxi Yang, et al.

In this article the authors describe a simple, low-cost assay for measuring blood hemoglobin concentrations at the point of care in resource-limited settings. Devices currently available for measuring hemoglobin are prohibitively expensive for resource-limited settings, which precludes proper diagnosis of anemia in low-income developing countries. The authors developed a paper-based hemoglobin assay that measures hemoglobin by simply quantifying the stain produced by the blood sample on paper. The hemoglobin measurements performed by the paper-based assay correlated well with a conventional hematology analyzer. This study demonstrates the feasibility of the novel paper-based hemoglobin assay that should be useful in resource-limited settings.

Quantification of a Proteotypic Peptide from Protein C Inhibitor by Liquid Chromatography–Free SISCAPA-MALDI Mass Spectrometry: Application to Identification of Recurrence of Prostate Cancer
By Morteza Razavi, et al.

In this article the authors describe a new liquid chromatography-free, mass spectrometry-based method that has a short sample cycle time, thus allowing biomarker validation using large sample sets. The assay was applied to the measurement of a prospective biomarker peptide from Protein C inhibitor in sera from patients with prostate cancer who had been treated with radiation with or without androgenic hormones. Patients with cancer recurrence showed decreased serum concentrations of the Protein C inhibitor peptide analyte within 18 months of treatment, whereas peptide concentrations remained increased in the sera of patients who did not experience cancer recurrence. The results suggest that the Protein C inhibitor peptide may be a biomarker for prediction of recurrence of prostate cancer, justifying further exploration using larger numbers of patients.

Circulating Fragments of N-Terminal Pro–B-Type Natriuretic Peptides in Plasma of Heart Failure Patients
By Jared Yong Yang Foo, et al.

The use of nonstandardized NT-proBNP assays with large intraindividual and interindividual variations can contribute to the misdiagnosis of heart failure. The authors of this study sought to identify and quantify the circulating forms of NT-proBNP in heart failure patients. Mass spectrometry analysis identified the presence of N- and C-terminally processed forms of circulating NT-proBNP. In-house developed AlphaLISA immunoassays demonstrated that the antibodies targeting NT-proBNP13-76 fragment gave the highest concentration whereas the antibodies targeting the NT-proBNP1-45 fragment gave the lowest concentration in circulation of heart failure patients. These findings will assist in the development of next generation NT-proBNP immunoassays to detect the presence of heart failure.