Clinical Chemistry

November 2016 Audio Summary

This is the November 2016 issue of *Clinical Chemistry*, Volume 62, Issue 11.

ON THE COVER: Catharine Sturgeon, consultant clinical scientist at the Royal Infirmary of Edinburgh and director of the National External Quality Assessment Service proficiency-testing center. A product of a nomadic youth, Dr. Sturgeon's career has been slightly off the beaten path. In fact, how she ended up in clinical chemistry is a rather nomadic story. Knowing absolutely nothing about chemistry, she decided at the age of 4 that she liked chemistry because they got to wear white coats. But when the time came, studying chemistry was far different than liking chemistry, as Catharine found out. To learn how the story ends, see our *Inspiring Minds* feature in this month's issue of *Clinical Chemistry*.

Is the $1000 Genome as Near as We Think? A Cost Analysis of Next-Generation Sequencing
By Kirsten JM van Nimwegen, et al.

Although several commercial parties report breaking the $1,000 barrier for sequencing a human genome, a valid cost overview for next generation sequencing is currently lacking. This study examined the costs of different next generation sequencing applications. To anticipate future developments in costs, parameter sensitivity analyses were performed. Per-sample costs were €1,669 for whole-genome sequencing, €587 for whole-exome sequencing, and €333 for targeted gene panel. To reach the $1,000 per genome price barrier, long-term and efficient use of the sequencing equipment will be needed, as well as large reductions in capital, and especially consumable costs.

Clinical Next Generation Sequencing Outperforms Standard Microbiological Culture for Characterizing Polymicrobial Samples
By Lisa A. Cummings, et al.

Next generation sequencing generates a reproducible, analytically sensitive, and accurate assessment of the identity and relative abundance of organisms present in polymicrobial samples, and outperforms standard non-selective culture. Interpretation of standard culture results, where multiple organisms are present in samples plated onto rich non-selective media, is much more complicated and biased than commonly presumed. In this study the authors confirm these observations in clinical samples. The data demonstrate the opportunity to use next generation sequencing to redefine the catalog of potential pathogens in human disease states and expand our view of polymicrobial contributions to the pathogenesis of infection.

Effect of Participating in a Quality Improvement System over Time for Point-of-Care C-Reactive Protein, Glucose, and Hemoglobin Testing
By Tone Bukve, et al.

The present study evaluates results from 19 external quality assessment surveys concerning point-of-care CRP, glucose, and hemoglobin testing in primary care. The probability of having poor performance decreased depending on the number of years the participants took part in the quality improvement system. The following independent factors predicted good participant performance for all three analytes: type of instrument, the number of times performing external quality assessments, performing internal quality control weekly, performing 10 or more tests weekly, and having laboratory-qualified personnel perform the tests.

Detection of KRAS Mutations in Circulating Tumor DNA by Digital PCR in Early Stages of Pancreatic Cancer
By Nora Brychta, et al.

In this study the authors show the feasibility of diagnosis of early stage pancreatic cancers based on KRAS mutations in circulating tumor DNA. Digital PCR can detect single mutant alleles in a large background of wild-type DNA. To examine the clinical utility of digital PCR, matched tumor and plasma samples from the same patient were tested. KRAS mutations were identified in 72% of the tumor samples. Analysis of the matching plasma samples showed KRAS-mutated circulating tumor DNA in 35% of these cases. The diagnosis of early stage pancreatic cancer by KRAS mutations in circulating tumor DNA appears feasible but is limited by the total tumor cell content of the primary tumor.

Analysis of Base-Position Error Rate of Next-Generation Sequencing to Detect Tumor Mutations in Circulating DNA
By Nicolas Pécuchet, et al.

In this study the authors aimed to detect mutations in circulating tumor DNA using targeted next-generation sequencing. They developed a method based on quantification of the error rate of each base position. To identify mutations, a binomial test was used to compare the minor-allele frequency to control error rate at each base position. This method was applied to plasma samples from cancer patients. It detected mutations at allele frequencies as low as 3 per thousand for single nucleotide variants and 1 per thousand for insertions and deletions. The method showed strong agreement with the base-position error rate method.

Accession of Tumor Heterogeneity by Multiplex Transcriptome Profiling of Single Circulating Tumor Cells
By Tobias M Gorges, et al.

In this study the authors established reliable workflows to simply the study of multi-marker profiles of single circulating tumor cells from patients with cancer. In principle, their assay could be combined with any circulating tumor cell enrichment system that provides circulating tumor cells with good RNA quality. Multivariate analysis of expression profiles indicated that subgroups of circulating tumor cells with different phenotypes were present within each patient. Intra-patient heterogeneity of circulating tumor cells might contribute to the evolution of resistance to therapy. This hypothesis can be now tested in future clinical studies with established endpoints such as time-to-progression or overall survival.

Sandwich ELISA Using a Mouse/Human Chimeric CSLEX-1 Antibody
By Jun Yamashita, et al.

This article describes the development of an anti-sialyl Lewis X antibody using unique expression system in transgenic silkworms. Many anti-sialyl Lewis X antibodies (abbreviated hereafter as anti-sLeX antibodies) are IgM isoforms and are not preferred for the establishment of an assay because the bulkiness generally causes worse accessibility to the antigen. To solve this problem, the authors developed an anti-sLeX mouse/human chimeric IgG antibody, CH-CSLEX-1. Results demonstrated that CH-CSLEX-1 allowed the establishment of a highly sensitive and specific sandwich ELISA for sLeX that was not affected by human anti-mouse antibodies. The improved clinical relevancy of the CH-CSLEX-1 assay should be confirmed by measuring a statistically sufficient number of specimens.

Glycated Albumin Identifies Prediabetes Not Detected by Hemoglobin A1c: The Africans in America Study
By Anne E Sumner, et al.

In Africa, 70% of people with diabetes are undiagnosed. Contributing to this low level of detection is the fact that current diagnostic tests for the detection of hyperglycemia perform suboptimally in Africans. Previous research in Africans demonstrated that to detect hyperglycemia, fasting glucose, and hemoglobin A1c had sensitivities of only 30% and 50%, respectively. This study evaluated the diagnostic efficacy of glycated albumin. The results indicated that glycated albumin identifies a substantial number of non-obese Africans with prediabetes not detected by hemoglobin A1c. Therefore, hemoglobin A1c had a diagnostic sensitivity of 45%, glycated albumin of 34%, and the combined tests of 72%. This work has public health implications for Africans, and low income countries in which the prevalence of diabetes is high in nonobese individuals.