Clinical Chemistry

May 2013 Audio Summary

This is the May 2013 issue of *Clinical Chemistry*: Volume 59, Issue 5.

On the cover this month, Eleftherios Diamandis. A Cyprian scientist. A soccer player. A tennis nut. A chemist who originally did not choose chemistry. A trumpeter. An expert in prostate-specific antigen and kallikreins. A scientist who named his laboratory after a 1970s rock band. A purveyor of slightly cheesy rock music videos. A grandfather. And that is just half of the story. Read more about this eminent scientist in this month's *Inspiring Minds*.

Low Plasma 25-Hydroxyvitamin D and Risk of Tobacco-Related Cancer

By Shoaib Afzal, et al.

Worldwide, both vitamin D deficiency and tobacco smoking are major risk factors for disease, and this study provides new evidence for the significance of vitamin D in cancers caused by smoking. The study utilized data from a large cohort of 9,791 participants from the general population, followed for up to 28 years without any loss to follow-up. The authors found that the risk of tobacco-related cancers was increased by 80% in those who were deficient in vitamin D. The lower plasma 25-hydroxyvitamin D concentrations were associated with higher risk of tobacco-related cancers, but not with risk of other cancers.

Targeting the Circulating MicroRNA Signature of Obesity

By Francisco Ortega, et al.

Genomic studies using adipose tissue from obese subjects have yielded important insights into the pathogenesis of obesity. New tools for genomic analyses such as microRNA profiling may not only solve common problems in clinical practice but also reveal new therapeutic targets. The authors present a careful comparative study which provides, for the first time, a set of circulating microRNAs significantly deregulated in severe obesity. The effects of surgery and diet-induced weight loss on circulating microRNAs were also investigated and further validated in independent cohorts. The findings reported here have potential prognostic and therapeutic value in the setting of obesity.

Vitamin D and Mortality: A Mendelian Randomization Study

By Olivia Trummer, et al.

Decreased 25-hydroxyvitamin D concentrations have been associated with mortality rates, but it is unclear whether this association is causal. The authors performed a Mendelian randomization study and analyzed whether 3 common single-nucleotide polymorphisms associated with circulating 25-hydroxyvitamin D concentrations are causal for mortality rates. In this investigation, these genetic variants associated with 25-hydroxyvitamin D concentrations were not found predictive of all-cause mortality, cardiovascular mortality, or noncardiovascular mortality. This suggests that low 25-hydroxyvitamin D concentrations are associated with but unlikely to be causal for higher mortality rates.

Diagnosis of 5α-Reductase 2 Deficiency: Is Measurement of Dihydrotestosterone Essential?
by Angel O.K. Chan, et al.

This paper examines the clinical value of dihydrotestosterone in the diagnosis of 5α-reductase deficiency, since testing for this hormone is not widely available. The authors performed a review on local patient data and published medical literature and observed that a majority of the local and reported cases did not rely on dihydrotestosterone testing for diagnosis. Alternative means should be considered for diagnosing this condition.

Laboratory Assessment of Novel Oral Anticoagulants: Method Suitability and Variability between Coagulation Laboratories
By Tuukka Helin, et al.

This survey assessed the effects of novel oral anticoagulants dabigatran and rivaroxaban on the coagulation screening tests international normalized ratio, prothrombin time, and activated partial thromboplastin time and on specific assays thrombin time and anti-factor Xa activity. Samples spiked with dabigatran or rivaroxaban were sent to European coagulation laboratories in 10 different countries as part of an external quality assessment round by Labquality Ltd. A wide variety of reagents was used for the coagulation screening tests, and results varied widely. Few laboratories applied specific assays. The results of this survey show that laboratories must be aware of the sensitivity of the assays they are using with the novel oral anticoagulants and interpret accordingly.

Multiplex Picoliter-Droplet Digital PCR for Quantitative Assessment of DNA Integrity in Clinical Samples
by Audrey Didelot, et al.

Assessment of DNA integrity and quantity remains a bottleneck for molecular genotyping technologies including next-generation sequencing. In particular, DNA extracted from paraffin-embedded tissues is often compromised, leading to unpredictable sequencing data. Here the authors describe a picodroplet-based digital PCR method that enables the simultaneous detection of DNA integrity and quantity of amplifiable DNA. The multiplex procedure was validated with fragmented genomic DNA. Tumor samples were then tested, with next-generation sequencing confirming the results. In addition to next-generation sequencing, such a procedure is well suited for the assessment of DNA integrity as a biomarker of cancer.

Quantification of 5-Methylcytosine and 5-Hydroxymethylcytosine in Genomic DNA from Hepatocellular Carcinoma Tissues by Capillary Hydrophilic-Interaction Liquid Chromatography/Quadrupole Time-of-Flight Mass Spectrometry
By Ming-Luan Chen, et al.

5-hydroxymethylcytosine modifications are known to be prevalent in DNA of embryonic stem cells and neurons, but the distribution of 5-hydroxymethylcytosine in human liver tumor has not been rigorously explored. The authors of this study developed an ultra-sensitive method based on mass spectrometry for the detection of 5-hydroxymethylcytosine from hepatocellular carcinoma tumor tissues. Their data demonstrated a 4-to-5-fold lower 5-hydroxymethylcytosine content in hepatocellular carcinoma tumor tissues as compared with tumor adjacent tissues. In addition, 5-hydroxymethylcytosine level was highly correlated with tumor stages. The significant depletion of 5-hydroxymethylcytosine in hepatocellular carcinoma could be a potential biomarker for the early detection and prognosis of hepatocellular carcinoma.

Preanalytical Aspects and Sample Quality Assessment in Metabolomics Studies of Human Blood
by Peiyuan Yin, et al.

Metabolomics is a powerful tool that is increasingly used in clinical research, but excellent sample quality is essential. This study set out to identify critical preanalytical steps and biomarkers that reflect preanalytical inaccuracies using a nontargeted liquid chromatographic-mass spectrometric metabolomics approach. This work led to the following recommendations for the preanalytical phase of nontargeted metabolomics studies: test the blood collection tubes, avoid hemolysis, place whole blood immediately in ice water, use EDTA plasma, and preferably use nonrefrozen biobank-samples. To exclude outliers due to preanalytical errors, the biomarker signal intensities reflecting systematic as well as accidental and preanalytical inaccuracies should be inspected prior to bioinformatics data processing.