Clinical Chemistry

August 2018 Audio Summary

This is the August 2018 issue of *Clinical Chemistry*, Volume 64, Issue 8.

ON THE COVER Opium Poppy Pods (*Papaver somniferum*). Opiates and synthetic opioids are abused by millions worldwide. For this reason, these drugs are included in most toxicology screens. Although the natural opiates (e.g., morphine) can be readily detected by common immunoassay screens, these immunoassays fail to detect synthetic opioids because they often have little structural homology to morphine. The lengthy process of developing new immunoassays, the rapid increase in the number and variety of new synthetic opioids, and the lack of certified reference materials for adding to mass spectral libraries adds to the challenge. This issue of *Clinical Chemistry* contains the description of a novel bioassay that uses activity-based screening as the principle for detecting the presence of opiates/ opioids not based on structure but on activation of the μ-opioid receptor. In this bioassay, this activation ultimately leads to the production of a bioluminescent signal that can be read out with a standard luminometer.

EurA1c: The European HbA1c Trial to Investigate the Performance of HbA1c Assays in 2166 Laboratories across 17 Countries and 24 Manufacturers by Use of the IFCC Model for Quality Targets
By The EurA1c Trial Group.

In a unique collaboration of IFCC and 17 countries, the performance of HbA1c assays in two thousand laboratories was evaluated. One out of twenty laboratories did not meet the IFCC criterion. Differentiation by country and by manufacturer showed substantial differences between countries and also between manufacturers. The major contribution to analytical error derived from between laboratory variation rather than from bias. These data show that standardization can be achieved in all countries and by nearly all manufacturers. Evaluation of fresh whole blood specimens and lyophilized hemolysates prepared from the same blood demonstrated that – with some limitations- both matrixes are suitable for external quality assessment and proficiency testing.

Commutability Assessment of Candidate Reference Materials for Pancreatic α-Amylase
By Liesbet Deprez, et al.

In this study the authors performed a commutability study with five candidate reference materials for pancreatic α-amylase; four materials had an artificial matrix and 1 was based on serum. Data were analyzed following the approach described in the guideline CLSI EP30-A and according to the recommendations of the IFCC Working Group on Commutability. One candidate reference material with an artificial matrix showed a good commutability profile similar to that of the material based on serum. This study shows that a reference material intended for trueness control of the reference measurement procedure can also be suitable for calibration and trueness control of routine measurement systems.

Dietary Intakes and Circulating Concentrations of Branched-Chain Amino Acids in Relation to Incident Type 2 Diabetes Risk Among High-Risk Women with a History of Gestational Diabetes Mellitus
By Dierdre K. Tobias, et al.

In this study the authors prospectively evaluated both the dietary intakes and circulating plasma metabolite concentrations of branched-chain amino acids, in relation to type 2 diabetes among high-risk women in the Nurses' Health Study II. Circulating branched-chain amino acid metabolites have been consistently associated with type 2 diabetes risk. The authors simultaneously evaluated both dietary intakes and circulating concentrations of branched-chain amino acids in relation to risk of incident type 2 diabetes. Independent of body mass index and other risk factors, higher diet and plasma branched-chain amino acid metabolite concentrations were associated with an increased type 2 diabetes risk among women with prior gestational diabetes, supporting the idea that impaired branched-chain amino acid metabolism may confer type 2 diabetes risk.

Association of Tryptophan Metabolites with Incident Type 2 Diabetes in the PREDIMED Trial: A Case–Cohort Study
By Edward Yu, et al.

The authors of this study investigated the association several plasma metabolites related to tryptophan with diabetes using a case-cohort design. Baseline tryptophan and 1-year increases in quinolinic acid were found predictive of diabetes incidence. Various metabolites further predicted the homeostatic model assessment for insulin resistance. Tryptophan metabolites may play an important role in diabetes pathogenesis.

Activity-Based Concept to Screen Biological Matrices for Opiates and (Synthetic) Opioids
By Annelies Cannaert, et al.

Highly potent synthetic opioids, which mimic the effects of heroin and morphine, are a growing health threat. Detection of novel opioids remains challenging as new compounds continue to enter the market. Here the authors present a novel screening method for the detection of opiates and (synthetic) opioids, not relying on antibody-based or mass spectrometry-based recognition of the structure of these compounds, but based on their opioid activity. The performance of the opioid reporter bioassay was evaluated on 107 blood samples from postmortem toxicology casework. This approach may be a useful tool to investigate potential opioid intoxications in clinical and forensic settings.

Clinical Assay for AFP-L3 by Using Multiple Reaction Monitoring–Mass Spectrometry for Diagnosing Hepatocellular Carcinoma
By Hyunsoo Kim, et al.

Lens culinaris agglutinin-reactive fraction of α-fetoprotein, or AFP-L3, is a serum biomarker for hepatocellular carcinoma. AFP-L3 is typically measured by liquid-phase binding assay or LiBA. Here the authors developed and validated a multiple reaction monitoring mass spectrometry assay for quantifying AFP-L3 in human serum to diagnose early-stage hepatocellular carcinoma. LiBA, the current standard method, cannot measure AFP-L3 concentrations accurately owing to its low sensitivity. The authors addressed this issue with immunoprecipitation in conjunction with fractionation with lens culinaris agglutinin lectin. Consequently, the multiple reaction monitoring mass spectrometry assay identified hepatocellular carcinoma patients that were missed by LiBA. In addition, they validated this approach in accordance with several multinational guidelines.

Liver- and Colon-Specific DNA Methylation Markers in Plasma for Investigation of Colorectal Cancers with or without Liver Metastases
By Wanxia Gai, et al.

In cancer patients, an increased amount of DNA is released to the circulation by the tumor cells and the tissues invaded by the cancer. In this study, the authors used colorectal cancer as a model to illustrate the use of tissue-specific DNA measurement for the investigation of cancer metastases. They developed a droplet digital PCR to measure the plasma concentration of DNA carrying liver-specific methylation signature, and showed that patients with liver metastases had significantly higher plasma concentrations of liver-derived DNA than those without liver metastases. This approach is generalizable for investigating cancer metastases to many other distant sites.