Clinical Chemistry

June 2018 Audio Summary

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ON THE COVER Damage to the brain of a patient with Alzheimer's disease. Alzheimer's is the most common form of dementia. Symptoms usually develop slowly and get worse over time, becoming severe enough to interfere with daily tasks. Ongoing efforts have sought to identify markers that are predictive and potentially useful for monitoring disease progression to aid in treatment intervention studies. One such marker is neurogranin, a postsynaptic protein involved in synaptic plasticity. This issue of *Clinical Chemistry* contains the results of a study of the performance of 3 commonly used neurogranin assays in the same cohort of patients to improve the interpretability of CSF neurogranin test results.

Noninvasive Detection of Cocaine and Heroin Use with Single Fingerprints: Determination of an Environmental Cutoff
By Mahado Ismail, et al.

The authors present a novel method for testing for cocaine and heroin from a single fingerprint, and explore the possibility of establishing an environmental cut-off for drug testing. Fingerprint samples were collected from the hands of 50 non-drug users to establish an environmental cut-off and testing protocol. The detection rate for washed hands of patients was 87.5% for cocaine and 100% for heroin, after application of the cut-off. Fingerprints show enhanced concentrations of cocaine, heroin and their respective metabolites in patients who testified taking the substances, compared with the background population surveyed, and a cut-off could be established.

Activity-Based Detection of Cannabinoids in Serum and Plasma Samples
By Annelies Cannaert, et al.

Synthetic cannabinoids continue to be the largest group of new psychoactive substances monitored in Europe. The rapid proliferation of novel analogs makes the detection of these new derivatives challenging and has initiated considerable interest in the development of so-called 'untargeted' screening strategies. Here, the authors developed an improved activity-based cannabinoid reporter assay and applied it for the detection of consumption of synthetic cannabinoids. The potential of bioassays to serve as a first-line screening tool for (synthetic) cannabinoid activity in serum or plasma was demonstrated. These bioassays may complement conventional targeted and untargeted analytical assays and/or precede analytical (mass spectrometry based) confirmation.

Neurogranin as Cerebrospinal Fluid Biomarker for Alzheimer Disease: An Assay Comparison Study
By Eline A J Willemse, et al.

An in-depth investigation of the analytical and diagnostic performance of three different immunoassays for neurogranin was performed in the same cohort of patients to improve the interpretability of CSF results. The three assays targeting different epitopes on neurogranin resulted in different absolute values, but carried similar information for dementia diagnostics. These findings may facilitate implementation of neurogranin as an additional CSF biomarker for dementia as all the assays can predict dementia.

Ultrasensitive Detection of Chimerism by Single-Molecule Molecular Inversion Probe Capture and High-Throughput Sequencing of Copy Number Deletion Polymorphisms
By David Wu, et al.

Genomic chimerism, cell populations from different people within the same body, is an important marker in multiple disease states, ranging from graft injury to cancer relapse. To improve diagnosis of genomic chimerism, the authors of this study performed next-generation sequencing of polymorphic genomic loci which are variably present or absent in given individuals, providing a universal detection platform independent of disease phenotype. They achieved ultrasensitve detection of chimeric cell populations and were able to identify trace residual patient cells in clinical samples from hematopoietic stem cell transplantation patients during remission. This approach will be generally useful and will enhance diagnosis of many medical conditions.

Accurate Pan-Cancer Molecular Diagnosis of Microsatellite Instability by Single-Molecule Molecular Inversion Probe Capture and High-Throughput Sequencing
By Adam Waalkes, et al.

Microsatellite instability is a molecular diagnostic finding that predicts tumor response to immune checkpoint pathway immunotherapies, independent of cancer type. However, there remains a need for microsatellite instability diagnostics that are low cost, have high accuracy, and are generalizable across cancer types. Here the authors have developed a next-generation sequencing assay for microsatellite instability using highly multiplexed targeting of informative microsatellite loci. The assay is analytically sensitive to low numbers of microsatellite instability positive cell populations and demonstrates superior performance to existing standards-of-care as a pan-cancer diagnostic for microsatellite instability. The approach allows accurate, standardized, and economical screening of tumors for microsatellite instability, regardless of tissue of origin.

Cell-Free Plasma DNA for Disease Stratification and Prognosis in Head and Neck Cancer
By Markus A Schirmer, et al.

This paper suggests a new biomarker in head and neck cancer patients. In locally limited stages, lymph node involvement is the strongest established predictor for clinical outcome. However, the pre-surgery lymph node status is often difficult to assess and clinicians are conflicted on whether to perform a neck dissection. The authors of this study present a copy number instability score based on comprehensive sequencing of chromosomal aberrations in tumor-derived cell-free DNA. This score is shown to predict tumor-involved lymph nodes and patient overall survival better than established disease features rendering it a promising biomarker for disease stratification and personalizing treatment.