Clinical Chemistry

June 2017 Audio Summary

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ON THE COVER Mikhail Semyonovich Tsvet (1872–1919). Mikhail Tsvet's research into plant pigments led him to invent chromatography in 1903. His technique was largely ignored and only came into the mainstream after Martin and Synge obtained the Nobel Prize for describing the theory behind the separation of components in a mixture by having each solute distributed between a liquid mobile phase and a stationary phase. But perhaps Tsvet received the highest recognition of all: the inscription on his grave states, "He invented chromatography, separating molecules but uniting peoples." Chromatography has advanced substantially since its early days, with affinity chromatography becoming a rapidly expanding application of chromatographic separation to clinical and pharmaceutical analyses. This issue of *Clinical Chemistry* contains a comprehensive review of the various methods used to examine biological interactions by affinity chromatography, with an emphasis on the recent applications of high performance affinity chromatography.

Thrombin-Mediated Degradation of Human Cardiac Troponin T
By Ivan A Katrukha, et al.

This study examined the degradation of one of the key markers of acute myocardial infarction – cardiac troponin T. The authors observed that the pattern of degradation of troponin T depends on the type of blood sample used for analysis. In heparin plasma samples of acute myocardial infarction patients troponin T was present mostly as a full-sized molecule, while in serum samples it was present as a 29 kDa fragment. They found that this difference was due to the action of thrombin that cleaves troponin T between the arginine and serine amino acid residues at positions 68 and 69. This cleavage activity of thrombin should be considered during both the investigation of troponin T degradation and development of new methods of troponin T measurement.

Prognostic Value of Inflammatory and Cardiovascular Biomarkers for Prediction of 90-Day All-Cause Mortality after Acute Ischemic Stroke—Results from the Linz Stroke Unit Study
By Benjamin Dieplinger, et al.

There is an unmet need of accurate prediction of outcome after stroke. This study assessed the prognostic value of interleukin-6, D-dimer, amino-terminal-proBNP, high sensitivity cardiac troponin T, and soluble ST2 in 721 patients after acute ischemic stroke. Only interleukin-6, and amino-terminal-proBNP at admission were strong and independent prognostic biomarkers for 90-day all-cause mortality, and provided complementary prognostic information to the routinely used NIHSS stroke severity score. The study authors developed a novel multi-marker model combining the NIHSS score, interleukin-6, and amino-terminal-proBNP, that allowed simple and accurate risk stratification. The multi-marker approach they developed needs further validation in independent cohorts, and ultimately, as part of a decision-making process.

Development of a BNP1-32 immunoassay that does not cross-react with proBNP
By Lynley K Lewis, et al.

Plasma B-type natriuretic peptide concentration, abbreviated BNP, reflects cardiac dysfunction and assists in the diagnosis and prognosis of heart failure. All current BNP assays measure not only BNP, but BNP metabolites and proBNP, thus overestimating bioactive BNP concentrations. The authors of this study developed a more specific BNP assay not influenced by proBNP or known circulating BNP metabolites. Their preliminary results indicate that this more specific assay distinguishes heart failure from control samples better than other BNP assays. This specific assay can now be used to evaluate larger study cohorts to assess its diagnostic and prognostic potential for heart failure compared to currently available assays.

Multiplex Tandem Mass Spectrometry Enzymatic Activity Assay for Newborn Screening of the Mucopolysaccharidoses and Type 2 Neuronal Ceroid Lipofuscinosis
By Yang Liu, et al.

Progress in the development and application of therapies for lysosomal storage disorders has created demand for fast and robust detection of low enzyme activities in dried blood spots from newborn populations. Here the authors report a new multiplex assay of six lysosomal enzymes in dried blood spots using new synthetic substrates in a format suitable for newborn screening. The analytical platform used was tandem mass spectrometry with liquid chromatography separation of enzyme products. Incubation of dried blood spots with an assay cocktail followed by separation and analysis gave activity readings that clearly distinguished affected children from a healthy cohort.

Single-Tube Dodecaplex PCR Panel of Polymorphic Microsatellite Markers Closely Linked to the DMPK CTG Repeat for Preimplantation Genetic Diagnosis of Myotonic Dystrophy Type 1
By Mulias Lian, et al.

Preimplantation genetic diagnosis of myotonic dystrophy type 1 currently utilizes conventional PCR to detect non-expanded alleles of the dystrophia myotonica protein kinase or DMPK gene, or triplet-primed PCR to detect the CTG-trinucleotide-repeat-expanded alleles of this gene, coupled with analysis of linked microsatellite markers, to increase diagnostic accuracy. Here the authors simplified the process of identification and selection of informative linked markers for application to the preimplantation genetic diagnosis, myotonic dystrophy type 1. Twelve markers with potentially high heterozygosity values and polymorphism information content were selected and optimized in a single-tube multiplex PCR panel. The multiplex PCR panel was found suitable for use either as a stand-alone linkage-based preimplantation genetic diagnosis assay or as a complement to DMPK CTG repeat expansion-mutation detection.

Biological Variation Estimates Obtained from 91 Healthy Study Participants for 9 Enzymes in Serum
By Anna Carobene, et al.

This paper presents new biological variation estimates with confidence limits for nine enzymes obtained by examining a cohort of 91 healthy individuals enrolled in the European Biological Variation Study. The study participants were phlebotomized for 10 consecutive weeks and their sera were stored at -80 degrees Celsius prior to analysis in duplicate. Reference materials were analyzed to obtain assay traceability. The results showed that all within-subject, and most between-subject biological variation estimates for these enzymes were clearly lower than those presented in the online 2014 updated biological variation database. The data obtained in this study can be used to derive new analytical performance specification for systems to be used internationally.

Plasma Urate, Cancer Incidence, and All-Cause Mortality: A Mendelian Randomization Study
By Camilla J Kobylecki, et al.

The authors of this study tested the hypothesis that high concentrations of plasma urate are associated with high cancer incidence and all-cause mortality using a Mendelian randomization design in 86,210 individuals from the Copenhagen General Population Study. The study authors found that high plasma urate was both observationally and genetically associated with high cancer incidence and high all-cause mortality, suggesting causal relationships. Replication of these findings in independent populations could suggest lowering of plasma urate as a potential target for cancer prevention as well as a role for plasma urate in risk prediction models for cancer incidence and all-cause mortality.