Clinical Chemistry

October 2017 Audio Summary

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ON THE COVER Ian Young. “When life gives you lemons, make lemonade” is an expression attributed to Dale Carnegie, who used it in his 1948 book *How to Stop Worrying and Start Living*. Ian Young is the embodiment of what Dale Carnegie wrote about. Growing up in Belfast, Northern Ireland, Ian personally witnessed the horrors of the social war that tore apart his country. Yet, the right high school teacher and, more importantly, Ian’s can-do attitude, turned adversity into a biochemistry major from Queen’s University. While at Queen’s University, Ian showed up late to a meeting where research projects were being assigned, ending up with a project on cattle. Yet, he was able to turn what others might consider a dead end project into a subsequent exploration of the importance of free radicals in diabetes and cardiovascular disease, for which he is now internationally recognized. And that is just a small part of what you will read about in our latest *Inspiring Minds* article.

Gene Expression Signatures in Circulating Tumor Cells Correlate with Response to Therapy in Metastatic Breast Cancer
By Maren Bredemeier, et al.

The authors of this study used a 46 gene qPCR panel for the characterization of circulating tumor cells from metastatic breast cancer patients undergoing palliative therapy. They investigated whether it is possible to predict treatment response based on gene expression, and whether differences in circulating tumor cell gene expression patterns could be identified in regard to therapy response. Expression of the ADAM metallopeptidase domain 17 gene appeared to be a key marker in distinguishing responders from non-responders, and, expression of the Keratin 19 gene was powerful in identifying circulating tumor cells. Circulating tumor cell gene expression profiling in the follow-up of metastatic breast cancer during palliative treatment could be a promising diagnostic tool to predict response or resistance to therapy, assuming the findings of this study can be confirmed in an independent validation set.

Diagnostic Performance of High Sensitivity Compared with Contemporary Cardiac Troponin I for the Diagnosis of Acute Myocardial Infarction
By Yader Sandoval, et al.

Studies comparing high-sensitivity cardiac troponin vs. contemporary cardiac troponin for diagnosing myocardial infarction (abbreviated MI) are needed. In a prospective, observational cohort study of consecutive emergency department patients, this study demonstrated that in the context of a normal electrocardiogram, instead of taking greater than 6h to safely rule-out MI using contemporary cardiac troponin I, the same performance can be obtained within 3h using high sensitivity cardiac troponin I with two measurements at 0 and 3h. Utilizing such an approach may expedite discharge, reduce overcrowding, and improve resource utilization. For ruling-in MI, the use of serial changes or deltas in cardiac troponin concentrations was found to improve the specificity for diagnosing MI, but the delta criteria varied according to whether the initial sample concentration was normal or increased.

Multiplexed Elimination of Wild-Type DNA and High-Resolution Melting Prior to Targeted Resequencing of Liquid Biopsies
By Ioannis Ladas, et al.

The use of clinical samples and circulating DNA collected from liquid biopsies for diagnostic and prognostic applications in cancer is burgeoning, and improved methods that reduce the influence of excess wild-type portion of the sample are desirable. This study presents an improved approach to enrich mutation-containing sequences using enzymatic degradation of wild-type DNA. Mutation enrichment is combined with high-resolution-melting performed in multiplexed closed-tube reactions, as a rapid, cost-effective screening tool prior to targeted re-sequencing.

DNA of Erythroid Origin is Present in Human Plasma and Informs the Types of Anemia
By W.K. Jacky Lam, et al.

This manuscript reports, for the first time, that DNA of erythroid origin constitutes approximately 25% of the circulating DNA in healthy subjects. This conclusion has been reached through the development of novel methylation markers for cells of the erythroid lineage. The data are cross-validated in three different sets of markers. Furthermore, the study authors have demonstrated that aberrant levels of erythroid DNA in plasma can be found in patients with anemia. Of great interest, measurements of circulating erythroid DNA allow differentiation between anemias of different etiologies. These developments raise the possibility of noninvasive bone marrow assessment and would have numerous applications in many branches of medicine.

High-Speed Melting Analysis: The Effect of Melting Rate on Small Amplicon Microfluidic Genotyping
By Robert J Pryor, et al.

DNA melting for genotyping typically takes 20-60 minutes on most commercial instruments. By using precise temperature control on a microfluidic instrument, the authors of this study demonstrated that this time can be reduced about 1000-fold. Indeed, for small amplicon genotpying, faster DNA melting is better than slower, conventional melting. High speed melting, along with extreme PCR, enables very rapid amplification and analysis for molecular diagnostics in less than one minute.

Surface Plasmon Resonance is an Analytically Sensitive Method for Antigen Profiling of Extracellular Vesicles
By Elmar L. Gool, et al.

Clinical research on extracellular vesicles is hampered by their small size, low refractive index and low numbers of antigens. Current clinical laboratory compatible techniques lack sensitivity to fulfill the biomarker potential of extracellular vesicles. This article demonstrates how surface plasmon resonance can be used to perform extracellular vesicle phenotyping by comparing it to antigen exposure measured by flow cytometry. Furthermore, it highlights that surface plasmon resonance can obtain information about particle concentration, diameter and antigen exposure during an individual measurement. Surface plasmon resonance therefore has potential to become a valuable technique for characterization of extracellular vesicles.

Standardization of Free Thyroxine Measurements Allows the Adoption of a More Uniform Reference Interval
By Linde AC De Grande, et al.

The IFCC Committee for Standardization of Thyroid Function Tests intends to standardize free thyroxine immunoassays based on a multi-assay method comparison study using a clinically relevant panel and targets set by the reference measurement procedure. Recalibration of the participating assays to those targets significantly reduced their bias. A subsequent reference interval study showed that the reference interval determined by the reference measurement procedure is suitable for common use within a margin of 12.5%. This should facilitate the development of modern public health standards, such as clinical guidelines quoting fixed decision limits and integration of laboratory data in electronic patient records.