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ON THE COVER *Klebsiella pneumoniae bacterium*. The rapid identification of respiratory pathogens is important for providing targeted rather than empiric therapy. Intact protein profiling of cultured bacterial colonies using MALDI-TOF-MS has become a standard means to identify microorganisms, but the presence of defensins (potent antimicrobial peptides made within the body) compromises the ability of MALDI-TOF-MS to identify bacteria. This issue of *Clinical Chemistry* contains an article describing an alternative, proof-of-concept method for identifying unique peptide markers of five Gram-negative bacteria in bronchoalveolar lavage specimens by LC-MS/MS, including Klebsiella pneumoniae. In this new method intact bacterial cells are digested with trypsin without lysis, protein denaturation, disulfide reduction or alkylation, which may provide the basis for the development of a multiplexed assay for rapid and direct pathogen identification in bronchoalveolar lavage specimens by LC-MS/MS.

Overinterpretation of Research Findings: Evidence of "Spin" in Systematic Reviews of Diagnostic Accuracy Studies
By Trevor A McGrath, et al.

The authors of this study sought to identify the frequency of overinterpretation (or 'spin') in systematic reviews of diagnostic accuracy studies. In their evaluation of 112 recently published diagnostic accuracy systematic reviews, the proportion of reviews identified as having at least one overinterpretation practice was 72%. The practice of frequent overinterpretation may lead to unjustified optimism about test performance in clinical practice and erroneous decisions and recommendations.

Lymphocyte Galactocerebrosidase Activity by LC-MS/MS for Post–Newborn Screening Evaluation of Krabbe Disease
By Hsuan-Chieh Liao, et al.

Newborn screening for Krabbe disease leads to the need for second-tier analysis for disease prognosis. Mass spectrometry has been shown to provide a much more accurate assay of the activity of the relevant enzyme, galactocerebrosidase (abbreviated GALC), than the existing radiometric assay. Here the authors describe a new mass spectrometry assay that better correlates with disease severity than the classic GALC assay. The assay should be useful to all newborn screening programs performing newborn screening for Krabbe disease.

Single-Nucleotide Polymorphism Leading to False Allelic Fraction by Droplet Digital PCR
By Eric Christenson, et al.

Mutation detection for cancer often relies upon sensitive and specific molecular probes. The authors of this paper used droplet digital PCR to assay for cancer mutations in cell free plasma DNA and found implausible results of a high allelic fraction with one patient sample. They sequenced this locus and discovered a SNP that interfered with assay performance. These results demonstrate the need for consideration of SNPs and other variants that could affect molecular assays leading to spurious results.

Stronger Together: Aggregated Z-values of Traditional Quality Control Measurements and Patient Medians Improve Detection of Biases
By Andreas Bietenbeck, et al.

This study analyzed traditional control measurements and medians of results from patients to facilitate the detection of biases. Measurements of five analytes were simulated with the newly developed software package "rSimLab". The required sample size to calculate meaningful medians was highly dependent on the ratio of the spread of sample values to their center. Control rules combined single quality control parameters. An algorithm similar to Westgard's rules applied a threshold to each parameter separately. A newly proposed aggregation of Z-values averaged the control parameters. Inclusion of patient medians improved bias detection for some analytes substantially. Patient result medians can supplement traditional quality control, and aggregations of Z-values are beneficial tools for quality control strategies to detect biases.

Rapid *RHD* Zygosity Determination Using Digital PCR
By Kelly A Sillence, et al.

Determination of paternal zygosity can be beneficial for the management of pregnancies at risk of hemolytic disease of the newborn and fetus. Current methods used to determine *RHD* zygosity, including assessment of the Rhesus box and real-time PCR, are complicated by the presence of variants and exponential PCR amplification. This small-cohort study reveals that digital PCR enables rapid determination of *RHD* zygosity and clearly distinguishes between hemizygous and homozygous individuals. In addition to paternal testing, further large scale validation studies could re-define the frequencies of RH haplotypes in different populations, which have previously been predicted solely using serological testing.

A Genoproteomic Approach to Detect Peptide Markers of Bacterial Respiratory Pathogens
By Honghui Wang, et al.

Rapid identification of bacteria causing hospital-acquired pneumonia may improve patient outcomes by providing a basis for targeted antimicrobial therapy. The direct application of MALDI-TOF to bronchoalveolar lavage is limited by host inflammatory cells, and by proteins that suppress bacterial spectra and generate peaks that interfere with pathogen identification. The authors of this study showed that a genoproteomic method for discovering bacterial peptide markers allowed for the identification of five pathogenic species, and demonstrated the simultaneous detection of Acinetobacter baumannii and Pseudomonas aeruginosa in spiked acellular inflammatory bronchoalveolar lavage. This approach provides the basis for a rapid method of identifying bacterial pathogens in bronchoalveolar lavage specimens.

Cardiac Troponins and Their Prognostic Importance in Patients with Suspected Acute Coronary Syndrome and Renal Dysfunction
By Kai M Eggers, et al.

The importance of the interrelation between troponin concentrations and renal dysfunction in patients with suspected acute coronary syndrome is not well established. In this large registry-based study, the authors investigated the association of troponin with renal dysfunction and 1-year mortality in patients admitted to coronary care units. Troponin T, in particular, when measured with a more sensitive assay, appeared to integrate prognostic information originating from both heart and kidneys to a greater extent than troponin I. However, these findings must be considered in the context of the severity of renal dysfunction and whether or not an acute coronary syndrome is present.