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Molecular Diagnostics: Going from Strength to Strength

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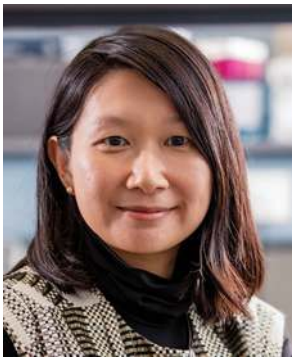
It has been 5 years since the last Molecular Diagnostics theme issue was published in *Clinical Chemistry*. In this new edition of the theme issue, the editors have highlighted some of the most exciting developments in the field. Because of the limitation of space within the issue, this selection is by no means exhaustive but, rather, is meant to be a sampler of some of the advances that will likely impact clinical practice.

Y.M. Dennis Lo

Linnea M. Baudhuin

In particular, with the maturation of massively parallel DNA sequencing technology, production of genomic data at the hospital or even population level is now feasible. Indeed, a number of countries around the world are engaged in pilot studies on population genomics, such as the 100 000 Genomes Project in the UK. Such developments necessitate debate of policies in genomic medicine. It is thus timely that in this issue, Klein discusses the policy challenges in genomic medicine *(1)*. With the ready elucidation of human genomic variations, there is also debate about the value of such information in the prediction of an individual's future health. In a Q&A article, Baudhuin et al. discuss the reality and hype of this potentially contentious area *(2)*.

Klaus Pantel



Rossa W.K. Chiu

With the generation of large amounts of clinical sequence data, quality assurance-related issues are also becoming increasingly important. One such example is the coverage of exome sequencing data studied by Gotway et al. in this issue *(3)*. Indeed, the generation of DNA sequencing data is only the first step in the process. The interpretation of sequencing data is often the more time-consuming and more expensive part of the process. Perhaps with the development of artificial intelligence, a significant part of this process would be automated in the future. In this regard, Sarmady et al. have explored the use of machine learning approaches in the classification of sequence variants *(4)*. Another important development in genomics is the potential of moving from genomic data generated from a population of cells to those generated from a single cell. Hence, it is timely that Valihrach et al. have studied the performance of different reverse transcriptases in single-cell transcriptomics analyses *(5)*.

One of the longstanding interests of *Clinical Chemistry* relates to cell-free nucleic acids. Noninvasive prenatal testing (NIPT) and cancer liquid biopsy are currently the 2 forerunners in this field. Hence, in a Reflections

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article, Dennis Lo has provided a personal view on some of the emerging developments in the field, especially as they relate to the study of the circulating DNA fragmentation, referred to as fragmentomics *(6)*. Although the first success of NIPT was to screen for fetal chromosomal aneuploidies, the next wave of clinical NIPT may cover the prenatal detection of single-gene disorders. Related to this, Chandler et al. have summarized their experience with the development of NIPT for cystic fibrosis *(7)*. With regard to the development of liquid biopsy for cancer, cell-free DNA is not the only approach; there are other strategies involving circulating tumor cells. Hence, we have a pair of Point/Counterpoint articles debating the pros and cons of cell-free vs cell-based approaches for liquid biopsy *(8, 9)*. Furthermore, 2 reviews addressing the biology and clinical applications of circulating tumor cells are presented *(10, 11)*.

Frederick S. Nolte

Carl T. Wittwer

The development of increasingly powerful methods for analyzing nucleic acids also allows pathogen-related nucleic acids to be examined for clinical applications. In this issue, multiple articles provide readers an up-to-date view on these major developments and how they are changing the paradigms for diagnosis and management of infectious diseases *(12–14)*.

Looking toward the future, are there novel therapeutic maneuvers that can be performed when a pathogenic variant is discovered through genome sequencing? The answer may lie in the development of practical tools of genome editing. One such technology that has taken the world by storm is the clustered regularly interspaced short palindromic repeats (CRISPR)—CRISPR-associated protein 9 (CRISPR-Cas9) technology. Hence, we are particularly excited to have an interview of George Church, one of the pioneers of genome editing in this issue *(15)*. Taken together, molecular diagnostics and genomic medicine are creating a paradigm shift in the future practice of medicine.

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