Molecular Diagnostics: At the Cutting Edge of Translational Research

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The goal of translational research is to advance basic research and new technology toward clinical utility. Molecular diagnostics focuses primarily on nucleic acids. Rapid advances in molecular diagnostics both enable basic research and result in practical diagnostic tests. This central position of molecular diagnostics in translational research has led us to bring you this special edition of Clinical Chemistry, Molecular Diagnostics: At the Cutting Edge of Translational Research.

We start the issue with a reminder that basic research is the foundation for advances in molecular diagnostics through an interview with Dr. Elizabeth Blackburn, a pioneer in telomere biology. This area of research holds promise in improving our understanding of aging, stem cell biology, and diseases like cancer and has stimulated the development of new molecular diagnostic tests.

Basic research has also provided us with new tools for molecular diagnostics, including high-density microarrays, massively parallel sequencing, extremely sensitive real-time PCR, and methods for rapid discrimination of very small differences between molecules. “Whole-genome” arrays are now available for mRNA expression, single-nucleotide polymorphism genotyping, and copy-number variants. Of course, clinical utility does not map directly to the number of tests performed or the number of spots on an array. A 100K chip does not imply 100K times the clinical value of a single test. Nevertheless, expression arrays are well suited to facilitate identification of important transcripts that may be included in reduced analysis sets for tumor subclassification. Genotyping arrays provide extraordinary power for association studies to map complex traits. Copy-number arrays have direct clinical applications with a resolution impossible by conventional cytogenetics. Next-generation sequencing leverages the power of parallel processing by use of emulsion or solid-phase PCR and even single-molecule sequencing. Hybrid applications have begun to appear: next-generation sequencing of mRNA can be used for expression analysis, and oligonucleotide arrays can be used for both single-nucleotide polymorphisms and copy-number variants.

Closed-tube amplification methods such as real-time PCR have enabled much of current molecular diagnostics. Very low concentrations of nucleic acids can be measured, promising early cancer detection, noninvasive prenatal diagnosis, minimal residual-disease monitoring, and personalized therapy. Nucleic acids turn up in unexpected places such as urine and saliva, and fetal nucleic acids appear in maternal plasma; all have diagnostic promise. New classes of nucleic acids, such as micro-RNAs, are being discovered that are highly specific as regulators, with strong potential as biomarkers. Very small differences between nucleic acids can be detected rapidly by mass spectroscopy or high-resolution melting.

Clinical chemistry today encompasses much more than measuring blood glucose. Nevertheless, like blood glucose, the best molecular correlates to disease are usually related to disease etiology. Molecular diagnostics will continue to evolve. Not all methods and markers will survive the test of time, but those that do will complement the rapidly expanding menu of molecular diagnostic tests focused on improving medical care and our quality of life.

As guest editors, we would like to dedicate this edition to our mentor and friend, David Bruns, former Editor-in-Chief of Clinical Chemistry.