From the Editor

A Birthday Party for the Human Genome

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It's been ten years since scientists completed the draft sequence of the human genome. At the time of its completion, many looked forward to an upcoming decade full of new clinical insights, which would in turn lead to cures for many human diseases. However, we have yet to see the series of new drugs and cures that we envisioned in 2000. On the other hand, basic biology has undergone a complete metamorphosis over this period. Perhaps the publishing of the human genome sequence is better celebrated not for its clinical impact, but for ushering in a new generation of high-throughput approaches and catalyzing a change in mindset among biologists.

Prior to the sequencing of the human genome, most biological research was conducted on a small, hypothesis-driven scale. Large-scale studies were mostly restricted to clinical trials or initiatives involving multiple centers. But with the debut of the sequence, and the dissemination of the technologies developed for the effort, there has been a steady rise in 'omics research. Genomics studies are now performed in even the smallest of labs using million-feature arrays that can be purchased at fairly low costs. Proteomics is moving forward rapidly with an ever-expanding number of antibodies and advancing mass spectrometry technology. Metabolomics is giving old-school biochemistry a large-scale twist, and interactomics is sitting in the background, mapping out all the molecular networks within the cell. All of these fields owe a debt to the Human Genome Project.

The move toward large-scale 'omics studies has unearthed a wealth of information about biological processes, protein interactions, and gene expression. But despite how naturally such studies lend themselves to the clinical realm, new and unique challenges have kept conclusions elusive. For instance, hundreds of genome-wide association (GWA) studies have been completed in the past ten years looking for the genetic underpinnings to a variety of human diseases, but most of these studies have failed to identify major sources of genetic susceptibility. Now, researchers are focusing on rare variants in the population with the hope that these are the missing pieces to the puzzle. Such rare variants are a challenge to identify, so many are looking to the new generation of DNA sequencing instrumentation—developed following the genome project and now at the cusp of the personalized medicine

movement—along with a reference human genome, to help find these important variations within the human population. But whether these variants explain the risk for a particular disease or not remains to be determined.

Decoding the human genome also established the base number of protein-coding genes, and now proteomics researchers are on the hunt for disease-predicting proteins. Protein biomarkers have had a long road to the clinic. While there are a large number of studies that have suggested potential biomarkers, very few have made their way to the doctor's office. The reason for this comes in validation: markers initially identified on a smaller scale can't pass the test when they are applied to a larger population of clinically relevant samples. Sarah A. Webb examines this issue, along with other challenges with biomarkers, in this month's Tech News feature.

Similar to rare variants in GWA studies, protein biomarkers are usually found at extremely low concentrations in serum among proteins at very high abundance, which creates a dynamic range issue. The dynamic range of serum—that is, the range of protein concentrations from the most to least abundant—can be as much as 12 orders of magnitude. Mass spectrometry, which is the technology most often used to identify biomarkers, only has a dynamic range of 5–6 orders of magnitude. So while it is improving, current mass spectrometry technology can't yet provide the sensitivity required to identify these potential markers.

Decoding the human genome was a milestone in the history of science, not only for the sequence it gave us, but also for the inspiration it provided when it came to large-scale studies. A decade of questions have been answered, but many more have also been uncovered. But as our understanding of the genetic basis of human biology and illness continues to grow, new drugs and treatments will one day be available for many diseases. In most cases, we will have the announcement ten years ago to thank for it. Happy Birthday. Please post your thoughts or comments to Molecular Biology Forums under "To the Editor" (<http://molecularbiology.forums.biotechniques.com>) or send an email directly to the editors (bioeditor@biotechniques.com).

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