Finding Cures in the Genome

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Rapid advances in human genetics offer clear potential for medical breakthroughs if supported by more genetic research collaborations.

In the quest to find cures for diseases, one of the primary hurdles we face is the extraordinary complexity of biology. The intricacy and molecular scale of biological systems make it hard to assemble more than a fragmented picture of the body in health and disease. But thanks to recent and stunningly rapid advances in human genetics, that picture is growing clearer, and the potential for medical breakthroughs is rising dramatically.

The 6 billion DNA nucleotides in the genome contain the complete instructions for assembling every protein and cell in our bodies. Changes in just one nucleotide can lead to disease or prevent it, and rarely occurring gene variants are often the most consequential. We need whole-genome data from many people to fully map disease risk.

This is why the payoff from human genetics is taking longer than first expected. Hopes were high that the Human Genome Project would quickly lead to a wave of treatment advances. That didn't happen, in part because the sequencing of whole genomes remained prohibitively expensive and time consuming.

In recent years, with the advent of ultrahigh-throughput DNA sequencing technology, our ability to read DNA has increased a million fold. As sequencing costs drop and methods for crunching genetic data improve, we now have the tools to map the molecular basis for all diseases.

Success in this great endeavor will require more than scientific prowess. The most productive models for gene discovery have involved collaborations that extend across broad elements of society. One excellent example is deCODE Genetics, the Iceland-based world leader in gene discovery and now a subsidiary of Amgen.

deCODE's success is based on a combination of great science and the generous participation of Icelanders in its research. On the scientific side, deCODE has developed sophisticated methods for collecting, analyzing, visualizing and storing huge amounts of genetic data. The Icelandic people, in turn, provided a wealth of data to analyze. About 160,000 Icelanders gave deCODE access to their genetic data as well as medical data collected through Iceland's universal health-care system.

By correlating genetic variations with health data, deCODE has discovered dozens of genes that impact the risk of common diseases. In a recent, highly significant example, Amgen and deCODE announced that a rare mutation in a gene called *ASGR1* was linked to a 34 percent decrease in heart disease risk. The discovery points to a new biological pathway that might be modulated to further reduce the risk for heart attacks.

The web of collaborations that supports such major findings extends beyond Iceland. It includes technology companies that make gene sequencers; academic researchers who replicate and extend gene discoveries to more diverse populations; scientific publications that announce discoveries; and companies like Amgen, which invest in genetic research and work to transform genetic insights into medicines.

There are many more disease genes waiting to be discovered. To find them more quickly, we need to augment and extend genetic research collaborations. Based on our current understanding of genetic variation, Amgen estimates that data from 50,000 patients who share a disease may be sufficient to identify every gene with a meaningful impact on that disease. Data from a million patients might explain the biology of diseases that account for most of the suffering and premature death in the world. Many patients would welcome the chance to take part in the search for cures by providing access to their genetic and medical data. Networks could be established to encourage such generosity and ensure that patients' privacy is protected.

Achieving the potential of human genetics will also require greater collaboration among health-care payers and innovators. We need to ensure our health-care system supports major medical advances, and coverage and payment systems need to be modernized to accommodate personalized medicine.

Unfortunately, there's a trend toward viewing innovative therapies in terms of their immediate costs. Little value is placed on their offsetting impact on other health-care expenses or on benefits to patients, including longer, healthier, more productive lives. This outlook reflects siloed thinking and insufficient cooperation among all the players that patients are counting on for help. If we're intent on finding cures, we need to find better ways to share the costs as well as the benefits that medical progress provides.

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