Genomic Tools for Precision and Personalized Medicine

Largely outside of public awareness, a revolution in clinical medicine has quietly taken root within the walls of academia and in start-up enterprises, worldwide. It is based on genomic technology and the fortuitous fact that biotech seems immune to Moore's Law: instead of halving about every 18 months, the cost of sequencing the human genome has dropped off a precipice. The first one, cobbled together in 2003, cost $3 billion. Twelve years later, thanks to next-generation sequencing, the thousand-dollar individual genome is almost within reach.

One indicator that the revolution has arrived is the awarding of the U.S. National Medal for Technology and Innovation late last year to Arthur Levinson, CEO of Google's Calico spinoff and former CEO of Genentech, in part for contributions to personalized medicine. Another is the imminence of do-it-yourself genetic hacking. Chai biotechnologies is developing a real-time, quantitative PCR machine for the home user, to sell for $1,500 or less.

Many orthomolecular practitioners have long ordered single-nucleotide polymorphism (SNP) tests for their patients, but that older technology is limited practically to detecting common SNPs at selected loci. The doctor cannot assure a patient that potentially hazardous polymorphisms aren't lurking in some dark, untested corner of his or her genome. Now that next-generation, high-throughput sequencing has lowered costs so greatly, genomic analysis becomes affordable for more people with modest incomes. In the future, look beyond full proteome expression to transcriptome profiling and epigenome characterization.

Forward-looking oncologists have embraced the new technology, sequencing entire cancer genomes to find vulnerabilities in genes like BCL and HER-2 that can be targeted with tyrosine kinase inhibitors, antisense nucleotides, microRNA, monoclonal antibodies, even vitamins A and D. Characteristically, cancers present several targets but not all histologically similar cancers possess the same set of targets. Targeted therapy prolongs survival of patients without the toxic risk of multi-agent "shotgun" chemotherapy.

Not only cancer cells, but every living being carries within itself its own pattern of genetic vulnerabilities. By one estimate, about a third of all genetic variations cause decreased affinity of an enzyme for its vitamin cofactor. Before long, some academician will perceive and proclaim an obvious insight: innate weaknesses are stepping-stones to future diseases, so they merit targeted, preventive therapy. That is the likely interface between genomic medicine and orthomolecular medicine: genomic analysis presents the road map, and orthomolecular therapies provide both the fuel for the journey and the means to monitor progress.

Widespread application of genomic tools will impact not only the practice of clinical medicine, but also its infrastructure. Diagnoses that are mere diatheses and chemical imbalances will challenge the existing Diagnostic and Statistical Manual (i.e., the DSM)-coding structure and insurers' tacit policy of only paying for "real" diseases. (Indeed, insurance may fall by the wayside and be replaced by a system based more on patients' preferences.) Suitable statistical methodologies will arise to validate multifactorial therapies, obviating the need for double-blind studies with their attendant ethical hazards.

Big Pharma will try to co-opt genomic technology, because individualized medicine is not compatible with its one-size-fits-all paradigm, based on the "average man" statistical fallacy. Big Pharma, in concert with (and often subservient to) governmental regulatory agencies like the FDA, will work to suppress natural therapies—the obvious remedy for many genetic defects—via political influence. That is a ploy with which most orthomolecular doctors, ruefully, are all too familiar. In the end, however, the advanced technology will oust the old and all of its baggage, no matter how long it takes.

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