candid conversations:
YOUR HUMAN GENOME

THE GENE SEERS:
Q&A WITH GREG LUCIER & JONATHAN ROTHBERG OF life technologies™

DNA &
THE DAWN OF DIGITAL MEDICINE
Perhaps the most exciting frontier in medicine today is the emerging field of personal genomics: the use of detailed knowledge about a patient’s individual genetics as a guide to better prevention and treatment. Much of what makes it possible are the rapid improvements in technology that determine the precise arrangement of paired nucleotide bases in someone’s DNA that defines his or her genome. Between 1990 and 2003, the U.S. federal government poured roughly $3 billion to produce a final draft of the first human genome (and to amass a wealth of research findings vital to making sense of it).

This year, the price for sequencing a genome will fall to just $1,000 with Life Technologies’ new Ion Proton technology. Medical policy planners have long considered the $1,000 price tag to be a crucial threshold because it puts the cost of sequencing a genome roughly in line with the cost of obtaining insurance.

To get their perspectives on personal genomics, we spoke with Greg Lucier, the CEO and chairman of Life Technologies, and Jonathan Rothberg, the CEO of the company’s sequencing division, Ion Torrent Systems. This conversation is edited from several interviews and discussions that took place in the days surrounding the Digital Health Summit at the 2012 Consumer Electronics Show (CES), where Life Technologies debuted its new Ion Proton sequencer.

Q: It’s interesting that Life Technologies has chosen to make this momentous announcement at the beginning of the CES, where people would traditionally expect to find out about new TVs, computers or appliances—not about cutting-edge biomedical technology. What’s the significance of doing it here and now?
Lucier: If you look back in history, most revolutions happened when a tool was created to make them happen. I think that’s what this announcement about the $1,000 genome is today in terms of setting us on the path to genomic medicine. It allows this to happen in a very fast, economical way and will bring about a whole new level of information that doctors can use to make decisions with their patients.

Rothberg: First, I agree with Greg that this digital genetic information will be part of your medical record that also contains the digital information from your CAT scans, your MRIs, pathology reports, and so on. So partly we’re here because your genome sequence is going to be part of your electronic medical record.

Second, in our sequencing technology, we leveraged the same CMOS technology that enables essentially all the devices that you see on the show floor. You have a chip in your cell phone that sees light, and it’s what allows you to have a camera in there. We made a chip that saw chemistry instead of light! That was the key “what” moment.

We’re leveraging that trillion dollar investment over the past 40 years in those chips, and the same supply chain, and of course, the same Moore’s Law. That’s why it was inevitable that we’d get the cost for sequencing a whole human genome in a couple of hours down to $1,000. And that’s why we selected Gordon Moore himself [co-founder of Intel, for whom Moore’s Law is named] to be the first person to be completely sequenced with the technology, which we published in Nature last year.

Q: So, as with Moore’s Law in computing, should we expect to see the cost of sequencing continue to drop?
Rothberg: Absolutely. It’s something I have to fight constantly, but people keep saying that DNA sequencing is going faster than Moore’s Law. That’s an illusion. With the switch to new, CMOS-based methods, we’re just catching up to what 40 years of accumulated Moore’s Law has done for progress in electronics. We estimate that we’ll probably be fully caught up somewhere around 2014, and then the progress and cost of sequencing will progress along with all other costs that are driven by Moore’s Law.

Q: As you know, one of the concerns often voiced is that sequencing technology may start pumping out genomic information faster than we know how to do with it. That we’ll be wallowing in sequence data that we can’t interpret intelligently, and that this will prove counterproductive to people’s health or well being. You seem to be more optimistic.
Rothberg: I’m optimistic for two reasons. One, Life Technologies in particular is putting a huge amount of work into it. We have a new effort with Carnegie-Mellon University to develop better artificial intelligence agents, like Siri [on Apple’s iPhone] or Watson [IBM’s Jeopardy! game-playing computer], that would help a doctor to access and interpret genetic information with more expertise. The other reason is because the more sequencing we do of individuals and the more we correlate gene sequences with their medical records, the more we know. If I sequence one person, I don’t know anything. But if I sequence one hundred thousand people with cancer—or with cardiovascular disease or with autism—and I have their medical records and I understand how they respond, I could know all about complex diseases.

Recently, I raised that same problem you did to a group of 16 computer scientists at Carnegie-Mellon who contributed three of the modules to Watson’s memory, and they told me that I shouldn’t worry about it. They felt reasonably confident there was enough progress going on in unstructured data applications, in genomics and in mining for relevant answers in pathology reports, radiology reports, and so on. The tools could interact with physicians to help them along the way.

Q: You’ve mentioned that in applying our newfound genomic information to specific problems, cancer is low-hanging fruit. What makes cancer so well-suited to be a target?
Lucier: Cancer is a disease of the DNA. It is a bit ironic that we haven’t been reading the DNA until now. But here we have a tool that will help in understanding the very thing that’s causing the disease, and in the future the physician can match up the specific defects in the DNA with the right therapeutic to help an individual patient with a particular malignancy.

One in five cancer drugs is effective today. That is just not an acceptable rate. And cancer progresses; time matters. Having an accurate ability to read the DNA and to select the right therapeutic in a timely fashion could make a world of difference in the quality of health we offer patients.

You can’t believe the groundwork of referrals I get, people calling me constantly: “I have a brother” or “I have a cousin,”...
can you please make the introduction to this doctor?" It shows you that people are getting activated. They are becoming aware. They don’t want just to place their care in the hands of the doctors and wait for the doctors to reach an understanding that may or may not help them. That’s what has to happen now, quite frankly. I think we’re on this irreversible course.

People are starting to understand genetics to a certain degree, and they will learn more. They will start talking to their doctors and they will expect their doctors to understand, too, and do something about their conditions. Q: This kind of personalized genomic medicine isn’t an abstract topic for either of you, is it?

**ROTHBERG:** When my newborn son developed breathing problems and the doctors weren’t sure whether it was something genetic, that was the moment when I understood what personal medicine meant. (See “The Inside Story of a Sequencing Chip,” on the facing page.)

**LUICER:** Two years ago, I had my own genome sequenced and spent time with some of Life Technologies’ researchers going over the results. It turns out that I carry a mutation that raises my risk for an unusual type of Parkinson’s disease. That’s a good thing for me to know and watch out for as I get older.

What was also significant about that, though, is that my mother happens to be suffering from a degenerative neurological condition that had been diagnosed as multiple systems atrophy. My results tipped us off to check her for the same mutation, which led us to discover that she has it too, and that her illness is really Parkinson’s. That didn’t point us to a cure for her, but it did suggest ways to improve her treatment.

My genome also showed that I carry the BRCA1 mutation that increases the risk of breast and ovarian cancer. We didn’t point us to a cure for her, but it did suggest ways to improve her treatment.

The second pivotal moment was in 2007, when Rothberg says he was bragging to his son that he had just read the “surreal” moments that led them to their breakthroughs. Yet Jonathan Rothberg, who created the system that will enable Life Technologies to sequence a whole human genome in hours, remembers precisely. He credits both of the inspirations to his son, Noah: “The first because he was sick and the other because he was crazy.” Rothberg says.

“Prior to his birth, I thought I was on top of the world,” he says. Back then, he was the founder and CEO of the company then called CuraGen, which was mining the cumulative information pouring out of the world’s genome projects to develop new drug candidate compounds. But in 1999, shortly after his birth, Noah turned blue because of breathing difficulties and was rushed to intensive care. Doctors were not sure whether his problem might be genetic. Helpless in the hospital’s waiting room, Rothberg says, “I was not interested in the human genome as a map for humanity. I really only cared about my son’s genome. That was really the moment when I understood what personal medicine meant.”

Then Rothberg noticed a photograph of a Pentium microprocessor on the cover of a magazine in the waiting room. He suddenly made a mental connection to genome sequencing and realized, he says, “everybody had been doing it wrong.” Big sequencing efforts had always involved scaling up the number of sequencing machines involved to increase output, like hiring more people to work in a factory. But Rothberg saw that semiconductor technology should make it possible to execute and monitor many chemical sequencing operations simultaneously on a chip. After Noah recovered— his problem turned out not to be genetic—Rothberg developed those ideas into the technology on which the company 454 Life Sciences was based.

The comment made Rothberg realize that an inefficiency in his sequencing approach was that it relied on chemical processes that emitted light detectable to a chip to signal the sequencing results. “What we needed was a chip that could see chemistry instead of photons,” Rothberg says. The semiconductor devices called ISFETs (ion-sensitive field effect transistors) invented in 1970 by Piet Bergveld offered a way to do it.

Rothberg’s Ion Torrent Systems team created an ISFET-based sensor chip similar to the light-sensitive one in a smartphone’s camera, except that the surface is an array of microscopic wells. On the original chip, 400 wells were packed into an area as the cross-section of a human hair; in the new Proton chip, the same area holds up to 10,000 wells.) Each well acts like a tiny beaker with a pH meter in it. Single-strand bits of DNA from the genome to be sequenced sit in each well as a template, along with the enzymes and other requirements to grow a complementary matching strand of DNA. During the sequencing process, solutions containing one DNA base sequentially wash through the wells. If that base matches the next open position in the template strand, it attaches to the growing complementary strand. That chemical process releases a single hydrogen ion into the well. The ISFET at the bottom of each well specifically registers that change in pH, thus revealing the identity of one more base in that well’s template DNA sequence.
Three years ago, all the people whose DNA had ever been fully sequenced—all seven of them—could have fit in the waiting room of the average doctor’s office. Today, the best estimates suggest the number of people with sequenced genomes has been chasing ever since the completion of the first human genome sequence a decade ago.

“Before this point, the machines were too big, far too expensive, and took weeks if not months to get the results,” remarks Greg Lucier, CEO and chairman of Life Technologies. “And now, literally, this machine is the size of a printer that could be on your desktop.”

Yet the new simplicity of sequencing is only part of the story. Genomics is converging with computing, wireless communications, sensors, imaging and new medical information technologies to create a framework for “digital health” that could transform the practice of medicine.

“Each individual is unique: we have our own biology, our own physiology, our own environment. And the way medicine is practiced today couldn’t be further from that,” observed Eric J. Topol, the director of the Scripps Translational Science Institute, during his opening remarks at the Digital Health Summit at the 2012 Consumer Electronics Show in January. As a result, he says, “We spend over $100 billion a year on drugs in this country alone. Most of that, believe it or not, is wasted, because we don’t match up the right drugs at the right dose with the right patient.”

Topol argues in his new book, The Creative Destruction of Medicine: How the Digital Revolution Will Create Better Health Care (Basic Books, 2012), that genomics and the rest of the new digital health infrastructure will make it possible to understand any individual’s health more profoundly and comprehensively than ever before. Consumers empowered by the new technologies and unprecedented access to their own medical information, he thinks, will transfigure healthcare, with colossal benefits in better outcomes, reduced suffering, and saved costs.

His vision is one that growing numbers of people, inside the genomics field and out, are coming to share. Jonathan Rothberg, the CEO of the Ion Torrent division of Life Technologies and the inventor of its high-throughput sequencing method, emphasizes that personal genomics is a tool that only becomes useful in the context of an individual’s full medical history, including specialists’ reports, imaging records and other data. “But here’s where I will be bold,” he says. “I think that this new addition will be as important to human health as clean water, antibiotics and imaging.”

Targeted Genome vs. Whole Genome Sequencing

Genetic tests for diseases have been around for a long time, so one might wonder why it’s a big deal that the technology has advanced enough to sequence all of someone’s DNA inexpensively in a couple of hours. After all, of the three billion base pairs in DNA, only about 1.5 percent code for proteins, which is what most genetic defects seem to affect—so sequencing it all might seem like overkill. In fact, for several reasons, it is hugely important.

Most of what one might consider medical genetic tests, however, do not really look directly at the genes at all. Instead, they check body chemistry for the presence of proteins or other metabolites that signal whether certain genes are active. For example, the phenylketonuria (PKU) test performed on newborns looks for a compound in their blood that signals whether they can make the enzyme that digests the amino acid phenylalanine. The results of such tests show whether a gene is working but don’t say much about what’s gone wrong if it isn’t. Genetic sequencing is potentially more accurate and can reveal precisely what mutation has shut down a gene—information that might be useful in devising a treatment.

Advances that make whole genome sequencing faster and affordable do the same for more targeted sequencing, too. Sequencing a panel of suspicious genes can become so easy that physicians stop needing to send DNA samples to expensive labs: they can do it themselves in the office with desktop equipment, maybe even while patients wait. The cost and ease of targeted sequencing can therefore potentially plummet.

For example, Life Technologies currently markets a product based on its $99-chip technology that looks at a targeted panel of 46 genes involved in tumor growth. In development, the company says, are ones that would look at a more comprehensive set of 400 cancer genes and at about 100 inherited diseases. (These products are currently only for research purposes, not medical diagnostics.)
Useful as targeted genetic tests can be, when used for diagnosti- c purposes, they are a bit like searching at night for your keys under a lamppost only because the light is better there. The tests can confirm a physician's suspicions about what is wrong but they don't flag unexpected sources of trouble, such as any other mutations that might be disturbing a patient's physiology more subtly.

Whole genome sequencing, however, illuminates every cor- ner of a patient's physiology and can suggest new hypotheses if the obvious causes for a medical condition don't apply. It also provides a single unified terminology for describing a patient— a lingua franca of base pairs, if you will—that all medical specialties can use to share detailed information.

As whole genome sequencing gets less expensive, it may eventually become a standard, preferable alternative to target- ed sequencing or metabolic screening. People sequenced at birth (or maybe even prenatally) could have all their genetic information tucked into their medical records for reference throughout their lives. The interpretation of the genome record could constantly evolve along with medical science. Patients and their doctors could use it to tailor prevention measures that would head off potential medical problems.

And it is here that the genomic medicine movement merges with Topol's ideas of a broader digital health revolution now brewing—a revolution that intends to liberate all our medical information from the Bastille and arm us with devices that can make healthful use of it every day.

**Drivers of Digital Health**

Several trends in concert are driving the rise of personal genomics and digital health. One is of course the increasingly molecular focus of modern medicine, in which being able to characterize a patient's state of health in terms of genetic information serves as a key to its management.

Digital health is also a fruit of Moore's Law, which relent- lessly makes computing, communications and all other chip-related technologies faster, cheaper and more compact. Computing has always been instrumental in genome sequencing efforts but the development of chip-based sequencing techniques has enabled personal genomics to suddenly “leverage 40 years worth of Moore's Law,” in Rothberg's words—and puts it in a position to ride the curve upward hereafter.

The advent of mobile digital technologies over the past two decades is playing a big part, too. Mobile technology offers largely unprecedented opportunities for collecting and distributing information on the go, so measurements of people's health under all conditions can be more complete and continuous than when medical instruments were anchored in one location.

Another factor might be the modern tendency to look for health answers outside the traditional medical establishment. For better or worse—or rather, for better and worse—unsatis- fied consumers are questioning their physicians' authority and looking for help within circles of their peers with relevant knowledge and experience. "Patients with rare conditions often understand more about their conditions than their physicians do," says Jesse Dylan, the founder of Lybba, a non-profit that advocates for open-source healthcare. Social media and the Web are instrumental in establishing those peer-to-peer connections easily.

**The Case of the Beery Twins**

If the cause of whole genome sequencing and personalized medicine needed further proof, they might be the 15-year-old fraternal twins Alexis and Noah, offspring of Retta and Joseph Beery of Encinitas, Calif. Joe, who is the chief information offi- cer of Life Technologies, joined the company in 2008 partly because the twins’ difficult medical history made him appreci- ate how much diagnostics needed to improve.

"And the only way we found that was through whole genome sequencing." At age two, Alexis and Noah, who had been constantly nauseated and colicky from birth, were diagnosed from an MRI as having cerebral palsy. But Alexis's condition started to get worse, and she showed symptoms inconsistent with that diagnosis. "At age five and a half, our daughter started losing the ability to walk during the day," Retta recalls.

Retta, who was studying everything she could find that might contain a clue about what was plaguing her children, eventually read a magazine article that mentioned a rare nervous disorder called a dystonia that mimicked cerebral palsy and which could be treated with the Parkinson's disease medication L-dopa. Doses of that neurotransmitter immediately allowed both children to function at a high level, she says.

Then in 2009, a chronic cough that had bothered Alexis for years suddenly blossomed into a severe breathing problem. "We almost lost her on many occasions over a period of about 18 months. We had paramedics in our house. We had taken her to the ER. Every other week we were going through this," Retta says. "We never knew if she was going to make it through the night." No one could figure out why Alexis couldn't breathe, Retta adds, but her neurologists were convinced the respira- tory problem was unconnected to her motor problems.

Desperate, the Beerys reached out through Life Technologies to scientists at the Baylor College of Medicine as part of a research study to do whole genome sequencing on Alexis and Noah to see if it could find the root of their problems. The Baylor group agreed, and eventually identified a single mutation responsible for both sets of symptoms: one that lowered not only the children's L-dopa levels but also those of a second neurotransmitter, serotonin.

Doctors put Alexis on a new medication that restored her levels of these chemicals. Her breathing returned to normal and within weeks she was back to participating in school track and field events. (A smaller dose of the same drug also helped Noah.) "It was all connected," Retta says. "And the only way we found that was through whole genome sequencing."

**First Target: Cancer**

Rare inherited disorders are obvious targets for personalized genomic medicine to go after because of the good that it could do, as the Beery twins' story attests. The condition that many of the medical genomics innovators are making a prime focus of their work, however, is far more common: cancer.
The digital movement is poised to process unprecedented amounts of health data about unprecedented numbers of people. But gathering and moving data around isn’t the goal—achieving better health outcomes is.

Aman Iyer, president and COO of the digital health solutions group WellDoc, points out that many of the monitoring capabilities and potential interventions that could improve patients’ health would not be possible without the rise of personal genomics. The cost to sequence a genome has fallen to $1,000, making medical sense of being able to share one’s medical data, she says, brings “a whole new level of accountability” and engagement. This kind of simplification or demystification will be especially important in systems that patients—and their physicians—will need to use to make sense of the huge, sprawling complexities of detailed biological study. They may not be doing it alone. People with shared health problems are banding together more often in online communities such as PatientsLikeMe and CureTogether to educate themselves and learn how to manage their conditions: digital technology makes it easier to find fellow sufferers and to share information.

We’ve seen a wave of people wanting to take action,” says Robbins, who pins her company’s recent success on its decision to offer consumer solutions, not just medical or research products. The social component of being able to share one’s medical data, she says, brings “a whole new level of accountability” and engagement. This kind of simplification or demystification will be especially important in systems that patients—and their physicians—will need to use to make sense of the huge, sprawling complexities of detailed biological study. They may not be doing it alone. People with shared health problems are banding together more often in online communities such as PatientsLikeMe and CureTogether to educate themselves and learn how to manage their conditions: digital technology makes it easier to find fellow sufferers and to share information.

Progress on computerized tools that can comb through huge amounts of medical data is making the interpretation problem less daunting. When people act on the basis of highly personalized data, they may not be doing it alone. People with shared health problems are banding together more often in online communities such as PatientsLikeMe and CureTogether to educate themselves and learn how to manage their conditions: digital technology makes it easier to find fellow sufferers and to share information.

“The problem that the raw materials aren’t available where the patients are, when and how they need it.” The key challenge for companies in the digital health space, he says, is to use people’s personal information—not just their medical data but seemingly unrelated facts like their social media preferences—to create and deliver “bite-size chunks” of actionable knowledge at exactly the right moment. “We need to take what we have and we need to deliver it in new ways,” he says.

Christine Robbins, president and CEO of Body Media, agrees. “What action do I take to help change behavior?” Because that’s what we’re all trying to do,” she says. Individual users might want behavioral changes that would help them get fit; meanwhile, insurance companies want the population to adopt behaviors that would bring down healthcare premiums. Smart design will also play a crucial role in making sure digital health offerings are actionable, says Robert McCray, CEO of the Wireless Health Science Alliance. Everything, from monitoring devices to messaging systems, will need to be inexpensive and simple to install and use. “No IT degree required,” he jokes. That kind of simplification or denystomization will be especially important in systems that patients—and their physicians—will need to make sense of the huge, sprawling complexities of detailed biological study. They may not be doing it alone. People with shared health problems are banding together more often in online communities such as PatientsLikeMe and CureTogether to educate themselves and learn how to manage their conditions: digital technology makes it easier to find fellow sufferers and to share information.

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The sky is falling” because the sheer volume of required data associated with it. “Human factors is the biggest issue that we have, and where there is a big opportunity,” McCray says. Good design can inform people without overwhelming them. By analogy, he cites the engine temperature on a BMW automobile, which is just a red light that doesn’t say what the temperature is. “As long as you trust that red light, or the amber one, that tells you you’re getting closer to needing an oil change, that’s all you need,” he says. “As a consumer, you just need to trust the application and the source.”

“When a person’s sequence differs from the canonical, reference version of the human genome at about 26,000 sites, and it will probably hold only about 400 differences that seem unique. “That’s not information overkill,” he says. Progress on computerized tools that can comb through databases of genome information and make the important correlations is also coming. Thanks to big genome-keeping with past methods, genome sequences have often been stored as full photographic images of electrophoretic gels, much as watercolor paintings are kept. “Geneticists, however, should not have to “find the sequence in the images,” he argues: switching to digital sequencing tech- niques is easier, requires as just an output stream of base- es would hugely reduce the amount of storage needed.

He adds that it shouldn’t be necessary to store a complete genome for everyone—the human genome is so vast that keeping a copy costs far too much. Progress on computerized tools that can comb through databases of genome information and make the important correlations is also coming. Thanks to big genome-keeping with past methods, genome sequences have often been stored as full photographic images of electrophoretic gels, much as watercolor paintings are kept. “Geneticists, however, should not have to “find the sequence in the images,” he argues: switching to digital sequencing tech- niques is easier, requires as just an output stream of base- es would hugely reduce the amount of storage needed.

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Many entrepreneurs in digital health are confident that, whatever the upfront costs might be, their products will end up sharply reducing medical costs by improving prevention and better matching drugs or other therapies to the specific ills of individual patients. Genomic information is clearly supposed to play a crucial role in achieving that goal.

“Employers today in the U.S. can’t afford double-digit health care cost increases any longer,” Lucier says. For that reason, he believes that aside from everyone’s desire for better treatment outcomes, natural financial incentives flow from the potential of genomic information to cut billions of dollars out of healthcare costs by better tailoring drug treatments to patients. “Innovation actually leads to lower healthcare costs,” he says.

“We spend so much money today on people getting therapies for which they are not appropriate. But more importantly, people are not getting the care that they need and are being subjected to side effects that they should not have to experience,” Tuckson says. The goal should be to “identify that patient who is at risk really early and then use new digital, behavioral, supportive technologies to send a message that, ‘You really are at high risk. This is not determined because of a population model or population-based assumptions. This is your genomics. And we can tell you what your risks are.’”

INVESTING IN THE REVOLUTION

Keeping healthcare affordable is only one of the complex economic variables that will determine whether the dream of genomically informed, personalized medicine materializes. Another is that neither the science nor the technology of personal genomics is yet so settled that most businesses can easily start offering services in the area. Much as U.S. federal investment into molecular biology research during the 1960s and ’70s paved the way for the later biotech boom, further robust government investment—by the U.S. and other nations—into genomics, bioinformatics, and related areas will be crucial for speeding personalized medicine into reality.

As Margaret A. Hamburg and Francis S. Collins noted in their 2010 article “The Path to Personalized Medicine” in The New England Journal of Medicine: “When the federal government created the national highway system, it did not tell people where to drive—it built the roads and set the standards for safety. Those investments supported a revolution in transportation, commerce, and personal mobility. We are now building a national highway system for personalized medicine, with substantial investments in infrastructure and standards.”

Therapeutics emerging from personalized medicine also may face severe obstacles. In theory, personal genomics could someday make it possible to prescribe a course of treatment perfectly optimized for a single patient. But as the target population for a treatment shrinks, finding appropriate ways to test its safety and efficacy gets harder and more expensive, too. Therapies that might be extremely effective for relatively few patients might risk getting caught in a regulatory limbo impeding their use outside of research settings. Insurers, too, might balk at seemingly thin evidence that a personalized treatment is worthwhile.

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Meanwhile, the pharmaceutical industry has largely been built on a model of developing drugs that work well for large patient populations. If it costs roughly a billion dollars to bring a new drug to market, companies may deem it impractical to turn certain genomic discoveries into drugs. It’s entirely possible, of course, that genomics research may help to lower those development costs, in part by identifying subgroups of patients who would strongly benefit from drug compounds that failed for the general population. Nevertheless, personal genomics could conceivably suggest a vast new number of “orphan drugs” that no one is prepared to develop for the sake of too few patients. Government support might therefore become important in helping to bring some of these potential treatments to fruition.

Notwithstanding these hurdles, however, the confluence of social, economic and technological factors favoring the emergence of personal genomics as an important part of how people will manage their health—with and without the direct involvement of traditional medical gatekeepers—seems all but irresistible. As Topol summarized the situation in The Creative Destruction of Medicine, “The foundation for genomic medicine has been laid. The revolution is ongoing: even though it has taken longer than initially projected, we are moving irrevocably forward in the second postsequence decade. Routine molecular biologic digitization of humankind is just around the corner.” •