SIGN HERE: Informed Consent in Personalized Medicine

by

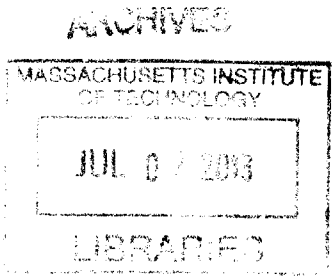
Abdul-Kareem H. Ahmed

B.S. Neuroscience
B.A. History & Philosophy of Science
University of Pittsburgh, 2012

SUBMITTED TO THE PROGRAM IN COMPARATIVE MEDIA STUDIES/WRITING IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE IN SCIENCE WRITING
AT THE
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

SEPTEMBER 2013



Signature of Author: _____
Department of Writing and Humanistic Studies
May 17, 2013

Certified by: _____
Alan Lightman
Professor of the Practice of the Humanities, Creative Writing, Physics
Graduate Program in Science Writing

Accepted by: _____
Seth Mnookin
Assistant Professor of Science Writing
Director, Graduate Program in Science Writing

SIGN HERE: Informed Consent in Personalized Medicine

by

Abdul-Kareem H. Ahmed

Submitted to the Program in Comparative Media Studies/Writing
on May 17, 2013 in Partial Fulfillment of the
Requirements for the Degree of Master of Science in
Science Writing

ABSTRACT

The next era of medicine will be one of personalization, scientists and physicians promise. Personalized medicine is a refined clinical approach in which clinicians will utilize your genomic information to help you prevent disease, and tailor targeted therapies for you when you fall ill. This is the future science has slowly been approaching. However, the human genome is not enough, not unless we can decipher its language. One ambitious study to this effect is the Personal Genome Project, led by Dr. George Church at Harvard Medical School. This project will eventually recruit 100,000 volunteers to donate their genomes and a full body of information concerning their biological health. With this data, Church hopes others can cross-analyze these profiles and better determine the role in disease of each gene of the human genome.

However, the Personal Genome Project is as much a study in the ethical, legal and social aspects of genomic studies as it is an effort toward personalized medicine. Church envisions a future where privacy cannot be guaranteed. Society is becoming more open and technology is more invasive than ever. Considering this, Church has informed his participants that their information will likely not remain anonymous. With their fully informed consent, he has in turn made all this data public, to promote open science. This ethical approach raises several important questions about expansive genomic studies. The scientific community will have to decide on an approach that will eventually deliver personalized medicine. On one end of the spectrum, there is Church's open approach, and the other, more security, more firewalls and more legislation. In order for personalized medicine to become a reality, society will have to prepare itself for our ever-changing ethical, technological and scientific landscape.

Thesis Supervisor: Alan P. Lightman
Title: Professor of the Practice of Humanities

SIGN HERE

Informed Consent in Personalized Medicine

Profile One

The first human analyzed in the Personal Genome Project was born on August 28, 1954. At 58 years old, this Caucasian male weighs 246 pounds and measures in at 6 feet 5 inches. He is narcoleptic, dyslexic and has survived a heart attack and skin cancer. On any given day, he has a high level of fat in his O positive blood. Every night, he takes lovastatin, to lower his cholesterol levels. The man is a carrier for several possibly dangerous diseases, signaled by dormant "mistakes" in his genetic code that could result in lung disease in any future children.

The sum of his genes, known as his genome, is the recipe book to every protein his body creates. And now it has been sequenced, or read, letter by letter and analyzed for any currently known mutations, mistakes which can lead to deleterious health. This man's entire genome, with all of its single nucleotide polymorphisms or unique single letters, is freely available for download to anyone with an Internet connection. It is a mere 272 megabytes and could fit comfortably on a compact disc.

Is his genome safe online? Can he be identified by his DNA? Did he know the risks before he donated his genome to science? The path to personalized medicine may prove not only to be a hurdle in science and technology, but also a challenge to scientific ethics.

A Journey to Medical Individualism

GATTACA, the 1997 science fiction film depicted a future of robust medicine. The technology was space age. You too have probably pondered a future of innovative medicine; a robotic heart, a cure-all superdrug, a stem-cell elixir of youth perhaps. Today, that vision of the future is referred to as 'personalized medicine', a refined practice of medicine where doctors will use your fully sequenced genetic code, your genome to help you live the fullest and healthiest life, and to flag down disease before it occurs. A child who possesses the tell-tale pattern of genes that increase his risk of diabetes will be prescribed a strict, healthy diet from a young age, avoiding the disease altogether.

Full genome sequencing will also help doctors prescribe you the most optimal drugs when you need them, harnessing pharmacogenomics. Genes, the basic components of heredity, can code for proteins like enzymes, and enzymes break down drugs. By knowing your particular genes, physicians can prescribe drug dosages that are specific to how your body responds.

Cancer is a disease especially suited to personalization. In healthy cells, two types of genes carefully balance the growth of a tissue: genes that act like fertilizers, promoting growth,

and those that act like pruning scissors, moderating growth where necessary. When mutations occur in these genes, tissues grow unbridled, resulting in cancer. With over 200 known types of cancer, over 60 organs where they can occur, and countless genetic mutations that can be responsible, each cancer patient is virtually unique. Reading the genome and mining that data for known mutations can be life saving. For one, physicians can see cancer years before it starts; by detecting the BRCA1 gene women can take action years before breast cancer has a chance to emerge. In a stirring editorial in the *New York Times*, Hollywood actress Angelina Jolie revealed her decision to have both of her breasts removed after learning she was a carrier of BRAC1. Additionally, physicians can test the cancerous tissue itself for genes that are known to respond well to certain treatments. Finally, these cancer genes themselves can serve as a target for drugs.

Genomic data, including all mutant genes will enhance the physician's perspective of a person's health and vulnerability. It will join the traditional inspection of patient history, family history, environmental factors like diet and exercise, and behavioral factors like mental health to inform health care professionals of your full state of health and need for treatment. Such a standard promises longer, healthier lives as disease will be prevented and quelled.

The term 'personalized medicine' is deceptive however. Medicine has long been individualized, since well before genes were postulated and discovered. From Hippocrates, the Greek medicine man who claimed that, "it is far more important to know what person the disease has than what disease the person has," to the Persian polymath Abu Sina and his renowned treatise, the *Canon of Medicine*, ancient, modern and alternative approaches to medicine have often stressed that each patient is unique, and not just another copy of the same model.

More often, however, the norm throughout the history of medicine has been for physicians to utilize one-size-fits-all medicine, pragmatic approaches like tonics and antibiotics. For medicine to overcome this tendency and to adopt individuality was a matter of scope. The human body is a collection of organ systems, like the nervous system. Each organ is made of tissue, like the neural tissue in the brain. Each tissue is made of cells, neurons. If science is an art, then technology is the paintbrush. The scope with which physicians viewed the human body, and thus defined the biological individual, narrowed only as the technology permitted.

The advent of fine microscopy not only revealed human cells, but also organisms that were then only postulated to exist. Microbes, bacteria, viruses, protists and fungi were finally recognized as the pathogens that were responsible for many human diseases, like tuberculosis, small pox, and cholera.

People respond to microbes differently. We're all jealous of those fortunate few that can weather the winter without a sniffle. This should have been a vote for individualism. Unfortunately, this wasn't the case, said Nathaniel Comfort, historian of medical genetics at the Johns Hopkins University and author of the recent book, *The Science of Human Perfection: How Genes Became the Heart of American Medicine.*

At the time, the medical community believed that, "the disease cholera is caused by the cholera germ," said Comfort. "If you kill [these germs] you will cure people of the disease. So all you need for that one disease is that one medicine," for example a generic antibiotic.

Not all contemporary scientists were convinced of this thinking. On October 7, 1892, the Bavarian hygienist Max Joseph Pettenkofer famously drank a cholera-cocktail prepared by the bacteriologist Robert Koch in front of a horror-stricken crowd. Pettenkofer didn't contract the disease and suffered only mild upset stomach. He used this triumph to advocate that the unique constitution of an individual matters. It's not only the pathogen or perturbation, but also some level of particularity about a person that tips the balance between health and illness.

The greatest testimony of individualism, the fuel to power biomedical science for decades was the development of the field of genetics.

The realization that heritable factors contributed to an individual's features was a delayed revolution. By 1866, Gregor Mendel established the intellectual framework of heredity. Some factors pass through generations influencing traits, like eye color or susceptibility to disease. He was ahead of his time, but several discoveries in molecular biology confirmed his theory, and demonstrated that those factors were genes, segments of DNA. Through the mid-20th century many landmark studies confirmed that DNA was in fact the material of heredity. Genes instruct the production of proteins that then determine a physical feature, capability or vulnerability, traits in general. Soon after, Franklin, Watson, and Crick made their famous discovery of the structure of this holy molecule.

The scope of individuality zoomed in on the sub-cellular.

In the latter half of the 20th century, technology again permitted better science. Full genome sequencing, the comprehensive reading of an individual's entire medley of genes became a tenable goal. As most cells in the body carry a copy of the genome, a simple sample of spit is all that's necessary. By breaking open the cells and extracting DNA from its hiding place inside, a full genome can be read. The technology developed through the efforts of Frederick Sanger, Walter Gilbert and many others. By the turn of the 21st century, the Human Genome Project had achieved a rough sketch of the human genome, a milestone for science. Not only did science appreciate that each individual has a unique genome, a biological fingerprint, but that it might now be possible to harness that information for use in individualized medical care.

The biomedical community is investing much time, energy and money into the study of genetics. Nothing emblemizes that zeal more than the Human Genome Project, the international race to sequence the human genome, starting in 1984 and concluding in 2000, with revisions made to the genome script ever since. When the Project was near completion, fervor quickly developed in the media. The human genome itself was hastily linked to lofty ambitions: the complete eradication of disease, a direct understanding of humanity, the secret to life itself.

One Milestone on a Long Road

On June 26, 2000, the completion of a rough script of the human genome was announced jointly by then U.S. President Bill Clinton and then British Prime Minister Tony Blair, a landmark for science, medicine and society itself, so everyone was told.

The project spanned over 15 years, and cost $3 billion, from conception to completion. It was accomplished by a consortium of global contributors working nonstop, including the U.S. Department of Energy, the National Institute of Health (NIH)—the efforts of which was headed by Francis Collins, then director of the National Human Genome Research Institute of the NIH-—and private efforts by J. Craig Venter through his corporation, Celera Genomics.

"Let us be in no doubt about what we are witnessing today," said Prime Minister Blair on a televised report... "A revolution in medical science whose implications far surpass even the discovery of antibiotics, the first great technological triumph of the 21st century."

Many headlines were idealistic in this nature. Science at the turn of the century could best be described as hyped. Somehow, having a rough script of the human genome (it wasn't perfectly accurate and only 92 percent complete) would allow physicians to prescribe you made-to-measure drugs. Disease would fall to the awesome wrath of science, as did bacterial infections, and polio virus decades before. If only.

Notably, some scientists in and around the Project were prudent about their comments. The *New York Times* was saturated with the news: *Genetic Code of Human Life is Cracked by Scientists*, and another, *The Human Genome Abounds in Complex Contradictions*. One molecular biologist quoted in the latter was skeptical.

"We've got another century of work ahead of us, to figure out how all these things relate to each other," said David Baltimore, a Nobel Laureate in Physiology or Medicine and then president of the California Institute of Technology.

"It's like a book in a foreign language that you don't understand," said Frederick Sanger, a biochemist from Cambridge, UK, a pioneer in DNA sequencing, and a two-time recipient of the Nobel Prize in Chemistry, offering some clairvoyance in a 2001 news report in *Science* magazine. "That's the first job, working the language out."

Sanger's analogy works on many levels. The human genome has been referred to as the Book of Life. Literally, the genetic code written out letter by letter could fill an encyclopedia that could be stacked up as tall as the Washington Monument. But further, the human genome script is like a disordered list of plot points in a story. Each point, each gene, refers to a would-be chapter. We need to analyze each point and determine where it fits into the grander account of human life. We have the book, but we are waiting to hear the story, and the raconteurs are few.

On its tenth anniversary, in 2010, the question on the minds of science and society was, 'where is the genome now?'

In the past decade the human genome has opened a window into human biology and nature. First, science is now easier to conduct. The genome script is available online with an open-access policy. Any laboratory large or small can utilize the data. The genome has also helped us understand our origins: the Out of Africa theory. Genomic data corroborates what archeologists and linguists have proposed for decades. Even Charles Darwin estimated a single point of origin for humanity in his *Descent of Man.*

Following that descent, the genome has been truly humbling. In a bout of genetic hubris, scientists estimated that an organism as complex as the human must have 100 thousand or so genes. Today we know that number is between 20 and 25 thousand. The freshwater crustacean *Daphnia pulex*, a water flea has 31,000 genes, putting *Homo sapiens* to shame. Perhaps our genes are more complex. Interestingly, the genome has allowed science to peer closer at so-called junk DNA. Only 1.5 percent of our genome is composed of genes. The rest, a full 98.5 percent, has purposes that scientists are only just discovering, for example, influencing how the 1.5 percent behaves. Which symphony an orchestra of genes plays depends on a fine-tuning of which genes are playing and producing proteins, and when.

Though discovering the genetic basis of disease is a gradual process, The Human Genome Project has not yet delivered personalized medicine. Patients aren't getting their genomes sequenced in droves, except the occasional genetic test for a specific disease. Physicians aren't scanning your genes in the same routine they check your blood pressure. People are still succumbing to diseases of genetic origin.

For individual genomes to truly become actionable, to serve a purpose in the clinic, genes need to be correlated with traits. Science needs to become fluent in the language of the Book of Life. It needs to develop a dictionary, to translate the full story.

"It made a great impact on science," said Lee Gutkind, a professor of creative nonfiction, at Arizona State University, and coauthor of the recent book, *An Immense New Power to Heal: The Promise of Personalized Medicine.* "It has yet to make a great impact on medicine. It has to make that big jump."

The technological jump has already been taken. In fact, it was a vigorous leap. The efficiency and accuracy of genome sequencing has grown at an exponential rate in only the last decade. Around the time the Human Genome Project concluded, sequencing a full genome would cost $100 million, prohibitively high for personalized medicine. Today, this cost has fallen to well below $10,000, rapidly approaching the ultimate feat: the $1000 genome.

Additionally, the accuracy with which genomes can be sequenced has improved. In April 2003, the Human Genome Project was reportedly 99.99 percent accurate in over 92 percent of the genome. Today, this number continues to climb, adding more 9's after the decimal point. Such incremental improvement is pivotal because with 3 billion base pairs in the genome, 99.99 percent accuracy means 300,000 base pairs are incorrectly read, whereas with 99.9999 percent accuracy, only 3,000 are incorrectly read: a 100-fold improvement.

Continuously improving technology only strengthens the allure of personalized medicine. In the near future, a $1000 medical bill for a sequenced genome is plenty reasonable. A routine X-ray costs your insurance company the same.

The technology is there but the intellectual link is missing. Even with accurate, cheap, fully sequenced genomes, there remains that next jump: deciphering how genes correlate with traits. "Determining how the genome functions will be the task of much of biomedical research for years to come," said Francis Collins, Director of the NIH. It might be unfair to fault the Human Genome Project for its tardiness in delivering personalized medicine.

Puzzle Pieces

To realize a future with personalized medicine, science must be able to accurately read a man's entire genome, and then mine it for unique DNA letters that are known to indicate risk for disease. A key that links genes to traits is direly needed.

Unfortunately, genes are not as simple as science might hope. Gene 1 produces trait 1 and gene 2 produces trait 2 is entirely too simplistic. At the molecular level, a genome is composed of two sets of 23 lengthy DNA molecules, wrapped up into packages called chromosomes. Four nitrogenous bases, represented by the letters A, T, G and C are the alphabet to each strand, which bind to each other in pairs. Thus, a full genome has nearly 6 billion bases, occurring as 3 billion pairs. Two people are unique because their DNA is different by a mere one percent, or roughly 30 million base pairs. Single letter differences in the code account for this one percent.

Crucial to quantifying that variability has been the effort to discover the genetic basis for phenotypes or traits. What makes one person an NBA player and another, a Nobel Prize winning physicist? Why do some women have weak bones and others, early baldness? The daily bread and butter of genetics research has been to identify the genes responsible for diseases like cancer, diabetes, cardiovascular disease, and even psychiatric aberrations. Genome-wide association studies, sifting through the whole genome to find peculiarities in the DNA correlated with a certain trait or disease have become universal. But, the whole story is not in the genome alone.

Not only does your DNA influence your traits, your susceptibility to disease, but so does your environment. Environment is an umbrella term, encompassing, literally, your environment; did you play outside when you were young, and thus, how strong is your immune system? It also includes your diet; eating sugary foods from a young age can give you early signs of diabetes. It refers to your lifestyle; how much do you exercise? The term comprises of upbringing as well; were your parents overly protective and what is your resulting mental health? Where and how you grew up and live can influence your eventual health in myriad ways.

Genes are not the only entries in your personal Book of Life. With the goal of personalizing medicine, genetic science must appreciate how genes and environment interact to influence an individual. Do genes cause dietary preferences? Do lifestyle choices influence how your genes behave (the ongoing question of an entire field of study, epigenetics)?

Fortunately, some classical genetic diseases are rather straightforward, but that's probably why they are classical. Huntington's disease is caused by a mutation in the *HTT* gene, where a group of 3 letters are repeated one too many times. This results in dysfunctional proteins, causing a terrible, incurable disease, characterized by brain degeneration, loss of muscle control and early death.

Almost all human diseases have a genetic component. Apart from these classical genetic disorders, genes only play a partial role. Environment accounts for the rest, but how? The complexity of personalizing medicine quickly becomes disheartening among this tangled web of cause and effect. It's the kind of puzzle you think you can complete when you see the enticing picture on the box. However, the picture has been painted by multiple, unknown artists. And then, you find billions of obscure shape-shifting pieces in the box.

Should this be a reason for despair? No. Science is the sharpest scalpel available to cut past the obscurity of nature. And perhaps that is the inherent beauty of this conundrum. If there was ever a question worthy of all this effort, this is it. What accounts for our individual abilities, disabilities and idiosyncrasies? As the father of modern medicine Sir William Osler proclaimed in 1892, "If it were not for the great variability among individuals, medicine might as well be a science, not an art."

If we are to comprehend this mosaic, we need to develop an artistic eye. One man is already developing that keen vision. He is searching for that sacred key which will tell all.

The Young Crystallographer

George MacDonald Church is Profile One of the Personal Genome Project, his scientific quest to find the key to the human genome.

Hundreds of bottles of different chemicals line the seemingly endless shelves in his vast laboratory at Harvard Medical School. Dozens of post-doctoral, graduate and medical students bustle about; in this corner or that, an experiment of some sort is underway. Located just outside downtown Boston and surrounded by some of the world's best hospitals, the modernist glass edifice buzzes with excitement about testing new ideas in genomic medicine.

Church has deep grey eyes, pale skin, a mane that won't quit and a lumberjack beard that has long since given way to more grey. His full frame is shrouded with a Steve Jobs-style black top, with sleeves pulled up ready to work. He has a commanding baritone voice with a slight Southern charm, always speaking with a hint of marvel of the world. Church sits comfortably in his chair before a wall of manuals and books enhancing his already imposing stature. He is director of the National Institute of Health Center of Excellence in Genomic Science at Harvard, MIT & Washington University, and advisor to 22 biomedical companies, a handful of which he co-founded.

Church's recent book *Regenesis*, which reveals the promise and perils of synthetic biology, altering the genomes of organisms to make slightly different organisms, sits on the closest shelf. Nearby is a small vial containing the entire manuscript of the book translated into DNA form, his tweak of biology. Storing data as DNA is just another side project of his.

"My father was a physician," said the scientist. Church would marvel at all the tools his father would use to treat his patients, from syringes to stethoscopes. "I thought, wow this is full of inventions. Someone had to invent every single thing in here. I thought how do you do that?"

He was curious about the world inside and outside the house. His childhood home was on a bay in MacDill Air Force Base, Florida. Low tide would reveal vast expanses of knee-deep mud full of critters and crawlers for young Church to sift through. In these early adventures, he was already showing the first mark of a scientist, curiosity. But was science all he aspired to?

Church showed an early knack for math and computers as well. By age 9, he had built his own computer. By age 15, the year the U.S. Apollo 11 landed on the Moon, he taught himself three different computer languages.

"I wanted to find some kind of connection between math and computers, which I was good at," he said. "I loved biology and medicine. I was desperate to find some connection [between all these disciplines]. It took a while."

The answer was crystallography, the science of determining the shape and folding of molecules by measuring their geometric angles. It was a "really good match," Church said. "It was related to the crystallography that Rosalind Franklin and Watson and Crick used to get the double helix." Crystallography was a natural fit for Church. While the world was looking at the heavens in awe, he was peering deeper into the microscopic universes of molecules. It was the nucleic acids he fell in love with, the DNA that composes the genome and the RNA that serves as a step of translation between the DNA and the proteins it instructs the production of. He focused on a small nucleic acid. "Actually it was this one here," he said, pointing to a beautiful crystal.

This gem popped out of the background for the first time. It was a laser-etched crystal of a tRNA or transfer RNA molecule, looking like a strand of spaghetti positioned in a V. To complete this project he wrote a computer program that helped create the first high-resolution image of the molecule, a program still in use today.

Unfortunately, he flunked out of Duke in 1976, focusing too much of his effort on research instead of coursework. Harvard University overlooked his academics and gave the young scientist another chance. Church subsequently earned his Ph.D. in Biochemistry & Molecular Biology in 1984 under the mentorship of Dr. Walter Gilbert, the winner of the Nobel Prize in Chemistry in 1980. Together, they developed a new standard of genomic sequencing.

"I fell in love with nucleic acids, automation and computers," said Church. He continued to develop genome sequencing technology, among other ventures in synthetic biology.

Math. Computers. Biology. Medicine. Call it a peculiar combination, but Church's varied interests merged at a most opportune time. The field of genomics was burgeoning. Only, the methodology of the science was cumbersome. "Biology was really, very primitive in terms of engineering," he said. It was begging for people like Church to come and streamline it. And he did. He developed Polony genome sequencing, which is a next-generation method that affords more than 99.9999 percent accuracy at one-ninth the cost of traditional sequencing.

Church's commitment to technology was fervent. He started off as an initial contributor to the Human Genome Project, being the only one to attend all three foundational meetings on the subject. Later on, he would break away due to a difference of opinion. Church wanted sequencing technology to become fast, cheap and efficient before the genome was attempted.

"I've always been a round peg trying to fit into square holes," he said. "I didn't really fit, even though I helped start it." He also wanted environmental factors like diet, exercise, and childhood upbringing, crucial influences to be considered alongside the human genome.

Church's recent brainchild, the Personal Genome Project, an expansive study to correlate genes, environment and traits, gives him a chance to see science and technology come together to advance medicine.

A Rosetta Stone for Personalized Medicine

"That's actually a second problem I had with the Human Genome Project," said Church. They were doing a genome without traits. My first grant, in 1987, the first [Human Genome Project] grant, was titled *Genome Sequence Comparisons*. I felt that without comparisons, it's hard to get to biology."

To achieve this translation, to communicate seamlessly between DNA, the features it instructs for and the external forces that influence this process, science needs to compare these data between a multitude of people. "What you need is a Rosetta stone that helps you connect genes, environment and traits," said George Church. For this reason, he started the Personal Genome Project, a logical step after the Human Genome Project.

This formidable, ongoing study based at Harvard Medical School envisions eventually recruiting 100,000 volunteers like Church who will submit their genomes, an exhaustive list of their phenotypes, their total phenome, and information about their environment into a database. With many profiles like this occurring in tandem on one database, researchers can mine the data for links: cross analysis.

They might comb the database for every person with one phenotype, say, occurrence of non-small cell lung carcinoma, a lung cancer particularly resistant to chemotherapy. They will then compare each the environmental factors and the genomes of those making the list. Did many of these people happen to live near industrial factories? Do they tend to consume sugary

drinks? Or, at the molecular level, what segments of their DNA are similar to each other? Perhaps that is a location of interest in the code, maybe a mutation has occurred there.

Misha Angrist, a geneticist at the Duke Institute for Genome Sciences & Policy, was a co-founder and the fourth participant of the Project in 2007. He describes his own journey as a participant in his recent book, *Here Is a Human Being: At the Dawn of Personal Genomics*. The level of data in his profile is rich. First, a participant's genome is sequenced. It is searched for any currently known disease-causing variations and marked as such. That annotated script is uploaded to his online profile, hosted on *personalgenomes.org*.

Next, he submits answers to numerous questions about ethnic background, family history, diet, exercise, lifestyle, and undergoes a full physician workup to record all his physical vulnerabilities. Functional magnetic resonance images, scans of his brain from several angles are uploaded. So are comprehensive blood tests and their results. Information about every last complaint he may have about his health is uploaded. Every prescription drug, illegal drug, sexually transmitted disease... every parameter of health is noted and uploaded. Participants even donate some cells, in case future research requires it. They are also asked to check with their families before participating; they share much of their genome with family. This data collection occurs over several visits to Church's lab. As new questions arise, participants can be asked to revisit to submit more images and answers. "The process was unprecedented and at times clunky, but it was necessary," said Angrist.

So far, Church has recruited nearly 3,000 people: 3,000 samples freely available to cross-analyze for anyone in the world that has a mind to. Several thousand more are already committed and await full collection of their information.

Given the enormity of data, researchers can tease apart the basis for different diseases. They can compare small groups of similar people with the same disease, instead of large groups of different people with a general disease, to truly target the genetic underpinnings at play. Normally, researchers conduct genome-wide association studies, GWAS to find similar single nucleotide polymorphisms, single DNA letters, between people with the same disease.

"I was a critic of the original definition of genome-wide association studies," said Church. In these studies, "the focus [is] on common variance and common disease, neither of which I feel is significant. 'Common diseases' is a misnomer, a mistaken way of looking at it. There are no common diseases; we're all going to die of something different. You can clump them together if you want."

By clumping together many people who have 'pancreatic cancer' in a genome-wide association study, scientists are ensuring that their results will be muddled and inconclusive; significant but hard to discern differences in genes will all be blended together. This is because many people develop 'pancreatic cancer' via different mutations. In reality, there may be several or a hundred different subtypes of pancreatic cancer, each with a slightly different genetic basis. "We need a large number of people, each of which is an N=1 study," said Church, at his annual GET Conference (Genes, Environments and Traits) which presents the status of the Project.

By studying much smaller groups of people with similar backgrounds and profiles, researchers can target the DNA letters that lead to a particular pancreatic cancer with more precision. The Personal Genome Project makes that possible. Pancreatic cancer can be studied among clusters based on age, sex, ethnicity, diet, or a combination of these as opposed to one giant amorphous sample: divide and conquer. "What we're trying to do is create a viewport into how precision, personalized medicine will occur in the future," said Church.

There are several other efforts that are similar to the Personal Genome Project in that they have a goal of linking genes with traits. The most prominent is the International Hap-Map Project, a follow-up to the Human Genome Project lead by Eric Lander, a prolific biologist and founding director of the Broad Institute of MIT and Harvard.

In the *Nature* journal article announcing the initial completion of the human genome, there were over 100 authors listed. Lander was the first. In addition to leading this project, he developed the Hap-Map Project to translate the genome into useful information. In this effort, nearly 300 human genomes were sequenced, but only at positions that are highly variable between people: the one percent difference. The project seeks to correlate diseases with these variations in the genome.

The Human Genome Project was a race that had a finish line. The finished script of the human genome was a tangible trophy. Conversely, translating that script, learning that language, piecing together the puzzle of life has no end in sight. It's not a race, it's an infinite marathon.

This effort, "certainly won't have a finish line in my lifetime," said Angrist. "I suppose at one point it will be considered fairly well-understood."

"I felt the ultimate comparison would be doing millions of people, comparing human genomes," said Church. "You need to get the price [of sequencing] down so everybody can get their genome, and then everybody who wants to can share their genome and compare it. And that's what the Personal Genome Project is about: genomes, environment and traits."

The Y's Have It

In studies like the Personal Genome Project, participants are uploading their entire genomes online, accessible by literally anyone in the world. But why?

Steven Pinker, an evolutionary psychologist at Harvard University and author of *The Blank Slate* among other works, participated in the Personal Genome Project, "to get firsthand acquaintance with a human genome [he] was particularly motivated to analyze." Observing your own marked genome fulfills a self-searching desire for some. In *The Daily Jewish Forward*, Pinker commented about himself that, "even this secular Jew experienced a primitive tribal stirring in learning [the] deep genealogy," his genome revealed.

In the same piece, Angrist shared some thoughts on participating as well. A personal genome "is simply a rich source of data that can give us additional clues about ourselves and our families, whether it's our ancestry or our health," he said.

Some candidates might participate out of pure generosity to science. As a perk, they receive their sequenced genome free of charge. They can use it to learn about risk of disease should they choose to. Church and his team are not medically responsible for the participants, as they make plenty clear, but can inform them of any concerns that might arise.

The researchers are sure to remove participants' names from their profiles, a modest effort toward anonymity. There's nothing to worry about right? Even if there were folks malicious enough to use your genome for ill purposes, there's no way they could identify you with it... it's not like your name is encoded in your genes. Wrong.

On January 18, 2013, a group of geneticists and ethicists caused a row in the scientific community. Using just publically available genomes and online resources, data and tools anyone can access, they correctly placed surnames on genomes samples. They published their results in *Science* magazine, instigating several key questions: are participants who donate their genomes to science being lied to? Can scientists keep a lid on the identity of their participants? Does informed consent need to change? Will the pursuit of privacy hinder personalized medicine?

Informed consent refers to a well-established practice in scientific research. Human participants in scientific studies must be informed of the benefits and risks of participation and then provide their written consent to enroll. Part of this legal agreement is that participants have a right to have their personal medical information kept private, an ethic dating back to Hippocrates, and today known as a U.S. law called HIPPA (Health Insurance Portability and Accountability Act). Medical information is inherently sensitive. By establishing this agreement, research institutions and universities protect themselves and scientists can establish an accord with their subjects.

To reach this agreement, some researchers keep the data they collect from participants secure, promising anonymity or at least low risk. "They're locking it with bigger locks and deeper vaults," said Church. Other studies have the inherent goal of publishing genomes for the general public, to promote open science. In these cases, identifying information, especially names, is removed from genome profiles.

Yaniv Erlich is a young geneticist and a fellow at the Whitehead Institute of Biomedical Research. He wasn't convinced that removing names did much for anonymity. That's when he and an international team of researchers decided to put public genomes to the test. The secret lies in Y chromosomes.

Females have two X chromosomes in their genome, which denote their sex. Males have an X and a Y. Coincidentally, and luckily for biomedical science, Y chromosomes and surnames are similarly inherited.

Fathers can contribute an X or a Y chromosome to a child, while mothers can only contribute an X. The father thus determines the sex of the child. When it's a boy, it's because daddy donated a Y chromosome. Interestingly, in many patriarchal cultures like our own, sons inherent surnames from their fathers, while daughters often adopt the surname of their eventual spouses. Therefore, surnames generally follow Y chromosomes in lineages.

Y chromosomes are part of the genome, and research participants are donating their full genomes to science, to the public sphere. The participant shouldn't worry about their genome being re-identified, as long as no one can provide a link between the genomic data in their Y chromosomes and surnames... wait.

There are currently eight companies that can estimate surnames using genomic data from Y chromosomes. The genetic information in Y chromosomes from one man to the next is mostly conserved: after all, aren't all men the same? But there are areas in the chromosome, 'short tandem repeats' that are highly variable between individuals, called Y-STRs. These companies have amassed data linking Y-STRs and surnames from participants and in turn provide them genealogic services when they're searching for relatives in their paternal line. With enough samples in their databases, they're able to provide a good estimate of potential surnames given Y chromosome data, considering that some people change names and mutations can occur.

Some of these services, Ysearch (www.ysearch.org) and SMGF (www.smgf.org) are public, free of charge, and usually intended for individuals personally seeking their own genealogy, providing their own genomic information. However, the slope between submitting your own genome and someone else's from a public genomic study to search for surnames is a slippery one. That was the concern on Erlich's mind. His team conducted such a study: they tested these databases submitting Y-STRs of publically available genomes with known surnames. The databases, which output the most probable surname, provided the correct name in 12 to 18 percent of the cases.

Erlich and his team pushed further, and considered how closely they could hone in by using genomic data, age, and state residency information. He tested some genomes of known individuals that are hosted by the National Center for Biotechnology Information. The team extracted the Y-STRs of these genomes, and searched for a surname. J. Craig Venter, one of the significant contributors of the Human Genome Project, was among these individuals. As expected, Erlich landed on several potential Venters using his Y-STRs. Dwindling down the list by age and state residency, from genealogical information hosted by the National Institute of General Medical Sciences (NIGMS, a branch of the NIH) and data from public resources like PeopleFinders.com, the team landed on J. Craig Venter himself, displaying full scientific sacrilege: from genome to full name, supposed anonymity to unabashed re-identification.

The study was received with much anxiety this past January in both genomic science and research ethic circles. Some scientists question if Erlich should have published such a study, it could have been damning to all genomic studies, scaring away vital participants. It was a proof of concept, an example that had to be shown. But as Erlich admits, he's not the first to attempt such a genome hack.

In 2005, an ambitious 15-year-old named Ryan Kramer took a similar route to identify his sperm-donor father. He used personal genome services to analyze his own Y chromosome (after all, that was a gift from dad) and searched the databases for a surname, eventually identifying his dad. His biological father must have been promised anonymity when donating.

Kramer's curiosity and Erlich's systematic study demonstrate that we can no longer be naïve about anonymity and privacy in genome studies. It was possible then, now, and it will only be more possible in the near future to place a name on a genome. It seems irresponsible to promise anonymity to study participants.

What is the appropriate response in light of this information? To achieve personalized medicine, scientists must analyze genomes to whittle out the underlying heritability and cause of disease, like the Personal Genome Project is doing. This means that multiple genomes will be amassed and hosted together, somewhere on some network. "If large scale data sharing is anticipated or planned then the participant should be explained what that involves and the potential risk of identifiability," said Amy McGuire, a medical ethicist at Baylor College of Medicine, and co-author of Erlich's study.

Erlich conducted this study to better inform the scientific community. He tipped off the NIH about his results before publishing them. As a countermeasure, the NIGMS removed information regarding the ages of participants in the study from public view said Laura Rodriguez, Director of Division of Policy, Communications, and Education at the NIGMS. "This did not remove all risk of re-identification, but it significantly diminishes the vulnerability."

Should scientists increase the security of this data? Define 'secure'. Erlich and his team got a question from the NIH about if they "should take all this data from the Y chromosomes of these people and put it into a secure database," he said. "We told them it doesn't matter," because other researchers have already taken this Y-STR information from these genomes and published it in publically available papers. "Unintentionally, there might be a leak of the data," said Erlich.

"Putting the data on [a] cloud with limited and importantly monitored access is very useful," said Dov Greenbaum, a molecular biophysicist and biochemist at Yale University. "Limiting access to the cloud to people who have passed some sort of basic exam as to the ethical, legal and social concerns might help." Greenbaum proposed altering public genomes by stripping them of immediately identifying information, a method with precedent. The famous James Watson donated his genome to science in 2008. However, he redacted the region of his genome, a gene that could reveal whether he is at risk for developing Alzheimer's disease. A study in response demonstrated that it is possible to ascertain this risk just from the nature of the DNA surrounding that gene. Watson redacted even more of his genome.

This illustrates the central predicament in studying public genomes. Do we increase security, do we encrypt, do we restrict? How far do we go in pursuit of anonymity? Angrist believes this issue to be grey. "We are not a homogeneous species," he said. "People have different preferences: researchers should do their best to honor them rather than to do what's most convenient for themselves or what keeps the lawyers and regulators at bay." Scientists can

either increase security and promise privacy or develop another approach. Whatever each group of scientists in each study decides, they must act to retain the trust of their participants and the public. Rich genomes and profiles come from ordinary people, not the laboratory.

Church, in his characteristic manner, observed this problem a decade ago. In a 2003 proposal to create the Molecular and Genomic Imaging Center at Harvard, he wrote,

> The core question is: how may the gathering of increasing amounts of genetic information be made compatible with ethical and legal requirements for privacy? Anything approaching a comprehensive genotype or phenotype ultimately reveals subjects' identity in our increasingly wired world as surely as conventional identifiers like name and social security number.

As part of his motive to start the Personal Genome Project, to set an example for science, Church wandered where few dared to. His foresight told him promising privacy was a futile goal. "We flipped the whole thing on its head," said Church. "Instead of saying how can we make the data more secure, I said, let's make it less secure, but get people who are okay with that."

Facebook, Myspace, Mygenes

Church often has a futuristic perspective, delivering copious anxiety to fellow scientists. In the 1980s, he was already concerned about making genome sequencing cheap. His book *Regenesis* tries to estimate what synthetic biology will achieve in the years to come. He predicted problems with genomic security well before the genomic boom of the last five years. Church has prepared the Personal Genome Project for this future.

He believes that in years to come, privacy will have ebbed away, either by will or by technological advances. "When I was a kid, no one would talk about almost any medical problem," said Church. "If you had someone in the family with psychiatric disorder, you just said, 'you know, Uncle Henry is a little odd.' That would be the end of the conversation." Today, people readily reveal even their own medical information, their illnesses and treatments.

"I don't know where it's going exactly," said Church, "but I see a general trend toward more openness." Erlich agrees. "I think the landscape of our feeling about private information is changing," he said. Greenbaum predicted that, "as a society we are moving in a direction that cares less about disclosure."

Today, people share a surprising level of personal information on social media websites. Google Earth software gives anyone a bird's eye view of where you live. Hackers constantly find new ways to crack computer vaults in an arms race with data security experts, some just for the thrill. Whenever you are in a public place, you are surrounded by a phalanx of smartphone cameras that can share your image with the world in seconds. Even by carrying a smartphone, you are revealing your distinct traveling fingerprint to cell phone providers and the advertising agencies that seek to use that information to increase sales. A group of researchers from MIT

demonstrated this year that with minimal phone data, they could identify a person 95 percent of the time; even your day to day travel is revealing.

Either because we choose so, or because the technology we immerse ourselves in is so good at it, privacy is becoming antiquated. The hinges of the floodgates are rusty. It's only a matter of time.

Invasive technology and a shift in privacy culture mean that personal information will not remain secret. Genomic data is as personal as it gets. With the way the culture is shifting, it's not so difficult to imagine a future where we might ourselves boast our genome as another feature on Facebook, Myspace and Twitter accounts. Maybe we will tweet about mutations we possess, and befriend fellow mutants. This would align perfectly with the 'me' culture of social media.

Not surprisingly, biotech companies that provide direct-to-consumer sequencing have been flourishing. For example, 23andMe Inc. provides people with information on 250 or so known sites in their genome that directly affect health for a mere $99. Sites like Ancestry.com allow people to track their genealogy. It's not difficult to imagine what sorts of searches and manipulations people are capable of with such services. Tomorrow will be the era of personal genomes, where people directly use their own genome, without a lab coat or suit serving as a middle man. They can do as they please with their genes.

"We're going to get to a world [with]—what I would call personal sequencers," said Church. "Your phone went from being a phone to a camera phone. At some point some phone company that differentiates itself from all the other companies is going to put in some biochemistry and genetics." Church believes that in time, you'll be able to place a little saliva on a receptacle on your phone, which will then sequence your genome and display the results for you. This is a future where nanotechnology, proficient sequencing and the attitude of 'why not' converge. With a click, you can share your results with the world.

Even if some of this is fantastical thinking, Church doesn't see the opposite occurring. There are no signs that as a society, we are keeping personal information more secure, that security systems are winning the arms race, or that we are striving toward privacy. "I don't think we are going to be able to convince the Twitter/Facebook/Tumblr generation to put the genie back in the bottle," said Greenbaum. It is time genomic science acknowledges this, and adapts for the better. "If you're honest with a research subject, that's a better protocol," said Church.

Truly Informed

On April 25, 2013, Latanya Sweeney, director of the Data Privacy Lab at Harvard, and her research assistants cracked the identity 241 of the participants in the Personal Genome Project. The friendly effort was meant to demonstrate vulnerability in public data.

Of the roughly 3,000 participant profiles online, about 579 included zip code, date of birth and gender. With just these three key pieces of information, (no genes, no DNA) she tried to re-identify participants using information from voter rolls and other public records. Sweeney was relatively successful, placing a name on about 40 percent of this subset.

As expected, Church had prepared for this before even beginning his project. Such an attempt is exactly what he had in mind when he started thinking about making genomes publically available. The Personal Genome Project is as much a prototype for a new standard of research ethics as it is a study in genomic science. The participants that come forth are those willing to give open consent, a type of informed consent where they acknowledge that privacy and anonymity are not guaranteed.

In many cases, study participants are briefly informed of what they're participating in, and quickly sign an agreement. In a study of say, 200 participants, few researchers have the time to make sure that each participant fully understands a thick legal document.

Church's approach is different. After coming forth and expressing interest, participants must complete six modules of a study guide, learning about everything from the nature of open consent, to what DNA is, to what the risks and benefits of participating are. Next, they must take a quiz on those subjects including 15-45 questions, and must attain a perfect score. In this way, participants get some idea of what it is they are donating. It's not just a drop of blood.

Next, they read, review and sign consent forms. These forms are entirely candid about the benefits and risks of participating in the study. Participants are informed in a straightforward manner that their genomic data could be used in malicious ways, and in ways that are yet unimaginable. Church and his team make sure that participants understand this. Their data can be used to "infer paternity or other features of the participant's genealogy, claim statistical evidence that could affect employment or insurance or the ability to obtain financial services for the participant, claim relatedness to criminals or incriminate relatives, make synthetic DNA corresponding to the participant and plant it at a crime scene, or reveal propensity for a disease currently lacking effective treatment options." These are grim outcomes, but at least the participants are informed as such.

When Church first started talking about this 180 degree turn in the scientific community, that privacy and anonymity are unfeasible, and that perhaps genomic science should seek and inform participants who will accept that, he was met with much criticism.

"Nobody really thought that I was saying anything reasonable," said Church. "They were worried that if they listened to me even for a moment, they would be held legally responsible for what they learned from me, and it would scare away all their patients from their studies."

Scientists would be hard-pressed to reveal their disagreement. "They never quite articulated this," he said, "because that would be admitting that you're actually consenting patients without their full knowledge of what could happen."

Instead of adopting open consent, like Church, some studies attempt to ensure low risk in their consent forms. An example is the 1000 Genomes Project, another comparison effort which is cross-analyzing genomes from a diversity of ethnic backgrounds. "It basically alternates paragraphs where it says 'Oh these are all the ways that you can get re-identified, but, it's very unlikely for the following reasons'," said Church. "It oscillates back and forth enough times that you're left with a notion that it's safe."

In most genomic studies other than the Personal Genome Project, participants are assured that the chances of being re-identified are low. If their genomes are public, their profiles are de-identified, stripped of any identifying information like name. Or, if they are private, their profiles are locked away with the best data security. This is the increase security, promise low risk path.

Church is taking the decrease security, inform of high risk path. As Erlich pointed out, data leaks. In fact, Church informs his participants of ways in which de-identified data can be re-identified, and how 'secure data' can end up in the wrong hands. Wherever their moral compass points, people can re-identify an individual from their genome just based on phenotype information; genes readily reveal eye and hair color, height, stature and even facial shape. Hackers can breach secure data servers, thieves can steal laptops, scientists can accidentally publish parts of genomes in papers.

Erlich was motivated to show the scientific community where the holes in the security are. "We just showed one technique," he said. "I'm sure there are another dozen techniques that we didn't think of."

There is no right solution to this conundrum. "It recommended that researchers and clinicians should evaluate and adopt robust and workable consent processes," said Kayte Spector-Bagdady, Associate Director of the Presidential Commission for the Study of Bioethical Issues. As long as those processes are honest and clear about the benefits and risks of participating, researchers are free to adopt any public/private, secure/open structure.

And there are multiple structures. "I think you see a continuum here," said Bradley Malin, professor of biomedical informatics and Director of the Health Information Privacy Laboratory at Vanderbilt University. However, Malin thinks research policy could be more proactive instead of letting the inevitable happen. A potential solution to re-identification problems is to implement laws prohibiting it. Currently, there are no explicit laws that prohibit people from doing what Erlich did, or preventing people from doing what Church warns can happen. Similarly, gun laws don't prevent illegal gun use, but they do lessen it.

Additionally, Malin is hesitant about adopting a completely open structure, as in the Personal Genome Project. "We do not know what all the repercussions are going to be," he said. "It would be really nice to know who's using the information." Like Greenbaum, Malin suggests as a potential solution some level of monitoring or control beyond completely open access which the Personal Genome Project currently uses. The fact that any unnamed, unknown person can download his genome if he was part of the Project makes Malin concerned.

Church structured the body of ethics in his Project to prepare for the worse, but the worse might never happen. "Just because you can identify a piece of DNA because you can analyze Y-STRs until the cows come home at the [Whitehead Institute] doesn't mean that other people are going to do that," said Malin. Though there is some merit in taking precautions, and assuming some people will simply hack genomes, there might not be enough evidence to assume that given some genomes and public software, everyone will be re-identifiable all the time always. And so, adopting a completely open access structure might need some rethinking.

With a rapidly evolving technological landscape, cheaper DNA sequencing, and a change in culture, no one, not even Church knows for sure what future consequences science might face in choosing one path or the other. For example, Church has his participants consult their family members before enrolling. Your genome represents half of each of your parents' genomes. It can also reveal crucial information about your children, and other relatives. Greenbaum points out that, "there really isn't a way around this issue – do we find all your relatives and get them to consent? What if there is a hold out?"

If scientists fight the long battle of trying to keep information private and anonymous, they might be stalling the inevitable. Locking up data, removing important information from profiles because it's identifying does not fit into a model of open-access science. Not acknowledging the reality runs the risk of people losing trust in the safety of genomic science. "If you want people to keep donating information to studies, you need to educate them about the risks and benefits of genetic studies," said Erlich. On the other hand, it might not be prudent to declare open season on public genomes and plan for the worst.

Just as sifting through genes, environments and traits, hammering out consent policies and study structures that are suitable to the society we live in, and for different-minded groups of researchers and participants is an intricate issue. It's a relatively young puzzle that scientists and society will have to piece together over time.

In the meantime, the pursuit of privacy might hinder the development of personalized medicine. The technology for personalized medicine is here and only advancing. The science is coming along. Church is simply adapting and evolving as he knows best. "That is one of the things that distinguishes the Personal Genome Project," said Church. "It's looking forward."

The Future, Not Science Fiction

If personalization is to become the new standard of medicine, the ethical, legal and social concerns on how the science will deliver this progress must evolve as well. "When you see something that is technically sweet, you go ahead and do it and you argue about what to do about it only after you have had your technical success," said J. Robert Oppenheimer in reference to the Manhattan Project, the effort to create atomic bombs. Though geneticists who compete in the race to translate the human genome are hardly committing the sin of World War II, they are similarly anticipating the science before acknowledging the reality of its ethical considerations.

"A lot of technologists just say, 'ethical-legal-social, that's distracting, it's irrelevant, it hasn't changed since Socrates any way, why should we mess around with it?'" said Church. But he did mess around with it. Church anticipated these concerns and addressed them in the Personal Genome Project in order that genomic science may progress rapidly and seamlessly. He has carved a new inroad for genomic science to follow.

How will life be different when that progress is finally complete? "I suppose at one point [the genome] will be considered fairly well-understood," said Angrist. Even if that point is 10, 50 or 100 years from now, the future of medicine looks more accurate and more efficient.

Imagine a child born in year 2100. When he is a developing fetus, physicians will conduct amniocentesis at the request of the parents, where they will collect a little fluid from his mother's womb which contains his fetal cells. In the nucleus of each cell, in that vital envelope are his 46 chromosomes, his parents' original DNA masterpiece. Physicians will reach that DNA by breaching the cell and nuclear membrane. The chromosomes will be unpackaged in a genome sequencing machine. The DNA will be read base by base, and a virtually 100 percent accurate script will be produced as a portable document; one copy to the parents for safekeeping, and the other which will be uploaded to the child's online medical folder. Before he is even born, the book of his life is written.

Next, that genome script will be searched letter to letter. Using software that will act like a genetic dictionary, physicians will note which mutations the child possesses, which risks he is prone to and perhaps even special abilities the child may have in life. That dictionary, that key, that Rosetta Stone will be the end result of a century of comparing genes, traits and environment. It will be an invaluable tool to medicine, a feat greater than the Polio vaccine and penicillin.

The physician will advise the parents on what measures to take to maximize their child's health. Eventually the physician will advise the child himself. He will inform the family on what particular lifestyle choices to adopt and what dietary considerations to make. The physician will also inform the patient of any genetic concerns should he choose. If he possesses the *HTT* mutation, he may want to live a full life before Huntingon's disease sets in, unless of course there is already a cure. If he possesses the *APOE4* mutation, he may want to engage his mind by frequently completing Sudoku puzzles well into old age, so as to stave off Alzheimer's disease.

In this future, genomes will not be as permanent as the ink with which they are written. Gene therapy will be the next generation of treatment. When there is an error in the genetic code that results in such terrible illnesses, there can be more direct treatments than Sudoku puzzles. Physicians will create therapies that will serve as genetic copy editors. Through gene therapy, innocuous viruses will be engineered to deliver new and correct genes to the segments of the DNA that are erroneous, to every nucleus of every cell in the body. This gene therapy will restore potential to the patient.

In addition to his genome and its interpretation being filed in his online medical records, so will every other facet of his health, every checkup and every visit. Perhaps by 2100, the Brain Activity Map project, the effort to map the human brain will be complete. Physicians will scan this man's brain and upload those images and their interpretation to his online records. In addition, maybe the Human Microbiome Project will be complete as well, the effort to track which microbes and bacteria inhabit the human gut. Every year or so, this man will submit a stool sample so that his own microbiome can be assessed and interpreted. This will help physicians understand how his digestion is influenced by these bacteria, and how he may respond to certain drugs. Finally, every parallel that can be drawn between these datasets will be drawn. If he possesses a mutation concerning how serotonin in his brain is produced, that will be compared to how the serotonin centers in his brain images appear. Quite simply, every measure of individual health will be made and collected on a central database folder accessible by health care professionals: completely personalized medicine.

With these efforts, medical care will become more efficient. No more will physicians treat the aftermath of a disease. They will prevent the disease from ever occurring. With all this data, and the expertise to act on it, the patient will avoid ailment and live the fullest life possible.

It sounds like science fiction, but so did the idea that microscopic organisms cause disease in the early 19th century and the idea that 100 billion neurons make up the human brain in the early 20th century. Imagine medicine just one or two centuries from now. What makes you one of a kind will be of the essence. That's a cheery future to look forward to.

BIOGRAPHY

Abdul-Kareem Ahmed grew up in Wakefield, Rhode Island. He attended the University of Pittsburgh, earning his bachelor's degrees in neuroscience and history & philosophy of science. During college, he tried his hand at sharing science through writing. Subsequently, he enrolled in the Graduate Program in Science Writing at MIT. Following MIT, Abdul will start his journey into medicine at the Warren Alpert Medical School of Brown University, with the ultimate hopes of becoming a physician-writer. Besides learning more biochemical pathways and writing the story of science, he likes spending time with family and friends, and enjoying the many waterways and beaches The Ocean State boasts.

ACKNOWLEDGEMENTS

I would like to thank my family for their infinite support. I would also like to express gratitude toward Alan Lightman for his wisdom and guidance. The faculty and staff of the Graduate Program in Science Writing at MIT were indispensable in this effort. And of course, the GPSW Class of 2013 was limitless in encouragement and assistance.

REFERENCES

INTERVIEW NOTES

Page 4-5

1) Interview with Nathaniel Comfort, Ph.D. The Johns Hopkins University. Conducted January 2, 2013.

Page 7

1) Interview with Lee Gutkind. Arizona State University. Conducted February 27, 2013.

Page 8

1) Interview with Francis Collins, M.D., Ph.D. National Institute of Health. Conducted via e-mail March 3, 2013.

Page 9-14, 17-23

1) Interview with George Church, Ph.D. Harvard Medical School. Conducted February 6, 2013, March 22, 2013, and April 9, 2013

Page 12-22

1) Interview with Misha Angrist, Ph.D. Duke University. Conducted March 5, 2013.

Page 13

1) Interview with Stephen Pinker, Ph.D. Harvard University. Conducted via e-mail April 28, 2013

Page 14-21

1) Interview with Yaniv Erlich, Ph.D. Whitehead Institute. Conducted April 26, 2013

Page 16-21

1) Interview with Amy McGuire, J.D., Ph.D. Baylor College of Medicine. Conducted via e-mail April 29, 2013
2) Interview with Laura Rodriguez, Ph.D. National Institute of Health. Conducted via e-mail May 13, 2013.
3) Interview with Dov Greenbaum , J.D., Ph.D. Yale University School of Medicine. Conducted via e-mail May 6-7, 2013
4) Interview with Misha Angrist, Ph.D. Duke University. Conducted via e-mail May 13, 2012.

Page 20-21

1) Interview with Kayte Spector-Bagdady, J.D. The Presidential Commission for the Study of Bioethical Issues. Conducted via e-mail May 10, 2013.

2) Interview with Bradley Malin, Ph.D. Vanderbilt University. Conducted via e-mail May 6, 2013.

BIBLIOGRAPHY

Page 3

1) personalgenomes.org
2) http://arep.med.harvard.edu/gmc/pers.html
3) http://www.personalizedmedicinecoalition.org/about/about-personalized-medicine/the-case-for-personalized-medicine
4) Dupuis, J. *et al.* New genetic loci implicated in fasting glucose homeostasis and their impact on type 2 diabetes risk. Nat. Genet. 42, 105–116 (2010)
5) http://ghr.nlm.nih.gov/handbook/genomicresearch/pharmacogenomics

Page 4

1) http://cancer.stanford.edu/information/geneticsAndCancer/genesCause.html
2) http://medical-dictionary.thefreedictionary.com/Cancer
3) http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA
4) http://www.nytimes.com/2013/05/14/opinion/my-medical-choice.html?_r=0
5) http://www.cancer.org/cancer/news/expertvoices/post/2012/04/18/the-future-is-now-personalized-medicine.aspx
6) Lee, MS. *et al.* Personalized medicine in cardiovascular diseases. Korean Circ J. 42, 583-591 (2012)
7) Abu-Asab, Mones, Amri, Hakima, and Micozzi, Marc. *Avicenna's Medicine.* New York City: Healing Arts Press, 2013. Print.
8) http://www.ucmp.berkeley.edu/history/leeuwenhoek.html

Page 5

1) http://ocp.hul.harvard.edu/contagion/vonpettenkofer.html
2) http://www.genome.gov/Pages/Education/GeneticTimeline.pdf
3) http://bioinfo.mbb.yale.edu/course/projects/final-4/
4) http://www.ornl.gov/sci/techresources/Human_Genome/project/hgp.shtml
5) http://www.nytimes.com/2010/06/13/health/research/13genome.html?pagewanted=all

Page 6

1) http://partners.nytimes.com/library/national/science/062600sci-human-genome.html
2) http://www.genome.gov/11006943
3) http://www.ornl.gov/sci/techresources/Human_Genome/research/sequencing.shtml
4) http://www.stanford.edu/group/hopes/cgi-bin/wordpress/2010/10/human-genome-project/
5) http://partners.nytimes.com/library/national/science/062700sci-genome.html
6) partners.nytimes.com/library/national/science/062700sci-genome-nature.html
7) Pennisi, E. The Human Genome. Science. 291, 117-1180 (2001)
8) http://www.broadinstitute.org/education/glossary/genome

Page 7

1) http://news.nationalgeographic.com/news/human-genome-project-tenth-anniversary/
2) Klein, RG. Darwin and the recent African origin of modern humans. Proc. Natl. Acad. Sci. 106, 16007–16009 (2009)
3) http://newsinfo.iu.edu/news/page/normal/17183.html
4) Pertea, M and Salzberg, S. Between a chicken and a grape: estimating the number of human genes. Genome Biology. 11, 206 (2010)
5) www.broadinstitute.org/blog/what-exome-sequencing
6) http://www.genome.gov/sequencingcosts/
7) http://www.ornl.gov/sci/techresources/Human_Genome/research/sequencing.shtml

Page 8

1) http://www.hsph.harvard.edu/obesity-prevention-source/obesity-causes/genes-and-obesity/
2) http://www.niehs.nih.gov/health/topics/science/gene-env/
3) http://www.dor.kaiser.org/external/DORExternal/rpgeh/index.aspx
4) http://www.sciencemag.org/site/feature/plus/sfg/resources/res_epigenetics.xhtml

Page 9

1) http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001775/
2) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2323540/
3) http://arep.med.harvard.edu/gmc/pers.html
4) http://www.nytimes.com/2010/06/08/science/08church.html

Page 10

1) http://arep.med.harvard.edu/gmc/pers.html

Page 11

1) http://arep.med.harvard.edu/Polonator/
2) Personalgenomes.org

Page 12

1) Personalgenomes.org
2) http://fora.tv/2013/04/25/Harvard_Professor_George_Church_Opens_the_GET_Conference
3) http://www.getconference.org/

Page 13

1) http://www.broadinstitute.org/history-leadership/scientific-leadership/core-members/eric-s-lander
2) Lander, ES. *et al.* Initial sequencing and analysis of the human genome. Nature. 409, 860-921 (2001)
3) http://forward.com/articles/140896/dna-and-you-personalized-genomics-goes-jewish/

Page 14

1) http://forward.com/articles/140896/dna-and-you-personalized-genomics-goes-jewish/
2) Personalgenomes.org
3) http://erlichlab.wi.mit.edu/
4) Gymrek, M. et al. Identifying Personal Genomes by Surname Inference. Science. 339, 321-324 (2013)
5) http://www.usc.edu/dept/source/HIPPA.html

Page 15

1) http://www.uic.edu/classes/bms/bms655/lesson6.html
2) www.smgf.org
3) www.ysearch.org
4) Gymrek, M. et al. Identifying Personal Genomes by Surname Inference. Science. 339, 321-324 (2013)

Page 16

1) http://www.nature.com/news/genetic-privacy-needs-a-more-nuanced-approach-1.12363
2) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2986051/

Page 17

1) Angrist, M. Eyes wide open: the personal genome project, citizen science and veracity in informed consent. Personalized Medicine. 6, 691-699 (2009)

Page 18

1) http://web.mit.edu/newsoffice/2013/de-anonymize-cellphone-data-0327.html
2) https://www.23andme.com/howitworks/
3) Ancestry.com

Page 19

1) http://www.forbes.com/sites/adamtanner/2013/04/25/harvard-professor-re-identifies-anonymous-volunteers-in-dna-study/
2) www.personalgenomes.org/participate.html
3) http://www.personalgenomes.org/consent/PGP_Consent_Approved_02212013.pdf

Page 20

1) http://www.1000genomes.org/about
2) http://www.personalgenomes.org/considerations.html

Page 22

1) http://quotes.dictionary.com/when_you_see_something_that_is_technically_sweet

Page 23

1) http://www.nytimes.com/2013/04/02/science/obama-to-unveil-initiative-to-map-the-human-brain.html
2) http://commonfund.nih.gov/hmp/
3) http://faculty.washington.edu/chudler/facts.html