



Your Genes Say No

Open Access Teaching Case Developed for the Tech for Humanity Pathways Minor

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*“But what *is* “natural”? I wonder. On one hand: variation, mutation, change, inconstancy, divisibility, flux. And on the other: constancy, permanence, indivisibility, fidelity. Bhed. Abhed. It should hardly surprise us that DNA, the molecule of contradictions, encodes an organism of contradictions. We seek constancy in heredity—and find its opposite: variation. Mutants are necessary to maintain the essence of our selves. Our genome has negotiated a fragile balance between counterpoised forces, pairing strand with opposing strand, mixing past and future, pitting memory against desire. It is the most human of all things that we possess. Its stewardship may be the ultimate test of knowledge and discernment for our species. ”*

— Siddhartha Mukherjee, *The Gene: An Intimate History*

Background

William was like many other boys. He liked sports, video games, going to the swimming pool, watching movies, reading spy novels, and dating girls. He had spent most of his youth just like any other child, dreaming about the future. From the time he was little until when he was a senior in high school, he wanted to be an engineer. He wanted to solve problems. In particular, he wanted to be a NASA engineer and develop technologies to explore space. He had known since he was a child that he himself could never be an astronaut. He could never board a Starship by SpaceX and travel to the Lunar colonies first built in 2030. He knew this because when he was only 5 years old, he had been identified as having a predisposition to Type 1

Diabetes (T1D) after a government mandated genetic test to enter public school. The tests were designed to help address and head off a broad array of medical issues prior to children entering school in the late 2020s.

A wave of student athlete heart failures during athletic events, rising concerns over autism, Attention Deficit/Hyperactivity Disorder, and a bevy of other genetic abnormalities resulted in the National Genetic Testing Act of 2027. The legislation made it possible (but optional) for parents to get free testing for their children at any age. By 2031, New York State had begun to mandate that all children receive genetic testing. This allowed the state to budget health care and special needs expenses years in advance and lock in funding for schools and programs. Despite some pushback from disability rights advocates and other communities, the program began to spread to other states.

William's father, Oliver, a T1D himself, wanted to head off issues with T1D and saw promise in Tzield—a vaccine that could delay the onset of T1D. When William was tested in 2031, prior to entering kindergarten, results indicated that he had variations of the HLA-DQA1 and HLA DQ81 genes, indicating a predisposition to T1D. William himself had not become diabetic, but his genetic predisposition to diabetes had imposed multiple restrictions on his life. He would be prohibited from joining the U.S. Military, and he would not be allowed to work as a commercial truck driver or a commercial pilot. All the restrictions associated with being a T1D applied to him as an individual predisposed to the disease.

The roots of genetic testing date back to the start of the Human Genome Project, which was initiated in 1990 with the goal of mapping the entire human genome within 13 years. Through the work of thousands of scientists, the first complete human genome was sequenced without gaps by 2002 at a cost of \$2.7 billion. By 2023, a complete human genome could be sequenced in approximately 5 hours, and the procedure cost less than \$2,000. By the time of the 2027 National Genetic Testing Act, a full human genome could be sequenced in about 2 hours for less than \$1,000. When William had his genome sequenced in 2031, his full genome took 1 hour to sequence and cost \$500. The trajectory of genetic testing for diseases of all kinds rapidly increased the efficiency of genetic testing, thus opening the process up to nearly everyone in the country.

Combined with a revision to the 2001 Health Records Act in 2026, the Genetic Testing Act created the basis for an enormous training database for artificial intelligence algorithms. The 2028 Health Records Anonymization and Transparency Act then paved the way for all patient records from providers to contribute to a national health information database. This database created a longitudinal national dataset that included a wealth of health data on millions of Americans over time. Health companies began to combine health records and genetics data over time to create new health care solutions tailored to individual patients. Yet the AIs could also be used by health insurance providers to set tailored rates based on individual predispositions to genetic diseases or other potential health risks.

Health-related AIs had been evolving since the early 2000s. IBM had released a health-related version of its Watson AI, but the AI was found to be extremely inaccurate. Despite early failures in health AIs, the industry did not decline, rather it continued to generate significant interest. Increasing research into bioinformatics over the intervening years began to foster an increasingly robust understanding of genetics and further informed AI model development. Yet concerns remained as to the efficacy of using AIs to influence individual futures.

Despite having a genetic predisposition to T1D, by the time William graduated from college he was still not diabetic. Nevertheless, because of his predisposition to a genetic disease his potential health insurance premiums were higher than those of others. Whenever he applied for jobs, the AI algorithms would search his health records. As a result, potential employers would either pass him over completely or else offer him a lower annual salary to offset his higher medical insurance premiums.

Unable to secure his dream job after graduating from college, William went back to school to earn Master's and Doctoral degrees in mechanical engineering and astrophysics. He excelled in all his studies. When he went back on the job market again after completing his degrees, he was still offered lower salaries by the private sector to offset his medical insurance premiums. Despite never developing diabetes, he was continually penalized for having a genetic predisposition to the disease.

In tandem with its passage of the 2027 National Genetics Testing Act, the U.S. government had passed legislation prohibiting discrimination in remuneration or hiring decisions for most

non-military or flight-restricted jobs for those with genetic predispositions to certain diseases. William was eventually hired by the National Aeronautics and Space Administration (NASA) to work on space related projects—his ideal job—and he never developed diabetes. Despite never becoming a T1D, over his lifetime he continued to run into problems associated with his genetic predisposition to the disease. He was unable to secure affordable rates on life insurance and disability insurance. His car insurance company charged him a higher rate due to correlations between diabetes and car accidents.

On top of these troubles, what most hurt William was the inability to have natural children with his future wife. They had discussed the possibility of having children without genetic engineering intervention, but to prevent the possibility of inherited diabetes, they decided to go to a genetic engineering fertility clinic. The clinic sequenced the genes of the sperm and eggs in order to edit out genetic issues prior to implantation in the uterus. While both parents recognized that the child they had was biologically theirs, they still felt that there was something odd about having to genetically modify their reproductive cells to prevent all genetic predispositions to disease.

The story above is science fiction. It includes elements of biology, artificial intelligence, health sciences and insurance markets, discrimination, and more. This same story is commonly told in different forms within the science fiction community. One famous version of this story is a 1997 movie titled *Gattaca*. The film's main character is a genetically unedited child who is prohibited from the career of his choice based on his genes. His brother, a genetically engineered child, is given every opportunity. The tale explores the moral and ethical considerations associated with genetic engineering. The movie ends with Ethan Hawke's character achieving his goal of becoming an astronaut by deceiving the testing mechanisms after entering a deal with another person to use their blood and identity.

How realistic is *Gattaca*? Today we may find the story quite conservative in its assessment of genetic testing and its costs. The trajectory of gene sequencing has been astounding. The ability to sequence the human genome in a matter of hours is a reality. Many gene sequencers can now run dozens of sequences in parallel at the same time, thereby lowering the cost associated with genetic testing for multiple individuals. The potential for companies to use genetic testing to further insurance or employment discrimination is part of an ongoing conversation within the global health community. The increasing use of AI in health care is

similarly an area of increasing interest and concern for healthcare providers and patients alike. AI is already used in biomedical devices such as artificial pancreas systems, pacemakers, implantable defibrillators, biventricular pacemakers, and more. AI is also being used in tandem with large data models to identify disease or other issues in fields such as radiology.

As particular technologies advance, they often are integrated with other types of technology to create new realities that shape the way we view and interact with the world. Being able to engage with complex topics across a range of integrated concepts is key to heading off problems before they arise. Below are a series of questions that examine the various issues raised in the case example above.

Question 1:

The case study above sets up a scenario whereby the federal government makes it possible for anyone and everyone to have their genome sequenced. As the technology becomes increasingly affordable, the potential for medical practices to sequence the genomes of every patient is likely to move closer to reality. Information from such sequencing might provide patients and their physicians with data that could lead to longer, healthier lives. Should the government consider providing or making gene sequencing available to the public as the relative costs go down? What are the benefits of knowing what your genes say about you and your health?

Question 2:

The case study above builds on the provision of access to gene sequencing potentially leading to its requirement by states. The logic behind this testing mandate seems comparable to state mandates for vaccinations. In the case study, the State of New York is attempting to predict the costs associated with supporting its citizens and school programs as far in advance as possible so that it can plan and budget resources to best serve its citizens. By using testing data to anticipate the likely medical care and schooling costs for children down the road, the state government can make sure that it has enough teachers for special education programs—even hiring and training them in advance. Such information might allow for tailored educational practices that might better prepare students to live with certain types of disease. It may also prevent or mitigate potential death or illness, for example if genetic issues affecting a child's heart might make it dangerous for them to play a particular sport. If it does become cost effective, what are some of the benefits and drawbacks of mandating genetic sequencing of

citizens? Should states be allowed to require such tests for children to play sports such as football or basketball? Would genetic sequencing really allow schools or the state to plan and budget more effectively in advance? Is this a valid concern?

Question 3:

The United States began requiring digital health records shortly after the passage of the Digital Health Records Act of 2001. The data collected under this law often forms the basis for research on health-related issues within various regions and health systems. The data in these research studies is always anonymized. The data is often used to identify trends in health care and to plan out health care investments and policies. Such datasets could also be useful in training large health AI models. By combining health data from hospitals and practitioners, these models could increase in accuracy, helping patients understand how their genes correlate to potential health outcomes. However, this big-data combination approach can depersonalize the relationship between patient and physician, turning the patient into a series of data points. These data points can drive patient and provider interactions. Should AI, data from practices, and genome data be combined? What are the potential consequences of such combinations? What are your thoughts on the use of data to drive health care decisions? Does it obviate the art of medicine in favor of sterile patient-physician interactions? Would you as a patient prefer a physician driven exclusively by data, or one who is more informed by the “art of medicine”?

Question 4:

One of the issues raised in the case above is all the restrictions placed on someone with a predisposition to T1D. Yet, all these same restrictions are already imposed on individuals actually diagnosed with T1D. Even using modern biomedical devices such as the artificial pancreas system, individuals with T1D cannot currently join the military, fly commercial planes, or be truck drivers. Laws as well as genes can be restrictive. Yet, what about the instances when genes never manifest into a disease or a condition? Should student athletes who have a predisposition for genetic issues with their heart be prevented from participating in certain sports? Should individuals genetically predisposed to T1D be prevented from becoming pilots or astronauts? What if these predispositions are predicated on information derived from large models of data and analyzed by artificial intelligence? Should algorithms and data determine our fate based on probabilities of future health maladies residing in our genes?

Question 5:

The case study discusses discrimination arising from gene sequencing. Private firms and insurance companies are both in the business of maximizing revenue and minimizing costs. Firms of any kind regularly use data analysis to direct business interactions across supply chains, investment decisions and more. An insurance company that has information indicating a potential client has or might have an expensive medical condition is likely to charge that person a higher rate. Similarly, because private employers must pay a large portion of their employees' health insurance premiums, they are also likely to bear part of the financial burden for hiring a person whose medical needs might result in a higher premium. In the case study, firms solved the higher costs issue in different ways. First, they denied a job offer without informing the candidate of the reason. This would be illegal under the U.S. Federal Law which prohibits employment discrimination:

The EEOC is responsible for protecting you from one type of discrimination - employment discrimination because of your race, color, religion, sex (including pregnancy, gender identity, and sexual orientation), national origin, disability, age (age 40 or older), or genetic information.

The second type of discrimination used by employers in the case was creating a pay gap between individuals with and without predispositions to genetic disease. Again, the Equal Employment Opportunity Commission (EEOC) would define paying someone differently based on their genetic information as a form of discrimination. Although both types of discrimination are illegal, EEOC claims are not uncommon—claims of EEOC violations typically exceed 60,000 per year. Differential rates for health insurance are also prohibited under The Genetic Information Nondiscrimination Act of 2008. Title 1 of the Act:

Prohibits a group health plan from requesting, requiring, or purchasing genetic information: (1) for underwriting purposes; or (2) with respect to any individual prior to such individual's enrollment in connection with such enrollment ...

Although these information requests are illegal in health insurance and employment practice, they are not illegal in other forms of insurance, such as life insurance. It is also important to note that the laws prohibiting these forms of discrimination are difficult to enforce and can even be

amended out of existence given sufficient lobbying by industry groups. Discrimination based on genetic information is difficult to identify, let alone prove. Why is discrimination based on genetic information immoral and unethical? Should firms be able to discriminate to increase market efficiency? Does it surprise you that laws are already on the books to prevent genetic discrimination? Are there areas where this kind of discrimination should be allowed?

Question 6:

Are we more than our genes, or are we simply the product of genetic outcomes? At the heart of this story, William suffers because his genetics are used to define his potential in life and curtail his opportunities. What if genes aren't the whole story, but rather only part of the story—to what extent can lifestyle decisions and a host of other actions change the relative impact of genes on our lives? What about genetic conditions that are immutable and thus extremely likely to impact one's quality of life or ability to function in society? Have you had a genetic test? How would you feel about the data in that test being used in studies, or to help identify health issues, or perhaps alter your rates for insurance?

“The desire to categorize humans along racial lines, and the impulse to superpose attributes such as intelligence (or criminality, creativity, or violence) on those lines, illustrates a general theme concerning genetics and categorization. Like the English novel, or the face, say, the human genome can be lumped and split in a million different ways. But whether to split or lump, to categorize or synthesize, is a choice. ... The narrower the definition of the heritable feature or the trait, the more likely we will find a genetic locus for that trait, and the more likely we will find that the trait will segregate within some human sub-population.”

— Siddhartha Mukherjee, *The Gene: An Intimate History*

“Biological determinism is a blight on science. It implies that the way things are is the way they must be. [...] This position is wrong, both empirically and morally.”

— John Horgan, *The End of Science: Facing the Limits of Knowledge in the Twilight of the Scientific Age*

Reflections

There is little doubt the biological sciences have advanced in awesome ways over the last several decades. Progress in genetic sequencing has paralleled advances in computational power and reduced the time it takes to analyze an entire genome from years to months, weeks, days, and now to hours. Concurrently the costs associated with that analysis have plummeted. Researchers around the world are now able to probe the mysteries of our genetic code and unlock many of its secrets. Frequently the unlocking of secrets is aided by algorithms and data. The impact of algorithms and data on the future of health, work, insurance, and much more is yet to be fully written. There are no doubt boundless opportunities for positive changes that might help humans live healthier and more fulfilling lives. Yet, as technologies advance and work in concert it is increasingly important to ask tough questions. It becomes necessary to examine the human impacts not on populations, but on individuals. In the story above, William is affected by what his genes supposedly say about him. He is barred or delayed from achieving some of his dreams. Although his genes tell a story, that story is not fully written. It says what may happen, not what will happen. Genetics can and does provide insight into many aspects of biological life, yet it doesn't always provide the correct answers or tell us what to do with that information. The story becomes increasingly complicated as data on genes and their impact on human biology and behavior are mixed with algorithms often constructed and run in black boxes and trained on data that contains its own biases and issues.

A move towards biological (genetic) determinism has often been used as a shortcut that oversimplifies the realities of life and leads to challenges of equality and accountability. Determinism is by its very nature dehumanizing, as it removes human agency and substitutes in numbers. Breaking these three issues down is the subject of the final pages below.

Theme 1: Equality

In *The Gene: An Intimate History*, Siddhartha Mukherjee rightly identifies the all-too-common human desire to categorize and segment populations off from one another. For thousands of years, societies have separated one another into groups based on prevailing beliefs about skin color, religion, geographical origin, or any other identifiable attribute. There is a tendency to ascribe to genetics an immutable reality based on “cold, hard facts”. This should be avoided. While genetic information can help identify issues as they arise or might help head off potential

health/medical issues before they become too serious, this data should not replace the assessment of the entire human being behind the genetic code being analyzed. The healthy functioning of an entire forest cannot be judged by the health of a blade of grass somewhere in its midst. Sometimes the information gained can be very valuable, but it is not more valuable than the whole living organism. Individuals can no more change their genes than they can alter their place of birth, skin color, or any number of other features used to categorize them. Genes may not give every person biological equity, but it is important that genes are not a determining factor in equality of opportunity. Should William be discriminated against based on something beyond his control? Only where a true safety concern arises should issues of access be considered; and then these concerns should be discussed transparently with the relevant individuals and communities.

While type one diabetics can and do occasionally lose consciousness due to fluctuations in their blood glucose, individuals predisposed to T1D but not yet diabetic have no such concerns. To close off certain opportunities to them, or to discriminate against individuals regardless of diagnoses or predisposition undermines the equality of individuals without reason, based on possibilities rather than realities. Entities may see encouragement to discriminate based on genetic information. As algorithms and information on the genome continue to shed light on medical conditions rooted in genes, it will become tempting to declare that someone with gene J or gene K should not do X or should not have opportunity Y. Such justifications might be rooted in good intentions, but they do not facilitate equality and they remove the humanity of individuals.

Theme 2: Accountability

There are several key accountability issues associated with genes, AI, and medical care. As science continues to unravel the mysteries of genes, there will be a temptation to identify initial or even secondary and substantiated findings as the declarative moment of understanding. The pressures to overestimate the functions and interactions of genes will increase as AI algorithms and big data training sets over time begin to highlight correlations between genes, diseases, traits, and other attributes of human biology. Accountability can occur through peer review processes, but that is only possible if everything from data collection, to processing, to analysis are transparent and replicable. Accountability is a critical component of science. Hiding behind patents, methods, or other obtuse frameworks while still reporting on findings is not acceptable.

It is equally important to admit when the result of a study was wrong or disproven. In the case of William, the fact that he has a predisposition to T1D does not equate to him developing the disease. Identifying a correlation between a gene and a disease is not the same as a gene causing a disease. Correlation does not equal causation. There are likely many intervening factors. The field of science and technologies studies has established sound frameworks for holding the scientific community accountable. Combining the oversight of different communities is likely to increase accountability.

Theme 3: Dehumanization

Perhaps the most significant aspect of the case is the dehumanization and removal of individual agency from William. He is more than his genetic code. By constraining his life to a reading of his genes, he is turned from an individual with hopes and desires for the future into a problem that must be addressed by the medical fields. He is a T1D patient-in waiting. He may not have diabetes yet, but his genes say he might, therefore we must treat him as a patient now. There is a tendency to think that humans are biological computer codes written and executed without interference from the operator; yet this biologically deterministic view is simply not true. While genes influence the resultant biology (and that influence can be great or small), the individual can in many instances impact the running of his or her code. Through exercise, food consumption, education, and a number of factors, the individual has partial sway over the code they have been given. Even where genetic indicators are clear and signs of disease are imminent, the code should not substitute for the person. Doctors do not treat gene sequences; they treat human beings.