Genetics Society of America
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Medical Genetics Ethics Cases
Student Handout

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Learning Objectives

At the end of this section, the student should be able to:

1. Consider the potential advantages and disadvantages of widespread use of whole genome sequencing approaches and direct-to-consumer initiatives.
2. Identify the critical need to protect individual privacy of genetic test results and genetic databases to safeguard their impact on a patient's family relationships, their employment status, and their ability to secure health insurance.
3. Appraise the nuances and consequences of the current recommendations around reporting of genetic test results with respect to whole genome sequencing.
4. Recognize the economic ramifications of genetic technology for precision medicines and patented inventions.

Cases

Implications of genetic testing

Case study 1: Cystic fibrosis testing

Mary and Bill Jones have a child, Kevin, with cystic fibrosis. Mary is 6 weeks pregnant with her second child, and they are pursuing prenatal diagnosis of this child for cystic fibrosis. Since the diagnosis is more accurate when the parental mutations are known, Mary and Bill are both genotyped for the CFTR gene. Mary carries the common ΔF508 mutation, but Bill was not found to have the same, or any recognizable, mutation. It is still possible that Bill has an undetected mutation, but it may not be possible to ascertain this by future testing.

Direct-to-consumer genetic testing

Case study 2: Direct-to-consumer tests in college

"Bring your genes to Cal" was launched as a common educational experience for incoming freshmen in the class of 2014 at UC Berkeley. Freshmen received testing kits in the mail and were invited to swab their own DNA and voluntarily submit DNA samples for testing of genes involved in folate metabolism, lactose intolerance, and alcohol metabolism. The original plan was to report the results back to the individual students in the absence of genetic counseling and to offer a prize of further genetic testing from 23andMe to students who won a creative contest on the theme of personalized medicine. After a ruling from the California State Department of Public Health, UC Berkeley modified their testing plans to proceed with the testing but not report individual results. Instead, they would consider only community results.

Case study 3: Advertising BRCA1 and BRCA2 testing

In late 2002, Myriad Genetics started television and print advertisements for "BRCAnalysis," their BRCA1 and BRCA2 testing kits. The kits cost approximately $440 if the familial mutation is known and over $4000 if complete analysis of both genes is required. In test markets, the advertisements increased calls to the company hotline by 40%. Myriad Genetics was targeting primary care doctors and gynecologists to conduct these tests.

Case study 4: Consumer genetic tests for athletic ability

In December 2008, Atlas Sports Genetics began selling a genetic test for ACTN3, the α-actinin-3 gene. One of the variants in this gene is a nonsense mutation (R577X) that prevents production of the protein. It has been found that individuals with reduced amounts of α-actinin-3 tend to have a higher proportion of slow twitch muscle fibers than fast twitch muscle fibers. Conversely, because α-actinin-3 is expressed only in fast twitch muscle fibers, the presence of 1 or 2 copies of the wild type allele of the gene can tilt the physiological balance in favor of fast twitch fibers. This physiological association has been extended to elite athletes to show a modest enrichment of XX genotypes among endurance athletes and RR genotypes among sprint and power athletes. The company advocated testing children, even before their first birthday, as a performance indicator for their future athletic ability. Moreover, they contended that this genetic test is a more accurate prognostic indicator than physical tests before age 9 because these young children have not developed mature motor skills yet. The test results were reported to the families as the client's "genetic advantage."

Case study 5: The Nash family

Molly Nash was a six-year-old with Fanconi anemia, an inherited anemia that leads to bone marrow failure. Bone marrow transplant from a matched sibling can cure 85% of these cases. Molly, however, did not have a sibling, so her parents decided to have a second child who was chosen through PGD for his healthy stem cells. After four in vitro fertilization attempts, Baby Adam was born and donated umbilical and placental stem cells to his sister. The transplant cured Molly's bone marrow failure, but she is still at risk for life-threatening complications from infections and for solid tumor cancers.

Privacy of genetic information

Case study 6: Burlington Northern Santa Fe Railroad

Burlington Northern Santa Fe Railroad (BNSF, Fort Worth, TX) medically tested employees seeking disability payments for carpal tunnel syndrome. Included in these tests were genetic tests for a mutation in HNPP, a gene connected to hereditary neuropathy and pressure palsies. The symptoms caused by mutations in HNPP either closely mimic the symptoms of or predispose patients to carpal tunnel syndrome itself. These genetic tests were conducted without the employees' knowledge or consent. The Equal Employment Opportunity Commission stopped the testing in 2002 and BNSF settled claims with its employees.

Case study 7: Sickle cell anemia population screening

In the 1970s, a population screening initiative was in place for sickle cell anemia in the African American population. Many employers used the information to terminate employment of heterozygous employees who were not in danger of even developing the condition.

Case study 8: Nitromed and BiDil

BiDil is a combination pill containing two drugs used to treat heart failure: isosorbide dinitrate (an NO donor) and hydralazine (a vasodilator and antioxidant). Roughly five million Americans suffer from heart failure, and many are successfully treated with ACE (angiotensin converting enzyme) inhibitors. In the original clinical trials conducted by Medco Research, BiDil did not seem to offer any statistically significant improvement to heart failure treatments and was not approved for use by the FDA. Later on, when Nitromed acquired the rights to the BiDil compound, they reanalyzed the same data and noticed a 47% reduction in one-year mortality among African Americans. Consequently, they rushed to file a patent for race-specific use of BiDil which protects this market for them until 2020. Clinical trials have verified the initial observation; in these studies, BiDil offers a 43% reduction in mortality after one year. Because of these dramatic effects, the trial was halted, and BiDil was offered to all participants, including those who had been taking placebos. The FDA Cardiovascular and Renal Drugs Division approved the use of BiDil as the first race-specific drug in June 2005. Under this definition, Nitromed risks overlooking numerous non-African American patients who could benefit from this drug. In fact, because most (70%) European American heart failure is due to heart attack or chronic heart disease while much (50%) African American heart failure is a result of hypertension, scientists have speculated that BiDil is actually more effective for hypertensive patients than the more general racial categories. In addition, racial groupings do not take into account environmental or social factors such as access to healthcare.

Case study 9: Cassidy v. SmithKline Beecham

SmithKline Beecham (SKB) developed a lyme disease vaccine that, after FDA approval, it became apparent that about one-third of the population would react poorly to the vaccine. Individuals with the HLS-DR4+ genotype were susceptible to developing autoimmune arthritis in response to the vaccine. SKB did not warn patients of this complication on the label, and was sued in a class action lawsuit by individuals who developed autoimmune arthritis in response to vaccination. Due to negative publicity, sales of the vaccine plummeted, and SKB had to pull the product from the market.

Case study 10: The Pseudo Xanthoma Elasticum patent

After having two children with Pseudo Xanthoma Elasticum (PXE), Sharon and Patrick Terry became founders and administrators of PXE International, a patient support group. PXE is a genetic disorder that causes connective tissue in the skin, eyes, and arteries to calcify, eventually leading to blindness, premature aging, and gastrointestinal bleeding. To understand the genetic basis of PXE, the two created a Biobank of samples that they provided to University of Hawaii researchers. Both PXE International and the University of Hawaii are listed as inventors on the patent application that resulted from the discovery of the PXE gene. This is the first example of intellectual property and benefit sharing by the patients and the inventors, and the Terry's are working towards establishing additional Biobanks for more genetic diseases with the same intellectual property conditions of use.

Whole exome / genome sequencing

Case study 11: The Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) Project

The National Human Genome Research Institute is sponsoring a series of studies to explore the implications, challenges, and opportunities associated with genomic sequencing of newborns. One of these studies, the BabySeq project, aims to assess the risks and benefits of sequencing newborns' DNA in comparison to conventional newborn screening using biochemical analysis of blood obtained from a neonatal heel prick. The project is designed to conduct full exome sequencing for both healthy and very sick infants to assess the full protein-coding portion of the babies' genomes. Initial results from the first 51 participants have uncovered a range of findings including frequent identification of carriers for recessive disorders, two babies with pharmacogenetic variants, three with mutations associated with heart conditions (although the babies and their parents appear healthy), and one with a mutation in the BRCA2 gene. The American Society of Human Genetics has taken the position that only newborns with undiagnosed conditions should undergo genome sequencing, preferably only analyzing genes that are likely to explain the disorder, ostensibly to minimize the possibility of incidental/secondary findings. Sequencing of healthy newborns does not fall within this guideline, and the sharing of the BRCA2 finding does not fall within this recommendation either, but it *is* considered an actionable medical finding by the American College of Medical Genetics and Genomics. As such, this result was returned to the family of the baby, after reconsideration of the scientists' initial agreement to only tell parents about variants that would impact babies during their childhood.

Along with the remarkable pace of scientific progress comes new responsibilities for the scientists, particularly in these cases, to make sure genetic information and concepts are used responsibly. It is the job of our health professionals to remain educated on these developments and to impart expertise to the many social debates of this post-genomic era. Good luck!