Chapter Ten

Ethics in Genetics

Introduction

In the previous chapter, various biotechnologies were presented that allow individuals to screen themselves or their embryos for genetic diseases. These DNA sequencing technologies can be divided into two categories: whole-genome sequencing (WGS) and whole-exome sequencing (WES). WGS is a procedure that determines the complete DNA sequence of an individual's genome at a single moment in his or her lifetime. WES technologies only allow the sequencing of the protein-coding genes in a genome (known as the exome). In addition, gene editing technologies can be applied to individuals or embryos to alter the DNA sequence of their genetic codes.

From an ethical perspective, the use of these technologies with a view to improve the health of a human being follows the bioethical principles of beneficence and human dignity (see chapter 2). Nonetheless, there are still many contentious issues that bioethicists raise regarding these technologies. In response to the press hype of gene editing technologies, a December of 2015 summit was convened in Washington, DC to explore the science and ethics of germline gene editing. The organizers concluded with the following words of caution:

> "It would be irresponsible to proceed with any clinical use of germline editing unless and until (i) the relevant safety and efficacy issues have been resolved … and (ii) there is broad societal consensus about the appropriateness of the proposed application."

This chapter will address the ethics of gene screening and gene editing. In order to assess the various bioethical dilemmas associated with these technologies, the reader must recognize two important caveats: a) these technologies are too recent and more time is needed to fully identify and explore ethical concerns, and b) there is no consensus on identifying what ethical guidelines these technologies may violate.

Genetic Sequencing and Screening in Adults and Newborns

Genetic screening is more than simply sequencing the base pairs of the human genome because it offers a window into personalized treatment. Both genomic and epigenetic genetic screenings in cell free blood DNA can be used to

diagnose disease states. In addition, exosome diagnosis in another method that is generating a great deal of excitement. Exosomes are lipid nanovesicles, on the order of 30–200 nm, secreted from cells and found in all bodily fluids such as plasma, urine, and cerebrospinal fluid (CSF). Although exosomes were discovered over 30 years ago, they were originally thought to be nothing more than a garbage disposal system for cellular debris and proteins. More recently, interest in exosomes has increased with better understanding of their capabilities to utilize exosomes in the development of biofluid-based, real-time molecular diagnostics, as drug delivery vehicles, and as tools for biomedical research. Exosomes contain not only proteins, but also different types of RNA transcripts, such as messenger RNA (mRNA), microRNA (miRNA), other noncoding RNA, ribosomal RNA (rRNA), and transfer RNA (tRNA). These differences in exosome-derived RNA profiles could be harnessed to distinguish healthy vs. disease states.

The ability to detect the nucleic acid profile of a tumor for example, in a noninvasive way, via a blood draw or urine sample, without the need for a potentially invasive tissue biopsy is a significant advance, especially when sample tissue is difficult to access. Prostate cancer is a good example of how exosomes could improve patient management. It is estimated that 30% of men age 50 or older will have some form of prostate cancer (although only about 15% of men will be diagnosed during his lifetime); however, many of these men have low-risk prostate cancer that will not likely progress to a life-threatening stage. Exosome analysis might help differentiate between low-risk and high risk prostate cancer. Exosome diagnosis is also being assessed to diagnose Alzheimer's disease and assess a patient's immunological compatibility for organ donations.

Screening Adults. As the cost of classical genomic sequencing or epigenetic sequencing dramatically decreases to under $1,000, its applications will impact many individuals. It is important to highlight several features of genomic sequencing. First, it differs from obtaining genetic information from a family history. A family history of a patient may reveal very little about an individual's biological propensity to disease, which could be easily gleaned from genetic testing. Yet, taking a family history will still reveal a great deal of information about the personality and environmental background of the patient within his or her family. Second, in genomic sequencing, tools are available to distinguish genetic factors from environmental and life course contributions to disease. Third, some outcomes of DNA analysis may reveal unsolicited (often referred to as incidental) findings that the patients do not expect and may not want (Rigter et al., 2014).

Genetic analysis can reveal diseases that are life-long, as well as predicting those that are late-onset. Yet, the accuracy of DNA sequencing analysis in predicting late-onset diseases is not as accurate, in part because the individual has not yet presented with any symptoms. Until science uncovers the role of each gene within the human genome and how all genes interact with one another, interpreting the DNA data related to late-onset diseases will remain a challenge. The sheer amount of information afforded by genome sequencing also raises ethical issues related but not limited to: informed consent, privacy, data ownership

and sharing, and the regulation of this technology. Despite these ethical concerns, there is a need for many volunteers to have their DNA sequenced and analyzed, even though they themselves may not gain any useful medical information for decades to come.

Children. What about the rights of parents to genetically analyze their newborn children? Newborn screening can benefit newborn children if there is a family history or other signs of a disease such as congenital hypothyroidism and phenylketonuria. Most bioethicists support genetic screening for diseases that manifest at birth or during childhood. However, genetic screening of newborns or young children, for late-onset diseases such as Hungtinton's disease, breast cancers, or Alzheimer's disease, presents serious bioethical challenges (Anderson et al., 2014). Specifically, the question is whether such testing or screening violates the autonomous right of the child to decide whether he or she wants to know if he or she is carrying the gene for Hungtinton's disease?

Incidental Genetic Findings

In 2013, the publication of the controversial "American College of Medical Genetics and Genomics (ACMG) Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing" created a huge debate regarding whether or not the recommendations in this report were ethical. These recommendations (Green et al., 2013) are summarized as follows:

1. Mutations found in the genes on the minimum list should be reported by the laboratory to the ordering clinician, regardless of the indication for which the clinical sequencing was ordered.

    a) Additional genes may be analyzed for incidental variants, as deemed appropriate by the laboratory.
    b) Incidental variants should be reported regardless of the age of the patient.
    c) Incidental variants should be reported for any clinical sequencing conducted on constitutional (but not tumor) tissue. This includes the normal sample of a tumor-normal sequenced dyad and unaffected members of a family member.

2. The Working Group recommends that laboratories seek and report only the types of variants within these genes that have delineated as causing diseases.

    a) For most genes, only variants that have been previously reported and are a recognized cause of the disorder or variants that are previously unreported, but are of the type that is expected to

cause the disorder, as defined by prior ACMG guidelines should be reported.
b) For some genes, predicted loss-of-function variants are not relevant (e.g., COL3A1 and most hypertrophic cardiomyopathy genes).

3. It is the responsibility of the ordering clinician/team to provide comprehensive pre-test and post-test counseling to the patient.

    a) Clinicians should be familiar with the basic attributes and limitations of clinical genetic sequencing.
    b) Clinicians should alert patients to the possibility that clinical sequencing may generate incidental findings that could require further evaluation or information that the patient may not want to know.
    c) Given the complexity of genomic information, the clinical geneticist should be consulted at the appropriate time, which may include ordering, interpreting, and communicating genomic testing.

There are three key bioethical issues that emerge from these recommendations: a) the long-standing inconsistencies between consensus guidelines and clinical practice regarding risk assessment, for adult-onset genetic disorders in children, obtained using family history and molecular analysis; b) the disparate assumptions regarding the nature of whole genome and exome sequencing and how they affect arguments for and against reporting; and c) the implicit differences in how to reveal genetic information to maintain the best interests of the child.

This working group defended their recommendations in stating: 1) the potential benefits of revealing incidental genetic findings outweigh any harm, and 2) in other areas of diagnosis such as radiology, incidental findings should be reported without ethical concerns. Those who criticize these recommendations claim that in fact, the potential harm of revealing information outweighs the benefits. In addition, they reject the analogies drawn between genetic sequencing and other areas of medicine. Finally, they maintain that these guidelines violate the longstanding consensus against testing children for adult-onset conditions. In many countries (USA, as well as Great Britain and other European countries) the practice is to not disclose to families the genetic information about a child, unless it is immediately relevant to their health care (Clarke, 2014).

Genetic Screening in Pre-Implanted Embryos

The use of genetic screening technologies (including PGD) to select for embryos that do not carry specific mutations seems at first to be uncontroversial.

It allows for the selection of healthy embryos. However, several highly contentious ethical concerns arise from PGD. What should be done with those pre-implanted embryos that are not selected for implantation into a woman's uterus? Is discarding an embryo that is a carrier for a genetic disease ever justified? Are there conditions when prospective parents can justifiably discard an embryos? Is it ethical to create savior siblings by selecting embryos that, after gestation and birth, might serve as an organ donor for an existing, sick sibling? These types of ethical questions are rooted in cultural and religious beliefs (see Chapters 5 and 7) rendering them difficult to resolve.

Thought Question: Under what circumstances should incidental genetic findings be revealed to the patient and/or the parents? In the 1990's diagnosis of Duchenne's muscular dystrophy (DMD) involved obtaining tissue or blood samples from the pregnant woman, her husband and the embryo that she was carrying to ascertain whether the embryo inherited the X-linked mutation responsible for DMD. In about 5-10% of the cases it was clear that the husband was not the biological father of the child. Should the physician present this information to the couple?

As mentioned in Chapter 7, several religions such as Catholicism believe that discarding a pre-implanted embryo is akin to murder because this embryo if implanted into a woman's uterus will generate a child. Some ethicists believe that allowing embryo selection will lead to a slippery slope situation in which embryos will be selected for non-medical reasons such as gender, increased athleticism or increased intelligence. Arthur Caplan, the director of the division of medical ethics at NYU Langone Medical Center in New York City states, "I believe that the future of PGD is in both looking for traits that parents do not want in their children and in selecting for traits that they do very much want to try to pass on. The morality of eugenics, both negative—eliminating unwanted traits—and positive—selecting for desired traits—will surely loom very large as the key moral question facing those offering PGD and those seeking to utilize it."[1]

Another ethical issue that is debated is the use of these technologies to screen for late-onset diseases. From a predictive perspective, Huntington's disease is a disease for which genetic analysis can accurately predict disease onset. In contrast, for other diseases such as cancer, genetic analysis only predicts the risk of developing a disease within the lifetime of the individual. For example, a woman who is a carrier for the BRCA mutation possesses a significant higher risk of developing ovarian and breast cancer during her lifetime than a woman lacking this mutation. But having this mutation does not mean that she will definitely develop breast or ovarian cancer, nor does it mean that a woman who does not have the mutation will not. As mentioned earlier, until the functions of all

[1] http://www.aacc.org/publications/cln/2014/january/Pages/Preimplantation.aspx

genes and their interactions are known, it will be difficult to make precise predictions from genetic sequencing technologies.

The question of whether a person wants to know his/her genetic predisposition for a specific disease is a final ethical concern that needs to be addressed. Some individuals who have a family history of Hungtinton's disease do not want to be genetically tested and know their fate. Yet, they do want to have a healthy, disease-free child. Several individuals, in particular, women, will undergo PGD and instruct the physician **not to tell her whether she is carrying the fatal Hungtinton's disease mutation**, but rather the physician should only implant a selected embryo that only inherited the normal but not Hungtinton's disease causing mutation.[2] In this case, her autonomous choice is to deny obtaining her genetic information regarding Hungtinton's disease and yet have a child that is free of the gene mutation that would cause Hungtinton's disease.

Legal Issues Related to Genomic Screening

From a legal standpoint, privacy concerns and the accuracy of genetic diagnosis are major issues regarding DNA sequencing and PGD. There have been several legal cases and judgments brought against commercial DNA testing laboratories due to incorrect PGD results. Currently genetic screening is not 100% accurate and raises the following question: under what circumstances is malpractice justified? Is there a legal justification to sue a physician if genetic screening is not offered to the couple or if the selected embryo implanted actually developed the disease that the DNA screen did not successfully target?

http://www.sciencemag.org/site/products/lst_20110304.xhtml

*Privacy Issues***:** Another legal issue relates to protecting the individual from having his genetic background revealed to unwanted recipients such as employers or maybe even health insurance companies. In light of these concerns, the US Government signed into law the Genetic Information Nondiscrimination Act (GINA) in 2008. This law bans U.S. employers from using genetic information in hiring, firing, promotion and compensation decisions, as well as from collecting genetic information from employees. Furthermore, GINA prevents health plans and insurers from denying coverage or boosting premium prices based on a person's genetic information, including his or her family history. It also forbids these organizations from requesting or requiring people to undergo genetic testing. GINA provides greater protection than the 2003 enacted law called the Privacy Rule, implemented as part of the Health Insurance Portability and Accountability Act (HIPAA) that established

[2] http://www.cnn.com/2014/02/22/opinion/klitzman-genetic-testing/

federal regulations for the use and disclosure of protected health information. What is frustrating to clinicians and researchers is the absence of evidence that such federal regulations are making patient records more secure.

Another unanswered question is whether federal legislation protecting genetic information might inadvertently foster the public's apprehension of genetic testing. GINA was initially designed to provide sufficient privacy protection so that the public feels safe to participate in genetic research, to pursue genetic testing for themselves and to share the findings with family members who might also be at risk, as well as with health care providers who can help affected individuals treat or manage their conditions. Is GINA meeting these expectations (Prince, 2014)?

Forensic Science: Interestingly, the capacity of law enforcement officials to use genetic information to identify a criminal is becoming quite sophisticated (Kayser and de Knijff, 2011). Over half of the States obtain DNA samples from arrestees, currently totaling over 10 million DNA samples collected and retained in the USA forensic bank.[3] Most often this data bank is used to identify an exact match with DNA obtained from crime scenes. If, however, the DNA obtained at a crime scene does not match the FBI data bank, the FBI could still use that DNA sample for DNA profiling. DNA profiling refers to the use of DNA sequencing technologies to predict physical characteristics (hair color, eye color, facial geometry, and height) and diseases that the criminal may possess. DNA profiling also can identify whether the DNA sample obtained at the crime scene is related to a person in the FBI data bank. As scientists learn more about the role of genetics and behavior, DNA profiling will eventually be used to predict violent behavior or anger management disorders from the suspect's DNA.

The following case presents an interesting ethical conundrum related to forensic DNA analysis. In a small town in Virginia, DNA obtained from a crime scene revealed that the criminal had four mutations commonly associated with Gaucher's disease. Most people with Gaucher's disease require biweekly treatments administered within a hospital setting. The law enforcement officers investigating this crime went to the only local hospital that treats patients with Gaucher's disease and demanded that the hospital administrators provide them with a list of all individuals being treated for this genetic disease. With this information, the police would be able to generate a list of suspects to interrogate. Did the hospital administration have the right to refuse to release this medical information because it violates private GINA laws? Some argue that the police have the right to this information because they have the right to contact hospitals and seek medical information on whether someone was admitted and/or treated for gunshot wounds. Others would argue that, in fact, the two situations are ethically different. The alleged criminal who was shot by the police is entering the hospital's ER in full view of the present public, and by default relinquishes their right to privacy. In the situation where the criminal has Gaucher's disease, the right

[3] http://www.pbs.org/wgbh/nova/next/body/dna-databases/

of privacy is legally protected when the patient comes in for treatments. **What do you think?**

One of the most famous legal cases involving the use of biological testing was the Charlie Chaplin paternity law suit. In 1943, the starlet Joan Barry accused actor Charlie Chaplin of fathering her child. At that time, research had begun to identify the ABO blood group classification of people. Although blood tests definitively excluded Chaplin as the father, the court did not allow this evidence to be admitted as evidence, and Chaplin was ordered to pay child support to Barry. It is unclear exactly why the court did not accept the blood type tests as evidence in this case. The media claimed that the blood tests were not scientifically accurate or that Chaplin had ingested some chemical to change his own blood type. Chaplin's second wife, Lita Grey (who was divorced from Chaplin in a bitter, proceeding), asserted that Chaplin had paid corrupt government officials to tamper with the blood test results. While the media and even the court did not understand the science of blood typing, this case did spur the passage of new laws regarding the use of biological data as forensic evidence.

A difficult obstacle in forensic medicine is establishing that the actual DNA obtained at the crime scene was from the alleged criminal who committed the crime. Sometimes, it is difficult to separate the perpetrator's tissue (e.g., sperm) from tissue belonging to the victim. Moreover, there are documented cases in which the alleged criminal DNA actually was contaminated with DNA from the law enforcers investigating the crime scene or from individuals working in the forensics laboratory.

Ethics of Gene Editing and Synthetic Biology

The potential power of using gene-editing systems (see Chapter 9) to treat a wide variety of genetic diseases does not deter bioethicists from raising bioethical concerns. Many of these concerns have been raised in regards to other biotechnologies such as human cloning and stem cell technologies. These ethical concerns include:

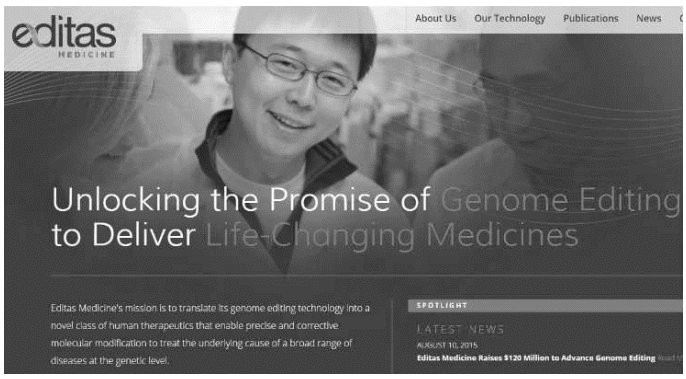
1. Playing God, (see Textbox 1)
2. Violating the principle of justice as the high cost of gene-editing will only benefit the rich,

Textbox I: Playing God

The argument that human beings should not "play God" has been used to claim that specific technologies, such as gene editing, are unethical. In fact, many of the technologies discovered have biological precedents. Gene editing, for example, is based on the discovery of an enzyme called CAS in bacteria that functions as a defense against foreign DNA, either viral or plasmid.

3. Negatively tampering with our genetic integrity by editing the "Book of Life",
4. Introducing technology to create more potent bioterror weapons,
5. Genetic engineering of human IVF embryos,
6. Engaging in germline therapies,
7. Parents who alter the genetics of their fertilized eggs or children violate the autonomous rights of their children,
8. Applications of these technologies for non-medical purposes, such as increasing EPO levels in athletes, or for non-medical enhancements (intelligence, looks (blond hair), athleticism, personality traits).

While these bioethical concerns need to be addressed, one must remember that if and when gene-editing systems[4] will be successfully used to treat diseases, many of these concerns will fade into the background. This is precisely the lesson we learnt from IVF technologies. As it became clear that IVF was an effective method for infertile couples to have healthy children, the ethical outcries (related to designer babies and discarding embryos) heard in the early nineties faded in the 21st century. Even the Catholic Church has lowered its noise in opposing IVF.



In 2015, Editas, a biotechnology company, was founded in part by Jennifer Doudna and Feng Zhang, two of the first developers of the CRISPR technology. One of the company's objectives is to initiate the first clinical trials using CRISPR to correct a rare eye disorder called Leber congenital amaurosis (LCA). The condition mainly affects the retina, resulting patients having a difficult time seeing anything other than large, bright shapes. Why does Editas want to try CRISPR for this condition? First, it's an easy disease to target. The treatment (which involves injecting people with modified viruses carrying the CRISPR technology that will go in and repair the faulty DNA) can be

[4] Gene-repair systems may convey a more ethical semantics then "gene-editing systems" see Loike, 2015.

injected directly into the retina and, in this case, used to delete the portion of the CEP290 gene that's responsible for the disease. Second, because this disease affects vision, it will be easy to assess the clinical effectiveness of the therapy. However, if CRISPR is effective, it may prove to be very expensive since there are only about 600 people who have the type of LCA that could be treated. From a bioethical perspective, we have a situation where the technology is expensive, rendering it inaccessible to many patients and violating the bioethical guideline of "justice". What remains unclear is whether the clinical success of using CRISPR to treat LCA patients will accelerate the use of CRISPR to treat other diseases and, in turn, significantly lower its costs thus making the technology more accessible to all patients. The fact that more than six companies are employing gene editing technologies for clinical applications highlights its great clinical potential.

In addition, technologies are being developed to reverse some of the gene editing systems. As discussed in Chapter 9, RNA-guided gene drives are capable of spreading genomic alterations made in laboratory organisms through wild populations to address environmental and public health problems. However, society must be aware of the possibility that unintended genome editing might occur through the escape of strains from laboratories, leading to the prospect of unanticipated and possibly harmful ecological changes. In 2015, scientists examined the efficacy of CRISPR-Cas9 gene drive systems in wild and laboratory strains of the yeast Saccharomyces cerevisiae (DiCarlo et al., 2015). The researchers designed two molecular confinement approaches capable of overwriting any changes introduced by an earlier gene drive. The first, called a split drive, involves separating Cas9 and guide RNAs so they are not encoded in the same organism. Cas9 was encoded on an unlinked episomal plasmid and the gene drive element contained only the guide RNA. Because the gene encoding Cas9 is required and is unlinked from the drive, and since wild yeast populations do not encode Cas9, the [guide] RNA-only drive is unable to spread in wild organisms lacking Cas9. In the second containment strategy, Cas9 is designed to target genes in which a DNA sequence not found in wild-type organisms has been inserted. As expected, gene drive-containing yeast was unable to affect yeast lacking the synthetic target sequence. These molecular safeguards should enable the development of safe CRISPR gene drives for diverse organisms and minimize the risk of unwanted genome editing. Lastly, these scientists showed that a trait imposed on yeast using a gene drive could be reversed by using another gene drive to overwrite the initial change. In doing so, the gene drive machinery remained in place, but rendered the genetic change inactive. **Once again, we have an example in which a scientific discovery can override a potential bioethical dilemma in which a technology could inflict unwanted harm (maleficence).**

In August of 2016 a survey carried out by Pew Research Centre[5] found that a majority of adults (~70%) in the USA are worried about the potential use of genome-editing technologies to give children a reduced risk of disease. Respondents who said they were familiar with genome editing were more likely to want it for their own child, and there was more acceptance of genome editing if people were allowed to choose which diseases would be affected. Yet, fifty-four percent of adults surveyed felt that genome editing to prevent serious disease in a baby and give it the average level of health would be appropriate. However, the same amount of people felt that genome editing to make someone healthier than any existing human was crossing a bioethical line. The survey also found that religious people are less likely to support such interventions, and that the more committed to religion someone is, the more likely they are to think that enhancement technologies are meddling with nature and 'playing god'. Interestingly, many respondents also said they had mixed views about current enhancements such as cosmetic surgery.

Equally important is the fact that ethical concerns related to synthetic biology technologies are equally as complex as gene editing, with some differences. Yet, there is a fundamental question that needs to be addressed regarding synthetic biology technologies. What are the actual benefits of synthetic biology? As mentioned in the previous chapter, the capacity to expand our genetic base pairs will eventually allow scientists to create a wide variety of new types of proteins. They hope that these proteins could be used to generate better vaccines for diseases. How valid is this scientific claim? Secondly, could synthetic biology technologies be applied to create more virulent bioterror weapons (see Chapter 14 on “Dual Use”)? Finally, as financial resources for biomedical research become more difficult to obtain, should this area of science be a top priority for governmental funding? The answers to these questions remain elusive at this time and questions remain regarding what clinical applications will be developed from research in synthetic biology. While it is quite difficult to regulate technological advancements, research in this area will most likely proceed because history has shown that human beings are often mesmerized by new technologies.

There are other ethical challenges in genetic engineering that need to be addressed. In August of 2015, Dr. Smolke and her team at Stanford University reported in the Journal Science the complete synthesis of opioids in genetically modified yeast. They created one form of yeast that converts sugar into hydrocodone, the active ingredient in Vicodin. Another yeast strain makes a compound called thebaine — which can easily be turned into many opioids, including oxycontin, codeine and morphine. Her goal was to open the door to the quick development of better medications of all sorts and to make morphine more available in developing countries, where there's a shortage of painkillers. Currently the opioid yields from these yeast strains are small. But once the process has been optimized, these modified yeast strains should make it much easier and cheaper

[5] http://www.pewresearch.org/fact-tank/2016/07/29/the-religious-divide-on-views-of-technologies-that-would-enhance-human-beings/

to manufacture new painkilling medicine. In addition, scientists will be able to leverage this technology to reduce some of the narcotics' side effects, and/or make medications that are less addictive.

The genetically modified yeast strains have triggered an ethical debate about how to regulate these organisms to prevent "home-brewing morphine." These genetically modified yeast could, one day, be grown at home and used to turn sugar into heroin — which is easily made from morphine or thebaine, and to put more inexpensive addicting drugs on the street. The DEA shares concerns about using yeast for home-brewing. But the agency is also worried about large drug cartels. These cartels could find a way to increase production and increase their profits — all on the backs of people who are addicted to opiates.

Thought Question: From an ethical perspective it is important to assess whether the harm emanating from the illegal opiof market is more important than the fact that over 5 billion individuals around the globe do not have sufficient access to pain killers because of their high cost. In this case should beneficence trump over maleficence?

What are your thoughts?

Conclusions

In this chapter, many ethical challenges were presented related to three types of genetic technologies: genetic screening, gene editing and synthetic biology. There is no doubt that ethicists have used and will continue to consider the classical ethical guidelines to limit the application or delay in engaging human trials of these technologies. Nonetheless, one must recognize the allure of basic scientific innovation and technology, even if the health benefits are not clearly defined (as in expanding our repertoire base pairs from 4-6) or and even if the health risks may be higher than society is normally comfortable with (i.e., gene editing). Coupled with the allure of these new technologies is the fact that patients with untreatable and fatal diseases are desperate and will engage in unproven therapies with the small hope that if may attenuate their disease. Thus, despite any bans or fund restriction, these technologies will develop at a rapid pace.

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Companies employing gene editing technologies

Editas: Editas, a company that we profiled before which was founded by 5 of the world's leaders in gene editing. Editas has exclusive rights to the one issued patent for CRISPR granted to the Broad Institute and Harvard University.

Caribou Biosciences: Backed by Atlas Venture, Caribou was founded by Jennifer Doudna who was also one of the cofounders of Editas. When the key CRISPR patent was granted to another Editas founder, Feng Zhang, Jennifer broke off from Editas taking her intellectual property in the form of her own pending patent for CRISPR. It is with this patent that she is hoping to stake her claim.

Intellia: Founded in 2014 by Caribou Biosciences and Atlas Venture, Intellia was funded by both Atlas Venture and Novartis Institutes for Biomedical Research (NIBR). Novartis has exclusive rights to use Intellia's CRISPR platforms to develop CAR-T therapies.

CRISPR Therapeutics: CRISPR Therapeutics was founded in April of 2014 by Emmanuelle Charpentier, also one of the co-inventors of the CRISPR/Cas9 technology.

Cellectis: Cellectis is a French company that is involved in both gene editing and cancer immunotherapy. The Company has worldwide rights to a patent family titled "Engineering Plant Genomes Using CRISPR/Cas Systems" upon which they have developed a platform to improve the quality of crops for the food and agriculture industries.

Precision Biosciences: Precision's Directed Nuclease Editor™ (DNE) technology enables the production of genome editing enzymes. Precision controls a growing patent estate consisting of over fifteen allowed genome engineering patents in the U.S., Europe and Australia.

Sangamo: California based Sangamo is a $1 billion company that uses a gene editing system based on zinc-finger nucleases and has quite a head start over Editas. Sangamo has entered Phase 1 clinical safety trials for their gene editing technique that is showing encouraging results as a possible functional cure for HIV.