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Genetic Manipulation

Photo by Herb Pilcher, USDA Agricultural Research Service, via Wikimedia.

Genetically manipulated peanut leaves (bottom image) that are protected from damage caused by the cornstalk borer (top image).

The History of Genetic Science

Though genetic editing is "cutting-edge" science, the process of influencing the genetic expression of organisms is not really a new concept. The idea of "inheritance," meaning that characteristics can be passed down and altered through reproduction, was discovered very early in history and as early as 10,000 years ago, humans were already engaging in genetic manipulation through selective breeding and propagation.

The global food crop known as "corn" provides an example of how these ancient experiments shaped human life. The common corn plant is classified as the species *Zea mays*, but scientists know that the species grown today bears little resemblance to the ancestor species that existed in North America before humans began growing corn as a food crop. Over the centuries, humans bred corn to have larger fruiting bodies with juicier, more flavorsome seeds. They did this by selecting individuals with larger fruits or that were more productive and harvesting the seeds from these selected individuals to propagate the next generation. Most of the species utilized in agriculture were produced in a similar way to corn, through selective propagation towards the goal of enhancing certain characteristics.

It was also ancient humans who created the first genetically modified (GM) animals by selecting individual animals to breed based on their traits. This is how humanity created cows, pigs, and horses, using lineages of animals bred to enhance their useful traits. Similarly, humanity created all the breeds and varieties of domestic dogs and cats utilizing this simple form of genetic engineering. In the twenty-first century, people are still utilizing the same techniques to create new animals, such as how tropical fish breeders select individuals or even mix species in an effort to create new "breeds" of fish.

Undoubtedly, manipulating genetics had tremendous influence on human life, shaping modern culture in many ways, but there are many ways in which genetic engineering has been problematic. The overpopulation of "pet" animals, hybrids and domesticated versions that cannot live in the wild, has created ecological problems around the world and many consider the breeding and harvesting of food animals as an immoral and unethical industry. Likewise, the cultivation of food plants facilitated environmental devastation in the form of monocultures and resulted in crops with reduced nutritional value.

Beginning in the late twentieth century, science and human agriculture merged through the implementation of new techniques that allowed humans to directly influence genes. This form of direct genetic modification also ushered in a new era of genetic manipulation targeting the human species and in which scientists seek to use genetic modification in medical treatment.

Discovering and Mastering the Gene

Genes are segments of genetic code stored within the cells of all organisms that contribute to certain characteristics displayed by the organism. The shape of a person's chin, the color of their hair, or even personality traits, are shaped, to some degree, by the "expression" of genes, which means the way that genes direct the development of bodies and minds.

The history of genetics can be traced to ancient Greece, where first imagined that there was some sort of atomic system in which parents were contributing some "component" to any resulting offspring. In the eighteenth century, work on plant and animal breeding led to the scientific documentation of phenomena that pointed the way towards the discovery of genes. It was Gregor Mendel who famously put these various pieces of evidence together in the 1850s and came up with the idea of genetic inheritance. Mendel introduced concepts such as "dominant" and "recessive" genes and helped to show how traits changed and were passed down through generations within a species or population.[1]

Then, in 1869, Swiss chemist Friedrich Miescher identified a substance inside white blood cells that would later become known as "nucleic acid," and, through further discovery, as "deoxyribonucleic acid" or "DNA." This, it was discovered, along with another substance called "ribonucleic acid" or "RNA" formed the basis of human inheritance and contained the "code," to use a simplified metaphor, for the expression of human physical properties.[2]

The discovery of genetics and of DNA and RNA changed the landscape of our understanding of human characteristics and bodies. Over the century that followed, humanity developed the ability to determine the sequences of individual genes and scientists got better and better and tracing certain genes or collections of genes to certain human traits. In the 1990s and early 2000s, many believed that there was a single, specific gene for many human traits. For many years, it was common to hear Americans speculate about a gene for blue eyes, or for baldness, or even for homosexuality. Many believed that when it was possible to find these genes, it would also become possible to change the traits connected to those genes. A person might therefore be able to genetically change their eye color to blue, or scientists might genetically cure baldness. On the darker side, prejudiced people speculated about using genetic manipulation to cure "homosexuality," which is neither a disorder that needs to be cured, nor a purely physical, genetic phenomenon. Over the years, scientists have found that genetic inheritance isn't as simple as was once believed and that it is rare for any trait to be controlled by just a single gene. The expression of physical traits like eye color and baldness are now understood to be connected to a number of different genes that collectively influence expression. More complex aspects of human existence, like personality traits or sexual preference, have genetic components but are not the matter of simple genetic expression alone.

However, while the idea of finding "the gene" for baldness and other things proved to be more illusory than productive, scientists were able to link many serious medical conditions to various genes or combinations of genes and further were able to discover how the absence of genes can affect the body. It was in the 1960s

that scientists first speculated about the possibility of "injecting" or "inserting" gene sequences into the human body to change how the body behaves. The research paper "Gene Therapy for Human Genetic Disease?" was published in the popular journal *Science* in 1972, with scientists Theodore Friedmann and Richard Roblin presenting the basic theory of how this might work, but also warning that active development of gene therapy was not advised because of the lack of understanding about how genes worked.

Around eighteen years later, in 1990, a four-year-old girl, Ashanthi DeSilva, became the first patient treated with gene therapy. DeSilva suffered from a rare genetic disorder called "severe combined immunodeficiency," which essentially meant that she could barely spend time with others without risking severe illness or death. Scientists discovered that this disease stemmed from the lack of an enzyme adenosine deaminase (ASA), which was created by way of a certain gene. Using a virus as a "vector" or "carrier," scientists were able to insert a functional copy of this gene into DeSilva's body, which allowed her to produce ASA herself, and increased the function of her immune system.[3]

This 1990 treatment was the beginning of gene therapy, but the field stalled in 1999 after the death of Jesse Gelsinger, a patient at the University of Pennsylvania suffering from ornithine transcarbamylase deficiency. When Gelsinger died, from an immune system reaction, the FDA suspended the University of Pennsylvania's entire gene therapy operation, which was, at the time, one of the largest and most productive in the country. Researchers turned their attention to looking into the safety concerns surrounding genetic treatments and, specifically, the use of viral vectors and development largely stopped for a few years.[4]

In the mid-2000s, gene therapy research began to resume in many countries and the Food and Drug Administration (FDA) again began to approve genetic treatments for certain disorders. Part of what changed, in the ensuing years, was that viral vector technology improved and became more reliable. The development of the viral vectors known as adeno-associated viruses (AAVs) was a big part of the return of gene therapy, providing a more targeted delivery system. In addition, utilizing the eye to introduce viral vectors proved to be another advancement, as eyes are relatively limited systems that typically don't allow introduced materials to reach other areas as easily. Advancements like these led to an explosion of development in gene therapy around the world.

Much of the modern focus on gene therapy focuses on Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) a system that can be used to edit genes. In traditional gene therapy, a functional copy of a gene is introduced, but this does not eliminate dysfunctional gene activity. Using CRISPR, which is a "gene-editing" technique, it is possible to eliminate dysfunctional genes from a cell. This is therefore a different, though related way, to eliminate a genetic disorder, by eliminating the genetic abnormality at the root of the dysfunction. The CRISPR program gained worldwide attention in the late 2010s as scientists began working on gene-editing solutions involving sickle cell anemia.[5]

Editing Human Life

While gene therapy and genetic editing have provided promising results when it comes to combating genetic diseases and disorders, the capability to edit the genome has also raised ethical issues that Americans are still struggling to understand. Some believe that the genetic manipulation of living organisms is unnatural or violates national patterns and processes. Others believe that humanity is meddling with biological and physical properties about which humans know very little and that there may yet be unforeseen consequences.

Ethical concern over genetic manipulation techniques can be seen in the ongoing debate over the cloning of animals and the potential to clone humans, which many Americans and citizens around the world consider a potentially dangerous or immoral path of development. Cloned organisms have demonstrated a high likelihood of developing genetic disorders, which is one of the primary ethical objections against experimentation with this kind of technology. In addition, many simply consider cloning to be unnatural or contrary to either the perceived "laws of nature" or some kind of "spiritual" principle against the technological creation of life. A similar controversy has developed over projects designed to recreate extinct organisms by using genetic manipulation to essentially "clone" extinct species. While there are numerous scientists working on "de-extinction" technology, many consider this process potentially dangerous and unethical given that it is unclear how a recreated species would survive or whether this process can be conducted without producing genetic abnormalities that might amount to animal cruelty.

Another controversy surrounding genetic editing and manipulation techniques concerns that possibility of eliminating genetic abnormalities from fetuses. While in some cases members of the public support such efforts, such as in the effort to eliminate genetic dysfunctions that negatively impact a person's quality of life, many have expressed concern that this kind of technology will be used to eliminate aspects of human life that differ from the norm but cannot be plainly labeled as dysfunction. For instance, if gene editing could eliminate deafness, some might consider this a benefit, but members of the deaf community have objected to characterizing deafness as a disability and instead argue that deafness is part of the natural diversity of human life. This view of characteristics like deafness, autism, or blindness is part of a movement known as "neurodiversity," which promotes the idea that human minds and bodies can work in various different ways without being considered dysfunctional or problematic in a way that needs to be "cured."

A Historical Stigma

The potential negative impact of genetic manipulation seen from past efforts colors the way that Americans and people around the world view genetic science in the twenty-first century as well. Many critics worry that unchecked genetic experimentation will lead to the unintentional increase in genetic abnormalities or illness. Others are concerned that genetic manipulation violates natural or spiritual principles. Others are concerned that this technology could fall into the "wrong hands"

becoming a weapon. The historical development of genetic manipulation techniques demonstrates that the technology has long been controversial and potentially problematic, but also demonstrates that genetic medicine and development might also hold the key to addressing some of humanity's most ancient threats.

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Notes

1. Miko, "Gregor Mendel and the Principles of Inheritance."
2. Pray, "Discovery of DNA Structure and Function: Watson and Crick."
3. Mitha, "The Return of Gene Therapy."
4. Rinde, "The Death of Jesse Gilsinger, 20 Years Later."
5. Gostimskaya, "CRISPR-Cas9: A History of Its Discovery and Ethical Consideration of Its Use in Genome Editing."