Genome Engineering in Humans

All the cells in our bodies contain exact, identical copies of our unique genome. The sequence of genes in DNA, or deoxyribonucleic acid, determine all the different characteristics of the human body from eye color, to muscular mass, to risk for a certain disease. Our bodies have a very specific, tedious process through which the genetic code in each of our cells is copied and reproduced. One mistake or mutation in this process can cause serious illnesses to the organism involved. These diseases range from minor problems like colorblindness, to life threatening illnesses like cancer. For the last fifty years, scientists have been striving to find a way to correct these mutations and cure the underlying disease. There has been a huge leap in progress in a process called genome editing or genome engineering. This development has given us the ability to edit the DNA of organisms and replace unwanted mutations with the corrected version. As of now, the most efficient and cost effective system of genetic editing is called CRISPR. However, even more advanced systems are already in the process of being designed.

**How CRISPR system was discovered**

 Bacterial cells are constantly competing with viral cells for space and resources. The way a virus attacks a bacterial cell is by sending out a phage to inject the bacterial cell with the virus’s genetic information. The bacterial cell then begins to replicate this information and creates copies of the virus. Eventually there are so many copies of the virus created that the cell bursts and all the new phages are released*.* Most bacterial cells are defenseless against this type of attack. If, however, the bacterial cell happens to survive, the cell keeps and stores a copy of a sequence of DNA from the virus in its own genetic code in a DNA archive. When the bacterial cell is under attack by the virus again, the bacterium finds the DNA from the archive and creates two types of RNA copies of the fragment. One of the RNA fragments is called the guide RNA and is an exact match to the virus DNA from the archive. These RNA fragments form a complex with a protein called Cas9. The Cas9 protein is a nuclease that can detect and cut the virus DNA strand. Cas9 scans the inside of the bacterium, comparing all DNA that it finds with the RNA copy. When an exact DNA match is found, Cas9 is activated and it then cuts the viral DNA strand, disabling the virus. After studying this mechanism, scientists found that the CRISPR system used in bacteria is programmable and any copy of DNA given to the system can be used in the same manner whenever it is injected into a living cell. They discovered that this system not only works for bacteria, but can be recreated to work in microorganisms, animals, plants and humans.

**Clustered Regularly Interspaced Short Palindromic Repeats**

The system that scientists designed is called **Clustered Regularly Interspaced Short Palindromic Repeats or CRISPR.** Its application for now is basic research, but it is believed that eventually it will be used for helping cure diseases caused by genetic mutations. We’ve had the ability to edit the genome of organisms for some time now, but CRISPR technology has increased the efficiency and accuracy significantly while decreasing the time and cost. In this method, scientists transcribe CRISPR sequences onto RNA strands that match the DNA sequence of the genetic mutation. This helps the protein Cas9 to locate the mutation and cut the DNA. Modified versions of Cas9 can also activate gene expression instead of just cutting it. This activation allows further study of the gene. In 2015 researchers used this method to cut the HIV DNA from living cells that came from patients infected with HIV. Less than a year later they were able to remove roughly 48% of the HIV virus from mice that were infected. This shows incredible promise for the future of this technology in being able to treat genetic diseases.

**Importance of Genome Engineering**

Genome editing is incredibly valuable because it gives us the possibility to cure serious diseases like cancer, Huntington’s, HIV and other genetic diseases. For example, in the case of cancer, certain cells in the body do not die and instead replicate exponentially creating a mass of cells that can spread and lead to death. These cells are effective in attacking their host because they hide from the immune system. In the future, we could be able to edit our immune cells to make them better at finding cancer cells by using the CRISPR system. Then, the treatment for cancer could be a few injections of these modified immune cells. This advancement would not only be extremely cost effective, but also way less invasive than other methods like chemotherapy and surgery.

**Other types of Genome Engineering Methods**

CRISPR is the most recent and most efficient form of genome editing, but genome editing has been developing since the early 1970’s and there are several other ways of genetically engineering DNA sequences.

1. Homologous Recombination

This particular technique of genetic recombination between two similar strands of DNA began taking shape in the late ‘70’s. It was discovered from studying yeast which naturally carries out this process. In the laboratory, researchers determine which section of the genome they want to edit and then engineer DNA sequences that match this portion of the genome. They then inject the fragments into the individual cells, or use chemicals to facilitate the uptake of the DNA by the cells using chemicals. The engineered DNA segments then recombine with the targeted cell’s DNA to replace the portion of the genome. This was the earliest form of genetic recombination and it is very expensive, difficult and very inefficient. One of the most common mistakes with this practice is when the fragment of DNA is inserted into the wrong area of the genome. This error is called an off-target edit.

1. Zinc-Finger Nucleases

**Zinc-Finger Nucleases** is another form of genetic editing that is ten percent more effective than homologous recombination. This form of genetic editing decreases the number of off target edits. In this method, scientists develop proteins, called Zinc-finger nucleases or ZFNs, that bind to a target DNA sequence in the desired genome. Once bound they then cut the DNA so that scientists can replace the desired area of DNA by using homologous recombination. The ZFN process is more successful than homologous recombination alone, but is still very hard, time consuming and not much more effective. The scientists have to create new ZFN proteins for every experiment, which is tedious and takes time.

1. Transcription Activator-like Effector Nucleases

**Transcription Activator-like Effector Nuclease or TALENS** is a form of genome editing that began in 2009 uses transcription activator-like effector nucleases or TALENs to cleave the DNA segment in the target. This form is similar to the method that uses Zinc-Finger Nucleases, but it is easier and to design and manufacture the proteins used.

**Ethical complications of genome engineering**

There are several ethical complications that could cause issues in the future if we pursue all the possibilities genome editing holds. There is a possibility that in the future, parents will be able to “design” their future children and choose their hair color, eye color, muscle mass, height, etc. They might also be able to use genome editing to make their child really athletic, intelligent or musically inclined. These genetic choices not only affect the child whose genes are modified, but it also affects generations after the child as the modified genes are passed down. There is also fear that if designing your own child and choosing the best traits for him or her becomes a reality, that the option will only be possible for those in the higher class who would be able to afford this luxury. This could create a very large gap between those who can afford to modify their children and those who can’t or choose not to. It might also be a possibility for humans to inject DNA sequences from other animals and acquire traits like webbed toes, whiskers or gills. Another justified fear is that certain countries could use genetic modification to create their own super army of soldiers with the perfect desirable genes to fight in wars. Perhaps the hardest possibility to grasp is the idea that we might be able to slow down or reverse aging of cells in our bodies. The wear and tear we endure from every day life is harder on cells as we get older because cells become less efficient at performing the tasks they were created to perform. Scientists believe that we could modify the genes associated with these cells and reverse their aging. This would make people not only look and feel younger, but also live longer as well. As we continue with our research in the area of genome engineering and new doors are opened for our society, we will have to decide together what is beneficial to our existence and which lines should not be crossed.

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