Gene Editing

Gene editing is a broad study that has become increasingly popular over the last few years. With the world’s population continuously increasing, problems such as world hunger begin to increase. With studies using genome editing to genetically modify crops to provide more substantial nutrition and increasing crop value, problems such as these can hopefully be solved. Gene editing also has a promising future in the medical field. Doctors and scientists hope to one day be able to use gene editing techniques to alter DNA sequences in patients with chronic diseases such as cancer or even alter genetic diseases in unborn babies. In this chapter we will cover the basic concepts of genome editing and the links between these studies and our everyday lives.

Enzyme: a protein molecule produced by living organisms that acts as a catalyst.

Gene editing can be described as the ability to make changes in the DNA sequence of living organisms by targeting specific enzymes. One of the keys to gene editing is the CRISPR-Cas9 system. This system was discovered in 2012 by scientists Jennifer Doudna, Emmanuelle Charpentier, and colleagues. The CRISPR-Cas9 system gives scientists the precision they need in order to target specific locations in DNA for insertion or removal of different enzymes. However, despite this being a fairly recent discover, the idea of gene editing dates back to the 1950s. During this time scientists really began to uncover the link between gene sequences and healthy or diseased offspring. In the 1980s, gene therapy made its debut as a potential to help combat genetic disorders in offspring. This approach proved to be effective for some genetic disorders, but for others the technology was not precise enough to alter the desired genes. Two other forms of gene editing were introduced before the CRISPR-Cas9 system to try and fix this problem: zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENS). ZFNs are DNA binding proteins that create double stranded breaks in DNA to edit the targeted genome. TALENS are proteins engineered to cut specific DNA sequences in order to alter the target genome. Unlike using ZFNs and TALENs, CRISPR-Cas9 uses RNA-DNA binding instead of protein-DNA binding. This makes working the CRISPR-Cas9 system much simpler than the two alternatives and allows for the system to reach a broad range of targeted sequences instead of a select few.

Gene: basis unit of heredity

Gene therapy: the process of transplanting normal genes in place of missing or defective ones

**The Many Uses of Gene Editing**

Gene editing is a concept that can be used in many ways and not only in humans. Many living organisms could benefit from the possibly beneficial outcomes of gene editing whether it be animals, crops or plants, or the bacteria surrounding us. Gene editing could influence our lives in many ways and with the popularity on the rise, is something we could be seeing making a huge impact in the near future.

**Gene Editing in Humans**

Genetic Disease: disease that is inherited by abnormalities in DNA structure.

As stated before, the idea of gene editing in humans began in the mid-20th century. Gene therapy has been used for decades in trying to fight against genetic diseases, but the results haven’t always been successful. In 2015, scientists used somatic gene therapy, and the genome editing technology TALENs, on one-year old Layla who had leukemia. Many other forms of treatment had been used but this was the only one the proved successful. Today Layal lives a happy, healthy life. However, despite this success, genetic editing is still a controversial topic when being used on humans. Many believe that genetic editing crosses technical barriers and raises too many ethical concerns. With necessary modifications and plenty of practice trials, gene editing can could help not only those with genetic diseases but help cure chronic illnesses like cancer.

Abiotic: caused by nonliving physical factors such as chemical reactions or weather

Biotic: caused by or related to living things

**Gene Editing in Plants**

Genome editing in plants and crops is a topic that has actually become more popular than that in humans. Without having to worry about crossing technical and ethical barriers regarding human life, the editing of crop genomes has little limitations when it comes to its research. Currently, almost 20 different crop species have been adapted with the use of genetic editing to help improve biotic and abiotic stress management. With the use of the CRISPR-Cas9 editing system, crop disease resistance and tolerance to abiotic factors such as drought have increased. With the world’s population constantly growing and world hunger becoming an even bigger issue, the need for crops to feed starving nations are in high demand. By using the CRISPR-Cas9 system to genetically modify crops such as rice, wheat, and maize, which are staple crops in many third-world countries, the nutritional value and overall quality of these crops could be increased.

**Gene Editing in Animals**

The most commonly used animals in gene editing research are mice and zebrafish. This is because both animals provide the idealistic lifestyle for testing due to reproducing quickly and having the same genes as humans. By using these species of animals, scientists are able to test, edit, and investigate different diseases in an approach that would simulate what would happen if that same approach were used in humans. The biggest benefit of this is scientists can conduct their gene therapy research without having to dodge the bioethical concerns of whether or not this is okay. The Burgess lab is a prime example of a research facility that uses zebrafish in their research. Their primary focus is the use of 50 zebrafish genes that closely resemble those of humans in hopes to better understand the basis of deafness and its genetic makeup. Zebrafish and mice are not the only animals used in this research as scientists have also tested ZFNs and TALENs on fruit flies, nematodes, livestock, and monarch butterflies.

ZFN: also known as Zinc Finger nucleases, is form of gene editing that binds and cuts DNA to allow the deletion or replacement of DNA

**How Gene Editing Works**

**Zinc-finger nucleases (ZFN)**

Zinc-finger nucleases was discovered in the 1990s and was used to reduce off-target edits and to improve the specificity of gene editing all together. In basic terms it is the process of binding to specific DNA sequences of the genome and cutting the DNA**.** Once the cut is made, scientists can either delete the sequence or replace it with a new one using homologous recombination. The first successful ZFN was performed in *Drosophila, also* known as a fruit fly. Since then ZFNs have been modified, constructed, and used in a variety of different organisms and cells. Zinc-finer nucleases is a time-consuming process and is much more complicated than the other alternatives to perform which is why it is not used very often.

Homologous recombination: the exchange of genetic information between similar strands of DNA.

**Transcriptions activator-like effector nucleases (TALENs)**

Brought about in 2009, TALENs are a different type of gene editing protein which can actually be found in nature. Much like the use of ZFNs, TALENs bind to specific DNA sequences to help scientists delete or replace corrupted DNA. Despite being about the same efficiency as ZFNs, TALENs are much simpler to engineer making it much more desirable than ZFNs. TALENs have even been used to inactive the LDL receptor gene in pigs which brings about a lot of excitement in the scientific community as the ability to induce mutations in different organisms could open the door to models of human diseases using different animal species.

TALENs: also known as transcriptions activator-like effector nucleases, is a type of gene editing that uses proteins found in nature to alter DNA sequences.

**Clustered regularly interspaced short palindromic repeats (CRISPR)**

When using CRISPR a short RNA strand is created to mimic the desired DNA target sequence in a genome, thus creating what we call a guide RNA. This guide RNA then directs the Cas9 enzyme to the targeted DNA sequence to be gutted and edits such as deletions or insertions of new DNA occur. The CRISPR-Cas9 system is a revolutionary breakthrough in the world of gene editing. The use of RNA sequences instead of engineered protein makes this technology much easier to use than that of TALENs or ZFNs and it is much more cost efficient. CRISPR can also be introduced to multiple genes at one time and is not limited to single gene editing like TALENs and ZFNs. Whitehead Research Institute recently revealed that they were successful in mutating five different genes in mous cells simultaneously using the CRISPR-Cas9 system. Plus, CRISPR is six times more efficient than that of its competitors making it the ideal technology to use in genetic editing as it guarantees a more successful outcome.

LDL: low density lipoproteins. Also known as bad cholesterol because a high LDL leads to the build up of cholesterol in the arteries

**Disadvantages to Gene Editing**

RNA: messenger that carries instructions from DNA to make proteins.

Although there are many good things about the use of gene editing, there are also many disadvantages to it as well. First of all, being a fairly new study, it is not completely accurate and could still use some modifications to increase target specificity and reduce off target cleavage. Another downside is that while gene editing is a revolutionary breakthrough in crop development and human pathology, if it were to fall into the wrong hands, its power could be abused. By manipulating germline genetics, the human race could fall victim to something far more nuclear than simply fixing genetic diseases. Cloning and superhumans are all concerns that scientists have worried about if gene editing were to advance too far. Lastly is the bioethical issue of the research. While everyone may want a healthy child, some question whether it is okay to manipulate the genes of an unborn child without their consent (even if the parents have said it was okay). Not only this but there can also be complications to the use of gene editing such as unwanted mutations. As stated before, the technique is not completely accurate, and mistakes are bound to be made.

Germline: germ cells descending from earlier cells

**Conclusion**

Overall the idea of gene therapy is a biotechnical breakthrough that could help thousands. Modifications made to crops could help in the fight against world hunger. If human genome editing is put into place, genetic diseases might cease to exist. People fighting cancer or other chronic illnesses could potentially be cured. With the study still being fairly new, there is still much room for improvement and results are still in the work of seeing how effective this research will be in the end. However, if this study continues to progress and gain popularity at the rate it is, we can hope to see it making an impact in this world very soon as the potential abilities of this research are endless!

Chronic illness: disease that is long-lasting or potentially lifelong.

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