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Group 6

Modern Techniques

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**CRISPR/Cas9**

Technology has rapidly changed over the last 30 years to create cheaper, faster, smaller, more accurate computers and devices to perform bigger and bigger tasks. What was science fiction in the 1980s is now a reality. Processors the size of rooms have shrunk down to fit into our palms and have become the norm within the market. A similar breakthrough has occurred within the world of genetic engineering over the last four years. Though bacteria have been using this mechanism, which is known as Clustered Regularly-Interspaced Short Palindromic Repeats, or CRISPR, for billions of years, its potential applications for genetic engineering was discovered in 2012 by Emmanuelle Charpentier and Jennifer Doudna of the University of California, Berkeley. This mechanism cut the costs of genetic engineering by 99% and the timeline of genetic engineering experiments by months (“Genetic Engineering”, 2016).

When a bacterium is attacked by a bacteriophage, the phage inserts its DNA into the bacterium’s DNA in order to reproduce. If a bacterium survives the attack, it saves the viral DNA in its CRISPR locus, which functions like a library of past infection. In the event of another attack, CRISPR searches for the viral DNA and makes a copy of it for CAS9, a protein which searches the rest of the bacterium for portions of DNA that match the old viral copy. If a perfect match is found, the viral DNA is cut out of the bacterial DNA, stopping the reproduction of viruses. CAS9 is extremely precise in cutting out the viral DNA, which makes it ideal for genetic engineering (CRISPR, 2016). Charpentier and Doudna discovered that one could manipulate CRISPR and CAS9 to find and cut out desired sections of DNA in any organism, while other scientists, such as Jonathan Weissman of the University of California, San Francisco and Stanley Qi of Stanford University discovered how to change CRISPR/CAS9 so that the desired gene is not cut out, but either inhibits or activates gene expression of the desired gene (Broad Institute, n.d.).

According to Kamel Khalili from Temple University in a paper in *Gene Therapy*, the CRISPR/Cas9 system was used to edit rats’ genomes to cut out HIV-1 genes that had been inserted into nearly every cell in the body. The CRISPR/Cas9 mechanism then cut out those genes, leaving the rest of the DNA as it was normally. The study found that CRISPR was able to completely eradicate the HIV-genes from more than 50% of the rat’s cells of each type (brain, blood, spleen, etc.), by only injecting CRISPR/Cas9 into the tail. Due to the success of this trial, Khalili is researching the dosage of CRISPR as well as any side effects of the treatment for future use in human trials.

The discovery of uses for the gene editing method of CRISPR/Cas9 has made such leaps and bounds that on June 21, 2016, it was approved by the National Institute of Health (NIH) to use CRISPR’s Cas9 to modify current cancer therapies. The purpose of this clinical trial is to see its impact on the body, and how well it will aid in the elimination of cancer cells. The team hypothesized that CRISPR will help the immune system detect and identify cancer cells so the T cells can eliminate them (Reardon, 2016). Although clinical trials have not officially started yet, patients should be getting treated with CRISPR at the start of 2017. CRISPR is making leaps and bounds to the point where it will be seen in gene therapy clinical trials very soon.

When CRISPR is used by bacteria, it is limited by the fact that the bacteria must survive the initial viral attack in order to run CRISPR. This limitation becomes unimportant when discussing CRISPR’s involvement in gene therapy, as it is mainly used for its gene editing capability. When talking in terms of gene therapy, there are very few things holding it back. The problem is the exact opposite; this gene manipulation can go so far as to invoke moral and ethical dilemmas.

The current goal is to find a way to use CRISPR/Cas9 to correct genetic disease. These diseases can range from something as harmless as color blindness to as life threatening as Huntington’s Disease. Although these genetic diseases are wildly different, they share the fact that they were caused by one or more mismatched nucleotides. The well-tested theory is that CRISPR can easily correct genetic mutations by editing the patient's DNA and correcting the mismatched nucleotides (Andersen, 2016). CRISPR could become the cure for over 3,000 genetic diseases, but once this is achieved, the question is, does science stop there? With such power to edit DNA and genes, what is stopping people from moving from gene therapy to gene manipulation?

Current studies and experiments are going into genetic manipulation of embryos (Andersen, 2016). This means one could make said person immune to some disease, but they would also be able to pass on this gene to their children, and in the long run make humanity immune to the disease. This would be one of the biggest breakthroughs in the medical field, but this also opens up the possibilities of modifying the genome of said personto get more desireable traits. This could begin to be implemented in the next 100 years. According to Dr. Perry from the University of Bath, “It is approaching 100% efficiency already; it’s a case of ‘you shoot you score.’” With this technology, scientists could then begin to modify people’s traits, make them tall, more muscular, have longer hair, etc.; any trait is an option for modification. This concept is also known as ‘designer babies’, where one would be able to customize a baby to one’s preference. Morally, this can be seen as having too much control and raises the question; should humans be allowed to make ‘perfect’ people? This would raise problems such as leaving un-edited ‘regular’ people at a disadvantage.

Along with the alteration of traits, there is the possibility of unlocking the key to stopping aging, which would introduce an ethical problem. The idea of being able to live 20, 100, 1000 more years than what is currently possible is fascinating, but ethically, it would not be right. Although there are animals that do not age, like lobsters, but they do not have the same impact on the planet that humans do. As of right now, humans are in constant need of expansion to meet the demands of the ever-growing population. If human lives were to be extended, that would mean fewer deaths and, in the long run, even worse overpopulation (“Human Population Growth and Extinction”, n.d.).

With the discovery of CRISPR/Cas9, humans have been able to harness the gene editing process that bacteria have been using to protect themselves against viruses for billions of years. It is an amazing mechanism that will do great things for humanity, such as the treatment and possible eradication of disease, but continuing these advances beyond the treatment of diseases can bring further ethical complications. Scientists must begin the discussion of where the line is drawn to stop the advancing of this technology to continue into unethical fields.

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