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Darren Stoub

Dordt College, darren.stoub@dordt.edu

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Science Associated with Producing GMOs

Abstract

"Are our understandings of GMOs based in reality? Are GMOs bad? Are they good? Should we make them? These are challenging questions. We, as a society, must discuss the issues."

Posting about the science associated with GMOs from *In All Things* - an online hub committed to the claim that the life, death, and resurrection of Jesus Christ has implications for the entire world.

<http://inallthings.org/the-science-associated-with-producing-gmos/>

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The Science Associated with Producing GMOs

 inallthings.org/the-science-associated-with-producing-gmos/

Darren Stoub

I am a medicinal biochemist, which means I discover new medicines and seek to understand how the medicine affects the physiology of diseased cells. Recently, my research has focused on looking for drugs that treat Systemic Lupus Erythematosus (SLE), which is one of the diseases called lupus. SLE is caused by genetic mutations in a protein involved in the immune system's inflammation pathways. While we could do our testing on patients with lupus, the amount of blood we need would be excessive and the continual drawing of blood would be intrusive; some might suggest it is even unethical. We could do our experiments on immortal cell lines, such as HEK or HeLa cells; however, we need cell lines that mimic lupus cells. As a result, we do genetic engineering on human cells to create mutated human cells that display the characteristics of lupus cells. In my daily work, I create GMOs.

In this article, I want to pull the curtain back on the science associated with GMOs, provide a few historical methods of generating GMOs and highlight a new method, termed CRISPR-Cas9, which will significantly impact the ease by which GMOs are created. Through an understanding of these ideas, we hope to provide a working vocabulary so that the resultant ethical discussions can be well-informed.

A **GMO** is “an organism or microorganism whose genetic material has been altered by means of genetic engineering.” Genetic engineering utilizes a wide variety of molecular biology techniques, all of which have the same goal: to modify the genetic code of an organism. By the modification of the genetic code of an organism—its genotype—the physical manifestations of the genes, its phenotype, can be altered. While the correlation between the genotype and phenotype is often complex, the central dogma of molecular biology defines a simple understanding. Briefly, deoxyribonucleic acid (DNA), the genetic information, codes for protein, the doers of almost all cellular processes. The chemical identity of DNA is based upon four chemical building blocks, called nucleotides: adenosine (A), thymidine (T), guanosine (G) and cytidine (C). The sequence of these building blocks, that is, the order in which these chemicals are connected, provides the genetic code. Proteins are chemicals produced in living systems based upon the genetic code. That is, proteins are a sequence of amino acids that are assembled into this sequence because of the sequence of the genetic code. Proteins, because of their sequence, are capable of doing many tasks such as:

- catalyzing biochemical reactions (for example, HMG-CoA Reductase, which is an important enzyme involved with the bodies normal production of cholesterol)
- facilitating organismal communication (for example, insulin, a protein, interacts with the insulin receptor, a protein, which allows the pancreas to tell the rest of the body that blood sugar levels are too high)
- providing structural support for an organism (for example, the protein dystrophin provides a tether between the cell and the actin fibers which allow muscles to work effectively)
- transporting chemicals into and out of cells (for example, cystic fibrosis transmembrane conductance regulator (CFTR) facilitates the transport of “salt” in lung tissue)

If proteins are not produced, are modified or new proteins are added to a cell, the cell will behave differently. As a result, if we change the DNA, which codes for a protein, we can change the function of the protein, which is the basis of all genetic engineering. An interesting observation about how we currently accomplish genetic engineering is that the methods/modifications are seen naturally, so we have learned

how to do genetic engineering, because we observe it in nature.

There are three main types of genetic modifications or mutations that affect the phenotype of an organism and are, therefore, used in genetic engineering. First, genes can be knocked-out, which means that a gene within the organism has been modified so that the cell no longer produces the protein. Genes are often knocked out by modifying the gene, which often results in the protein not being produced and, therefore, the change in genotype results in a different phenotype. An example of a naturally occurring knock-out mutation can be seen in Duchenne's muscular dystrophy, in which the protein dystrophin is not produced, thereby substantially impacting the structure of muscles.

Second, genes can be added, which means all of the genetic information required for a new or different protein is provided to an organism. By doing so, an organism is given new abilities that were not historically present in the organism. A natural example of this is seen during viral infections, such as HIV, in which the HIV virus will insert its genes into the DNA of white blood cells, causing the cells to produce new proteins, specifically the ones used to make new HIV particles.

Third, genes can be modified through point mutations, which cause subtle changes in the protein function. By exchanging even one nucleotide within a gene, the resulting protein may have one different amino acid, which will change its chemical structure, which will change its ability to function normally. A naturally occurring example of a point mutation is seen in sickle cell anemia, in which an A is changed to a T within one of the genes for hemoglobin, which results in a valine being inserted at position 6 within the hemoglobin instead of a glutamic acid, which results in a new propensity for the hemoglobin proteins to form "non-natural" protein fibers, which forces the cells to change shape, which seriously impacts the circulatory system, which causes significant disease.

Using these natural examples, humans have developed four main methods to introduce genetic changes into an organism. First, we use crossing experiments, which has been part of agronomy and animal husbandry for millennia. Simply, we take two different, yet genetically related organisms and cross fertilize the organisms so that when they produce progeny, the progeny are genetically different. This method has been used to create award winning tomatoes, hairless cats, and amazing children. Using current genome sequencing techniques, we are now able to see that the results of genetic crossing is often one of the aforementioned genetic changes.

Second, we can use a process termed mutation breeding, in which an organism is bombarded with destructive conditions, such as gamma irradiation, reactive chemicals or nutritionally modified diets. Often these conditions damage the DNA, which the organism attempts to repair, which sometimes results in mistakes, which results in genetic changes. Examples of products we use that are created using this method include the Rio Star grapefruit, which is loved for its deep red color, and Golden Promise barley, which can be grown using salt water. It should be noted that even our own sun can cause these types of mutations.

Third, we can transfect or transduce the organism. In this experiment, genes, in the form of purified DNA or DNA appropriately packaged in viruses, can be introduced to an organism and, under the correct conditions, the gene can be permanently added to the affected cell's genome. An example is seen in Round-up ready crops, which are created by the addition of a bacterial gene, which codes for a point mutant of an enzyme normally found in plants; however, the bacterial enzyme is unaffected by glyphosate, the active ingredient in Round-up. Plants without this added gene are killed when Round-up is administered. A second example is used to treat patients with a specific genetic variation of cystic fibrosis, which makes the aforementioned CFTR not function well, which results in the production of a suffocating mucus in the patient's lungs. In the therapy, a normal gene for CFTR protein is added to a cells within the patient's lungs using a lentivirus. The new gene provides the patient's cells the ability to regulate the consistency of the mucus coating their lungs, thereby mitigating the symptoms of CF.

One of the drawbacks for each of the first three techniques is that either generation of the mutation or incorporation of the new DNA is random. While such an approach can be valid if the added DNA is tested to ensure that it will not cause other problems (the round-up example) or if the cells are not immortal (CF example). However, the randomness does cause me pause, either because of the random nature or because of the amount of work it requires to test the new cells generated using these techniques.

The fourth technique used to generate mutations is called [CRISPR-Cas9](#). Using this technique, we are now able to modify DNA with unprecedented specificity and precision, which might alleviate my pause related to the randomness of the older techniques. Without describing the details, CRISPR-Cas9 represents an atomic-level scissors, with which I can modify any gene, and an atomic-level thread, which I can insert any piece of DNA, so that I can make any subtle (or grandiose) changes in a living organism's DNA. In the last 2 years, over 300 articles have used this technique to modify the genome of various organisms, from plants to bacteria to human blood cells and reportedly even to human embryos. One example of its use is that the bone marrow from a sickle cell anemia patient has been genetically modified to remove and repair the aberrant hemoglobin gene, thereby, providing a treatment for the disease.

CRISPR-Cas9 is a game changer for all things related to genetic engineering. Genetic engineering is now simple and CRISPR-Cas9 replaces the other techniques which could take years, with a technique that can be completed in a manner of weeks. Despite its power and beauty, I once again pause in my use of genetic engineering. While it can be a useful technique to bring healing, if it is used poorly, there is the potential for unbridled harm. If we mess around with the wrong genes, there could be introduction of new disease. It is such a revolution that the developer of the technique is calling for a moratorium on the use of the technique on humans in order to encourage all of society to discuss the implications of this powerful tool on eugenics.

In my work, I create GMOs, using the same methods that God has used to create his GMOs, that is, as He has revealed Himself throughout His creation. I do so to seek treatments for disease; He has done so to reveal His glory through the processes by which He has created an intricate and detailed world. Am I playing God when I do these experiments? Can CRISPR be used to bring glory to God? Is it justified to use this technique? Is part of God's unveiling of His kingdom the fact that we now have a glimmer into how God creates or redeems His creation? Does our understanding of genetic modification further show that the heavens (and the inner workings of a cell) declare the glory of God? Does using CRISPR bring glory to God? Are GMOs bad?

I'll leave you with a scientific and political conundrum. Dr. Kevin Dorn, during his tenure at the University of Minnesota, was seeking to develop a new cover crop that could be used to decrease soil erosion on farmland and increase soil resilience and productivity, while not impacting the subsequent year's crop rotation. Using a detailed understanding of the genetics of various cover crops, Dr. Dorn performed crossing experiments, hoping for genetic changes in several specific genes. After conducting the crossing experiments, analyzing the genetic sequences of thousands of plant progeny and several years of work, Dr. Dorn was successful in generating a few mutants that had desirable phenotypical traits, but was unsuccessful at targeting all of the genes of interest. When I asked him why he didn't use CRISPR to generate his mutants and save himself several years of work, his answer was that plants derived from crossing experiments are not considered GMOs and, therefore, acceptable, while plants generated using "genetic engineering" are considered GMOs and, therefore, less acceptable and federally regulated. The plants would be identical, irrespective of the methodology used to produce them.

Are our understandings of GMOs based in reality? Are GMOs bad? Are they good? Should we make them? These are challenging questions. We, as a society, must discuss the issues. Hopefully, this article has provided some common language and understanding that will allow us to have these discussions.