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GENE THERAPY IN BIOENGINEERING: WHAT DO I THINK?

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HISTORY

Engineers' defining element is that they solve the world's problems. Specifically, bioengineers design devices and procedures that help other people solve medical issues. Experts are constantly debating diverse issues that range from advancing health informatics to reverse-engineering the brain [1]. For as long as medicine has been around, there have been people trying to eradicate disease and strive to achieve a healthier future. As more and more discoveries are made about the body and how it works, new technologies arise that help more people. For example, after DNA mutations were discovered, doctors were able to develop prenatal tests that test for genetic diseases such as cystic fibrosis, hemophilia, and familial hypercholesterolemia. From there, researchers are working on fixing not only the inherited genetic disorders but also to cure acquired diseases like cancer, AIDS, Parkinson's, Alzheimer's and other infectious diseases [2]. The method that allows engineers to do all this is called gene therapy. Gene therapy is a new technology that allows engineering and medicine to combine with the goal of creating new cures to disease.

Ever since the first gene therapy trial in a human in 1990[3], gene therapy has been controversial, but still continued to expand. There has been more than 2,200 clinical trials since 1989[4], however, only few have been approved as treatments by the FDA. Even though the FDA is extremely strict with calling gene therapy a cure to diseases, there are still many clinical trials that help patients. Cancers are the most commonly treated diseases followed with single gene diseases and cardiovascular diseases [5].

The basis of gene therapy is to introduce "functional genetic material such as therapeutic pDNA and siRNA to human cells, tissues, or organs to provide therapeutic functions for the purpose of preventing for treating disease, or to fix a genetic defect" [6]. For example, doctors would inject healthy cells into say, the heart, to have them create new, normal cells to hopefully extend the life of the organ. Some methods are even able to correct the gene mutations at the genome or primary mRNA levels [6]. In the grand scheme of gene therapy, it is only just beginning and has endless potential.

CURRENT TECHNOLOGY

Advances in gene therapy are constantly being made and taking larger steps towards eradicating disease. A specific hot topic of research over recent years has been cardiovascular disease, as it affects and takes the lives of so many Americans annually.

A group over in Europe is currently working on myocardial remodeling to develop gene therapies that prevent and strengthen the heart after failure. The cause of cardiac arrest is the unbearable stress put on it by the body; the probability of cardiac arrest can be increased by factors such as diet, smoking, or genetics. In the past, solutions to heart failure included vasodilators and diuretics, which relieve the pressure on the heart. Recently, there have been developments into the molecular basis of heart dysfunction, so that treatments can be created that target specific areas that restore specific muscle function. These treatments are still in the early experimental stages, in order to find the right target that allows the heart to rebuild its muscle function.[11]

Another group of researchers in China is working on combining mesenchymal stem cell therapy with the drug, interleukin-10. The combination of these two treatments was tested on the injured hearts of rats where four weeks after the induction, cardiac functions oxygen flow to cells and inflammation was assessed. They found that, compared to either treatment alone, the animals' hearts improved and were returning close to normal functioning.[12]

Nanoparticles are another aspect of gene therapy, that are currently being studied by Russian organizations that believe they could be a solution to atherosclerotic disease. Nanoparticles are used as a delivery methods to get the healthy genes to the damaged organ. Using nanoparticles to transport the healthy cells is not only efficient, but also enhances the survival and regenerative capacity of the transported stem cells, therefore decreasing the chance of cell death. When the nanoparticles were modified with chemical agents or specific proteins, they were able to aim more accurately to a specific organ. Not only can they deliver accurately, but nanoparticles allow for characterization and tracking of the post-transplant behavior of stem cells [13].

There is yet another gene therapy study being researched and tested in animals to prevent heart disease. This focuses in on the efficiency of a re-engineered virus to carry inhibitor 1-

c, that prevents a certain protein from depleting cardiac cells. They first had the protein injected to destroy some of the heart and resemble heart disease. Then, after one month, they injected the special virus, in hopes that it would somewhat restore the heart's functions. The treated pigs experienced a significant increase in efficiency of the left artery and after two months, it only improved more. In addition, they found no evidence of adverse effects of signaling from the heart to the brain, irregular heartbeats, bad immune responses towards the cells, or organ damage[14].

Lastly, for the lucky patients that are able to find heart donors, there are researchers in China that have found ways to decrease the likelihood that the organ will reject its new owner. Testing this method in rats, they use a combination of modern imaging techniques and immuno-suppressive genetic therapy to achieve better graft survival. The gene therapy used in this case in preventative, not only of transplant rejection, but, after the successful transplant, decreases infections, tumor growths and other side effects of going on the standard lifelong immuno-suppressive medication. This gene therapy also has been shown to "achieve immune-suppression of T cells with better durability, less toxicity and cost effectiveness" [15]. However, they are still in need of new strategies that diagnose acute rejection of the organ earlier on, so they are able to treat it with gene therapy before it rejects. [15]

All of these breaking gene therapies would not be able to done or improved upon without the help of biomedical engineers. We are able to use our knowledge of the body and medical procedures and combine that with the knowledge of current technology to assist in gene therapy. For example, bioengineers used their knowledge of imaging devices to help the researchers in China know where to use their gene therapy [15]. Without bioengineers, these researchers would not have tools to inject modified stem cells or viruses to improve functions of the heart. Those in gene therapy could not do their jobs without bioengineers.

WHY IS IT IMPORTANT?

As a very adaptable treatment for countless diseases, genetically inherited or acquired, gene therapy has almost a limitless spread of research to choose from. An area of genetic therapy interest growing in popularity is heart disease. Cardiovascular disease is an all too common disease that was the leading cause of death for both men and women in 2015 [7]. So, if we have a solution that can possibly save about 630,000 Americans every year [7], why not research it? With gene therapy being offered more and more as a solution, it becomes more refined with every clinical trial and is able to help more and more people.

Not only is gene therapy an important area of research because it could help loads of people, but it also is cost effective for those people. According to the American Heart Association, the cost of cardiovascular disease treatment in comparatively much higher than any other disease group [8]. The AHA also stated the total direct and indirect cost of heart diseases and stroke in the US was estimated to be $315.4 billion in 2010 [8]. While as pharmaceuticals treat symptoms and require long-term administration, gene therapy has the potential to modify the mechanisms of those specific diseases [6]. Then if people are not paying for any more long-term medications, it could then save years of pharmaceutical costs.

In addition to gene therapy solving the issue of expensive medications, it would also significantly decrease the need for transplants. Penn Medicine describes the lengthy process it takes to successfully acquire a new heart. Donors must have the same blood type and body size. Wait time can last anywhere from days to months, and sometimes even years [9]. At this moment, there are 116,592 people waiting to receive a lifesaving transplant and on average, 20 of those people die each day while waiting for a transplant from the United Network for Organ Sharing [10]. These people could possibly be helped by the lifesaving gene therapy. Gene therapy would save these people years of anxiety and pain they would experience while being on the transplant list, hoping that the next organ donated would be a match for them.

For all of these reasons, gene therapy is an important field in bioengineering, as it is versatile and can help many groups of people. Those affected by cardiovascular disease would especially appreciate its amazing abilities and even greater possibilities. Continued research needs to be done, as the possibilities for gene therapy are endless. This topic is extremely important to me, as a future bioengineer, because working to improve gene therapy would consequently improve the lives of so many of my peers.

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