It's In The Genes

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Abstract

The CRISPR-Cas9 genome editing technology is a groundbreaking discovery that allows for scientists to alter a person's genome. This would stop genetic diseases from being passed down, and as many are hoping, end disease. The CRISPR-Cas9 process is done in a lab where fermented cells are taken and their genomes are cut, edited and replaced by the correct sequence. When the correct sequence has been implemented or the incorrect one deleted, the disease or disability is gone too. There are also other types of enzymes that have assisted CRISPR but they are nowhere near as efficient as Cas9. There have been human and animal trials, as well as two human babies successfully born using the CRISPR method. The CRISPR - Cas9 has also raised many questions and concerns about ethics and how this methodology may one day corrupt society.

Introduction

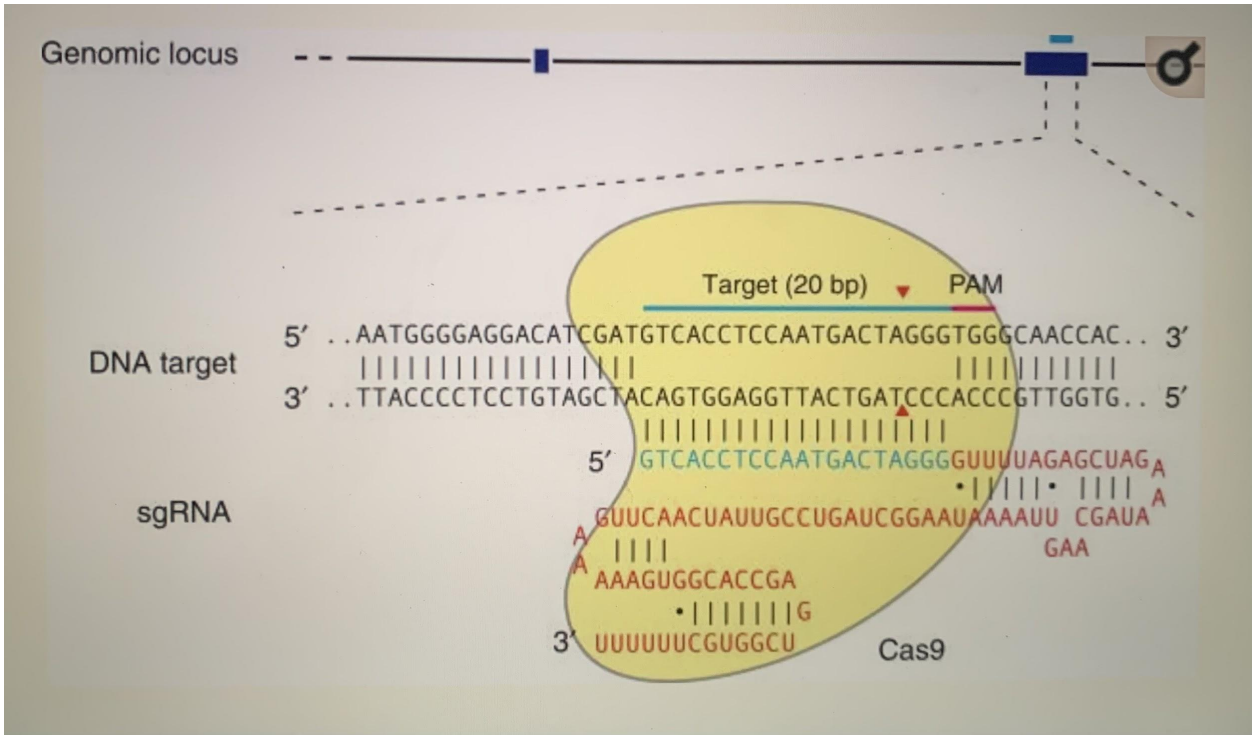
The CRISPR- Cas9 is a new and exciting way for genes to be edited in fertilized cells. This occurs when a sperm and egg cell are fertilized outside of the cell, then go through the CRISPR-Cas9 process and are put in the uterus using in vitro fertilization. For now, this process is strictly experimental and not being used by any clinics.

Process / Experiment

CRISPR stands for clustered regularly interspaced short palindromic repeats [ADD]. Cas9 stands for CRISPR associated protein 9 [5]. This technology is used to find a specific point on a strand of DNA where there's a disease, and change it. CRISPR-Cas9 was adapted from a naturally occurring genome editing system in bacteria [1]. The bacteria capture a small piece of DNA from invading viruses and use them to make CRISPR arrays. CRISPR arrays are like small pieces of broken up DNA that correspond to the viruses. The arrays allow the bacteria to remember the virus, so it's prepared if the virus comes back. If the viruses do come back the bacteria produce segments of RNA (ribonucleic acid), from the CRISPR arrays to target the DNA in the virus [1]. The bacteria then uses a Cas9 or a similar enzyme to cut the virus's DNA apart, which disables the virus and stops it from being able to attack the bacteria.

This tech was discovered by Emmanuelle Charpentier and Jennifer A. Doudna who both won the nobel prize for chemistry this year for the CRISPR-Cas9. They realized that the bacteria could be similarly edited to work for genes in humans. The actual crispr system starts with scientists creating a small piece of RNA with a guide sequence. The guide sequence allows the RNA to bind to a specific target sequence of DNA in a genome. The RNA also binds to the Cas9 enzyme. The modified RNA is then used to

recognize the DNA sequence that is going to be edited and the Cas9 enzyme goes in and cuts the DNA strand at the targeted location. Once the DNA has been cut, researchers use the cell's own DNA repair mechanisms to add or delete pieces of genetic material [1]. They also make changes to the DNA by replacing an existing segment with a customized DNA sequence that will alter the disease sequence.



In the above image, it depicts a schematic representation of the RNA-guided Cas9 nuclease [3]. The yellow is the Cas9 nuclease which originated from a bacteria important for humans. The nuclease is targeted toward genomic DNA by a guide RNA with a 20 letter sequence in blue. This is also followed by a scaffold which helps the formation of the new piece of DNA in red. The guide sequence pairs with the DNA target, represented as the blue bar which is followed by the pink bar which is PAM. Pam is a protospacer adjacent motif that follows the target sequence, and is a required piece for the function to be able to cut the strand of DNA correctly. Then the Cas9 mediates a double strand break on the DNA at the red triangle.

Other processes

The crispr-cas9 method is the most well known and recognized way to edit genomes but there are two predecessors to the Cas9 enzyme. Zinc finger nucleases (ZFN) and transcription activator like effector nucleases (TALEN). ZFN are artificial endonucleases which are like lab made knives that need direction of knowing what to cut. The ZFN is attached to the endonuclease and acts as the hand for the knife, guiding it to certain strands of DNA. TALENs are nonspecific DNA nucleases that have been connected to a

DNA binding domain; these two together allow the TALEN to target and find a sequence of DNA [3]. While these may sound like very similar processes to the CRISPR-Cas9, they lack the ability to be easily customized, have a higher targeting efficiency and a higher ability to facilitate a certain type of genome editing.

Results

There have been animal trials and human trials are in the process of starting. As of April 2019 human trials began, testing inherited blindness. In the upcoming trial the ‘molecular scissors’ will be injected into the eyes in hopes of the CRISPR-Cas9 fighting the disease [9]. There have also been animal trials. One trial was tested on canines with a genetic disorder that disables their bodies from making enough muscle proteins. In humans this disorder is very similar to muscular dystrophy which is another genetic disorder that's passed down. Each dog received the CRISPR-Cas9 system, and one dog experienced a 92% more normal level of dystrophin [10]. Also in 2018 a geneticist known as He Jiankui successfully and unethically did a human trial that produced two twin girls. The gene edited was to stop HIV from entering the cells of the infants, while there is no evidence yet to see if Jiankui successfully edited the DNA but that doesnt matter [7]. Jiankui has since been given three years in prison for illegal medical practice and many of his cohorts have also been charged.

Conclusion

This technology has the potential to change society and the way diseases are treated forever..If all diseases can be cured using CRISPR or even before birth, this could lead to loss of key professionals in society. The role of ethics also becomes questionable, many questioning where the line will be crossed. Since diseases and genetic defects can be changed so can other characteristics like eye color, hair color or athletic and intellectual status. Jiankui has since been given three years in prison for illegal medical practice and many of his cohorts have also been charged [8]. only further endorsing how dangerous and potentially problematic this process could be if it's not regulated sooner rather than later.

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