DNA DISCOVERIES IN CRISPR

DNA Basics

DNA or deoxyribonucleic acid A long two strand molecule contains unique genetic codes, a ‘double helix’ shape; like a twisted ladder.

Four basic building blocks or ‘bases’: adenine(A), cytosine (C), guanine(G) and thymine(T). The sequence of these bases form the instructions in the genome.

Each strand is composed of long sequences of the four bases, A, C, G, and T, paired with hydrogen bonds.

What is DNA? (2016, January 25). Retrieved April 3, 2020, from https://www.yourgenome.org/facts/what-is-dna

Introduction to CRISPR

"CRISPR": "clusters of regularly interspaced short palindromic repeats." A special region of DNA with two distinct characteristics: the presence of nucleotide repeats and spacers.

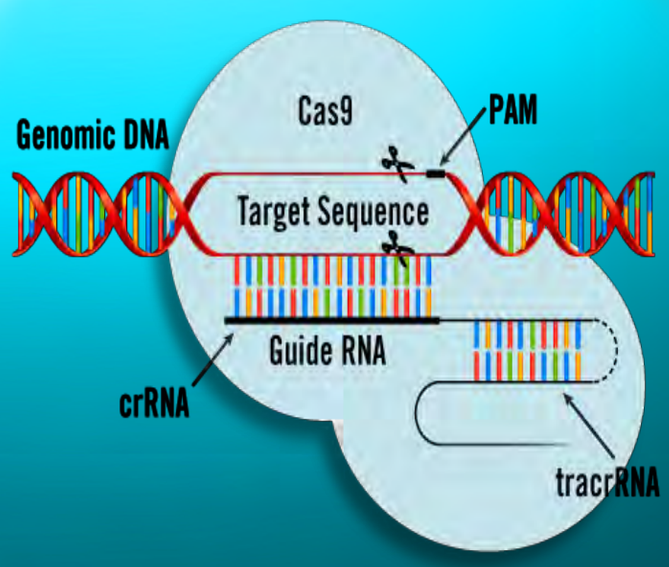
CRISPR technology was adapted from the natural defense mechanisms of bacteria and archaea. CRISPR-Cas9 was adapted from these technologies in bacteria. Bacteria capture invading viruses through DNA snippets. CRISPR arrays or DNA segments are then made, allowing the bacteria to recall these viruses or very similar ones.

If such viruses to attack again, RNA segments are produced from the CRISPR arrays to combat the virus. The bacteria use Cas9, or something similar to snip the DNA disabling the virus.

Vidyasagar, A. (2018, April 21). What Is CRISPR? Retrieved April 2, 2020, from https://www.livescience.com/58790-crispr-explained.html

CRISPR RESEARCH

Genome Editing



What is it?

A group of technologies that allow genetic material to be added, removed, or altered at particular locations in the genome: changing the organism's DNA.

How is it being tested?

A small segment of RNA is created containing a short guiding sequence that binds to a particular targeted sequence of genome DNA, Cas9 enzyme. The modified RNA is now using for recognition of such DNA sequence, Cas9 enzyme; cu ing the DNA at such location.

The new cut DNA is studied by using the individual cells repair machinery through add/delete/change the genetic material; making custom DNA sequences.

Current Progress:

Great interest, exploration in the prevention and treatment of human diseases; like cystic fibrosis, or sickle cell disease.

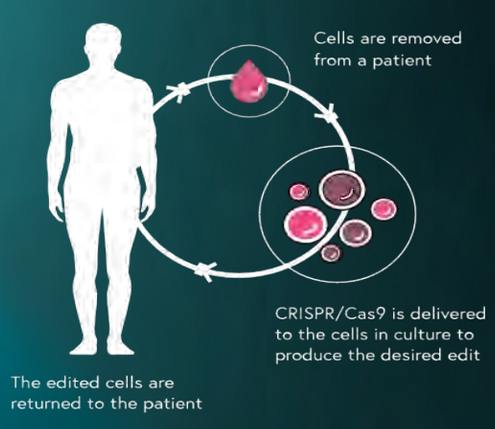
Genome editing research done on cell, animal models.

Testing state for effectiveness and safety.

Holds promise to treating, preventing more complex diseases like cancer or HIV

“What Are Genome Editing and CRISPR-Cas9? - Genetics Home Reference - NIH.” U.S. National Library of Medicine, National Institutes of Health, 31 Mar. 2020, ghr.nlm.nih.gov/primer/genomicresearch/genomeediting.

Ex Vino



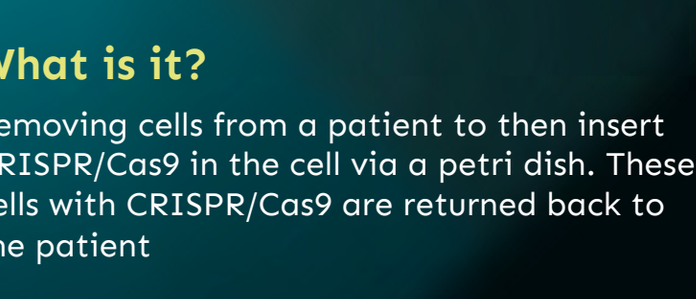
What is it?

Removing cells from a patient to then insert CRISPR/Cas9 in the cell via a petri dish. These cells with CRISPR/Cas9 are returned back to the patient

How is it being tested?

Studying the treatment β-thalassemia, SCD by making them to increase levels of fetal hemoglobin (HbF), a naturally-occurring form of hemoglobin present in all people before birth.

HbF can substitute for the diseased hemoglobin in β-thalassemia and SCD patients, reducing or eliminating symptoms.



Current Progress:

Cell therapy with CTX001 is isolating a patient’s blood stem cells, editing them with CRISPR/Cas9 to increase HbF expression, then returning the edited cells to the patient. Over time the belief is these edited blood stem cells will generate red blood cells with increased levels of HbF, which may reduce or eliminate patients’ symptoms. .

2017 signed an agreement agreement to co-develop and commercialize this program with our partner Vertex Pharmaceuticals.

“Hemoglobinopathies.” CRISPR, www.crisprtx.com/programs/hemoglobinopathies.

In Vino

What is it?

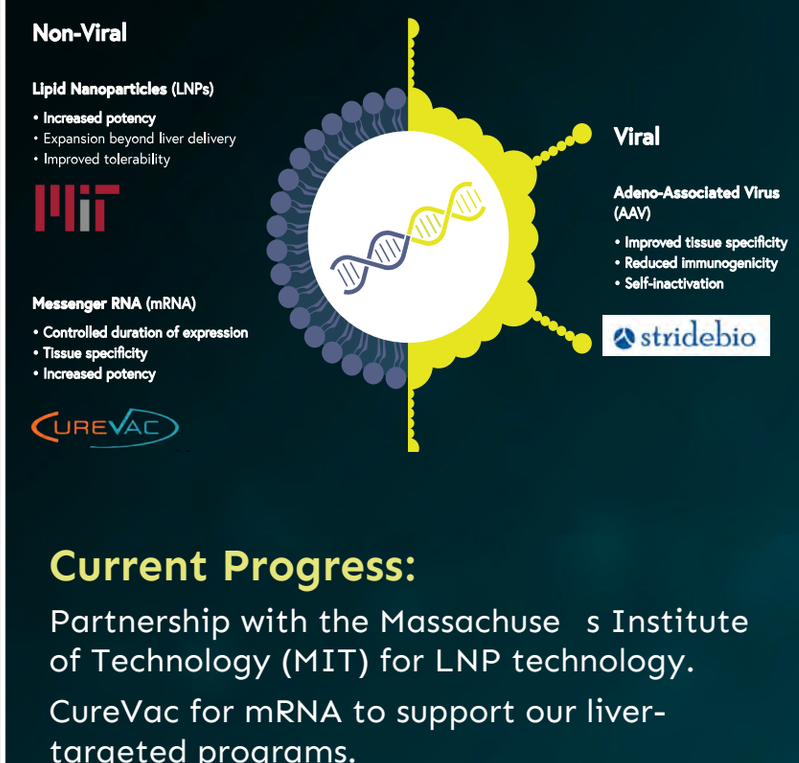
Targeting genes during cell therapy by inserting new genes; giving cells new abilites.Can improve cell therapy safety and efficany via ex, in- vivo.

Ex vivo: edit cells outside the body.

How is it being tested?

Non-viral: Focused on lipid nanoparticles (LNPs), targeting the liver. Encapsulate messenger RNA encoding Cas9, guide RNA, a donor DNA template, into LNPs to shu le these components to the liver.

Viral: Focused on other organ systems using adeno-associated viral (AAV) vectors. They can deliver DNA encoding for Cas9 and guide RNAs into specific tissues of the body.



Current Progress:

Partnership with the Massachuse s Institute of Technology (MIT) for LNP technology.

CureVac for mRNA to support our liver-targeted programs.

Collaboration with StrideBio, aiming to engineer novel AAV vectors that target individual tissue types with avoiding pre-existing immunity.

“What Are Genome Editing and CRISPR-Cas9? - Genetics Home Reference - NIH.” U.S. National Library of Medicine, National Institutes of Health, 31 Mar. 2020, ghr.nlm.nih.gov/primer/genomicresearch/genomeediting.