Author: Roberto Thompson

Major: Chemical Engineering

Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Targeted lipid nanoparticles with CRISPR-Cas9 gene editing for cancer therapy

Abstract

Since its discovery more than a decade ago, CRISPR has evolved into a verb as well as an acronym, revolutionizing biomedical research and opening up new paths for the study of cells in general. When it comes to cancer genetics, the non-coding genome, and tumor heterogeneity in cancer research, CRISPR-associated technologies have opened up previously unsolvable challenges. They have also provided fresh insights on therapeutic vulnerabilities in cancer research. The development of CRISPR systems as a tool for cancer research and the application of these technologies to better cancer detection and treatment are discussed in this article.

Introduction

Cancer is a complex disease with many dimensions and complications. Tumor suppressors are turned off as a result of a genetic mutation in the DNA that causes oncogenes to become active and tumor suppressors to become inactive, as well as abnormalities in the epigenome, which are the root causes of this disease. Also known as cellulitis, it is a disease of the cell that thrives in sterile conditions by utilizing changes in metabolism, cell structure, and motility to sustain itself. Finally, an organism-specific illness infiltrates and evades the host's defense mechanisms by utilizing the host's own cells and tissues to infiltrate and escape them. It is estimated that there are

1.4 million new cancer cases identified each year, and it is critical to understand how these diseases begin, progress, and are treated in order to develop more effective treatment choices and improve outcomes for those impacted. Since its initial use to mammalian cells, CRISPR has evolved into a powerful and versatile tool for studying practically all aspects of cell function in a variety of settings. A significant influence has been made on our understanding of cancer biology, and new discoveries that have the potential to speed up detection and treatment are still being driven by this knowledge base today.

For many years, the bacterial adaptive immune system has relied on CRISPR and CRISPR-associated proteins (Cas). The advancement of the understanding of CRISPR biology has been aided by various scientists who have made substantial contributions to the knowledge, including landmark studies that revealed programmable DNA editing in mammalian cells. Since then, nearly all cell types have made use of it as a tool for modifying their genomes in a controlled manner.

Recent progress

Using CRISPR, a new tool that allows scientists to change the DNA of an individual cell, scientists were able to destroy late-stage cancer cells in mice. However, no human trials have been conducted with the study's early findings, which focused on two forms of metastatic cancers: ovarian cancer and brain cancer. According to the researchers, Lipid nanoparticles may be utilized in the production of CRISPR enzymes, which are capable of destroying the genetic material of cancer cells and killing them. The development of safe and efficient delivery mechanisms for drugs into cancer cells after they have been introduced into human bodies has been a significant bottleneck in the development of new cancer therapies. Researchers at Tel Aviv University have devised a new CRISPR gene-editing therapy that makes use of a cutting-edge delivery system to

achieve success. They are able to insert mutations into DNA by cutting specific DNA sequences with a unique protein known as an enzyme, which is made possible by CRISPR technology. Because of the vast size of the CRISPR enzyme, which makes it challenging to penetrate cancer cells in current studies, CRISPR cancer treatments have exhibited poor efficiency. It was discovered that a delivery system was developed that encases the RNA molecule responsible for enzyme synthesis in a coating of long fatty molecules known as lipids, making it easier for cancer cells to absorb the RNA molecule (DANIEL ROSENBLUM, 2020).

Discussion

When it comes to genome editing, the CRISPR-Cas9 technology creates quite a commotion among those working in the scientific world. It is faster, more cost-effective, and more precise than previous methods of DNA editing, which are all advantages of CRISPR. Using CRISPR-Cas9, geneticists and medical researchers may make modifications to the genome by removing, adding, or altering DNA sequences. This is known as genome editing. In the scientific world, it is now considered to be the most straightforward, most versatile, and most precise method of genetic manipulation. Two critical components of the CRISPR-Cas9 system are responsible for inducing a change (mutation) in DNA. Specifically, it is the Cas9 enzyme that is responsible for this process. It is possible to utilize them as a pair of "molecular scissors" to make precise cuts in the genome, allowing new DNA to be inserted into or deleted from a specific spot. The RNA known as guide RNA (gRNA) is one of many varieties. In this instance, a more extended RNA structure contains a shorter pre-designed RNA sequence. It is Cas9 that directs itself to the correct chromosomal site by utilizing previously defined sequences as guides. Cas9 is after that able to cut at the right chromosomal site as a result of this development.

To produce the guide RNA, knowing the exact DNA sequence was necessary. The guide RNA is composed of RNA nucleotides that are identical to the DNA sequence of the target genome, which is called a guide RNA sequence. The guide RNA should, therefore, at least theoretically, bind to the target region exclusively and not to any other regions of the genome. After identifying the guide RNA in the DNA, the Cas9 enzyme precisely cuts through both strands of DNA. Cells begin to repair DNA damage as soon as they recognize harm has occurred. Scientists can manipulate the DNA repair machinery in a cell's genome to change the expression of one or more genes of interest.

CRISPR, a gene-editing technique, is used by scientists to make changes to DNA. It is envisaged that this would pave the way for the development of medicines for genetic diseases. It is possible that nanoparticles, which can enter cancer cells and deliver the essential instructions for CRISPR enzyme creation to cancer cells, would develop enzymes that will rip up the genetic material of cancer cells and destroy them.

Because of its revolutionary potential, CRISPR has piqued the interest of many scientists. New treatments based on this technology, on the other hand, have experienced particular challenges. According to recent research, cells have a built-in defense system that prevents them from having their genetic material tampered with (Ledford, 2015).

Researchers at the University of Tel Aviv, New York University, Harvard, and the startup Integrated DNA Technologies have successfully delivered CRISPR-Cas9 enzyme instructions into cells. Integrated DNA Technologies has manufactured tiny lipid particles that are approximately 50,000 times smaller in size than the diameter of a human hair, allowing them to be delivered into

cells. In order to rip the DNA of cancer cells, a cancer-killing enzyme must be produced within the diseased cell itself (Xiaoyu Xuab, 2021).

This research aims to determine which cell is the most effective at delivering this payload. Because they possess patents on the technique, the researchers have a financial incentive to continue developing the treatment.

Unlike other treatments, this one does not edit healthy cells in the proximity of the diseased ones, as is the case with many others in the field. This is because there is a significant probability of unintended effects occurring. In the therapy, it is demonstrated that the approach does not affect neighboring cells' activity. Cells in close proximity are not being altered. Similarly, Pfizer's COVID-19 vaccine uses the exact mechanism of immunization as the previous vaccine. The experiment was carried out on mice. After receiving only one dose of an anti-tumor agent, tumor development was reduced, and survival rates were enhanced in mice treated with the agent (Diana Raquel Rodríguez-Rodríguez, 2019).

A second modification was made to the lipid particles to target cancer cells by attaching them to cancer-specific proteins found outside cancer cells. It has been discovered that cancer cells die due to the development of an enzyme that breaks the DNA of a gene required for cell multiplication. It was decided that glioblastoma and metastatic ovarian cancer would serve as the study's primary focus because of their tremendous aggressiveness and difficulty in treating them. After studying these two lethal tumors in mice, they discovered that they could edit up to 80% of the tumor cells, that tumor development was significantly reduced, and that overall survival could be increased by up to 80% by editing the cancer cells. There was no evidence of toxicity or immunological response in response to the treatment.

After a single treatment, these studies provide the largest statistically meaningful survival improvement in these two aggressive cancers. However, this delivery technique, combined with high-efficiency editing, offers a fascinating promise for broad clinical translation before more rigorous toxicity testing is performed, which is still in the early stages. This study is notable in that the lipid delivery mechanism used here is remarkably similar to the mRNA vaccine delivery technology now under development for the COV19 virus infection outbreak. A similar technique could be used to treat other inherited disorders, including tumor-dependent genes and tumor-specific oncogene mutations (Ledford, Could mixing COVID vaccines bolster immune response, 2021).

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