Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 4 Issue 8 August 2021

Short Communication

CRISPR Genome Editing: A Boon to Medical Science

Hemshankar Laugi*

Department of Biology, Bal Kalyan Vidhya Mandir Ma. Vi., Nepal

***Corresponding Author:** Hemshankar Laugi, Department of Biology, Bal Kalyan Vidhya Mandir Ma. Vi., Nepal.

Received: July 07, 2021

Published: July 20, 2021

© All rights are reserved by **Hemshankar Laugi.**

CRISPR, an acronym for Clustered Regularly Interspaced Short Palindromic Repeats, is one of the major discoveries in the field of medical science. It is a type of bacterial adaptive immunity used to fight against bacteriophages. It is a type of memory. Whenever a virus attacks a bacterium for the first time, it creates a memory which is used to fight with that virus if it attacks the second time. In this system, small guide RNAs (crRNAs) are employed for sequence-specific interference with invading nucleic acids. CRISPR-Cas comprises a genomic locus called CRISPR that has short repetitive elements (repeats) separated by unique sequences (spacers), which can originate from mobile genetic elements (MGEs) such as bacteriophages, transposons, or plasmids [1].

The molecular mechanism of the CRISPR-Cas system, by which it works, can be divided into 3 steps; spacer acquisition, crRNA biogenesis, and target interference. When bacteriophage infects bacteria for the first time, bacteria take snippets of viral DNA segments similar to PAM (Protospacer Adjacent Motif) and insert them into spacer DNA present in the CRISPR array. Hence, the DNA spacer consists of segments of DNA of bacteriophage that has infected the bacteria before [2]. Bacteria repeat this each time a new bacteriophage virus infects them. The second step deals with crRNA biogenesis. In this, one of the two DNA strands transcribes into mRNA that has complementary sequences to that of coding strand. Hence, it also consists of CRISPR repeats and viral genes. The last step deals with target interference. In this, crRNAs will be integrated by Cas protein ending with a complex that contains both Cas protein and crRNAs. In short, viral DNA is incorporated into spacer DNA, the first time it infects bacteria. Now, mRNA/pre-crRNA is transcribed and cut into crRNAs which get merged with Cas enzymes to form Cas complex. Now, this complex recognizes the viral genome, the second time it attacks and finally cuts viral DNA into segments thereby destroying the viral genome [3].

Nowadays, CRISPR has been used to edit the genome of a patient infected with a particular disease. It helps to replace the defective allele in the genome of the patient with the normal one. With the high positive results, this technology has been used in the treatment of many dreadful diseases. For instance, when a nucleotide cytosine (C) at the eight SNP location of the gene at cytogenetic location 8q24.21 is replaced with adenine (A), an individual is susceptible to acute lymphoblastic leukemia (ALL). Hence, CRISPR genome editing can be implied to edit the genome of the patient infected with ALL by replacing the nucleotide adenine (A) with cytosine (C). Moreover, Sickle cell disease is caused by a mutation in the hemoglobin-Beta gene found on chromosome 11. When the nucleotide Adenine (A) at eleventh SNP position of wildtype gene is replaced by Thymine (T), valine amino acid is produced instead of Glutamic acid thereby causing sickle cell anemia. Hence, CRISPR-genome editing can be used to replace T by A at the eleventh SNP position. Hence, this technology could be a great boon to free humanity from life-threatening diseases.

CRISPR genome editing technologies allow modifying the genome at a precise location by inserting a therapeutic transgene and replacing the defected one associated with a disease [4]. This requires a vector to deliver the engineered material into the host cell. Viral delivery vectors are the most-used delivery vectors due to their high transduction efficiency. This allows *in vivo* delivery of engineered genetic material into the host cells. Among many viral vectors, Adeno-associated virus (AAV) is largely used for CRISPR genome editing [5]. AAV is a non-enveloped, single-stranded DNA

virus in the parvovirus family [4]. It is less immunogenic and triggers mild toxicity in humans even at high doses. Moreover, the integration site of AAV is considered safe that also prevents tumorigenesis [5]. After the *in vivo* viral delivery of gene-editing tools, Cas 9 nuclease causes a direct cut at a precise location in the host DNA. This triggers a single 20-nucleotide RNA strand to mark the exact breakage point [6]. After the breakage of DNA, the DNA repair machinery of the host cell leads to repair errors and promotes modification of the original genome by replacing defective allele responsible for causing the disease with the normal one.

However, the CRISPR-Cas system often leads to off-target gene editing at unintended sites thereby causing chromosomal deletions and translocations, disruption of tumor suppressor genes or other genes, and even activation of oncogenes. Hence, this creates a major hindrance in using CRISPR. The use of the CRISPRitz platform, as the bioinformatics tool, helps to detect off-target sites. Moreover, the large cargo size (4.3 Kb) of the CRISPR-Cas9 system impedes the delivery of viral vectors into the host cells [4]. Sometimes, the nuclease enzyme - used as a part of the CRISPR-Cas system - may not be able to cut the desired copies of the target gene, or the target cell may divide before the completion of genome editing. This often leads to genetic mosaicism: the presence of genetically different somatic cells in an individual and is often masked [7].

In gist, CRISPR-Cas9 genome editing could be the potential gene therapy technique to edit the genome of the infected patient. However, extreme care is to be taken to prevent off-target genome editing and other bioethical issues associated with it. Moreover, further research is needed in CRISPR genome editing technology to get a better insight of how this system works and could be used to control many genetic diseases.

Bibliography

1. Hille F and Charpentier E. "CRISPR-Cas: biology, mechanisms and relevance. Philosophical transactions of the Royal Society of London". *Series B, Biological Sciences* 371.1707 (2016): 20150496.

2. Fineran PC and Charpentier E. "Memory of viral infections by CRISPR-Cas adaptive immune systems:acquisition of new information". *Virology* 434 (2012): 202-209.

3. Gholizadeh P., *et al*. "How CRISPR-Cas System Could Be Used to Combat Antimicrobial Resistance". *Infect Drug Resist* 13 (2020): 1111-1121.

4. Xu CL., *et al*. "Viral Delivery Systems for CRISPR". *Viruses* 11.1 (2019): 28.

5. Montaño A., *et al*. "Targeted genome editing in acute lymphoblastic leukemia: a review". *BMC Biotechnology* 18.1 (2018): 45.

6. Ayanoğlu FB., *et al*. "Bioethical issues in genome editing by CRISPR-Cas9 technology". *Turkish Journal of Biology = Turk Biyoloji Dergisi* 44.2 (2020): 110-120.

7. Maryam Mehravar., *et al*. "Mosaicism in CRISPR/Cas9-mediated genome editing". *Developmental Biology* 445.2 (2019): 156-162.

Volume 4 Issue 8 August 2021
© All rights are reserved by Hemshankar Laugi.