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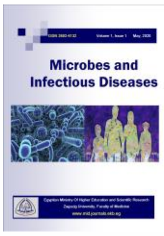

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Mini review

CRISPR in dentistry: A boon or bane!

***Mirna Garhnayak* [1], *Shakti Rath* [*2], *Loknath Garhnayak* [3], *Sangram Panda* [1]**

1- *Department of Prosthodontics and Crown and Bridge, Institute of Dental Sciences, Siksha O Anusandhan (Deemed to be University), Bhubaneswar 751003, Odisha, India.*
2- *Central Research Laboratory, Institute of Dental Sciences, Siksha O Anusandhan Deemed to be University, Bhubaneswar, Odisha.*
3- *Department of Prosthodontics and Crown and Bridge, SCB Dental College and Hospital, Cuttack 753007, Odisha, India.*
4- *Department of Prosthodontics and Crown and Bridge, Institute of Dental Sciences, Siksha O Anusandhan (Deemed to be University), Bhubaneswar 751003, Odisha, India.*

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ABSTRACT

Background: Clustered Regularly Inter Spaced Palindromic Repeats (CRISPR) is programmable protein that can change the genome's content, remove it, and switch it on and off. This cutting-edge technology offers a wide range of uses and has the potential to change the future of oral health. Because of its efficacy and precision, the CRISPR-associated protein 9 (Cas9) genome editing technology could be a promising therapeutic tool in the treatment of oral cancer. It quickly changes the genetic makeup of cell lines, organs, and animals. As a result, gene editing has expanded to include genome-wide screening for both loss and augmentation of function. The CRISPR-Cas9 genome editing method and its uses in dentistry have been summarised in this study.

Introduction

The 21st century revolutionized the technology of molecular biology by changing the methods of genome editing. Typically, modulation of the host genome is achieved by the precise manipulation of DNA sequences to combat various oral diseases [1]. However, this is a time-consuming procedure that can only be carried out in laboratories equipped with powerful molecular biology techniques [2, 3]. Because of its simplicity, specificity, effectiveness, low cost, and versatility, the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) gene-editing method has revolutionised gene therapy. CRISPR was found as a mechanism for bacterial acquired immunity [4, 5].

Typically, CRISPR is used by prokaryotes to inactivate invading plasmids or bacteriophages [6]. This steered RNA genome editing tool is based on CRISPR technology to destroy viral DNA, thus ensuring host immunity. Since Cas9 proteins are coded by scientists to target a specific piece of DNA, they are also called "DNA localization systems". They can deactivate/reactivate the gene, edit it and replace it with a slightly different object. The literature reveals the potential use of the CRISPR-Cas9 system in clinical practice. This molecular technology can effectively combat diseases associated with

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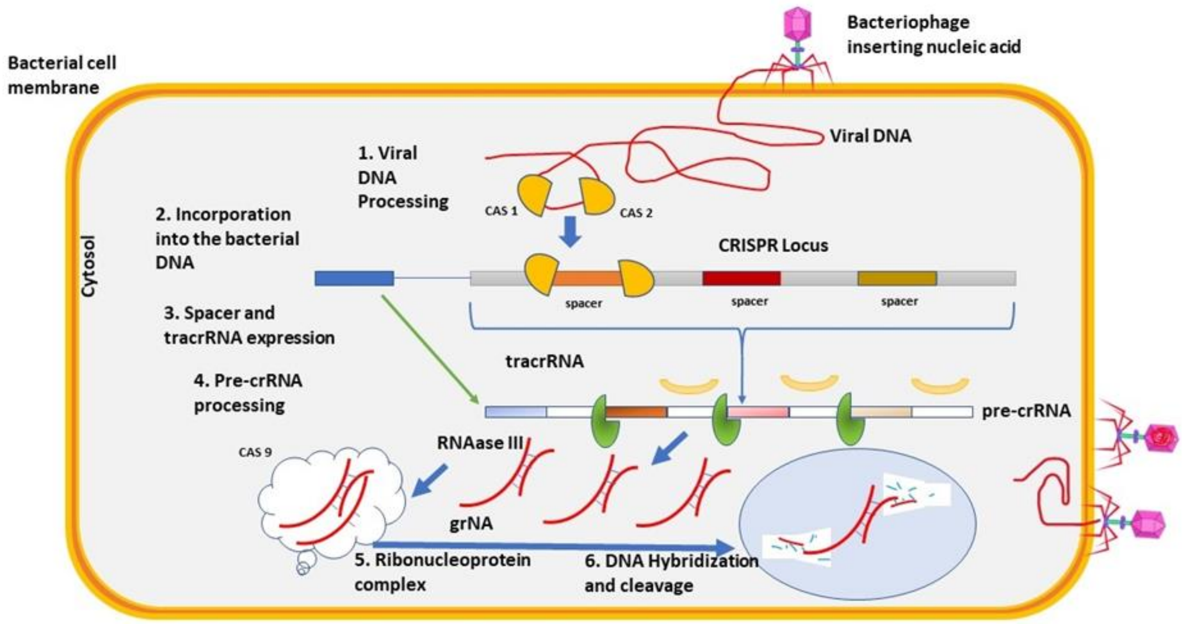
* *Corresponding author:* Shakti Rath
E-mail address: dr.shaktirath@gmail.com

a genomic mutation, and genomic oral health disorder is no exception [7]. Therefore, a clear understanding of its mechanism of action is required.

Mechanism Of CRISPR–Cas9 technology

The natural immunological response of a bacteria against the virus is the activation of the CRISPR–Cas9 mechanism. When a virus infects a bacteria, a little section of its DNA gets incorporated as spacers in the bacterial genome's CRISPR locus. As a result, the bacteria develop an adaptive immunity against the virus. Subsequent infection with a similar virus activates the CRISPR locus to form pre-rRNA and tracrRNA. They facilitate the formation of guide RNAs (gRNAs). The guide RNAs (gRNAs) form a cleavage in the complementary segments of the attacking virus genome, using Cas9 **(Figure 1)** [4, 5].

Figure 1. Mechanism Of CRISPR–Cas9 Technology



Role Of CRISPR in dentistry

CRISPR-Cas9 technology is in a very nascent stage. Though it can be a potent therapeutic tool for genomic mutation-induced oral diseases, literature regarding the same is few. The following are some of the applications of CRISPR-Cas9 in the disciplines of human nasal chondrocytes (HNC), tissue engineering, craniofacial defects, and infectious dental illnesses.

Oral cancer

A menace to human lives has been oral cancer originating from epigenetic and genetic changes [7]. Oral squamous cell carcinoma (OSCC) is a common HNC with a low survival rate. CRISPRCas9 is an emerging technology that is highly effective in identifying faulty genes responsible for oral cancer pathobiology and helping to eliminate HNC cell lines. **Huang et al.** in their study have defined the role of the p75NTR gene on human tongue carcinoma. As per the study, removal of the p75NTR gene can suppress a whole lot of features of SCC-9 cells [8]. In another study, Kim et al discovered that HSPA5/GRP78/BiP plays an important role in tumour progression or cell survival. HSPA5 promotes HNC survival by maintaining lysosomal activity. As a result, targeting the MUL1-HSPA5 axis for HNC treatment would be a novel approach [9].

Similarly, **Chai and colleagues** performed genome-wide CRISPR-Cas9 screens in 21 Asian OSCC cell lines to find therapeutic targets for oral squamous cell carcinoma (OSCC). They found that OSCCs with WWTR1 dependency signature respond favourably to immunotherapy. So, YAP1 and WWTR1 prioritize as therapeutic targets, for OSCC.

Congenital malformations, wound healing

The potential applications of CRISPR on plastic and reconstructive surgery are many and have reformed the treatment procedure [10].

Craniofacial malformations

Because many craniofacial abnormalities originate early in the embryonic stage, genetic modifications in embryonic tissue are extremely appealing. Basic scientific studies using the CRISPR technique have led to new knowledge of craniofacial development pathways [11]. CRISPR enables rapid identification of individual gene mutations. Mesenchymal stem cells (MSCs) have gotten a lot of interest in the treatment of oral and craniofacial illnesses in recent years. Subsets of MSCs have been found in the alveolar bone, periodontal ligament, and pulp. Oral, periodontal, and craniofacial abnormalities can all benefit from CRISPR / Cas9 altered MSCs [12].

Wound healing and tissue regeneration

Gene therapy has the potential to speed up wound and tissue healing. CRISPR could lead to novel ways of mending and regenerating bones, cartilage, nerves, and muscles, as well as cleft palate and other birth abnormalities, in addition to quickening skin wound healing.

Cell therapy and tissue engineering

CRISPR techniques can be used to generate or modify a patient's autologous cells to transplant or swap damaged tissue, encourage cell growth, or modulate immune function, for generating skin grafts with therapeutic potential.

Flap biology and grafts

Gene editing with CRISPR will not only modify tissue flaps but also allow reprogramming of vascularized complex allografts of the face or hand transplants, to increase tolerance and prevent rejection by the recipient's immune system. Similarly, immune modulation might uphold tissue tolerance from donor animals (xenotransplantation).

Infectious diseases

Caries

Dental caries is usually caused by *Streptococcus mutans* [13]. They produce biofilm dysbiosis, which leads to tooth surface demineralization and the possibility of cavities. [14]. Scientists used RNA-gated nucleases (RGN) CRISPR / Cas to produce antimicrobial drugs with pre-selected activity ranges. RGN also manipulates bacterial populations by knocking out specific strains depending on genetic fingerprints [15].

Gingivitis and periodontitis

Chronic periodontitis is caused by a gram-negative anaerobic rod called *Porphyromonas gingivalis*. Ninety-five per cent of these bacteria were found to carry CRISPR arrays. As a result, CRISPR technology appears to be a viable technique in dental clinics for preventing plaque buildup, which leads to periodontitis [16].

Viral infection

Various oral lesions are caused by herpes viruses (herpes simplex virus), human cytomegalovirus (HCMV) (infectious mononucleosis), and Epstein-Barr virus (EBV) (hairy ndleukoplakia, mucocutaneous ulcers). The CRISPR/Cas9 system can be used to target virus-infected cells' genomes. This, in turn, renders the virus inactive and prevents it from replicating in the host cell [17].

Salivary dysfunction

Cancer patients treated with ionizing radiation often suffer from xerostomia. In this case, the CRISPR/Ca9 system can be utilised to boost the expression of the AQP1 gene. [16] Aquaporin 1 (AQP1), a water-specific protein, may promote salivation. The CRISPR/Cas9 system has recently been utilised to successfully target key genes in the treatment of primary Sjogren's syndrome [18,19].

Limitations of CRISPR technology

The safety and effectiveness of CRISPRCas9 technology still require the validation of extensive research. Further, the CRISPRCas9 methodology can be complicated and time-consuming to develop. Choosing a target site and developing a sgRNA are difficult tasks. The universality of CRISPRCas9 technology is not high [20]. Unexpected results can be obtained in the experimental treatment of critically ill patients. The greatest fear of CRISPR is that the modified gene may be passed down from generation to generation [21].

Conclusions

CRISPR technology treats oral diseases by modulating or completely removing defective genes. While this technology appears to be saving lives, related research is in its infancy. Changes in the human genetic code can have eternal and random consequences for future generations. Therefore, evidence-based research is needed for their use in dentistry.

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