

Transforming Regeneration and Disease Management in Oral Biology through Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and Gene Editing

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Abstract

Biomedical research has been dramatically transformed with the creation of gene editing technologies such as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). Their application spans across multiple systemic diseases as they allow for precise, cost-effective, and reliable genome modifications. But their potential in the field of oral biology remains underexplored. This editorial discusses the emerging role CRISPR is having in oral biology, especially its uses in regeneration and oral related diseases treatment. Modifications of oral defective cleft lip or amelogenesis imperfecta or dentinogenesis imperfecta can be treated with mutation targeting techniques that CRISPR offer us. Not only this, but new oral microbiome modulation approaches can be employed to target and prevent dental caries and periodontitis. The broader adoption of emerging technologies, including in vivo delivery systems and CRISPR diagnostics, pose additional opportunities, but issues such as effective delivery to oral tissues, off-target mutations, and ethical implications persist. Multidisciplinary CRISPR implementation will help advance medicine and quite literally change the game for oral health and patient care across the globe.

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Gene editing technology has significantly revolutionized biomedical research, especially in understanding, preventing, and treating diseases that were previously inconceivable. One of the most successful technologies is Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) which provides high reliability, precision, and cost-effective modifications of genomes.¹ While this technology has gained significant attention for its work in systemic diseases, its application in the field of oral biology is still very limited. This editorial provides an insight into the transformative role CRISPR offers in oral biology with an emphasis on regeneration and disease management.

Oral biology involves numerous structures and systems including the teeth and salivary glands, oral microbiome and craniofacial tissues. These features are commonly influenced by genetic, developmental and acquired factors. CRISPR technology provides an opportunity to address these challenges with the aid of modification on specific genes.¹ Some of the commonly seen craniofacial defects are cleft lip and palate, craniosynostosis, as well as syndromic orofacial deformities and these are oftentimes the result of certain genetic mutations.² Conventional methods are based on surgery, which is both costly and invasive. With CRISPR being an effective means of treating these diseases at their source, it helps to alter the specific genes causing them.³ Enamel and dentin – the two major mineralized tissues that compose teeth are vital to ensuring functionality and durability of the teeth. Genetic disorders like amelogenesis imperfecta or dentinogenesis imperfecta results in defective production of enamel and dentin and leading to lifelong oral health challenges. Through CRISPR, these conditions may be addressed by targeting the underlying genetic mutations that are responsible for impaired mineralization.⁴ Another example is the ability of CRISPR to repair AMELX (Amelogenin) and

DSPP (Dentin Sialophosphoprotein) gene mutations which are crucial for formation of enamel and dentin.⁵ Furthermore, CRISPR gene activation can also be used to enhance the stem cell's ability to regenerate which will lead to new prospects of treatments in restorative of dental stem cells.^{5,6} Such approaches could eliminate the use of traditional crowns and fillings and other treatments with biologically integrated solutions.

The oral microbiome plays a dual role in oral health and disease. A balanced oral microbiome is beneficial for oral health, however, dysbiosis results in dental caries, periodontal disease, and even endodontic infections. CRISPR approaches can target and change specific oral microbiome bacteria - a great alternative to broad spectrum antibiotics.⁷ For example, CRISPR-Cas systems can be designed to target and destroy cariogenic microbes such as *Streptococcus mutans* while preserving other essential microbes.⁷ In periodontitis, it is quite possible to use the same techniques to target and destroy pathogens such as *Porphyromonas gingivalis*.⁸ These types of strategies have the potential to revolutionize oral disease from dealing with the effects of a condition to preventing its occurrence by modifying the makeup of the oral microbiome.

Apart from certain structural defects, CRISPR have a lot of potential when it comes to treating heritable disorders for oral tissues such as conditions like those of amelogenesis imperfecta dentinogenesis, and some rare genetic syndromes that affect salivary glands can be dealt with by choosing gene editing.⁴ There are in vivo delivery systems, such as or lipid nano particles or viral vectors are being developed to deliver CRISPR directly to the area needed genetic modification.⁹ Furthermore, CRISPR can be useful in alleviating some systemic oral genetic disorders like epidermolysis bullosa or Ehlers Danlos syndrome which affect numerous body systems.¹⁰ Treating such oral related issues at the genetic level will enhance the oral and life conditions of all the affected people.

There is extensive scope for CRISPR in oral biology, but it has numerous challenges before being used in clinical settings. One major challenge is the delivery of the CRISPR components to oral tissues, which is particularly difficult due to their unique structural and biological traits. There are also concerns regarding unintended genetic edits which may pose unknown side effects, which calls for new and highly specific CRISPR variants to be developed.¹¹ There are also ethical questions surrounding the use of CRISPR, especially in regard to germline editing such as - how far genetic modification can be taken.¹¹ This, like many other applications of CRISPR in oral science will be influenced by the public acceptance as well as regulatory oversight.

With high certainty, repairing or editing mutations of key genes during craniofacial development can prevent anomalies during the embryonic period. Animal models have recently illustrated the viability of applying CRISPR technology for these specific purposes, with candidates *MSX1* and *FGFR2* being significantly studied for their ability to cause craniofacial abnormalities.¹² However, there are some ethical implications that accompanies the alteration of germline DNA using CRISPR, as such a line of research can put into question the manner and the extent in which genomic modification can be accepted.^{13,14} There is also corroborating evidence which shows that attributes such as genomic defects or other alterations may come to be expected which has sounded alarms in the technological editing of human embryos for clinical purposes.^{13,14} Public acceptance and regulatory oversight will play critical roles in shaping the future of CRISPR applications in dentistry.

To develop CRISPR in oral biology, research must be approached in a holistic manner, which means integrating learning from genetics, bioengineering, and dental science. Some of the other areas that need focus are the creation of CRISPR-specific diagnostics for oral and other diseases using salivary biomarkers, development of stem cell tissue engineering where 3D bioprinting is used for dental and craniofacial construction along with CRISPR edited cells, and epigenetic

modification of oral tissues to gain insights on diseases and their regeneration processes. The integration of CRISPR technology into oral biology research requires a multidisciplinary approach, combining expertise in genetics, bioengineering, and dental science. Gene editing technologies like CRISPR has the potential of revolutionizing oral biology by creating innovative ways of regeneration and treating diseases. Modifying a microbiome or even correcting genetic disorders are now easier because of CRISPR methodology. Despite the advantages associated, comprehensive efforts need to be made to make it a possibility in clinical environments since there exist ethical, technical and regulatory challenges. Exploiting the power of CRISPR should facilitate oral biological sciences to transition towards the flavor of the day: precision medicine - which is key to improving outcomes for patients worldwide.

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Conflict of Interest

It is declared that the author don't have any conflict of interest.

References

1. Xu Y, Li Z. CRISPR-Cas systems: Overview, innovations and applications in human disease research and gene therapy. *Comput Struct Biotechnol J*. 2020;18:2401-15.
2. Kohli SS, Kohli VS. A comprehensive review of the genetic basis of cleft lip and palate. *J Oral Maxillofac Pathol*. 2012;16(1):64-72.
3. Garhnayak M, Rath S, Garhnayak L, Panda S. CRISPR in dentistry: A boon or bane! *Microbes Infect Dis*. 2023;4(4):1178-82.
4. Schindeler A, Lee LR, O'Donohue AK, Ginn SL, Munns CF. Curative cell and gene therapy for osteogenesis imperfecta. *J Bone Miner Res*. 2022;37(5).
5. Kaushal K, Kim EJ, Tyagi A, Karapurkar JK, Haq S, Jung HS, et al. Genome-wide screening for deubiquitinase subfamily identifies ubiquitin-specific protease 49 as a novel regulator of odontogenesis. *Cell Death Differ*. 2022;29(9):1689-704.
6. Patel VB, Vanasi M, Dhimole A, Saini RJ, KS. Harnessing CRISPR-Cas9 technology in dentistry: A promising avenue for precision oral health - A literature review. *J Oral Med Dent Res*. 2024;5(1):55.
7. Javed MU, Hayat MT, Mukhtar H, Imre K. CRISPR-Cas9 system: A prospective pathway toward combatting antibiotic resistance. *Antibiotics*. 2023;12(6):1075.
8. Yadalam PK, Arumuganainar D, Anegundi RV, Shrivastava D, Alftaikhah SAA, Almutairi HA, et al. CRISPR-Cas-based adaptive immunity mediates phage resistance in periodontal red complex pathogens. *Microorganisms*. 2023;11(8):2060.
9. Behr M, Zhou J, Xu B, Zhang H. In vivo delivery of CRISPR-Cas9 therapeutics: Progress and challenges. *Acta Pharm Sin B*. 2021;11(8):2150-71.
10. Cattaneo C, Enzo E, Rosa LD, Sercia L, Consiglio G, Forcato M, et al. Allele-specific CRISPR-Cas9 editing of dominant epidermolysis bullosa simplex in human epidermal stem cells. *Mol Ther*. 2024;32(2):372-83.
11. Hunt JMT, Samson CA, Rand AD, Sheppard HM. Unintended CRISPR-Cas9 editing outcomes: A review of the detection and prevalence of structural variants generated by gene-editing in human cells. *Hum Genet*. 2023;142(6):705-20.
12. Yue YY, Lai CZ, Guo XS, Yang CS, Wang Y, Song GD, et al. New CRISPR/Cas9-based Fgfr2C361Y/+ mouse model of Crouzon syndrome exhibits skull and behavioral abnormalities. *J Mol Med*. 2024;102(10):1255-66.
13. Wiley L, Cheek M, LaFar E, Ma X, Sekowski J, Tanguturi N, et al. The ethics of human embryo editing via CRISPR-Cas9 technology: A systematic review of ethical arguments, reasons, and concerns. *HEC Forum*. 2024.
14. Rubeis G, Steger F. Risks and benefits of human germline genome editing: An ethical analysis. *Asian Bioethics Rev*. 2018;10(2):133-41.

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