


# Chapter 9


## CRISPR–Cas9 Technology for Epigenome Editing in Precision Medicine: Opportunities and Challenges

**M. M. Nidhilangelo**

 <https://orcid.org/0000-0003-1497-9865>

*Pondicherry University, India*

**Ranjith Kumavath**

 <https://orcid.org/0000-0002-0751-5491>

*Pondicherry University, India*

### ABSTRACT

*CRISPR–Cas9, originally derived from a bacterial adaptive immune system, has rapidly evolved into a transformative platform for genome and epigenome engineering with broad applications in biology and precision medicine. Guided by single-guide RNAs, the Cas9 nuclease introduces targeted DNA modifications through cellular repair pathways. Meanwhile, engineered variants, such as high-fidelity nucleases, nickases, and nuclease-deficient dCas9, extend their functionality to precise gene regulation, epigenetic modulation, RNA editing, and live-cell genomic imaging. dCas9-based effectors enable locus-specific control of transcription by directing DNA methylation, histone modifications, or chromatin remodelling, offering reversible and non-permanent alternatives to conventional epigenetic drugs. In vivo models, including somatically engineered mouse models and xenografts, enable physiologically relevant studies of tumorigenesis and therapeutic response, while base and prime editors offer safer, DNA break-free approaches for the precision correction of pathogenic variants. Clinically, CRISPR is driving innovation in adoptive immunotherapies, regenerative medicine, and targeted delivery systems,*

DOI: 10.4018/979-8-3373-4857-5.ch009

*with nanoparticle- and ligand-modified carriers improving tissue-specific targeting and reducing systemic toxicity. Despite these advances, major challenges remain, including off-target activity, inefficient and tissue-restricted delivery, instability of epigenetic edits, and ethical concerns surrounding germline modification and long-term safety. Ongoing innovations in CRISPR engineering, delivery technologies, and regulatory oversight are addressing these barriers. Collectively, CRISPR-based platforms represent a cornerstone of next-generation personalised therapeutics, offering programmable, scalable, and clinically relevant strategies to understand and treat human disease.*

## **1. ABBREVIATIONS**

- CRISPR – Clustered Regularly Interspaced Short Palindromic Repeats
- Cas9 – CRISPR-associated protein 9
- gRNA / sgRNA – guide RNA / single-guide RNA
- dCas9 – dead Cas9 (catalytically inactive Cas9)
- PAM – Protospacer Adjacent Motif
- NHEJ – Non-Homologous End Joining
- HDR – Homology-Directed Repair
- DSB – Double-Strand Break
- AAV – Adeno-Associated Virus
- iPSCs – Induced Pluripotent Stem Cells
- DNMT3A / DNMT3L – DNA (cytosine-5)-methyltransferase 3A / 3L
- TET1 – Ten–Eleven Translocation methylcytosine dioxygenase 1
- KRAB – Krüppel-associated box
- VP64 – Viral Protein 64
- LOF – Loss-of-Function
- GOF – Gain-of-Function

## **2. GLOSSARY**

- CRISPR-Cas9 – A bacterial-derived gene-editing system that uses a guide RNA and Cas9 nuclease to target specific DNA sequences. Adapted for epigenome editing with catalytically inactive Cas9 (dCas9).
- Cas9 – DNA-cutting enzyme used in CRISPR to introduce double-strand breaks at targeted genomic loci.

34 more pages are available in the full version of this document, which may be purchased using the "Add to Cart" button on the publisher's webpage: [www.igi-global.com/chapter/crispr-cas9-technology-for-epigenome-editing-in-precision-medicine/399098](http://www.igi-global.com/chapter/crispr-cas9-technology-for-epigenome-editing-in-precision-medicine/399098)

## Related Content

---

### GPdotNET Open Source Software for Running Genetic Programming

(2019). *Optimized Genetic Programming Applications: Emerging Research and Opportunities* (pp. 183-242).

[www.irma-international.org/chapter/gpdotnet-open-source-software-for-running-genetic-programming/207402](http://www.irma-international.org/chapter/gpdotnet-open-source-software-for-running-genetic-programming/207402)

### Computer Implementation of Genetic Programming

(2019). *Optimized Genetic Programming Applications: Emerging Research and Opportunities* (pp. 132-182).

[www.irma-international.org/chapter/computer-implementation-of-genetic-programming/207401](http://www.irma-international.org/chapter/computer-implementation-of-genetic-programming/207401)

### Genome Editing and CRISPR/Cas System of Extremophiles and Its Applications

Suneeta Gireesh Panicker (2022). *Physiology, Genomics, and Biotechnological Applications of Extremophiles* (pp. 136-160).

[www.irma-international.org/chapter/genome-editing-and-crisprcas-system-of-extremophiles-and-its-applications/291496](http://www.irma-international.org/chapter/genome-editing-and-crisprcas-system-of-extremophiles-and-its-applications/291496)

### Genes: Expression and Regulation

(2019). *Examining the Causal Relationship Between Genes, Epigenetics, and Human Health* (pp. 186-204).

[www.irma-international.org/chapter/genes/223542](http://www.irma-international.org/chapter/genes/223542)

### Personal Development Plans (PDPs) Supporting Employee Learning and Job Satisfaction: Lightening Role of Emotional Intelligence

Trupti Suresh Patole, Swati Sharmaand Kshitiz Sharma (2024). *Embracing Transhumanism and Genomics in Human Resources Management* (pp. 183-210).

[www.irma-international.org/chapter/personal-development-plans-pdps-supporting-employee-learning-and-job-satisfaction/355097](http://www.irma-international.org/chapter/personal-development-plans-pdps-supporting-employee-learning-and-job-satisfaction/355097)