
Epigenome Editing for Stress Tolerance

Sriram Karthikeyan

UG Scholar, Agriculture, SRM College of Agricultural Sciences, SRM Institute of Science and Technology, Vendhar Nagar, Baburayanpettai, Elapakkam (Post), Chengalpattu (Dt.), Tamil Nadu, India.

Corresponding author's e-mail: Sriramkarthikeyan88@gmail.com

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ABSTRACT

Epigenome editing refers to the process of altering the expression of genes in organisms via the modification of epigenetic marks in DNA, while not affecting its sequence. Plants are faced with many different adverse factors in their environment like drought, salinity, high and low temperatures, as well as biotic stresses from the likes of pathogens and pests. This usually leads to decreased yields from agriculture. Epigenome editing techniques use biological systems like zinc fingers, TALENs, and CRISPR/Cas9 in order to edit the locus of certain genes and change their state. They do so using DNA methylation and demethylation, histone modifications and chromatin remodeling. The use of this technique can be useful for developing stress-resistant plants, and thus boost yields and help develop more climate-resistant agriculture. Examples of stressors include drought, salinity, heat, cold, floods, disease and pest resistance. Nevertheless, there are some difficulties in this field: off-target effects, effective delivery methods, complexity, regulations and heritability of epigenetic changes.

INTRODUCTION

Plants are always exposed to various forms of stress such as drought, salt, heat/cold, and stress from pathogens causing diseases to plants affecting yield levels. The breeding methods adopted to improve plant resistance to environmental stress have proven to be very lengthy due to a low number of genotypes. The recent advances in the field of biotechnology have led to the discovery of epigenome editing technology that is based on the regulation of gene expressions without altering the DNA sequences. Some of the epigenetic mechanisms such as DNA

methylation, histone modification, and RNA interference control the activity of genes adapting to environmental stresses. (Kang, 2019; Jogam *et al.*, 2022).

WHAT IS EPIGENOME EDITING?

Epigenome editing is a biotechnological method, in which epigenetic marks at particular locations on genomic DNA may be added or eliminated without changing the genetic information in order to control gene expression. This technology involves genetically modified enzymes which alter the epigenome through introducing certain epigenetic modifications such as DNA methylation, histone acetylation/methylation, and chromatin organization. As a result, regulation of genes' functions occurs, influencing their phenotypes, e.g., stress resistance. (Kungulovski & Jeltsch, 2016; Moreno *et al.*, 2021).

MAIN TOOLS FOR EPIGENOME EDITING

The major approaches for epigenome editing are zinc finger proteins (ZFPs), transcription activator-like effector nucleases (TALENs), and CRISPR/dCas9 system. The CRISPR/dCas9 system is especially popular because of its higher accuracy and simpler guide RNA designing (Moreno *et al.*, 2021).

STEPS INVOLVED IN EPIGENOME EDITING?

Epigenome editing involves several steps required for the development of stress-resistant plants.

Step 1: Identifying Targeted Gene. Stress-resistant genes, providing resistance to drought, salt, and high temperatures, are selected as targets.

Step 2: Preparing Guide RNA (gRNA)

Guide RNA is designed for the regulation of specific gene promoters and control sequences.

Step 3: Employing Engineered Cas9 (dCas9)

Engineered Cas9 enzyme that is incapable of making any cuts into the DNA is joined with epigenetic modifiers such as:

- DNA methyltransferase (DNMT),
- Demethylase (TET1)
- Histone acetyltransferase.

Step 4: Modifying Epigenome of Targeted Gene

Epigenetic modifications are carried out by targeting the desired gene using the Cas9-gRNA complex that involves DNA methylation and histone acetylation.

Step 5: Controlling Gene Expression

Expression of:

- Genes involved in stress tolerance can be increased,
- Sensitivity genes can be reduced as a result of the process.

Step 6: Generating Plants

Plantlets are prepared through tissue culture techniques.

(Jogam *et al.*, 2022; Johnston *et al.*, 2026).

REASONS FOR EPIGENOME EDITING TECHNOLOGY DEVELOPMENT

The development of this technology is done for different reasons.

1. Increase in Resistance to Stress - Stress causes tremendous damage to crop production. Epigenome editing plays a role in managing stress response genes.
2. Fast Improvement of Crop Yield - Traditional crop breeding takes a lot of time while epigenome editing can give the results in a few generations.
3. Reversible Gene Expression Regulation - Unlike other gene editing methods, epigenomic editing is reversible, so it doesn't cause any irreversible genetic alterations.
4. Resistance to Climate Changes - Rising temperatures, droughts, and high soil salinity require climatically resistant crops.
5. Sustainable Agriculture - Epigenome editing makes it possible to improve the production capacity of crops without altering their genetic characteristics.

WHO DEVELOPED IT FIRST?

INTERNATIONAL LEVEL

An early example of epigenome editing was reported by Mendenhall *et al.* in 2013 when the authors used TALE-fused LSD1 proteins to regulate and modify the gene expression from the enhancer regions.

Example

- Scientists: Mendenhall *et al.*
- Technique of Epigenome Editing: TALE
- Function: Gene Enhancer Silencing
- Systems: Human, Model

Recently, the epigenome editing using CRISPR/dCas9 technique is extensively used in plants and animals.

NATIONAL LEVEL (INDIA)

Epigenome editing and the technology of CRISPR have been involved in research studies conducted by Indians in relation to the improvement of crops using epigenetics.

Example

- Institute: Indian Agricultural Research Institute (IARI), New Delhi
- Crop: Rice
- Theme: Drought Responsive Genes in Rice through CRISPR Techniques.

TAMIL NADU LEVEL

Studying epigenetics and genome editing is a common activity at Indian agricultural universities in Tamil Nadu.

Example

- Institutes: Tamil Nadu Agricultural University (TNAU), Coimbatore
- Crops: Rice and Millets
- Theme: Resistance against abiotic stresses using genetic and epigenetic regulation and gene expression in rice and millets using CRISPR techniques.

These experiments would produce crops resistant to climatic variations suitable for South India agriculture.

APPLICATIONS

ABIOTIC STRESS

Type of stress	Crop	Action
Drought	Rice	dCas9 fused with transcriptional activator targets
Salinity	Rice	Epigenetic activation of ion transporter genes
Heat	Wheat	activation of Heat Shock Factor (HSF) and Heat Shock Protein (HSP) genes through histone acetyltransferase recruitment.
Cold	Rice	Targeted demethylation of promoters of CBF (C-repeat binding factor) genes to activate cold-responsive gene expression.
Flood	Rice	Epigenetic regulation of SUB1A gene controlling ethylene signaling, allowing plants to survive prolonged submergence.

BIOTIC STRESS

Type of stress	Crop	Action
Bacterial disease	Bacterial blight - Rice	Salicylic acid pathway are epigenetically activated through histone acetylation to enhance bacterial resistance.
Fungal disease	Powdery mildew – Wheat	Susceptibility gene MLO is epigenetically silenced using CRISPR-dCas9 by inducing DNA methylation, improving fungal resistance.
Viral disease	Yellow leaf curl virus - Tomato	Activation of RNA-silencing genes that suppress viral replication and movement within plant tissues
Feeding pest	Maize – corn borer	Genes involved in secondary metabolite production and protease inhibitors are epigenetically activated to reduce insect feeding damage.
Sucking pest	Brinjal – Aphids	Jasmonic-acid defense genes are epigenetically activated to increase defensive metabolites that reduce sap feeding.

(Jogam et al., 2022; Moreno et al., 2021). (Kungulovski & Jeltsch, 2016; Jogam et al., 2022).

MERITS

- The genetic manipulation is precise
- It precisely selects parts of particular genes.
- DNA itself is not affected
- Just makes some changes to DNA.
- The modifications are reversible
- Because there are some reversible modifications.
- Low tolerance to stress
- Because it increases tolerance against drought, salt, and heat.

- Faster method to grow plants
- By saving time than in traditional selective breeding.
- Contributes towards sustainable agriculture
- By reducing dependence on chemicals and irrigation.

DEMERITS

- Off-target effects
 - Can result in unintended epigenetic changes.
 - Technical challenges
 - The technology employed is very advanced.
 - Delivery issues
 - Delivering CRISPR into plant cells is difficult.
 - Regulatory challenges
 - Some epigenetic modifications may not be stable across generations.
- (Moreno et al., 2021; Johnston et al., 2026).

CONCLUSION

Epigenome editing is a recently developed technique in biotechnological modification of plants that allows regulating the expression of genes while leaving their sequences unchanged. This technology is extremely promising for developing climate-resistant varieties of crops and higher production efficiency. Nevertheless, some problems related to the stability, delivery, and regulation of modifications need to be resolved before using it on a large scale

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