Modulating Prime Editing Efficiency Through Epigenetic Reprogramming

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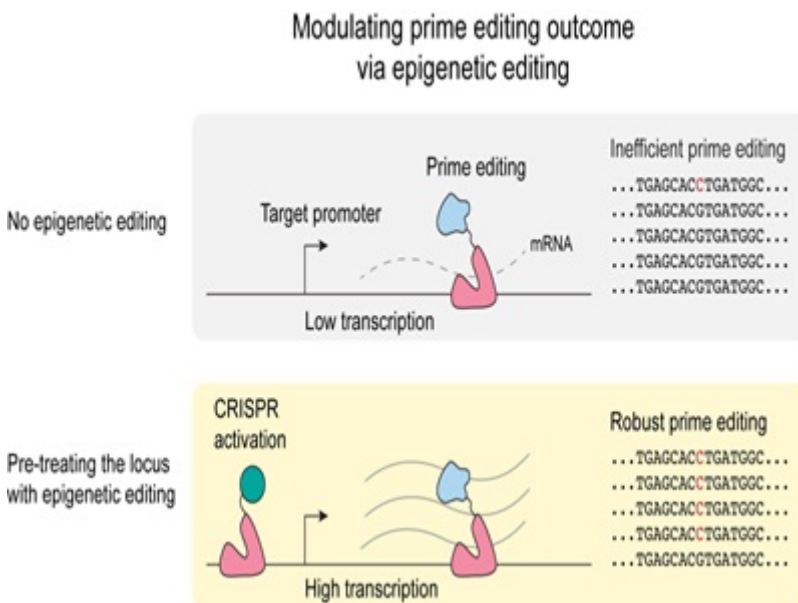
What is the Problem?

Prime editing, a CRISPR-based genome engineering tool, facilitates the precise introduction of genetic variants in the genome. However, prime editing faces challenges such as suboptimal efficiency and variable editing outcomes which limits its widespread adoption in basic research and clinical settings. As a result, understanding the epigenetic regulation of prime editing is crucial for improving its efficacy and expanding the therapeutic potential of this promising genome editing tool.

What is the Solution?

The solution is a method that involves reprogramming the epigenetic environment in the vicinity of a target site to modulate prime editing efficiency. Prime editing efficiency of a desired target can be modulated by regulating the transcriptional activity of the nearby gene. For example, if the desired site is targeted with CRISPRa, which activates gene expression, prime editing efficiency is increased at that site. If the desired site is targeted with CRISPRi, which inhibits gene expression, prime editing efficiency is decreased at that site.

What is the Competitive Advantage?

The competitive advantage of this technology lies in its ability to increase the efficiency of prime editing, thus expanding the therapeutic applications of prime editing. Coupling epigenetic reprogramming with prime editing demonstrates that transient gene activation before prime editing can enhance editing efficiency. This strategy will advance stem-cell based gene therapies, in which the target gene remains transcriptionally silenced and is only expressed in differentiated cell types. As the global genome editing market size is valued at $6.4 billion in 202 with an expected CAGR of 17.8%, there is a significant opportunity for this technology to advance the field of gene therapy and genetic engineering.

References

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