Programmable Genome Editing Using Molecular Proximity Sensors

The innovation is a strategy called P3 editing, which links protein-protein proximity to the formation of a functional CRISPR-Cas9 dual-component guide RNA.

What is the Problem?

Genome editing can be used in the design of synthetic molecular circuits to modulate the expression of a target gene or to record information into genomic DNA. However, current genome editing technologies are unable to program molecular events such as protein-protein interactions or proximity-triggered mechanisms for genome editing. The potential application of genome editing in synthetic biology circuits, where diverse cellular events can serve as programmable triggers for genome editing, requires the development of a molecular interaction sensor that transduces molecular events to functional genome editing events.

What is the Solution?

The solution is a strategy called P3 editing, which links protein-protein proximity to the formation of a functional CRISPR-Cas9 dual-component guide RNA. The molecular interaction between two protein or RNA molecules is sensed by two adaptor modules attached to dual-RNA-guide molecules. The dimerization of the adaptor modules induces the formation of a functional guide RNA, which activates prime editing or base editing in human cells to record its occurrence into the genomic DNA. The genome editing efficiency depends on the strength of the dimerization interactions, therefore the strength of interaction between two molecules can be measured.

What is the Competitive Advantage?

The competitive advantage of this technology lies in its ability to program protein-protein interactions and trigger precise genome editing using a molecular interaction sensor. This strategy can be used to record specific molecular interaction strength between biomolecules, detect expression of specific protein and/or RNA molecules, and form a genetic circuitry where cellular events are sensed and integrated to modulate changes in gene expression. 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 CRISPR genome editing and synthetic biology.

References

Technology ID

BDP 8768

Category

Research Tools

Selection of Available Technologies

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1. Choi, J., Chen, W., Liao, H., Li, X., & Shendure, J.(2024) , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10461971/, https://www.biorxiv.org/