



Technology Offer

High-precision base editors for site-specific single nucleotide conversion

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Background

The CRISPR-Cas system is a powerful tool for site-specific genome editing. The Cas9 endonuclease is capable of introducing DNA double strand breaks at a desired location with high precision. The lesion is repaired either in an error prone process leading to gene inactivation or in a highly accurate way relying on an external template. Modification of the template may serve to introduce selected mutations, modified sequences or entirely new genes. The accurate pathway comes with low endogenous efficiency.

Most hereditary diseases in humans are caused by single point mutations, the correction of which requires only subtle changes to the DNA. Recently, base editors were developed that allow the introduction of selective nucleotide substitutions. A mutant Cas9 enzyme that does not induce double strand breaks is fused to a nucleobase deaminase catalysing C-to-T mutations (by C-to-U deamination) or A-to-G mutations (by A-to-I deamination). Such base editors have enormous potential in genome editing, gene therapy and precision breeding. Yet, current editors suffer from limited specificity in that they edit different and/or multiple nucleobases within a larger sequence window. For broad application, especially in human therapies, improved systems will be needed that provide extraordinary accuracy of site-specific editing, ideally without any off-target effects.

Technology

Researchers from the Max-Planck-Institute of Molecular Plant Physiology in Golm invented high-precision C-to-T base editors with narrow activity windows that can selectively edit a single nucleobase at a specific position with high accuracy and high efficiency (1). The scientists hypothesized that structural flexibility between the Cas9 module and the deaminase module caused the observed inaccuracies of previously designed base editors, and decided to engineer the connection between the modules. The use of rigidifying linkers and the truncation of non-essential and flexible protein parts resulted in new fusion proteins that show a strong increase in editing precision while maintaining full deaminase activity. The narrow-window base editors combine superior editing precision with high editing efficiency and product purity, and will be widely applicable in many areas of basic and applied research.

We are seeking licensing partners for the further development and exploitation of this technology.



Literature

(1) Tan, J. et al., Nat Commun 2019 Jan 25;10(1):439. doi: 10.1038/s41467-018-08034-8

Patent Information

A PCT application was filed in March 2019.

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