Technology Opportunity, Ref. No. UZ-25/420

Improved Prime Editing Enzyme

This invention relates to improved variants of the prime editing enzyme for gene editing applications comprised of a *Sp*Cas9 nickase fused to an engineered reverse transcriptase (RT) derived from Moloney Murine leukaemia virus. Enhanced activities of the discovered variants were investigated biochemically, in a diverse set of cultured mammalian cells and in the murine liver and brain when applied through AAV-mediated delivery.

Keywords Gene therapy, genome editing, prime editing, SpCas9, reverse transcriptase

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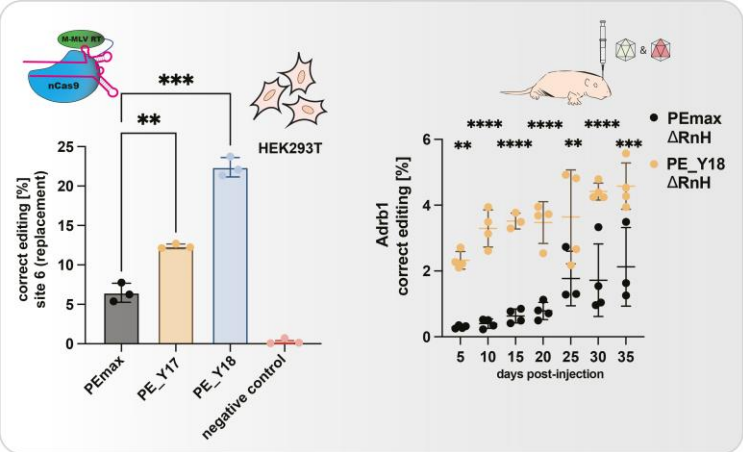
Reference Weber, Y., Böck, D., Ivașcu, A. et al. Enhancing prime editor activity by directed protein evolution in yeast. Nat Commun 15, 2092 (2024). https://doi.org/10.1038/s41467-024-46107-z

Background Prime editors are gene-editing tools that use a prime editing guide RNA and a complex of SpCas9 nickase fused to a reverse transcriptase from the Moloney Murine Leukemia virus. Though versatile, PEs are less efficient than traditional Cas9 nucleases or base editors. To overcome this limitation, a directed evolution strategy in yeast led to the identification of PE variants, which showed enhanced activities in various cellular backgrounds.

Invention The invention lies in the identification of prime editing variants that showed enhanced editing rates in biochemical assays, multiple mammalian cell lines, the mouse brain and the liver.



Fields of Use Gene therapy, genome editing, cell line engineering

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