Base editing and its applications in various organisms

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In place of nuclease activity of conventional genome editing, DNA base-modifying reactions allow direct introduction of point mutations (base editing). Deaminase-mediated base editing tools (BE and Target-AID) have been developed by tethering DNA cytidine deaminases to nuclease-deficient CRISPR-Cas9 system, enabling pinpoint mutagenesis within the target range of 3-5 bases. The tools now have been applied to wide range of organisms. Whole genome sequencing in yeast showed no significant off-target or non-specific mutagenesis induced. In mammals and plants, use of nickase Cas9 (D10A), which retains single-strand cleaving activity, greatly increased the efficiency, although it also occasionally induced insertion/deletion (indel). Co-expression of Uracil-DNA glycosylase inhibitor (UGI) further boosted the efficiency and reduced the indel formation. Transgene-free mutant tomato and rice were obtained. In *E.coli*, multiplex editing of up to 41 loci of multicopy elements was demonstrated. Several modifications and improvements have been made available for highest efficiency and mitigating unwanted effects, depending on the application. Other DNA base-modifying enzymes are also explored.

References

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