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Opportunities and challenges with CRISPR-Cas mediated homologous recombination based precise editing in plants and animals

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摘要	The genome editing has revolutionized the agriculture and human therapeutic sectors by its ability to create precise, stable and predictable mutations in the genome. It depends upon targeted double-strand breaks induction by the engineered endonucleases, which then gets repaired by highly conserved endogenous DNA repair mechanisms. The repairing could be done either through non-homologous end joining (NHEJ) or homology-directed repair (HDR) pathways. The HDR-based editing can be applied for precise gene targeting such as insertion of a new gene, gene replacement and altering of the regulatory sequence of a gene to control the existing protein expression. However, HDR-mediated editing is considered challenging because of lower efficiency in higher eukaryotes, thus, preventing its widespread application. This article reviews the recent progress of HDR-mediated editing and discusses novel strategies such as cell cycle synchronization, modulation of DNA damage repair factors, engineering of Cas protein favoring HDR and CRISPR-Cas reagents delivery methods to improve efficiency for generating knock-in events in both plants and animals. Further, multiplexing of described methods may be promising towards achieving higher donor template-assisted homologous recombination efficiency at the target locus.
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