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(54) Title: PRECISE GENOME DELETION AND REPLACEMENT METHOD BASED ON PRIME EDITING

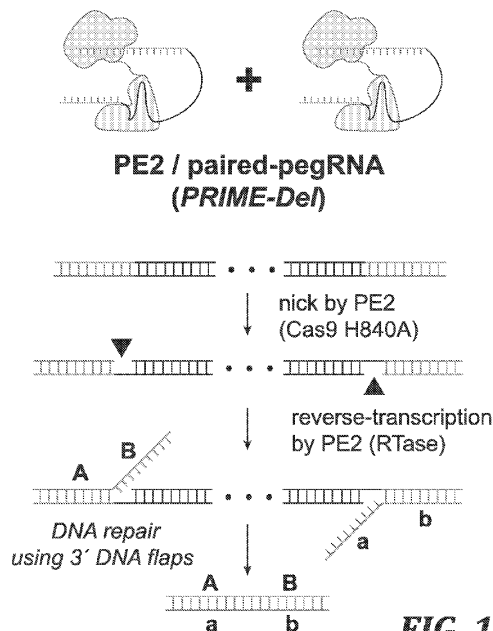


FIG. 1C

(57) Abstract: Disclosed are methods and related compositions for genomic editing. In one aspect, methods of editing double stranded DNA (dsDNA) use first and second editing complexes specific for first and second target sequences on the sense and antisense strands of the dsDNA molecule, respectively. Each editing complex comprises an extended guide RNA associated with a fusion editor protein, which comprises a functional nickase domain and a functional reverse transcriptase domain. The respective guide RNAs guide their associated fusion editor proteins to the dsDNA, which implement single stranded breaks on opposite strands of the dsDNA. The respective reverse transcriptase domains generate 3' overhangs. Repair of the dsDNA excises the portion of dsDNA disposed between the two single-stranded breaks. A variety of configurations and applications of the method are disclosed, providing flexible, facile, efficient, and precise methods to impose genetic manipulations.

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