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Supplemental information

A novel base editor SpRY-ABE8e^{F148A} mediates efficient A-to-G base editing with a reduced off-target effect

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Supplemental Material

Table S1 Guide sequences used for endogenous gene editing.

Table S2 Primers used in this study.

Table S3 The sequences of main plasmids used in this study.

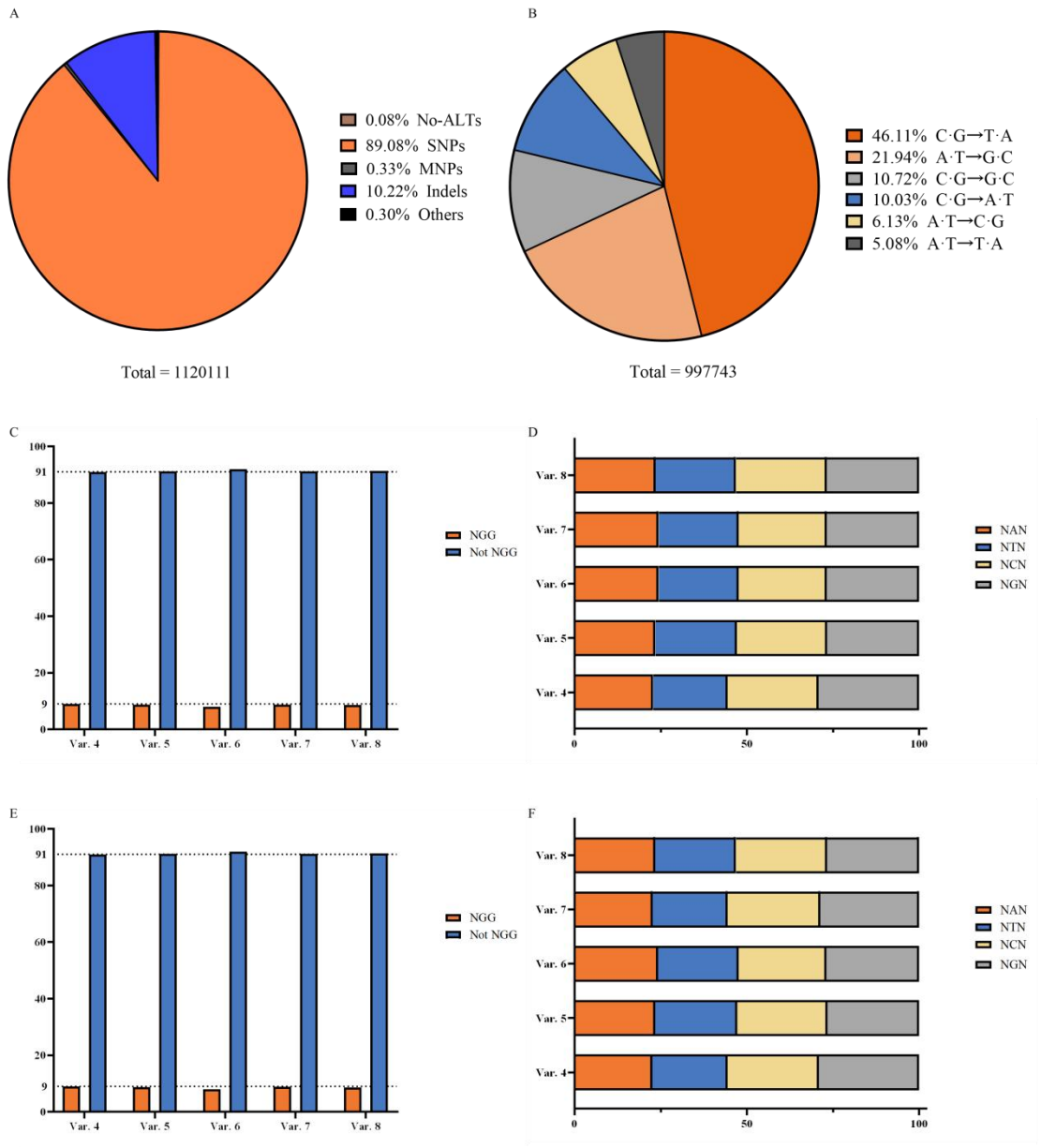

Fig. S1 The PAM distributions of reverse C•G-to-T•A pathogenic point mutations via ABE-mediated base editing.

A. The classification of human pathogenic genetic variants in the ClinVar database (accessed Feb, 2022). ALTs represent alternate base(s); SNPs (single-nucleotide polymorphisms), represent point mutations; MNPs represent multi-nucleotide polymorphisms.

B. The distributions of mutation required-to-reverse pathogenic point mutation.

B. The distributions of NGG and not NGG PAM by reversion C-to-T pathogenic point mutation by ABE.

C. The distributions of 4 types of PAM by reversion C-to-T pathogenic point mutation by ABE.

D. The distributions of NGG and not NGG PAM by reversion G-to-A pathogenic point mutation by ABE.

E. The distributions of 4 types of PAM by reversion G-to-A pathogenic point mutation by ABE.

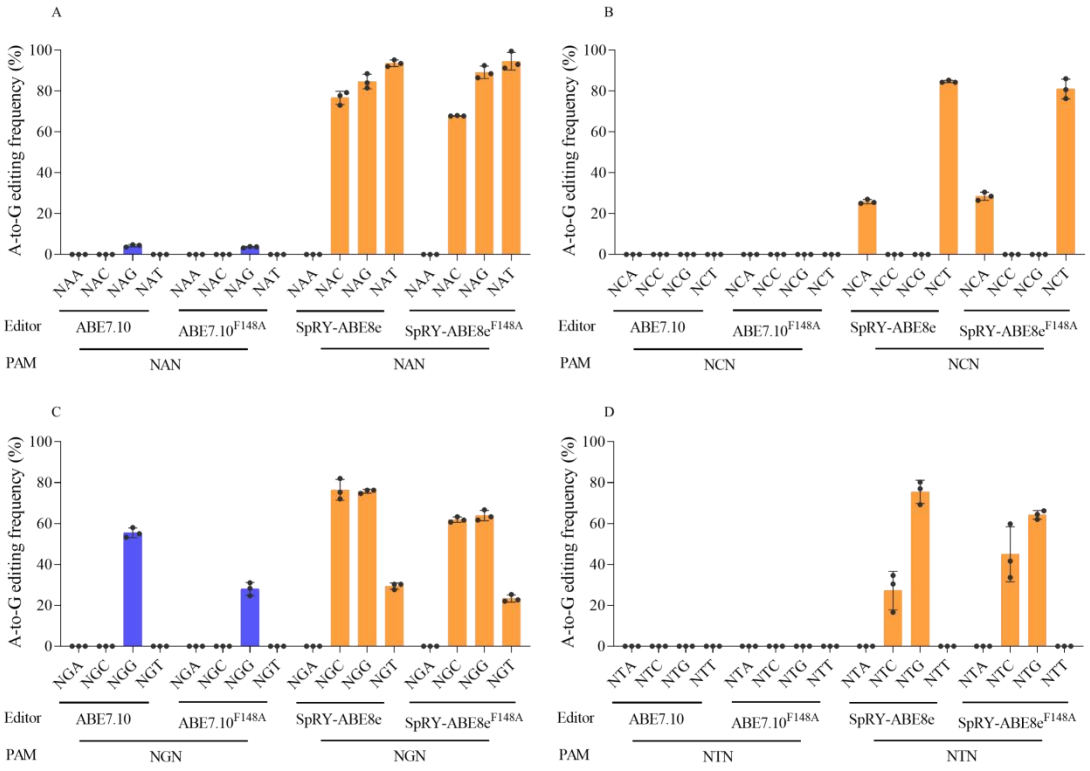

Fig. S2 Comparison of ABE7.10, ABE7.10^{F148A}, SpRY-ABE8e and SpRY-ABE8e^{F148A} base editors' activities across NR/YN PAM sites in VISTA enhancer site hs267.

A. A-to-G base editing of VISTA enhancer site hs267 bearing NAN PAM.

B. A-to-G base editing of VISTA enhancer site hs267 bearing NCN PAM.

C. A-to-G base editing of VISTA enhancer site hs267 bearing NGN PAM.

D. A-to-G base editing of VISTA enhancer site hs267 bearing NTN PAM.

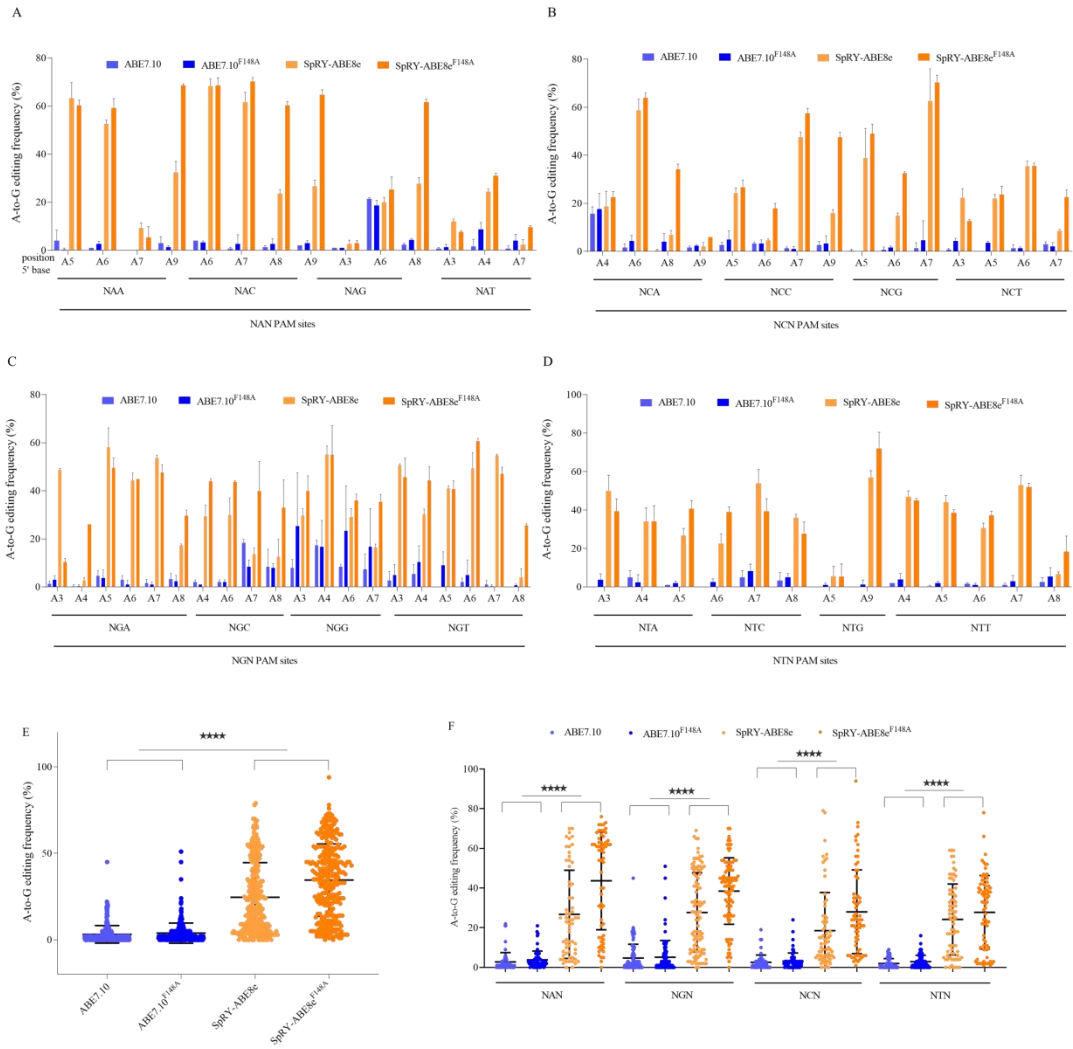

Fig. S3 Comparison of ABE7.10, ABE7.10^{F148A}, SpRY-ABE8e and SpRY-ABE8e^{F148A} base editors' activities across NR/YN PAM sites in Hela cells.

A. A-to-G base editing of endogenous sites in Hela cells bearing NAN PAM.

B. A-to-G base editing of endogenous sites in Hela cells bearing NCN PAM.

C. A-to-G base editing of endogenous sites in Hela cells bearing NGN PAM.

D. A-to-G base editing of endogenous sites in Hela cells bearing NTN PAM.

E. Editing efficiencies across target sites with NR/YN PAMs in Hela cells.

F. Editing efficiencies across target sites with NAN, NGN, NCN, and NTN in Hela cells, respectively.

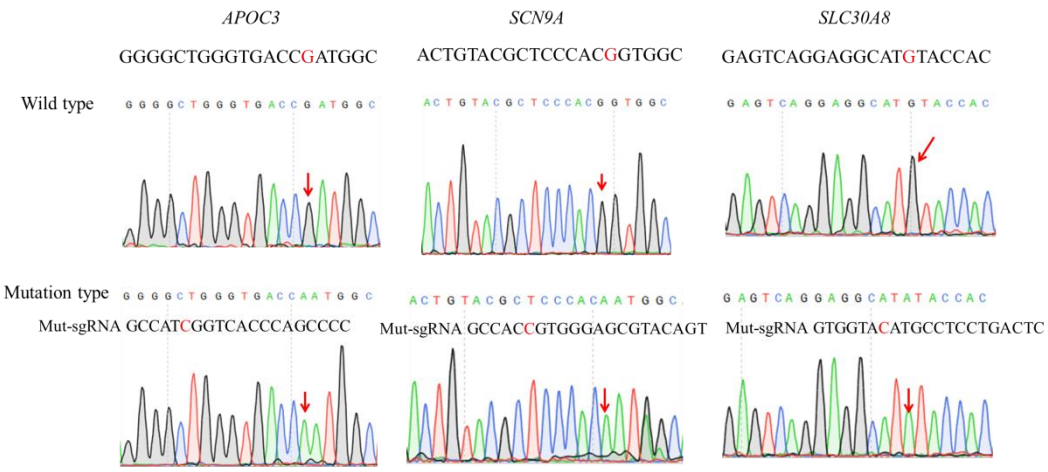

Fig. S4 Sequence chromatograms of installating *APOC3*, *SCN9A* and *SLC30A8* mutations in HEK293T cells.