CLAIMS

1. A composition for editing a gene target comprising:

(i) an mRNA encoding a base editor protein comprising a DNA binding domain and a deaminase, wherein the mRNA comprises a sequence having at least 95% sequence identity to SEQ ID NO: 2192, and

(ii) a guide RNA comprising a tracr sequence that serves as a binding scaffold for the base editor protein, and a spacer sequence that corresponds to a protospacer on PCSK9.

2. The composition of claim 1, wherein the mRNA comprises a sequence having at least 99% sequence identity to SEQ ID NO: 2192.
3. The composition of any one of claims 1 to 2, wherein the mRNA comprises a 5'UTR having at least 95% identity to the sequence of AGGAAAu'AAGAGAGAAAAGAAGAGu'AAGAAGAAAu'Au'AAGAGCCACC (SEQ ID NO: 2138).
4. The composition of any one of claims 1 to 3, wherein mRNA comprises a 3'UTR having at least 95% identity to the sequence of GCGGCCGCu'u'AAu'u'AAGCu'GCCu'u'Cu'GCGGGGCu'u'GCCu'u'Cu'GGCCAu'GCCCu'u'Cu'u'Cu'Cu'CCCu'u'GCACCu'Gu'ACCu'Cu'u'GGu'Cu'u'u'GAAu'AAAGCCu'GAGu'AGGAAGu'Cu'AGA (SEQ ID NO: 2147).
5. The composition of any one of claims 1 to 4, wherein the mRNA encoding the base editor protein comprises a GC% content greater than 50%.
6. The composition of any one of claims 1 to 5, wherein the base editor protein further comprises an adenine tTNA deaminase (TadA) region, a Cas9 region and a nuclear localization sequence (NLS) region.
7. The composition of claim 6, wherein the GC% content of the mRNA encoding the TadA region of the base editor protein is greater than 60%.
8. The composition of claim 6, wherein the GC% content of the mRNA encoding the Cas9 nickase region of the base editor protein is greater than 56%.
9. The composition of claim 6, wherein the GC% content of the mRNA encoding the NLS region of the base editor protein is greater than 54%.

10. The composition of any one of claims 1 to 9, wherein the mRNA encodes a base editor protein selected from the group consisting of MA004, MA040, MA041, and MA045.
11. The composition of claim 10, wherein mRNA encodes MA004.
12. The composition of any one of claims 1 to 11, wherein the ratio of the guide RNA and the mRNA encoding the base editor protein is from about 1:10 to about 10:1 by weight.
13. The composition of any one of claims 1 to 12, wherein the guide RNA further comprises a chemical modification on one or more nucleotides.
14. The composition of claim 13, wherein the chemical modification is selected from the group consisting of 2'-O-methyl modifications, 2'-O-(2-methoxyethyl) modifications, 2'-fluoro modifications, phosphonothioate modifications, inverted abasic modifications, deoxyribonucleotides, bicylic ribose analog (e.g., locked nucleic acid (LNA), C-ethylene-bridged nucleic acid (ENA), bridged nucleic acid (BNA), unlocked nucleic acid (UNA)), base or nucleobase modifications, internucleoside linkage modifications, ribonebularine, 2'-O-methylnebularine, and 2'-deoxynebularine.
15. The composition of any one of claims 1 to 14, wherein the guide RNA directs the base editor protein to effect a nucleobase alteration in the PCSK9 gene.
16. The composition of claim 15, wherein the nucleobase alteration results in a frame shift, a premature stop codon, an insertion or deletion in a transcript encoded by the PCSK9 gene.
17. The composition of claim 15, wherein the nucleobase alteration results in an aberrant transcript encoded by the PCSK9 gene.
18. The composition of any one of claims 15 to 17, wherein the nucleobase alteration is at a splice donor site of the PCSK9 gene.
19. The composition of claim 18, wherein the splice donor site is at 5' end of PCSK9 intron 1 as referenced in SEQ ID NO: 5.
20. The composition of claim 15, wherein the nucleobase alteration is at a splice acceptor site of the PCSK9 gene.
21. The composition of any one of claims 1 to 20, wherein the protospacer comprises a sequence having at least 80% sequence identity to the sequence of 5'-CCCGCACCTTGGCGCAGCGG-3' (SEQ ID No: 13) or to the sequence of 5'-CCGCACCTTGGCGCAGCGG-3' (SEQ ID No: 247).

22. The composition of any one of claims 1 to 21, wherein the guide RNA comprises a spacer sequence having at least 80% sequence identity to a spacer sequence of a guide RNA selected from the group consisting of SEQ ID NO: 9, ~~SEQ ID NO: 5,~~ SEQ ID NO: 428, SEQ ID NO: 429, SEQ ID NO: 430, SEQ ID NO: 431, SEQ ID NO: 432, SEQ ID NO: 433, SEQ ID NO: 434, SEQ ID NO: 435, SEQ ID NO: 11, SEQ ID NO: 436, and SEQ ID NO: 437.
23. The composition of claim 22, wherein the guide RNA comprises an RNA sequence having the sequence of SEQ ID NO: 9.