CLAIMS

1. An adenosine deaminase that deaminates adenine in deoxyribonucleic acid (DNA).

2. The adenosine deaminase of claim 1, comprising one or more amino acid substitutions at positions corresponding to amino acids that are involved in H-bond contacts with tRNA in a wild-type adenosine deaminase.

3. The adenosine deaminase of claim 2, wherein the wild-type adenosine deaminase is a TadA deaminase.

4. The adenosine deaminase of any one of claims 1-3, comprising an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 1, with the exception of one or more substitutions at positions selected from the group consisting of amino acid residues corresponding to positions 8, 17, 18, 23, 34, 36, 45, 48, 51, 56, 59, 84, 85, 94, 95, 102, 104, 106, 107, 108, 110, 118, 123, 127, 138, 142, 146, 147, 149, 151, 152, 153, 154, 155, 156, and 157 of the amino acid sequence of SEQ ID NO: 1.

5. The adenosine deaminase of any one of claims 2-4, wherein the one or more substitutions are substitutions selected from the group consisting of W23R, W23L, H36L, P48S, P48A, R51L, L84F, A106V, D108N, H123Y, A142N, S146C, D147Y, R152P, E155V, I156F, and K157N of the amino acid sequence of SEQ ID NO: 1.

6. The adenosine deaminase of any one of claims 2-5, wherein the one or more substitutions comprise a group of substitutions at positions selected from the group of substitutions at positions consisting of:

(i) W23, H36, P48, R51, L84, A106, D108, H123, A142, S146, D147, R152, E155, I156, and K157;

(ii) W23, H36, P48, R51, L84, A106, D108, H123, S146, D147, R152, E155, I156, and K157;

(iii) H36, P48, R51, L84, A106, D108, H123, A142, S146, D147, E155, I156, and K157;

(iv) H36, P48, R51, L84, A106, D108, H123, S146, D147, E155, I156, and K157;

(v) H36, R51, L84, A106, D108, H123, S146, D147, E155, I156, and K157;

(vi) L84, A106, D108, H123, D147, E155, and I156;
(vii) A106, D108, D147, and E155;
(viii) A106, and D108; and
(ix) D108;
of the amino acid sequence of SEQ ID NO: 1.

7. The adenosine deaminase of any one of claims 2-6, wherein the one or more substitutions comprise a group of substitutions selected from the groups of substitutions consisting of:
(i) W23L, H36L, P48A, R51L, L84F, A106V, D108N, H123Y, A142N, S146C, D147Y, R152P, E155V, I156F, and K157N;
(ii) W23R, H36L, P48A, R51L, L84F, A106V, D108N, H123Y, S146C, D147Y, R152P, E155V, I156F, and K157N;
(iii) H36L, P48S, R51L, L84F, A106V, D108N, H123Y, A142N, S146C, D147Y, E155V, I156F, and K157N;
(iv) H36L, P48S, R51L, L84F, A106V, D108N, H123Y, S146C, D147Y, E155V, I156F, and K157N;
(v) H36L, R51L, L84F, A106V, D108N, H123Y, S146C, D147Y, E155V, I156F, and K157N;
(vi) L84F, A106V, D108N, H123Y, D147Y, E155V, and I156F;
(vii) A106V, D108N, D147Y, and E155V;
(viii) A106V, and D108N; and
(ix) D108N;
of the amino acid sequence of SEQ ID NO: 1.

8. A base editor comprising: (i) a nucleic acid programmable DNA binding protein (napDNAbp) domain, and (ii) the adenosine deaminase of any one of claims 1-7.

9. The base editor of claim 8, wherein the napDNAbp domain comprises a Cas9 domain, a Cpf1 domain, a CasX domain, a CasY domain, a C2C1 domain, a C2C2 domain, or a C2C3 domain.

10. The base editor of claim 8 or 9, wherein the napDNAbp domain comprises a nuclease dead Cas9 (dCas9), a Cas9 nickase (nCas9), or a nuclease active Cas9.

11. The base editor of any one of claims 8-10, wherein the adenosine deaminase is fused to the napDNAbp domain via a linker.

12. The base editor of claim 11, wherein the linker is a polymer linker.

13. The base editor of claim 11 or 12, wherein the linker is a peptide linker.

14. The base editor of any one of claims 8-13, further comprising a second adenosine deaminase.

15. The base editor of any one of claims 8-14, wherein the base editor comprises the structure:

[adenosine deaminase]-[second adenosine deaminase]-[napDNAbp];
[adenosine deaminase]-[napDNAbp]-[second adenosine deaminase]; or
[napDNAbp]-[adenosine deaminase]-[second adenosine deaminase].

16. The base editor of claim 14 or 15, wherein the second adenosine deaminase does not deaminate adenosine in DNA.

17. The base editor of claim 14 or 15, wherein the second adenosine deaminase is capable of deaminating adenosine in DNA.

18. The base editor of any one of claims 14-17, wherein any of the adenosine deaminase and the second adenosine deaminase, the adenosine deaminase and the napDNAbp or the second adenosine deaminase and the napDNAbp are fused via a linker comprising the amino acid sequence SGGS (SEQ ID NO: 37), SGSETPGTSESATPES (SEQ ID NO: 10), SGGSSGGSSGSETPGTSESATPESSGGSSGGS (SEQ ID NO: 385), or GGSGGSPGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGSEPATSGGSGGS (SEQ ID NO: 386).

19. The base editor of any one of claims 8-18 further comprising one or more nuclear localization sequences (NLS).

20. The base editor of any one of claims 8-19 further comprising an amino acid sequence that is at least 90% identical to any one of the amino acid sequences of SEQ ID NOs: 11-28, 387-388, 440, or 691-706.

21. A complex comprising the base editor of any one of claims 8-20 and a guide RNA bound to the nucleic acid programmable DNA binding protein (napDNAbp) domain of the base editor.

22. A nucleic acid encoding the adenosine deaminase of any one of claims 1-7.

23. A nucleic acid encoding the base editor of any one of claims 8-20.

24. A vector comprising the nucleic acid of claim 22 or 23.

25. A cell comprising the adenosine deaminase of any one of claims 1-7 or the base editor of any one of claims 8-20.

26. A method for editing a nucleobase of a target DNA sequence, the method comprising:
(a) contacting the target DNA sequence with the base editor of any one of claims 8-18 or the complex of claim 19;
(b) converting a first nucleobase of the target DNA sequence to a second nucleobase; and
(c) cutting no more than one strand of the target DNA sequence, wherein a third nucleobase complementary to the first nucleobase is replaced by a fourth nucleobase complementary to the second nucleobase.

27. The method of claim 24, wherein the target DNA sequence comprises a point mutation associated with a disease or disorder.

28. The method of claim 24 or 25, wherein the method causes less than 20%, 19%, 18%, 16%, 14%, 12%, 10%, 8%, 6%, 4%, 2%, 1%, 0.5%, 0.2%, or 0.1% indel formation.