CLAIMS

1. An adenosine deaminase that deaminates adenine in deoxyribonucleic acid (DNA), wherein the adenosine deaminase comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 1, and further comprises one or more substitutions at the positions selected from the group consisting of amino acid residues 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~~is an engineered tRNA adenosine deaminase A (TadA)~~.

2. The adenosine deaminase of claim 1, wherein the adenosine deaminase is an engineered tRNA TadA deaminase A (TadA)~~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 TadA adenosine deaminase~~.

~~3. The adenosine deaminase of claim 1 or 2, 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 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.~~

3. The adenosine deaminase of claim 1 or 2, wherein the adenosine deaminase comprises an amino acid sequence that is at least 95%, at least 98%, at least 99%, or at least 99.5% identical to the amino acid sequence of SEQ ID NO: 1.

4. The adenosine deaminase of any one of claims ~~2-3~~1-3, 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.

5. The adenosine deaminase of any one of claims ~~2-4~~1-4, wherein the one or more substitutions comprise a group of substitutions at the 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.

6. The adenosine deaminase of any one of claims ~~2-5~~1-5, wherein the one or more substitutions comprise a group of substitutions selected from the group~~s 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.

7. The adenosine deaminase of any one of claims 1-6, wherein the amino acid sequence of the adenosine deaminase comprises an amino acid sequence that is an amino acid sequence that is at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 99.5% identical to any one of the amino acid sequences of SEQ ID NOs: 65-83, 420-437, or 672-684.

~~7~~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 ~~1-6~~1-7.

~~8~~9. The base editor of claim ~~7~~8, wherein the napDNAbp domain comprises a Cas9 domain, a Cpf1 domain, a CasX domain, a CasY domain, a ~~C2C1~~ C2c1 domain, a ~~C2C2~~ C2c2 domain, or a ~~C2C3~~ C2c3 domain.

~~9~~10. The base editor of claim ~~7~~ 8 or ~~8~~9, wherein the napDNAbp domain comprises a nuclease dead Cas9 (dCas9) domain, a Cas9 nickase (nCas9) domain, or a nuclease active Cas9 domain.

~~10~~11. The base editor of any one of claims ~~7-9~~8-10, wherein the adenosine deaminase is fused to the napDNAbp domain via a linker.

~~11~~12. The base editor of claim ~~10~~11, wherein the linker is a polymer linker.

~~12~~13. The base editor of claim ~~10~~ 11 or ~~11~~12, wherein the linker is a peptide linker.

14. The base editor of any one of claims 8-13, wherein the adenosine deaminase domain is fused to the N-terminus of the napDNAbp domain.

~~13~~15. The base editor of any one of claims ~~7-12,~~8-13 further comprising a second adenosine deaminase domain.

~~14~~16. The base editor of ~~any one of claims 7-13~~claim 15, wherein the base editor comprises the structure:

[adenosine deaminase domain]-[second adenosine deaminase domain]-[napDNAbp domain];

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

[napDNAbp domain]-[adenosine deaminase domain]-[second adenosine deaminase domain].

~~15~~17. The base editor of claim ~~13~~ 15 or ~~14~~16, wherein the second adenosine deaminase domain is a wild-type adenosine deaminase domain.

~~16~~18. The base editor of claim ~~13~~ 15 or ~~14~~16, wherein the second adenosine deaminase domain is capable of deaminating adenine in DNA.

~~17~~19. The base editor of any one of claims ~~13-16~~15-18, wherein any of the adenosine deaminase domain and the second adenosine deaminase domain, the adenosine deaminase domain and the napDNAbp domain, or the second adenosine deaminase domain and the napDNAbp domain 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).

~~18~~20. The base editor of any one of claims ~~7-17~~8-19 further comprising one or more nuclear localization sequences (NLS).

21. The base editor of claim 20, wherein the NLS comprises the amino acid sequence set forth in SEQ ID NO: 4.

~~19~~22. The base editor of any one of claims ~~7-18~~8-20, wherein the base editor comprises an amino acid sequence that is at least 90%, at least 95%, at least 98%, at least 99%, or at least 99.5% identical to any one of the amino acid sequences of SEQ ID NOs: 11-28, 387-388, 440, or 691-706~~, or~~

~~an amino acid sequence that is at least 90%, at least 95%, at least 98%, at least 99%, or at least 99.5% identical to any one of the amino acid sequences of SEQ ID NOs: 64-84, 420-437, or 672-684~~.

23. The base editor of any one of claims 8-22 further comprising an inhibitor of base excision repair.

24. The base editor of claim 23, wherein the inhibitor of base excision repair is a catalytically inactive inosine-specific nuclease (dISN).

~~20~~25. A complex comprising the base editor of any one of claims ~~7-19~~8-24 and a guide RNA bound to the ~~nucleic acid programmable DNA binding protein (~~napDNAbp~~)~~ domain of the base editor.

~~21~~26. A nucleic acid encoding the adenosine deaminase of any one of claims ~~1-6~~1-7.

~~22~~27. A nucleic acid encoding the base editor of any one of claims ~~7-19~~8-24.

~~23~~28. A vector comprising the nucleic acid of claim ~~21-~~26 or ~~22~~27.

~~24~~29. A cell comprising the adenosine deaminase of any one of claims ~~1-6~~1-7, ~~or~~ the base editor of any one of claims ~~7-19~~8-24, the nucleic acid of claim 26 or 27, or the vector of claim 28.

~~25~~30. An *in vitro* or *ex vivo* 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 ~~7-19~~8-24 or the complex of claim ~~20~~25; thereby converting a first nucleobase of the target DNA sequence to a second nucleobase and cutting no more than one strand of the target DNA sequence, ~~wherein~~ whereby a third nucleobase complementary to the first nucleobase is replaced by a fourth nucleobase complementary to the second nucleobase.

~~26~~31. The method of claim ~~25~~30, wherein the target DNA sequence comprises a point mutation associated with a disease or disorder.

~~27~~32. The method of claim ~~25~~ 30 or ~~26~~31, 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.

~~28~~33. A composition comprising the base editor of any one of claims ~~7-19~~8-24, the complex of claim ~~20~~25, the nucleic acid of claim ~~21~~ 26 or ~~22~~27, the vector of claim ~~23~~28, or the cell of claim ~~24~~29, for use as a medicament.

34. An *in vitro* or *ex vivo* method comprising introducing the adenosine deaminase of any one of claims 1-7, the base editor of any one of claims 8-24, the complex of claim 25, the nucleic acid of claim 26 or 27, or the vector of claim 28 into a cell.