WHAT IS CLAIMED IS:

1. A gene targeting nuclease expression cassette comprising a nucleic acid comprising a nuclease coding sequence which is operably linked to regulatory sequences which direct expression of the nuclease following delivery to a host cell having a sequence to which the nuclease is targeted, wherein the regulatory sequences comprise a promoter which has low transcriptional activity.

2. The nuclease expression cassette according to claim 1, wherein the promoter is a liver-specific promoter.

3. The nuclease expression cassette according to claim 1 or claim 2, wherein the promoter is a TBG-S1 promoter variant.

4. The nuclease expression cassette according to claim 3, wherein the TBG-S1 variant is truncated at the 5' end or the 3' end, or both.

5. The nuclease expression cassette according to claim 4, wherein the TBG-S1 variant is truncated at the 5' end.

6. The nuclease expression cassette according to any one of claims 1 to 5, wherein the promoter is TBG-S1-F64 (SEQ ID NO: 6).

7. The nuclease expression cassette according to any one of claims 1 to 5, wherein the promoter is TBG-S1-F113 (SEQ ID NO: 7).

8. The nuclease expression cassette according to any one of claims 1 to 5, wherein the promoter is TBG-S1-F140 (SEQ ID NO: 8).

9. The nuclease expression cassette according to claim 1 or claim 2, wherein the promoter is a CCL16 promoter.

10. The nuclease expression cassette according to claim 1 or claim 2, wherein the promoter is a SCLC22A9 promoter.

11. The nuclease expression cassette according to claim 1 or claim 2, wherein the promoter is a CYP26A1 promoter.

12. The nuclease expression cassette according to any one of claims 1 to 11, wherein the nuclease is a meganuclease, a CRISPR/Cas nuclease, zinc finger nuclease, or TALEN.

13. The nuclease expression cassette according to any one of claims 1 to 11, wherein the nuclease is a meganuclease.

14. A pharmaceutical composition comprising a nuclease expression cassette according to any one of claims 1 to 13 and one or more of a carrier, suspending agent, and/or excipient.

15. The pharmaceutical composition according to claim 14, wherein the expression is in a non-viral delivery system.

16. The pharmaceutical composition according to claim 15, wherein the non-viral delivery system is a lipid nanoparticle.

17. A viral vector comprising nuclease expression cassette according to any one of claims 1 to 13.

18. A recombinant AAV useful for gene editing comprising an AAV capsid and a vector genome packaged in the AAV capsid, said vector genome comprising:

(a) an expression cassette according to any of claims 1 to 13, and

(b) AAV inverted terminal repeat required for packaging the expression cassette into the capsid.

19. A composition comprising a viral vector according to claim 17 or a recombinant AAV according to claim 18 and one or more of a carrier, diluent, and/or excipient.

20. A method for editing a targeted gene, said method comprising delivering a nuclease expression cassette according to any one of claims 1 to 13, a composition according to any of claims 14 to 16, a viral vector according to claim 17, or an rAAV according to claim 18.

21. A method for reducing off-target activity of a gene targeting nuclease, said method comprising delivering a nuclease expression cassette according to any one of claims 1 to 13, a composition according to any of claims 14 to 16, a viral vector according to claim 17, or an rAAV according to claim 18.

22. A promoter comprising the sequence of SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8.

23. An expression cassette comprising the promoter of claim 22.

24. An expression vector comprising the promoter of claim 22.