CLAIMS

What is claimed is:

1. A composition comprising a nucleic acid sequence comprising a guide RNA (gRNA) sequence that specifically binds a first target RNA sequence, wherein the first target RNA sequence encodes a protein component of an adaptive immune response, and wherein the gRNA sequence comprises a first spacer sequence that binds a portion of a nucleic acid sequence encoding the protein component, and wherein the protein component is selected from the group consisting of Beta-2-microglobulin (β2M), Human Leukocyte Antigen A (HLA-A), Human Leukocyte Antigen B (HLA-B), Human Leukocyte Antigen C (HLA-C), Cluster of Differentiation 28 (CD28), Cluster of Differentiation 80 (CD80), Cluster of Differentiation 86 (CD86), Inducible T-cell Costimulator (ICOS), ICOS Ligand (ICOSLG), OX40L, Interleukin 12 (IL12), and CC Chemokine Receptor 7 (CCR7); and

wherein the composition further comprises a second spacer sequence which specifically binds a second target RNA sequence, wherein the first spacer sequence and the second spacer sequence bind different target RNA sequences.

2. The composition of claim 1, wherein a component of the adaptive immune response is selected from the group consisting of type I major histocompatibility complex (MHC I), type II major histocompatibility complex (MHC II), T-cell receptor (TCR), costimulatory molecule and a combination thereof.

3. The composition of claim 1, wherein the spacer sequence is about 20 or 21 nucleotides in length.

4. The composition of claim 1, wherein the spacer sequence and the target RNA sequence are reverse complements of one another.

5. The composition of claim 1, wherein the gRNA sequence comprises a scaffold sequence that specifically binds to a CRISPR/Cas polypeptide or portion thereof.

6. The composition of claim 5, wherein the CRISPR/Cas polypeptide or portion thereof is selected from the group consisting of Cas9, Cpf1, Cas13a, Cas13b, Cas13c and Cas13d, wherein the CRISPR/Cas polypeptide has native, reduced or null activity.

7. The composition of claim 1, wherein the nucleic acid sequence comprises a promoter which drives expression of the gRNA sequence.

8. The composition of claim 7, wherein the promoter is selected from the group consisting of a polymerase III promoter and a tRNA promoter.

9. The composition of claim 8, wherein the polymerase III promoter is a U6 promoter.

10. The composition of claim 1, wherein the gRNA sequence is a first gRNA sequence, and wherein the second spacer sequence is comprised within a second gRNA sequence.

11. The composition of claim 1, wherein the second target RNA sequence encodes a protein component of an adaptive immune response.

12. The composition of claim 1, wherein the second spacer sequence binds a portion of a nucleic acid sequence encoding a protein component selected from the group consisting of Beta-2-microglobulin (β2M), Human Leukocyte Antigen A (HLA-A), Human Leukocyte Antigen B (HLA-B), Human Leukocyte Antigen C (HLA-C), Cluster of Differentiation 28 (CD28), Cluster of Differentiation 80 (CD80), Cluster of Differentiation 86 (CD86), Inducible T-cell Costimulator (ICOS), ICOS Ligand (ICOSLG), OX40L, Interleukin 12 (IL12), and CC Chemokine Receptor 7 (CCR7).

13. The composition of claim 1, wherein the second spacer sequence binds a target sequence comprising at least 1, 2, 3, 4, 5, 6, or 7 repeats of a nucleic acid sequence selected from the group consisting of: CUG (SEQ ID NO: 18), CCUG (SEQ ID NO: 19), CAG (SEQ ID NO: 80), GGGGCC (SEQ ID NO: 81), and a combination thereof.

14. A composition comprising a nucleic acid sequence comprising: (a) the guide RNA (gRNA) sequence of claim 1 and (b) a nucleic acid sequence encoding a fusion protein, wherein the fusion protein comprises a first RNA-binding polypeptide and a second RNA-binding polypeptide, wherein neither the first RNA-binding polypeptide nor the second RNA-binding polypeptide comprises a significant DNA-nuclease activity, wherein the first RNA-binding polypeptide and the second RNA-binding polypeptide are not identical, and wherein the second RNA-binding polypeptide comprises an RNA-nuclease activity.

15. A composition comprising a nucleic acid sequence comprising: (a) the first and second guide RNA (gRNA) sequences of claim 10 and (b) a nucleic acid sequence encoding a fusion protein, wherein the fusion protein comprises a first RNA-binding polypeptide and a second RNA-binding polypeptide, wherein neither the first RNA-binding polypeptide nor the second RNA-binding polypeptide comprises a

significant DNA-nuclease activity, wherein the first RNA-binding polypeptide and the second RNA-binding polypeptide are not identical, and wherein the second RNA-binding polypeptide comprises an RNA-nuclease activity.

16. The composition of claim 14, wherein the first RNA-binding polypeptide or portion thereof is a CRISPR/Cas polypeptide or portion thereof.

17. The composition of claim 16, wherein the CRISPR/Cas polypeptide or portion thereof is selected from the group consisting of Cas9, Cpf1, Cas13a, Cas13b, Cas13c and Cas13d, wherein the CRISPR/Cas polypeptide has native, reduced or null activity.

18. The composition of claim 14, wherein the second RNA-binding polypeptide binds RNA in a manner in which it associates with RNA.

19. The composition of claim 18, wherein the second RNA-binding polypeptide associates with RNA in a manner in which it cleaves RNA.

20. The composition of claim 14, wherein the nucleic acid sequence comprises a promoter.

21. The composition of claim 14, wherein the fusion protein comprises an NLS, NES or tag.

22. A vector comprising the composition of claim 1.

23. The vector of claim 22, wherein the vector is selected from the group consisting of: adeno-associated virus, retrovirus, lentivirus, adenovirus, nanoparticle, micelle, liposome, lipoplex, polymersome, polyplex, and dendrimer.

24. A cell comprising the vector of claim 22.

25. The composition of claim 14, wherein the second RNA-binding polypeptide is selected from the group consisting of: RNAse1, RNAse4, RNAse6, RNAse7, RNAse8, RNAse2, RNAse6PL, RNAseL, RNAseT2, RNAse11, RNAseT2-like, NOB1, ENDOV, ENDOG, ENDOD1, hFEN1, hSLFN14, hLACTB2, APEX2, ANG, HRSP12, ZC3H12A, RIDA, PDL6, NTHL, KIAA0391, APEX1, AGO2, EXOG, ZC3H12D, ERN2, PELO, YBEY, CPSF4L, hCG_2002731, ERCC1, RAC1, RAA1, RAB1, DNA2, FLJ35220, FLJ13173, ERCC4, RNAse1(K41R), RNAse1(K41R, D121E), RNAse1(K41R, D121E, H119N), RNAse1(H119N), RNAse1(R39D, N67D, N88A, G89D, R91D, H119N), RNAse1(R39D, N67D, N88A, G89D, R91D, H119N, K41R, D121E), RNAse1(R39D, N67D, N88A, G89D, R91D), TENM1, TENM2, RNAseK, TALEN, ZNF638, and hSMG6 PIN.