Claims

We claim:

1. An engineered nucleic acid whose nucleotide sequence includes a sequence element that is or is a complement of an oncoselective translation sequence element, wherein the oncoselective translation sequence element is or comprises an oncoselective read-through motif.

2. The engineered nucleic acid of claim 1, wherein the engineered nucleic acid's nucleotide sequence includes an open reading frame or complement thereof.

3. The engineered nucleic acid of claim 2, wherein the oncoselective read-through motif is within or upstream of the open reading frame.

4. The engineered nucleic acid of claim 3 wherein the oncoselective read-through motif comprises an upstream flanking sequence, a stop codon, and a downstream flanking sequence.

5. The engineered nucleic acid of claim 4 , wherein the oncoselective read-through motif comprises a sequence selected from the group comprising: VNNNNNNMNNMWK, NNNVWNNKGHHNH, DVHVNNNCWNNNB, MWBNNNNNNNNNN, WGNNSNHNHDNNN, VNNNNNNMNNMWK or VMNNWNKNNNNNN, wherein V stands for A, C or G, M stands for A or C, W stands for A or T/U, K stands for G or T/U, H stands for A, C or T/U, D stands for A,G or T/U, B stands for C, G or T/U, S stands for G or C, N stands for any nucleotide, within the region that spans the read-through stop codon and the first 14 nucleotides of the downstream flanking sequence.

6. The engineered nucleic acid of claim 4, wherein the oncoselective read-through motif comprises a stem loop; a bulge loop, a pseudoknot, or a combination thereof within the first 50 nucleotides of the downstream flanking sequence and part of this stem loop located preferably within stop codon and the first 16 nucleotides of the downstream flanking sequence, or a combination thereof.

7. The engineered nucleic acid of claim 6, wherein the stem loop comprises more than 20 base paired nucleotides within first 50 nucleotides of the downstream flanking sequence.

8. The engineered nucleic acid of any of the preceding claims, wherein the oncoselective read-through motif comprises a downstream flanking sequence with a GC content of more than 42%, more than 48%, preferably more than 54%.

9. The engineered nucleic acid of any of the preceding claims, wherein the oncoselective read-through motif comprises a codon that encodes proline residue.

10. The engineered nucleic acid of claim 2, wherein the open reading frame or complement thereof encodes a suicide protein.

11. The engineered nucleic acid of claim 10, wherein the suicide protein induces necroptosis.

12. The engineered nucleic acid of claim 11, wherein the suicide protein is constitutively active MLKL.

13. The engineered nucleic acid of claim 10, wherein the suicide protein induces pyroptosis.

14. The engineered nucleic acid of claim 13, wherein the suicide protein is constitutively active gasdermin D.

15. The engineered nucleic acid of claim 1, wherein the engineered nucleic acid has reduced immunogenicity.

16. A nucleic acid whose sequence includes an open reading frame, or a complement thereof, wherein an oncoselective read-through motif has been inserted into or before the open reading frame, and wherein the open reading frame encodes a payload protein selected from the group consisting of a suicide protein, cell surface antigen, an antibody agent, a toxin, a genetic modification protein, or a viral replication protein.

17. A pharmaceutical composition comprising the nucleic acid of claim 16.

18. The pharmaceutical composition of claim 17, wherein the pharmaceutical composition comprises nanoparticles.

19. The pharmaceutical composition of claim 18, wherein the nanoparticles are lipid nanoparticles.

20. The pharmaceutical composition of claim 18, wherein the engineered nucleic acid is or comprises RNA.

21. The pharmaceutical composition of claim 18, wherein the engineered nucleic acid is or comprises DNA.

22. The pharmaceutical composition of claim 18, wherein the engineered nucleic acid is expressed in a cell so that administration of the pharmaceutical composition delivers RNA to the cell.

23. The engineered nucleic acid of claim 16 or the pharmaceutical composition of claim 17 for use in therapy.

24. Use of the engineered nucleic acid of claim 16 or the pharmaceutical composition of claim 17 in the manufacture of a medicament for the treatment of cancer in a subject, wherein the engineered nucleic acid or the pharmaceutical composition is to be administered to the subject.

25. The use according to claim 24, wherein the cancer in the subject comprises oncogenic ribosomes.

26. The use according to claim 25, wherein the oncogenic ribosomes comprises at least one of loss of p53 activity, loss of RB activity, FBL overexpression, or hemizygous loss of ribosomal protein genes.

27. The use according to claim 24, wherein aminoglycoside antibiotics, macrolide antibiotics, ataluren, or ivacaftor, ivacaftor/lumacaftor is not received by the subject.

28. The use according to claim 24, wherein the subject is not suffering from Diamond–Blackfan anemia, Dyskeratosis congenita, Shwachman–Diamond syndrome, 5q- myelodysplastic syndrome, Treacher Collins syndrome, Cartilage–hair hypoplasia, Isolated congenital asplenia, Bowen–Conradi syndrome, or North American Indian childhood cirrhosis.

29. The use according to claim 24, wherein the subject is to be administered a plurality of doses.

30. The use according to claim 24, wherein one or more features of an immune response to the cancer is to be monitored in the subject.

31. The use according to claim 30, wherein further doses are to be administered until the immune response is detected from monitoring the subject.

32. An oncoselective translation sequence element comprising a read-through consensus sequence, sequence with high G-C content; a codon encoding proline; a stem loop; a bulge loop, a pseudoknot or a combination thereof.