CLAIMS

1. A DNA construct comprising:
   (a) a starter exon encoding a start codon;
   (b) a first frame-switch exon located downstream of the starter exon, the first frame-switch exon comprising a first acceptor splice site, wherein inclusion or exclusion of the first frame-switch exon during alternative splicing determines the downstream reading frame of the mature mRNA transcript; and
   (c) a first specific exon located downstream of the first frame-switch exon, the first specific exon comprising a second acceptor splice site, a first reporter gene and a second reporter gene, wherein the first reporter gene is upstream or downstream of the second reporter gene and wherein the first reporter gene is in a different reading frame from the second reporter gene,

   wherein the exclusion of the first frame-switch exon causes the first reporter gene to be in-frame with the start codon and to be translated as a discrete protein terminating at a stop codon without the second reporter gene being translated as a functional protein, and wherein the inclusion of the first frame-switch exon causes the second reporter gene to be in-frame with the start codon and to be translated as a discrete protein terminating at a stop codon without the first reporter gene being translated as a functional protein.

2. The DNA construct of claim 1, further comprising a second specific exon located downstream of the first specific exon.

3. The DNA construct of claims 1 or 2, further comprising a second frame-switch exon located downstream of the first frame-switch exon and upstream of the first specific exon, the second frame-switch exon comprising a third acceptor splice site, wherein the second frame-switch exon is in a different reading frame from the first frame-switch exon and wherein the combination of inclusion or exclusion of the first frame-switch exon and the second frame-switch exon during alternative splicing determines the downstream reading frame of the mature mRNA transcript.

4. The DNA construct of claim 2 or 3, further comprising a third reporter gene, wherein the third reporter gene is located in the first specific exon or second specific exon.

5. The DNA construct of claim 3, wherein the third reporter gene is in the same reading frame as the first or second reporter genes.

6. The DNA construct of claim 3, wherein the third reporter gene is in a different reading frame from the first and second reporter genes.

7. The DNA construct of any one of claims 2 to 6, further comprising a fourth reporter gene, wherein the third reporter gene is located in the first specific exon or second specific exon.

8. The DNA construct of claim 1, comprising the sequence of SEQ ID NO:67.

9. A method of measuring the efficacy of a nucleic acid delivery into a cell by a delivery agent, the method comprising:
   (a) using the delivery agent to introduce the nucleic acid into the cell, wherein the cell expresses the DNA construct of any one of claims 1 to 8 and wherein the nucleic acid is configured to modify the DNA construct or to modulate the expression or processing of a pre-mRNA or mature mRNA expressed from the DNA construct; and
   (b) quantifying the functional uptake of the nucleic acid into the cell by measuring the relative expression of two of the reporter genes, wherein the functional uptake of the nucleic acid is indicative of the efficacy of delivery of the nucleic acid by the delivery agent.

10. The method of claim 9, wherein step (b) comprises quantifying the functional uptake of the nucleic acid into the cell by measuring the relative expression of the first reporter gene and the second reporter gene.

11. The method of claims 9 or 10, wherein the nucleic acid is selected from the group consisting of a steric blocker antisense oligonucleotide, a RNaseH-activating GAPmer, an siRNA, a CRISPR/Cas-sgRNA and a snRNA.

12. The method of claim 11, wherein the steric blocker antisense oligonucleotide is a splice-switching oligonucleotide (SSO).

13. The method of any one of claims 9 to 12, wherein the delivery agent is selected from the group consisting of an intra-molecular chemical modification, an inter-molecular delivery agent, an encapsulation delivery agent, a complexation delivery agent, a viral-based delivery agent, a cellular delivery agent and a sub-cellular delivery agent.

14. The method of any one of claims 9 to 13, wherein the expression of the reporter genes is measured by fluorescence, luminescence, immunohistochemistry or quantitative PCR.

15. A method for measuring the effect of chemical modification on the potency or activity of a nucleic acid, the method comprising:

(a) introducing a chemically-modified nucleic acid into a cell, wherein the cell expresses the DNA construct of any one of claims 1 to 8 and wherein the chemically-modified nucleic acid is configured to modify the DNA construct or to modulate the expression or processing of a pre-mRNA or mature mRNA expressed from the DNA construct; and

(b) quantifying the potency or activity of the chemically-modified nucleic acid by measuring the relative expression of two of the reporter genes.

16. The method of claim 15, wherein step (b) comprises quantifying the potency or activity of the chemically-modified nucleic acid by measuring the relative expression of the first reporter gene and the second reporter gene.

17. A transgenic animal that expresses the DNA construct of any one of claims 1 to 8.

18. The transgenic animal of claim 17, wherein the animal is a rodent.

19. A system for characterizing the functional cellular uptake of a nucleic acid, the system comprising:

(a) a DNA construct comprising at least two reporter genes; and

(b) a nucleic acid configured to modify the DNA construct or to modulate the expression or processing of a pre-mRNA or mature mRNA expressed from the DNA construct such that one of the at least two reporter genes is preferentially expressed, wherein the DNA construct comprises the DNA construct of any one of claims 1 to 8.