TREM COMPOSITIONS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application No. 63/009,669, filed on April 14, 2020, the entire contents of which is hereby incorporated by reference.

BACKGROUND

Transfer RNAs (tRNAs) are complex, naturally occurring RNA molecules that possess a number of functions including initiation and elongation of proteins.

SUMMARY

The present disclosure features modified tRNA-based effector molecules (TREMs, e.g., a TREM or TREM fragment), as well as related compositions and uses thereof. As provided herein, TREMs are complex molecules which can mediate a variety of cellular processes. The TREMs disclosed herein comprise at least one modification (e.g., a non-naturally occurring modification), e.g., on a component nucleotide (e.g., a nucleobase or sugar) or within an internucleotide region, e.g., the TREM backbone. In one aspect, provided herein is a TREM comprising a sequence of Formula A: [L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2], wherein independently, [L1] and [VL Domain], are optional; and one of [L1], [ASt Domain1], [L2]-[DH Domain], [L3], [ACH Domain], [VL Domain], [TH Domain], [L4], and [ASt Domain2] comprises a nucleotide comprising a non-naturally occurring modification.

In an embodiment, the TREM: (a) has the ability to: (i) support protein synthesis, (ii) be charged by a synthetase, (iii) be bound by an elongation factor, (iv) introduce an amino acid into a peptide chain, (v) support elongation, or (vi) support initiation; (b) comprises at least X contiguous nucleotides without a non-naturally occurring modification, wherein X is greater than 3, 4, 5, 6, 7, 8, 9, or 10; (c) comprises at least 3, but less than all of the nucleotides of a type (e.g., A, T, C, G or U) comprise the same non-naturally occurring modification; (d) comprises at least X nucleotides of a type (e.g., A, T, C, G or U) that do not comprise a non-naturally occurring modification, wherein X=1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48,

49 or 50; (e) comprises no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) that comprise a non-naturally occurring modification; and/or (f) comprises no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) that do not comprise a non-naturally occurring modification.

In an embodiment, the TREM comprises feature (a)(i). In an embodiment, the TREM comprises feature (a)(ii). In an embodiment, the TREM comprises feature (a)(iii). In an embodiment, the TREM comprises feature (a)(iv). In an embodiment, the TREM comprises feature (a)(v). In an embodiment, the TREM comprises feature (a)(vi). In an embodiment, the TREM comprises feature (b). In an embodiment, the TREM comprises feature (c). In an embodiment, the TREM comprises feature (d). In an embodiment, the TREM comprises feature (e). In an embodiment, the TREM comprises feature (f). In an embodiment, the TREM comprises all of features (a)-(f) or a combination thereof.

In an embodiment, the TREM Domain comprising the non-naturally occurring modification has a function, e.g., a domain function described herein.

In an aspect, provided herein is a TREM core fragment comprising a sequence of Formula B:

$[L1]_y$-[ASt Domain1]$_x$-$[L2]_y$-[DH Domain]$_y$-$[L3]_y$-[ACH Domain]$_x$-[VL Domain]$_y$-[TH Domain]$_y$-$[L4]_y$-[ASt Domain2]$_x$,

wherein x=1 and y=0 or 1; and one of [ASt Domain1], [ACH Domain], and [ASt Domain2] comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, the TREM has the ability to support protein synthesis. In an embodiment, the TREM has the ability to be able to be charged by a synthetase. In an embodiment, the TREM has the ability to be bound by an elongation factor. In an embodiment, the TREM has the ability to introduce an amino acid into a peptide chain. In an embodiment, the TREM has the ability to support elongation. In an embodiment, the TREM has the ability to support initiation.

In an embodiment, the [ASt Domain 1] and/or [ASt Domain 2] comprising the non-naturally occurring modification has the ability to initiate or elongate a polypeptide chain.

In an embodiment, the [ACH Domain] comprising the non-naturally occurring modification has the ability to mediate pairing with a codon.

In an embodiment, y=1 for any one, two, three, four, five, six, all or a combination of [L1], [L2], [DH Domain], [L3], [VL Domain], [TH Domain], [L4].

In an embodiment, y=0 for any one, two, three, four, five, six, all or a combination of [L1], [L2], [DH Domain], [L3], [VL Domain], [TH Domain], [L4].

In an embodiment, y=1 for linker [L1], and L1 comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, y=1 for linker [L2], and L2 comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, y=1 for [DH Domain (DHD)], and DHD comprises a nucleotide having a non-naturally occurring modification. In an embodiment, the DHD comprising the non-naturally occurring modification has the ability to mediate recognition of aminoacyl-tRNA synthetase.

In an embodiment, y=1 for linker [L3], and L3 comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, y=1 for [VL Domain (VLD)], and VLD comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, y=1 for [TH Domain (THD)], and THD comprises a nucleotide having a non-naturally occurring modification. In an embodiment, the THD comprising the non-naturally occurring modification has the ability to mediate recognition of the ribosome.

In an embodiment, y=1 for linker [L4], and L4 comprises a nucleotide having a non-naturally occurring modification.

In another aspect, the disclosure provides a TREM fragment comprising a portion of a TREM, wherein the TREM comprises a sequence of Formula A:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2], and wherein the TREM fragment comprises a non-naturally occurring modification.

In an embodiment, the TREM fragment comprises one, two, three or all or any combination of the following: (a) a TREM half (*e.g.*, from a cleavage in the ACH Domain, *e.g.*, in the anticodon sequence, *e.g.*, a 5'half or a 3' half); (b) a 5' fragment (*e.g.*, a fragment comprising the 5' end, *e.g.*, from a cleavage in a DH Domain or the ACH Domain); (c) a 3' fragment (*e.g.*, a fragment comprising the 3' end, *e.g.*, from a cleavage in the TH Domain); or (d)

an internal fragment (*e.g.*, from a cleavage in any one of the ACH Domain, DH Domain or TH Domain).

In an embodiment, the TREM fragment comprise (a) a TREM half which comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, the TREM fragment comprise (b) a 5' fragment which comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, the TREM fragment comprise (c) a 3' fragment which comprises a nucleotide having a non-naturally occurring modification.

In an embodiment, the TREM fragment comprise (d) an internal fragment which comprises a nucleotide having a non-naturally occurring modification.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the TREM Domain comprises a plurality of nucleotides each having a non-naturally occurring modification. In an embodiment, the non-naturally occurring modification comprises a nucleobase modification, a sugar (e.g., ribose) modification, or a backbone modification. In an embodiment, tbe non-naturally occurring modification is a sugar (e.g., ribose) modification. In an embodiment, tbe non-naturally occurring modification is 2'-ribose modification, e.g., a 2'-OMe, 2'-halo (e.g., 2'-F), 2'-MOE, or 2'-deoxy modification. In an embodiment, tbe non-naturally occurring modification is a backbone modification, e.g., a phosphorothioate modification.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the TREM sequence comprises a CCA sequence on a terminus, e.g., the 3' terminus. In an embodiment, the TREM sequence does not comprise a CCA sequence on a terminus, e.g., the 3' terminus.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the non-naturally occurring modification is a modification in a base or a backbone of a nucleotide, e.g., a modification chosen from any one of Tables 5, 6, 7, 8 or or 9.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the non-naturally occurring modification is a base modification chosen from a modification listed in Table 5.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the non-naturally occurring modification is a base modification chosen from a modification listed in Table 6.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the non-naturally occurring modification is a base modification chosen from a modification listed in Table 7.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the non-naturally occurring modification is a backbone modification chosen from a modification listed in Table 8.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the non-naturally occurring modification is a backbone modification chosen from a modification listed in Table 9.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 1, e.g., any one of SEQ ID NOs 1-451.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the TREM, TREM core fragment, or TREM fragment is encoded by a consensus sequence chosen from any one of SEQ ID NOs: 562-621.

In an embodiment of any of the TREMs, TREM core fragments, or TREM fragments disclosed herein, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in any one of Tables 15-22, e.g., any one of SEQ ID NOs: 622-1187. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 15, e.g., any one of SEQ ID NOs: 622-698. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 16, e.g., any one of SEQ ID NOs: 699-774. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 17, e.g., any one of SEQ ID NOs: 775-841. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 18, e.g., any one of SEQ ID NOs: 842-917. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 19, e.g., any one of SEQ ID NOs: 918-992. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 20, e.g., any one of

SEQ ID NOs: 993-1078. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 21, e.g., any one of SEQ ID NOs: 1079-1154. In an embodiment, the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 22, e.g., any one of SEQ ID NOs: 1155-1187.

In another aspect, the disclosure provides a pharmaceutical composition comprising a TREM, a TREM core fragment, or a TREM fragment disclosed herein.

In another aspect, the disclosure provides a method of making a TREM, a TREM core fragment, or a TREM fragment disclosed herein, comprising linking a first nucleotide to a second nucleotide to form the TREM.

In an embodiment, the TREM, TREM core fragment or TREM fragment is non-naturally occurring (e.g., synthetic).

In an embodiment, the TREM, TREM core fragment or TREM fragment is made by cell-free solid phase synthesis.

In another aspect, the disclosure provides a method of modulating a tRNA pool in a cell comprising: providing a TREM, a TREM core fragment, or a TREM fragment disclosed herein, and contacting the cell with the TREM, TREM core fragment or TREM fragment, thereby modulating the tRNA pool in the cell.

In an aspect, the disclosure provides a method of contacting a cell, tissue, or subject with a TREM, a TREM core fragment, or a TREM fragment disclosed herein, comprising: contacting the cell, tissue or subject with the TREM, TREM core fragment or TREM fragment, thereby contacting the cell, tissue, or subject with the TREM, TREM core fragment or TREM fragment.

In another aspect, the disclosure provides a method of delivering a TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject, comprising: providing a cell, tissue, or subject, and contacting the cell, tissue, or subject, a TREM, a TREM core fragment, or a TREM fragment disclosed herein.

In an aspect, the disclosure provides a method of modulating a tRNA pool in a cell comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a first sequence, comprising:

optionally, acquiring knowledge of the abundance of one or both of (i) and (ii), e.g., acquiring knowledge of the relative amounts of: (i) and (ii) in the cell, wherein (i) is a tRNA moiety having an anticodon that pairs with the codon of the ORF having a first sequence (the

first tRNA moiety) and (ii) is an isoacceptor tRNA moiety having an anticodon that pairs with a codon other than the codon having the first sequence (the second tRNA moiety) in the cell;

contacting the cell with a TREM, a TREM core fragment, or a TREM fragment disclosed herein, wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with: the codon having the first sequence; or the codon other than the codon having the first sequence, in an amount and/or for a time sufficient to modulate the relative amounts of the first tRNA moiety and the second tRNA moiety in the cell,

thereby modulating the tRNA pool in the cell.

In another aspect, the disclosure provides a method of modulating a tRNA pool in a subject having an ORF, which ORF comprises a codon having a first sequence, comprising:

optionally, acquiring knowledge of the abundance of one or both of (i) and (ii), e.g., acquiring knowledge of the relative amounts of: (i) and (ii) in the subject, wherein (i) is a tRNA moiety having an anticodon that pairs with the codon of the ORF having a first sequence (the first tRNA moiety) and (ii) is an isoacceptor tRNA moiety having an anticodon that pairs with a codon other than the codon having the first sequence (the second tRNA moiety) in the subject;

contacting the subject with a TREM, a TREM core fragment, or a TREM fragment disclosed herein, wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with: the codon having the first sequence; or the codon other than the codon having the first sequence, in an amount and/or for a time sufficient to modulate the relative amounts of the first tRNA moiety and the second tRNA moiety in the subject,

thereby modulating the tRNA pool in the subject.

In an aspect, the disclosure provides a method of modulating a tRNA pool in a subject having an endogenous ORF comprising a codon comprising a synonymous mutation (a synonymous mutation codon or SMC), comprising:

providing a composition comprising a TREM, a TREM core fragment, or a TREM fragment disclosed herein, wherein the TREM, TREM core fragment or TREM fragment comprises an isoacceptor tRNA moiety comprising an anticodon sequence that pairs with the SMC (the TREM);

contacting the subject with the composition in an amount and/or for a time sufficient to modulate the tRNA pool in the subject,

thereby modulating the tRNA pool in the subject.

In another aspect, the disclosure provides a method of modulating a tRNA pool in a cell comprising an endogenous ORF comprising a codon comprising a SMC, comprising:

providing a composition comprising a TREM, a TREM core fragment, or a TREM fragment disclosed herein, wherein the TREM, TREM core fragment or TREM fragment comprises an isoacceptor tRNA moiety comprising an anticodon sequence that pairs with the SMC (the TREM);

contacting the cell with the composition comprising a TREM in an amount and/or for a time sufficient to modulate the tRNA pool in the cell,

thereby modulating the tRNA pool in the cell.

In an aspect, the disclosure provides a method of modulating expression of a protein in a cell, wherein the protein is encoded by a nucleic acid comprising an ORF, which ORF comprises a codon having a mutation, comprising:

contacting the cell with a composition comprising a TREM, a TREM core fragment, or a TREM fragment disclosed herein in an amount and/or for a time sufficient to modulate expression of the encoded protein,

wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with the codon having the mutation,

thereby modulating expression of the protein in the cell.

In another aspect, the disclosure provides a method of modulating expression of a protein in a subject, wherein the protein is encoded by a nucleic acid comprising an endogenous ORF, which ORF comprises a codon having a mutation, comprising:

contacting the subject with a composition comprising a TREM, a TREM core fragment, or a TREM fragment disclosed herein, in an amount and/or for a time sufficient to modulate expression of the encoded protein,

wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with the codon having the mutation,

thereby modulating expression of the protein in the subject.

In an embodiment of any of the methods disclosed herein, the mutation in the ORF is a nonsense mutation, e.g., resulting in a premature stop codon chosen from UAA, UGA or UAG. In an embodiment, the stop codon is UAA. In an embodiment, the stop codon is UGA. In an embodiment, the stop codon is UAG.

In an embodiment of any of the methods disclosed herein, the TREM comprises an anticodon that pairs with a stop codon.

TREMs of the disclosure include TREMs, TREM core fragments and TREM fragments. TREMs, TREM core fragments or TREM fragments can be modified with non-naturally occurring modifications to, e.g., increase the level and/or activity (e.g., stability) of the TREM. Pharmaceutical TREM compositions, e.g., comprising TREMs having a non-naturally occurring modification, can be administered to cells, tissues or subjects to modulate these functions, *e.g.*, *in vitro* or *in vivo*. Disclosed herein are TREMs, TREM core fragments or TREM fragments comprising non-naturally occurring modifications, TREM compositions, preparations, methods of making TREM compositions and preparations, and methods of using the same.

Additional features of any of the aforesaid TREMs, TREM core fragments, TREM fragments, TREM compositions, preparations, methods of making TREM compositions and preparations, and methods of using TREM compositions and preparations include one or more of the features in the Enumerated Embodiments, Figures, Description, Examples, or Claims.

Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following Enumerated Embodiments, Figures, Description, Examples, or Claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic illustrating the activity (log2 fold change) of modified TREMs containing a 2'-OMe, 2'-F, 2'-OME, 2'-deoxy, and PS modification at each position along an exemplary TREM sequence (TREM-Arg-TGA) over an unmodified TREM, as outlined in Example 11.

ENUMERATED EMBODIMENTS

Enumerated Embodiments I

1. A TREM comprising a sequence of Formula A:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2],

wherein:

independently, [L1] and [VL Domain], are optional;

one of [L1], [ASt Domain1], [L2]-[DH Domain], [L3], [ACH Domain], [VL Domain], [TH Domain], [L4], and [ASt Domain2] comprises a nucleotide having a non-naturally occurring modification; and

wherein:

(a) the TREM has the ability to: support protein synthesis, be charged by a synthetase, be bound by an elongation factor, introduce an amino acid into a peptide chain, support elongation, or support initiation;

(b) the TREM comprises at least X contiguous nucleotides without a non-naturally occurring modification, wherein X is greater than 10;

(c) at least 3, but less than all of the nucleotides of a type (e.g., A, T, C, G or U) comprise the same non-naturally occurring modification;

(d) at least X nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification, wherein X=1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50;

(e) no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) comprise a non-naturally occurring modification; and/or

(f) no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification.

2. The TREM of embodiment 1, comprising the feature provided in embodiment 1(a).

3. The TREM of embodiment 1, comprising the feature provided in embodiment 1(b).

4. The TREM of embodiment 1, comprising the feature provided in embodiment 1(c).

5. The TREM of embodiment 1, comprising the feature provided in embodiment 1(d).

6. The TREM of embodiment 1, comprising the feature provided in embodiment 1(e).

7. The TREM of embodiment 1, comprising the feature provided in embodiment 1(f).

8. The TREM of embodiment 1, comprising all of the features provided in embodiments 1(a)-(f).

9. The TREM of any one of embodiments 1-8, wherein the Domain comprising the non-naturally occurring modification has a function, e.g., a domain function described herein.

10. The TREM of any one of embodiments 1-8, comprising an [L1].

11. The TREM of any one of embodiments 1-8, comprising a [VL Domain].

12. The TREM of any one of embodiments 1-8, wherein: [L1] is a linker comprising a nucleotide having a non-naturally occurring modification.

13. The TREM of any one of embodiments 1-8, wherein [ASt Domain1 (AstD1)] comprises a nucleotide having a non-naturally occurring modification.

14. The TREM of any one of embodiments 1-8, wherein [L2] is a linker comprising a nucleotide having a non-naturally occurring modification.

15. The TREM of any one of embodiments 1-8, wherein [DH Domain (DHD)] comprises a nucleotide having a non-naturally occurring modification.

16. The TREM of any one of embodiments 1-8, wherein [L3] is a linker comprising a nucleotide having a non-naturally occurring modification.

17. The TREM of any one of embodiments 1-8, wherein [ACH Domain (ACHD)] comprises a nucleotide having a non-naturally occurring modification.

18. The TREM of any one of embodiments 1-8, wherein [VL Domain (VLD)] comprises a nucleotide having a non-naturally occurring modification.

19. The TREM of any one of embodiments 1-8, wherein [TH Domain (THD)] comprises a nucleotide having a non-naturally occurring modification.

20. The TREM of any one of embodiments 1-8, wherein [L4] is a linker comprises a nucleotide having a non-naturally occurring modification.

21. The TREM of any one of embodiments 1-8, wherein: [ASt Domain2 (AStD2)] comprises a nucleotide having a non-naturally occurring modification.

22. A TREM core fragment comprising a sequence of Formula B:

$[L1]_y$-[ASt Domain1]$_x$-$[L2]_y$-[DH Domain]$_y$-$[L3]_y$-[ACH Domain]$_x$-[VL Domain]$_y$-[TH Domain]$_y$-$[L4]_y$-[ASt Domain2]$_x$,

wherein:

x=1 and y=0 or 1;

one of [ASt Domain1], [ACH Domain], and [ASt Domain2] comprises a nucleotide having a non-naturally occurring modification; and

the TREM has the ability to: support protein synthesis; be able to be charged by a synthetase, be bound by an elongation factor, introduce an amino acid into a peptide chain, support elongation, or support initiation.

23. The TREM core fragment of embodiment 22, wherein AStD1 and AStD2 comprise an ASt Domain (AStD).

24. The TREM core fragment of embodiment 22, wherein the [ASt Domain 1], and/or [ASt Domain 2] comprising the non-naturally occurring modification has the ability to initiate or elongate a polypeptide chain.

25. The TREM core fragment of embodiment 22, wherein the [ACH Domain] comprising the non-naturally occurring modification has the ability to mediate pairing with a codon.

26. The TREM core fragment of embodiment 22, wherein y=1 for any one, two, three, four, five, six, all or a combination of [L1], [L2], [DH Domain], [L3], [VL Domain], [TH Domain], [L4].

27. The TREM core fragment of embodiment 22, wherein y=0 for any one, two, three, four, five, six, all or a combination of [L1], [L2], [DH Domain], [L3], [VL Domain], [TH Domain], [L4].

28. The TREM core fragment of embodiment 22, wherein y=1 for linker [L1], and L1 comprises a nucleotide having a non-naturally occurring modification.

29. The TREM core fragment of embodiment 22, wherein y=1 for linker [L2], and L2 comprises a nucleotide having a non-naturally occurring modification.

30. The TREM core fragment of embodiment 22, wherein y=1 for [DH Domain (DHD)], and DHD comprises a nucleotide having a non-naturally occurring modification.

31. The TREM core fragment of embodiment 30, wherein the DHD comprising the non-naturally occurring modification has the ability to mediate recognition of aminoacyl-tRNA synthetase.

32. The TREM core fragment of embodiment 22, wherein y=1 for linker [L3], and L3 comprises a nucleotide having a non-naturally occurring modification.

33. The TREM core fragment of embodiment 22, wherein y=1 for [VL Domain (VLD)], and VLD comprises a nucleotide having a non-naturally occurring modification.

34. The TREM core fragment of embodiment 22, wherein y=1 for [TH Domain (THD)], and THD comprises a nucleotide having a non-naturally occurring modification.

35. The TREM core fragment of embodiment 34, wherein the THD comprising the non-naturally occurring modification has the ability to mediate recognition of the ribosome.

36. The TREM core fragment of embodiment 22, wherein y=1 for linker [L4], and L4 comprises a nucleotide having a non-naturally occurring modification.

37. A TREM fragment comprising a portion of a TREM, wherein the TREM comprises a sequence of Formula A:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2], and wherein:

the TREM fragment comprises:

a non-naturally occurring modification; and

one, two, three or all or any combination of the following:

(a) a TREM half (*e.g.*, from a cleavage in the ACH Domain, *e.g.*, in the anticodon sequence, *e.g.*, a 5'half or a 3' half);

(b) a 5' fragment (*e.g.*, a fragment comprising the 5' end, *e.g.*, from a cleavage in a DH Domain or the ACH Domain);

(c) a 3' fragment (*e.g.*, a fragment comprising the 3' end, *e.g.*, from a cleavage in the TH Domain); or

(d) an internal fragment (*e.g.*, from a cleavage in any one of the ACH Domain, DH Domain or TH Domain).

38. The TREM of embodiment 37, wherein the TREM fragment comprise (a) a TREM half which comprises a nucleotide having a non-naturally occurring modification.

39. The TREM of embodiment 37, wherein the TREM fragment comprise (b) a 5' fragment which comprises a nucleotide having a non-naturally occurring modification.

40. The TREM of embodiment 37, wherein the TREM fragment comprise (c) a 3' fragment which comprises a nucleotide having a non-naturally occurring modification.

41. The TREM of embodiment 37, wherein the TREM fragment comprise (d) an internal fragment which comprises a nucleotide having a non-naturally occurring modification.

42. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM Domain comprises a plurality of nucleotides each having a non-naturally occurring modification.

43. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of AStD1 have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6 or 7.

44. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of AStD1 have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6 or 7.

45. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of AStD2 have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6 or 7.

46. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of AStD2 have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6 or 7.

47. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of ACHD have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6,7, 8, 9, or 10.

48. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of ACHD have a non-naturally occurring modification, wherein X is equal to or greater than 11, 12, 13, 14, 15, 16, or 17.

49. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of ACHD have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

50. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of ACHD have a non-naturally occurring modification, wherein X is equal to or greater than 11, 12, 13, 14, 15, or 16.

51. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of THD have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

52. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of THD have a non-naturally occurring modification, wherein X is equal to or greater than 11, 12, 13, 14, 15, 16, or 17.

53. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of THD have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

54. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of THD have a non-naturally occurring modification, wherein X is equal to or greater than 11, 12, 13, 14, 15, or 16.

55. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of DHD have a non-naturally occurring modification, wherein X is equal to or greater than 2, 3, 4, 5, 6,7, 8, 9 or 10.

56. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of DHD have a non-naturally occurring modification, wherein X is equal to or greater than 11, 12, 13, 14, 15, 16, 17, 18 or 19.

57. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of DHD have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

58. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than X of the nucleotides of DHD have a non-naturally occurring modification, wherein X is equal to or greater than 11, 12, 13, 14, 15, 16, 17, or 18.

59. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of the VLD have a non-naturally occurring modification, wherein X is equal to or greater than 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 50, 100, 150, 200 or 271.

60. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein all of the nucleotides of the AStD1, AStD2, ACHD, DHD, and/or THD have a non-naturally occurring modification.

61. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of AStD1 and/or

AStD2 do not have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6 or 7.

62. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of ACHD do not have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6,7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or 17.

63. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of THD do not have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6,7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or 17.

64. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of DHD do not have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6,7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19.

65. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of VLD do not have a non-naturally occurring modification, wherein X is equal to or greater than 1, 2, 3, 4, 5, 6,7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 50, 100, 150, 200 or 271.

66. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM Linker L2 comprises two nucleotides each having a non-naturally occurring modification.

67. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X of the nucleotides of the TREM Linker do not have a non-naturally occurring modification, wherein X is equal to 1 or 2.

68. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein:

each of a plurality of TREM Domains and Linkers comprises a nucleotide having a non-naturally occurring modification.

69. The TREM, TREM core fragment or TREM fragment of embodiment 68, wherein one of the TREM Domains and Linkers of the plurality comprises a plurality of nucleotides each having a non-naturally occurring modification.

70. The TREM, TREM core fragment or TREM fragment of any of the preceding embodiments, wherein the non-naturally occurring modification is a modification in a base or a backbone of a nucleotide, e.g., a modification chosen from any one of Tables 5-9.

71. The TREM, TREM core fragment or TREM fragment of any of the preceding embodiments, wherein the non-naturally occurring modification is a base modification chosen from a modification listed in Table 5.

72. The TREM, TREM core fragment or TREM fragment of any of the preceding embodiments, wherein the non-naturally occurring modification is a base modification chosen from a modification listed in Table 6.

73. The TREM, TREM core fragment or TREM fragment of any of the preceding embodiments, wherein the non-naturally occurring modification is a base modification chosen from a modification listed in Table 7.

74. The TREM, TREM core fragment or TREM fragment of any of the preceding embodiments, wherein the non-naturally occurring modification is a backbone base modification chosen from a modification listed in Table 8.

75. The TREM, TREM core fragment or TREM fragment of any of the preceding embodiments, wherein the non-naturally occurring modification is a backbone modification chosen from a modification listed in Table 9.

76. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, comprising a nucleotide of a first type comprising a non-naturally occurring modification.

77. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, comprising a nucleotide of a first type and a nucleotide of a second type comprising a non-naturally occurring modification.

78. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein the non-naturally occurring modification on the nucleotide of the first type and the non-naturally occurring modification on the nucleotide of the second type are the same non-naturally occurring modification.

79. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein the non-naturally occurring modification on the nucleotide of the first type and the non-naturally occurring modification on the nucleotide of the second type are different non-naturally occurring modifications.

80. The TREM, TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the first type is chosen from: A, T, C, G or U.

81. The TREM, TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the second type is chosen from: A, T, C, G or U.

82. The TREM, TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the first type is an A.

83. The TREM, TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the first type is a G.

84. The TREM, TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the first type is a C.

85. The TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the first type is a T.

86. The TREM, TREM core fragment or TREM fragment of embodiments 76 or 77, wherein the nucleotide of the first type is a U.

87. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein when the nucleotide of the first type is an A, the nucleotide of the second type is chosen from: T, C, G or U.

88. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein when the nucleotide of the first type is a G, the nucleotide of the second type is chosen from: T, C, A or U.

89. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein when the nucleotide of the first type is a C, the nucleotide of the second type is chosen from: T, A, G or U.

90. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein when the nucleotide of the first type is a T, the nucleotide of the second type is chosen from: A, C, G or U.

91. The TREM, TREM core fragment or TREM fragment of embodiment 77, wherein when the nucleotide of the first type is a U, the nucleotide of the second type is chosen from: T, C, G or A.

92. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the non-naturally modification is in a purine (A or G).

93. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the non-naturally modification is not in a purine (A or G).

94. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the non-naturally modification is in a pyrimidine (U, T or C).

95. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the non-naturally modification is not in a pyrimidine (U, T or C).

96. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the DHD has a first sequence, a second sequence and a third sequence, optionally wherein the first sequence and the third sequence form a stem and the second sequence forms a loop, e.g., under physiological conditions.

97. The TREM, TREM core fragment or TREM fragment of embodiment 96, wherein the DHD comprises a non-naturally occurring modification in the first sequence or the third sequence, e.g., in the stem.

98. The TREM, TREM core fragment or TREM fragment of embodiment 96, wherein the DHD comprises a non-naturally occurring modification in the second sequence, e.g., in the loop.

100. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the ACHD has a first sequence, a second sequence and a third sequence, optionally wherein the first sequence and the third sequence form a stem and the second sequence forms a loop, e.g., under physiological conditions.

101. The TREM, TREM core fragment or TREM fragment of embodiment 100, wherein the ACHD comprises a non-naturally occurring modification in the first sequence or the third sequence, e.g., in the stem.

102. The TREM, TREM core fragment or TREM fragment of embodiment 100, wherein the ACHD comprises a non-naturally occurring modification in the second sequence, e.g., in the loop.

103. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the THD has a first sequence, a second sequence and a third sequence, optionally wherein the first sequence and the third sequence form a stem and the second sequence forms a loop, e.g., under physiological conditions.

104. The TREM, TREM core fragment or TREM fragment of embodiment 103, wherein the THD comprises a non-naturally occurring modification in the first sequence or the third sequence, e.g., in the stem.

105. The TREM, TREM core fragment or TREM fragment of embodiment 103, wherein the THD comprises a non-naturally occurring modification in the second sequence, e.g., in the loop.

106. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the VLD comprises a variable region having 1-271 nucleotides.

107. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM comprises at least X contiguous nucleotides without a non-naturally occurring modification, wherein X is greater than 10.

108. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least 3, but less than all of the nucleotides of a type (e.g., A, T, C, G or U) comprise the same non-naturally occurring modification.

109. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein at least X nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification, wherein X=1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50.

110. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than 5, 10, or 15 of a type (e.g., A, T, C, G or U) comprise a non-naturally occurring modification.

111. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein no more than 5, 10, or 15 of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification.

112. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, which specifies X, wherein X is an amino acid selected from alanine, arginine, asparagine, aspartate, cysteine, glutamine, glutamate, glycine, histidine, isoleucine, methionine, leucine, lysine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

113. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, which recognizes a codon provided in Table 8 or Table 9.

114. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM is a cognate TREM.

115. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM is a non-cognate TREM.

116. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment, or TREM fragment is encoded by a sequence provided in Table 1, e.g., any one of SEQ ID NOs 1-451.

117. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment, or TREM fragment is encoded by a consensus sequence chosen from any one of SEQ ID NOs: 562-621.

118. The TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment, or TREM fragment is encoded by a consensus sequence chosen from any one of SEQ ID NOs: 622-1187.

119. A pharmaceutical composition comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37.

120. The pharmaceutical composition of embodiment 119, comprising a pharmaceutically acceptable component, *e.g.*, an excipient.

121. A lipid nanoparticle formulation comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37.

122. A method of making a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, comprising linking a first nucleotide to a second nucleotide to form the TREM.

123. The method of embodiment 122, wherein the TREM, TREM core fragment or TREM fragment is synthetic (e.g, non-naturally occurring).

124. The method of embodiment 122 or 123, wherein the synthesis is performed in vitro.

125. The method of embodiment 122, wherein the TREM, TREM core fragment or TREM fragment is made by cell-free solid phase synthesis.

126. A cell comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37.

127. A cell comprising a TREM, TREM core fragment or TREM fragment made according to the method of embodiment 122.

128. A method of modulating a tRNA pool in a cell comprising:

providing a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, and

contacting the cell with the TREM, TREM core fragment or TREM fragment,

thereby modulating the tRNA pool in the cell.

129. A method of contacting a cell, tissue, or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, comprising

contacting the cell, tissue or subject with the TREM, TREM core fragment or TREM fragment,

thereby contacting the cell, tissue, or subject with the TREM, TREM core fragment or TREM fragment.

130. A method of presenting a TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject with a TREM, TREM core fragment or TREM fragment, comprising

contacting the cell, tissue or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby presenting the TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject.

131. A method of forming a TREM, TREM core fragment or TREM fragment -contacted cell, tissue, or subject, comprising

contacting the cell, tissue or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby forming a TREM, TREM core fragment or TREM fragment -contacted cell, tissue, or subject.

132. A method of using a TREM, TREM core fragment or TREM fragment comprising,

contacting the cell, tissue or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby using the TREM.

133. A method of applying a TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject, comprising

contacting the cell, tissue or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby applying a TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject.

134. A method of exposing a cell, tissue, or subject to a TREM, comprising

contacting the cell, tissue or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby exposing a cell, tissue, or subject to a TREM, TREM core fragment or TREM fragment.

135. A method of forming an admixture of a TREM, TREM core fragment or TREM fragment and a cell, tissue, or subject, comprising

contacting the cell, tissue or subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby forming an admixture of a TREM, TREM core fragment or TREM fragment and a cell, tissue, or subject.

136. A method of delivering a TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject, comprising:

providing a cell, tissue, or subject, and contacting the cell, tissue, or subject, a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37.

137. A method, e.g., an ex vivo method, of modulating the metabolism, *e.g.*, the translational capacity of an organelle, comprising:

providing a preparation of an organelle, *e.g.*, mitochondria or chloroplasts, and contacting the organelle with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37.

138. A method of treating a subject, *e.g.*, modulating the metabolism, *e.g.*, the translational capacity of a cell, in a subject, comprising:

providing, *e.g.*, administering to the subject a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37,

thereby treating the subject.

139. A method of modulating a tRNA pool in a cell comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a first sequence, comprising:

optionally, acquiring knowledge of the abundance of one or both of (i) and (ii), e.g., acquiring knowledge of the relative amounts of: (i) and (ii) in the cell, wherein (i) is a tRNA moiety having an anticodon that pairs with the codon of the ORF having a first sequence (the first tRNA moiety) and (ii) is an isoacceptor tRNA moiety having an anticodon that pairs with a codon other than the codon having the first sequence (the second tRNA moiety) in the cell;

contacting the cell with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with: the codon having the first sequence; or the codon other than the codon having the first sequence, in an amount and/or for a time sufficient to modulate the relative amounts of the first tRNA moiety and the second tRNA moiety in the cell,

thereby modulating the tRNA pool in the cell.

140. A method of modulating a tRNA pool in a subject having an endogenous open reading frame (ORF), which ORF comprises a codon having a first sequence, comprising:

optionally, acquiring knowledge of the abundance of one or both of (i) and (ii), e.g., acquiring knowledge of the relative amounts of: (i) and (ii) in the subject, wherein (i) is a tRNA moiety having an anticodon that pairs with the codon of the ORF having a first sequence (the first tRNA moiety) and (ii) is an isoacceptor tRNA moiety having an anticodon that pairs with a codon other than the codon having the first sequence (the second tRNA moiety) in the subject;

contacting the subject with a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with: the codon having the first sequence; or the codon other than the codon having the first sequence, in an amount and/or for a time sufficient to modulate the relative amounts of the first tRNA moiety and the second tRNA moiety in the subject,

thereby modulating the tRNA pool in the subject.

141. A method of modulating a tRNA pool in a subject having an endogenous open reading frame (ORF) comprising a codon comprising a synonymous mutation (a synonymous mutation codon or SMC), comprising:

providing a composition comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment or TREM fragment comprises an isoacceptor tRNA moiety comprising an anticodon sequence that pairs with the SMC (the TREM);

contacting the subject with the composition in an amount and/or for a time sufficient to modulate the tRNA pool in the subject,

thereby modulating the tRNA pool in the subject.

142. A method of modulating a tRNA pool in a cell comprising an endogenous open reading frame (ORF) comprising a codon comprising a synonymous mutation (a synonymous mutation codon or SMC), comprising:

providing a composition comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, wherein the TREM, TREM core fragment or TREM fragment comprises an isoacceptor tRNA moiety comprising an anticodon sequence that pairs with the SMC (the TREM);

contacting the cell with the composition comprising a TREM in an amount and/or for a time sufficient to modulate the tRNA pool in the cell,

thereby modulating the tRNA pool in the cell.

143. A method of modulating expression of a protein in a cell, wherein the protein is encoded by a nucleic acid comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a mutation, comprising:

contacting the cell with a composition comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37 in an amount and/or for a time sufficient to modulate expression of the encoded protein,

wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with the codon having the mutation,

thereby modulating expression of the protein in the cell.

144. A method of modulating expression of a protein in a subject, wherein the protein is encoded by a nucleic acid comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a mutation, comprising:

contacting the subject with a composition comprising a TREM of any one of embodiments 1-8, the TREM core fragment of embodiment 22, or the TREM fragment of embodiment 37, in an amount and/or for a time sufficient to modulate expression of the encoded protein,

wherein the TREM, TREM core fragment or TREM fragment has an anticodon that pairs with the codon having the mutation,

thereby modulating expression of the protein in the subject.

145. The method of embodiment 143 or 144, wherein the mutation in the ORF is a nonsense mutation, e.g., resulting in a premature stop codon chosen from UAA, UGA or UAG.

146. The method of embodiment 143 or 144, wherein the TREM comprises an anticodon that pairs with a stop codon.

Enumerated Embodiments II

1000. A TREM comprising a nucleotide (at a position identified herein) comprising a non-naturally occurring modification or a nucleotide (at a position identified herein) lacking a non-naturally occurring modification.

1001. The TREM of embodiment 1000, comprising the following structure:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain]-[VL Domain]-[TH Domain]-[L4]-[ASt Domain2].

1002. A TREM comprising a sequence of Formula A:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain]-[VL Domain]-[TH Domain]-[L4]-[ASt Domain2],

wherein:

independently, [L1] and [VL Domain], are optional;

one of [L1], [ASt Domain1], [L2]-[DH Domain], [L3], [ACH Domain], [VL Domain], [TH Domain], [L4], and [ASt Domain2] comprises a nucleotide having a non-naturally occurring modification; and

wherein:

(a) the TREM has the ability to: (i) support protein synthesis, (ii) be charged by a synthetase, (iii) be bound by an elongation factor, (iv) introduce an amino acid into a peptide chain, (v) support elongation, or (vi) support initiation;

(b) the TREM comprises X_1 contiguous nucleotides without a non-naturally occurring modification, wherein X_1 is 3, 4, 5, 6, 7, 8, 9, 10 or greater;

(c) the TREM comprises X_2 non-naturally occurring modifications, wherein X_2 is, 2, 3, 4, or greater;

(d) the TREM comprises X_3 different non-naturally occurring modifications, wherein X_3 is, 2, 3, 4, or greater;

(e) 3 nucleotides, wherein less than all of the nucleotides of a type (e.g., A, T, C, G or U) comprise the same non-naturally occurring modification;

(f) X_4 nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification, wherein X_4 is equal to or greater than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50;

(g) no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) comprise a non-naturally occurring modification; and/or

(h) no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification; and/or the ACH Domain comprises a non-extended anticodon.

1003. The TREM of any preceding embodiment, wherein:

(a) the TREM has the ability to: (i) support protein synthesis, (ii) be charged by a synthetase, (iii) be bound by an elongation factor, (iv) introduce an amino acid into a peptide chain, (v) support elongation, or (vi) support initiation.

1004. The TREM of any preceding embodiment, wherein:

(b) the TREM comprises X_1 contiguous nucleotides without a non-naturally occurring modification, wherein X_1 is 10 or greater.

1005. The TREM of any preceding embodiment, wherein: the TREM comprises at X_2 non-naturally occurring modifications, wherein X_2 is, 2, 3, 4, or greater.

1006. The TREM of any preceding embodiment, wherein:

(c) the TREM comprises X_3 different non-naturally occurring modifications, wherein X_3 is, 2, 3, 4, or greater.

1007. The TREM of any preceding embodiment, wherein:

(d) 3 nucleotides, wherein less than all of the nucleotides of a type (e.g., A, T, C, G or U) comprise the same non-naturally occurring modification.

1008. The TREM of any preceding embodiment, wherein:

(e) X_4 nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification, wherein X_4 is equal to or greater than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50.

1009. The TREM of any preceding embodiment, wherein:

(f) no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) comprise a non-naturally occurring modification.

1010. The TREM of any preceding embodiment, wherein:

(g) no more than 5, 10, or 15 nucleotides of a type (e.g., A, T, C, G or U) do not comprise a non-naturally occurring modification; and/or the ACH Domain comprises a non-extended anticodon.

1011. The TREM of any preceding embodimentwherein the ACH Domain comprises a non-extended anticodon or does not include an extended anticodon.

1012. A TREM fragment comprising a portion of a TREM, wherein the TREM comprises a sequence of Formula A:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2], and wherein:

the TREM fragment comprises:

a non-naturally occurring modification; and

one, two, three or all or any combination of the following:

(a) a TREM half (*e.g.*, from a cleavage in the ACH Domain, *e.g.*, in the anticodon sequence, *e.g.*, a 5'half or a 3' half);

(b) a 5' fragment (*e.g.*, a fragment comprising the 5' end, *e.g.*, from a cleavage in a DH Domain or the ACH Domain);

(c) a 3' fragment (*e.g.*, a fragment comprising the 3' end, *e.g.*, from a cleavage in the TH Domain); or

(d) an internal fragment (*e.g.*, from a cleavage in any one of the ACH Domain, DH Domain or TH Domain).

1013. The TREM or TREM fragment of any of the above embodiments, comprising a non-naturally occurring modification on a nucleotide sugar moiety (2'-modification) or in the TREM backbone.

1014. The TREM or TREM fragment of any of the above embodiments, comprising a nucleotide comprising a 2' non-naturally occurring modification on the sugar moiety.

1015. The TREM or TREM fragment of any of the above embodiments, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622, nucleotides 1-85 of SEQ ID NO: 993, or nucleotides 1-75 of SEQ ID NO: 1079 is modified.

1016. The TREM or TREM fragment of embodiments 1000-1015, wherein the nucleotide is in the ASt Domain1.

1017. The TREM or TREM fragment of embodiments 1000-1016, wherein the nucleotide is in the DH Domain.

1018. The TREM or TREM fragment of embodiments 1000-1017, wherein the nucleotide is in the ACH Domain.

1019. The TREM or TREM fragment of embodiments 1000-1018, wherein the nucleotide is in the VL Domain.

1020. The TREM or TREM fragment of embodiments 1000-1019, wherein the nucleotide is in the TH Domain.

1021. The TREM or TREM fragment of embodiments 1000-1020, wherein the nucleotide is in the ASt Domain2.

1022. The TREM or TREM fragment of embodiments 1000-10021, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1023. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 1, 2, 4, 6, 10, 12, 13, 17, 18, 20, 22, 29, 30, 42, 43, 45, 50, 52, 56, 59, 61, 65, 66, 68, 69, 71, 72, and 73 of SEQ ID NO: 622 is modified.

1024. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 20, 29, 33, 40, 41, 44, 45, 48, 49, 50, 52, 53, 54, 56, 59, 61, 62, 63, 65, 67, 68, 69, 71, 72, 75, and 76 of SEQ ID NO: 622 is modified.

1025. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 1, 4, 14, 15, 16, 17, 20, 29, 44, 45, 47, 49, 50, 52, 54, 56, 57, 59, 65, 72, and 73 of SEQ ID NO: 622 is modified.

1026. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 3, 4, 5, 6, 14, 15, 16, 20, 22, 23, 33, 54, 59, 62, 63, 72, and 76 of SEQ ID NO: 622 is modified.

1027. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 1, 2, 3, 9, 14, 15, 16, 17, 18, 19, 20, 21, 35, 37, 38, 44, 45, 46, 52, 54, 55, 56, 57, 58, 73, and 74 of SEQ ID NO: 622 is modified.

1028. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 1, 17, 18, 20, 29, 30, 50, 52, and 73 of SEQ ID NO: 622 is modified.

1029. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 1, 4, 5, 34, 38, 39, 61, 79, 80, and 82 of SEQ ID NO: 993 is modified.

1030. The TREM or TREM fragment of embodiments 1000-1022, wherein the nucleotide corresponding to any one of nucleotides 1, 4, 12, 13, 17, 18, 23, 28, 29, 30, 38, 39, 41, 44, 48, 49, 51, 52, 53, 58, 60, 61, 63, 64, 65, 66, 68, 69, 71, 72, 73, 74, and 75 of SEQ ID NO: 1079 is modified.

1031. The TREM or TREM fragment of embodiments 1000-1014, wherein the 2' non-naturally occurring modification comprises an ester, halo, hydrogen, alkyl group.

1032. The TREM or TREM fragment of embodiments 1000-1014, wherein the 2' non-naturally occurring modification comprises a 2'-OMe moiety.

1033. The TREM or TREM fragment of embodiments 1000-1024, wherein the 2' non-naturally occurring modification comprises a 2'-MOE moiety.

1034. The TREM or TREM fragment of embodiments 1000-1014, wherein the 2' non-naturally occurring modification comprises a 2'-halo (e.g., 2'-F or 2'Cl).

1035. The TREM or TREM fragment of embodiments 1000-1014, wherein the 2' non-naturally occurring modification comprises a 2'-deoxy group (e.g., a 2'-H).

1036. The TREM or TREM fragment of any of embodiments 1000-1035, comprising a nucleotide that lacks a non-naturally occurring modification, e.g., lacks a 2' non-naturally occurring modification on a sugar moiety.

1037. The TREM or TREM fragment of any of embodiment 1036, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO:622 and lacks a non-naturally occurring modification.

1038. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in the ASt Domain1.

1039. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in the DH Domain.

1040. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in the ACH Domain.

1041. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in the VL Domain.

1042. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in the TH Domain.

1043. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in the ASt Domain2.

1044. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1045. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide corresponds to any one of nucleotides 1-76 of SEQ ID NO: 622 and lacks a non-naturally occurring modification, e.g., 2' non-naturally occurring modification on a sugar.

1046. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide corresponding to any one of nucleotides 1-85 of SEQ ID NO: 993 lacks a non-naturally occurring modification, e.g., a 2' non-naturally occurring modification on a sugar.

1047. The TREM or TREM fragment of embodiment 1036, wherein the nucleotide corresponding to any one of nucleotides 1-75 of SEQ ID NO: 1079 lacks a non-naturally occurring modification, e.g., a 2' non-naturally occurring modification on a sugar.

1048. The TREM or TREM fragment of any one of embodiments 1000-1047, comprising a nucleotide comprising a 2' OMe non-naturally occurring modification.

1049. The TREM or TREM fragment of embodiment 1000-1048, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622 is modified.

1050. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in the ASt Domain1.

1051. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in the DH Domain.

1052. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in the ACH Domain.

1053. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in the VL Domain.

1054. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in the TH Domain.

1055. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in the ASt Domain2.

1056. The TREM or TREM fragment of any of embodiment 1048-1049, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1057. The TREM or TREM fragment of any of embodiment 1048-1056, wherein the nucleotide corresponding to any one of nucleotides 1, 2, 4, 6, 10, 12, 13, 17, 18, 20, 22, 29, 30, 42, 43, 45, 50, 52, 56, 59, 61, 65, 66, 68, 69, 71, 72, and 73 of SEQ ID NO: 622 is modified (e.g., a sequence in Table 15).

1058. The TREM or TREM fragment of any of embodiment 1000-1047, comprising a nucleotide comprising a nucleotide that lacks a non-naturally occurring modification, e.g., lacks a 2' OMe modification on a sugar moiety.

1059. The TREM or TREM fragment of embodiment 1058, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622 lacks a non-naturally occurring modification, e.g., lacks a 2' OMe modification on a sugar moiety.

1060. The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in the ASt Domain1.

1061. The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in the DH Domain.

1062. The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in the ACH Domain.

1063 The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in the VL Domain.

1064. The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in the TH Domain.

1065. The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in the ASt Domain2.

1066. The TREM or TREM fragment of any of embodiment 1058-1059, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1067. The TREM or TREM fragment of any of embodiment 1000-1066, comprising a nucleotide comprising a 2' halo, e.g., a 2' fluoro, non-naturally occurring modification on a sugar moiety.

1068. The TREM or TREM fragment of embodiment 1067, wherein the 2' halo is 2' fluoro.

1069. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide corresponding to any of nucleotides 1-76 of SEQ ID NO: 622 is modified.

1070. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide is in the ASt Domain1.

1071. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide is in the DH Domain.

1072. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide is in the ACH Domain.

1073. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide is in the VL Domain.

1074. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide is in the TH Domain.

1075. The TREM or TREM fragment of embodiment 1067-1068, wherein the nucleotide is in the ASt Domain2.

1076. The TREM or TREM fragment of any of embodiment 1067-1068, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1077. The TREM or TREM fragment of any of embodiment 1067-1076, wherein the nucleotide corresponding to any one of nucleotides 20, 29, 33, 40, 41, 44, 45, 48, 49, 50, 52, 53, 54, 56, 59, 61, 62, 63, 65, 67, 68, 69, 71, 72, 75, and 76 of SEQ ID NO: 622 is modified.

1078. The TREM or TREM fragment of any of embodiment 1000-1035, comprising a nucleotide that lacks a non-naturally occurring modification, e.g., lacks a 2' halo, e.g., a 2' fluoro, non-naturally occurring modification on a sugar moiety.

1079. The TREM or TREM fragment of embodiment 1078, wherein 2' halo is 2' fluoro.

1080. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622 and lacks a non-naturally occurring modification.

1081. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in the ASt Domain1.

1082. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in the DH Domain.

1083. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in the ACH Domain.

1084. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in the VL Domain.

1085. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in the TH Domain.

1086. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in the ASt Domain2.

1087. The TREM or TREM fragment of any of embodiments 1078-1079, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1088. The TREM or TREM fragment of any of embodiment 1000-1013, wherein the nucleotide corresponding to any one of nucleotides 20, 29, 33, 40, 41, 44, 45, 48, 49, 50, 52, 53, 54, 56, 59, 61, 62, 63, 67, 68, 69, 71, 72, 75, and 76 of SEQ ID NO: 622 lacks a non-naturally occurring modification, e.g., a 2' fluoro non-naturally occurring modification on the sugar.

1089. The TREM or TREM fragment of any of embodiments 1000-1088, wherein the non-naturally occurring modification comprises a 2' deoxy nucleotide.

1090. The TREM or TREM fragment of embodiment 1084, wherein the 2' deoxy nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622 is modified.

1091. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the 2' deoxy nucleotide is in the ASt Domain1.

1092. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the 2' deoxy nucleotide is in the DH Domain.

1093. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the 2' deoxy nucleotide is in the ACH Domain.

1094. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the 2' deoxy nucleotide is in the VL Domain.

1095. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the 2' deoxy nucleotide is in the TH Domain.

1096. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the 2' deoxy nucleotide is in the ASt Domain2.

1097. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1098. The TREM or TREM fragment of any of embodiments 1089-1090, wherein the nucleotide corresponding to any one of nucleotides 3, 4, 5, 6, 14, 15, 16, 20, 22, 23, 33, 54, 59, 62, 63, 72, and 76 of SEQ ID NO: 622 is a 2' deoxy nucleotide.

1099. The TREM or TREM fragment of any of embodiments 1000-1092, comprising an 2'-OH nucleotide.

1100. The TREM or TREM fragment of embodiment 1099, wherein the 2'-OH nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO:622.

1101. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in the ASt Domain1.

1102. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in the DH Domain.

1103. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in the ACH Domain.

1104. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in the VL Domain.

1105. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in the TH Domain.

1106. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in the ASt Domain2.

1107. The TREM or TREM fragment of any of embodiments 1099-1100, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1109. The TREM or TREM fragment of any of embodiment 1000-1100, wherein the nucleotide corresponding to any one of nucleotides 3, 4, 5, 6, 14, 15, 16, 20, 22, 23, 33, 54, 59, 62, 63, 72, and 76 of SEQ ID NO: 622 is a 2'-OH nucleotide.

1110. The TREM or TREM fragment of any of embodiments 1000-1109, wherein the non-naturally occurring modification comprises a 2' methoxyethyl (MOE) nucleotide.

1111. The TREM or TREM fragment of embodiment 1110, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622.

1112. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the 2'-MOE nucleotide is in the ASt Domain1.

1113. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the 2'-MOE nucleotide is in the DH Domain.

1114. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the 2'-MOE nucleotide is in the ACH Domain.

1115. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the 2'-MOE nucleotide is in the VL Domain.

1116. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the 2'-MOE nucleotide is in the TH Domain.

1117. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the 2'-MOE nucleotide is in the ASt Domain2.

1118. The TREM or TREM fragment of any of embodiments 1110-1111, wherein the2'-MOE nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1119. The TREM or TREM fragment of any of embodiments 1110-1118, wherein the nucleotide corresponding to any one of nucleotides 1, 4, 14, 15, 16, 17, 20, 29, 44, 45, 47, 49, 50, 52, 54, 56, 57, 59, 65, 72, and 73 of SEQ ID NO: 622 is a 2'-MOE nucleotide.

1120. The TREM or TREM fragment of any of embodiments 1000-1109, comprising a nucleotide that lacks a non-naturally occurring modification, e.g., lacks a 2-MOE, e.g., a non-naturally occurring modification on a sugar moiety.

1121. The TREM or TREM fragment of embodiment 1120, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622 and lacks a non-naturally occurring modification.

1122. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in the ASt Domain1.

1123. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in the DH Domain.

1124. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in the ACH Domain.

1125. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in the VL Domain.

1126. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in the TH Domain.

1127. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in the ASt Domain2.

1128. The TREM or TREM fragment of any of embodiments 1120-1121, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1129. The TREM or TREM fragment of any of embodiments 1120-1128, wherein the nucleotide corresponding to any one of nucleotides 1, 4, 14, 15, 16, 17, 20, 29, 44, 45, 47, 49, 50, 52, 54, 56, 57, 59, 65, 72, and 73 of SEQ ID NO: 622 and lacks a 2'-MOE nucleotide.

1130. The TREM or TREM fragment of any of embodiment 1000-1129, comprising a modified backbone, e.g., a modification of the phosphate moiety attached to the 5' or 3' carbon of the sugar moiety of a nucleotide.

1131. The TREM or TREM fragment of embodiment 1130, wherein the phosphate moiety attached to the 5' carbon is modified.

1132. The TREM or TREM fragment of embodiment 1130, wherein the phosphapte moiety attached to the 3' carbon is modified.

1133. The TREM or TREM fragment of embodiment 1130, wherein the modification comprises a phosphothioate moiety.

1134. The TREM or TREM fragment of embodiments 1130-1133, wherein the nucleotide corresponds to any of nucleotides 1-76 of SEQ ID NO: 622 is modified.

1135. The TREM or TREM fragment of embodiments 1130-1133, wherein the modified nucleotide is in the ASt Domain1.

1136. The TREM or TREM fragment of embodiments 1130-1133, wherein the modified nucleotide is in the DH Domain.

1137. The TREM or TREM fragment of embodiments 1130-1133, wherein the modified nucleotide is in the ACH Domain.

1138. The TREM or TREM fragment of embodiments 1130-1133, wherein the modified nucleotide is in the VL Domain.

1139. The TREM or TREM fragment of embodiments 1130-1133, wherein the modified nucleotide is in the TH Domain.

1140. The TREM or TREM fragment of embodiments 1130-1133, wherein the modified nucleotide is in the ASt Domain2.

1141. The TREM or TREM fragment of any of embodiments 1130-1133, wherein the nucleotide is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1142. The TREM or TREM fragment of embodiments 1130-1133, wherein the nucleotide corresponding to any one of nucleotides 1, 2, 3, 9, 14, 15, 16, 17, 18, 19, 20, 21, 35, 37, 38, 44,

45, 46, 52, 54, 55, 56, 57, 58, 73, and 74 of SEQ ID NO: 622 is backbone modified, e.g., with a phosphorothioate moiety.

1142. The TREM or TREM fragment of embodiments 1130-1141, wherein the nucleotide corresponding to any one of nucleotides 14, 15, 16, 17, 18, 20, 44, 45, 47, 54, 56, 57, and 59 of SEQ ID NO: 622 is backbone modified, e.g., with a phosphorothioate moiety.

1143. The TREM or TREM fragment of embodiments 1000-1142, lacking a backbone modification, e.g., a phosphorothioate moiety.

1144. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified corresponds to any of nucleotides 1-76 of SEQ ID NO: 622.

1145. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in the ASt Domain1.

1146. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in the DH Domain.

1147. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in the ACH Domain.

1148. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in the VL Domain.

1149. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in the TH Domain.

1150. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in the ASt Domain2.

1151. The TREM or TREM fragment of embodiment 1143, wherein the nucleotide which is not backbone modified is in a linker domain (e.g., [L1], [L2], [L3], or [L4]).

1152. The TREM or TREM fragment of any of embodiments 1000-1151, wherein the nucleotide corresponding to any one of nucleotides 1, 2, 3, 9, 14, 15, 16, 17, 18, 19, 20, 21, 35, 37, 38, 44, 45, 46, 52, 54, 55, 56, 57, 58, 73, and 74 of SEQ ID NO: 622 is not backbone modified.

1153. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 15 is modified with a 2'-O Me.

1154. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 15 is modified with a 2'-O Me.

1155. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 15 is modified with a 2'-O Me.

1156. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 15 is not modified.

1157. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 15 is not modified.

1158. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 15 is not modified.

1159. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 21 is modified with a 2'-O Me.

1160. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 21 is modified with a 2'-O Me.

1161. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 21 is modified with a 2'-O Me.

1162. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 21 is not modified.

1163. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 21 is not modified.

1164. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 21 is not modified.

1165. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 22 is modified with a 2'-O Me.

1166. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 22 is modified with a 2'-O Me.

1167. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 22 is modified with a 2'-O Me.

1168. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 22 is not modified.

1169. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 22 is not modified.

1170. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 22 is not modified.

1171 The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 17 is modified with a 2'-MOE.

1172. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 17 is modified with a 2'-MOE.

1173.The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 17 is modified with a 2'-MOE.

1174. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 17 is not modified.

1175. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 17 is not modified.

1176. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 17 is not modified.

1177. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 16 is modified with a 2'- fluoro.

1178. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 16 is modified with a 2'- fluoro.

1179. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 16 is modified with a 2'- fluoro.

1180. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 16 is not modified.

1181. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 16 is not modified.

1182. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 16 is not modified.

1183. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 18 is modified to be a 2'- deoxy.

1184. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 18 is modified to be a 2'- deoxy.

1185. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 18 is modified to be a 2'- deoxy.

1186. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 18 is not modified.

1187. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 18 is not modified.

1188. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 18 is not modified.

1189. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 19 comprises a phosphorothate.

1190. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 19 comprises a phosphorothate.

1191. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 19 comprises a phosphorothate.

1192. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 3 for the 100 nm for the sequence in Table 19 is not modified.

1193. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 2 for the 100 nm for the sequence in Table 19 is not modified.

1194. The TREM or TREM fragment of any of embodiments 1000-1152, wherein a position corresponding to a modified position having a value of 1 for the 100 nm for the sequence in Table 19 is not modified.

1195. The TREM or TREM fragment of any of embodiments 1000-1152, wherein the TREM comprises an anticodon specific for an amino acid from Table 1.

1196. The TREM or TREM fragment of any of embodiments 1000-1152, wherein the TREM comprises an anticodon of Table 1.

1197. The TREM or TREM fragment of any of embodiments 1000-1196, comprising a first and a second non-naturally occurring modification.

1198. The TREM or TREM fragment of embodiment 1197, comprising comprising a third non-naturally occurring modification.

1199. The or TREM fragment of any of embodiments 1197-1198, comprising, wherein the first and second non-naturally occurring modifications are the same non-naturally occurring modification.

1200. The TREM or TREM fragment of any of embodiments 1197-1198, comprising wherein the first and second non-naturally occurring modifications are different non-naturally occurring modifications.

1201. The TREM or TREM fragment of any of embodiments 1197-1198, comprising wherein the first and second non-naturally occurring modification are on the same nucleotide.

1202. The TREM or TREM fragment of any of embodiments 1197-1198, wherein the first and second non-naturally occurring modification are on the different nucleotides.

1203. The TREM or TREM fragment of any of embodiments 1197-1198, wherein the first and second non-naturally occurring modifications are in the same domain.

1204. The TREM or TREM fragment of any of embodiments 1197-1198, wherein the first and second non-naturally occurring modifications are in different domains.

1205. The TREM or TREM fragment of any one the preceding embodiments, wherein the domain comprising the non-naturally occurring modification has a function, e.g., a domain function described herein.

1206. The TREM or TREM fragment of any of the preceding embodiments, wherein the TREM has at least X % sequence sequence identity with a sequence described herein, e.g., with SEQ ID NO: 622, SEQ ID NO: 993, or SEQ ID NO: 1079, or a consensus sequence disclosed herein, e.g., from Table 9 or 10, wherein X=60, 70, 75, 80, 85, 90, or 95.

1207. The TREM or TREM fragment of embodiment 1206, wherein X=60.

1208. The TREM or TREM fragment of embodiment 1206, wherein X=70.

1209. The TREM or TREM fragment of embodiment 1206, wherein X=75.

1210. The TREM or TREM fragment of embodiment 1206, wherein X=80.

1211. The TREM or TREM fragment of embodiment 1206, wherein X=85.

1212. The TREM or TREM fragment of embodiment 1206, wherein X=90.

1213. The TREM or TREM fragment of embodiment 1206, wherein X=95.

1214. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of any of Tables 15-22.

1215. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 15.

1216. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 16.

1217. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 17.

1218. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 18.

1219. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 19.

1220. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 20.

1221. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 21.

1222. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a position corresponding to a position that is modified in a row of Table 22.

1223. The TREM or TREM fragment of any of embodiments 1001-1213, having a modified nucleotide at a first and a modified nucleotide at a second position, wherein the first and second positions correspond to positions that are modified in any one row of Table 22.

1224. A pharmaceutical composition comprising a TREM or TREM fragment of any of the preceding embodiments.

1225. The pharmaceutical composition of embodiment 1224, comprising a pharmaceutically acceptable component, *e.g.*, an excipient.

1226. A lipid nanoparticle formulation comprising a TREM or TREM fragment of any one of embodiments 1000-1213, or a pharmaceutical composition of any one of claims 1224-1225.

1227. A method of making a TREM or TREM fragment of any of embodiments 1000-1213, comprising linking a first nucleotide to a second nucleotide to form the TREM or TREM fragment.

1228. The method of embodiment 1227, wherein the TREM or TREM fragment is non-naturally occurring (e.g., synthetic).

1229. The method of embodiment 1227, wherein the synthesis is performed in vitro.

1230. The method of embodiment 1227, wherein the TREM or TREM fragment is made by cell-free solid phase synthesis.

1231. A cell comprising a TREM or TREM fragment of any of embodiments 1000-1213.

1232. A method of modulating a tRNA pool in a cell comprising:
providing a TREM or TREM fragment of any of embodiments 1000-1213, and
contacting the cell with the TREM,
thereby modulating the tRNA pool in the cell.

1233. A method of contacting a cell, tissue, or subject with a TREM or TREM fragment of any of embodiments 1000-1213, comprising
contacting the cell, tissue or subject with the TREM,
thereby contacting the cell, tissue, or subject with the TREM.

1234. A method of presenting a TREM or TREM fragment, to a cell, tissue, or subject , comprising
contacting the cell, tissue or subject with a TREM or TREM fragment of any of embodiments 1000-1213,
thereby presenting the TREM, TREM core fragment or TREM fragment to a cell, tissue, or subject.

1235. A method of forming a TREM-contacted cell, tissue, or subject, comprising:
contacting the cell, tissue or subject with a TREM or TREM fragment of any of embodiments 1000-1213,
thereby forming a TREM-contacted cell, tissue, or subject.

1236. A method of using a TREM comprising,
contacting a cell, tissue or subject with a TREM or TREM fragment of any of embodiments 1000-1213,
thereby using the TREM.

1237. A method of applying a TREM to a cell, tissue, or subject, comprising

contacting the cell, tissue or subject with a TREM or TREM fragment of any of embodiments 1000-1213,
thereby applying a TREM to a cell, tissue, or subject.

1238. A method of exposing a cell, tissue, or subject to a TREM, comprising
contacting the cell, tissue or subject with a TREM or TREM fragment of any of embodiments 1000-1213,
thereby exposing a cell, tissue, or subject to a TREM.

1239. A method of forming an admixture of a TREM, and a cell, tissue, or subject, comprising
contacting the cell, tissue or subject with a TREM or TREM fragment of any of embodiments 1000-1213,
thereby forming an admixture of a TREM and a cell, tissue, or subject.

1240. A method of delivering a TREM to a cell, tissue, or subject, comprising:
providing a cell, tissue, or subject, and contacting the cell, tissue, or subject, a TREM or TREM fragment of any of embodiments 1000-1213.

1241. A method, e.g., an ex vivo method, of modulating the metabolism, *e.g.*, the translational capacity of an organelle, comprising:
providing a preparation of an organelle, *e.g.*, mitochondria or chloroplasts, and contacting the organelle with a TREM or TREM fragment of any of embodiments 1000-1213.

1242. A method of treating a subject, *e.g.*, modulating the metabolism, *e.g.*, the translational capacity of a cell, in a subject, comprising:
providing, *e.g.*, administering to the subject a TREM or TREM fragment of any of embodiments 1000-1213,
thereby treating the subject.

1243. A method of modulating a tRNA pool in a cell comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a first sequence, comprising:

optionally, acquiring knowledge of the abundance of one or both of (i) and (ii), e.g., acquiring knowledge of the relative amounts of: (i) and (ii) in the cell, wherein (i) is a tRNA moiety having an anticodon that pairs with the codon of the ORF having a first sequence (the first tRNA moiety) and (ii) is an isoacceptor tRNA moiety having an anticodon that pairs with a codon other than the codon having the first sequence (the second tRNA moiety) in the cell;

contacting the cell with a TREM or TREM fragment of any of embodiments 1000-1213, wherein the TREM has an anticodon that pairs with: the codon having the first sequence; or the codon other than the codon having the first sequence, in an amount and/or for a time sufficient to modulate the relative amounts of the first tRNA moiety and the second tRNA moiety in the cell,

thereby modulating the tRNA pool in the cell.

1244. A method of modulating a tRNA pool in a subject having an endogenous open reading frame (ORF), which ORF comprises a codon having a first sequence, comprising:

optionally, acquiring knowledge of the abundance of one or both of (i) and (ii), e.g., acquiring knowledge of the relative amounts of: (i) and (ii) in the subject, wherein (i) is a tRNA moiety having an anticodon that pairs with the codon of the ORF having a first sequence (the first tRNA moiety) and (ii) is an isoacceptor tRNA moiety having an anticodon that pairs with a codon other than the codon having the first sequence (the second tRNA moiety) in the subject;

contacting the subject with a TREM or TREM fragment of any of embodiments 1000-1213, wherein the TREM has an anticodon that pairs with: the codon having the first sequence; or the codon other than the codon having the first sequence, in an amount and/or for a time sufficient to modulate the relative amounts of the first tRNA moiety and the second tRNA moiety in the subject,

thereby modulating the tRNA pool in the subject.

1245. A method of modulating a tRNA pool in a subject having an endogenous open reading frame (ORF) comprising a codon comprising a synonymous mutation (a synonymous mutation codon or SMC), comprising:

providing a composition comprising a TREM or TREM fragment of any of embodiments 1000-1213, wherein the TREM comprises an isoacceptor tRNA moiety comprising an anticodon sequence that pairs with the SMC (the TREM);

contacting the subject with the composition in an amount and/or for a time sufficient to modulate the tRNA pool in the subject,

thereby modulating the tRNA pool in the subject.

1246. A method of modulating a tRNA pool in a cell comprising an endogenous open reading frame (ORF) comprising a codon comprising a synonymous mutation (a synonymous mutation codon or SMC), comprising:

providing a composition comprising a TREM or TREM fragment of any of embodiments 1000-1213, wherein the TREM comprises an isoacceptor tRNA moiety comprising an anticodon sequence that pairs with the SMC (the TREM);

contacting the cell with the composition comprising a TREM in an amount and/or for a time sufficient to modulate the tRNA pool in the cell,

thereby modulating the tRNA pool in the cell.

1247. A method of modulating expression of a protein in a cell, wherein the protein is encoded by a nucleic acid comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a mutation, comprising:

contacting the cell with a composition comprising a TREM or TREM fragment of any of embodiments 1000-1213, in an amount and/or for a time sufficient to modulate expression of the encoded protein,

wherein the TREM has an anticodon that pairs with the codon having the mutation,

thereby modulating expression of the protein in the cell.

1248. A method of modulating expression of a protein in a subject, wherein the protein is encoded by a nucleic acid comprising an endogenous open reading frame (ORF), which ORF comprises a codon having a mutation, comprising:

contacting the subject with a composition comprising a TREM or TREM fragment of any of embodiments 1000-1213, in an amount and/or for a time sufficient to modulate expression of the encoded protein,

wherein the TREM has an anticodon that pairs with the codon having the mutation,

thereby modulating expression of the protein in the subject.

1249. The method of embodiment 1247 or 1248, wherein the mutation in the ORF is a nonsense mutation, e.g., resulting in a premature stop codon chosen from UAA, UGA or UAG.

1250. The method of embodiment 1247 or 1248, wherein the TREM comprises an anticodon that pairs with a stop codon.

Other features, objects, and advantages of the invention will be apparent from the description and from the claims.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

The present disclosure features tRNA-based effector molecules (TREMs) comprising a non-naturally occurring modification and methods relating thereto. As disclosed herein, TREMs are complex molecules which can mediate a variety of cellular processes. Pharmaceutical TREM compositions, e.g., TREMs comprising a non-naturally occurring modification, can be administered to a cell, a tissue, or to a subject to modulate these functions.

Definitions

A "nucleotide," as that term is used herein, refers to an entity comprising a sugar, typically a pentameric sugar; a nucleobase; and a phosphate linking group. In an embodiment, a nucleotide comprises a naturally occurring, e.g., naturally occurring in a human cell, nucleotide, e.g., an adenine, thymine, guanine, cytosine, or uracil nucleotide.

A "modification," as that term is used herein with reference to a nucleotide, refers to a modification of the chemical structure, e.g., a covalent modification, of the subject nucleotide. The modification can be naturally occurring or non-naturally occurring. In an embodiment, the modification is non-naturally occurring. In an embodiment, the modification is naturally

occurring. In an embodiment, the modification is a synthetic modification. In an embodiment, the modification is a modification provided in Tables 5, 6, 7 , 8 or 9.

A "non-naturally occurring modification," as that term is used herein with reference to a nucleotide, refers to a modification that: (a) a cell, e.g., a human cell, does not make on an endogenous tRNA; or (b) a cell, e.g., a human cell, can make on an endogenous tRNA but wherein such modification is in a location in which it does not occur on a native tRNA, e.g., the modification is in a domain, linker or arm, or on a nucleotide and/or at a position within a domain, linker or arm, which does not have such modification in nature. In either case, the modification is added synthetically, e.g., in a cell free reaction, e.g., in a solid state or liquid phase synthetic reaction. In an embodiment, the non-naturally occurring modification is a modification that is not present (in identity, location or position) if a sequence of the TREM is expressed in a mammalian cell, e.g., a HEK293 cell line. Exemplary non-naturally occurring modifications are found in Tables 5, 6, 7, 8 or 9.

A "non-naturally modified nucleotide," as that term is used herein, refers a nucleotide comprising a non-naturally occurring modification on or of a sugar, nucleobase, or phosphate moiety.

A "naturally occurring nucleotide," as that term is used herein, refers to a nucleotide that does not comprise a non-naturally occurring modification. In an embodiment, it includes a naturally occurring modification.

A "tRNA-based effector molecule" or "TREM," as that term is used herein, refers to an RNA molecule comprising a structure or property from (a)-(v) below, and which is a recombinant TREM, a synthetic TREM, or a TREM expressed from a heterologous cell. The TREMs described in the present invention are synthetic molecules and are made, e.g., in a cell free reaction, e.g., in a solid state or liquid phase synthetic reaction. TREMs are chemically distinct, e.g., in terms of primary sequence, type or location of modifications from the endogenous tRNA molecules made in cells, e.g., in mammalian cells, e.g., in human cells. A TREM can have a plurality (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9) of the structures and functions of (a)-(v).

In an embodiment, a TREM is non-native, as evaluated by structure or the way in which it was made.

In an embodiment, a TREM comprises one or more of the following structures or properties:

(a') an optional linker region of a consensus sequence provided in the "Consensus Sequence" section, *e.g.*, a Linker 1 region;

(a) an amino acid attachment domain that binds an amino acid, *e.g.*, an acceptor stem domain (AStD), wherein an AStD comprises sufficient RNA sequence to mediate, *e.g.*, when present in an otherwise wildtype tRNA, acceptance of an amino acid, *e.g.*, its cognate amino acid or a non-cognate amino acid, and transfer of the amino acid (AA) in the initiation or elongation of a polypeptide chain. Typically, the AStD comprises a 3'-end adenosine (CCA) for acceptor stem charging which is part of synthetase recognition. In an embodiment the AStD has at least 75, 80, 85, 85, 90, 95, or 100% identity with a naturally occurring AStD, *e.g.*, an AStD encoded by a nucleic acid in Table 1. In an embodiment, the TREM can comprise a fragment or analog of an AStD, *e.g.*, an AStD encoded by a nucleic acid in Table 1, which fragment in embodiments has AStD activity and in other embodiments does not have AStD activity. (One of ordinary skill can determine the relevant corresponding sequence for any of the domains, stems, loops, or other sequence features mentioned herein from a sequence encoded by a nucleic acid in Table 1. *E.g.*, one of ordinary skill can determine the sequence which corresponds to an AStD from a tRNA sequence encoded by a nucleic acid in Table 1.)

In an embodiment the AStD falls under the corresponding sequence of a consensus sequence provided in the "Consensus Sequence" section, or differs from the consensus sequence by no more than 1, 2, 5, or 10 positions;

In an embodiment, the AStD comprises residues R_1-R_2-R_3-R_4 -R_5-R_6-R_7 and residues R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71} of Formula I $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the AStD comprises residues R_1-R_2-R_3-R_4 -R_5-R_6-R_7 and residues R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71} of Formula II $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the AStD comprises residues R_1-R_2-R_3-R_4 -R_5-R_6-R_7 and residues R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71} of Formula III $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

(a'-1) a linker comprising residues R_8-R_9 of a consensus sequence provided in the "Consensus Sequence" section, *e.g.*, a Linker 2 region;

(b) a dihydrouridine hairpin domain (DHD), wherein a DHD comprises sufficient RNA sequence to mediate, *e.g.*, when present in an otherwise wildtype tRNA, recognition of aminoacyl-tRNA synthetase, *e.g.*, acts as a recognition site for aminoacyl-tRNA synthetase for

amino acid charging of the TREM. In embodiments, a DHD mediates the stabilization of the TREM's tertiary structure. In an embodiment the DHD has at least 75, 80, 85, 85, 90, 95, or 100% identity with a naturally occurring DHD, *e.g.*, a DHD encoded by a nucleic acid in Table 1. In an embodiment, the TREM can comprise a fragment or analog of a DHD, *e.g.*, a DHD encoded by a nucleic acid in Table 1, which fragment in embodiments has DHD activity and in other embodiments does not have DHD activity.

In an embodiment the DHD falls under the corresponding sequence of a consensus sequence provided in the "Consensus Sequence" section, or differs from the consensus sequence by no more than 1, 2, 5, or 10 positions;

In an embodiment, the DHD comprises residues R_{10}-R_{11}-R_{12}-R_{13}-R_{14} R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28} of Formula I $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the DHD comprises residues R_{10}-R_{11}-R_{12}-R_{13}-R_{14} R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28} of Formula II $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the DHD comprises residues R_{10}-R_{11}-R_{12}-R_{13}-R_{14} R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28} of Formula III $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

(b'-1) a linker comprising residue R_{29} of a consensus sequence provided in the "Consensus Sequence" section, *e.g.*, a Linker 3 region;

(c) an anticodon that binds a respective codon in an mRNA, *e.g.*, an anticodon hairpin domain (ACHD), wherein an ACHD comprises sufficient sequence, *e.g.*, an anticodon triplet, to mediate, *e.g.*, when present in an otherwise wildtype tRNA, pairing (with or without wobble) with a codon; In an embodiment the ACHD has at least 75, 80, 85, 85, 90, 95, or 100% identity with a naturally occurring ACHD, *e.g.*, an ACHD encoded by a nucleic acid in Table 1. In an embodiment, the TREM can comprise a fragment or analog of an ACHD, *e.g.*, an ACHD encoded by a nucleic acid in Table 1, which fragment in embodiments has ACHD activity and in other embodiments does not have ACHD activity.

In an embodiment the ACHD falls under the corresponding sequence of a consensus sequence provided in the "Consensus Sequence" section, or differs from the consensus sequence by no more than 1, 2, 5, or 10 positions;

In an embodiment, the ACHD comprises residues -R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}-R_{43}-R_{44}-R_{45}-R_{46} of Formula I $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the ACHD comprises residues -R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}-R_{43}-R_{44}-R_{45}-R_{46} of Formula II $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the ACHD comprises residues -R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}-R_{43}-R_{44}-R_{45}-R_{46} of Formula III $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

(d) a variable loop domain (VLD), wherein a VLD comprises sufficient RNA sequence to mediate, *e.g.*, when present in an otherwise wildtype tRNA, recognition of aminoacyl-tRNA synthetase, *e.g.*, acts as a recognition site for aminoacyl-tRNA synthetase for amino acid charging of the TREM. In embodiments, a VLD mediates the stabilization of the TREM's tertiary structure. In an embodiment, a VLD modulates, *e.g.*, increases, the specificity of the TREM, *e.g.*, for its cognate amino acid, *e.g.*, the VLD modulates the TREM's cognate adaptor function. In an embodiment the VLD has at least 75, 80, 85, 85, 90, 95, or 100% identity with a naturally occurring VLD, *e.g.*, a VLD encoded by a nucleic acid in Table 1. In an embodiment, the TREM can comprise a fragment or analog of a VLD, *e.g.*, a VLD encoded by a nucleic acid in Table 1, which fragment in embodiments has VLD activity and in other embodiments does not have VLD activity.

In an embodiment the VLD falls under the corresponding sequence of a consensus sequence provided in the "Consensus Sequence" section.

In an embodiment, the VLD comprises residue -$[R_{47}]_x$ of a consensus sequence provided in the "Consensus Sequence" section, wherein x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28,

x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271);

(e) a thymine hairpin domain (THD), wherein a THD comprises sufficient RNA sequence, to mediate, *e.g.*, when present in an otherwise wildtype tRNA, recognition of the ribosome, *e.g.*, acts as a recognition site for the ribosome to form a TREM-ribosome complex during translation. In an embodiment the THD has at least 75, 80, 85, 85, 90, 95, or 100% identity with a naturally occurring THD, *e.g.*, a THD encoded by a nucleic acid in Table 1. In an embodiment, the TREM can comprise a fragment or analog of a THD, *e.g.*, a THD encoded by a nucleic acid in Table 1, which fragment in embodiments has THD activity and in other embodiments does not have THD activity.

In an embodiment the THD falls under the corresponding sequence of a consensus sequence provided in the "Consensus Sequence" section, or differs from the consensus sequence by no more than 1, 2, 5, or 10 positions;

In an embodiment, the THD comprises residues -R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64} of Formula I $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the THD comprises residues -R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64} of Formula II $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

In an embodiment, the THD comprises residues -R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64} of Formula III $_{ZZZ}$, wherein ZZZ indicates any of the twenty amino acids;

(e'1) a linker comprising residue R_{72} of a consensus sequence provided in the "Consensus Sequence" section, *e.g.*, a Linker 4 region;

(f) under physiological conditions, it comprises a stem structure and one or a plurality of loop structures, *e.g.*, 1, 2, or 3 loops. A loop can comprise a domain described herein, *e.g.*, a domain selected from (a)-(e). A loop can comprise one or a plurality of domains. In an embodiment, a stem or loop structure has at least 75, 80, 85, 85, 90, 95, or 100% identity with a naturally occurring stem or loop structure, *e.g.*, a stem or loop structure encoded by a nucleic acid in Table 1. In an embodiment, the TREM can comprise a fragment or analog of a stem or loop structure, *e.g.*, a stem or loop structure encoded by a nucleic acid in Table 1, which

fragment in embodiments has activity of a stem or loop structure, and in other embodiments does not have activity of a stem or loop structure;

(g) a tertiary structure, *e.g.*, an L-shaped tertiary structure;

(h) adaptor function, i.e., the TREM mediates acceptance of an amino acid, *e.g.*, its cognate amino acid and transfer of the AA in the initiation or elongation of a polypeptide chain;

(i) cognate adaptor function wherein the TREM mediates acceptance and incorporation of an amino acid (*e.g.*, cognate amino acid) associated in nature with the anti-codon of the TREM to initiate or elongate a polypeptide chain;

(j) non-cognate adaptor function, wherein the TREM mediates acceptance and incorporation of an amino acid (*e.g.*, non-cognate amino acid) other than the amino acid associated in nature with the anti-codon of the TREM in the initiation or elongation of a polypeptide chain;

(k) a regulatory function, *e.g.*, an epigenetic function (*e.g.*, gene silencing function or signaling pathway modulation function), cell fate modulation function, mRNA stability modulation function, protein stability modulation function, protein transduction modulation function, or protein compartmentalization function;

(l) a structure which allows for ribosome binding;

(m) a post-transcriptional modification, e.g., a naturally occurring post-trasncriptional modification;

(n) the ability to inhibit a functional property of a tRNA, *e.g.*, any of properties (h)-(k) possessed by a tRNA;

(o) the ability to modulate cell fate;

(p) the ability to modulate ribosome occupancy;

(q) the ability to modulate protein translation;

(r) the ability to modulate mRNA stability;

(s) the ability to modulate protein folding and structure;

(t) the ability to modulate protein transduction or compartmentalization;

(u) the ability to modulate protein stability; or

(v) the ability to modulate a signaling pathway, *e.g.*, a cellular signaling pathway.

In an embodiment, a TREM comprises a full-length tRNA molecule or a fragment thereof.

In an embodiment, a TREM comprises the following properties: (a)-(e).

In an embodiment, a TREM comprises the following properties: (a) and (c).

In an embodiment, a TREM comprises the following properties: (a), (c) and (h).

In an embodiment, a TREM comprises the following properties: (a), (c), (h) and (b).

In an embodiment, a TREM comprises the following properties: (a), (c), (h) and (e).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (b) and (e).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (b), (e) and (g).

In an embodiment, a TREM comprises the following properties: (a), (c), (h) and (m).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (m), and (g).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (m) and (b).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (m) and (e).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (m), (g), (b) and (e).

In an embodiment, a TREM comprises the following properties: (a), (c), (h), (m), (g), (b), (e) and (q).

In an embodiment, a TREM comprises:

(i) an amino acid attachment domain that binds an amino acid (*e.g.*, an AStD, as described in (a) herein; and

(ii) an anticodon that binds a respective codon in an mRNA (*e.g.*, an ACHD, as described in (c) herein).

In an embodiment the TREM comprises a flexible RNA linker which provides for covalent linkage of (i) to (ii).

In an embodiment, the TREM mediates protein translation.

In an embodiment a TREM comprises a linker, *e.g.*, an RNA linker, *e.g.*, a flexible RNA linker, which provides for covalent linkage between a first and a second structure or domain. In an embodiment, an RNA linker comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 ribonucleotides. A TREM can comprise one or a plurality of linkers, *e.g.*, in embodiments a TREM comprising (a), (b), (c), (d) and (e) can have a first linker between a first and second domain, and a second linker between a third domain and another domain.

In an embodiment, the TREM comprises a sequence of Formula A: [L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2].

In an embodiment, a TREM comprises an RNA sequence at least 60, 65, 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99% identical with, or which differs by no more than 1, 2, 3, 4, 5, 10, 15, 20, 25, or 30 ribonucleotides from, an RNA sequence encoded by a DNA sequence listed in Table 1, or a fragment or functional fragment thereof. In an embodiment, a TREM comprises an RNA sequence encoded by a DNA sequence listed in Table 1, or a fragment or functional fragment thereof. In an embodiment, a TREM comprises an RNA sequence encoded by a DNA sequence at least 60, 65, 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99% identical with a DNA sequence listed in Table 1, or a fragment or functional fragment thereof. In an embodiment, a TREM comprises a TREM domain, *e.g.*, a domain described herein, comprising at least 60, 65, 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99% identical with, or which differs by no more than 1, 2, 3, 4, 5, 10, or 15, ribonucleotides from, an RNA encoded by a DNA sequence listed in Table 1, or a fragment or a functional fragment thereof. In an embodiment, a TREM comprises a TREM domain, *e.g.*, a domain described herein, comprising an RNA sequence encoded by DNA sequence listed in Table 1, or a fragment or functional fragment thereof. In an embodiment, a TREM comprises a TREM domain, *e.g.*, a domain described herein, comprising an RNA sequence encoded by DNA sequence at least 60, 65, 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99% identical with a DNA sequence listed in Table 1, or a fragment or functional fragment thereof.

In an embodiment, a TREM is 76-90 nucleotides in length. In embodiments, a TREM or a fragment or functional fragment thereof is between 10-90 nucleotides, between 10-80 nucleotides, between 10-70 nucleotides, between 10-60 nucleotides, between 10-50 nucleotides, between 10-40 nucleotides, between 10-30 nucleotides, between 10-20 nucleotides, between 20-90 nucleotides, between 20-80 nucleotides, 20-70 nucleotides, between 20-60 nucleotides, between 20-50 nucleotides, between 20-40 nucleotides, between 30-90 nucleotides, between 30-80 nucleotides, between 30-70 nucleotides, between 30-60 nucleotides, or between 30-50 nucleotides.

In an embodiment, a TREM is aminoacylated, *e.g.*, charged, with an amino acid by an aminoacyl tRNA synthetase.

In an embodiment, a TREM is not charged with an amino acid, *e.g.*, an uncharged TREM (uTREM).

In an embodiment, a TREM comprises less than a full length tRNA. In embodiments, a TREM can correspond to a naturally occurring fragment of a tRNA, or to a non-naturally occurring fragment. Exemplary fragments include: TREM halves (*e.g.*, from a cleavage in the ACHD, *e.g.*, in the anticodon sequence, *e.g.*, 5'halves or 3' halves); a 5' fragment (*e.g.*, a fragment comprising the 5' end, *e.g.*, from a cleavage in a DHD or the ACHD); a 3' fragment (*e.g.*, a fragment comprising the 3' end, *e.g.*, from a cleavage in the THD); or an internal fragment (*e.g.*, from a cleavage in one or more of the ACHD, DHD or THD).

A "TREM core fragment," as that term is used herein, refers to a portion of the sequence of Formula B: [L1]$_y$-[ASt Domain1]$_x$-[L2]$_y$-[DH Domain]$_y$-[L3]$_y$-[ACH Domain]$_x$-[VL Domain]$_y$-[TH Domain]$_y$-[L4]$_y$-[ASt Domain2]$_x$, wherein: x=1 and y=0 or 1.

A "TREM fragment," as used herein, refers to a portion of a TREM, wherein the TREM comprises a sequence of Formula A: [L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2].

A "cognate adaptor function TREM," as that term is used herein, refers to a TREM which mediates initiation or elongation with the AA (the cognate AA) associated in nature with the anti-codon of the TREM.

"Decreased expression," as that term is used herein, refers to a decrease in comparison to a reference, *e.g.*, in the case where altered control region, or addition of an agent, results in a decreased expression of the subject product, it is decreased relative to an otherwise similar cell without the alteration or addition.

An "exogenous nucleic acid," as that term is used herein, refers to a nucleic acid sequence that is not present in or differs by at least one nucleotide from the closest sequence in a reference cell, *e.g.*, a cell into which the exogenous nucleic acid is introduced. In an embodiment, an exogenous nucleic acid comprises a nucleic acid that encodes a TREM.

An "exogenous TREM," as that term is used herein, refers to a TREM that:

(a) differs by at least one nucleotide or one post transcriptional modification from the closest sequence tRNA in a reference cell, *e.g.*, a cell into which the exogenous nucleic acid is introduced;

(b) has been introduced into a cell other than the cell in which it was transcribed;

(c) is present in a cell other than one in which it naturally occurs; or

(d) has an expression profile, *e.g.*, level or distribution, that is non-wildtype, *e.g.*, it is expressed at a higher level than wildtype. In an embodiment, the expression profile can be mediated by a change introduced into a nucleic acid that modulates expression or by addition of an agent that modulates expression of the RNA molecule. In an embodiment an exogenous TREM comprises 1, 2, 3 or 4 of properties (a)-(d).

A "GMP-grade composition," as that term is used herein, refers to a composition in compliance with current good manufacturing practice (cGMP) guidelines, or other similar requirements. In an embodiment, a GMP-grade composition can be used as a pharmaceutical product.

As used herein, the terms "increasing" and "decreasing" refer to modulating that results in, respectively, greater or lesser amounts of function, expression, or activity of a particular metric relative to a reference. For example, subsequent to administration to a cell, tissue or subject of a TREM described herein, the amount of a marker of a metric (*e.g.*, protein translation, mRNA stability, protein folding) as described herein may be increased or decreased by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 98%, 2X, 3X, 5X, 10X or more relative to the amount of the marker prior to administration or relative to the effect of a negative control agent. The metric may be measured subsequent to administration at a time that the administration has had the recited effect, *e.g.*, at least 12 hours, 24 hours, one week, one month, 3 months, or 6 months, after a treatment has begun.

"Increased expression," as that term is used herein, refers to an increase in comparison to a reference, *e.g.*, in the case where altered control region, or addition of an agent, results in an increased expression of the subject product, it is increased relative to an otherwise similar cell without the alteration or addition.

A "non-cognate adaptor function TREM," as that term is used herein, refers to a TREM which mediates initiation or elongation with an AA (a non-cognate AA) other than the AA associated in nature with the anti-codon of the TREM. In an embodiment, a non-cognate adaptor function TREM is also referred to as a mischarged TREM (mTREM).

A "non-naturally occurring sequence," as that term is used herein, refers to a sequence wherein an Adenine is replaced by a residue other than an analog of Adenine, a Cytosine is replaced by a residue other than an analog of Cytosine, a Guanine is replaced by a residue other

than an analog of Guanine, and a Uracil is replaced by a residue other than an analog of Uracil. An analog refers to any possible derivative of the ribonucleotides, A, G, C or U. In an embodiment, a sequence having a derivative of any one of ribonucleotides A, G, C or U is a non-naturally occurring sequence.

A "pharmaceutical TREM composition," as that term is used herein, refers to a TREM composition that is suitable for pharmaceutical use. Typically, a pharmaceutical TREM composition comprises a pharmaceutical excipient. In an embodiment the TREM will be the only active ingredient in the pharmaceutical TREM composition. In embodiments the pharmaceutical TREM composition is free, substantially free, or has less than a pharmaceutically acceptable amount, of host cell proteins, DNA, *e.g.*, host cell DNA, endotoxins, and bacteria.

A "post-transcriptional processing," as that term is used herein, with respect to a subject molecule, *e.g.*, a TREM, RNA or tRNAs, refers to a covalent modification of the subject molecule. In an embodiment, the covalent modification occurs post-transcriptionally. In an embodiment, the covalent modification occurs co-transcriptionally. In an embodiment the modification is made *in vivo, e.g.*, in a cell used to produce a TREM. In an embodiment the modification is made *ex vivo*, *e.g.*, it is made on a TREM isolated or obtained from the cell which produced the TREM. In an embodiment, the post-transcriptional modification is selected from a post-transcriptional modification listed in Table 2.

A "synthetic TREM," as that term is used herein, refers to a TREM which was synthesized other than in or by a cell having an endogenous nucleic acid encoding the TREM, *e.g.*, a synthetic TREM is synthetized by cell-free solid phase synthesis. A synthetic TREM can have the same, or a different, sequence, or tertiary structure, as a native tRNA.

A "recombinant TREM," as that term is used herein, refers to a TREM that was expressed in a cell modified by human intervention, having a modification that mediates the production of the TREM, *e.g.*, the cell comprises an exogenous sequence encoding the TREM, or a modification that mediates expression, *e.g.*, transcriptional expression or post-transcriptional modification, of the TREM. A recombinant TREM can have the same, or a different, sequence, set of post-transcriptional modifications, or tertiary structure, as a reference tRNA, *e.g.*, a native tRNA.

A "tRNA", as that term is used herein, refers to a naturally occurring transfer ribonucleic acid in its native state.

A "TREM composition," as that term is used herein, refers to a composition comprising a plurality of TREMs, a plurality of TREM core fragments and/or a plurality of TREM fragments. A TREM composition can comprise one or more species of TREMs, TREM core fragments or TREM fragments. In an embodiment, the composition comprises only a single species of TREM, TREM core fragment or TREM fragment. In an embodiment, the TREM composition comprises a first TREM, TREM core fragment or TREM fragment species; and a second TREM, TREM core fragment or TREM fragment species. In an embodiment, the TREM composition comprises X TREM, TREM core fragment or TREM fragment species, wherein X=2, 3, 4, 5, 6, 7, 8, 9, or 10. In an embodiment, the TREM, TREM core fragment or TREM fragment has at least 70, 75, 80, 85, 90, or 95, or has 100%, identity with a sequence encoded by a nucleic acid in Table 1. A TREM composition can comprise one or more species of TREMs, TREM core fragments or TREM fragments. In an embodiment, the TREM composition is at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 95 or 99% dry weight TREMs (for a liquid composition dry weight refers to the weight after removal of substantially all liquid, *e.g.*, after lyophilization). In an embodiment, the composition is a liquid. In an embodiment, the composition is dry, *e.g.*, a lyophilized material. In an embodiment, the composition is a frozen composition. In an embodiment, the composition is sterile. In an embodiment, the composition comprises at least 0.5 g, 1.0 g, 5.0 g, 10 g, 15 g, 25 g, 50 g, 100 g, 200 g, 400 g, or 500 g (*e.g.*, as determined by dry weight) of TREM.

In an embodiment, at least X% of the TREMs in a TREM composition has a non-naturally occurring modification at a selected position, and X is 80, 90, 95, 96, 97, 98, 99, or 99.5.

In an embodiment, at least X% of the TREMs in a TREM composition has a non-naturally occurring modification at a first position and a non-naturally occurring modification at a second position, and X, independently, is 80, 90, 95, 96, 97, 98, 99, or 99.5. In embodiments, the modification at the first and second position is the same. In embodiments, the modification at the first and second position are different. In embodiments, the nucleiotide at the first and second position is the same, e.g., both are adenine. In embodiments, the nucleiotide at the first and second position are different, e.g., one is adenine and one is thymine.

In an embodiment, at least X% of the TREMs in a TREM composition has a non-naturally occurring modification at a first position and less than Y% have a non-naturally

occurring modification at a second position, wherein X is 80, 90, 95, 96, 97, 98, 99, or 99.5 and Y is 20, 20, 5, 2, 1, .1, or .01. In embodiments, the nucleotide at the first and second position is the same, e.g., both are adenine. In embodiments the nucleotide at the first and second position are different, e.g., one is adenine and one is thymine.

TREM, TREM core fragment and TREM fragment

A "tRNA-based effector molecule" or "TREM" refers to an RNA molecule comprising one or more of the properties described herein. A TREM can comprise a non-naturally occurring modification, e.g., as provided in Tables 4, 5, 6 or 7.

In an embodiment, a TREM includes a TREM comprising a sequence of Formula A; a TREM core fragment comprising a sequence of Formula B; or a TREM fragment comprising a portion of a TREM which TREM comprises a sequence of Formula A.

In an embodiment, a TREM comprises a sequence of Formula A: [L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2]. In an embodiment, [VL Domain] is optional. In an embodiment, [L1] is optional.

In an embodiment, a TREM core fragment comprises a sequence of Formula B: $[L1]_y$-$[ASt\ Domain1]_x$-$[L2]_y$-$[DH\ Domain]_y$-$[L3]_y$-$[ACH\ Domain]_x$-$[VL\ Domain]_y$-$[TH\ Domain]_y$-$[L4]_y$-$[ASt\ Domain2]_x$, wherein: x=1 and y=0 or 1. In an embodiment, y=0. In an embodiment, y=1.;

In an embodiment, a TREM fragment comprises a portion of a TREM, wherein the TREM comprises a sequence of Formula A: [L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2], and wherein the TREM fragment comprises: one, two, three or all or any combination of the following: a TREM half (*e.g.*, from a cleavage in the ACH Domain, *e.g.*, in the anticodon sequence, *e.g.*, a 5'half or a 3' half); a 5' fragment (*e.g.*, a fragment comprising the 5' end, *e.g.*, from a cleavage in a DH Domain or the ACH Domain); a 3' fragment (*e.g.*, a fragment comprising the 3' end, *e.g.*, from a cleavage in the TH Domain); or an internal fragment (*e.g.*, from a cleavage in any one of the ACH Domain, DH Domain or TH Domain). Exemplary TREM fragments include TREM halves (*e.g.*, from a cleavage in the ACHD, *e.g.*, 5'TREM halves or 3' TREM halves), a 5' fragment (*e.g.*, a fragment comprising the 5' end, *e.g.*, from a cleavage in a DHD or the ACHD), a 3'

fragment (*e.g.*, a fragment comprising the 3' end of a TREM, *e.g.*, from a cleavage in the THD), or an internal fragment (*e.g.*, from a cleavage in one or more of the ACHD, DHD or THD).

In an embodiment, a TREM, a TREM core fragment or a TREM fragment can be charged with an amino acid (*e.g.*, a cognate amino acid); charged with a non-cognate amino acid (*e.g.*, a mischarged TREM (mTREM)); or not charged with an amino acid (*e.g.*, an uncharged TREM (uTREM)). In an embodiment, a TREM, a TREM core fragment or a TREM fragment can be charged with an amino acid selected from alanine, arginine, asparagine, aspartate, cysteine, glutamine, glutamate, glycine, histidine, isoleucine, methionine, leucine, lysine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

In some embodiments, a non-extended anticodon is an anticodon of no more than three nucleotides. In an embodiment, a non-extended codon pairs with no more than three codon nucleotides on a nucleic acid being translated.

In an embodiment, the TREM, TREM core fragment or TREM fragment is a cognate TREM. In an embodiment, the TREM, TREM core fragment or TREM fragment is a non-cognate TREM. In an embodiment, the TREM, TREM core fragment or TREM fragment recognizes a codon provided in Table 2 or Table 3.

Table 2: List of codons

AAA	CAG	GCA
AAC	CAU	GCC
AAG	CCA	GCG
AAU	CCC	GCU
ACA	CCG	GGA
ACC	CCU	GGC
ACG	CGA	GGG
ACU	CGC	GGU
AGA	CGG	GUA
AGC	CGU	GUC
AGG	CUA	GUG
AGU	CUC	GUU
AUA	CUG	UAA
AUC	CUU	UAC
AUG	GAA	UAG
AUU	GAC	UAU
CAA	GAG	UCA
CAC	GAU	UCC

UCG
UCU
UGA
UGC
UGG
UGU
UUA
UUC
UUG
UUU

Table 3: Amino acids and corresponding codons

Amino Acid	**mRNA codons**
Alanine	GCU, GCC, GCA, GCG
Arginine	CGU, CGC, CGA, CGG, AGA, AGG
Asparagine	AAU, AAC
Aspartate	GAU, GAC
Cysteine	UGU, UGC
Glutamate	GAA, GAG
Glutamine	CAA, CAG
Glycine	GGU, GGC, GGA, GGG
Histidine	CAU, CAC
Isoleucine	AUU, AUC, AUA
Leucine	UUA, UUG, CUU, CUC, CUA, CUG
Lysine	AAA, AAG
Methionine	AUG
Phenylalanine	UUU, UUC
Proline	CCU, CCC, CCA, CCG
Serine	UCU, UCC, UCA, UCG, AGU, AGC
Stop	UAA, UAG, UGA
Threonine	ACU, ACC, ACA, ACG
Tryptophan	UGG
Tyrosine	UAU, UAC
Valine	GUU, GUC, GUA, GUG

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In an embodiment, a TREM comprises a ribonucleic acid (RNA) sequence encoded by a deoxyribonucleic acid (DNA) sequence disclosed in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM comprises an RNA sequence at least 60%, 65%, 70%, 75%, 80%, 82%, 85%, 87%, 88%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to an RNA sequence encoded by a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM comprises an RNA sequence encoded by a DNA sequence at least 60%, 65%, 70%, 75%, 80%, 82%, 85%, 87%, 88%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1.

In an embodiment, a TREM, a TREM core fragment, or TREM fragment comprises at least 5, 10, 15, 20, 25, or 30 consecutive nucleotides of an RNA sequence encoded by a DNA sequence disclosed in Table 1, *e.g.*, at least 5, 10, 15, 20, 25, or 30 consecutive nucleotides of an RNA sequence encoded by any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM, a TREM core fragment, or TREM fragment comprises at least 5, 10, 15, 20, 25, or 30 consecutive nucleotides of an RNA sequence at least 60%, 65%, 70%, 75%, 80%, 82%, 85%, 87%, 88%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to an RNA sequence encoded by a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM, a TREM core fragment, or TREM fragment comprises at least 5, 10, 15, 20, 25, or 30 consecutive nucleotides of an RNA sequence encoded by a DNA sequence at least 60%, 65%, 70%, 75%, 80%, 82%, 85%, 87%, 88%, 90%, 92%, 95%, 96%, 97%, 98%, or 99% identical to a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1.

In an embodiment, a TREM core fragment or a TREM fragment comprises at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% of an RNA sequence encoded by a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM core fragment or a TREM fragment comprises at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% of an RNA sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to an RNA sequence encoded by a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM core fragment or a TREM fragment comprises

at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% of an RNA sequence encoded by a DNA sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1.

In an embodiment, a TREM core fragment or a TREM fragment comprises at least 5 ribonucleotides (nt), 10 nt, 15 nt, 20 nt, 25 nt, 30 nt, 35 nt, 40 nt, 45 nt, 50 nt, 55 nt or 60 nt (but less than the full length) of an RNA sequence encoded by a DNA sequence disclosed in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM core fragment or a TREM fragment comprises at least 5 ribonucleotides (nt), 10 nt, 15 nt, 20 nt, 25 nt, 30 nt, 35 nt, 40 nt, 45 nt, 50 nt, 55 nt or 60 nt (but less than the full length) of an RNA sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to an RNA sequence encoded by a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1. In an embodiment, a TREM core fragment or a TREM fragment comprises at least 5 ribonucleotides (nt), 10 nt, 15 nt, 20 nt, 25 nt, 30 nt, 35 nt, 40 nt, 45 nt, 50 nt, 55 nt or 60 nt (but less than the full length) of an RNA sequence encoded by a DNA sequence with at least 80%, 82%, 85%, 87%, 88%, 90%, 92%, 95%, 96%, 97%, 98%, 99% or 100% identity to a DNA sequence provided in Table 1, *e.g.*, any one of SEQ ID NOs: 1-451 disclosed in Table 1.

In an embodiment, a TREM core fragment or a TREM fragment comprises a sequence of a length of between 10-90 ribonucleotides (rnt), between 10-80 rnt, between 10-70 rnt, between 10-60 rnt, between 10-50 rnt, between 10-40 rnt, between 10-30 rnt, between 10-20 rnt, between 20-90 rnt, between 20-80 rnt, 20-70 rnt, between 20-60 rnt, between 20-50 rnt, between 20-40 rnt, between 30-90 rnt, between 30-80 rnt, between 30-70 rnt, between 30-60 rnt, or between 30-50 rnt

Table 1: List of tRNA Sequences

SEQ ID NO	**tRNA name**	**tRNA sequence**
1	Ala_AGC_chr6:28763741-28763812 (-)	GGGGGTATAGCTCAGTGGTAGAGCGCGTGCTTAGCATGCACGAGGTCCTGGGTTCGATCCCC
2	Ala_AGC_chr6:26687485-26687557 (+)	GGGGAATTAGCTCAAGTGGTAGAGCGCTTGCTTAGCACGCAAGAGGTAGTGGGATCGATGCC
3	Ala_AGC_chr6:26572092-26572164 (-)	GGGGAATTAGCTCAAATGGTAGAGCGCTCGCTTAGCATGCGAGAGGTAGCGGGATCGATGCC

4	Ala_AGC_chr6:26682715-26682787 (+)	GGGGAATTAGCTCAAGTGGTAGAGCGCTTGCTTAGCATGCAAGAGGTAGTGGGATCGATGCC
5	Ala_AGC_chr6:26705606-26705678 (+)	GGGGAATTAGCTCAAGCGGTAGAGCGCTTGCTTAGCATGCAAGAGGTAGTGGGATCGATGCC
6	Ala_AGC_chr6:26673590-26673662 (+)	GGGGAATTAGCTCAAGTGGTAGAGCGCTTGCTTAGCATGCAAGAGGTAGTGGGATCAATGCC
7	Ala_AGC_chr14:894455442-89445514 (+)	GGGGAATTAGCTCAAGTGGTAGAGCGCTCGCTTAGCATGCGAGAGGTAGTGGGATCGATGCC
8	Ala_AGC_chr6:58196623-58196695 (-)	GGGGAATTAGCCCAAGTGGTAGAGCGCTTGCTTAGCATGCAAGAGGTAGTGGGATCGATGCC
9	Ala_AGC_chr6:28806221-28806292 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGCACGAGGCCCCGGGTTCAATCCCC
10	Ala_AGC_chr6:28574933-28575004 (+)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGTACGAGGTCCCGGGTTCAATCCCC
11	Ala_AGC_chr6:28626014-28626085 (-)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTAGCATGCATGAGGTCCCGGGTTCGATCCCC
12	Ala_AGC_chr6:28678366-28678437 (+)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGCACGAGGCCCTGGGTTCAATCCCC
13	Ala_AGC_chr6:28779849-28779920 (-)	GGGGGTATAGCTCAGCGGTAGAGCGCGTGCTTAGCATGCACGAGGTCCTGGGTTCAATCCCC
14	Ala_AGC_chr6:28687481-28687552 (+)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGCACGAGGCCCCGGGTTCAATCCCT
15	Ala_AGC_chr2:27274082-27274154 (+)	GGGGGATTAGCTCAAATGGTAGAGCGCTCGCTTAGCATGCGAGAGGTAGCGGGATCGATGCC
16	Ala_AGC_chr6:26730737-26730809 (+)	GGGGAATTAGCTCAGGCGGTAGAGCGCTCGCTTAGCATGCGAGAGGTAGCGGGATCGACGCC
17	Ala_CGC_chr6:26553731-26553802 (+)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTCGCATGTATGAGGTCCCGGGTTCGATCCCC
18	Ala_CGC_chr6:28641613-28641684 (-)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTCGCATGTATGAGGCCCCGGGTTCGATCCCC
19	Ala_CGC_chr2:157257281-157257352 (+)	GGGGATGTAGCTCAGTGGTAGAGCGCGCGCTTCGCATGTGTGAGGTCCCGGGTTCAATCCCC
20	Ala_CGC_chr6:28697092-28697163 (+)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTCGCATGTACGAGGCCCCGGGTTCGACCCCC
21	Ala_TGC_chr6:28757547-28757618 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGCATGCTTTGCATGTATGAGGTCCCGGGTTCGATCCCC
22	Ala_TGC_chr6:28611222-28611293 (+)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTTGCATGTATGAGGTCCCGGGTTCGATCCCC
23	Ala_TGC_chr5:180633868-180633939 (+)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTTGCATGTATGAGGCCCCGGGTTCGATCCCC
24	Ala_TGC_chr12:125424524512-125424583 (+)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTTGCACGTATGAGGCCCCGGGTTCAATCCCC
25	Ala_TGC_chr6:28785012-28785083 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGCATGCTTTGCATGTATGAGGCCTCGGGTTCGATCCCC

26	Ala_TGC_chr6:28726141-28726212 (-)	GGGGGTGTAGCTCAGTGGTAGAGCACATGCTTTGCATGTGTGAGGCCCCGGGTTCGATCCCC
27	Ala_TGC_chr6:28770577-28770647 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGCATGCTTTGCATGTATGAGGCCTCGGTTCGATCCCCG
28	Arg_ACG_chr6:26328368-26328440 (+)	GGGCCAGTGGCGCAATGGATAACGCGTCTGACTACGGATCAGAAGATTCCAGGTTCGACTCC
29	Arg_ACG_chr3:45730491-45730563 (-)	GGGCCAGTGGCGCAATGGATAACGCGTCTGACTACGGATCAGAAGATTCTAGGTTCGACTCC
30	Arg_CCG_chr6:28710729-28710801 (-)	GGCCGCGTGGCCTAATGGATAAGGCGTCTGATTCCGGATCAGAAGATTGAGGGTTCGAGTCC
31	Arg_CCG_chr17:66016013-66016085 (-)	GACCCAGTGGCCTAATGGATAAGGCATCAGCCTCCGGAGCTGGGGATTGTGGGTTCGAGTCC
32	Arg_CCT_chr17:73030001-73030073 (+)	GCCCCAGTGGCCTAATGGATAAGGCACTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTCC
33	Arg_CCT_chr17:73030526-73030598 (-)	GCCCCAGTGGCCTAATGGATAAGGCACTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTCC
34	Arg_CCT_chr16:3202901-3202973 (+)	GCCCCGGTGGCCTAATGGATAAGGCATTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTCC
35	Arg_CCT_chr7:139025446-139025518 (+)	GCCCCAGTGGCCTAATGGATAAGGCATTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTCC
36	Arg_CCT_chr16:3243918-3243990 (+)	GCCCCAGTGGCCTGATGGATAAGGTACTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTTC
37	Arg_TCG_chr15:898783 04-89878376 (+)	GGCCGCGTGGCCTAATGGATAAGGCGTCTGACTTCGGATCAGAAGATTGCAGGTTCGAGTCC
38	Arg_TCG_chr6:26323046-26323118 (+)	GACCACGTGGCCTAATGGATAAGGCGTCTGACTTCGGATCAGAAGATTGAGGGTTCGAATCC
39	Arg_TCG_chr17:73031208-73031280 (+)	GACCGCGTGGCCTAATGGATAAGGCGTCTGACTTCGGATCAGAAGATTGAGGGTTCGAGTCC
40	Arg_TCG_chr6:26299905-26299977 (+)	GACCACGTGGCCTAATGGATAAGGCGTCTGACTTCGGATCAGAAGATTGAGGGTTCGAATCC
41	Arg_TCG_chr6:28510891-28510963 (-)	GACCACGTGGCCTAATGGATAAGGCGTCTGACTTCGGATCAGAAGATTGAGGGTTCGAATCC
42	Arg_TCG_chr9:112960803-112960875 (+)	GGCCGTGTGGCCTAATGGATAAGGCGTCTGACTTCGGATCAAAAGATTGCAGGTTTGAGTTC
43	Arg_TCT_chr1:94313129-94313213 (+)	GGCTCCGTGGCGCAATGGATAGCGCATTGGACTTCTAGAGGCTGAAGGCATTCAAAGGTTCC
44	Arg_TCT_chr17:8024243-8024330 (+)	GGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGTGACGAATAGAGCAATTCAAAGGT
45	Arg_TCT_chr9:131102355-131102445 (-)	GGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGCTGAGCCTAGTGTGGTCATTCAAA
46	Arg_TCT_chr11:59318767-59318852 (+)	GGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGATAGTTAGAGAAATTCAAAGGTTG
47	Arg_TCT_chr1:159111401-159111474 (-)	GTCTCTGTGGCGCAATGGACGAGCGCGCTGGACTTCTAATCCAGAGGTTCCGGGTTCGAGTC

48	Arg_TCT_chr6:27529963-27530049 (+)	GGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGCCTAAATCAAGAGATTCAAAGGTT
49	Asn_GTT_chr1:161510031-161510104 (+)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGATCC
50	Asn_GTT_chr1:143879832-143879905 (-)	GTCTCTGTGGCGCAATCGGCTAGCGCGTTTGGCTGTTAACTAAAAGGTTGGCGGTTCGAACC
51	Asn_GTT_chr1:144301611-144301684 (+)	GTCTCTGTGGTGCAATCGGTTAGCGCGTTCCGCTGTTAACCGAAAGCTTGGTGGTTCGAGCCC
52	Asn_GTT_chr1:149326272-149326345 (-)	GTCTCTGTGGCGCAATCGGCTAGCGCGTTTGGCTGTTAACTAAAAAGTTGGTGGTTCGAACA
53	Asn_GTT_chr1:148248115-148248188 (+)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
54	Asn_GTT_chr1:148598314-148598387 (-)	GTCTCTGTGGCGCAATCGGTTAGCGCATTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
55	Asn_GTT_chr1:17216172-17216245 (+)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGATTGGTGGTTCGAGCC
56	Asn_GTT_chr1:16847080-16847153 (-)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACTGAAAGGTTGGTGGTTCGAGCC
57	Asn_GTT_chr1:149230570-149230643 (-)	GTCTCTGTGGCGCAATGGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
58	Asn_GTT_chr1:148000805-148000878 (+)	GTCTCTGTGGCGTAGTCGGTTAGCGCGTTCGGCTGTTAACCGAAAAGTTGGTGGTTCGAGCC
59	Asn_GTT_chr1:149711798-149711871 (-)	GTCTCTGTGGCGCAATCGGCTAGCGCGTTTGGCTGTTAACTAAAAGGTTGGTGGTTCGAACC
60	Asn_GTT_chr1:145979034-145979107 (-)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACTGAAAGGTTAGTGGTTCGAGCC
61	Asp_GTC_chr12:98897281-98897352 (+)	TCCTCGTTAGTATAGTGGTTAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCAATTCCCC
62	Asp_GTC_chr1:161410615-161410686 (-)	TCCTCGTTAGTATAGTGGTGAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCGATTCCCC
63	Asp_GTC_chr6:27551236-27551307 (-)	TCCTCGTTAGTATAGTGGTGAGTGTCCCCGTCTGTCACGCGGGAGACCGGGGTTCGATTCCCC
64	Cys_GCA_chr7:149007281-149007352 (+)	GGGGGCATAGCTCAGTGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCTGGTTCAAATCCA
65	Cys_GCA_chr7:149074601-149074672 (-)	GGGGGTATAGCTCAGGGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCTGGTTCAAATCCA
66	Cys_GCA_chr7:149112229-149112300 (-)	GGGGGTATAGCTTAGCGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCCGGTTCAAATCCG
67	Cys_GCA_chr7:149344046-149344117 (-)	GGGGGTATAGCTTAGGGGTAGAGCATTTGACTGCAGATCAAAAGGTCCCTGGTTCAAATCCA
68	Cys_GCA_chr7:149052766-149052837 (-)	GGGGGTATAGCTCAGGGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCCAGTTCAAATCTG
69	Cys_GCA_chr17:37017937-37018008 (-)	GGGGGTATAGCTCAGGGGTAGAGCATTTGACTGCAGATCAAGAAGTCCCCGGTTCAAATCCG

70	Cys_GCA_chr7:14928 1816-149281887 (+)	GGGGGTATAGCTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCTCTGGTTCAAATCCA
71	Cys_GCA_chr7:14924 3631-149243702 (+)	GGGGGTATAGCTCAGGGGTAGAGCACTTGAC TGCAGATCAAGAAGTCCTTGGTTCAAATCCA
72	Cys_GCA_chr7:14938 8272-149388343 (-)	GGGGATATAGCTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCGGTTCAAATCCG
73	Cys_GCA_chr7:14907 2850-149072921 (-)	GGGGGTATAGTTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCTGGTTCAAATCCA
74	Cys_GCA_chr7:14931 0156-149310227 (-)	GGGGGTATAGCTCAGGGGTAGAGCATTTGAC TGCAAATCAAGAGGTCCCTGATTCAAATCCA
75	Cys_GCA_chr4:12443 0005-124430076 (-)	GGGGGTATAGCTCAGTGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCGGTTCAAATCCG
76	Cys_GCA_chr7:14929 5046-149295117 (+)	GGGCGTATAGCTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCAGTTCAAATCTG
77	Cys_GCA_chr7:14936 1915-149361986 (+)	GGGGGTATAGCTCACAGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCGGTTCAAATCTG
78	Cys_GCA_chr7:14925 3802-149253871 (+)	GGGCGTATAGCTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCAGTTCAAATCTG
79	Cys_GCA_chr7:14929 2305-149292376 (-)	GGGGGTATAGCTCACAGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCGGTTCAAATCCG
80	Cys_GCA_chr7:14928 6164-149286235 (-)	GGGGGTATAGCTCAGGGGTAGAGCACTTGAC TGCAGATCAAGAGGTCCCTGGTTCAAATCCA
81	Cys_GCA_chr17:3702 5545-37025616 (-)	GGGGGTATAGCTCAGTGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCTGGTTCAAATCCG
82	Cys_GCA_chr15:8003 6997-80037069 (+)	GGGGGTATAGCTCAGTGGGTAGAGCATTTGA CTGCAGATCAAGAGGTCCCCGGTTCAAATCC
83	Cys_GCA_chr3:13194 7944-131948015 (-)	GGGGGTGTAGCTCAGTGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCTGGTTCAAATCCA
84	Cys_GCA_chr1:93981 834-93981906 (-)	GGGGGTATAGCTCAGGTGGTAGAGCATTTGA CTGCAGATCAAGAGGTCCCCGGTTCAAATCC
85	Cys_GCA_chr14:7342 9679-73429750 (+)	GGGGGTATAGCTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCCGGTTCAAATCCG
86	Cys_GCA_chr3:13195 0642-131950713 (-)	GGGGGTATAGCTCAGGGGTAGAGCATTTGAC TGCAGATCAAGAGGTCCCTGGTTCAAATCCA
87	Gln_CTG_chr6:18836 402-18836473 (+)	GGTTCCATGGTGTAATGGTTAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCAAATCTC
88	Gln_CTG_chr6:27515 531-27515602 (-)	GGTTCCATGGTGTAATGGTTAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCAAGTCTC
89	Gln_CTG_chr1:14596 3304-145963375 (+)	GGTTCCATGGTGTAATGGTGAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCGAGTCTC
90	Gln_CTG_chr1:14773 7382-147737453 (-)	GGTTCCATGGTGTAATGGTAAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCGAGTCTC
91	Gln_CTG_chr6:27263 212-27263283 (+)	GGTTCCATGGTGTAATGGTTAGCACTCTGGA CTCTGAATCCGGTAATCCGAGTTCAAATCTC

92	Gln_CTG_chr6:27759135-27759206 (-)	GGCCCCATGGTGTAATGGTCAGCACTCTGGACTCTGAATCCAGCGATCCGAGTTCAAATCTC
93	Gln_CTG_chr1:147800937-147801008 (+)	GGTTCCATGGTGTAATGGTAAGCACTCTGGACTCTGAATCCAGCCATCTGAGTTCGAGTCTCT
94	Gln_TTG_chr17:47269890-47269961 (+)	GGTCCCATGGTGTAATGGTTAGCACTCTGGACTTTGAATCCAGCGATCCGAGTTCAAATCTC
95	Gln_TTG_chr6:28557156-28557227 (+)	GGTCCCATGGTGTAATGGTTAGCACTCTGGACTTTGAATCCAGCAATCCGAGTTCGAATCTC
96	Gln_TTG_chr6:26311424-26311495 (-)	GGCCCCATGGTGTAATGGTTAGCACTCTGGACTTTGAATCCAGCGATCCGAGTTCAAATCTC
97	Gln_TTG_chr6:145503859-145503930 (+)	GGTCCCATGGTGTAATGGTTAGCACTCTGGGCTTTGAATCCAGCAATCCGAGTTCGAATCTTG
98	Glu_CTC_chr1:145399233-145399304 (-)	TCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCTCTCACCGCCGCGGCCCGGGTTCGATTCCC
99	Glu_CTC_chr1:249168447-249168518 (+)	TCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCTCTCACCGCCGCGGCCCGGGTTCGATTCCC
100	Glu_TTC_chr2:131094701-131094772 (-)	TCCCATATGGTCTAGCGGTTAGGATTCCTGGTTTTCACCCAGGTGGCCCGGGTTCGACTCCCG
101	Glu_TTC_chr13:45492062-45492133 (-)	TCCCACATGGTCTAGCGGTTAGGATTCCTGGTTTTCACCCAGGCGGCCCGGGTTCGACTCCCG
102	Glu_TTC_chr1:17199078-17199149 (+)	TCCCTGGTGGTCTAGTGGCTAGGATTCGGCGCTTTCACCGCCGCGGCCCGGGTTCGATTCCCG
103	Glu_TTC_chr1:16861774-16861845 (-)	TCCCTGGTGGTCTAGTGGCTAGGATTCGGCGCTTTCACCGCCGCGGCCCGGGTTCGATTCCCG
104	Gly_CCC_chr1:16872434-16872504 (-)	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTCCCACGCGGGAGACCCGGGTTCAATTCCCGG
105	Gly_CCC_chr2:70476123-70476193 (-)	GCGCCGCTGGTGTAGTGGTATCATGCAAGATTCCCATTCTTGCGACCCGGGTTCGATTCCCGG
106	Gly_CCC_chr17:19764175-19764245 (+)	GCATTGGTGGTTCAATGGTAGAATTCTCGCCTCCCACGCAGGAGACCCAGGTTCGATTCCTGG
107	Gly_GCC_chr1:161413094-161413164 (+)	GCATGGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTCGATTCCCG
108	Gly_GCC_chr1:161493637-161493707 (-)	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTCGATTCCCGG
109	Gly_GCC_chr16:70812114-70812184 (-)	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTTGATTCCCGG
110	Gly_GCC_chr1:161450356-161450426 (+)	GCATAGGTGGTTCAGTGGTAGAATTCTTGCCTGCCACGCAGGAGGCCCAGGTTTGATTCCTG
111	Gly_GCC_chr16:70822597-70822667 (+)	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCCATGCGGGCGGCCGGGCTTCGATTCCTGG
112	Gly_TCC_chr19:4724082-4724153 (+)	GCGTTGGTGGTATAGTGGTTAGCATAGCTGCCTTCCAAGCAGTTGACCCGGGTTCGATTCCC
113	Gly_TCC_chr1:145397864-145397935 (-)	GCGTTGGTGGTATAGTGGTGAGCATAGCTGCCTTCCAAGCAGTTGACCCGGGTTCGATTCCC

114	Gly_TCC_chr17:8124866-8124937 (+)	GCGTTGGTGGTATAGTGGTAAGCATAGCTGCCTTCCAAGCAGTTGACCCGGGTTCGATTCCC
115	Gly_TCC_chr1:161409961-161410032 (-)	GCGTTGGTGGTATAGTGGTGAGCATAGTTGCCTTCCAAGCAGTTGACCCGGGCTCGATTCCC
116	His_GTG_chr1:145396881-145396952 (-)	GCCGTGATCGTATAGTGGTTAGTACTCTGCGTTGTGGCCGCAGCAACCTCGGTTCGAATCCGA
117	His_GTG_chr1:149155828-149155899 (-)	GCCATGATCGTATAGTGGTTAGTACTCTGCGCTGTGGCCGCAGCAACCTCGGTTCGAATCCG
118	Ile_AAT_chr6:58149254-58149327 (+)	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGCGCTAATAACGCCAAGGTCGCGGGTTCGATCC
119	Ile_AAT_chr6:27655967-27656040 (+)	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCC
120	Ile_AAT_chr6:27242990-27243063 (-)	GGCTGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCC
121	Ile_AAT_chr17:8130309-8130382 (-)	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGAACC
122	Ile_AAT_chr6:26554350-26554423 (+)	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCC
123	Ile_AAT_chr6:26745255-26745328 (-)	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCTAAGGTCGCGGGTTCGATCC
124	Ile_AAT_chr6:26721221-26721294 (-)	GGCCGGTTAGCTCAGTTGGTCAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCC
125	Ile_AAT_chr6:27636362-27636435 (+)	GGCCGGTTAGCTCAGTCGGCTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCC
126	Ile_AAT_chr6:27241739-27241812 (+)	GGCTGGTTAGTTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGTGGGTTCGATCC
127	Ile_GAT_chrX:3756418-3756491 (-)	GGCCGGTTAGCTCAGTTGGTAAGAGCGTGGTGCTGATAACACCAAGGTCGCGGGCTCGACTC
128	Ile_TAT_chr19:39902808-39902900 (-)	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATATGACAGTGCGAGCGGAGCAATGCC
129	Ile_TAT_chr2:43037676-43037768 (+)	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATACAGCAGTACATGCAGAGCAATGCC
130	Ile_TAT_chr6:26988125-26988218 (+)	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATATGGCAGTATGTGTGCGAGTGATGC
131	Ile_TAT_chr6:27599200-27599293 (+)	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATACAACAGTATATGTGCGGGTGATGC
132	Ile_TAT_chr6:28505367-28505460 (+)	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATAAGACAGTGCACCTGTGAGCAATGC
133	Leu_AAG_chr5:180524474-180524555 (-)	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTAAGGCTCCAGTCTCTTCGGAGGCGTGGG
134	Leu_AAG_chr5:180614701-180614782 (+)	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTAAGGCTCCAGTCTCTTCGGGGGCGTGGG
135	Leu_AAG_chr6:28956779-28956860 (+)	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTAAGGCTCCAGTCTCTTCGGGGGCGTGGG

136	Leu_AAG_chr6:28446400-28446481 (-)	GGTAGCGTGGCCGAGTGGTCTAAGACGCTGG ATTAAGGCTCCAGTCTCTTCGGGGGCGTGGG
137	Leu_CAA_chr6:28864000-28864105 (-)	GTCAGGATGGCCGAGTGGTCTAAGGCGCCAG ACTCAAGCTAAGCTTCCTCCGCGGTGGGGAT
138	Leu_CAA_chr6:28908830-28908934 (+)	GTCAGGATGGCCGAGTGGTCTAAGGCGCCAG ACTCAAGCTTGGCTTCCTCGTGTTGAGGATTC
139	Leu_CAA_chr6:27573417-27573524 (-)	GTCAGGATGGCCGAGTGGTCTAAGGCGCCAG ACTCAAGCTTACTGCTTCCTGTGTTCGGGTCT
140	Leu_CAA_chr6:27570348-27570454 (-)	GTCAGGATGGCCGAGTGGTCTAAGGCGCCAG ACTCAAGTTGCTACTTCCCAGGTTTGGGGCTT
141	Leu_CAA_chr1:249168054-249168159 (+)	GTCAGGATGGCCGAGTGGTCTAAGGCGCCAG ACTCAAGGTAAGCACCTTGCCTGCGGGCTTT
142	Leu_CAA_chr11:9296790-9296863 (+)	GCCTCCTTAGTGCAGTAGGTAGCGCATCAGT CTCAAAATCTGAATGGTCCTGAGTTCAAGCC
143	Leu_CAA_chr1:161581736-161581819 (-)	GTCAGGATGGCCGAGCAGTCTTAAGGCGCTG CGTTCAAATCGCACCCTCCGCTGGAGGCGTG
144	Leu_CAG_chr1:161411323-161411405 (+)	GTCAGGATGGCCGAGCGGTCTAAGGCGCTGC GTTCAGGTCGCAGTCTCCCCTGGAGGCGTGG
145	Leu_CAG_chr16:57333863-57333945 (+)	GTCAGGATGGCCGAGCGGTCTAAGGCGCTGC GTTCAGGTCGCAGTCTCCCCTGGAGGCGTGG
146	Leu_TAA_chr6:144537684-144537766 (+)	ACCAGGATGGCCGAGTGGTTAAGGCGTTGGA CTTAAGATCCAATGGACATATGTCCGCGTGG
147	Leu_TAA_chr6:27688898-27688980 (-)	ACCGGGATGGCCGAGTGGTTAAGGCGTTGGA CTTAAGATCCAATGGGCTGGTGCCCGCGTGG
148	Leu_TAA_chr11:59319228-59319310 (+)	ACCAGAATGGCCGAGTGGTTAAGGCGTTGGA CTTAAGATCCAATGGATTCATATCCGCGTGG
149	Leu_TAA_chr6:27198334-27198416 (-)	ACCGGGATGGCTGAGTGGTTAAGGCGTTGGA CTTAAGATCCAATGGACAGGTGTCCGCGTGG
150	Leu_TAG_chr17:8023632-8023713 (-)	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGG ATTTAGGCTCCAGTCTCTTCGGAGGCGTGGG
151	Leu_TAG_chr14:21093529-21093610 (+)	GGTAGTGTGGCCGAGCGGTCTAAGGCGCTGG ATTTAGGCTCCAGTCTCTTCGGGGGCGTGGG
152	Leu_TAG_chr16:22207032-22207113 (-)	GGTAGCGTGGCCGAGTGGTCTAAGGCGCTGG ATTTAGGCTCCAGTCATTTCGATGGCGTGGGT
153	Lys_CTT_chr14:58706613-58706685 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGGGA CTCTTAATCCCAGGGTCGTGGGTTCGAGCCC
154	Lys_CTT_chr19:36066750-36066822 (+)	GCCCAGCTAGCTCAGTCGGTAGAGCATAAGA CTCTTAATCTCAGGGTTGTGGATTCGTGCCCC
155	Lys_CTT_chr19:52425393-52425466 (-)	GCAGCTAGCTCAGTCGGTAGAGCATGAGACT CTTAATCTCAGGGTCATGGGTTCGTGCCCCAT
156	Lys_CTT_chr1:145395522-145395594 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGA CTCTTAATCTCAGGGTCGTGGGTTCGAGCCCC
157	Lys_CTT_chr16:3207406-3207478 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGA CCCTTAATCTCAGGGTCGTGGGTTCGAGCCC

158	Lys_CTT_chr16:3241501-3241573 (+)	GCCCGGCTAGCTCAGTCGGTAGAGCATGGGACTCTTAATCTCAGGGTCGTGGGTTCGAGCCCC
159	Lys_CTT_chr16:3230555-3230627 (-)	GCCCGGCTAGCTCAGTCGATAGAGCATGAGACTCTTAATCTCAGGGTCGTGGGTTCGAGCCG
160	Lys_CTT_chr1:55423542-55423614 (-)	GCCCAGCTAGCTCAGTCGGTAGAGCATGAGACTCTTAATCTCAGGGTCATGGGTTTGAGCCCC
161	Lys_CTT_chr16:3214939-3215011 (+)	GCCTGGCTAGCTCAGTCGGCAAAGCATGAGACTCTTAATCTCAGGGTCGTGGGCTCGAGCTCC
162	Lys_CTT_chr5:26198539-26198611 (-)	GCCCGACTACCTCAGTCGGTGGAGCATGGGACTCTTCATCCCAGGGTTGTGGGTTCGAGCCCC
163	Lys_TTT_chr16:7351 2216-73512288 (-)	GCCTGGATAGCTCAGTTGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
164	Lys_TTT_chr12:2784 3306-27843378 (+)	ACCCAGATAGCTCAGTCAGTAGAGCATCAGACTTTTAATCTGAGGGTCCAAGGTTCATGTCCC
165	Lys_TTT_chr11:1224 30655-122430727 (+)	GCCTGGATAGCTCAGTTGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
166	Lys_TTT_chr1:20447 5655-204475727 (+)	GCCCGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
167	Lys_TTT_chr6:27559593-27559665 (-)	GCCTGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
168	Lys_TTT_chr11:5932 3902-59323974 (+)	GCCCGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCGGGGTTCAAGTCCC
169	Lys_TTT_chr6:27302769-27302841 (-)	GCCTGGGTAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
170	Lys_TTT_chr6:28715521-28715593 (+)	GCCTGGATAGCTCAGTTGGTAGAACATCAGACTTTTAATCTGACGGTGCAGGGTTCAAGTCCC
171	Met_CAT_chr8:124169470-124169542 (-)	GCCTCGTTAGCGCAGTAGGTAGCGCGTCAGTCTCATAATCTGAAGGTCGTGAGTTCGATCCTC
172	Met_CAT_chr16:7146 0396-71460468 (+)	GCCCTCTTAGCGCAGTGGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCGAGCCT
173	Met_CAT_chr6:28912352-28912424 (+)	GCCTCCTTAGCGCAGTAGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCGAACCT
174	Met_CAT_chr6:26735574-26735646 (-)	GCCCTCTTAGCGCAGCGGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCGAGCCT
175	Met_CAT_chr6:26701712-26701784 (+)	GCCCTCTTAGCGCAGCTGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCAAGCCT
176	Met_CAT_chr16:8741 7628-87417700 (-)	GCCTCGTTAGCGCAGTAGGCAGCGCGTCAGTCTCATAATCTGAAGGTCGTGAGTTCGAGCCT
177	Met_CAT_chr6:58168492-58168564 (-)	GCCCTCTTAGTGCAGCTGGCAGCGCGTCAGTTTCATAATCTGAAAGTCCTGAGTTCAAGCCTC
178	Phe_GAA_chr6:28758499-28758571 (-)	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTAAAGGTCCCTGGTTCGATCCC
179	Phe_GAA_chr11:5933 3853-59333925 (-)	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTAAAGGTCCCTGGTTCAATCCC

180	Phe_GAA_chr6:28775610-28775682 (-)	GCCGAGATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTAAAGGTCCCTGGTTCAATCCC
181	Phe_GAA_chr6:28791093-28791166 (-)	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGACCGAAGATCTTAAAGGTCCCTGGTTCAATCC
182	Phe_GAA_chr6:28731374-28731447 (-)	GCTGAAATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTTAAAGTTCCCTGGTTCAACCCT
183	Pro_AGG_chr16:3241989-3242060 (+)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTTAGGATGCGAGAGGTCCCGGGTTCAAATCCCG
184	Pro_AGG_chr1:167684725-167684796 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTTAGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
185	Pro_CGG_chr1:167683962-167684033 (+)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTTCGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
186	Pro_CGG_chr6:27059521-27059592 (+)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTTCGGGTGTGAGAGGTCCCGGGTTCAAATCCCG
187	Pro_TGG_chr14:2110 1165-21101236 (+)	GGCTCGTTGGTCTAGTGGTATGATTCTCGCTTTGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
188	Pro_TGG_chr11:7594 6869-75946940 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGGTTTGGGTCCGAGAGGTCCCGGGTTCAAATCCCG
189	Pro_TGG_chr5:18061 5854-180615925 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTTTGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
190	SeC_TCA_chr19:4598 1859-45981945 (-)	GCCCGGATGATCCTCAGTGGTCTGGGGTGCAGGCTTCAAACCTGTAGCTGTCTAGCGACAGA
191	SeC_TCA_chr22:4454 6537-44546620 (+)	GCTCGGATGATCCTCAGTGGTCTGGGGTGCAGGCTTCAAACCTGTAGCTGTCTAGTGACAGA
192	Ser_AGA_chr6:27509554-27509635 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGACTAGAAATCCATTGGGGTTTCCCCGCGCAGG
193	Ser_AGA_chr6:26327817-26327898 (+)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGACTAGAAATCCATTGGGGTCTCCCCGCGCAGG
194	Ser_AGA_chr6:27499987-27500068 (+)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGACTAGAAATCCATTGGGGTTTCCCCACGCAGG
195	Ser_AGA_chr6:27521192-27521273 (-)	GTAGTCGTGGCCGAGTGGTTAAGGTGATGGACTAGAAACCCATTGGGGTCTCCCCGCGCAGG
196	Ser_CGA_chr17:8042199-8042280 (-)	GCTGTGATGGCCGAGTGGTTAAGGCGTTGGACTCGAAATCCAATGGGGTCTCCCCGCGCAGG
197	Ser_CGA_chr6:27177628-27177709 (+)	GCTGTGATGGCCGAGTGGTTAAGGCGTTGGACTCGAAATCCAATGGGGTCTCCCCGCGCAGG
198	Ser_CGA_chr6:27640229-27640310 (-)	GCTGTGATGGCCGAGTGGTTAAGGTGTTGGACTCGAAATCCAATGGGGGTTCCCCGCGCAGG
199	Ser_CGA_chr12:5658 4148-56584229 (+)	GTCACGGTGGCCGAGTGGTTAAGGCGTTGGACTCGAAATCCAATGGGGTTTCCCCGCACAGG
200	Ser_GCT_chr6:27065085-27065166 (+)	GACGAGGTGGCCGAGTGGTTAAGGCGATGGACTGCTAATCCATTGTGCTCTGCACGCGTGG
201	Ser_GCT_chr6:27265775-27265856 (+)	GACGAGGTGGCCGAGTGGTTAAGGCGATGGACTGCTAATCCATTGTGCTCTGCACGCGTGG

202	Ser_GCT_chr11:66115591-66115672 (+)	GACGAGGTGGCCGAGTGGTTAAGGCGATGG ACTGCTAATCCATTGTGCTTTGCACGCGTGGG
203	Ser_GCT_chr6:28565117-28565198 (-)	GACGAGGTGGCCGAGTGGTTAAGGCGATGG ACTGCTAATCCATTGTGCTCTGCACGCGTGG
204	Ser_GCT_chr6:28180815-28180896 (+)	GACGAGGTGGCCGAGTGGTTAAGGCGATGG ACTGCTAATCCATTGTGCTCTGCACACGTGG
205	Ser_GCT_chr6:26305718-26305801 (-)	GGAGAGGCCTGGCCGAGTGGTTAAGGCGATG GACTGCTAATCCATTGTGCTCTGCACGCGTG
206	Ser_TGA_chr10:69524261-69524342 (+)	GCAGCGATGGCCGAGTGGTTAAGGCGTTGGA CTTGAAATCCAATGGGGTCTCCCCGCGCAGG
207	Ser_TGA_chr6:27513468-27513549 (+)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGA CTTGAAATCCATTGGGGTTTCCCCGCGCAGG
208	Ser_TGA_chr6:26312824-26312905 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGA CTTGAAATCCATTGGGGTCTCCCCGCGCAGG
209	Ser_TGA_chr6:27473607-27473688 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGA CTTGAAATCCATTGGGGTTTCCCCGCGCAGG
210	Thr_AGT_chr17:8090478-8090551 (+)	GGCGCCGTGGCTTAGTTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC
211	Thr_AGT_chr6:26533145-26533218 (-)	GGCTCCGTGGCTTAGCTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC
212	Thr_AGT_chr6:28693795-28693868 (+)	GGCTCCGTAGCTTAGTTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGACTC
213	Thr_AGT_chr6:27694473-27694546 (+)	GGCTTCGTGGCTTAGCTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC
214	Thr_AGT_chr17:8042770-8042843 (-)	GGCGCCGTGGCTTAGCTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC
215	Thr_AGT_chr6:27130050-27130123 (+)	GGCCCTGTGGCTTAGCTGGTCAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC
216	Thr_CGT_chr6:28456770-28456843 (-)	GGCTCTATGGCTTAGTTGGTTAAAGCGCCTGT CTCGTAAACAGGAGATCCTGGGTTCGACTCC
217	Thr_CGT_chr16:143799750-14379821 (+)	GGCGCGGTGGCCAAGTGGTAAGGCGTCGGTC TCGTAAACCGAAGATCACGGGTTCGAACCCC
218	Thr_CGT_chr6:28615984-28616057 (-)	GGCTCTGTGGCTTAGTTGGCTAAAGCGCCTG TCTCGTAAACAGGAGATCCTGGGTTCGAATC
219	Thr_CGT_chr17:298777093-29877164 (+)	GGCGCGGTGGCCAAGTGGTAAGGCGTCGGTC TCGTAAACCGAAGATCGCGGGTTCGAACCCC
220	Thr_CGT_chr6:27586135-27586208 (+)	GGCCCTGTAGCTCAGCGGTTGGAGCGCTGGT CTCGTAAACCTAGGGGTCGTGAGTTCAAATC
221	Thr_TGT_chr6:28442329-28442402 (-)	GGCTCTATGGCTTAGTTGGTTAAAGCGCCTGT CTTGTAAACAGGAGATCCTGGGTTCGAATCC
222	Thr_TGT_chr1:222638347-222638419 (+)	GGCTCCATAGCTCAGTGGTTAGAGCACTGGT CTTGTAAACCAGGGGTCGCGAGTTCGATCCT
223	Thr_TGT_chr14:21081949-21082021 (-)	GGCTCCATAGCTCAGGGGTTAGAGCGCTGGT CTTGTAAACCAGGGGTCGCGAGTTCAATTCT

224	Thr_TGT_chr14:21099319-21099391 (-)	GGCTCCATAGCTCAGGGGTTAGAGCACTGGT CTTGTAAACCAGGGGTCGCGAGTTCAAATCT
225	Thr_TGT_chr14:21149849-21149921 (+)	GGCCCTATAGCTCAGGGGTTAGAGCACTGGT CTTGTAAACCAGGGGTCGCGAGTTCAAATCT
226	Thr_TGT_chr5:180618687-180618758 (-)	GGCTCCATAGCTCAGGGGTTAGAGCACTGGT CTTGTAAACCAGGGTCGCGAGTTCAAATCTC
227	Trp_CCA_chr17:8124187-8124258 (-)	GGCCTCGTGGCGCAACGGTAGCGCGTCTGAC TCCAGATCAGAAGGTTGCGTGTTCAAATCAC
228	Trp_CCA_chr17:19411494-19411565 (+)	GACCTCGTGGCGCAATGGTAGCGCGTCTGAC TCCAGATCAGAAGGTTGCGTGTTCAAGTCAC
229	Trp_CCA_chr6:26319330-26319401 (-)	GACCTCGTGGCGCAACGGTAGCGCGTCTGAC TCCAGATCAGAAGGTTGCGTGTTCAAATCAC
230	Trp_CCA_chr12:98898030-98898101 (+)	GACCTCGTGGCGCAACGGTAGCGCGTCTGAC TCCAGATCAGAAGGCTGCGTGTTCGAATCAC
231	Trp_CCA_chr7:99067307-99067378 (+)	GACCTCGTGGCGCAACGGCAGCGCGTCTGAC TCCAGATCAGAAGGTTGCGTGTTCAAATCAC
232	Tyr_ATA_chr2:219110549-219110641 (+)	CCTTCAATAGTTCAGCTGGTAGAGCAGAGGA CTATAGCTACTTCCTCAGTAGGAGACGTCCTT
233	Tyr_GTA_chr6:26569086-26569176 (+)	CCTTCGATAGCTCAGTTGGTAGAGCGGAGGA CTGTAGTTGGCTGTGTCCTTAGACATCCTTAG
234	Tyr_GTA_chr2:27273650-27273738 (+)	CCTTCGATAGCTCAGTTGGTAGAGCGGAGGA CTGTAGTGGATAGGGCGTGGCAATCCTTAGG
235	Tyr_GTA_chr6:26577332-26577420 (+)	CCTTCGATAGCTCAGTTGGTAGAGCGGAGGA CTGTAGGCTCATTAAGCAAGGTATCCTTAGG
236	Tyr_GTA_chr14:21125623-21125716 (-)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGATTGTATAGACATTTGCGGACATCCT
237	Tyr_GTA_chr8:67025602-67025694 (+)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGCTACTTCCTCAGCAGGAGACATCCTT
238	Tyr_GTA_chr8:67026223-67026311 (+)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGGCGCGCGCCCGTGGCCATCCTTAGG
239	Tyr_GTA_chr14:21121258-21121351 (-)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGCCTGTAGAAACATTTGTGGACATCC
240	Tyr_GTA_chr14:21131351-21131444 (-)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGATTGTACAGACATTTGCGGACATCC
241	Tyr_GTA_chr14:21151432-21151520 (+)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGTACTTAATGTGTGGTCATCCTTAGGT
242	Tyr_GTA_chr6:26595102-26595190 (+)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGGGGTTTGAATGTGGTCATCCTTAGGT
243	Tyr_GTA_chr14:21128117-21128210 (-)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGACTGCGGAAACGTTTGTGGACATCC
244	Tyr_GTA_chr6:26575798-26575887 (+)	CTTTCGATAGCTCAGTTGGTAGAGCGGAGGA CTGTAGGTTCATTAAACTAAGGCATCCTTAG
245	Tyr_GTA_chr8:66609532-66609619 (-)	TCTTCAATAGCTCAGCTGGTAGAGCGGAGGA CTGTAGGTGCACGCCCGTGGCCATTCTTAGG

246	Val_AAC_chr3:169490018-169490090 (+)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TAACACGCGAAAGGTCCCCGGTTCGAAACCG
247	Val_AAC_chr5:180615416-180615488 (-)	GTTTCCGTAGTGTAGTGGTCATCACGTTCGCC TAACACGCGAAAGGTCCCCGGTTCGAAACCG
248	Val_AAC_chr6:27618707-27618779 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TAACACGCGAAAGGTCCCTGGATCAAAACCA
249	Val_AAC_chr6:27648885-27648957 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TAACACGCGAAAGGTCCGCGGTTCGAAACCG
250	Val_AAC_chr6:27203288-27203360 (+)	GTTTCCGTAGTGTAGTGGTTATCACGTTTGCC TAACACGCGAAAGGTCCCCGGTTCGAAACCG
251	Val_AAC_chr6:28703206-28703277 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGTATGCT TAACATTCATGAGGCTCTGGGTTCGATCCCC
252	Val_CAC_chr1:161369490-161369562 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TCACACGCGAAAGGTCCCCGGTTCGAAACCG
253	Val_CAC_chr6:27248049-27248121 (-)	GCTTCTGTAGTGTAGTGGTTATCACGTTCGCC TCACACGCGAAAGGTCCCCGGTTCGAAACCG
254	Val_CAC_chr19:4724647-4724719 (-)	GTTTCCGTAGTGTAGCGGTTATCACATTCGCC TCACACGCGAAAGGTCCCCGGTTCGATCCCG
255	Val_CAC_chr1:149298555-149298627 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TCACACGCGAAAGGTCCCCGGTTCGAAACTG
256	Val_CAC_chr1:149684088-149684161 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TCACACGCGTAAAGGTCCCCGGTTCGAAACC
257	Val_CAC_chr6:27173867-27173939 (-)	GTTTCCGTAGTGGAGTGGTTATCACGTTCGCC TCACACGCGAAAGGTCCCCGGTTTGAAACCA
258	Val_TAC_chr11:59318102-59318174 (-)	GGTTCCATAGTGTAGTGGTTATCACGTCTGCT TTACACGCAGAAGGTCCTGGGTTCGAGCCCC
259	Val_TAC_chr11:59318460-59318532 (-)	GGTTCCATAGTGTAGCGGTTATCACGTCTGCT TTACACGCAGAAGGTCCTGGGTTCGAGCCCC
260	Val_TAC_chr10:5895674-5895746 (-)	GGTTCCATAGTGTAGTGGTTATCACATCTGCT TTACACGCAGAAGGTCCTGGGTTCAAGCCCC
261	Val_TAC_chr6:27258405-27258477 (+)	GTTTCCGTGGTGTAGTGGTTATCACATTCGCC TTACACGCGAAAGGTCCTCGGGTCGAAACCG
262	iMet_CAT_chr1:153643726-153643797 (+)	AGCAGAGTGGCGCAGCGGAAGCGTGCTGGG CCCATAACCCAGAGGTCGATGGATCGAAACC
263	iMet_CAT_chr6:27745664-27745735 (+)	AGCAGAGTGGCGCAGCGGAAGCGTGCTGGG CCCATAACCCAGAGGTCGATGGATCTAAACC
264	Glu_TTC_chr1:16861773-16861845 (-)	TCCCTGGTGGTCTAGTGGCTAGGATTCGGCG CTTTCACCGCCGCGGCCCGGGTTCGATTCCCG
265	Gly_CCC_chr1:17004765-17004836 (-)	GCGTTGGTGGTTTAGTGGTAGAATTCTCGCCT CCCATGCGGGAGACCCGGGTTCAATTCCCGG
266	Gly_CCC_chr1:17053779-17053850 (+)	GGCCTTGGTGGTGCAGTGGTAGAATTCTCGC CTCCCACGTGGGAGACCCGGGTTCAATTCCC
267	Glu_TTC_chr1:17199077-17199149 (+)	GTCCCTGGTGGTCTAGTGGCTAGGATTCGGC GCTTTCACCGCCGCGGCCCGGGTTCGATTCCC

268	Asn_GTT_chr1:17216171-17216245 (+)	TGTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGATTGGTGGTTCGAGCC
269	Arg_TCT_chr1:94313128-94313213 (+)	TGGCTCCGTGGCGCAATGGATAGCGCATTGGACTTCTAGAGGCTGAAGGCATTCAAAGGTTC
270	Lys_CTT_chr1:145395521-145395594 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGACTCTTAATCTCAGGGTCGTGGGTTCGAGCCCC
271	His_GTG_chr1:145396880-145396952 (-)	GCCGTGATCGTATAGTGGTTAGTACTCTGCGTTGTGGCCGCAGCAACCTCGGTTCGAATCCGA
272	Gly_TCC_chr1:145397863-145397935 (-)	GCGTTGGTGGTATAGTGGTGAGCATAGCTGCCTTCCAAGCAGTTGACCCGGGTTCGATTCCC
273	Glu_CTC_chr1:145399232-145399304 (-)	TCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCTCTCACCGCCGCGGCCCGGGTTCGATTCCC
274	Gln_CTG_chr1:145963303-145963375 (+)	AGGTTCCATGGTGTAATGGTGAGCACTCTGGACTCTGAATCCAGCGATCCGAGTTCGAGTCT
275	Asn_GTT_chr1:148000804-148000878 (+)	TGTCTCTGTGGCGTAGTCGGTTAGCGCGTTCGGCTGTTAACCGAAAAGTTGGTGGTTCGAGCC
276	Asn_GTT_chr1:148248114-148248188 (+)	TGTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
277	Asn_GTT_chr1:148598313-148598387 (-)	GTCTCTGTGGCGCAATCGGTTAGCGCATTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
278	Asn_GTT_chr1:149230569-149230643 (-)	GTCTCTGTGGCGCAATGGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
279	Val_CAC_chr1:149294665-149294736 (-)	GCACTGGTGGTTCAGTGGTAGAATTCTCGCCTCACACGCGGGACACCCGGGTTCAATTCCCG
280	Val_CAC_chr1:149298554-149298627 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCCTCACACGCGAAAGGTCCCCGGTTCGAAACTG
281	Gly_CCC_chr1:149680209-149680280 (-)	GCACTGGTGGTTCAGTGGTAGAATTCTCGCCTCCCACGCGGGAGACCCGGGTTTAATTCCCG
282	Val_CAC_chr1:149684087-149684161 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCCTCACACGCGTAAAGGTCCCCGGTTCGAAACC
283	Met_CAT_chr1:153643725-153643797 (+)	TAGCAGAGTGGCGCAGCGGAAGCGTGCTGGGCCCATAACCCAGAGGTCGATGGATCGAAAC
284	Val_CAC_chr1:161369489-161369562 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCCTCACACGCGAAAGGTCCCCGGTTCGAAACCG
285	Asp_GTC_chr1:161410614-161410686 (-)	TCCTCGTTAGTATAGTGGTGAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCGATTCCCC
286	Gly_GCC_chr1:161413093-161413164 (+)	TGCATGGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTCGATTCCC
287	Glu_CTC_chr1:161417017-161417089 (-)	TCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCTCTCACCGCCGCGGCCCGGGTTCGATTCCC
288	Asp_GTC_chr1:161492934-161493006 (+)	ATCCTTGTTACTATAGTGGTGAGTATCTCTGCCTGTCATGCGTGAGAGAGGGGGTCGATTCCC
289	Gly_GCC_chr1:161493636-161493707 (-)	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTCGATTCCCGG

290	Leu_CAG_chr1:161500131-161500214 (-)	GTCAGGATGGCCGAGCGGTCTAAGGCGCTGC GTTCAGGTCGCAGTCTCCCCTGGAGGCGTGG
291	Gly_TCC_chr1:161500902-161500974 (+)	CGCGTTGGTGGTATAGTGGTGAGCATAGCTG CCTTCCAAGCAGTTGACCCGGGTTCGATTCCC
292	Asn_GTT_chr1:161510030-161510104 (+)	CGTCTCTGTGGCGCAATCGGTTAGCGCGTTC GGCTGTTAACCGAAAGGTTGGTGGTTCGATC
293	Glu_TTC_chr1:161582507-161582579 (+)	CGCGTTGGTGGTGTAGTGGTGAGCACAGCTG CCTTTCAAGCAGTTAACGCGGGTTCGATTCCC
294	Pro_CGG_chr1:167683961-167684033 (+)	CGGCTCGTTGGTCTAGGGGTATGATTCTCGCT TCGGGTGCGAGAGGTCCCGGGTTCAAATCCC
295	Pro_AGG_chr1:167684724-167684796 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTT AGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
296	Lys_TTT_chr1:204475654-204475727 (+)	CGCCCGGATAGCTCAGTCGGTAGAGCATCAG ACTTTTAATCTGAGGGTCCAGGGTTCAAGTC
297	Lys_TTT_chr1:204476157-204476230 (-)	GCCCGGATAGCTCAGTCGGTAGAGCATCAGA CTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
298	Leu_CAA_chr1:249168053-249168159 (+)	TGTCAGGATGGCCGAGTGGTCTAAGGCGCCA GACTCAAGGTAAGCACCTTGCCTGCGGGCTT
299	Glu_CTC_chr1:249168446-249168518 (+)	TTCCCTGGTGGTCTAGTGGTTAGGATTCGGCG CTCTCACCGCCGCGGCCCGGGTTCGATTCCC
300	Tyr_GTA_chr2:27273649-27273738 (+)	GCCTTCGATAGCTCAGTTGGTAGAGCGGAGG ACTGTAGTGGATAGGGCGTGGCAATCCTTAG
301	Ala_AGC_chr2:27274081-27274154 (+)	CGGGGGATTAGCTCAAATGGTAGAGCGCTCG CTTAGCATGCGAGAGGTAGCGGGATCGATGC
302	Ile_TAT_chr2:43037675-43037768 (+)	AGCTCCAGTGGCGCAATCGGTTAGCGCGCGG TACTTATACAGCAGTACATGCAGAGCAATGC
303	Gly_CCC_chr2:70476122-70476193 (-)	GCGCCGCTGGTGTAGTGGTATCATGCAAGAT TCCCATTCTTGCGACCCGGGTTCGATTCCCGG
304	Glu_TTC_chr2:131094700-131094772 (-)	TCCCATATGGTCTAGCGGTTAGGATTCCTGGT TTTCACCCAGGTGGCCCGGGTTCGACTCCCG
305	Ala_CGC_chr2:157257280-157257352 (+)	GGGGGATGTAGCTCAGTGGTAGAGCGCGCGC TTCGCATGTGTGAGGTCCCGGGTTCAATCCCC
306	Gly_GCC_chr2:157257658-157257729 (-)	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCT GCCACGCGGGAGGCCCGGGTTCGATTCCCGG
307	Arg_ACG_chr3:45730490-45730563 (-)	GGGCCAGTGGCGCAATGGATAACGCGTCTGA CTACGGATCAGAAGATTCTAGGTTCGACTCC
308	Val_AAC_chr3:169490017-169490090 (+)	GGTTTCCGTAGTGTAGTGGTTATCACGTTCGC CTAACACGCGAAAGGTCCCCGGTTCGAAACC
309	Val_AAC_chr5:180596609-180596682 (+)	AGTTTCCGTAGTGTAGTGGTTATCACGTTCGC CTAACACGCGAAAGGTCCCCGGTTCGAAACC
310	Leu_AAG_chr5:180614700-180614782 (+)	AGGTAGCGTGGCCGAGCGGTCTAAGGCGCTG GATTAAGGCTCCAGTCTCTTCGGGGGCGTGG
311	Val_AAC_chr5:180615415-180615488 (-)	GTTTCCGTAGTGTAGTGGTCATCACGTTCGCC TAACACGCGAAAGGTCCCCGGTTCGAAACCG

312	Pro_TGG_chr5:18061 5853-180615925 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTT TGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
313	Thr_TGT_chr5:18061 8686-180618758 (-)	GGCTCCATAGCTCAGGGGTTAGAGCACTGGT CTTGTAAACCAGGGTCGCGAGTTCAAATCTC
314	Ala_TGC_chr5:18063 3867-180633939 (+)	TGGGGATGTAGCTCAGTGGTAGAGCGCATGC TTTGCATGTATGAGGCCCCGGGTTCGATCCCC
315	Lys_CTT_chr5:18063 4754-180634827 (+)	CGCCCGGCTAGCTCAGTCGGTAGAGCATGAG ACTCTTAATCTCAGGGTCGTGGGTTCGAGCC
316	Val_AAC_chr5:18064 5269-180645342 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TAACACGCGAAAGGTCCCCGGTTCGAAACCG
317	Lys_CTT_chr5:18064 8978-180649051 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGA CTCTTAATCTCAGGGTCGTGGGTTCGAGCCCC
318	Val_CAC_chr5:18064 9394-180649467 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCC TCACACGCGAAAGGTCCCCGGTTCGAAACCG
319	Met_CAT_chr6:26286 753-26286825 (+)	CAGCAGAGTGGCGCAGCGGAAGCGTGCTGG GCCCATAACCCAGAGGTCGATGGATCGAAAC
320	Ser_GCT_chr6:26305 717-26305801 (-)	GGAGAGGCCTGGCCGAGTGGTTAAGGCGATG GACTGCTAATCCATTGTGCTCTGCACGCGTG
321	Gln_TTG_chr6:26311 423-26311495 (-)	GGCCCCATGGTGTAATGGTTAGCACTCTGGA CTTTGAATCCAGCGATCCGAGTTCAAATCTC
322	Gln_TTG_chr6:26311 974-26312046 (-)	GGCCCCATGGTGTAATGGTTAGCACTCTGGA CTTTGAATCCAGCGATCCGAGTTCAAATCTC
323	Ser_TGA_chr6:26312 823-26312905 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGA CTTGAAATCCATTGGGGTCTCCCCGCGCAGG
324	Met_CAT_chr6:26313 351-26313423 (-)	AGCAGAGTGGCGCAGCGGAAGCGTGCTGGG CCCATAACCCAGAGGTCGATGGATCGAAACC
325	Arg_TCG_chr6:26323 045-26323118 (+)	GGACCACGTGGCCTAATGGATAAGGCGTCTG ACTTCGGATCAGAAGATTGAGGGTTCGAATC
326	Ser_AGA_chr6:26327 816-26327898 (+)	TGTAGTCGTGGCCGAGTGGTTAAGGCGATGG ACTAGAAATCCATTGGGGTCTCCCCGCGCAG
327	Met_CAT_chr6:26330 528-26330600 (-)	AGCAGAGTGGCGCAGCGGAAGCGTGCTGGG CCCATAACCCAGAGGTCGATGGATCGAAACC
328	Leu_CAG_chr6:26521 435-26521518 (+)	CGTCAGGATGGCCGAGCGGTCTAAGGCGCTG CGTTCAGGTCGCAGTCTCCCCTGGAGGCGTG
329	Thr_AGT_chr6:26533 144-26533218 (-)	GGCTCCGTGGCTTAGCTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC
330	Arg_ACG_chr6:26537 725-26537798 (+)	AGGGCCAGTGGCGCAATGGATAACGCGTCTG ACTACGGATCAGAAGATTCCAGGTTCGACTC
331	Val_CAC_chr6:26538 281-26538354 (+)	GGTTTCCGTAGTGTAGTGGTTATCACGTTCGC CTCACACGCGAAAGGTCCCCGGTTCGAAACC
332	Ala_CGC_chr6:26553 730-26553802 (+)	AGGGGATGTAGCTCAGTGGTAGAGCGCATGC TTCGCATGTATGAGGTCCCGGGTTCGATCCCC
333	Ile_AAT_chr6:265543 49-26554423 (+)	TGGCCGGTTAGCTCAGTTGGTTAGAGCGTGG TGCTAATAACGCCAAGGTCGCGGGTTCGATC

334	Pro_AGG_chr6:26555497-26555569 (+)	CGGCTCGTTGGTCTAGGGGTATGATTCTCGCTTAGGGTGCGAGAGGTCCCGGGTTCAAATCCC
335	Lys_CTT_chr6:26556773-26556846 (+)	AGCCCGGCTAGCTCAGTCGGTAGAGCATGAGACTCTTAATCTCAGGGTCGTGGGTTCGAGCC
336	Tyr_GTA_chr6:26569085-26569176 (+)	TCCTTCGATAGCTCAGTTGGTAGAGCGGAGGACTGTAGTTGGCTGTGTCCTTAGACATCCTTA
337	Ala_AGC_chr6:26572091-26572164 (-)	GGGGAATTAGCTCAAATGGTAGAGCGCTCGCTTAGCATGCGAGAGGTAGCGGGATCGATGCC
338	Met_CAT_chr6:26766443-26766516 (+)	CGCCCTCTTAGCGCAGCGGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCGAGCCT
339	Ile_TAT_chr6:26988124-26988218 (+)	TGCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATATGGCAGTATGTGTGCGAGTGATG
340	His_GTG_chr6:27125905-27125977 (+)	TGCCGTGATCGTATAGTGGTTAGTACTCTGCGTTGTGGCCGCAGCAACCTCGGTTCGAATCCG
341	Ile_AAT_chr6:27144993-27145067 (-)	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCC
342	Val_AAC_chr6:27203287-27203360 (+)	AGTTTCCGTAGTGTAGTGGTTATCACGTTTGCCTAACACGCGAAAGGTCCCCGGTTCGAAACC
343	Val_CAC_chr6:27248048-27248121 (-)	GCTTCTGTAGTGTAGTGGTTATCACGTTCGCCTCACACGCGAAAGGTCCCCGGTTCGAAACCG
344	Asp_GTC_chr6:27447452-27447524 (+)	TTCCTCGTTAGTATAGTGGTGAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCGATTCCC
345	Ser_TGA_chr6:27473606-27473688 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGACTTGAAATCCATTGGGGTTTCCCCGCGCAGG
346	Gln_CTG_chr6:27487307-27487379 (+)	AGGTTCCATGGTGTAATGGTTAGCACTCTGGACTCTGAATCCAGCGATCCGAGTTCAAATCT
347	Asp_GTC_chr6:27551235-27551307 (-)	TCCTCGTTAGTATAGTGGTGAGTGTCCCCGTCTGTCACGCGGGAGACCGGGGTTCGATTCCCC
348	Val_AAC_chr6:27618706-27618779 (-)	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCCTAACACGCGAAAGGTCCCTGGATCAAAACCA
349	Ile_AAT_chr6:27655966-27656040 (+)	CGGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATC
350	Gln_CTG_chr6:27759134-27759206 (-)	GGCCCCATGGTGTAATGGTCAGCACTCTGGACTCTGAATCCAGCGATCCGAGTTCAAATCTC
351	Gln_TTG_chr6:27763639-27763711 (-)	GGCCCCATGGTGTAATGGTTAGCACTCTGGACTTTGAATCCAGCGATCCGAGTTCAAATCTC
352	Ala_AGC_chr6:28574932-28575004 (+)	TGGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGTACGAGGTCCCGGGTTCAATCCC
353	Ala_AGC_chr6:28626013-28626085 (-)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTAGCATGCATGAGGTCCCGGGTTCGATCCCC
354	Ala_CGC_chr6:28697091-28697163 (+)	AGGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTCGCATGTACGAGGCCCCGGGTTCGACCCC
355	Ala_AGC_chr6:28806220-28806292 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGCACGAGGCCCCGGGTTCAATCCCC

356	Ala_AGC_chr6:28831461-28831533 (-)	GGGGGTGTAGCTCAGTGGTAGAGCGCGTGCTTAGCATGCACGAGGCCCCGGGTTCAATCCCC
357	Leu_CAA_chr6:28863999-28864105 (-)	GTCAGGATGGCCGAGTGGTCTAAGGCGCCAGACTCAAGCTAAGCTTCCTCCGCGGTGGGGAT
358	Leu_CAA_chr6:28908829-28908934 (+)	TGTCAGGATGGCCGAGTGGTCTAAGGCGCCAGACTCAAGCTTGGCTTCCTCGTGTTGAGGATT
359	Gln_CTG_chr6:28909377-28909449 (-)	GGTTCCATGGTGTAATGGTTAGCACTCTGGACTCTGAATCCAGCGATCCGAGTTCAAATCTC
360	Leu_AAG_chr6:28911398-28911480 (-)	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTAAGGCTCCAGTCTCTTCGGGGGCGTGGG
361	Met_CAT_chr6:28912351-28912424 (+)	TGCCTCCTTAGCGCAGTAGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCGAACCT
362	Lys_TTT_chr6:28918805-28918878 (+)	AGCCCGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTC
363	Met_CAT_chr6:28921041-28921114 (-)	GCCTCCTTAGCGCAGTAGGCAGCGCGTCAGTCTCATAATCTGAAGGTCCTGAGTTCGAACCT
364	Glu_CTC_chr6:28949975-28950047 (+)	TTCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCTCTCACCGCCGCGGCCCGGGTTCGATTCCC
365	Leu_TAA_chr6:144537683-144537766 (+)	CACCAGGATGGCCGAGTGGTTAAGGCGTTGGACTTAAGATCCAATGGACATATGTCCGCGTG
366	Pro_AGG_chr7:128423503-128423575 (+)	TGGCTCGTTGGTCTAGGGGTATGATTCTCGCTTAGGGTGCGAGAGGTCCCGGGTTCAAATCCC
367	Arg_CCT_chr7:139025445-139025518 (+)	AGCCCCAGTGGCCTAATGGATAAGGCATTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTC
368	Cys_GCA_chr7:149388271-149388343 (-)	GGGGATATAGCTCAGGGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCCGGTTCAAATCCG
369	Tyr_GTA_chr8:67025601-67025694 (+)	CCCTTCGATAGCTCAGCTGGTAGAGCGGAGGACTGTAGCTACTTCCTCAGCAGGAGACATCC
370	Tyr_GTA_chr8:67026222-67026311 (+)	CCCTTCGATAGCTCAGCTGGTAGAGCGGAGGACTGTAGGCGCGCGCCCGTGGCCATCCTTAG
371	Ala_AGC_chr8:67026423-67026496 (+)	TGGGGGATTAGCTCAAATGGTAGAGCGCTCGCTTAGCATGCGAGAGGTAGCGGGATCGATGC
372	Ser_AGA_chr8:96281884-96281966 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGACTAGAAATCCATTGGGGTCTCCCCGCGCAGG
373	Met_CAT_chr8:124169469-124169542 (-)	GCCTCGTTAGCGCAGTAGGTAGCGCGTCAGTCTCATAATCTGAAGGTCGTGAGTTCGATCCTC
374	Arg_TCT_chr9:131102354-131102445 (-)	GGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGCTGAGCCTAGTGTGGTCATTCAAA
375	Asn_GTT_chr10:22518437-22518511 (-)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
376	Ser_TGA_chr10:69524260-69524342 (+)	GGCAGCGATGGCCGAGTGGTTAAGGCGTTGGACTTGAAATCCAATGGGGTCTCCCCGCGCAG
377	Val_TAC_chr11:59318101-59318174 (-)	GGTTCCATAGTGTAGTGGTTATCACGTCTGCTTTACACGCAGAAGGTCCTGGGTTCGAGCCCC

378	Val_TAC_chr11:59318459-59318532 (-)	GGTTCCATAGTGTAGCGGTTATCACGTCTGCTTTACACGCAGAAGGTCCTGGGTTCGAGCCCC
379	Arg_TCT_chr11:59318766-59318852 (+)	TGGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGATAGTTAGAGAAATTCAAAGGTT
380	Leu_TAA_chr11:59319227-59319310 (+)	TACCAGAATGGCCGAGTGGTTAAGGCGTTGGACTTAAGATCCAATGGATTCATATCCGCGTG
381	Lys_TTT_chr11:59323901-59323974 (+)	GGCCCGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCGGGGTTCAAGTC
382	Phe_GAA_chr11:59324969-59325042 (-)	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTAAAGGTCCCTGGTTCGATCCC
383	Lys_TTT_chr11:59327807-59327880 (-)	GCCCGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC
384	Phe_GAA_chr11:59333852-59333925 (-)	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTAAAGGTCCCTGGTTCAATCCC
385	Ser_GCT_chr11:66115590-66115672 (+)	GGACGAGGTGGCCGAGTGGTTAAGGCGATGGACTGCTAATCCATTGTGCTTTGCACGCGTGG
386	Pro_TGG_chr11:75946868-75946940 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGGTTTGGGTCCGAGAGGTCCCGGGTTCAAATCCCG
387	Ser_CGA_chr12:56584147-56584229 (+)	AGTCACGGTGGCCGAGTGGTTAAGGCGTTGGACTCGAAATCCAATGGGGTTTCCCCGCACAG
388	Asp_GTC_chr12:98897280-98897352 (+)	CTCCTCGTTAGTATAGTGGTTAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCAATTCCC
389	Trp_CCA_chr12:98898029-98898101 (+)	GGACCTCGTGGCGCAACGGTAGCGCGTCTGACTCCAGATCAGAAGGCTGCGTGTTCGAATCA
390	Ala_TGC_chr12:125406300-125406372 (-)	GGGGATGTAGCTCAGTGGTAGAGCGCATGCTTTGCATGTATGAGGCCCCGGGTTCGATCCCC
391	Phe_GAA_chr12:125412388-125412461 (-)	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGACTGAAGATCTAAAGGTCCCTGGTTCGATCCC
392	Ala_TGC_chr12:125424511-125424583 (+)	AGGGGATGTAGCTCAGTGGTAGAGCGCATGCTTTGCACGTATGAGGCCCCGGGTTCAATCCC
393	Asn_GTT_chr13:31248100-31248174 (-)	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCGGCTGTTAACCGAAAGGTTGGTGGTTCGAGCC
394	Glu_TTC_chr13:45492061-45492133 (-)	TCCCACATGGTCTAGCGGTTAGGATTCCTGGTTTTCACCCAGGCGGCCCGGGTTCGACTCCCG
395	Thr_TGT_chr14:21081948-21082021 (-)	GGCTCCATAGCTCAGGGGTTAGAGCGCTGGTCTTGTAAACCAGGGGTCGCGAGTTCAATTCT
396	Leu_TAG_chr14:21093528-21093610 (+)	TGGTAGTGTGGCCGAGCGGTCTAAGGCGCTGGATTTAGGCTCCAGTCTCTTCGGGGGCGTGG
397	Thr_TGT_chr14:21099318-21099391 (-)	GGCTCCATAGCTCAGGGGTTAGAGCACTGGTCTTGTAAACCAGGGGTCGCGAGTTCAAATCT
398	Pro_TGG_chr14:21101164-21101236 (+)	TGGCTCGTTGGTCTAGTGGTATGATTCTCGCTTTGGGTGCGAGAGGTCCCGGGTTCAAATCCC
399	Tyr_GTA_chr14:21131350-21131444 (-)	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGACTGTAGATTGTACAGACATTTGCGGACATCC

400	Thr_TGT_chr14:21149848-21149921 (+)	AGGCCCTATAGCTCAGGGGTTAGAGCACTGG TCTTGTAAACCAGGGGTCGCGAGTTCAAATC
401	Tyr_GTA_chr14:21151431-21151520 (+)	TCCTTCGATAGCTCAGCTGGTAGAGCGGAGG ACTGTAGTACTTAATGTGTGGTCATCCTTAGG
402	Pro_TGG_chr14:21152174-21152246 (+)	TGGCTCGTTGGTCTAGGGGTATGATTCTCGCT TTGGGTGCGAGAGGTCCCGGGTTCAAATCCC
403	Lys_CTT_chr14:58706612-58706685 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGGGA CTCTTAATCCCAGGGTCGTGGGTTCGAGCCC
404	Ile_AAT_chr14:102783428-102783502 (+)	CGGCCGGTTAGCTCAGTTGGTTAGAGCGTGG TGCTAATAACGCCAAGGTCGCGGGTTCGATC
405	Glu_TTC_chr15:26327380-26327452 (-)	TCCCACATGGTCTAGCGGTTAGGATTCCTGGT TTTCACCCAGGCGGCCCGGGTTCGACTCCCG
406	Ser_GCT_chr15:40886022-40886104 (-)	GACGAGGTGGCCGAGTGGTTAAGGCGATGG ACTGCTAATCCATTGTGCTCTGCACGCGTGG
407	His_GTG_chr15:45490803-45490875 (-)	GCCGTGATCGTATAGTGGTTAGTACTCTGCGT TGTGGCCGCAGCAACCTCGGTTCGAATCCGA
408	His_GTG_chr15:45493348-45493420 (+)	CGCCGTGATCGTATAGTGGTTAGTACTCTGC GTTGTGGCCGCAGCAACCTCGGTTCGAATCC
409	Gln_CTG_chr15:66161399-66161471 (-)	GGTTCCATGGTGTAATGGTTAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCAAATCTC
410	Lys_CTT_chr15:79152903-79152976 (+)	TGCCCGGCTAGCTCAGTCGGTAGAGCATGGG ACTCTTAATCCCAGGGTCGTGGGTTCGAGCC
411	Arg_TCG_chr15:89878303-89878376 (+)	GGGCCGCGTGGCCTAATGGATAAGGCGTCTG ACTTCGGATCAGAAGATTGCAGGTTCGAGTC
412	Gly_CCC_chr16:686735-686806 (-)	GCGCCGCTGGTGTAGTGGTATCATGCAAGAT TCCCATTCTTGCGACCCGGGTTCGATTCCCGG
413	Arg_CCG_chr16:3200674-3200747 (+)	GGGCCGCGTGGCCTAATGGATAAGGCGTCTG ATTCCGGATCAGAAGATTGAGGGTTCGAGTC
414	Arg_CCT_chr16:3202900-3202973 (+)	CGCCCCGGTGGCCTAATGGATAAGGCATTGG CCTCCTAAGCCAGGGATTGTGGGTTCGAGTC
415	Lys_CTT_chr16:3207405-3207478 (-)	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGA CCCTTAATCTCAGGGTCGTGGGTTCGAGCCC
416	Thr_CGT_chr16:14379749-14379821 (+)	AGGCGCGGTGGCCAAGTGGTAAGGCGTCGGT CTCGTAAACCGAAGATCACGGGTTCGAACCC
417	Leu_TAG_chr16:22207031-22207113 (-)	GGTAGCGTGGCCGAGTGGTCTAAGGCGCTGG ATTTAGGCTCCAGTCATTTCGATGGCGTGGGT
418	Leu_AAG_chr16:22308460-22308542 (+)	GGGTAGCGTGGCCGAGCGGTCTAAGGCGCTG GATTAAGGCTCCAGTCTCTTCGGGGGCGTGG
419	Leu_CAG_chr16:57333862-57333945 (+)	AGTCAGGATGGCCGAGCGGTCTAAGGCGCTG CGTTCAGGTCGCAGTCTCCCCTGGAGGCGTG
420	Leu_CAG_chr16:57334391-57334474 (-)	GTCAGGATGGCCGAGCGGTCTAAGGCGCTGC GTTCAGGTCGCAGTCTCCCCTGGAGGCGTGG
421	Met_CAT_chr16:87417627-87417700 (-)	GCCTCGTTAGCGCAGTAGGCAGCGCGTCAGT CTCATAATCTGAAGGTCGTGAGTTCGAGCCT

422	Leu_TAG_chr17:8023631-8023713 (-)	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTTAGGCTCCAGTCTCTTCGGAGGCGTGGG
423	Arg_TCT_chr17:8024242-8024330 (+)	TGGCTCTGTGGCGCAATGGATAGCGCATTGGACTTCTAGTGACGAATAGAGCAATTCAAAGG
424	Gly_GCC_chr17:8029063-8029134 (+)	CGCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTCGATTCCC
425	Ser_CGA_chr17:8042198-8042280 (-)	GCTGTGATGGCCGAGTGGTTAAGGCGTTGGACTCGAAATCCAATGGGGTCTCCCCGCGCAGG
426	Thr_AGT_chr17:8042769-8042843 (-)	GGCGCCGTGGCTTAGCTGGTTAAAGCGCCTGTCTAGTAAACAGGAGATCCTGGGTTCGAATC
427	Trp_CCA_chr17:8089675-8089747 (+)	CGACCTCGTGGCGCAACGGTAGCGCGTCTGACTCCAGATCAGAAGGTTGCGTGTTCAAATCA
428	Ser_GCT_chr17:8090183-8090265 (+)	AGACGAGGTGGCCGAGTGGTTAAGGCGATGGACTGCTAATCCATTGTGCTCTGCACGCGTG
429	Thr_AGT_chr17:8090477-8090551 (+)	CGGCGCCGTGGCTTAGTTGGTTAAAGCGCCTGTCTAGTAAACAGGAGATCCTGGGTTCGAAT
430	Trp_CCA_chr17:8124186-8124258 (-)	GGCCTCGTGGCGCAACGGTAGCGCGTCTGACTCCAGATCAGAAGGTTGCGTGTTCAAATCAC
431	Gly_TCC_chr17:8124865-8124937 (+)	AGCGTTGGTGGTATAGTGGTAAGCATAGCTGCCTTCCAAGCAGTTGACCCGGGTTCGATTCCC
432	Asp_GTC_chr17:8125555-8125627 (-)	TCCTCGTTAGTATAGTGGTGAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCGATTCCCC
433	Pro_CGG_chr17:8126150-8126222 (-)	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTTCGGGTGCGAGAGGTCCCGGGTTCAAATCCCG
434	Thr_AGT_chr17:8129552-8129626 (-)	GGCGCCGTGGCTTAGTTGGTTAAAGCGCCTGTCTAGTAAACAGGAGATCCTGGGTTCGAATC
435	Ser_AGA_chr17:8129927-8130009 (-)	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGACTAGAAATCCATTGGGGTCTCCCCGCGCAGG
436	Trp_CCA_chr17:19411493-19411565 (+)	TGACCTCGTGGCGCAATGGTAGCGCGTCTGACTCCAGATCAGAAGGTTGCGTGTTCAAGTCA
437	Thr_CGT_chr17:29877092-29877164 (+)	AGGCGCGGTGGCCAAGTGGTAAGGCGTCGGTCTCGTAAACCGAAGATCGCGGGTTCGAACCC
438	Cys_GCA_chr17:37023897-37023969 (+)	AGGGGGTATAGCTCAGTGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCCGGTTCAAATCC
439	Cys_GCA_chr17:37025544-37025616 (-)	GGGGGTATAGCTCAGTGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCTGGTTCAAATCCG
440	Cys_GCA_chr17:37309986-37310058 (-)	GGGGGTATAGCTCAGTGGTAGAGCATTTGACTGCAGATCAAGAGGTCCCCGGTTCAAATCCG
441	Gln_TTG_chr17:47269889-47269961 (+)	AGGTCCCATGGTGTAATGGTTAGCACTCTGGACTTTGAATCCAGCGATCCGAGTTCAAATCT
442	Arg_CCG_chr17:66016012-66016085 (-)	GACCCAGTGGCCTAATGGATAAGGCATCAGCCTCCGGAGCTGGGGATTGTGGGTTCGAGTCC
443	Arg_CCT_chr17:73030000-73030073 (+)	AGCCCCAGTGGCCTAATGGATAAGGCACTGGCCTCCTAAGCCAGGGATTGTGGGTTCGAGTC

444	Arg_CCT_chr17:73030525-73030598 (-)	GCCCCAGTGGCCTAATGGATAAGGCACTGGC CTCCTAAGCCAGGGATTGTGGGTTCGAGTCC
445	Arg_TCG_chr17:73031207-73031280 (+)	AGACCGCGTGGCCTAATGGATAAGGCGTCTG ACTTCGGATCAGAAGATTGAGGGTTCGAGTC
446	Asn_GTT_chr19:1383561-1383635 (+)	CGTCTCTGTGGCGCAATCGGTTAGCGCGTTC GGCTGTTAACCGAAAGGTTGGTGGTTCGAGC
447	Gly_TCC_chr19:4724081-4724153 (+)	GGCGTTGGTGGTATAGTGGTTAGCATAGCTG CCTTCCAAGCAGTTGACCCGGGTTCGATTCCC
448	Val_CAC_chr19:4724646-4724719 (-)	GTTTCCGTAGTGTAGCGGTTATCACATTCGCC TCACACGCGAAAGGTCCCCGGTTCGATCCCG
449	Thr_AGT_chr19:33667962-33668036 (+)	TGGCGCCGTGGCTTAGTTGGTTAAAGCGCCT GTCTAGTAAACAGGAGATCCTGGGTTCGAAT
450	Ile_TAT_chr19:39902807-39902900 (-)	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGT ACTTATATGACAGTGCGAGCGGAGCAATGCC
451	Gly_GCC_chr21:18827106-18827177 (-)	GCATGGGTGGTTCAGTGGTAGAATTCTCGCC TGCCACGCGGGAGGCCCGGGTTCGATTCCCG

Non-naturally occurring modification

A TREM, a TREM core fragment or a TREM fragment described herein comprises a non-naturally occurring modification, e.g., a modification described in any one of Tables 5-9. A non-naturally occurring modification can be made according to methods known in the art. Exemplary methods of making non-naturally occurring modifications are provided in Examples 4-7.

In an embodiment, a non-naturally occurring modification is a modification that a cell, e.g., a human cell, does not make on an endogenous tRNA.

In an embodiment, a non-naturally occurring modification is a modification that a cell, e.g., a human cell, can make on an endogenous tRNA, but wherein such modification is in a location in which it does not occur on a native tRNA. In an embodiment, the non-naturally occurring modification is in a domain, linker or arm which does not have such modification in nature. In an embodiment, the non-naturally occurring modification is at a position within a domain, linker or arm, which does not have such modification in nature. In an embodiment, the non-naturally occurring modification is on a nucleotide which does not have such modification in nature. In an embodiment, the non-naturally occurring modification is on a nucleotide at a position within a domain, linker or arm, which does not have such modification in nature.

In an embodiment, a TREM, a TREM core fragment or a TREM fragment described herein comprises a non-naturally occurring modification provided in Table 5, or a combination thereof.

Table 5: Exemplary non-naturally occurring modifications

Modification
7-deaza-adenosine
Nl-methyl-adenosine
N6, N6 (dimethyl)adenine
N6-cis-hydroxy-isopentenyl-adenosine
thio-adenosine
2-(amino)adenine
2-(aminopropyl)adenine
2-(methylthio) N6 (isopentenyl)adenine
2-(alkyl)adenine
2-(aminoalkyl)adenine
2-(aminopropyl)adenine
2-(halo)adenine
2-(propyl)adenine
2'-azido-2'-deoxy-adenosine
2'-Deoxy-2'-alpha-aminoadenosine
2'-Deoxy-2'-alpha-azidoadenosine
6-(alkyl)adenine
6-(methyl)adenine
6-(alkyl)adenine
6-(methyl)adenine
7-(deaza)adenine
8-(alkenyl)adenine
8-(alkynyl)adenine
8-(amino)adenine
8-(thioalkyl)adenine
8-(alkenyl)adenine

Modification
8-(alkyl)adenine
8-(alkynyl)adenine
8-(amino)adenine
8-(halo)adenine
8-(hydroxyl)adenine
8-(thioalkyl)adenine
8-(thiol)adenine
8-azido-adenosine
azaadenine
deazaadenine
N6-(methyl)adenine
N6-(isopentyl)adenine
7-deaza-8-aza-adenosine
7-methyladenine
1-deazaadenosine
2'-Fluoro-N6-Bz-deoxyadenosine
2' -OMe-2-Amino-adenosine
2'O-methyl-N6-Bz-deoxyadenosine
2'-alpha-ethynyladenosine
2-aminoadenine
2-Aminoadenosine
2-Amino-adenosine
2' -alpha-Trifluoromethyladenosine
2-Azidoadenosine
2' -beta-Ethynyladenosine
2-Bromoadenosine

Modification
2’-beta-Trifluoromethyladenosine
2-Chloroadenosine
2’ -Deoxy-2’,2’-difluoroadenosine
2’ -Deoxy-2’-alpha-mercaptoadenosine
2’ -Deoxy-2’-alpha-thiomethoxyadenosine
2’ -Deoxy-2’-beta-aminoadenosine
2’ -Deoxy-2’-beta-azidoadenosine
2’ -Deoxy-2’-beta-bromoadenosine
2’ -Deoxy-2’-beta-chloroadenosine
2’ -Deoxy-2’-beta-fluoroadenosine
2’ -Deoxy-2’-beta-iodoadenosine
2’ -Deoxy-2’-beta-mercaptoadenosine
2’ -Deoxy-2’-beta-thiomethoxyadenosine
2-Fluoroadenosine
2-Iodoadenosine
2-Mercaptoadenosine
2-methoxy-adenine
2-methylthio-adenine
2-Trifluoromethyladenosine
3-Deaza-3-bromoadenosine
3-Deaza-3-chloroadenosine
3-Deaza-3-fluoroadenosine
3-Deaza-3-iodoadenosine
3-Deazaadenosine
4’ -Azidoadenosine
4’-Carbocyclic adenosine
4’ -Ethynyladenosine
5’-Homo-adenosine
8-Aza-adenosine
8-bromo-adenosine

Modification
8-Trifluoromethyladenosine
9-Deazaadenosine
2-aminopurine
7-deaza-2,6-diaminopurine
7-deaza-8-aza-2,6-diaminopurine
7-deaza-8-aza-2-aminopurine
2,6-diaminopurine
7-deaza-8-aza-adenine, 7-deaza-2-aminopurine
4-methylcytidine
5-aza-cytidine
Pseudo-iso-cytidine
pyrrolo-cytidine
alpha-thio-cytidine
2-(thio)cytosine
2’ -Amino-2’ -deoxy-cytosine
2’ -Azido-2’-deoxy-cytosine
2’ -Deoxy-2’-alpha-aminocytidine
2’ -Deoxy-2’-alpha-azidocytidine
3 (deaza) 5 (aza)cytosine
3 (methyl)cytosine
3-(alkyl)cytosine
3-(deaza) 5 (aza)cytosine
3-(methyl)cytidine
4,2’-O-dimethylcytidine
5 (halo)cytosine
5 (methyl)cytosine
5 (propynyl)cytosine
5 (trifluoromethyl)cytosine
5-(alkyl)cytosine
5-(alkynyl)cytosine

Modification
5-(halo)cytosine
5-(propynyl)cytosine
5-(trifluoromethyl)cytosine
5-bromo-cytidine
5-iodo-cytidine
5-propynyl cytosine
6-(azo)cytosine
6-aza-cytidine
aza cytosine
deaza cytosine
N4 (acetyl)cytosine
l-methyl-1-deaza-pseudoisocytidine
1-methyl-pseudoisocytidine
2-methoxy-5-methyl-cytidine
2-methoxy-cytidine
2-thio-5-methyl-cytidine
4-methoxy-1-methyl-pseudoisocytidine
4-methoxy-pseudoisocytidine
4-thio- l-methyl-1-deaza-pseudoisocytidine
4-thio-1-methyl-pseudoisocytidine
4-thio-pseudoisocytidine
5-aza-zebularine
5-methyl-zebularine
pyrrolo-pseudoisocytidine
zebularine
(E)-5-(2-Bromo-vinyl)cytidine
2,2'-anhydro-cytidine
2'-Fluor-N4-Bz-cytidine
2'-Fluoro-N4-Acetyl-cytidine
2'-O-Methyl-N4-Acetyl-cytidine

Modification
2'-O-methyl-N4-Bz-cytidine
2' -a-Ethynylcytidine
2' -a-Trifluoromethylcytidine
2' -b-Ethynylcytidine
2'-b-Trifluoromethylcytidine
2' -Deoxy-2',2'-difluorocytidine
2' -Deoxy-2'-alpha-mercaptocytidine
2' -Deoxy-2'-alpha-thiomethoxycytidine
2' -Deoxy-2'-betab-aminocytidine
2' -Deoxy-2'-beta-azidocytidine
2' -Deoxy-2'-beta-bromocytidine
2' -Deoxy-2'-beta-chlorocytidine
2' -Deoxy-2'-beta-fluorocytidine
2' -Deoxy-2'-beta-iodocytidine
2' -Deoxy-2'-beta-mercaptocytidine
2' -Deoxy-2'-beta-thiomethoxycytidine TP
2' -O-Methyl-5-(1-propynyl)cytidine
3'-Ethynylcytidine
4'-Azidocytidine
4'-Carbocyclic cytidine
4' -Ethynylcytidine
5-(1-Propynyl)ara-cytidine
5-(2-Chloro-phenyl)-2-thiocytidine
5-(4-Amino-phenyl)-2-thiocytidine
5-Aminoallyl-cytosine
5-Cyanocytidine
5-Ethynylara-cytidine
5-Ethynylcytidine
5'-Homo-cytidine
5-Methoxycytidine

Modification
5-Trifluoromethyl-Cytidine
N4-Amino-cytidine
N4-Benzoyl-cytidine
pseudoisocytidine
6-thio-guanosine
7-deaza-guanosine
8-oxo-guanosine
Nl-methyl-guanosine
alpha-thio-guanosine
2-(propyl)guanine
2-(alky1)guanine
2'-Amino-2' -deoxy-guanosine
2'-Azido-2'-deoxy-guanosine
2'-Deoxy-2'-alpha-aminoguanosine
2'-Deoxy-2'-alpha-azidoguanosine
6-(methyl)guanine
6-(alky1)guanine
6-(methyl)guanine
6-methyl-guanosine
7-(alkyl)guanine
7-(deaza)guanine
7-(methyl)guanine
7-(alkyl)guanine
7-(deaza)guanine
7-(methyl)guanine
8-(alkyl)guanine
8-(alkynyl)guanine
8-(halo)guanine
8-(thioalkyl)guanine
8-(alkenyl)guanine
8-(alkyl)guanine

Modification
8-(alkynyl)guanine
8-(amino)guanine
8-(halo)guanine
8-(hydroxyl)guanine
8-(thioalkyl)guanine
8-(thiol)guanine
azaguanine
deaza guanine
N (methyl)guanine
N-(methyl)guanine
l-methyl-6-thio-guanosine
6-methoxy-guanosine
6-thio-7-deaza-8-aza-guanosine
6-thio-7-deaza-guanosine
6-thio-7-methyl-guanosine
7-deaza-8-aza-guanosine
7-methyl-8-oxo-guanosine
N2,N2-dimethyl-6-thio-guanosine
N2-methyl-6-thio-guanosine
1-Me-guanosine
2'Fluoro-N2-isobutyl-guanosine
2'O-methyl-N2-isobutyl-guanosine
2' -alpha-Ethynylguanosine
2' -alpha-Trifluoromethylguanosine
2' -beta-Ethynylguanosine
2'-beta-Trifluoromethylguanosine
2' -Deoxy-2',2'-difluoroguanosine
2' -Deoxy-2'-alpha-mercaptoguanosine
2' -Deoxy-2'-alpha-thiomethoxyguanosine
2' -Deoxy-2'-beta-aminoguanosine

Modification
2’ -Deoxy-2’-beta-azidoguanosine
2’ -Deoxy-2’-beta-bromoguanosine
2’ -Deoxy-2’-beta-chloroguanosine
2’ -Deoxy-2’-beta-fluoroguanosine
2’ -Deoxy-2’-beta-iodoguanosine
2’ -Deoxy-2’-beta-mercaptoguanosine
2’-Deoxy-2’-beta-thiomethoxyguanosine
4’-Azidoguanosine
4’-Carbocyclic guanosine
4’ -Ethynylguanosine
5’-Homo-guanosine
8-bromo-guanosine
9-Deazaguanosine
N2-isobutyl-guanosine
7-methylinosine
allyamino- thymidine
aza thymidine
deaza thymidine
deoxy-thymidine
5-propynyl uracil
alpha-thio-uridine
1-(aminoalkylamino-carbonylethylenyl)-2(thio)-pseudouracil
1-(aminoalkylaminocarbonylethylenyl)-2,4-(dithio)pseudouracil
1-(aminoalkylaminocarbonylethylenyl)-4 (thio)pseudouracil
1-(aminoalkylaminocarbonylethylenyl)-pseudouracil
1-(aminocarbonylethylenyl)-2(thio)-pseudouracil
1-(aminocarbonylethylenyl)-2,4-(dithio)pseudouracil
1-(aminocarbonylethylenyl)-4 (thio)pseudouracil

Modification
1-(aminocarbonylethylenyl)-pseudouracil
1-substituted 2-(thio)-pseudouracil
1-substituted 2,4-(dithio)pseudouracil
1-substituted 4 (thio)pseudouracil
1-substituted pseudouracil
1-(aminoalkylamino-carbonylethylenyl)-2- (thio)-pseudouracil
l-Methyl-3-(3-amino-3-carboxypropyl) pseudouridine
l-Methyl-3-(3-amino-3-carboxyproovl)pseudo-Uradine
1-Methyl-pseudo-UTP
2 (thio)pseudouracil
2’ deoxy uridine
2’ fluorouridine
2-(thio)uracil
2,4-(dithio)psuedouracil
2’-methyl, 2’-amino, 2’azido, 2’fluro-guanosine
2’-Amino-2’-deoxy-uridine
2’-Azido-2’-deoxy-uridine
2’ -Azido-deoxyuridine
2’-O-methylpseudouridine
2’ deoxyuridine
2’ fluorouridine
2’ -Deoxy-2’-alpha-aminouridine TP
2’ -Deoxy-2’-alpha-azidouridine TP
2-methylpseudouridine
3-(3 amino-3-carboxypropyl)uracil
4-(thio)pseudouracil
4-(thio)pseudouracil
4-(thio)uracil
4-thiouracil

Modification
5-(l ,3-diazole-1-alkyl)uracil
5-(2-aminopropyl)uracil
5-(aminoalkyl)uracil
5-(dimethylaminoalkyl)uracil
5-(guanidiniumalkyl)uracil
5-(methoxycarbonylmethyl)-2-(thio)uracil
5-(methoxycarbonyl-methyl)uracil
5-(methyl)-2-(thio)uracil
5-(methyl)-2,4-(dithio)uracil
5 (methyl) 4 (thio)uracil
5 (methylaminomethyl)-2 (thio)uracil
5 (methylaminomethyl)-2,4 (dithio)uracil
5 (methylaminomethyl)-4 (thio)uracil
5 (propynyl)uracil
5 (trifluoromethyl)uracil
5-(2-aminopropyl)uracil
5-(alky1)-2-(thio)pseudouracil
5-(alkyl)-2,4 (dithio)pseudouracil
5-(alky1)-4 (thio)pseudouracil
5-(alkyl)pseudouracil
5-(alkyl)uracil
5-(alkynyl)uracil
5-(allylamino)uracil
5-(cyanoalkyl)uracil
5-(dialkylaminoalkyl)uracil
5-(dimethylaminoalkyl)uracil
5-(guanidiniumalkyl)uracil
5-(halo)uracil
5-(1,3-diazole-l-alkyl)uracil
5-(methoxy)uracil

Modification
5-(methoxycarbonylmethyl)-2-(thio)uracil
5-(methoxycarbonyl-methyl)uracil
5-(methyl) 2(thio)uracil
5-(methyl) 2,4 (dithio)uracil
5-(methyl) 4 (thio)uracil
5-(methyl)-2-(thio)pseudouracil
5-(methyl)-2,4 (dithio)pseudouracil
5-(methyl)-4 (thio)pseudouracil
5-(methyl)pseudouracil
5-(methylaminomethyl)-2 (thio)uracil
5-(methylaminomethyl)-2,4(dithio)uracil
5-(methylaminomethyl)-4-(thio)uracil
5-(propyny1)uracil
5-(trifluoromethyl)uracil
5-aminoallyl-uridine
5-bromo-uridine
5-iodo-uridine
5-uracil
6 (azo)uracil
6-(azo)uracil
6-aza-uridine
allyamino-uracil
aza uracil
deaza uracil
N3 (methyl)uracil
Pseudo-uridine-1-2-ethanoic acid
pseudouracil
4-Thio-pseudouridine
1-carboxymethyl-pseudouridine
l-methyl-1-deaza-pseudouridine

Modification
1-propynyl-uridine
l-taurinomethyl-1-methyl-uridine
l-taurinomethyl-4-thio-uridine
1-taurinomethyl-pseudouridine
2-methoxy-4-thio-pseudouridine
2-thio- l-methyl-1-deaza-pseudouridine
2-thio-1-methyl-pseudouridine
2-thio-5-aza-uridine
2-thio-dihydropseudouridine
2-thio-dihydrouridine
2-thio-pseudouridine
4-methoxy-2-thio-pseudouridine
4-methoxy-pseudouridine
4-thio-1-methyl-pseudouridine
4-thio-pseudouridine
5-aza-uridine
dihydropseudouridine
(±)1-(2-Hydroxypropyl)pseudouridine
(2R)- l -(2-Hydroxypropyl)pseudouridine
(2S)- l -(2-Hydroxypropyl)pseudouridine
(E)-5-(2-Bromo-vinyl)ara-uridine
(E)-5-(2-Bromo-vinyl)uridine
(Z)-5-(2-Bromo-vinyl)ara-uridine
(Z)-5-(2-Bromo-vinyl)uridine
1-(2,2,2-Trifluoroethyl)-pseudouridine
1-(2,2,3,3,3-Pentafluoropropyl)pseudouridine
1-(2,2-Diethoxyethy l)pseudouridine
1-(2,4,6-Trimethylbenzyl)pseudouridine
1-(2,4,6-Trimethyl-benzyl)pseudo-uridine
1-(2,4,6-Trimethyl-phenyl)pseudo-uridine

Modification
1-(2-Amino-2-carboxyethyl)pseudo-uridine
1-(2-Amino-ethyl)pseudouridine
1-(2-Hydroxyethyl)pseudouridine
1-(2-Methoxyethyl)pseudouridine
1-(3,4-Bis-trifluoromethoxvbenzvl)pseudouridine
1-(3,4-Dimethoxybenzyl)pseudouridine
1-(3-Amino-3-carboxypropyl)pseudo-uridine
1-(3-Amino-propyl)pseudouridine
1-(3-Cyclopropyl-prop-2-ynyl)pseudouridine TP
1-(4-Amino-4-carboxybutyl)pseudouridine
1-(4-Amino-benzyl)pseudouridine
1-(4-Amino-buty l)pseudouridine
1-(4-Amino-phenyl)pseudouridine
1-(4-Azidobenzyl)pseudouridine
1-(4-Bromobenzyl)pseudouridine
1-(4-Chlorobenzyl)pseudouridine
1-(4-Fluorobenzyl)pseudouridin
1-(4-Iodobenzyl)pseudouridine
1-(4-Methanesulfonvlbenzvl)pseudouridine
1-(4-Methoxybenzy l)pseudouridine
1-(4-Methoxy-benzyl)pseudouridine
1-(4-Methoxy-phenyl)pseudouridine
1-(4-Methylbenzyl)pseudouridine
1-(4-Methyl-benzyl)pseudouridine
1-(4-Nitrobenzyl)pseudouridine
1-(4-Nitro-benzy!)pseudouridine
1(4-Nitro-phenyl)pseudouridine
1-(4-Thiomethoxybenzyl)pseudouridine
1-(4-

Modification
Trifluoromethoxybenzvl)pseudouridine
1-(4-Trifluoromethylbenzyl)pseudouridine
1-(5-Amino-pentyl)pseudouridine
1-(6-Amino-hexyl)pseudouridine
1,6-Dimethyl-pseudouridine
l-[3-(2-{2-[2-(2-Aminoethoxy)-ethoxy]-ethoxy}-ethoxy)-propionyl]pseudouridine
1-{3-[2-(2-Aminoethoxy)-ethoxy]-propionvl } pseudouridine
1-Acetylpseudouridine
l-Alkyl-6-(1-propynyl)-pseudo-uridine
l-Alkyl-6-(2-propynyl)-pseudo-uridine
l-Alkyl-6-allyl-pseudo-uridine
l-Alkyl-6-ethynyl-pseudo-uridine
l -Alkyl-6-homoallyl-pseudo-uridine
l-Alkyl-6-vinyl-pseudo-uridine
1-Allylpseudouridine
1-Aminomethyl-pseudo-uridine
1-Benzoylpseudouridine
1-Benzyloxymethylpseudouridine
1-Benzyl-pseudo-uridine
l-Biotinyl-PEG2-pseudouridine
1-Biotinylpseudouridine
1-Butyl-pseudo-uridine
1-Cyanomethylpseudouridine
1-Cyclobutylmethyl-pseudo-uridine
1-Cyclobutyl-pseudo-uridine
1-Cycloheptylmethyl-pseudo-uridine
1-Cycloheptyl-pseudo-uridine
1-Cyclohexylmethyl-pseudo-uridine
1-Cyclohexyl-pseudo-uridine
1-Cyclooctylmethyl-pseudo-uridine

Modification
1-Cyclooctyl-pseudo-uridine
1-Cyclopentylmethyl-pseudo-uridine
1-Cyclopentyl-pseudo-uridine
1-Cyclopropylmethyl-pseudo-uridine
1-Cyclopropyl-pseudo-uridine
1-Ethyl-pseudo-uridine
1-Hexyl-pseudo-uridine
1-Homoallylpseudouridine
1-Hydroxymethylpseudouridine
1-iso-propyl-pseudo-uridine
1-Me-2-thio-pseudo-uridine
1-Me-4-thio-pseudo-uridine
1-Me-alpha-thio-pseudo-uridine
1-Methanesulfonylmethylpseudouridine
1-Methoxymethylpseudouridine uridine
l -Methyl-6-(2,2,2-Trifluoroethyl)pseudo-uridine
l-Methyl-6-(4-morpholino)-pseudo-uridine
l -Methyl-6-(4-thiomorpholino)-pseudo-uridine
l-Methyl-6-(substituted phenyl)pseudo-uridine
1-Methyl-6-amino-pseudo-uridine
l -Methyl-6-azido-pseudo-uridine
1-Methyl-6-bromo-pseudo-uridine
l-Methyl-6-butyl-pseudo-uridine
l -Methyl-6-chloro-pseudo-uridine
1-Methyl-6-cyano-pseudo-uridine
l -Methyl-6-dimethylamino-pseudo-uridine
l -Methyl-6-ethoxy-pseudo-uridine
l -Methyl-6-ethylcarboxylate-pseudo-uridine
l-Methyl-6-ethyl-pseudo-uridine

Modification
l -Methyl-6-fluoro-pseudo-uridine
l-Methyl-6-formyl-pseudo-uridine
1-Methyl-6-hydroxyamino-pseudo-uridine
l -Methyl-6-hydroxy-pseudo-uridine
l -Methyl-6-iodo-pseudo-uridine
l-Methyl-6-iso-propyl-pseudo-uridine
l-Methyl-6-methoxy-pseudo-uridine
l -Methyl-6-methylamino-pseudo-uridine
l-Methyl-6-phenyl-pseudo-uridine
l-Methyl-6-propyl-pseudo-uridine
l-Methyl-6-tert-butyl-pseudo-uridine
1-Methyl-6-trifluoromethoxy-pseudo-uridine
l-Methyl-6-trifluoromethyl-pseudo-uridine
1-Morpholinomethylpseudouridine
1-Pentyl-pseudo-uridineuridine
1-Phenyl-pseudo-uridine
1-Pivaloylpseudouridine
1-Propargylpseudouridine
1-Propyl-pseudo-uridine
1-propynyl-pseudouridine
1-p-tolyl-pseudo-uridine
1-tert-Butyl-pseudo-uridine
1-Thiomethoxymethylpseudouridine
1-Thiomorpholinomethylpseudouridine
1-Trifluoroacetylpseudouridine
1-Trifluoromethyl-pseudouridine
1-Vinylpseudouridine
2,2'-anhydro-uridine
2' -bromo-deoxyuridine
2' -F-5-Methyl-2'-deoxy-uridine

Modification
2' -OMe-5-Me-uridine
2' -OMe-pseudouridine
2' -alpha-Ethynyluridine
2' -alpha-Trifluoromethyluridine
2' -beta-Ethynyluridine
2' -beta-Trifluoromethyluridiner
2' -Deoxy-2',2'-difluorouridine
2' -Deoxy-2'-a-mercaptouridin
2' -Deoxy-2'-alpha-thiomethoxyuridine
2' -Deoxy-2'-beta-aminouridine
2' -Deoxy-2'-beta-azidouridine
2' -Deoxy-2'-beta-bromouridine
2' -Deoxy-2'-beta-chlorouridine
2' -Deoxy-2'-beta-fluorouridine
2' -Deoxy-2'-beta-iodouridine
2' -Deoxy-2'-beta-mercaptouridine
2' -Deoxy-2'-beta-thiomethoxyuridine
2-methoxy-4-thio-uridine
2-methoxyuridine
2' -O-Methyl-5-(1-propynyl)uridine
3-Alkyl-pseudo-uridine
4' -Azidouridine
4'-Carbocyclic uridine
4' -Ethynyluridine
5-(1-Propynyl)ara-uridine
5-(2-Furanyl)uridine
5-Cyanouridine
5-Dimethylaminouridine
5'-Homo-uridine
5-iodo-2'-fluoro-deoxyuridine
5-Phenylethynyluridine

Modification
5-Trideuteromethyl-6-deuterouridine
5-Trifluoromethyl-Uridine
5-Vinylarauridine
6-(2,2,2-Trifluoroethyl)-pseudo-uridine
6-(4-Morpholino)-pseudo-uridine
6-(4-Thiomorpholino)-pseudo-uridine
6-(Substituted-Phenyl)-pseudo-uridine
6-Amino-pseudo-uridine
6-Azido-pseudo-uridine
6-Bromo-pseudo-uridine
6-Butyl-pseudo-uridine
6-Chloro-pseudo-uridine
6-Cyano-pseudo-uridine
6-Dimethylamino-pseudo-uridine
6-Ethoxy-pseudo-uridine
6-Ethylcarboxylate-pseudo-uridine
6-Ethyl-pseudo-uridine
6-Fluoro-pseudo-uridine
6-Formyl-pseudo-uridine
6-Hydroxyamino-pseudo-uridine
6-Hydroxy-pseudo-uridine
6-Iodo-pseudo-uridine
6-iso-Propyl-pseudo-uridine
6-Methoxy-pseudo-uridine
6-Methylamino-pseudo-uridine
6-Methyl-pseudo-uridine
6-Phenyl-pseudo-uridine

Modification
6-Phenyl-pseudo-uridine
6-Propyl-pseudo-uridine
6-tert-Butyl-pseudo- uridine
6-Trifluoromethoxy-pseudo-uridine
6-Trifluoromethyl-pseudo-uridine
alpha-thio-pseudo-uridine
Pseudouridine 1-(4-methylbenzenesulfonic acid)
Pseudouridine 1-(4-methylbenzoic acid) TP
Pseudouridine l-[3-(2-ethoxy)]propionic acid
Pseudouridine l-[3-{2-(2-[2-(2-ethoxy)-ethoxy]-ethoxy)-ethoxy}]propionic acid
Pseudouridine l-[3-{2-(2-[2-{2(2-ethoxy)-ethoxy}-ethoxy]-ethoxy)-ethoxy}]propionic acid
Pseudouridine l-[3-{2-(2-[2-ethoxy]-ethoxy)-ethoxv}]propionic acid
Pseudouridine l-[3-{2-(2-ethoxy)-ethoxv}] propionic acid
Pseudouridine 1-methylphosphonic acid
Pseudouridine TP 1-methylphosphonic acid diethyl ester
Pseudo-uridine-N1-3-propionic acid
Pseudo-uridine-N1-4-butanoic acid
Pseudo-uridine-N 1-5-pentanoic acid
Pseudo-uridine-N1-6-hexanoic acid
Pseudo-uridine-Nl-7-heptanoic acid
Pseudo-uridine-N1-methy1-p-benzoic acid
Pseudo-uridine-N1-p-benzoic acid

In an embodiment, a TREM, a TREM core fragment or a TREM fragment described herein comprises a modification provided in Table 6, or a combination thereof. The modifications provided in Table 6 occur naturally in RNAs, and are used herein on a synthetic TREM, a TREM core fragment or a TREM fragment at a position that does not occur in nature.

Table 6: Additional exemplary modifications

Modification
2-methylthio-N6-(cis-hydroxvisopentenvl)adenosine
2-methylthio-N6-methyladenosine
2-methylthio-N6-threonyl carbamoyladenosine
N6-glycinylcarbamoyladenosine
N6-isopentenyladenosine
N6-methyladenosine
N6-threonylcarbamoyladenosine
1,2'-O-dimethyladenosine
1-methyladenosine
2'-O-methyladenosine
2'-O-ribosyladenosine (phosphate)
2-methyladenosine
2-methylthio-N6 isopentenyladenosine
2-methylthio-N6-hydroxynorvalyl carbamoyladenosine
2' -O-methyladenosine
2' -O-ribosyladenosine (phosphate)
isopenteny ladenosine
N6-(cis-hydroxyisopentenyl)adenosine
N6,2'-O-dimethyladenosine
N6,2'-O-dimethyladenosine
N6,N6,2'-O-trimethyladenosine
N6,N6-dimethyladenosine
N6-acetyladenosine
N6-hydroxynorvalylcarbamoyladenosine
N6-methyl-N6-threonylcarbamoyladenosine
2-methyladenosine
2-methylthio-N^6-isopentenyladenosine

Modification
2-thiocytidine
3-methylcytidine
5-formylcytidine
5-hydroxymethylcytidine
5-methylcytidine
N4-acetylcytidine
2'-O-methylcytidine
2' -O-methylcytidine
5,2'-O-dimethylcytidine
5-formyl-2'-O-methylcytidine
lysidine
N4,2'-O-dimethy lcytidine
N4-acetyl-2'-O-methylcytidine
N4-methylcytidine
N4,N4-Dimethyl-2'-OMe-Cytidine
7-methylguanosine
N2,2'-O-dimethylguanosine
N2-methylguanosine
wyosme
1,2'-O-dimethylguanosine
1-methylguanosine
2'-O-methylguanosine
2'-O-ribosylguanosine (phosphate)
2' -O-methylguanosine
2'-O-ribosylguanosine (phosphate)

Modification
7-aminomethyl-7-deazaguanosine
7-cyano-7-deazaguanosine
archaeosine
methylwyosine
N2,7-dimethylguanosine
N2,N2,2'-O-trimethylguanosine
N2,N2,7-trimethylguanosine
N2,N2-dimethylguanosine
N2, 7,2 '-O-trimethylguanosine
1-methylinosine
mosme
1,2'-O-dimethylinosine
2'-O-methylinosine
2' -O-methylinosine
epoxyqueuosine
galactosyl-queuosine
mannosyl-queuosine
2' -O-methyluridine
2-thiouridine
3-methyluridine
5-carboxymethyluridine
5-hydroxyuridine
5-methyluridine
5-taurinomethyl-2-thiouridine
5-taurinomethyluridine
dihydrouridine
pseudouridine
(3-(3-amino-3-carboxypropyl)uridine
l-methyl-3-(3-amino-5-carboxypropyl)pseudouridine
1-methylpseduouridine

Modification
1-methyl-pseudouridine
2'-O-methyluridine
2'-O-methylpseudouridine
2' -O-methyluridine
2-thio-2'-O-methyluridine
3-(3-amino-3-carboxypropyl)uridine
3,2'-0-dimethyluridine
3-Methyl-pseudo-Uridine
4-thiouridine
5-(carboxyhydroxymethyl)uridine
5-(carboxyhydroxymethyl)uridine methyl ester
5,2'-O-dimethyluridine
5,6-dihydro-uridine
5-aminomethy1-2-thiouridine
5-carbamoylmethyl-2'-0-methyluridine
5-carbamoylmethyluridine
5-carboxyhydroxymethyluridine
5-carboxyhydroxymethyluridine methyl ester
5-carboxymethylaminomethyl-2'-O-methyluridine
5-carboxymethylaminomethyl-2-thiouridine
5-carboxymethylaminomethyl-2-thiouridine
5-carboxymethylaminomethyluridine
5-carboxymethylaminomethyluridine
5-Carbamoylmethyluridine
5-methoxycarbonylmethyl-2'-O-methyluridine
5-methoxycarbonylmethy1-2-thiouridine
5-methoxycarbonylmethyluridine
5-methoxyuridine

Modification
5-methyl-2-thiouridine
5-methylaminomethyl-2-selenouridine
5-methylaminomethyl-2-thiouridine
5-methylaminomethyluridine
5-Methyldihydrouridine
5-Oxyacetic acid- Uridine
5-Oxyacetic acid-methyl ester-Uridin Nl-methyl-pseudo-uridine
uridine 5-oxyacetic acid
uridine 5-oxyacetic acid methyl ester
3-(3-Amino-3-carboxypropyl)-Uridine

Modification
5-(iso-Pentenylaminomethyl)- 2-thiouridine
5-(iso-Pentenylaminomethyl)-2 '-O-methyluridine
5-(iso-Pentenylaminomethyl)uridine
wybutosine
hydroxywybutosine
isowyosme
peroxywybutosine
undermodified hydroxywybutosine
4-demethylwyosine
altriol

In an embodiment, a TREM, a TREM core fragment or a TREM fragment described herein comprises a non-naturally occurring modification provided in Table 7, or a combination thereof.

Table 7: Additional exemplary non-naturally occurring modifications

Modification
2,6-(diamino)purine
1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl
1,3-(diaza)-2-(oxo)-phenthiazin-1-yl
1,3-(diaza)-2-(oxo)-phenoxazin-1-yl
1,3,5-(triaza)-2,6-(dioxa)-naphthalene
2 (amino)purine
2,4,5-(trimethyl)phenyl
2' methyl, 2'amino, 2'azido, 2'fluro-cytidine
2' methyl, 2'amino, 2'azido, 2'fluro-adenine
2'methyl, 2'amino, 2'azido, 2'fluro-uridine
2' -amino-2' -deoxyribose
2-amino-6-Chloro-purine
2-aza-inosinyl
2' -azido-2'-deoxyribose

Modification
2'fluoro-2 '-deoxyribose
2' -fluoro-modified bases
2' -O-methyl-ribose
2-oxo-7-aminopyridopyrimidin-3-yl
2-oxo-pyridopyrimidine-3-yl
2-pyridinone
3 nitropyrrole
3-(methyl)-7-(propynyl)isocarbostyrilyl
3-(methyl)isocarbostyrilyl
4-(fluoro)-6-(methyl)benzimidazole
4-(methyl)benzimidazole
4-(methyl)indolyl
4,6-(dimethyl)indolyl
5 nitroindole
5 substituted pyrimidines
5-(methyl)isocarbostyrilyl

Modification
5-nitroindole
6-(aza)pyrimidine
6-(azo)thymine
6-(methyl)-7-(aza)indolyl
6-chloro-purine
6-phenyl-pyrrolo-pyrimidin-2-on-3-yl
7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)- phenthiazin-1-yl
7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)- phenoxazin-1-yl
7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1- yl
7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenthiazin- 1-yl
7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-l- yl
7-(aza)indolyl
7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)- phenoxazinl-yl
7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)- phenthiazin-1-yl
7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)- phenoxazin-1-yl
7-(guanidiniumalkylhydroxy)-1,3-(diaza)-2-(oxo)- phenoxazin-1-yl
7-(guanidiniumalkyl-hydroxy)-1,3-(diaza)-2-(oxo)- phenthiazin-1-yl
7-(guanidiniumalkylhydroxy)-1,3-(diaza)-2-(oxo)- phenoxazin-1-yl
7-(propynyl)isocarbostyrilyl
7-(propynyl)isocarbostyrilyl, propynyl-7-(aza)indolyl
7-deaza-inosinyl
7-substituted 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl
7-substituted 1,3-(diaza)-2-(oxo)-phenoxazin-1-yl
9-(methyl)-imidizopyridinyl
aminoindolyl
anthracenyl

Modification
bis-ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo- nvrimidin-2-on-3-yl
bis-ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3- yl
difluorotolyl
hypoxanthine
imidizopyridinyl
inosinyl
isocarbostyrilyl
isoguanosine
N2-substituted purines
N6-methyl-2-amino-purine
N6-substituted purines
N-alkylated derivative
napthalenyl
nitrobenzimidazolyl
nitroimidazolyl
nitroindazolyl
nitropyrazolyl
nubularine
O6-substituted purines
O-alkylated derivative
ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2- on-3-yl
ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl
Oxoformycin TP
para-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2- on-3-yl
para-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl
pentacenyl
phenanthracenyl
phenyl
propynyl-7-(aza)indolyl
pyrenyl
pyridopyrimidin-3-yl
pyridopyrimidin-3-yl, 2-oxo-7-amino-pyridopyrimidin-3- yl
pyrrolo-pyrimidin-2-on-3-yl
pyrrolopyrimidinyl

Modification
pyrrolopyrizinyl
stilbenzyl
substituted 1,2,4-triazoles
tetracenyl
tubercidine
xanthine
Xanthosine
2-thio-zebularine
5-aza-2-thio-zebularine
7-deaza-2-amino-purine
pyridin-4-one ribonucleoside

Modification
2-Amino-riboside
Formycin A
Formycin B
Pyrrolosine
2' -OH-ara-adenosine
2' -OH-ara-cytidine
2' -OH-ara-uridine
2' -OH-ara-guanosine
5-(2-carbomethoxyvinyl)uridine
N6-(19-Amino-pentaoxanonadecyl)adenosine

In an embodiment, a TREM, a TREM core fragment or a TREM fragment described herein comprises a non-naturally occurring modification provided in Table 8, or a combination thereof.

Table 8: Exemplary backbone modifications

Modification
3'-alkylene phosphonates
3'-amino phosphoramidate
alkene containing backbones
aminoalkylphosphoramidates
aminoalkylphosphotriesters
boranophosphates
-CH2-0-N(CH3)-CH2-
-CH2-N(CH3)-N(CH3)-CH2-
-CH2-NH-CH2-
chiral phosphonates
chiral phosphorothioates
formacetyl and thioformacetyl backbones
methylene (methylimino)
methylene formacetyl and thioformacetyl backbones
methyleneimino and methylenehydrazino backbones
morpholino linkages

Modification
-N(CH3)-CH2-CH2-
oligonucleosides with heteroatom intenucleoside linkage
phosphinates
phosphoramidates
phosphorodithioates
phosphorothioate intenucleoside linkages
phosphorothioates
phosphotriesters
PNA
siloxane backbones
sulfamate backbones
sulfide sulfoxide and sulfone backbones
sulfonate and sulfonamide backbones
thionoalkylphosphonates
thionoalkylphosphotriesters
thionophosphoramidates
methylphosphonates

Modification
phosphonoacetates
Phosphorothioate
Constrained nucleic acid (CNA)
2'-O-methyl
2'-O-methoxyethyl (MOE)
2' Fluoro
Locked nucleic acid (LNA)
(*S*)-constrained ethyl (*cEt*)
Fluoro hexitol nucleic acid (FHNA)
5'-phosphorothioate
Phosphorodiamidate Morpholino Oligomer (PMO)
Tricyclo-DNA (tcDNA)
(*S*) 5'-C-methyl
(*E*)-vinylphosphonate
Methyl phosphonate
(*S*) 5'-C-methyl with phosphate
(R) 5'-C-methyl with phosphate
DNA
(R) 5'-C-methyl
GNA (glycol nucleic acid)
alkyl phosphonates

Modification
Phosphorothioate
Constrained nucleic acid (CNA)
2'-O-methyl
2'-O-methoxyethyl (MOE)
2' Fluoro
Locked nucleic acid (LNA)
(*S*)-constrained ethyl (*cEt*)
Fluoro hexitol nucleic acid (FHNA)
5'-phosphorothioate
Phosphorodiamidate Morpholino Oligomer (PMO)
Tricyclo-DNA (tcDNA)
(*S*) 5'-C-methyl
(*E*)-vinylphosphonate
Methyl phosphonate
(*S*) 5'-C-methyl with phosphate
(R) 5'-C-methyl with phosphate
DNA
(R) 5'-C-methyl
GNA (glycol nucleic acid)
alkyl phosphonates

In an embodiment, a TREM, a TREM core fragment or a TREM fragment described herein comprises a non-naturally occurring modification provided in Table 9, or a combination thereof.

Table 9: Exemplary non-naturally occurring backbone modificiations

Name of synthetic backbone modifications
Phosphorothioate
Constrained nucleic acid (CNA)
2' O'methylation
2'-O-methoxyethylribose (MOE)
2' Fluoro
Locked nucleic acid (LNA)
(*S*)-constrained ethyl (*cEt*)
Fluoro hexitol nucleic acid (FHNA)
5'phosphorothioate
Phosphorodiamidate Morpholino Oligomer (PMO)
Tricyclo-DNA (tcDNA)

(*S*) 5'-C-methyl
(*E*)-vinylphosphonate
Methyl phosphonate
(*S*) 5'-C-methyl with phosphate

TREM, TREM core fragment and TREM fragment fusions

In an embodiment, a TREM, a TREM core fragment or a TREM fragment disclosed herein comprises an additional moiety, *e.g.*, a fusion moiety. In an embodiment, the fusion moiety can be used for purification, to alter folding of the TREM, TREM core fragment or TREM fragment, or as a targeting moiety. In an embodiment, the fusion moiety can comprise a tag, a linker, can be cleavable or can include a binding site for an enzyme. In an embodiment, the fusion moiety can be disposed at the N terminal of the TREM or at the C terminal of the TREM, TREM core fragment or TREM fragment. In an embodiment, the fusion moiety can be encoded by the same or different nucleic acid molecule that encodes the TREM, TREM core fragment or TREM fragment.

TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises a consensus sequence provided herein.

In an embodiment, a TREM disclosed herein comprises a consensus sequence of Formula I $_{ZZZ}$, wherein $_{ZZZ}$ indicates any of the twenty amino acids and Formula I corresponds to all species.

In an embodiment, a TREM disclosed herein comprises a consensus sequence of Formula II $_{ZZZ}$, wherein $_{ZZZ}$ indicates any of the twenty amino acids and Formula II corresponds to mammals.

In an embodiment, a TREM disclosed herein comprises a consensus sequence of Formula III $_{ZZZ}$, wherein $_{ZZZ}$ indicates any of the twenty amino acids and Formula III corresponds to humans.

In an embodiment, $_{ZZZ}$ indicates any of the twenty amino acids: alanine, arginine, asparagine, aspartate, cysteine, glutamine, glutamate, glycine, histidine, isoleucine, methionine, leucine, lysine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

In an embodiment, a TREM disclosed herein comprises a property selected from the following:

a) under physiological conditions residue R_0 forms a linker region, *e.g.*, a Linker 1 region;

b) under physiological conditions residues R_1-R_2-R_3-R_4 -R_5-R_6-R_7 and residues R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71} form a stem region, *e.g.*, an AStD stem region;

c) under physiological conditions residues R_8-R_9 forms a linker region, *e.g.*, a Linker 2 region;

d) under physiological conditions residues -R_{10}-R_{11}-R_{12}-R_{13}-R_{14} R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28} form a stem-loop region, *e.g.*, a D arm Region;

e) under physiological conditions residue -R_{29} forms a linker region, *e.g.*, a Linker 3 Region;

f) under physiological conditions residues -R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}-R_{43}-R_{44}-R_{45}-R_{46} form a stem-loop region, *e.g.*, an AC arm region;

g) under physiological conditions residue -$[R_{47}]_x$ comprises a variable region, *e.g.*, as described herein;

h) under physiological conditions residues -R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64} form a stem-loop region, *e.g.*, a T arm Region; or

i) under physiological conditions residue R_{72} forms a linker region, *e.g.*, a Linker 4 region.

Alanine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{ALA} (SEQ ID NO: 562),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}, wherein R is a ribonucleotide residue and the consensus for Ala is: R_0= absent; R_{14}, R_{57}=are independently A or absent; R_{26}= A, C, G or absent; R_5, R_6, R_{15}, R_{16}, R_{21}, R_{30}, R_{31}, R_{32}, R_{34}, R_{37}, R_{41}, R_{42}, R_{43}, R_{44}, R_{45}, R_{48}, R_{49}, R_{50}, R_{58}, R_{59}, R_{63}, R_{64}, R_{66}, R_{67}= are independently N or absent; R_{11}, R_{35}, R_{65}= are independently A, C, U or absent; R_1, R_9, R_{20}, R_{38}, R_{40}, R_{51}, R_{52}, R_{56}= are independently A, G or absent; R_7, R_{22}, R_{25}, R_{27}, R_{29}, R_{46}, R_{53}, R_{72}= are independently A, G, U or absent; R_{24}, R_{69}= are independently A, U or absent; R_{70}, R_{71}=are independently C or absent; R_3, R_4= are independently C, G or absent; R_{12}, R_{33}, R_{36}, R_{62}, R_{68}= are independently C, G, U or absent; R_{13}, R_{17}, R_{28}, R_{39}, R_{55}, R_{60}, R_{61}= are independently C, U or absent; R_{10}, R_{19}, R_{23}= are independently G or absent; R_2= G, U or absent; R_8, R_{18}, R_{54}= are

independently U or absent; $[R_{47}]_x$ = N or absent; wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271),

provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II_{ALA} (SEQ ID NO: 563),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ala is:

R_0, R_{18}= are absent;

R_{14}, R_{24}, R_{57}=are independently A or absent;

R_{15}, R_{26}, R_{64}= are independently A, C, G or absent;

R_{16}, R_{31}, R_{50}, R_{59}= are independently N or absent;

R_{11}, R_{32}, R_{37}, R_{41}, R_{43}, R_{45}, R_{49}, R_{65}, R_{66}= are independently A, C, U or absent;

R_1, R_5, R_9, R_{25}, R_{27}, R_{38}, R_{40}, R_{46}, R_{51}, R_{56}= are independently A, G or absent;

R_7, R_{22}, R_{29}, R_{42}, R_{44}, R_{53}, R_{63}, R_{72}= are independently A, G, U or absent;

R_6, R_{35}, R_{69}= are independently A, U or absent;

R_{55}, R_{60}, R_{70}, R_{71}= are independently C or absent;

R_3= C, G or absent;

R_{12}, R_{36}, R_{48}= are independently C, G, U or absent;

R_{13}, R_{17}, R_{28}, R_{30}, R_{34}, R_{39}, R_{58}, R_{61}, R_{62}, R_{67}, R_{68}= are independently C, U or absent;

R_4, R_{10}, R_{19}, R_{20}, R_{23}, R_{52}= are independently G or absent;

R_2, R_8, R_{33}= are independently G, U or absent;

R_{21}, R_{54}= are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III_{ALA} (SEQ ID NO: 564),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ala is:

R_0, R_{18}= are absent;

R_{14}, R_{24}, R_{57}, R_{72}=are independently A or absent;

R_{15}, R_{26}, R_{64}= are independently A, C, G or absent;

R_{16}, R_{31}, R_{50}= are independently N or absent;

R_{11}, R_{32}, R_{37}, R_{41}, R_{43}, R_{45}, R_{49}, R_{65}, R_{66}= are independently A, C, U or absent;

R_5, R_9, R_{25}, R_{27}, R_{38}, R_{40}, R_{46}, R_{51}, R_{56}= are independently A, G or absent;

R_7, R_{22}, R_{29}, R_{42}, R_{44}, R_{53}, R_{63}= are independently A, G, U or absent;

R_6, R_{35}= are independently A, U or absent;

R_{55}, R_{60}, R_{61}, R_{70}, R_{71}= are independently C or absent;

R_{12}, R_{48}, R_{59}= are independently C, G, U or absent;

R_{13}, R_{17}, R_{28}, R_{30}, R_{34}, R_{39}, R_{58}, R_{62}, R_{67}, R_{68}= are independently C, U or absent;

R_1, R_2, R_3, R_4, R_{10}, R_{19}, R_{20}, R_{23}, R_{52}= are independently G or absent;

R_{33}, R_{36}= are independently G, U or absent;

R_8, R_{21}, R_{54}, R_{69}= are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Arginine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{ARG} (SEQ ID NO: 565),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Arg is:

R_{57}=A or absent;

R_9,R_{27}=are independently A,C,G or absent;

R_1,R_2,R_3,R_4,R_5,R_6,R_7,R_{11},R_{12},R_{16},R_{21},R_{22},R_{23},R_{25},R_{26},R_{29},R_{30},R_{31},R_{32},R_{33},R_{34},R_{37},R_{42},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{51},R_{58},R_{62},R_{63},R_{64},R_{65},R_{66},R_{67},R_{68},R_{69},R_{70},R_{71}=are independently N or absent;

R_{13},R_{17},R_{41}=are independently A,C,U or absent;

R_{19},R_{20},R_{24},R_{40},R_{56}=are independently A,G or absent;

R_{14},R_{15},R_{72}=are independently A,G,U or absent;

R_{18}= A,U or absent;

R_{38}= C or absent;

R_{35},R_{43},R_{61}=are independently C,G,U or absent;

R_{28},R_{55},R_{59},R_{60}=are independently C,U or absent;

R_0,R_{10},R_{52}=are independently G or absent;

R_8,R_{39}=are independently G,U or absent;

R_{36},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{ARG}$ (SEQ ID NO: 566),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Arg is:

R_{18}= absent;

R_{24},R_{57}=are independently A or absent;

R_{41}= A,C or absent;

R_3,R_7,R_{34},R_{50}=are independently A,C,G or absent;

R_2,R_5,R_6,R_{12},R_{26},R_{32},R_{37},R_{44},R_{58},R_{66},R_{67},R_{68},R_{70}=are independently N or absent;

R_{49},R_{71}=are independently A,C,U or absent;

R_1,R_{15},R_{19},R_{25},R_{27},R_{40},R_{45},R_{46},R_{56},R_{72}=are independently A,G or absent;

R_{14},R_{29},R_{63}=are independently A,G,U or absent;

R_{16},R_{21}=are independently A,U or absent;

R_{38},R_{61}=are independently C or absent;

R_{33},R_{48}=are independently C,G or absent;

R_4,R_9,R_{11},R_{43},R_{62},R_{64},R_{69}=are independently C,G,U or absent;

R_{13},R_{22},R_{28},R_{30},R_{31},R_{35},R_{55},R_{60},R_{65}=are independently C,U or absent;

R_0,R_{10},R_{20},R_{23},R_{51},R_{52}=are independently G or absent;

R_8,R_{39},R_{42}=are independently G,U or absent;

R_{17},R_{36},R_{53},R_{54},R_{59}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{ARG}$ (SEQ ID NO: 567),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Arg is:

R_{18}=is absent;

R_{15},R_{21},R_{24},R_{41},R_{57}=are independently A or absent;

R_{34},R_{44}=are independently A,C or absent;

R_{3},R_{5},R_{58}=are independently A,C,G or absent;

R_{2},R_{6},R_{66},R_{70}=are independently N or absent;

R_{37},R_{49}=are independently A,C,U or absent;

R_{1},R_{25},R_{29},R_{40},R_{45},R_{46},R_{50}=are independently A,G or absent;

R_{14},R_{63},R_{68}=are independently A,G,U or absent;

R_{16}= A,U or absent;

R_{38},R_{61}=are independently C or absent;

R_{7},R_{11},R_{12},R_{26},R_{48}=are independently C,G or absent;

R_{64},R_{67},R_{69}=are independently C,G,U or absent;

R_{4},R_{13},R_{22},R_{28},R_{30},R_{31},R_{35},R_{43},R_{55},R_{60},R_{62},R_{65},R_{71}=are independently C,U or absent;

R_{0},R_{10},R_{19},R_{20},R_{23},R_{27},R_{33},R_{51},R_{52},R_{56},R_{72}=are independently G or absent;

R_{8},R_{9},R_{32},R_{39},R_{42}=are independently G,U or absent;

R_{17},R_{36},R_{53},R_{54},R_{59}=are independently U or absent;

$[R_{47}]_{x}$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Asparagine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{ASN} (SEQ ID NO: 568),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Asn is:

R_0,R_{18}=are absent;

R_{41}= A or absent;

R_{14},R_{48},R_{56}=are independently A,C,G or absent;

R_2,R_4,R_5,R_6,R_{12},R_{17},R_{26},R_{29},R_{30},R_{31},R_{44},R_{45},R_{46},R_{49},R_{50},R_{58},R_{62},R_{63},R_{65},R_{66},R_{67},R_{68},R_{70},R_{71}= are independently N or absent;

R_{11},R_{13},R_{22},R_{42},R_{55},R_{59}=are independently A,C,U or absent;

R_9,R_{15},R_{24},R_{27},R_{34},R_{37},R_{51},R_{72}=are independently A,G or absent;

R_1,R_7,R_{25},R_{69}=are independently A,G,U or absent;

R_{40},R_{57}=are independently A,U or absent;

R_{60}= C or absent;

R_{33}= C,G or absent;

R_{21},R_{32},R_{43},R_{64}=are independently C,G,U or absent;

R_3,R_{16},R_{28},R_{35},R_{36},R_{61}=are independently C,U or absent;

R_{10},R_{19},R_{20},R_{52}=are independently G or absent;

R_{54}= G,U or absent;

R_8,R_{23},R_{38},R_{39},R_{53}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271),

provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{ASN}$ (SEQ ID NO: 569),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Asn is:

$R_{0,}R_{18}$=are absent

$R_{24},R_{41},R_{46},R_{62}$=are independently A or absent;

R_{59}= A,C or absent;

R_{14},R_{56},R_{66}=are independently A,C,G or absent;

R_{17},R_{29}=are independently N or absent;

$R_{11},R_{26},R_{42},R_{55}$=are independently A,C,U or absent;

$R_1,R_9,R_{12},R_{15},R_{25},R_{34},R_{37},R_{48},R_{51},R_{67},R_{68},R_{69},R_{70},R_{72}$=are independently A,G or absent;

R_{44},R_{45},R_{58}=are independently A,G,U or absent;

R_{40},R_{57}=are independently A,U or absent;

R_5,R_{28},R_{60}=are independently C or absent;

R_{33},R_{65}=are independently C,G or absent;

R_{21},R_{43},R_{71}=are independently C,G,U or absent;

$R_3,R_6,R_{13},R_{22},R_{32},R_{35},R_{36},R_{61},R_{63},R_{64}$=are independently C,U or absent;

$R_7,R_{10},R_{19},R_{20},R_{27},R_{49},R_{52}$=are independently G or absent;

R_{54}= G,U or absent;

$R_2,R_4,R_8,R_{16},R_{23},R_{30},R_{31},R_{38},R_{39},R_{50},R_{53}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-

271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{ASN}$ (SEQ ID NO: 570),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Asn is:

$R_{0,}R_{18}$=are absent

R_{24},R_{40},R_{41},R_{46},R_{62}=are independently A or absent;

R_{59}= A,C or absent;

R_{14},R_{56},R_{66}=are independently A,C,G or absent;

R_{11},R_{26},R_{42},R_{55}=are independently A,C,U or absent;

R_1,R_9,R_{12},R_{15},R_{34},R_{37},R_{48},R_{51},R_{67},R_{68},R_{69},R_{70}=are independently A,G or absent;

R_{44},R_{45},R_{58}=are independently A,G,U or absent;

R_{57}= A,U or absent;

R_5,R_{28},R_{60}=are independently C or absent;

R_{33},R_{65}=are independently C,G or absent;

R_{17},R_{21},R_{29}=are independently C,G,U or absent;

R_3,R_6,R_{13},R_{22},R_{32},R_{35},R_{36},R_{43},R_{61},R_{63},R_{64},R_{71}=are independently C,U or absent;

R_7,R_{10},R_{19},R_{20},R_{25},R_{27},R_{49},R_{52},R_{72}=are independently G or absent;

R_{54}= G,U or absent;

R_2,R_4,R_8,R_{16},R_{23},R_{30},R_{31},R_{38},R_{39},R_{50},R_{53}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Aspartate TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{ASP} (SEQ ID NO: 571),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Asp is:

R_0=absent

R_{24},R_{71}=are independently A,C or absent;

R_{33},R_{46}=are independently A,C,G or absent;

R_2,R_3,R_4,R_5,R_6,R_{12},R_{16},R_{22},R_{26},R_{29},R_{31},R_{32},R_{44},R_{48},R_{49},R_{58},R_{63},R_{64},R_{66},R_{67},R_{68},R_{69}=are independently N or absent;

R_{13},R_{21},R_{34},R_{41},R_{57},R_{65}=are independently A,C,U or absent;

R_9,R_{10},R_{14},R_{15},R_{20},R_{27},R_{37},R_{40},R_{51},R_{56},R_{72}=are independently A,G or absent;

R_7,R_{25},R_{42}=are independently A,G,U or absent;

R_{39}= C or absent;

R_{50},R_{62}=are independently C,G or absent;

R_{30},R_{43},R_{45},R_{55},R_{70}=are independently C,G,U or absent;

R_8,R_{11},R_{17},R_{18},R_{28},R_{35},R_{53},R_{59},R_{60},R_{61}=are independently C,U or absent;

R_{19},R_{52}=are independently G or absent;

R_1= G,U or absent;

R_{23},R_{36},R_{38},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{ASP}$ (SEQ ID NO: 572),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Asp is:

R_0,R_{17},R_{18},R_{23}=are independently absent;

R_9,R_{40}=are independently A or absent;

R_{24},R_{71}=are independently A,C or absent;

R_{67},R_{68}=are independently A,C,G or absent;

R_2,R_6,R_{66}=are independently N or absent;

R_{57},R_{63}=are independently A,C,U or absent;

R_{10},R_{14},R_{27},R_{33},R_{37},R_{44},R_{46},R_{51},R_{56},R_{64},R_{72}=are independently A,G or absent;

R_7,R_{12},R_{26},R_{65}=are independently A,U or absent;

R_{39},R_{61},R_{62}=are independently C or absent;

R_3,R_{31},R_{45},R_{70}=are independently C,G or absent;

R_4,R_5,R_{29},R_{43},R_{55}=are independently C,G,U or absent;

R_8,R_{11},R_{13},R_{30},R_{32},R_{34},R_{35},R_{41},R_{48},R_{53},R_{59},R_{60}=are independently C,U or absent;

R_{15},R_{19},R_{20},R_{25},R_{42},R_{50},R_{52}=are independently G or absent;

R_1,R_{22},R_{49},R_{58},R_{69}=are independently G,U or absent;

R_{16},R_{21},R_{28},R_{36},R_{38},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{ASP}$ (SEQ ID NO: 573),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Asp is:

R_0,R_{17},R_{18},R_{23}=are absent

R_9,R_{12},R_{40},R_{65},R_{71}=are independently A or absent;

R_2,R_{24},R_{57}=are independently A,C or absent;

R_6,R_{14},R_{27},R_{46},R_{51},R_{56},R_{64},R_{67},R_{68}=are independently A,G or absent;

R_3,R_{31},R_{35},R_{39},R_{61},R_{62}=are independently C or absent;

R_{66}= C,G or absent;

R_5,R_8,R_{29},R_{30},R_{32},R_{34},R_{41},R_{43},R_{48},R_{55},R_{59},R_{60},R_{63}=are independently C,U or absent;

R_{10},R_{15},R_{19},R_{20},R_{25},R_{33},R_{37},R_{42},R_{44},R_{45},R_{49},R_{50},R_{52},R_{69},R_{70},R_{72}=are independently G or absent;

R_{22},R_{58}=are independently G,U or absent;

R_1,R_4,R_7,R_{11},R_{13},R_{16},R_{21},R_{26},R_{28},R_{36},R_{38},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Cysteine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{CYS} (SEQ ID NO: 574),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Cys is:

R_0 =absent

R_{14},R_{39},R_{57}=are independently A or absent;

R_{41}= A,C or absent;

R_{10},R_{15},R_{27},R_{33},R_{62}=are independently A,C,G or absent;

R_3,R_4,R_5,R_6,R_{12},R_{13},R_{16},R_{24},R_{26},R_{29},R_{30},R_{31},R_{32},R_{34},R_{42},R_{44},R_{45},R_{46},R_{48},R_{49},R_{58},R_{63},R_{64},R_{66}, R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{65}= A,C,U or absent;

R_9,R_{25},R_{37},R_{40},R_{52},R_{56}=are independently A,G or absent;

R_7,R_{20},R_{51}=are independently A,G,U or absent;

R_{18},R_{38},R_{55}=are independently C or absent;

R_2= C, G or absent;

R_{21},R_{28},R_{43},R_{50}=are independently C,G,U or absent;

R_{11},R_{22},R_{23},R_{35},R_{36},R_{59},R_{60},R_{61},R_{71},R_{72}=are independently C,U or absent;

R_1,R_{19}=are independently G or absent;

R_{17}= G,U or absent;

R_8,R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{CYS}$ (SEQ ID NO: 575),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Cys is:

R_0,R_{18},R_{23}=are absent;

R_{14},R_{24},R_{26},R_{29},R_{39},R_{41},R_{45},R_{57}=are independently A or absent;

R_{44}= A,C or absent;

R_{27},R_{62}=are independently A,C,G or absent;

R_{16}= A,C,G,U or absent;

R_{30},R_{70}=are independently A,C,U or absent;

R_5,R_7,R_9,R_{25},R_{34},R_{37},R_{40},R_{46},R_{52},R_{56},R_{58},R_{66}=are independently A,G or absent;

R_{20},R_{51}=are independently A,G,U or absent;

R_{35},R_{38},R_{43},R_{55},R_{69}=are independently C or absent;

R_2,R_4,R_{15}=are independently C,G or absent;

R_{13}= C,G,U or absent;

R_6,R_{11},R_{28},R_{36},R_{48},R_{49},R_{50},R_{60},R_{61},R_{67},R_{68},R_{71},R_{72}=are independently C,U or absent;

R_1,R_3,R_{10},R_{19},R_{33},R_{63}=are independently G or absent;

R_8,R_{17},R_{21},R_{64}=are independently G,U or absent;

R_{12},R_{22},R_{31},R_{32},R_{42},R_{53},R_{54},R_{65}=are independently U or absent;

R_{59}= U, or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{CYS}$ (SEQ ID NO: 576),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Cys is:

$R_{0,}R_{18,}R_{23}$=are absent

$R_{14},R_{24},R_{26},R_{29},R_{34},R_{39},R_{41},R_{45},R_{57},R_{58}$=are independently A or absent;

R_{44},R_{70}=are independently A,C or absent;

R_{62}= A,C,G or absent;

R_{16}= N or absent;

$R_{5},R_{7},R_{9},R_{20},R_{40},R_{46},R_{51},R_{52},R_{56},R_{66}$=are independently A,G or absent;

$R_{28},R_{35},R_{38},R_{43},R_{55},R_{67},R_{69}$=are independently C or absent;

R_{4},R_{15}=are independently C,G or absent;

$R_{6},R_{11},R_{13},R_{30},R_{48},R_{49},R_{50},R_{60},R_{61},R_{68},R_{71},R_{72}$=are independently C,U or absent;

$R_{1},R_{2},R_{3},R_{10},R_{19},R_{25},R_{27},R_{33},R_{37},R_{63}$=are independently G or absent;

R_{8},R_{21},R_{64}=are independently G,U or absent;

$R_{12},R_{17},R_{22},R_{31},R_{32},R_{36},R_{42},R_{53},R_{54}$, R_{59},R_{65}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Glutamine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{GLN}$ (SEQ ID NO: 577),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Gln is:

R_0,R_{18}=are absent;

R_{14},R_{24},R_{57}=are independently A or absent;

R_9,R_{26},R_{27},R_{33},R_{56}=are independently A,C,G or absent;

R_2,R_4,R_5,R_6,R_{12},R_{13},R_{16},R_{21},R_{22},R_{25},R_{29},R_{30},R_{31},R_{32},R_{34},R_{41},R_{42},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{58},R_{62},R_{63},R_{66},R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{17},R_{23},R_{43},R_{65},R_{71}=are independently A,C,U or absent;

R_{15},R_{40},R_{51},R_{52}=are independently A,G or absent;

R_1,R_7,R_{72}=are independently A,G,U or absent;

R_3,R_{11},R_{37},R_{60},R_{64}=are independently C,G,U or absent;

R_{28},R_{35},R_{55},R_{59},R_{61}=are independently C,U or absent;

R_{10},R_{19},R_{20}=are independently G or absent;

R_{39}= G,U or absent;

R_8,R_{36},R_{38},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{GLN}$ (SEQ ID NO: 578),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-

R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Gln is:

$R_{0,}R_{18,}R_{23}$=are absent

R_{14},R_{24},R_{57}=are independently A or absent;

R_{17},R_{71}=are independently A,C or absent;

$R_{25},R_{26},R_{33},R_{44},R_{46},R_{56},R_{69}$=are independently A,C,G or absent;

$R_4,R_5,R_{12},R_{22},R_{29},R_{30},R_{48},R_{49},R_{63},R_{67},R_{68}$=are independently N or absent;

$R_{31},R_{43},R_{62},R_{65},R_{70}$=are independently A,C,U or absent;

$R_{15},R_{27},R_{34},R_{40},R_{41},R_{51},R_{52}$=are independently A,G or absent;

$R_2,R_7,R_{21},R_{45},R_{50},R_{58},R_{66},R_{72}$=are independently A,G,U or absent;

$R_3,R_{13},R_{32},R_{37},R_{42},R_{60},R_{64}$=are independently C,G,U or absent;

$R_6,R_{11},R_{28},R_{35},R_{55},R_{59},R_{61}$=are independently C,U or absent;

R_9,R_{10},R_{19},R_{20}=are independently G or absent;

R_1,R_{16},R_{39}=are independently G,U or absent;

$R_8,R_{36},R_{38},R_{53},R_{54}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{GLN}$ (SEQ ID NO: 579),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Gln is:

$R_{0,}R_{18,}R_{23}$=are absent

R_{14},R_{24},R_{41},R_{57}=are independently A or absent;

R_{17},R_{71}=are independently A,C or absent;

R_5,R_{25},R_{26},R_{46},R_{56},R_{69}=are independently A,C,G or absent;

R_4,R_{22},R_{29},R_{30},R_{48},R_{49},R_{63},R_{68}=are independently N or absent;

R_{43},R_{62},R_{65},R_{70}=are independently A,C,U or absent;

R_{15},R_{27},R_{33},R_{34},R_{40},R_{51},R_{52}=are independently A,G or absent;

R_2,R_7,R_{12},R_{45},R_{50},R_{58},R_{66}=are independently A,G,U or absent;

R_{31}= A,U or absent;

R_{32},R_{44},R_{60}=are independently C,G or absent;

R_3,R_{13},R_{37},R_{42},R_{64},R_{67}=are independently C,G,U or absent;

R_6,R_{11},R_{28},R_{35},R_{55},R_{59},R_{61}=are independently C,U or absent;

R_9,R_{10},R_{19},R_{20}=are independently G or absent;

R_1,R_{21},R_{39},R_{72}=are independently G,U or absent;

R_8,R_{16},R_{36},R_{38},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271),

provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Glutamate TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{GLU}$ (SEQ ID NO: 580),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Glu is:

R_0=absent;

R_{34},R_{43},R_{68},R_{69}=are independently A,C,G or absent;

R_1,R_2,R_5,R_6,R_9,R_{12},R_{16},R_{20},R_{21},R_{26},R_{27},R_{29},R_{30},R_{31},R_{32},R_{33},R_{41},R_{44},R_{45},R_{46},R_{48},R_{50},R_{51},R_{58},R_{63},R_{64},R_{65},R_{66},R_{70},R_{71}=are independently N or absent;

R_{13},R_{17},R_{23},R_{61}=are independently A,C,U or absent;

R_{10},R_{14},R_{24},R_{40},R_{52},R_{56}=are independently A,G or absent;

R_7,R_{15},R_{25},R_{67},R_{72}=are independently A,G,U or absent;

R_{11},R_{57}=are independently A,U or absent;

R_{39}= C,G or absent;

R_3,R_4,R_{22},R_{42},R_{49},R_{55},R_{62}=are independently C,G,U or absent;

R_{18},R_{28},R_{35},R_{37},R_{53},R_{59},R_{60}=are independently C,U or absent;

R_{19}= G or absent;

R_8,R_{36},R_{38},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1,

x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{GLU}$ (SEQ ID NO: 581),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Glu is:

$R_{0,}R_{18,}R_{23}$=are absent

R_{17},R_{40}=are independently A or absent;

$R_{26},R_{27},R_{34},R_{43},R_{68},R_{69},R_{71}$=are independently A,C,G or absent;

$R_1,R_2,R_5,R_{12},R_{21},R_{31},R_{33},R_{41},R_{45},R_{48},R_{51},R_{58},R_{66},R_{70}$=are independently N or absent;

R_{44},R_{61}=are independently A,C,U or absent;

$R_9,R_{14},R_{24},R_{25},R_{52},R_{56},R_{63}$=are independently A,G or absent;

$R_7,R_{15},R_{46},R_{50},R_{67},R_{72}$=are independently A,G,U or absent;

R_{29},R_{57}=are independently A,U or absent;

R_{60}= C or absent;

R_{39}= C,G or absent;

$R_3,R_6,R_{20},R_{30},R_{32},R_{42},R_{55},R_{62},R_{65}$=are independently C,G,U or absent;

$R_4,R_8,R_{16},R_{28},R_{35},R_{37},R_{49},R_{53},R_{59}$=are independently C,U or absent;

R_{10},R_{19}=are independently G or absent;

R_{22},R_{64}=are independently G,U or absent;

$R_{11},R_{13},R_{36},R_{38},R_{54}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24,

x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{GLU}$ (SEQ ID NO: 582),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Glu is:

$R_{0,}R_{17,}R_{18,}R_{23}$=are absent

R_{14},R_{27},R_{40},R_{71}=are independently A or absent;

R_{44}= A,C or absent;

R_{43}= A,C,G or absent;

R_1,R_{31},R_{33},R_{45},R_{51},R_{66}=are independently N or absent;

R_{21},R_{41}=are independently A,C,U or absent;

R_7,R_{24},R_{25},R_{50},R_{52},R_{56},R_{63},R_{68},R_{70}=are independently A,G or absent;

R_5,R_{46}=are independently A,G,U or absent;

R_{29},R_{57},R_{67},R_{72}=are independently A,U or absent;

R_2,R_{39},R_{60}=are independently C or absent;

R_3,R_{12},R_{20},R_{26},R_{34},R_{69}=are independently C,G or absent;

R_6,R_{30},R_{42},R_{48},R_{65}=are independently C,G,U o rabsent;

R_4,R_{16},R_{28},R_{35},R_{37},R_{49},R_{53},R_{55},R_{58},R_{61},R_{62}=are independently C,U or absent;

R_9,R_{10},R_{19},R_{64}=are independently G or absent;

R_{15},R_{22},R_{32}=are independently G,U or absent;

R_8,R_{11},R_{13},R_{36},R_{38},R_{54},R_{59}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Glycine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{GLY} (SEQ ID NO: 583),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Gly is:

R_0=absent;

R_{24}= A or absent;

R_3,R_9,R_{40},R_{50},R_{51}=are independently A,C,G or absent;

R_4,R_5,R_6,R_7,R_{12},R_{16},R_{21},R_{22},R_{26},R_{29},R_{30},R_{31},R_{32},R_{33},R_{34},R_{41},R_{42},R_{43},R_{44},R_{45},R_{46},R_{48},R_{49},R_{58},R_{63},R_{64},R_{65},R_{66},R_{67},R_{68}=are independently N or absent;

R_{59}= A,C,U or absent;

R_1,R_{10},R_{14},R_{15},R_{27},R_{56}=are independently A,G or absent;

R_{20},R_{25}=are independently A,G,U or absent;

R_{57},R_{72}=are independently A,U or absent;

R_{38},R_{39},R_{60}=are independently C or absent;

R_{52}= C,G or absent;

R_2,R_{19},R_{37},R_{54},R_{55},R_{61},R_{62},R_{69},R_{70}=are independently C,G,U or absent;

R_{11},R_{13},R_{17},R_{28},R_{35},R_{36},R_{71}=are independently C,U or absent;

R_8,R_{18},R_{23},R_{53}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{GLY}$ (SEQ ID NO: 584),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Gly is:

R_0,R_{18},R_{23}=are absent

R_{24},R_{27},R_{40},R_{72}=are independently A or absent;

R_{26}= A,C or absent;

R_3,R_7,R_{68}=are independently A,C,G or absent;

R_5,R_{30},R_{41},R_{42},R_{44},R_{49},R_{67}=are independently A,C,G,U or absent;

R_{31},R_{32},R_{34}=are independently A,C,U or absent;

R_9,R_{10},R_{14},R_{15},R_{33},R_{50},R_{56}=are independently A,G or absent;

R_{12},R_{16},R_{22},R_{25},R_{29},R_{46}=are independently A,G,U or absent;

R_{57}= A,U or absent;

R_{17},R_{38},R_{39},R_{60},R_{61},R_{71}=are independently C or absent;

R_6,R_{52},R_{64},R_{66}=are independently C,G or absent;

R_2,R_4,R_{37},R_{48},R_{55},R_{65}=are independently C,G,U or absent;

R_{13},R_{35},R_{43},R_{62},R_{69}=are independently C,U or absent;

R_1,R_{19},R_{20},R_{51},R_{70}=are independently G or absent;

R_{21},R_{45},R_{63}=are independently G,U or absent;

R_8,R_{11},R_{28},R_{36},R_{53},R_{54},R_{58},R_{59}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{GLY}$ (SEQ ID NO: 585),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Gly is:

R_0,R_{18},R_{23}=are absent

R_{24},R_{27},R_{40},R_{72}=are independently A or absent;

R_{26}= A,C or absent;

R_3,R_7,R_{49},R_{68}=are independently A,C,G or absent;

R_5,R_{30},R_{41},R_{44},R_{67}=are independently N or absent;

R_{31},R_{32},R_{34}=are independently A,C,U or absent;

R_9,R_{10},R_{14},R_{15},R_{33},R_{50},R_{56}=are independently A,G or absent;

R_{12},R_{25},R_{29},R_{42},R_{46}=are independently A,G,U or absent;

R_{16},R_{57}=are independently A,U or absent;

R_{17},R_{38},R_{39},R_{60},R_{61},R_{71}=are independently C or absent;

R_6,R_{52},R_{64},R_{66}=are independently C,G or absent;

R_{37},R_{48},R_{65}=are independently C,G,U or absent;

R_2,R_4,R_{13},R_{35},R_{43},R_{55},R_{62},R_{69}=are independently C,U or absent;

R_1,R_{19},R_{20},R_{51},R_{70}=are independently G or absent;

R_{21},R_{22},R_{45},R_{63}=are independently G,U or absent;

R_8,R_{11},R_{28},R_{36},R_{53},R_{54},R_{58},R_{59}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Histidine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{HIS} (SEQ ID NO: 586),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for His is:

R_{23}=absent;

R_{14},R_{24},R_{57}=are independently A or absent;

R_{72}= A,C or absent;

R_{9},R_{27},R_{43},R_{48},R_{69}=are independently A,C,G or absent;

R_{3},R_{4},R_{5},R_{6},R_{12},R_{25},R_{26},R_{29},R_{30},R_{31},R_{34},R_{42},R_{45},R_{46},R_{49},R_{50},R_{58},R_{62},R_{63},R_{66},R_{67},R_{68}=are independently N or absent;

R_{13},R_{21},R_{41},R_{44},R_{65}=are independently A,C,U or absent;

R_{40},R_{51},R_{56},R_{70}=are independently A,G or absent;

R_{7},R_{32}=are independently A,G,U or absent;

R_{55},R_{60}=are independently C or absent;

R_{11},R_{16},R_{33},R_{64}=are independently C,G,U or absent;

R_{2},R_{17},R_{22},R_{28},R_{35},R_{53},R_{59},R_{61},R_{71}=are independently C,U or absent;

R_{1},R_{10},R_{15},R_{19},R_{20},R_{37},R_{39},R_{52}=are independently G or absent;

R_{0}= G,U or absent;

R_{8},R_{18},R_{36},R_{38},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{HIS}$ (SEQ ID NO: 587),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-

R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for His is:

$R_{0,}R_{17,}R_{18,}R_{23}$=are absent;

$R_7,R_{12},R_{14},R_{24},R_{27},R_{45},R_{57},R_{58},R_{63},R_{67},R_{72}$=are independently A or absent;

R_3= A,C,U or absent;

R_4,R_{43},R_{56},R_{70}=are independently A,G or absent;

R_{49}= A,U or absent;

$R_2,R_{28},R_{30},R_{41},R_{42},R_{44},R_{48},R_{55},R_{60},R_{66},R_{71}$=are independently C or absent;

R_{25}= C,G or absent;

R_9= C,G,U or absent;

$R_8,R_{13},R_{26},R_{33},R_{35},R_{50},R_{53},R_{61},R_{68}$=are independently C,U or absent;

$R_1,R_6,R_{10},R_{15},R_{19},R_{20},R_{32},R_{34},R_{37},R_{39},R_{40},R_{46},R_{51},R_{52},R_{62},R_{64},R_{69}$=are independently G or absent;

R_{16}= G,U or absent;

$R_5,R_{11},R_{21},R_{22},R_{29},R_{31},R_{36},R_{38},R_{54},R_{59},R_{65}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{HIS}$ (SEQ ID NO: 588),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for His is:

$R_{0,}R_{17,}R_{18,}R_{23}$=are absent

R_7,R_{12},R_{14},R_{24},R_{27},R_{45},R_{57},R_{58},R_{63},R_{67},R_{72}=are independently A or absent;

R_3= A,C or absent;

R_4,R_{43},R_{56},R_{70}=are independently A,G or absent;

R_{49}= A,U or absent;

R_2,R_{28},R_{30},R_{41},R_{42},R_{44},R_{48},R_{55},R_{60},R_{66},R_{71}=are independently C or absent;

R_8,R_9,R_{26},R_{33},R_{35},R_{50},R_{61},R_{68}=are independently C,U or absent;

R_1,R_6,R_{10},R_{15},R_{19},R_{20},R_{25},R_{32},R_{34},R_{37},R_{39},R_{40},R_{46},R_{51},R_{52},R_{62},R_{64},R_{69}=are independently G or absent;

R_5,R_{11},R_{13},R_{16},R_{21},R_{22},R_{29},R_{31},R_{36},R_{38},R_{53},R_{54},R_{59},R_{65}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Isoleucine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{ILE} (SEQ ID NO: 589),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-

R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ile is:

R_{23}=absent;

R_{38},R_{41},R_{57},R_{72}=are independently A or absent;

R_{1},R_{26}=are independently A,C,G or absent;

R_{0},R_{3},R_{4},R_{6},R_{16},R_{31},R_{32},R_{34},R_{37},R_{42},R_{43},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{58},R_{59},R_{62},R_{63},R_{64},R_{66},R_{67},R_{68},R_{69}=are independently N or absent;

R_{22},R_{61},R_{65}=are independently A,C,U or absent;

R_{9},R_{14},R_{15},R_{24},R_{27},R_{40}=are independently A,G or absent;

R_{7},R_{25},R_{29},R_{51},R_{56}=are independently A,G,U or absent;

R_{18},R_{54}=are independently A,U or absent;

R_{60}= C or absent;

R_{2},R_{52},R_{70}=are independently C,G or absent;

R_{5},R_{12},R_{21},R_{30},R_{33},R_{71}=are independently C,G,U or absent;

R_{11},R_{13},R_{17},R_{28},R_{35},R_{53},R_{55}=are independently C,U or absent;

R_{10},R_{19},R_{20}=are independently G or absent;

R_{8},R_{36},R_{39}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{ILE}$ (SEQ ID NO: 590),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ile is:

$R_{0,}R_{18,}R_{23}$=are absent

$R_{24},R_{38},R_{40},R_{41},R_{57},R_{72}$=are independently A or absent;

R_{26},R_{65}=are independently A,C or absent;

R_{58},R_{59},R_{67}=are independently N or absent;

R_{22}= A,C,U or absent;

$R_6,R_9,R_{14},R_{15},R_{29},R_{34},R_{43},R_{46},R_{48},R_{50},R_{51},R_{63},R_{69}$=are independently A,G or absent;

R_{37},R_{56}=are independently A,G,U or absent;

R_{54}= A,U or absent;

$R_{28},R_{35},R_{60},R_{62},R_{71}$=are independently C or absent;

R_2,R_{52},R_{70}=are independently C,G or absent;

R_5= C,G,U or absent;

$R_3,R_4,R_{11},R_{13},R_{17},R_{21},R_{30},R_{42},R_{44},R_{45},R_{49},R_{53},R_{55},R_{61},R_{64},R_{66}$=are independently C,U or absent;

$R_1,R_{10},R_{19},R_{20},R_{25},R_{27},R_{31},R_{68}$=are independently G or absent;

R_7,R_{12},R_{32}=are independently G,U or absent;

$R_8,R_{16},R_{33},R_{36},R_{39}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17,

x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{ILE}$ (SEQ ID NO: 591),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ile is:

$R_{0,}R_{18,}R_{23}$=are absent

$R_{14},R_{24},R_{38},R_{40},R_{41},R_{57},R_{72}$=are independently A or absent;

R_{26},R_{65}=are independently A,C or absent;

R_{22},R_{59}=are independently A,C,U or absent;

$R_6,R_9,R_{15},R_{34},R_{43},R_{46},R_{51},R_{56},R_{63},R_{69}$=are independently A,G or absent;

R_{37}= A,G,U or absent;

$R_{13},R_{28},R_{35},R_{44},R_{55},R_{60},R_{62},R_{71}$=are independently C or absent;

R_2,R_5,R_{70}=are independently C,G or absent;

R_{58},R_{67}=are independently C,G,U or absent;

$R_3,R_4,R_{11},R_{17},R_{21},R_{30},R_{42},R_{45},R_{49},R_{53},R_{61},R_{64},R_{66}$=are independently C,U or absent;

$R_1,R_{10},R_{19},R_{20},R_{25},R_{27},R_{29},R_{31},R_{32},R_{48},R_{50},R_{52},R_{68}$=are independently G or absent;

R_7,R_{12}=are independently G,U or absent;

$R_8,R_{16},R_{33},R_{36},R_{39},R_{54}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1,

x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Methionine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{MET}$ (SEQ ID NO: 592),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Met is:

R_0,R_{23}=are absent;

R_{14},R_{38},R_{40},R_{57}=are independently A or absent;

R_{60}= A,C or absent;

R_{33},R_{48},R_{70}=are independently A,C,G or absent;

R_1,R_3,R_4,R_5,R_6,R_{11},R_{12},R_{16},R_{17},R_{21},R_{22},R_{26},R_{27},R_{29},R_{30},R_{31},R_{32},R_{42},R_{44},R_{45},R_{46},R_{49},R_{50},R_{58},R_{62},R_{63},R_{66},R_{67},R_{68},R_{69},R_{71}=are independently N or absent;

R_{18},R_{35},R_{41},R_{59},R_{65}=are independently A,C,U or absent;

R_9,R_{15},R_{51}=are independently A,G or absent;

R_7,R_{24},R_{25},R_{34},R_{53},R_{56}=are independently A,G,U or absent;

R_{72}= A,U or absent;

R_{37}= C or absent;

R_{10},R_{55}=are independently C,G or absent;

R_2,R_{13},R_{28},R_{43},R_{64}=are independently C,G,U or absent;

R_{36},R_{61}=are independently C,U or absent;

R_{19},R_{20},R_{52}=are independently G or absent;

R_8,R_{39},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{MET}$ (SEQ ID NO: 593),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Met is:

$R_{0,}R_{18,}R_{22,}R_{23}$=are absent

R_{14},R_{24},R_{38},R_{40},R_{41},R_{57},R_{72}=are independently A or absent;

R_{59},R_{60},R_{62},R_{65}=are independently A,C or absent;

R_6,R_{45},R_{67}=are independently A,C,G or absent;

R_4= N or absent;

R_{21},R_{42}=are independently A,C,U or absent;

R_1,R_9,R_{27},R_{29},R_{32},R_{46},R_{51}=are independently A,G or absent;

R_{17},R_{49},R_{53},R_{56},R_{58}=are independently A,G,U or absent;

R_{63}=A,U or absent;

R_3,R_{13},R_{37}=are independently C or absent;

R_{48},R_{55},R_{64},R_{70}=are independently C,G or absent;

R_2,R_5,R_{66},R_{68}=are independently C,G,U or absent;

R_{11},R_{16},R_{26},R_{28},R_{30},R_{31},R_{35},R_{36},R_{43},R_{44},R_{61},R_{71}=are independently C,U or absent;

R_{10},R_{12},R_{15},R_{19},R_{20},R_{25},R_{33},R_{52},R_{69}=are independently G or absent;

R_{7},R_{34},R_{50}=are independently G,U or absent;

R_{8},R_{39},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{MET}$ (SEQ ID NO: 594),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Met is:

R_{0},R_{18},R_{22},R_{23}=are absent

R_{14},R_{24},R_{38},R_{40},R_{41},R_{57},R_{72}=are independently A or absent;

R_{59},R_{62},R_{65}=are independently A,C or absent;

R_{6},R_{67}=are independently A,C,G or absent;

R_{4},R_{21}=are independently A,C,U or absent;

R_{1},R_{9},R_{27},R_{29},R_{32},R_{45},R_{46},R_{51}=are independently A,G or absent;

R_{17},R_{56},R_{58}=are independently A,G,U or absent;

R_{49},R_{53},R_{63}=are independently A,U or absent;

R_3,R_{13},R_{26},R_{37},R_{43},R_{60}=are independently C or absent;

R_2,R_{48},R_{55},R_{64},R_{70}=are independently C,G or absent;

R_5,R_{66}=are independently C,G,U or absent;

R_{11},R_{16},R_{28},R_{30},R_{31},R_{35},R_{36},R_{42},R_{44},R_{61},R_{71}=are independently C,U or absent;

R_{10},R_{12},R_{15},R_{19},R_{20},R_{25},R_{33},R_{52},R_{69}=are independently G or absent;

R_7,R_{34},R_{50},R_{68}=are independently G,U or absent;

R_8,R_{39},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Leucine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{LEU} (SEQ ID NO: 595),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Leu is:

R_0=absent;

R_{38},R_{57}=are independently A or absent;

R_{60}= A,C or absent;

R_1,R_{13},R_{27},R_{48},R_{51},R_{56}=are independently A,C,G or absent;

R_2,R_3,R_4,R_5,R_6,R_7,R_9,R_{10},R_{11},R_{12},R_{16},R_{23},R_{26},R_{28},R_{29},R_{30},R_{31},R_{32},R_{33},R_{34},R_{37},R_{41},R_{42},R_{43},R_{44}, R_{45},R_{46},R_{49},R_{50},R_{58},R_{62},R_{63},R_{65},R_{66},R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{17},R_{18},R_{21},R_{22},R_{25},R_{35},R_{55}=are independently A,C,U or absent;

R_{14},R_{15},R_{39},R_{72}=are independently A,G or absent;

R_{24},R_{40}=are independently A,G,U or absent;

R_{52},R_{61},R_{64},R_{71}=are independently C,G,U or absent;

R_{36},R_{53},R_{59}=are independently C,U or absent;

R_{19}= G or absent;

R_{20}= G,U or absent;

R_8,R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{LEU}$ (SEQ ID NO: 596),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Leu is:

R_0 =absent

R_{38},R_{57},R_{72}=are independently A or absent;

R_{60}= A,C or absent;

R_4,R_5,R_{48},R_{50},R_{56},R_{69}=are independently A,C,G or absent;

R_6,R_{33},R_{41},R_{43},R_{46},R_{49},R_{58},R_{63},R_{66},R_{70}=are independently N or absent;

R_{11},R_{12},R_{17},R_{21},R_{22},R_{28},R_{31},R_{37},R_{44},R_{55}=are independently A,C,U or absent;

R_1,R_9,R_{14},R_{15},R_{24},R_{27},R_{34},R_{39}=are independently A,G or absent;

R_7,R_{29},R_{32},R_{40},R_{45}=are independently A,G,U or absent;

R_{25}= A,U or absent;

R_{13}= C,G or absent;

R_2,R_3,R_{16},R_{26},R_{30},R_{52},R_{62},R_{64},R_{65},R_{67},R_{68}=are independently C,G,U or absent;

R_{18},R_{35},R_{42},R_{53},R_{59},R_{61},R_{71}=are independently C,U or absent;

R_{19},R_{51}=are independently G or absent;

R_{10},R_{20}=are independently G,U or absent;

R_8,R_{23},R_{36},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{LEU}$ (SEQ ID NO: 597),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Leu is:

R_0 =absent

R_{38},R_{57},R_{72}=are independently A or absent;

R_{60}= A,C or absent;

R_4,R_5,R_{48},R_{50},R_{56},R_{58},R_{69}=are independently A,C,G or absent;

R_6,R_{33},R_{43},R_{46},R_{49},R_{63},R_{66},R_{70}=are independently N or absent;

R_{11},R_{12},R_{17},R_{21},R_{22},R_{28},R_{31},R_{37},R_{41},R_{44},R_{55}=are independently A,C,U or absent;

R_1,R_9,R_{14},R_{15},R_{24},R_{27},R_{34},R_{39}=are independently A,G or absent;

R_7,R_{29},R_{32},R_{40},R_{45}=are independently A,G,U or absent;

R_{25}= A,U or absent;

R_{13}= C,G or absent;

R_2,R_3,R_{16},R_{30},R_{52},R_{62},R_{64},R_{67},R_{68}=are independently C,G,U or absent;

R_{18},R_{35},R_{42},R_{53},R_{59},R_{61},R_{65},R_{71}=are independently C,U or absent;

R_{19},R_{51}=are independently G or absent;

R_{10},R_{20},R_{26}=are independently G,U or absent;

R_8,R_{23},R_{36},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Lysine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{LYS} (SEQ ID NO: 598),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Lys is:

R_0 =absent

R_{14}= A or absent;

R_{40},R_{41}=are independently A,C or absent;

R_{34},R_{43},R_{51}=are independently A,C,G or absent;

R_1,R_2,R_3,R_4,R_5,R_6,R_7,R_{11},R_{12},R_{16},R_{21},R_{26},R_{30},R_{31},R_{32},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{58},R_{62},R_{63},R_{65}, R_{66},R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{13},R_{17},R_{59},R_{71}=are independently A,C,U or absent;

R_9,R_{15},R_{19},R_{20},R_{25},R_{27},R_{52},R_{56}=are independently A,G or absent;

R_{24},R_{29},R_{72}=are independently A,G,U or absent;

R_{18},R_{57}=are independently A,U or absent;

R_{10},R_{33}=are independently C,G or absent;

R_{42},R_{61},R_{64}=are independently C,G,U or absent;

R_{28},R_{35},R_{36},R_{37},R_{53},R_{55},R_{60}=are independently C,U or absent;

R_8,R_{22},R_{23},R_{38},R_{39},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{LYS}$ (SEQ ID NO: 599),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Lys is:

$R_{0,}R_{18,}R_{23}$=are absent

R_{14}= A or absent;

R_{40},R_{41},R_{43}=are independently A,C or absent;

R_3,R_7=are independently A,C,G or absent;

R_1,R_6,R_{11},R_{31},R_{45},R_{48},R_{49},R_{63},R_{65},R_{66},R_{68}=are independently N or absent;

R_2,R_{12},R_{13},R_{17},R_{44},R_{67},R_{71}=are independently A,C,U or absent;

R_9,R_{15},R_{19},R_{20},R_{25},R_{27},R_{34},R_{50},R_{52},R_{56},R_{70},R_{72}=are independently A,G or absent;

R_5,R_{24},R_{26},R_{29},R_{32},R_{46},R_{69}=are independently A,G,U or absent;

R_{57}= A,U or absent;

R_{10},R_{61}=are independently C,G or absent;

R_4,R_{16},R_{21},R_{30},R_{58},R_{64}=are independently C,G,U or absent;

R_{28},R_{35},R_{36},R_{37},R_{42},R_{53},R_{55},R_{59},R_{60},R_{62}=are independently C,U or absent;

R_{33},R_{51}=are independently G or absent;

R_8=G,U or absent;

R_{22},R_{38},R_{39},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17,

x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{LYS}$ (SEQ ID NO: 600),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Lys is:

$R_{0,}R_{18,}R_{23}$=absent

R_9,R_{14},R_{34},R_{41}=are independently A or absent;

R_{40}= A,C or absent;

R_1,R_3,R_7,R_{31}=are independently A,C,G or absent;

R_{48},R_{65},R_{68}=are independently N or absent;

$R_2,R_{13},R_{17},R_{44},R_{63},R_{66}$=are independently A,C,U or absent;

$R_5,R_{15},R_{19},R_{20},R_{25},R_{27},R_{29},R_{50},R_{52},R_{56},R_{70},R_{72}$=are independently A,G or absent;

R_6,R_{24},R_{32},R_{49}=are independently A,G,U or absent;

$R_{12},R_{26},R_{46},R_{57}$=are independently A,U or absent;

$R_{11},R_{28},R_{35},R_{43}$=are independently C or absent;

R_{10},R_{45},R_{61}=are independently C,G or absent;

R_4,R_{21},R_{64}=are independently C,G,U or absent;

$R_{37},R_{53},R_{55},R_{59},R_{60},R_{62},R_{67},R_{71}$=are independently C,U or absent;

R_{33},R_{51}=are independently G or absent;

R_8,R_{30},R_{58},R_{69}=are independently G,U or absent;

$R_{16},R_{22},R_{36},R_{38},R_{39},R_{42},R_{54}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24,

x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Phenylalanine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{PHE}$ (SEQ ID NO: 601),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Phe is:

R_0,R_{23}=are absent

R_9,R_{14},R_{38},R_{39},R_{57},R_{72}=are independently A or absent;

R_{71}= A,C or absent;

R_{41},R_{70}=are independently A,C,G or absent;

R_4,R_5,R_6,R_{30},R_{31},R_{32},R_{34},R_{42},R_{44},R_{45},R_{46},R_{48},R_{49},R_{58},R_{62},R_{63},R_{66},R_{67},R_{68},R_{69}=are independently N or absent;

R_{16},R_{61},R_{65}=are independently A,C,U or absent;

R_{15},R_{26},R_{27},R_{29},R_{40},R_{56}=are independently A,G or absent;

R_7,R_{51}=are independently A,G,U or absent;

R_{22},R_{24}=are independently A,U or absent;

R_{55},R_{60}=are independently C or absent;

R_2,R_3,R_{21},R_{33},R_{43},R_{50},R_{64}=are independently C,G,U or absent;

R_{11},R_{12},R_{13},R_{17},R_{28},R_{35},R_{36},R_{59}=are independently C,U or absent;

R_{10},R_{19},R_{20},R_{25},R_{37},R_{52}=are independently G or absent;

R_1= G,U or absent;

R_8,R_{18},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{PHE}$ (SEQ ID NO: 602),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Phe is:

R_0,R_{18},R_{23}=absent

R_{14},R_{24},R_{38},R_{39},R_{57},R_{72}=are independently A or absent;

R_{46},R_{71}=are independently A,C or absent;

R_4,R_{70}=are independently A,C,G or absent;

R_{45}= A,C,U or absent;

R_6,R_7,R_{15},R_{26},R_{27},R_{32},R_{34},R_{40},R_{41},R_{56},R_{69}=are independently A,G or absent;

R_{29}= A,G,U or absent;

R_5,R_9,R_{67}=are independently A,U or absent;

R_{35},R_{49},R_{55},R_{60}=are independently C or absent;

R_{21},R_{43},R_{62}=are independently C,G or absent;

R_{2},R_{33},R_{68}=are independently C,G,U or absent;

R_{3},R_{11},R_{12},R_{13},R_{28},R_{30},R_{36},R_{42},R_{44},R_{48},R_{58},R_{59},R_{61},R_{66}=are independently C,U or absent;

R_{10},R_{19},R_{20},R_{25},R_{37},R_{51},R_{52},R_{63},R_{64}=are independently G or absent;

R_{1},R_{31},R_{50}=are independently G,U or absent;

R_{8},R_{16},R_{17},R_{22},R_{53},R_{54},R_{65}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{PHE}$ (SEQ ID NO: 603),

R_{0}- R_{1}-R_{2}- R_{3}-R_{4} -R_{5}-R_{6}-R_{7}-R_{8}-R_{9}-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Phe is:

R_{0},R_{18},R_{22},R_{23}=absent

R_{5},R_{7},R_{14},R_{24},R_{26},R_{32},R_{34},R_{38},R_{39},R_{41},R_{57},R_{72}=are independently A or absent;

R_{46}= A,C or absent;

R_{70}= A,C,G or absent;

R_{4},R_{6},R_{15},R_{56},R_{69}=are independently A,G or absent;

R_9,R_{45}=are independently A,U or absent;

R_2,R_{11},R_{13},R_{35},R_{43},R_{49},R_{55},R_{60},R_{68},R_{71}=are independently C or absent;

R_{33}= C,G or absent;

R_3,R_{28},R_{36},R_{48},R_{58},R_{59},R_{61}=are independently C,U or absent;

R_1,R_{10},R_{19},R_{20},R_{21},R_{25},R_{27},R_{29},R_{37},R_{40},R_{51},R_{52},R_{62},R_{63},R_{64}=are independently G or absent;

R_8,R_{12},R_{16},R_{17},R_{30},R_{31},R_{42},R_{44},R_{50},R_{53},R_{54},R_{65},R_{66},R_{67}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Proline TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{PRO} (SEQ ID NO: 604),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Pro is:

R_0 =absent

R_{14},R_{57}=are independently A or absent;

R_{70},R_{72}=are independently A,C or absent;

R_9,R_{26},R_{27}=are independently A,C,G or absent;

R_4,R_5,R_6,R_{16},R_{21},R_{29},R_{30},R_{31},R_{32},R_{33},R_{34},R_{37},R_{41},R_{42},R_{43},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{58},R_{61},R_{62}, R_{63},R_{64},R_{66},R_{67},R_{68}=are independently N or absent;

R_{35},R_{65}=are independently A,C,U or absent;

R_{24},R_{40},R_{56}=are independently A,G or absent;

R_{7},R_{25},R_{51}=are independently A,G,U or absent;

R_{55},R_{60}=are independently C or absent;

R_{1},R_{3},R_{71}=are independently C,G or absent;

R_{11},R_{12},R_{20},R_{69}=are independently C,G,U or absent;

R_{13},R_{17},R_{18},R_{22},R_{23},R_{28},R_{59}=are independently C,U or absent;

R_{10},R_{15},R_{19},R_{38},R_{39},R_{52}=are independently G or absent;

R_{2}= are independently G,U or absent;

R_{8},R_{36},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{PRO}$ (SEQ ID NO: 605),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Pro is:

R_{0},R_{17},R_{18},R_{22},R_{23}=absent;

R_{14},R_{45},R_{56},R_{57},R_{58},R_{65},R_{68}=are independently A or absent;

R_{61}= A,C,G or absent;

R_{43}=N or absent;

R_{37}= A, C,U or absent;

R_{24},R_{27},R_{33},R_{40},R_{44},R_{63}=are independently A,G or absent;

R_3,R_{12},R_{30},R_{32},R_{48},R_{55},R_{60},R_{70},R_{71},R_{72}=are independently C or absent;

R_5,R_{34},R_{42},R_{66}=are independently C,G or absent;

R_{20}= C,G,U or absent;

R_{35},R_{41},R_{49},R_{62}=are independently C,U or absent;

R_1,R_2,R_6,R_9,R_{10},R_{15},R_{19},R_{26},R_{38},R_{39},R_{46},R_{50},R_{51},R_{52},R_{64},R_{67},R_{69}=are independently G or absent;

R_{11},R_{16}=are independently G,U or absent;

R_4,R_7,R_8,R_{13},R_{21},R_{25},R_{28},R_{29},R_{31},R_{36},R_{53},R_{54},R_{59}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{PRO}$ (SEQ ID NO: 606),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Pro is:

$R_{0,}R_{17,}R_{18,}R_{22,}R_{23}$=absent

$R_{14,}R_{45,}R_{56,}R_{57,}R_{58,}R_{65,}R_{68}$=are independently A or absent;

R_{37}= A,C,U or absent;

$R_{24,}R_{27,}R_{40}$=are independently A,G or absent;

$R_{3,}R_{5,}R_{12,}R_{30,}R_{32,}R_{48,}R_{49,}R_{55,}R_{60,}R_{61,}R_{62,}R_{66,}R_{70,}R_{71,}R_{72}$=are independently C or absent;

$R_{34,}R_{42}$=are independently C,G or absent;

R_{43}= C,G,U or absent;

R_{41}= C,U or absent;

$R_{1,}R_{2,}R_{6,}R_{9,}R_{10,}R_{15,}R_{19,}R_{20,}R_{26,}R_{33,}R_{38,}R_{39,}R_{44,}R_{46,}R_{50,}R_{51,}R_{52,}R_{63,}R_{64,}R_{67,}R_{69}$=are independently G or absent;

R_{16}= G,U or absent;

$R_{4,}R_{7,}R_{8,}R_{11,}R_{13,}R_{21,}R_{25,}R_{28,}R_{29,}R_{31,}R_{35,}R_{36,}R_{53,}R_{54,}R_{59}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Serine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{SER} (SEQ ID NO: 607),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ser is:

R_0=absent;

R_{14},R_{24},R_{57}=are independently A or absent;

R_{41}= A,C or absent;

R_2,R_3,R_4,R_5,R_6,R_7,R_9,R_{10},R_{11},R_{12},R_{13},R_{16},R_{21},R_{25},R_{26},R_{27},R_{28},R_{30},R_{31},R_{32},R_{33},R_{34},R_{37},R_{42},R_{43}, R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{62},R_{63},R_{64},R_{65},R_{66},R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{18}= A,C,U or absent;

R_{15},R_{40},R_{51},R_{56}=are independently A,G or absent;

R_1,R_{29},R_{58},R_{72}=are independently A,G,U or absent;

R_{39}= A,U or absent;

R_{60}= C or absent;

R_{38}= C,G or absent;

R_{17},R_{22},R_{23},R_{71}=are independently C,G,U or absent;

R_8,R_{35},R_{36},R_{55},R_{59},R_{61}=are independently C,U or absent;

R_{19},R_{20}=are independently G or absent;

R_{52}= G,U or absent;

R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{SER}$ (SEQ ID NO: 608),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ser is:

$R_{0,}R_{23}$=absent

$R_{14},R_{24},R_{41},R_{57}$=are independently A or absent;

R_{44}= A,C or absent;

R_{25},R_{45},R_{48}=are independently A,C,G or absent;

$R_2,R_3,R_4,R_5,R_{37},R_{50},R_{62},R_{66},R_{67},R_{69},R_{70}$=are independently N or absent;

R_{12},R_{28},R_{65}=are independently A,C,U or absent;

$R_9,R_{15},R_{29},R_{34},R_{40},R_{56},R_{63}$=are independently A,G or absent;

$R_7,R_{26},R_{30},R_{33},R_{46},R_{58},R_{72}$=are independently A,G,U or absent;

R_{39}= A,U or absent;

$R_{11},R_{35},R_{60},R_{61}$=are independently C or absent;

R_{13},R_{38}=are independently C,G or absent;

$R_6,R_{17},R_{31},R_{43},R_{64},R_{68}$=are independently C,G,U or absent;

$R_{36},R_{42},R_{49},R_{55},R_{59},R_{71}$=are independently C,U or absent;

$R_{10},R_{19},R_{20},R_{27},R_{51}$=are independently G or absent;

R_1,R_{16},R_{32},R_{52}=are independently G,U or absent;

$R_8,R_{18},R_{21},R_{22},R_{53},R_{54}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17,

x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{SER}$ (SEQ ID NO: 609),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Ser is:

R_0,R_{23}=absent

R_{14},R_{24},R_{41},R_{57},R_{58}=are independently A or absent;

R_{44}= A,C or absent;

R_{25},R_{48}=are independently A,C,G or absent;

R_2,R_3,R_5,R_{37},R_{66},R_{67},R_{69},R_{70}=are independently N or absent;

R_{12},R_{28},R_{62}=are independently A,C,U or absent;

R_7,R_9,R_{15},R_{29},R_{33},R_{34},R_{40},R_{45},R_{56},R_{63}=are independently A,G or absent;

R_4,R_{26},R_{46},R_{50}=are independently A,G,U or absent;

R_{30},R_{39}=are independently A,U or absent;

R_{11},R_{17},R_{35},R_{60},R_{61}=are independently C or absent;

R_{13},R_{38}=are independently C,G or absent;

R_6,R_{64}=are independently C,G,U or absent;

R_{31},R_{42},R_{43},R_{49},R_{55},R_{59},R_{65},R_{68},R_{71}=are independently C,U or absent;

R_{10},R_{19},R_{20},R_{27},R_{51},R_{52}=are independently G or absent;

R_1,R_{16},R_{32},R_{72}=are independently G,U or absent;

R_8,R_{18},R_{21},R_{22},R_{36},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24,

x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Threonine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{THR}$ (SEQ ID NO: 610),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Thr is:

$R_{0,}R_{23}$=absent

R_{14},R_{41},R_{57}=are independently A or absent;

R_{56},R_{70}=are independently A,C,G or absent;

$R_4,R_5,R_6,R_7,R_{12},R_{16},R_{26},R_{30},R_{31},R_{32},R_{34},R_{37},R_{42},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{58},R_{62},R_{63},R_{64},R_{65},R_{66},R_{67},R_{68},R_{72}$=are independently N or absent;

$R_{13},R_{17},R_{21},R_{35},R_{61}$=are independently A,C,U or absent;

$R_1,R_9,R_{24},R_{27},R_{29},R_{69}$=are independently A,G or absent;

R_{15},R_{25},R_{51}=are independently A,G,U or absent;

R_{40},R_{53}=are independently A,U or absent;

R_{33},R_{43}=are independently C,G or absent;

R_2,R_3,R_{59}=are independently C,G,U or absent;

$R_{11},R_{18},R_{22},R_{28},R_{36},R_{54},R_{55},R_{60},R_{71}$=are independently C,U or absent;

$R_{10},R_{20},R_{38},R_{52}$=are independently G or absent;

R_{19}= G,U or absent;

R_8,R_{39}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{THR}$ (SEQ ID NO: 611),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Thr is:

R_0,R_{18},R_{23}=absent

R_{14},R_{41},R_{57}=are independently A or absent;

R_9,R_{42},R_{44},R_{48},R_{56},R_{70}=are independently A,C,G or absent;

R_4,R_6,R_{12},R_{26},R_{49},R_{58},R_{63},R_{64},R_{66},R_{68}=are independently N or absent;

R_{13},R_{21},R_{31},R_{37},R_{62}=are independently A,C,U or absent;

R_1,R_{15},R_{24},R_{27},R_{29},R_{46},R_{51},R_{69}=are independently A,G or absent;

R_7,R_{25},R_{45},R_{50},R_{67}=are independently A,G,U or absent;

R_{40},R_{53}=are independently A,U or absent;

R_{35}= C or absent;

R_{33},R_{43}=are independently C,G or absent;

R_2,R_3,R_5,R_{16},R_{32},R_{34},R_{59},R_{65},R_{72}=are independently C,G,U or absent;

R_{11},R_{17},R_{22},R_{28},R_{30},R_{36},R_{55},R_{60},R_{61},R_{71}=are independently C,U or absent;

R_{10},R_{19},R_{20},R_{38},R_{52}=are independently G or absent;

R_8,R_{39},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{THR}$ (SEQ ID NO: 612),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Thr is:

R_0,R_{18},R_{23}=absent

R_{14},R_{40},R_{41},R_{57}=are independently A or absent;

R_{44}= A,C or absent;

R_9,R_{42},R_{48},R_{56}=are independently A,C,G or absent;

R_4,R_6,R_{12},R_{26},R_{58},R_{64},R_{66},R_{68}=are independently N or absent;

R_{13},R_{21},R_{31},R_{37},R_{49},R_{62}=are independently A,C,U or absent;

R_1,R_{15},R_{24},R_{27},R_{29},R_{46},R_{51},R_{69}=are independently A,G or absent;

R_7,R_{25},R_{45},R_{50},R_{63},R_{67}=are independently A,G,U or absent;

R_{53}= A,U or absent;

R_{35}= C or absent;

R_2,R_{33},R_{43},R_{70}=are independently C,G or absent;

R_5,R_{16},R_{34},R_{59},R_{65}=are independently C,G,U or absent;

R_3,R_{11},R_{22},R_{28},R_{30},R_{36},R_{55},R_{60},R_{61},R_{71}=are independently C,U or absent;

R_{10},R_{19},R_{20},R_{38},R_{52}=are independently G or absent;

R_{32}= G,U or absent;

R_8,R_{17},R_{39},R_{54},R_{72}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Tryptophan TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I_{TRP} (SEQ ID NO: 613),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Trp is:

R_0= absent;

R_{24},R_{39},R_{41},R_{57}=are independently A or absent;

R_2,R_3,R_{26},R_{27},R_{40},R_{48}=are independently A,C,G or absent;

R_4,R_5,R_6,R_{29},R_{30},R_{31},R_{32},R_{34},R_{42},R_{44},R_{45},R_{46},R_{49},R_{51},R_{58},R_{63},R_{66},R_{67},R_{68}=are independently N or absent;

R_{13},R_{14},R_{16},R_{18},R_{21},R_{61},R_{65},R_{71}=are independently A,C,U or absent;

R_1,R_9,R_{10},R_{15},R_{33},R_{50},R_{56}=are independently A,G or absent;

R_7,R_{25},R_{72}=are independently A,G,U or absent;

R_{37},R_{38},R_{55},R_{60}=are independently C or absent;

R_{12},R_{35},R_{43},R_{64},R_{69},R_{70}=are independently C,G,U or absent;

R_{11},R_{17},R_{22},R_{28},R_{59},R_{62}=are independently C,U or absent;

R_{19},R_{20},R_{52}=are independently G or absent;

R_8,R_{23},R_{36},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{TRP}$ (SEQ ID NO: 614),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Trp is:

R_0,R_{18},R_{22},R_{23}=absent

R_{14},R_{24},R_{39},R_{41},R_{57},R_{72}=are independently A or absent;

R_3,R_4,R_{13},R_{61},R_{71}=are independently A,C or absent;

R_6,R_{44}=are independently A,C,G or absent;

R_{21}= A,C,U or absent;

R_2,R_7,R_{15},R_{25},R_{33},R_{34},R_{45},R_{56},R_{63}=are independently A,G or absent;

R_{58}= A,G,U or absent;

R_{46}= A,U or absent;

R_{37},R_{38},R_{55},R_{60},R_{62}=are independently C or absent;

R_{12},R_{26},R_{27},R_{35},R_{40},R_{48},R_{67}=are independently C,G or absent;

R_{32},R_{43},R_{68}=are independently C,G,U or absent;

R_{11},R_{16},R_{28},R_{31},R_{49},R_{59},R_{65},R_{70}=are independently C,U or absent;

R_1,R_9,R_{10},R_{19},R_{20},R_{50},R_{52},R_{69}=are independently G or absent;

R_5,R_8,R_{29},R_{30},R_{42},R_{51},R_{64},R_{66}=are independently G,U or absent;

R_{17},R_{36},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{TRP}$ (SEQ ID NO: 615),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-

R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Trp is:

$R_{0,}R_{18,}R_{22,}R_{23}$=absent

R_{14},R_{24},R_{39},R_{41},R_{57},R_{72}=are independently A or absent;

R_3,R_4,R_{13},R_{61},R_{71}=are independently A,C or absent;

R_6,R_{44}=are independently A,C,G or absent;

R_{21}= A,C,U or absent;

R_2,R_7,R_{15},R_{25},R_{33},R_{34},R_{45},R_{56},R_{63}=are independently A,G or absent;

R_{58}= A,G,U or absent;

R_{46}= A,U or absent;

R_{37},R_{38},R_{55},R_{60},R_{62}=are independently C or absent;

R_{12},R_{26},R_{27},R_{35},R_{40},R_{48},R_{67}=are independently C,G or absent;

R_{32},R_{43},R_{68}=are independently C,G,U or absent;

R_{11},R_{16},R_{28},R_{31},R_{49},R_{59},R_{65},R_{70}=are independently C,U or absent;

R_1,R_9,R_{10},R_{19},R_{20},R_{50},R_{52},R_{69}=are independently G or absent;

R_5,R_8,R_{29},R_{30},R_{42},R_{51},R_{64},R_{66}=are independently G,U or absent;

R_{17},R_{36},R_{53},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Tyrosine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{TYR}$ (SEQ ID NO: 616),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Tyr is:

R_0 =absent

R_{14},R_{39},R_{57}=are independently A or absent;

R_{41},R_{48},R_{51},R_{71}=are independently A,C,G or absent;

R_3,R_4,R_5,R_6,R_9,R_{10},R_{12},R_{13},R_{16},R_{25},R_{26},R_{30},R_{31},R_{32},R_{42},R_{44},R_{45},R_{46},R_{49},R_{50},R_{58},R_{62},R_{63},R_{66}, R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{22},R_{65}=are independently A,C,U or absent;

R_{15},R_{24},R_{27},R_{33},R_{37},R_{40},R_{56}=are independently A,G or absent;

R_7,R_{29},R_{34},R_{72}=are independently A,G,U or absent;

R_{23},R_{53}=are independently A,U or absent;

R_{35},R_{60}=are independently C or absent;

R_{20}= C,G or absent;

R_1,R_2,R_{28},R_{61},R_{64}=are independently C,G,U or absent;

R_{11},R_{17},R_{21},R_{43},R_{55}=are independently C,U or absent;

R_{19},R_{52}=are independently G or absent;

R_8,R_{18},R_{36},R_{38},R_{54},R_{59}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17,

x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{TYR}$ (SEQ ID NO: 617),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Tyr is:

$R_{0,}R_{18,}R_{23}$=absent

R_7,R_9,R_{14},R_{24},R_{26},R_{34},R_{39},R_{57}=are independently A or absent;

R_{44},R_{69}=are independently A,C or absent;

R_{71}= A,C,G or absent;

R_{68}= N or absent;

R_{58}= A,C,U or absent;

R_{33},R_{37},R_{41},R_{56},R_{62},R_{63}=are independently A,G or absent;

R_6,R_{29},R_{72}=are independently A,G,U or absent;

R_{31},R_{45},R_{53}=are independently A,U or absent;

R_{13},R_{35},R_{49},R_{60}=are independently C or absent;

R_{20},R_{48},R_{64},R_{67},R_{70}=are independently C,G or absent;

R_1,R_2,R_5,R_{16},R_{66}=are independently C,G,U or absent;

R_{11},R_{21},R_{28},R_{43},R_{55},R_{61}=are independently C,U or absent;

R_{10},R_{15},R_{19},R_{25},R_{27},R_{40},R_{51},R_{52}=are independently G or absent;

R_3,R_4,R_{30},R_{32},R_{42},R_{46}=are independently G,U or absent;

R_8,R_{12},R_{17},R_{22},R_{36},R_{38},R_{50},R_{54},R_{59},R_{65}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24,

x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{TYR}$ (SEQ ID NO: 618),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Tyr is:

$R_{0,}R_{18,}R_{23}$=absent

$R_7,R_9,R_{14},R_{24},R_{26},R_{34},R_{39},R_{57},R_{72}$=are independently A or absent;

R_{44},R_{69}=are independently A,C or absent;

R_{71}= A,C,G or absent;

$R_{37},R_{41},R_{56},R_{62},R_{63}$=are independently A,G or absent;

R_6,R_{29},R_{68}=are independently A,G,U or absent;

R_{31},R_{45},R_{58}=are independently A,U or absent;

$R_{13},R_{28},R_{35},R_{49},R_{60},R_{61}$=are independently C or absent;

$R_5,R_{48},R_{64},R_{67},R_{70}$=are independently C,G or absent;

R_1,R_2=are independently C,G,U or absent;

$R_{11},R_{16},R_{21},R_{43},R_{55},R_{66}$=are independently C,U or absent;

$R_{10},R_{15},R_{19},R_{20},R_{25},R_{27},R_{33},R_{40},R_{51},R_{52}$=are independently G or absent;

$R_3,R_4,R_{30},R_{32},R_{42},R_{46}$=are independently G,U or absent;

$R_8,R_{12},R_{17},R_{22},R_{36},R_{38},R_{50},R_{53},R_{54},R_{59},R_{65}$=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Valine TREM Consensus sequence

In an embodiment, a TREM disclosed herein comprises the sequence of Formula I $_{VAL}$ (SEQ ID NO: 619),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Val is:

R_0,R_{23}=absent;

R_{24},R_{38},R_{57}=are independently A or absent;

R_9,R_{72}=are independently A,C,G or absent;

R_2,R_4,R_5,R_6,R_7,R_{12},R_{15},R_{16},R_{21},R_{25},R_{26},R_{29},R_{31},R_{32},R_{33},R_{34},R_{37},R_{41},R_{42},R_{43},R_{44},R_{45},R_{46},R_{48},R_{49},R_{50},R_{58},R_{61},R_{62},R_{63},R_{64},R_{65},R_{66},R_{67},R_{68},R_{69},R_{70}=are independently N or absent;

R_{17},R_{35},R_{59}=are independently A,C,U or absent;

R_{10},R_{14},R_{27},R_{40},R_{52},R_{56}=are independently A,G or absent;

R_1,R_3,R_{51},R_{53}=are independently A,G,U or absent;

R_{39}= C or absent;

R_{13},R_{30},R_{55}=are independently C,G,U or absent;

R_{11},R_{22},R_{28},R_{60},R_{71}=are independently C,U or absent;

R_{19}= G or absent;

R_{20}= G ,U or absent;

R_8,R_{18},R_{36},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula II $_{VAL}$ (SEQ ID NO: 620),

R_0- R_1- R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Val is:

R_0,R_{18},R_{23}=absent;

R_{24},R_{38},R_{57}=are independently A or absent;

R_{64},R_{70},R_{72}=are independently A,C,G or absent;

R_{15},R_{16},R_{26},R_{29},R_{31},R_{32},R_{43},R_{44},R_{45},R_{49},R_{50},R_{58},R_{62},R_{65}=are independently N or absent;

R_6,R_{17},R_{34},R_{37},R_{41},R_{59}=are independently A,C,U or absent;

R_9,R_{10},R_{14},R_{27},R_{40},R_{46},R_{51},R_{52},R_{56}=are independently A,G or absent;

R_7,R_{12},R_{25},R_{33},R_{53},R_{63},R_{66},R_{68}=are independently A,G,U or absent;

R_{69}= A,U or absent;

R_{39}= C or absent;

R_5,R_{67}=are independently C,G or absent;

R_2,R_4,R_{13},R_{48},R_{55},R_{61}=are independently C,G,U or absent;

R_{11},R_{22},R_{28},R_{30},R_{35},R_{60},R_{71}=are independently C,U or absent;

R_{19}= G or absent;

R_1,R_3,R_{20},R_{42}=are independently G,U or absent;

R_8,R_{21},R_{36},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

In an embodiment, a TREM disclosed herein comprises the sequence of Formula III $_{VAL}$ (SEQ ID NO: 621),

R_0- R_1-R_2- R_3-R_4 -R_5-R_6-R_7-R_8-R_9-R_{10}-R_{11}-R_{12}-R_{13}-R_{14}-R_{15}-R_{16}-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-R_{30}-R_{31}-R_{32}-R_{33}-R_{34}-R_{35}-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-R_{42}- R_{43}- R_{44}-R_{45}-R_{46}- $[R_{47}]_x$-R_{48}-R_{49}-R_{50}-R_{51}-R_{52}-R_{53}-R_{54}-R_{55}-R_{56}-R_{57}-R_{58}-R_{59}-R_{60}-R_{61}-R_{62}-R_{63}-R_{64}-R_{65}-R_{66}-R_{67}-R_{68}-R_{69}-R_{70}-R_{71}-R_{72}

wherein R is a ribonucleotide residue and the consensus for Val is:

R_0,R_{18},R_{23}=absent

R_{24},R_{38},R_{40},R_{57},R_{72}=are independently A or absent;

R_{29},R_{64},R_{70}=are independently A,C,G or absent;

R_{49},R_{50},R_{62}=are independently N or absent;

R_{16},R_{26},R_{31},R_{32},R_{37},R_{41},R_{43},R_{59},R_{65}=are independently A,C,U or absent;

R_9,R_{14},R_{27},R_{46},R_{52},R_{56},R_{66}=are independently A,G or absent;

R_7,R_{12},R_{25},R_{33},R_{44},R_{45},R_{53},R_{58},R_{63},R_{68}=are independently A,G,U or absent;

R_{69}= A,U or absent;

R_{39}= C or absent;

R_5,R_{67}=are independently C,G or absent;

R_2,R_4,R_{13},R_{15},R_{48},R_{55}=are independently C,G,U or absent;

R_6,R_{11},R_{22},R_{28},R_{30},R_{34},R_{35},R_{60},R_{61},R_{71}=are independently C,U or absent;

R_{10},R_{19},R_{51}=are independently G or absent;

R_1,R_3,R_{20},R_{42}=are independently G,U or absent;

R_8,R_{17},R_{21},R_{36},R_{54}=are independently U or absent;

$[R_{47}]_x$ = N or absent;

wherein, *e.g.*, x=1-271 (*e.g.*, x=1-250, x=1-225, x=1-200, x=1-175, x=1-150, x=1-125, x=1-100, x=1-75, x=1-50, x=1-40, x=1-30, x=1-29, x=1-28, x=1-27, x=1-26, x=1-25, x=1-24, x=1-23, x=1-22, x=1-21, x=1-20, x=1-19, x=1-18, x=1-17, x=1-16, x=1-15, x=1-14, x=1-13, x=1-12, x=1-11, x=1-10, x=10-271, x=20-271, x=30-271, x=40-271, x=50-271, x=60-271, x=70-271, x=80-271, x=100-271, x=125-271, x=150-271, x=175-271, x=200-271, x=225-271, x=1, x=2, x=3, x=4, x=5, x=6, x=7, x=8, x=9, x=10, x=11, x=12, x=13, x=14, x=15, x=16, x=17, x=18, x=19, x=20, x=21, x=22, x=23, x=24, x=25, x=26, x=27, x=28, x=29, x=30, x=40, x=50, x=60, x=70, x=80, x=90, x=100, x=110, x=125, x=150, x=175, x=200, x=225, x=250, or x=271), provided that the TREM has one or both of the following properties: no more than 15% of the residues are N; or no more than 20 residues are absent.

Variable region consensus sequence

In an embodiment, a TREM disclosed herein comprises a variable region at position R_{47}. In an embodiment, the variable region is 1-271 ribonucleotides in length (*e.g.* 1-250, 1-225, 1-200, 1-175, 1-150, 1-125, 1-100, 1-75, 1-50, 1-40, 1-30, 1-29, 1-28, 1-27, 1-26, 1-25, 1-24, 1-23, 1-22, 1-21, 1-20, 1-19, 1-18, 1-17, 1-16, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 10-271, 20-271, 30-271, 40-271, 50-271, 60-271, 70-271, 80-271, 100-271, 125-271, 150-271, 175-271, 200-271, 225-271, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 40, 50, 60, 70, 80, 90, 100, 110, 125, 150, 175, 200, 225, 250, or 271 ribonucleotides). In an embodiment, the variable region comprises any one, all or a combination of Adenine, Cytosine, Guanine or Uracil.

In an embodiment, the variable region comprises a ribonucleic acid (RNA) sequence encoded by a deoxyribonucleic acid (DNA) sequence disclosed in Table 4, *e.g.*, any one of SEQ ID NOs: 452-561 disclosed in Table 4.

Table 4: Exemplary variable region sequences.

	SEQ ID NO	**SEQUENCE**
1	452	AAAATATAAATATATTTC
2	453	AAGCT
3	454	AAGTT
4	455	AATTCTTCGGAATGT
5	456	AGA
6	457	AGTCC
7	458	CAACC
8	459	CAATC
9	460	CAGC
10	461	CAGGCGGGTTCTGCCCGCGC
11	462	CATACCTGCAAGGGTATC
12	463	CGACCGCAAGGTTGT
13	464	CGACCTTGCGGTCAT
14	465	CGATGCTAATCACATCGT
15	466	CGATGGTGACATCAT
16	467	CGATGGTTTACATCGT
17	468	CGCCGTAAGGTGT
18	469	CGCCTTAGGTGT
19	470	CGCCTTTCGACGCGT
20	471	CGCTTCACGGCGT
21	472	CGGCAGCAATGCTGT
22	473	CGGCTCCGCCTTC
23	474	CGGGTATCACAGGGTC
24	475	CGGTGCGCAAGCGCTGT
25	476	CGTACGGGTGACCGTACC
26	477	CGTCAAAGACTTC
27	478	CGTCGTAAGACTT
28	479	CGTTGAATAAACGT
29	480	CTGTC
30	481	GGCC
31	482	GGGGATT
32	483	GGTC
33	484	GGTTT
34	485	GTAG
35	486	TAACTAGATACTTTCAGAT
36	487	TACTCGTATGGGTGC

37	488	TACTTTGCGGTGT
38	489	TAGGCGAGTAACATCGTGC
39	490	TAGGCGTGAATAGCGCCTC
40	491	TAGGTCGCGAGAGCGGCGC
41	492	TAGGTCGCGTAAGCGGCGC
42	493	TAGGTGGTTATCCACGC
43	494	TAGTC
44	495	TAGTT
45	496	TATACGTGAAAGCGTATC
46	497	TATAGGGTCAAAAACTCTATC
47	498	TATGCAGAAATACCTGCATC
48	499	TCCCCATACGGGGGC
49	500	TCCCGAAGGGGTTC
50	501	TCTACGTATGTGGGC
51	502	TCTCATAGGAGTTC
52	503	TCTCCTCTGGAGGC
53	504	TCTTAGCAATAAGGT
54	505	TCTTGTAGGAGTTC
55	506	TGAACGTAAGTTCGC
56	507	TGAACTGCGAGGTTCC
57	508	TGAC
58	509	TGACCGAAAGGTCGT
59	510	TGACCGCAAGGTCGT
60	511	TGAGCTCTGCTCTC
61	512	TGAGGCCTCACGGCCTAC
62	513	TGAGGGCAACTTCGT
63	514	TGAGGGTCATACCTCC
64	515	TGAGGGTGCAAATCCTCC
65	516	TGCCGAAAGGCGT
66	517	TGCCGTAAGGCGT
67	518	TGCGGTCTCCGCGC
68	519	TGCTAGAGCAT
69	520	TGCTCGTATAGAGCTC
70	521	TGGACAATTGTCTGC
71	522	TGGACAGATGTCCGT
72	523	TGGACAGGTGTCCGC
73	524	TGGACGGTTGTCCGC
74	525	TGGACTTGTGGTC
75	526	TGGAGATTCTCTCCGC
76	527	TGGCATAGGCCTGC
77	528	TGGCTTATGTCTAC
78	529	TGGGAGTTAATCCCGT
79	530	TGGGATCTTCCCGC

80	531	TGGGCAGAAATGTCTC
81	532	TGGGCGTTCGCCCGC
82	533	TGGGCTTCGCCCGC
83	534	TGGGGGATAACCCCGT
84	535	TGGGGGTTTCCCCGT
85	536	TGGT
86	537	TGGTGGCAACACCGT
87	538	TGGTTTATAGCCGT
88	539	TGTACGGTAATACCGTACC
89	540	TGTCCGCAAGGACGT
90	541	TGTCCTAACGGACGT
91	542	TGTCCTATTAACGGACGT
92	543	TGTCCTTCACGGGCGT
93	544	TGTCTTAGGACGT
94	545	TGTGCGTTAACGCGTACC
95	546	TGTGTCGCAAGGCACC
96	547	TGTTCGTAAGGACTT
97	548	TTCACAGAAATGTGTC
98	549	TTCCCTCGTGGAGT
99	550	TTCCCTCTGGGAGC
100	551	TTCCCTTGTGGATC
101	552	TTCCTTCGGGAGC
102	553	TTCTAGCAATAGAGT
103	554	TTCTCCACTGGGGAGC
104	555	TTCTCGAGAGGGAGC
105	556	TTCTCGTATGAGAGC
106	557	TTTAAGGTTTTCCCTTAAC
107	558	TTTCATTGTGGAGT
108	559	TTTCGAAGGAATCC
109	560	TTTCTTCGGAAGC
110	561	TTTGGGGCAACTCAAC

Corresponding Nucleotide Positions

To determine if a selected nucleotide position in a candidate sequence corresponds to a selected position in a reference sequence (e.g., SEQ ID NO: 622, SEQ ID NO: 993, SEQ ID NO: 1079), one or more of the following Evaluations is performed.

Evaluation A:

1.The candidate sequence is aligned with each of the consensus sequences in Tables 9 and 10. The consensus sequence(s) having the most positions aligned (and which has at least 60% of the positions of the candidate sequence aligned) is selected.

The alignment is performed as is follows. The candidate sequence and an isodecoder consensus sequence from Tables 10A-10B are aligned based on a global pairwise alignment calculated with the Needleman–Wunsch algorithm when run with match scores from Table 11, a mismatch penalty of -1, a gap opening penalty of -1, and a gap extension penalty of -0.5, and no penalty for end gaps. The alignment with the highest overall alignment score is then used to determine the percent similarity between the candidate and the consensus sequence by counting the number of matched positions in the alignment, dividing it by the larger of the number of non-N bases in the candidate sequence or the consensus sequence, and multiplying the result by 100. In cases where multiple alignments (of the candidate and a single consensus sequence) tie for the same score, the percent similarity is the largest percent similarity calculated from the tied alignments. This process is repeated for the candidate sequence with each of the remaining isodecoder consensus sequences in Tables 10A-10B, and the alignment resulting in the greatest percent similarity is selected. If this alignment has a percent similarity equal to or greater than 60%, it is considered a valid alignment and used to relate positions in the candidate sequence to those in the consensus sequence, otherwise the candidate sequence is considered to have not aligned to any of the isodecoder consensus sequences. If there is a tie at this point, all tied consensus sequences are taken forward to step 2 in the analysis.

2. Using the selected consensus sequence(s) from step 1, one determines the consensus sequence position number that aligns with the selected position (e.g., a modified position) in the candidate sequence. One then assigns the position number of the aligned position in the consensus sequence to the selected position in the candidate sequence, in other words, the selected position in the candidate sequence is numbered according to the numbering of the consensus sequence. If there were tied consensus sequences from step one, and they give different position numbers in this step 2, then all such position numbers are taken forward to step 5.

3. The reference sequence is aligned with the consensus sequence chosen in step 1. The alignment is performed as described in step 1.

4. From the alignment in step 3, one determines the consensus sequence position number that aligns with the selected position (e.g., a modified position) in the reference sequence. One then assigns the position number of the aligned position in the consensus sequence to the selected position in the reference sequence, in other words, the selected position in the reference sequence is numbered according to the numbering of the consensus sequence. If there is a tie at this point, all tied consensus sequences are taken forward to step 5 in the analysis.

5. If a value for a position number determined for the reference sequence in step 2 is the same as the value for the position number determined for the candidate sequence in step 4, the positions are defined as corresponding.

Evaluation B:

The reference sequence (e.g., a TREM sequence described herein) and the candidate sequence are aligned with one another. The alignment is performed as follows.

The reference sequence and the candidate sequence are aligned based on a global pairwise alignment calculated with the Needleman–Wunsch algorithm when run with match scores from Table 11, a mismatch penalty of -1, a gap opening penalty of -1, and a gap extension penalty of -0.5, and no penalty for end gaps. The alignment with the highest overall alignment score is then used to determine the percent similarity between the candidate and reference sequence by counting the number of matched based in the alignment, dividing it by the larger of the number of non-N bases in the candidate or reference sequence, and multiplying the result by 100. In cases where multiple alignments tie for the same score, the percent similarity is the largest percent similarity calculated from the tied alignments. If this alignment has a percent similarity equal to or greater than 60%, it is considered a valid alignment and used to relate positions in the candidate sequence to those in the reference sequence, otherwise the candidate sequence is considered to have not aligned to the reference sequence.

If the selected nucleotide position in the reference sequence (e.g., a modified position) is paired with a selected nucleotide position (e.g., a modified position) in the candidate sequence, the positions are defined as corresponding.

If the selected position in the reference sequence and the candidate sequence are found to be corresponding in at least one of Evaluations A and B, the positions correspond. Thus, e.g., if two positions are found to be corresponding under Evaluation A, but do not correspond under Evaluation B, the positions are defined as corresponding.

The numbering given above is used for ease of presentation and does not imply a required sequence. If more than one Evaluation is performed, they can be performed in any order.

Table 10A. Consensus sequence computationally generated for each isodecoder by aligning members of the isodecoder family

SEQ ID NO.	Amino Acid	Anticodon	Consensus sequence
1200	Ala	AGC	GGGGAATTAGCTCAAGTGGTAGAGCGCTTG CTTAGCATGCAAGAGGTAGTGGGATCGATG CCCACATTCTCCA
1201	Ala	CGC	GGGGATGTAGCTCAGTGGTAGAGCGCATGC TTCGCATGTATGAGGTCCCGGGTTCGATCCC CGGCATCTCCA
1202	Ala	TGC	GGGGGTGTAGCTCAGTGGTAGAGCGCATGC TTTGCATGTATGAGGCCCCGGGTTCGATCCC CGGCACCTCCA
1203	Arg	ACG	GGGCCAGTGGCGCAATGGATAACGCGTCTG ACTACGGATCAGAAGATTCCAGGTTCGACTC CTGGCTGGCTCG
1204	Arg	CCG	GGCCGCGTGGCCTAATGGATAAGGCGTCTG ATTCCGGATCAGAAGATTGAGGGTTCGAGTC CCTTCGTGGTCG
1205	Arg	CCT	GCCCCAGTGGCCTAATGGATAAGGCACTGG CCTCCTAAGCCAGGGATTGTGGGTTCGAGTC CCACCTGGGGTA
1206	Arg	TCG	GACCGCGTGGCCTAATGGATAAGGCGTCTG ACTTCGGATCAGAAGATTGAGGGTTCGAGTC CCTCCGTGGTCG
1207	Arg	TCT	GGCTCTGTGGCGCAATGGATNAGCGCATTG GACTTCTAATTCAAAGGTTGCGGGTTCGAGT CCCNCCAGAGTCG
1208	Asn	GTT	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCG GCTGTTAACCGNAAAGGTTGGTGGTTCGAGC CCACCCAGGGACG
1209	Asp	GTC	TCCTCGTTAGTATAGTGGTGAGTATCCCCGC CTGTCACGCGGGAGACCGGGGTTCGATTCCC CGACGGGGAG
1210	Cys	GCA	GGGGGTATAGCTCAGNGGGTAGAGCATTTG ACTGCAGATCAAGAGGTCCCCGGTTCAAATC CGGGTGCCCCCT
1211	Gln	CTG	GGTTCCATGGTGTAATGGTNAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCAAGTCTC GGTGGAACCT

1212	Gln	TTG	GGTCCCATGGTGTAATGGTTAGCACTCTGGACTTTGAATCCAGCGATCCGAGTTCAAATCTCGGTGGGACCT
1213	Glu	CTC	TCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCTCTCACCGCCGCGGCCCGGGTTCGATTCCCGGTCAGGGAA
1214	Glu	TTC	TCCCTGGTGGTCTAGTGGCTAGGATTCGGCGCTTTCACCGCNGCGGCCCGGGTTCGATTCCCGGTCAGGGAA
1215	Gly	CCC	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTCCCACGCNGGAGACCCGGGTTCGATTCCCGGCCAATGCA
1216	Gly	GCC	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCCACGCGGGAGGCCCGGGTTCGATTCCCGGCCAATGCA
1217	Gly	TCC	GCGTTGGTGGTATAGTGGTGAGCATAGCTGCCTTCCAAGCAGTTGACCCGGGTTCGATTCCCGGCCAACGCA
1218	Ile	AAT	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGTGCTAATAACGCCAAGGTCGCGGGTTCGATCCCCGTACGGGCCA
1219	Ile	TAT	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGTACTTATAATGCCGAGGTTGTGAGTTCGAGCCTCACCTGGAGCA
1220	Leu	AAG	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTAAGGCTCCAGTCTCTTCGGGGGCGTGGGTTCGAATCCCACCGCTGCCA
1221	Leu	CAA	GTCAGGATGGCCGAGTGGTCNTAAGGCGCCAGACTCAAGTTCTGGTCTCCGNATGGAGGCGTGGGTTCGAATCCCACTTCTGACA
1222	Leu	CAG	GTCAGGATGGCCGAGCGGTCTAAGGCGCTGCGTTCAGGTCGCAGTCTCCCCTGGAGGCGTGGGTTCGAATCCCACTCCTGACA
1223	Leu	TAA	ACCAGGATGGCCGAGTGGTTAAGGCGTTGGACTTAAGATCCAATGGACAGATGTCCGCGTGGGTTCGAACCCCACTCCTGGTA
1224	Leu	TAG	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGGATTTAGGCTCCAGTCTCTTCGGNGGCGTGGGTTCGAATCCCACCGCTGCCA
1225	Lys	CTT	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGACTCTTAATCTCAGGGTCGTGGGTTCGAGCCCCACGTTGGGCGNNN
1226	Lys	TTT	GCCTGGATAGCTCAGTCGGTAGAGCATCAGACTTTTAATCTGAGGGTCCAGGGTTCAAGTCCCTGTTCAGGCG

1227	Met	CAT	GCCCTCTTAGCGCAGTNGGCAGCGCGTCAGT CTCATAATCTGAAGGTCCTGAGTTCGAGCCT CAGAGAGGGCA
1228	Phe	GAA	GCCGAAATAGCTCAGTTGGGAGAGCGTTAG ACTGAAGATCNTAAAGGTCCCTGGTTCAATC CCGGGTTTCGGCA
1229	Pro	AGG	GGCTCGTTGGTCTAGGGGTATGATTCTCGCT TAGGATGCGAGAGGTCCCGGGTTCAAATCC CGGACGAGCCC
1230	Pro	CGG	GGCTCGTTGGTCTAGGGGTATGATTCTCGCT TCGGGTGCGAGAGGTCCCGGGTTCAAATCCC GGACGAGCCC
1231	Pro	TGG	GGCTCGTTGGTCTAGGGGTATGATTCTCGCT TTGGGTGCGAGAGGTCCCGGGTTCAAATCCC GGACGAGCCC
1232	Ser	AGA	GTAGTCGTGGCCGAGTGGTTAAGGCGATGG ACTAGAAATCCATTGGGGTTTCCCCGCGCAG GTTCGAATCCTGCCGACTACG
1233	Ser	CGA	GCTGTGATGGCCGAGTGGTTAAGGCGTTGG ACTCGAAATCCAATGGGGTCTCCCCGCGCAG GTTCGAATCCTGCTCACAGCG
1234	Ser	GCT	GACGAGGNNTGGCCGAGTGGTTAAGGCGAT GGACTGCTAATCCATTGTGCTCTGCACGCGT GGGTTCGAATCCCATCCTCGTCG
1235	Ser	TGA	GTAGTCGTGGCCGAGTGGTTAAGGCGATGG ACTTGAAATCCATTGGGGTCTCCCCGCGCAG GTTCGAATCCTGCCGGCTACG
1236	Thr	AGT	GGCTCCGTGGCTTAGCTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC CCAGCGGGGCCT
1237	Thr	CGT	GGCNCTGTGGCTNAGTNGGNTAAAGCGCCG GTCTCGTAAACCNGGAGATCNTGGGTTCGA ATCCCANCNGGGCCT
1238	Thr	TGT	GGCTCCATAGCTCAGNGGGTTAGAGCACTG GTCTTGTAAACCAGGGGTCGCGAGTTCAAAT CTCGCTGGGGCCT
1239	Trp	CCA	GACCTCGTGGCGCAACGGTAGCGCGTCTGA CTCCAGATCAGAAGGTTGCGTGTTCAAATCA CGTCGGGGTCA
1240	Tyr	GTA	CCTTCGATAGCTCAGCTGGTAGAGCGGAGG ACTGTAGATCCTTAGGTCGCTGGTTCGATTC CGGCTCGAAGGA
1241	Val	AAC	GTTTCCGTAGTGTAGTGGTTATCACGTTCGC CTAACACGCGAAAGGTCCCCGGTTCGAAAC CGGGCGGAAACA

1242	Val	CAC	GTTTCCGTAGTGTAGTGGTTATCACGTTCGC CTCACACGCGAAAGGTCCCCGGTTCGAAAC CGGGCGGAAACA
1243	Val	TAC	GGTTCCATAGTGTAGTGGTTATCACGTCTGC TTTACACGCAGAAGGTCCTGGGTTCGAGCCC CAGTGGAACCA
1244	iMet	CAT	AGCAGAGTGGCGCAGCGGAAGCGTGCTGGG CCCATAACCCAGAGGTCGATGGATCGAAAC CATCCTCTGCTA

Table 10B. Consensus sequence computationally generated for each isodecoder by aligning members of the isodecoder family

SEQ ID NO	Amino Acid	Anticodon	Consensus sequence
1245	Ala	AGC	GGGGAATTAGCTCAAGTGGTAGAGCGCTTGC TTAGCATGCAAGAGGTAGTGGGATCGATGCC CACATTCTCCANNN
1246	Ala	CGC	GGGGATGTAGCTCAGTGGTAGAGCGCATGCT TCGCATGTATGAGGTCCCGGGTTCGATCCCC GGCATCTCCANNN
1247	Ala	TGC	GGGGGTGTAGCTCAGTGGTAGAGCGCATGCT TTGCATGTATGAGGCCCCGGGTTCGATCCCC GGCACCTCCANNN
1248	Arg	ACG	GGGCCAGTGGCGCAATGGATAACGCGTCTGA CTACGGATCAGAAGATTCCAGGTTCGACTCC TGGCTGGCTCGNNN
1249	Arg	CCG	GGCCGCGTGGCCTAATGGATAAGGCGTCTGA TTCCGGATCAGAAGATTGAGGGTTCGAGTCC CTTCGTGGTCGNNN
1250	Arg	CCT	GCCCCAGTGGCCTAATGGATAAGGCACTGGC CTCCTAAGCCAGGGATTGTGGGTTCGAGTCC CACCTGGGGTANNN
1251	Arg	TCG	GACCGCGTGGCCTAATGGATAAGGCGTCTGA CTTCGGATCAGAAGATTGAGGGTTCGAGTCC CTCCGTGGTCGNNN
1252	Arg	TCT	GGCTCTGTGGCGCAATGGATNAGCGCATTGG ACTTCTAATTCAAAGGTTGCGGGTTCGAGTC CCNCCAGAGTCGNNN
1253	Asn	GTT	GTCTCTGTGGCGCAATCGGTTAGCGCGTTCG GCTGTTAACCGNAAAGGTTGGTGGTTCGAGC CCACCCAGGGACGNNN
1254	Asp	GTC	TCCTCGTTAGTATAGTGGTGAGTATCCCCGCC TGTCACGCGGGAGACCGGGGTTCGATTCCCC GACGGGGAGNNN

1255	Cys	GCA	GGGGGTATAGCTCAGNGGGTAGAGCATTTGA CTGCAGATCAAGAGGTCCCCGGTTCAAATCC GGGTGCCCCCTNNN
1256	Gln	CTG	GGTTCCATGGTGTAATGGTNAGCACTCTGGA CTCTGAATCCAGCGATCCGAGTTCAAGTCTC GGTGGAACCTNNN
1257	Gln	TTG	GGTCCCATGGTGTAATGGTTAGCACTCTGGA CTTTGAATCCAGCGATCCGAGTTCAAATCTC GGTGGGACCTNNN
1258	Glu	CTC	TCCCTGGTGGTCTAGTGGTTAGGATTCGGCG CTCTCACCGCCGCGGCCCGGGTTCGATTCCC GGTCAGGGAANNN
1259	Glu	TTC	TCCCTGGTGGTCTAGTGGCTAGGATTCGGCG CTTTCACCGCNGCGGCCCGGGTTCGATTCCC GGTCAGGGAANNN
1260	Gly	CCC	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCT CCCACGCNGGAGACCCGGGTTCGATTCCCGG CCAATGCANNN
1261	Gly	GCC	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCT GCCACGCGGGAGGCCCGGGTTCGATTCCCGG CCAATGCANNN
1262	Gly	TCC	GCGTTGGTGGTATAGTGGTGAGCATAGCTGC CTTCCAAGCAGTTGACCCGGGTTCGATTCCC GGCCAACGCANNN
1263	Ile	AAT	GGCCGGTTAGCTCAGTTGGTTAGAGCGTGGT GCTAATAACGCCAAGGTCGCGGGTTCGATCC CCGTACGGGCCANNN
1264	Ile	TAT	GCTCCAGTGGCGCAATCGGTTAGCGCGCGGT ACTTATAATGCCGAGGTTGTGAGTTCGAGCC TCACCTGGAGCANNN
1265	Leu	AAG	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGG ATTAAGGCTCCAGTCTCTTCGGGGGCGTGGG TTCGAATCCCACCGCTGCCANNN
1266	Leu	CAA	GTCAGGATGGCCGAGTGGTCNTAAGGCGCCA GACTCAAGTTCTGGTCTCCGNATGGAGGCGT GGGTTCGAATCCCACTTCTGACANNN
1267	Leu	CAG	GTCAGGATGGCCGAGCGGTCTAAGGCGCTGC GTTCAGGTCGCAGTCTCCCCTGGAGGCGTGG GTTCGAATCCCACTCCTGACANNN
1268	Leu	TAA	ACCAGGATGGCCGAGTGGTTAAGGCGTTGGA CTTAAGATCCAATGGACAGATGTCCGCGTGG GTTCGAACCCCACTCCTGGTANNN
1269	Leu	TAG	GGTAGCGTGGCCGAGCGGTCTAAGGCGCTGG ATTTAGGCTCCAGTCTCTTCGGNGGCGTGGG TTCGAATCCCACCGCTGCCANNN

1270	Lys	CTT	GCCCGGCTAGCTCAGTCGGTAGAGCATGAGA CTCTTAATCTCAGGGTCGTGGGTTCGAGCCCC ACGTTGGGCGNNNNNN
1271	Lys	TTT	GCCTGGATAGCTCAGTCGGTAGAGCATCAGA CTTTTAATCTGAGGGTCCAGGGTTCAAGTCCC TGTTCAGGCGNNN
1272	Met	CAT	GCCCTCTTAGCGCAGTNGGCAGCGCGTCAGT CTCATAATCTGAAGGTCCTGAGTTCGAGCCT CAGAGAGGGCANNN
1273	Phe	GAA	GCCGAAATAGCTCAGTTGGGAGAGCGTTAGA CTGAAGATCNTAAAGGTCCCTGGTTCAATCC CGGGTTTCGGCANNN
1274	Pro	AGG	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTT AGGATGCGAGAGGTCCCGGGTTCAAATCCCG GACGAGCCCNNN
1275	Pro	CGG	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTT CGGGTGCGAGAGGTCCCGGGTTCAAATCCCG GACGAGCCCNNN
1276	Pro	TGG	GGCTCGTTGGTCTAGGGGTATGATTCTCGCTT TGGGTGCGAGAGGTCCCGGGTTCAAATCCCG GACGAGCCCNNN
1277	Ser	AGA	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGA CTAGAAATCCATTGGGGTTTCCCCGCGCAGG TTCGAATCCTGCCGACTACGNNN
1278	Ser	CGA	GCTGTGATGGCCGAGTGGTTAAGGCGTTGGA CTCGAAATCCAATGGGGTCTCCCCGCGCAGG TTCGAATCCTGCTCACAGCGNNN
1279	Ser	GCT	GACGAGGNNTGGCCGAGTGGTTAAGGCGAT GGACTGCTAATCCATTGTGCTCTGCACGCGT GGGTTCGAATCCCATCCTCGTCGNNN
1280	Ser	TGA	GTAGTCGTGGCCGAGTGGTTAAGGCGATGGA CTTGAAATCCATTGGGGTCTCCCCGCGCAGG TTCGAATCCTGCCGGCTACGNNN
1281	Thr	AGT	GGCTCCGTGGCTTAGCTGGTTAAAGCGCCTG TCTAGTAAACAGGAGATCCTGGGTTCGAATC CCAGCGGGGCCTNNN
1282	Thr	CGT	GGCNCTGTGGCTNAGTNGGNTAAAGCGCCGG TCTCGTAAACCNGGAGATCNTGGGTTCGAAT CCCANCNGGGCCTNNN
1283	Thr	TGT	GGCTCCATAGCTCAGNGGGTTAGAGCACTGG TCTTGTAAACCAGGGGTCGCGAGTTCAAATC TCGCTGGGGCCTNNN
1284	Trp	CCA	GACCTCGTGGCGCAACGGTAGCGCGTCTGAC TCCAGATCAGAAGGTTGCGTGTTCAAATCAC GTCGGGGTCANNN

1285	Tyr	GTA	CCTTCGATAGCTCAGCTGGTAGAGCGGAGGACTGTAGATCCTTAGGTCGCTGGTTCGATTCCGGCTCGAAGGANNN
1286	Val	AAC	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCCTAACACGCGAAAGGTCCCCGGTTCGAAACCGGGCGGAAACANNN
1287	Val	CAC	GTTTCCGTAGTGTAGTGGTTATCACGTTCGCCTCACACGCGAAAGGTCCCCGGTTCGAAACCGGGCGGAAACANNN
1288	Val	TAC	GGTTCCATAGTGTAGTGGTTATCACGTCTGCTTTACACGCAGAAGGTCCTGGGTTCGAGCCCCAGTGGAACCANNN
1289	iMet	CAT	AGCAGAGTGGCGCAGCGGAAGCGTGCTGGGCCCATAACCCAGAGGTCGATGGATCGAAACCATCCTCTGCTANNN

Table 11: Score values alignment

Row	Candidate nucleotide	Reference nucleotide	Match score
1	A	A	1
2	T	T	1
3	U	T	1
4	C	C	1
5	G	G	1
6	A	N	0
7	T	N	0
8	C	N	0
9	G	N	0
10	N	A	0
11	N	T	0
12	N	C	0
13	N	G	0
14	N	N	0

5

Method of making TREMs, TREM core fragments, and TREM fragments

In vitro methods for synthesizing oligonucleotides are known in the art and can be used to make a TREM, a TREM core fragment or a TREM fragment disclosed herein. For example, a

TREM, TREM core fragment or TREM fragment can be synthesized using solid state synthesis or liquid phase synthesis.

In an embodiment, a TREM, a TREM core fragment or a TREM fragment made according to an in vitro synthesis method disclosed herein has a different modification profile compared to a TREM expressed and isolated from a cell, or compared to a naturally occurring tRNA.

An exemplary method for making a modified TREM is provided in Example 1. The method provided in Example 1 can also be used to make a synthetic TREM core fragment or synthetic TREM fragment. Additional exemplary methods for making a synthetic TREM via 5'-Silyl-2'-Orthoester (2'- ACE) Chemistry is provided in Example 4. The method provided in Example 4 can also be used to make a synthetic TREM core fragment or synthetic TREM fragment. Additional synthetic methods are disclosed in Hartsel SA et al., (2005) *Oligonucleotide Synthesis*, 033–050, the entire contents of which are hereby incorporated by reference.

TREM composition

In an embodiment, a TREM composition, *e.g.*, a TREM pharmaceutical composition, comprises a pharmaceutically acceptable excipient. Exemplary excipients include those provided in the FDA Inactive Ingredient Database (https://www.accessdata.fda.gov/scripts/cder/iig/index.Cfm).

In an embodiment, a TREM composition, *e.g.*, a TREM pharmaceutical composition, comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100 or 150 grams of TREM, TREM core fragment or TREM fragment. In an embodiment, a TREM composition, *e.g.*, a TREM pharmaceutical composition, comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50 or 100 milligrams of TREM, TREM core fragment or TREM fragment.

In an embodiment, a TREM composition, *e.g.*, a TREM pharmaceutical composition, is at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 95 or 99% dry weight TREMs, TREM core fragments or TREM fragments.

In an embodiment, a TREM composition comprises at least 1 x 10^6 TREM molecules, at least 1 x 10^7 TREM molecules, at least 1 x 10^8 TREM molecules or at least 1 x 10^9 TREM molecules.

In an embodiment, a TREM composition comprises at least 1 x 10^6 TREM core fragment molecules, at least 1 x 10^7 TREM core fragment molecules, at least 1 x 10^8 TREM core fragment molecules or at least 1 x 10^9 TREM core fragment molecules.

In an embodiment, a TREM composition comprises at least 1 x 10^6 TREM fragment molecules, at least 1 x 10^7 TREM fragment molecules, at least 1 x 10^8 TREM fragment molecules or at least 1 x 10^9 TREM fragment molecules.

In an embodiment, a TREM composition produced by any of the methods of making disclosed herein can be charged with an amino acid using an in vitro charging reaction as known in the art.

In an embodiment, a TREM composition comprise one or more species of TREMs, TREM core fragments, or TREM fragments. In an embodiment, a TREM composition comprises a single species of TREM, TREM core fragment, or TREM fragment. In an embodiment, a TREM composition comprises a first TREM, TREM core fragment, or TREM fragment species and a second TREM, TREM core fragment, or TREM fragment species. In an embodiment, the TREM composition comprises X TREM, TREM core fragment, or TREM fragment species, wherein X=2, 3, 4, 5, 6, 7, 8, 9, or 10.

In an embodiment, the TREM, TREM core fragment, or TREM fragment has at least 70, 75, 80, 85, 90, or 95, or has 100%, identity with a sequence encoded by a nucleic acid in Table 1.

In an embodiment, the TREM comprises a consensus sequence provided herein.

A TREM composition can be formulated as a liquid composition, as a lyophilized composition or as a frozen composition.

In some embodiments, a TREM composition can be formulated to be suitable for pharmaceutical use, e.g., a pharmaceutical TREM composition. In an embodiment, a pharmaceutical TREM composition is substantially free of materials and/or reagents used to separate and/or purify a TREM, TREM core fragment, or TREM fragment.

In some embodiments, a TREM composition can be formulated with water for injection. In some embodiments, a TREM composition formulated with water for injection is suitable for pharmaceutical use, e.g., comprises a pharmaceutical TREM composition.

TREM characterization

A TREM, TREM core fragment, or TREM fragment, or a TREM composition, *e.g.*, a pharmaceutical TREM composition, produced by any of the methods disclosed herein can be assessed for a characteristic associated with the TREM, TREM core fragment, or TREM fragment or the TREM composition, such as purity, sterility, concentration, structure, or functional activity of the TREM, TREM core fragment, or TREM fragment. Any of the above-mentioned characteristics can be evaluated by providing a value for the characteristic, *e.g.*, by evaluating or testing the TREM, TREM core fragment, or TREM fragment, or the TREM composition, or an intermediate in the production of the TREM composition. The value can also be compared with a standard or a reference value. Responsive to the evaluation, the TREM composition can be classified, *e.g.*, as ready for release, meets production standard for human trials, complies with ISO standards, complies with cGMP standards, or complies with other pharmaceutical standards. Responsive to the evaluation, the TREM composition can be subjected to further processing, *e.g.*, it can be divided into aliquots, *e.g.*, into single or multi-dosage amounts, disposed in a container, *e.g.*, an end-use vial, packaged, shipped, or put into commerce. In embodiments, in response to the evaluation, one or more of the characteristics can be modulated, processed or re-processed to optimize the TREM composition. For example, the TREM composition can be modulated, processed or re-processed to (i) increase the purity of the TREM composition; (ii) decrease the amount of fragments in the composition; (iii) decrease the amount of endotoxins in the composition; (iv) increase the in vitro translation activity of the composition; (v) increase the TREM concentration of the composition; or (vi) inactivate or remove any viral contaminants present in the composition, *e.g.*, by reducing the pH of the composition or by filtration.

In an embodiment, the TREM, TREM core fragment, or TREM fragment (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) has a purity of at least 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, i.e., by mass.

In an embodiment, the TREM (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) has less than 0.1%, 0,5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25% TREM fragments relative to full length TREMs.

In an embodiment, the TREM, TREM core fragment, or TREM fragment (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) has low levels or absence of endotoxins, *e.g.*, a negative result as measured by the Limulus amebocyte lysate (LAL) test.

In an embodiment, the TREM, TREM core fragment, or TREM fragment (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) has in-vitro translation activity, *e.g.*, as measured by an assay described in Examples 12-13.

In an embodiment, the TREM, TREM core fragment, or TREM fragment (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) has a TREM concentration of at least 0.1 ng/mL, 0.5 ng/mL, 1 ng/mL, 5 ng/mL, 10 ng/mL, 50 ng/mL, 0.1 ug/mL, 0.5 ug/mL,1 ug/mL, 2 ug/mL, 5 ug/mL, 10 ug/mL, 20 ug/mL, 30 ug/mL, 40 ug/mL, 50 ug/mL, 60 ug/mL, 70 ug/mL, 80 ug/mL, 100 ug/mL, 200 ug/mL, 300 ug/mL, 500 ug/mL, 1000 ug/mL, 5000 ug/mL, 10,000 ug/mL, or 100,000 ug/mL.

In an embodiment, the TREM, TREM core fragment, or TREM fragment (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) is sterile, *e.g.*, the composition or preparation supports the growth of fewer than 100 viable microorganisms as tested under aseptic conditions, the composition or preparation meets the standard of USP <71>, and/or the composition or preparation meets the standard of USP <85>.

In an embodiment, the TREM, TREM core fragment, or TREM fragment (*e.g.*, TREM composition or an intermediate in the production of the TREM composition) has an undetectable level of viral contaminants, *e.g.*, no viral contaminants. In an embodiment, any viral contaminant, *e.g.*, residual virus, present in the composition is inactivated or removed. In an embodiment, any viral contaminant, *e.g.*, residual virus, is inactivated, *e.g.*, by reducing the pH of the composition. In an embodiment, any viral contaminant, *e.g.*, residual virus, is removed, *e.g.*, by filtration or other methods known in the field.

TREM administration

Any TREM composition or pharmaceutical composition described herein can be administered to a cell, tissue or subject, *e.g.*, by direct administration to a cell, tissue and/or an organ in vitro, ex-vivo or in vivo. In-vivo administration may be via, *e.g.*, by local, systemic and/or parenteral routes, for example intravenous, subcutaneous, intraperitoneal, intrathecal,

intramuscular, ocular, nasal, urogenital, intradermal, dermal, enteral, intravitreal, intracerebral, intrathecal, or epidural.

Vectors and Carriers

In some embodiments the TREM, TREM core fragment, or TREM fragment or TREM composition described herein, is delivered to cells, *e.g.* mammalian cells or human cells, using a vector. The vector may be, *e.g.*, a plasmid or a virus. In some embodiments, delivery is *in vivo, in vitro*, *ex vivo*, or *in situ*. In some embodiments, the virus is an adeno associated virus (AAV), a lentivirus, or an adenovirus. In some embodiments, the system or components of the system are delivered to cells with a viral-like particle or a virosome. In some embodiments, the delivery uses more than one virus, viral-like particle or virosome.

Carriers

A TREM, a TREM composition or a pharmaceutical TREM composition described herein may comprise, may be formulated with, or may be delivered in, a carrier.

Viral vectors

The carrier may be a viral vector (*e.g.*, a viral vector comprising a sequence encoding a TREM, a TREM core fragment or a TREM fragment). The viral vector may be administered to a cell or to a subject (*e.g.*, a human subject or animal model) to deliver a TREM, a TREM core fragment or a TREM fragment, a TREM composition or a pharmaceutical TREM composition.

A viral vector may be systemically or locally administered (*e.g.*, injected). Viral genomes provide a rich source of vectors that can be used for the efficient delivery of exogenous genes into a mammalian cell. Viral genomes are known in the art as useful vectors for delivery because the polynucleotides contained within such genomes are typically incorporated into the nuclear genome of a mammalian cell by generalized or specialized transduction. These processes occur as part of the natural viral replication cycle, and do not require added proteins or reagents in order to induce gene integration. Examples of viral vectors include a retrovirus (*e.g.*, Retroviridae family viral vector), adenovirus (*e.g.*, Ad5, Ad26, Ad34, Ad35, and Ad48), parvovirus (*e.g.*, adeno-associated viruses), coronavirus, negative strand RNA viruses such as orthomyxovirus (*e.g.*, influenza virus), rhabdovirus (*e.g.*, rabies and vesicular stomatitis virus), paramyxovirus (*e.g.*, measles and Sendai), positive strand RNA viruses, such as picornavirus and alphavirus, and double stranded DNA viruses including adenovirus, herpesvirus (*e.g.*, Herpes

Simplex virus types 1 and 2, Epstein-Barr virus, cytomegalovirus, replication deficient herpes virus), and poxvirus (*e.g.*, vaccinia, modified vaccinia Ankara (MVA), fowlpox and canarypox). Other viruses include Norwalk virus, togavirus, flavivirus, reoviruses, papovavirus, hepadnavirus, human papilloma virus, human foamy virus, and hepatitis virus, for example. Examples of retroviruses include: avian leukosis-sarcoma, avian C-type viruses, mammalian C-type, B-type viruses, D-type viruses, oncoretroviruses, HTLV-BLV group, lentivirus, alpharetrovirus, gammaretrovirus, spumavirus (Coffin, J. M., Retroviridae: The viruses and their replication, Virology (Third Edition) Lippincott-Raven, Philadelphia, 1996). Other examples include murine leukemia viruses, murine sarcoma viruses, mouse mammary tumor virus, bovine leukemia virus, feline leukemia virus, feline sarcoma virus, avian leukemia virus, human T-cell leukemia virus, baboon endogenous virus, Gibbon ape leukemia virus, Mason Pfizer monkey virus, simian immunodeficiency virus, simian sarcoma virus, Rous sarcoma virus and lentiviruses. Other examples of vectors are described, for example, in US Patent No. 5,801,030, the teachings of which are incorporated herein by reference. In some embodiments the system or components of the system are delivered to cells with a viral-like particle or a virosome.

Cell and vesicle-based carriers

A TREM, a TREM core fragment or a TREM fragment, a TREM composition or a pharmaceutical TREM composition described herein can be administered to a cell in a vesicle or other membrane-based carrier.

In embodiments, a TREM, a TREM core fragment or a TREM fragment, or TREM composition, or pharmaceutical TREM composition described herein is administered in or via a cell, vesicle or other membrane-based carrier. In one embodiment, the TREM, TREM core fragment, TREM fragment, or TREM composition or pharmaceutical TREM composition can be formulated in liposomes or other similar vesicles. Liposomes are spherical vesicle structures composed of a uni- or multilamellar lipid bilayer surrounding internal aqueous compartments and a relatively impermeable outer lipophilic phospholipid bilayer. Liposomes may be anionic, neutral or cationic. Liposomes are biocompatible, nontoxic, can deliver both hydrophilic and lipophilic drug molecules, protect their cargo from degradation by plasma enzymes, and transport their load across biological membranes and the blood brain barrier (BBB) (see, *e.g.*, Spuch and Navarro, Journal of Drug Delivery, vol. 2011, Article ID 469679, 12 pages, 2011. doi:10.1155/2011/469679 for review).

Vesicles can be made from several different types of lipids; however, phospholipids are most commonly used to generate liposomes as drug carriers. Methods for preparation of multilamellar vesicle lipids are known in the art (see for example U.S. Pat. No. 6,693,086, the teachings of which relating to multilamellar vesicle lipid preparation are incorporated herein by reference). Although vesicle formation can be spontaneous when a lipid film is mixed with an aqueous solution, it can also be expedited by applying force in the form of shaking by using a homogenizer, sonicator, or an extrusion apparatus (see, *e.g.*, Spuch and Navarro, Journal of Drug Delivery, vol. 2011, Article ID 469679, 12 pages, 2011. doi:10.1155/2011/469679 for review). Extruded lipids can be prepared by extruding through filters of decreasing size, as described in Templeton et al., Nature Biotech, 15:647-652, 1997, the teachings of which relating to extruded lipid preparation are incorporated herein by reference.

Lipid nanoparticles are another example of a carrier that provides a biocompatible and biodegradable delivery system for the TREM, TREM core fragment, TREM fragment, or TREM composition or pharmaceutical TREM composition described herein. Nanostructured lipid carriers (NLCs) are modified solid lipid nanoparticles (SLNs) that retain the characteristics of the SLN, improve drug stability and loading capacity, and prevent drug leakage. Polymer nanoparticles (PNPs) are an important component of drug delivery. These nanoparticles can effectively direct drug delivery to specific targets and improve drug stability and controlled drug release. Lipid–polymer nanoparticles (PLNs), a new type of carrier that combines liposomes and polymers, may also be employed. These nanoparticles possess the complementary advantages of PNPs and liposomes. A PLN is composed of a core–shell structure; the polymer core provides a stable structure, and the phospholipid shell offers good biocompatibility. As such, the two components increase the drug encapsulation efficiency rate, facilitate surface modification, and prevent leakage of water-soluble drugs. For a review, see, *e.g.*, Li et al. 2017, Nanomaterials 7, 122; doi:10.3390/nano7060122.

Exemplary lipid nanoparticles are disclosed in International Application PCT/US2014/053907, the entire contents of which are hereby incorporated by reference. For example, an LNP described in paragraphs [403-406] or [410-413] of PCT/US2014/053907 can be used as a carrier for the TREM, TREM core fragment, TREM fragment, or TREM composition or pharmaceutical TREM composition described herein.

Additional exemplary lipid nanoparticles are disclosed in U.S. Patent 10,562,849 the entire contents of which are hereby incorporated by reference. For example, an LNP of formula (I) as described in columns 1-3 of U.S. Patent 10,562,849 can be used as a carrier for the TREM, TREM core fragment, TREM fragment, or TREM composition or pharmaceutical TREM composition described herein.

Lipids that can be used in nanoparticle formations (e.g., lipid nanoparticles) include, for example those described in Table 4 of WO2019217941, which is incorporated by reference, e.g., a lipid-containing nanoparticle can comprise one or more of the lipids in Table 4 of WO2019217941. Lipid nanoparticles can include additional elements, such as polymers, such as the polymers described in Table 5 of WO2019217941, incorporated by reference.

In some embodiments, conjugated lipids, when present, can include one or more of PEG-diacylglycerol (DAG) (such as l-(monomethoxy-polyethyleneglycol)-2,3- dimyristoylglycerol (PEG-DMG)), PEG-dialkyloxypropyl (DAA), PEG-phospholipid, PEG- ceramide (Cer), a pegylated phosphatidylethanoloamine (PEG-PE), PEG succinate diacylglycerol (PEGS-DAG) (such as 4-0-(2',3'-di(tetradecanoyloxy)propyl-l-0-(w- methoxy(polyethoxy)ethyl) butanedioate (PEG-S-DMG)), PEG dialkoxypropylcarbam, N- (carbonyl-methoxypoly ethylene glycol 2000)-1 ,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt, and those described in Table 2 of WO2019051289 (incorporated by reference), and combinations of the foregoing.

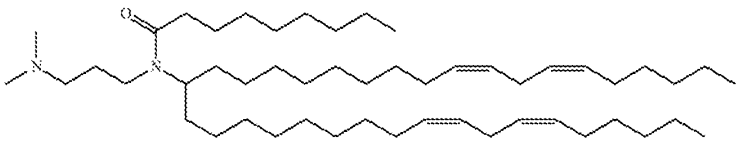
In some embodiments, sterols that can be incorporated into lipid nanoparticles include one or more of cholesterol or cholesterol derivatives, such as those in W02009/127060 or US2010/0130588, which are incorporated by reference. Additional exemplary sterols include phytosterols, including those described in Eygeris et al (2020), incorporated herein by reference.

In some embodiments, the lipid particle comprises an ionizable lipid, a non-cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a sterol. The amounts of these components can be varied independently and to achieve desired properties. For example, in some embodiments, the lipid nanoparticle comprises an ionizable lipid is in an amount from about 20 mol % to about 90 mol % of the total lipids (in other embodiments it may be 20-70% (mol), 30-60% (mol) or 40-50% (mol); about 50 mol % to about 90 mol % of the total lipid present in the lipid nanoparticle), a non-cationic lipid in an amount from about 5 mol % to about 30 mol % of the total lipids, a conjugated lipid in an amount from about 0.5 mol % to about 20 mol % of the total lipids, and a sterol in an amount from about 20 mol % to about 50 mol % of

the total lipids. The ratio of total lipid to nucleic acid can be varied as desired. For example, the total lipid to nucleic acid (mass or weight) ratio can be from about 10: 1 to about 30: 1.

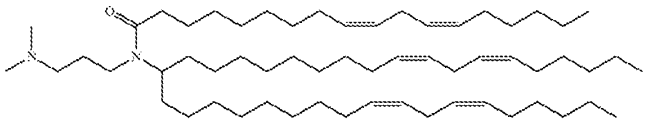
In some embodiments, the lipid to nucleic acid ratio (mass/mass ratio; w/w ratio) can be in the range of from about 1 : 1 to about 25: 1, from about 10: 1 to about 14: 1, from about 3 : 1 to about 15: 1, from about 4: 1 to about 10: 1, from about 5: 1 to about 9: 1, or about 6: 1 to about 9: 1. The amounts of lipids and nucleic acid can be adjusted to provide a desired N/P ratio, for example, N/P ratio of 3, 4, 5, 6, 7, 8, 9, 10 or higher. Generally, the lipid nanoparticle formulation's overall lipid content can range from about 5 mg/ml to about 30 mg/mL.

Some non-limiting example of lipid compounds that may be used (e.g., in combination with other lipid components) to form lipid nanoparticles for the delivery of compositions described herein, e.g., nucleic acid (e.g., RNA) described herein includes,



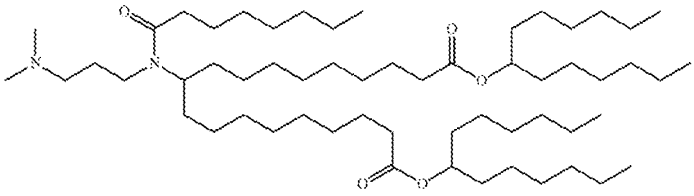
(i)

In some embodiments an LNP comprising Formula (i) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.



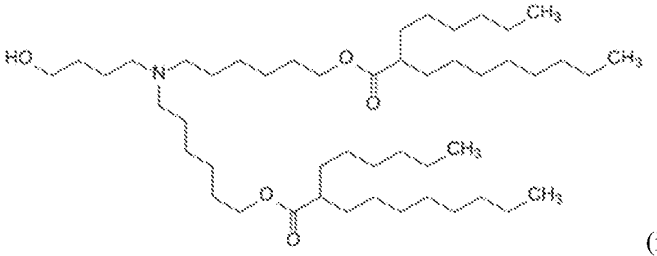
(ii)

In some embodiments an LNP comprising Formula (ii) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

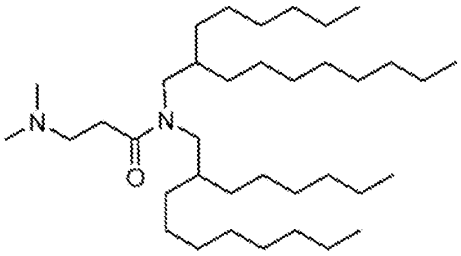


(iii)

In some embodiments an LNP comprising Formula (iii) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

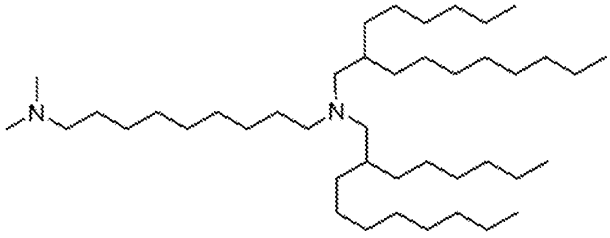


(iv)



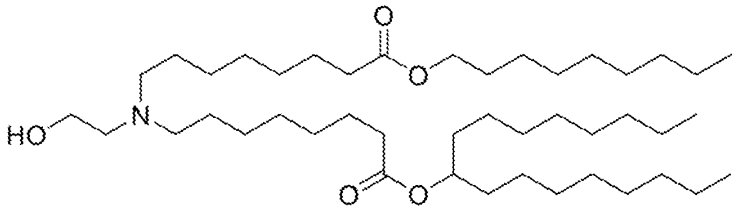
(v)

In some embodiments an LNP comprising Formula (v) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

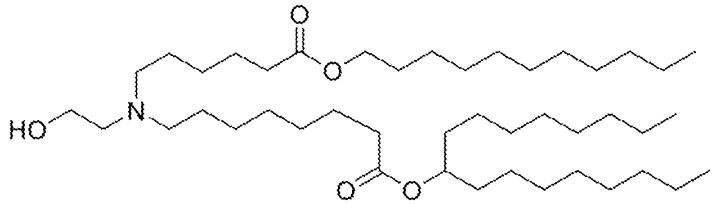


(vi)

In some embodiments an LNP comprising Formula (vi) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

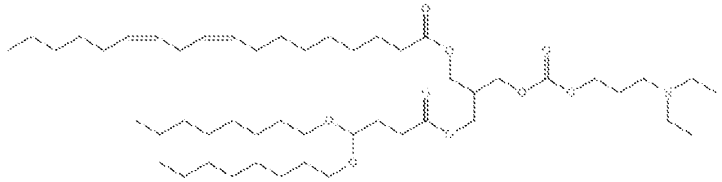


(vii)



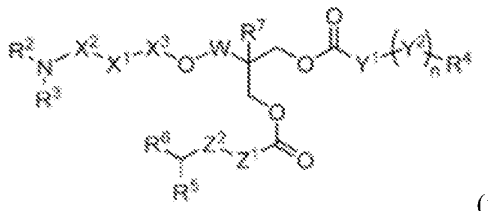
(viii)

In some embodiments an LNP comprising Formula (viii) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.



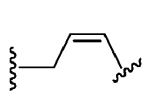
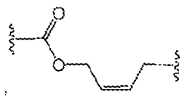
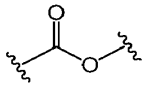
(ix)

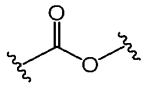
In some embodiments an LNP comprising Formula (ix) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

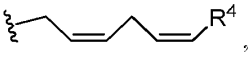


(x)

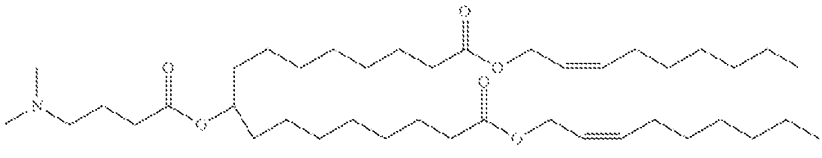
wherein X^1 is O, NR^1, or a direct bond, X^2 is C2-5 alkylene, X^3 is C(=O) or a direct bond, R^1 is H or Me, R^3 is Ci-3 alkyl, R^2 is Ci-3 alkyl, or R^2 taken together with the nitrogen atom to which it is attached and 1-3 carbon atoms of X^2 form a 4-, 5-, or 6-membered ring, or X^1 is NR^1, R^1 and R^2 taken together with the nitrogen atoms to which they are attached form a 5- or 6-membered ring, or R^2 taken together with R^3 and the nitrogen atom to which they are attached form a 5-, 6-, or 7-membered ring, Y^1 is C2-12 alkylene, Y^2 is selected from


(in either orientation),

(in either orientation),

(in either orientation),

n is 0 to 3, R^4 is Ci-15 alkyl, Z^1 is Ci-6 alkylene or a direct bond, Z^2 is , (in either orientation) or absent, provided that if Z^1 is a direct bond, Z^2 is absent; R^5 is C5-9 alkyl or C6-10 alkoxy, R^6 is C5-9 alkyl or C6-10 alkoxy, W is methylene or a direct bond, and R^7 is H or Me, or a salt thereof, provided that if R^3 and R^2 are C2 alkyls, X^1 is O, X^2 is linear C3 alkylene, X^3 is

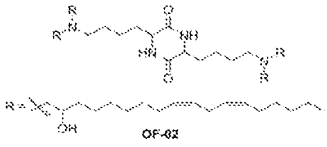
C(=O), Y^1 is linear C6 alkylene, $(Y^2)_n$-R^4 is , R^4 is linear C5 alkyl, Z^1 is C2 alkylene, Z^2 is absent, W is methylene, and R^7 is H, then R^5 and R^6 are not Cx alkoxy.

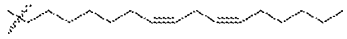
In some embodiments an LNP comprising Formula (xii) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.



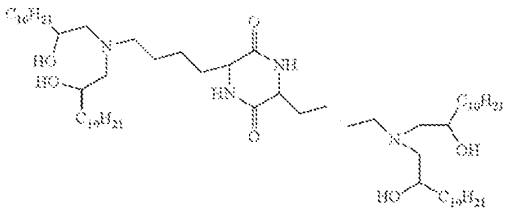
(xi)

In some embodiments an LNP comprising Formula (xi) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

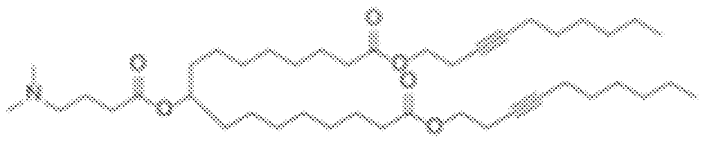


where R= 

(xii)

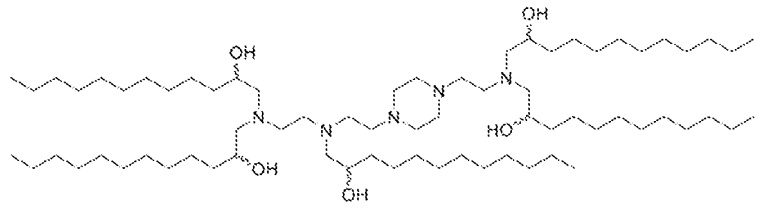


(xiii)



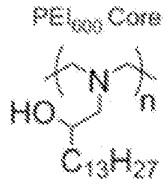
(xiv)

In some embodiments an LNP comprises a compound of Formula (xiii) and a compound of Formula (xiv).



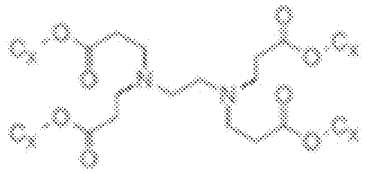
(xv)

In some embodiments, an LNP comprising Formula (xv) is used to deliver a TREM composition described herein to the liver and/or hepatocyte cells.

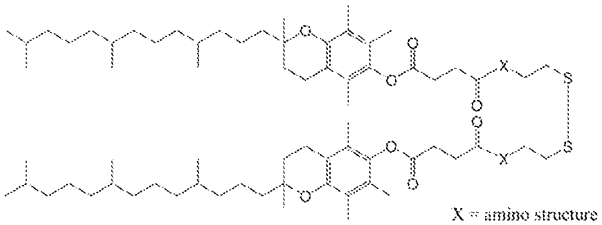


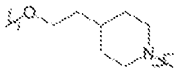
(xvi)

In some embodiments an LNP comprising a formulation of Formula (xvi) is used to deliver a TREM composition described herein to the lung endothelial cells.

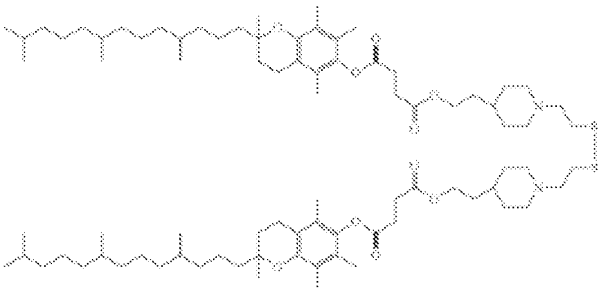


(xvii)

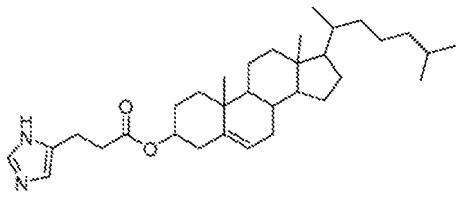


where X=  (xviii)

(a)

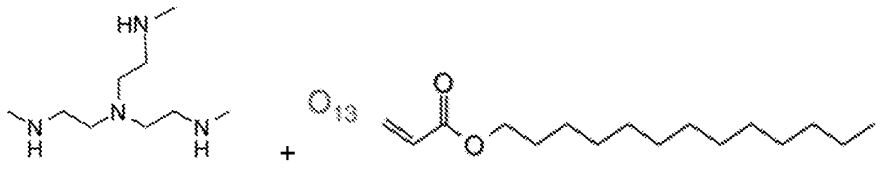


(xviii)(b)

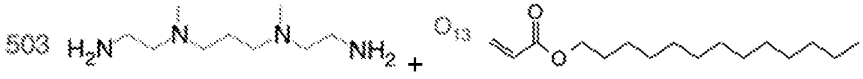


(xix)

In some embodiments, a lipid compound used to form lipid nanoparticles for the delivery of compositions described herein, e.g., a TREM described herein is made by one of the following reactions:



(xx) (a)



(xx)(b)

In some embodiments, a composition described herein (e.g., TREM composition) is provided in an LNP that comprises an ionizable lipid. In some embodiments, the ionizable lipid is heptadecan-9-yl 8-((2-hydroxyethyl)(6-oxo-6-(undecyloxy)hexyl)amino)octanoate (SM-102); e.g., as described in Example 1 of US9,867,888 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is 9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate (LP01), e.g., as synthesized in Example 13 of WO2015/095340 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is Di((Z)-non-2-en-1-yl) 9-((4-dimethylamino)-butanoyl)oxy)heptadecanedioate (L319), e.g. as synthesized in Example 7, 8, or 9 of US2012/0027803 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is 1,1'-((2-(4-(2-((2-(Bis(2-hydroxydodecyl)amino)ethyl)(2-hydroxydodecyl) amino)ethyl)piperazin-1-yl)ethyl)azanediyl)bis(dodecan-2-ol) (C12-200), e.g., as synthesized in Examples 14 and 16 of WO2010/053572 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is Imidazole cholesterol ester (ICE) lipid (3S, 10R, 13R, 17R)-10, 13-dimethyl-17- ((R)-6-methylheptan-2-yl)-2, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17-tetradecahydro-lH- cyclopenta[a]phenanthren-3-yl 3-(1H-imidazol-4-yl)propanoate, e.g., Structure (I) from WO2020/106946 (incorporated by reference herein in its entirety).

In some embodiments, an ionizable lipid may be a cationic lipid, an ionizable cationic lipid, e.g., a cationic lipid that can exist in a positively charged or neutral form depending on pH, or an amine-containing lipid that can be readily protonated. In some embodiments, the cationic lipid is a lipid capable of being positively charged, e.g., under physiological conditions. Exemplary cationic lipids include one or more amine group(s) which bear the positive charge. In

some embodiments, the lipid particle comprises a cationic lipid in formulation with one or more of neutral lipids, ionizable amine-containing lipids, biodegradable alkyne lipids, steroids, phospholipids including polyunsaturated lipids, structural lipids (e.g., sterols), PEG, cholesterol and polymer conjugated lipids. In some embodiments, the cationic lipid may be an ionizable cationic lipid. An exemplary cationic lipid as disclosed herein may have an effective pKa over 6.0. In embodiments, a lipid nanoparticle may comprise a second cationic lipid having a different effective pKa (e.g., greater than the first effective pKa), than the first cationic lipid. A lipid nanoparticle may comprise between 40 and 60 mol percent of a cationic lipid, a neutral lipid, a steroid, a polymer conjugated lipid, and a therapeutic agent, e.g., a TREM described herein, encapsulated within or associated with the lipid nanoparticle. In some embodiments, the TREM is co-formulated with the cationic lipid. The TREM may be adsorbed to the surface of an LNP, e.g., an LNP comprising a cationic lipid. In some embodiments, the TREM may be encapsulated in an LNP, e.g., an LNP comprising a cationic lipid. In some embodiments, the lipid nanoparticle may comprise a targeting moiety, e.g., coated with a targeting agent. In embodiments, the LNP formulation is biodegradable. In some embodiments, a lipid nanoparticle comprising one or more lipid described herein, e.g., Formula (i), (ii), (ii), (vii) and/or (ix) encapsulates at least 1%, at least 5%, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 92%, at least 95%, at least 97%, at least 98% or 100% of a TREM.

Exemplary ionizable lipids that can be used in lipid nanoparticle formulations include, without limitation, those listed in Table 1 of WO2019051289, incorporated herein by reference. Additional exemplary lipids include, without limitation, one or more of the following formulae: X of US2016/0311759; I of US20150376115 or in US2016/0376224; I, II or III of US20160151284; I, IA, II, or IIA of US20170210967; I-c of US20150140070; A of US2013/0178541; I of US2013/0303587 or US2013/0123338; I of US2015/0141678; II, III, IV, or V of US2015/0239926; I of US2017/0119904; I or II of WO2017/117528; A of US2012/0149894; A of US2015/0057373; A of WO2013/116126; A of US2013/0090372; A of US2013/0274523; A of US2013/0274504; A of US2013/0053572; A of W02013/016058; A of W02012/162210; I of US2008/042973; I, II, III, or IV of US2012/01287670; I or II of US2014/0200257; I, II, or III of US2015/0203446; I or III of US2015/0005363; I, IA, IB, IC, ID, II, IIA, IIB, IIC, IID, or III-XXIV of US2014/0308304; of US2013/0338210; I, II, III, or IV of

W02009/132131; A of US2012/01011478; I or XXXV of US2012/0027796; XIV or XVII of US2012/0058144; of US2013/0323269; I of US2011/0117125; I, II, or III of US2011/0256175; I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XII of US2012/0202871; I, II, III, IV, V, VI, VII, VIII, X, XII, XIII, XIV, XV, or XVI of US2011/0076335; I or II of US2006/008378; I of US2013/0123338; I or X-A-Y-Z of US2015/0064242; XVI, XVII, or XVIII of US2013/0022649; I, II, or III of US2013/0116307; I, II, or III of US2013/0116307; I or II of US2010/0062967; I-X of US2013/0189351; I of US2014/0039032; V of US2018/0028664; I of US2016/0317458; I of US2013/0195920; 5, 6, or 10 of US10,221,127; III-3 of WO2018/081480; I-5 or I-8 of WO2020/081938; 18 or 25 of US9,867,888; A of US2019/0136231; II of WO2020/219876; 1 of US2012/0027803; OF-02 of US2019/0240349; 23 of US10,086,013; cKK-E12/A6 of Miao et al (2020); C12-200 of WO2010/053572; 7C1 of Dahlman et al (2017); 304-O13 or 503-O13 of Whitehead et al; TS-P4C2 of US9,708,628; I of WO2020/106946; I of WO2020/106946.

In some embodiments, the ionizable lipid is MC3 (6Z,9Z,28Z,3 lZ)-heptatriaconta-6,9,28,3 l-tetraen-l9-yl-4-(dimethylamino) butanoate (DLin-MC3-DMA or MC3), e.g., as described in Example 9 of WO2019051289A9 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is the lipid ATX-002, e.g., as described in Example 10 of WO2019051289A9 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is (l3Z,l6Z)-A,A-dimethyl-3- nonyldocosa-l3, l6-dien-l-amine (Compound 32), e.g., as described in Example 11 of WO2019051289A9 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is Compound 6 or Compound 22, e.g., as described in Example 12 of WO2019051289A9 (incorporated by reference herein in its entirety).

Exemplary non-cationic lipids include, but are not limited to, distearoyl-sn-glycero-phosphoethanolamine, distearoylphosphatidylcholine (DSPC), dioleoylphosphatidylcholine (DOPC), dipalmitoylphosphatidylcholine (DPPC), dioleoylphosphatidylglycerol (DOPG), dipalmitoylphosphatidylglycerol (DPPG), dioleoyl-phosphatidylethanolamine (DOPE), palmitoyloleoylphosphatidylcholine (POPC), palmitoyloleoylphosphatidylethanolamine (POPE), dioleoyl-phosphatidylethanolamine 4-(N-maleimidomethyl)-cyclohexane- 1 - carboxylate (DOPE-mal), dipalmitoyl phosphatidyl ethanolamine (DPPE), dimyristoylphosphoethanolamine (DMPE), distearoyl-phosphatidyl-ethanolamine (DSPE), monomethyl-phosphatidylethanolamine (such as 16-O-monomethyl PE), dimethyl- phosphatidylethanolamine (such as 16-O-dimethyl

PE), l8-l-trans PE, l-stearoyl-2-oleoyl- phosphatidyethanolamine (SOPE), hydrogenated soy phosphatidylcholine (HSPC), egg phosphatidylcholine (EPC), dioleoylphosphatidylserine (DOPS), sphingomyelin (SM), dimyristoyl phosphatidylcholine (DMPC), dimyristoyl phosphatidylglycerol (DMPG), distearoylphosphatidylglycerol (DSPG), dierucoylphosphatidylcholine (DEPC), palmitoyloleyolphosphatidylglycerol (POPG), dielaidoyl-phosphatidylethanolamine (DEPE), lecithin, phosphatidylethanolamine, lysolecithin, lysophosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, sphingomyelin, egg sphingomyelin (ESM), cephalin, cardiolipin, phosphatidicacid,cerebrosides, dicetylphosphate, lysophosphatidylcholine, dilinoleoylphosphatidylcholine, or mixtures thereof. It is understood that other diacylphosphatidylcholine and diacylphosphatidylethanolamine phospholipids can also be used. The acyl groups in these lipids are preferably acyl groups derived from fatty acids having C10-C24 carbon chains, e.g., lauroyl, myristoyl, paimitoyl, stearoyl, or oleoyl. Additional exemplary lipids, in certain embodiments, include, without limitation, those described in Kim et al. (2020) dx.doi.org/10.1021/acs.nanolett.0c01386, incorporated herein by reference. Such lipids include, in some embodiments, plant lipids found to improve liver transfection with mRNA (e.g., DGTS).

Other examples of non-cationic lipids suitable for use in the lipid nanoparticles include, without limitation, nonphosphorous lipids such as, e.g., stearylamine, dodeeylamine, hexadecylamine, acetyl palmitate, glycerol ricinoleate, hexadecyl stereate, isopropyl myristate, amphoteric acrylic polymers, triethanolamine-lauryl sulfate, alkyl-aryl sulfate polyethyloxylated fatty acid amides, dioctadecyl dimethyl ammonium bromide, ceramide, sphingomyelin, and the like. Other non-cationic lipids are described in WO2017/099823 or US patent publication US2018/0028664, the contents of which is incorporated herein by reference in their entirety.

In some embodiments, the non-cationic lipid is oleic acid or a compound of Formula I, II, or IV of US2018/0028664, incorporated herein by reference in its entirety. The non-cationic lipid can comprise, for example, 0-30% (mol) of the total lipid present in the lipid nanoparticle. In some embodiments, the non-cationic lipid content is 5-20% (mol) or 10-15% (mol) of the total lipid present in the lipid nanoparticle. In embodiments, the molar ratio of ionizable lipid to the neutral lipid ranges from about 2:1 to about 8:1 (e.g., about 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, or 8:1).

In some embodiments, the lipid nanoparticles do not comprise any phospholipids.

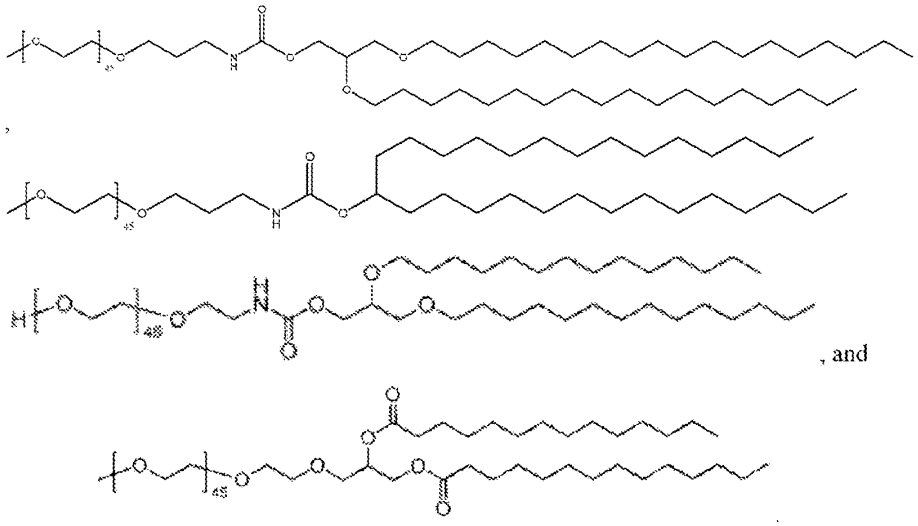
In some aspects, the lipid nanoparticle can further comprise a component, such as a sterol, to provide membrane integrity. One exemplary sterol that can be used in the lipid nanoparticle is cholesterol and derivatives thereof. Non-limiting examples of cholesterol derivatives include polar analogues such as 5a-choiestanol, 53-coprostanol, choiesteryl-(2'-hydroxy)-ethyl ether, choiesteryl-(4'- hydroxy)-butyl ether, and 6-ketocholestanol; non-polar analogues such as 5a-cholestane, cholestenone, 5a-cholestanone, 5p-cholestanone, and cholesteryl decanoate; and mixtures thereof. In some embodiments, the cholesterol derivative is a polar analogue, e.g., choiesteryl-(4 '-hydroxy)-buty1 ether. Exemplary cholesterol derivatives are described in PCT publication W02009/127060 and US patent publication US2010/0130588, each of which is incorporated herein by reference in its entirety.

In some embodiments, the component providing membrane integrity, such as a sterol, can comprise 0-50% (mol) (e.g., 0-10%, 10-20%, 20-30%, 30-40%, or 40-50%) of the total lipid present in the lipid nanoparticle. In some embodiments, such a component is 20-50% (mol) 30-40% (mol) of the total lipid content of the lipid nanoparticle.

In some embodiments, the lipid nanoparticle can comprise a polyethylene glycol (PEG) or a conjugated lipid molecule. Generally, these are used to inhibit aggregation of lipid nanoparticles and/or provide steric stabilization. Exemplary conjugated lipids include, but are not limited to, PEG-lipid conjugates, polyoxazoline (POZ)-lipid conjugates, polyamide-lipid conjugates (such as ATTA-lipid conjugates), cationic-polymer lipid (CPL) conjugates, and mixtures thereof. In some embodiments, the conjugated lipid molecule is a PEG-lipid conjugate, for example, a (methoxy polyethylene glycol)-conjugated lipid.

Exemplary PEG-lipid conjugates include, but are not limited to, PEG-diacylglycerol (DAG) (such as l-(monomethoxy-polyethyleneglycol)-2,3-dimyristoylglycerol (PEG-DMG)), PEG-dialkyloxypropyl (DAA), PEG-phospholipid, PEG-ceramide (Cer), a pegylated phosphatidylethanoloamine (PEG-PE), PEG succinate diacylglycerol (PEGS-DAG) (such as 4-0-(2',3'-di(tetradecanoyloxy)propyl-l-0-(w-methoxy(polyethoxy)ethyl) butanedioate (PEG-S-DMG)), PEG dialkoxypropylcarbam, N-(carbonyl-methoxypolyethylene glycol 2000)-l,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt, or a mixture thereof. Additional exemplary PEG-lipid conjugates are described, for example, in US5,885,613, US6,287,591, US2003/0077829, US2003/0077829, US2005/0175682, US2008/0020058, US2011/0117125, US2010/0130588, US2016/0376224, US2017/0119904, and US/099823, the contents of all of

which are incorporated herein by reference in their entirety. In some embodiments, a PEG-lipid is a compound of Formula III, III-a-I, III-a-2, III-b-1, III-b-2, or V of US2018/0028664, the content of which is incorporated herein by reference in its entirety. In some embodiments, a PEG-lipid is of Formula II of US20150376115 or US2016/0376224, the content of both of which is incorporated herein by reference in its entirety. In some embodiments, the PEG-DAA conjugate can be, for example, PEG-dilauryloxypropyl, PEG- dimyristyloxypropyl, PEG-dipalmityloxypropyl, or PEG-distearyloxypropyl. The PEG-lipid can be one or more of PEG-DMG, PEG-dilaurylglycerol, PEG-dipalmitoylglycerol, PEG- disterylglycerol, PEG-dilaurylglycamide, PEG-dimyristylglycamide, PEG- dipalmitoylglycamide, PEG-disterylglycamide, PEG-cholesterol (l-[8'-(Cholest-5-en-3[beta]- oxy)carboxamido-3',6'-dioxaoctanyl] carbamoyl-[omega]-methyl-poly(ethylene glycol), PEG- DMB (3,4-Ditetradecoxylbenzyl- [omega]-methyl-poly(ethylene glycol) ether), and 1,2- dimyristoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]. In some embodiments, the PEG-lipid comprises PEG-DMG, 1,2- dimyristoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]. In some embodiments, the PEG-lipid comprises a structure selected from:



, and

In some embodiments, lipids conjugated with a molecule other than a PEG can also be used in place of PEG-lipid. For example, polyoxazoline (POZ)-lipid conjugates, polyamide-lipid conjugates (such as ATTA-lipid conjugates), and cationic-polymer lipid (GPL) conjugates can be used in place of or in addition to the PEG-lipid.

Exemplary conjugated lipids, i.e., PEG-lipids, (POZ)-lipid conjugates, ATTA-lipid conjugates and cationic polymer-lipids are described in the PCT and LIS patent applications listed in Table 2 of WO2019051289A9, the contents of all of which are incorporated herein by reference in their entirety.

In some embodiments, the PEG or the conjugated lipid can comprise 0-20% (mol) of the total lipid present in the lipid nanoparticle. In some embodiments, PEG or the conjugated lipid content is 0.5- 10% or 2-5% (mol) of the total lipid present in the lipid nanoparticle. Molar ratios of the ionizable lipid, non-cationic-lipid, sterol, and PEG/conjugated lipid can be varied as needed. For example, the lipid particle can comprise 30-70% ionizable lipid by mole or by total weight of the composition, 0-60% cholesterol by mole or by total weight of the composition, 0-30% non-cationic-lipid by mole or by total weight of the composition and 1-10% conjugated lipid by mole or by total weight of the composition. Preferably, the composition comprises 30-40% ionizable lipid by mole or by total weight of the composition, 40-50% cholesterol by mole or by total weight of the composition, and 10- 20% non-cationic-lipid by mole or by total weight of the composition. In some other embodiments, the composition is 50-75% ionizable lipid by mole or by total weight of the composition, 20-40% cholesterol by mole or by total weight of the composition, and 5 to 10% non-cationic-lipid, by mole or by total weight of the composition and 1-10% conjugated lipid by mole or by total weight of the composition. The composition may contain 60-70% ionizable lipid by mole or by total weight of the composition, 25-35% cholesterol by mole or by total weight of the composition, and 5-10% non-cationic-lipid by mole or by total weight of the composition. The composition may also contain up to 90% ionizable lipid by mole or by total weight of the composition and 2 to 15% non-cationic lipid by mole or by total weight of the composition. The formulation may also be a lipid nanoparticle formulation, for example comprising 8-30% ionizable lipid by mole or by total weight of the composition, 5-30% non- cationic lipid by mole or by total weight of the composition, and 0-20% cholesterol by mole or by total weight of the composition; 4-25% ionizable lipid by mole or by total weight of the composition, 4-25% non-cationic lipid by mole or by total weight of the composition, 2 to 25% cholesterol by mole or by total weight of the composition, 10 to 35% conjugate lipid by mole or by total weight of the composition, and 5% cholesterol by mole or by total weight of the composition; or 2-30% ionizable lipid by mole or by total weight of the composition, 2-30% non-cationic lipid by mole or by total weight of the composition, 1 to 15% cholesterol by mole or

by total weight of the composition, 2 to 35% conjugate lipid by mole or by total weight of the composition, and 1-20% cholesterol by mole or by total weight of the composition; or even up to 90% ionizable lipid by mole or by total weight of the composition and 2-10% non-cationic lipids by mole or by total weight of the composition, or even 100% cationic lipid by mole or by total weight of the composition. In some embodiments, the lipid particle formulation comprises ionizable lipid, phospholipid, cholesterol and a PEG-ylated lipid in a molar ratio of 50: 10:38.5: 1.5. In some other embodiments, the lipid particle formulation comprises ionizable lipid, cholesterol and a PEG-ylated lipid in a molar ratio of 60:38.5: 1.5.

In some embodiments, the lipid particle comprises ionizable lipid, non-cationic lipid (e.g. phospholipid), a sterol (e.g., cholesterol) and a PEG-ylated lipid, where the molar ratio of lipids ranges from 20 to 70 mole percent for the ionizable lipid, with a target of 40-60, the mole percent of non-cationic lipid ranges from 0 to 30, with a target of 0 to 15, the mole percent of sterol ranges from 20 to 70, with a target of 30 to 50, and the mole percent of PEG-ylated lipid ranges from 1 to 6, with a target of 2 to 5.

In some embodiments, the lipid particle comprises ionizable lipid / non-cationic- lipid / sterol / conjugated lipid at a molar ratio of 50: 10:38.5: 1.5.

In an aspect, the disclosure provides a lipid nanoparticle formulation comprising phospholipids, lecithin, phosphatidylcholine and phosphatidylethanolamine.

In some embodiments, one or more additional compounds can also be included. Those compounds can be administered separately, or the additional compounds can be included in the lipid nanoparticles of the invention. In other words, the lipid nanoparticles can contain other compounds in addition to the nucleic acid or at least a second nucleic acid, different than the first. Without limitations, other additional compounds can be selected from the group consisting of small or large organic or inorganic molecules, monosaccharides, disaccharides, trisaccharides, oligosaccharides, polysaccharides, peptides, proteins, peptide analogs and derivatives thereof, peptidomimetics, nucleic acids, nucleic acid analogs and derivatives, an extract made from biological materials, or any combinations thereof.

In some embodiments, LNPs are directed to specific tissues by the addition of targeting domains. For example, biological ligands may be displayed on the surface of LNPs to enhance interaction with cells displaying cognate receptors, thus driving association with and cargo delivery to tissues wherein cells express the receptor. In some embodiments, the biological

ligand may be a ligand that drives delivery to the liver, e.g., LNPs that display GalNAc result in delivery of nucleic acid cargo to hepatocytes that display asialoglycoprotein receptor (ASGPR). The work of Akinc et al. *Mol Ther* 18(7):1357-1364 (2010) teaches the conjugation of a trivalent GalNAc ligand to a PEG-lipid (GalNAc-PEG-DSG) to yield LNPs dependent on ASGPR for observable LNP cargo effect (see, e.g., FIG. 6 of Akinc et al. 2010, *supra*). Other ligand-displaying LNP formulations, e.g., incorporating folate, transferrin, or antibodies, are discussed in WO2017223135, which is incorporated herein by reference in its entirety, in addition to the references used therein, namely Kolhatkar et al., Curr Drug Discov Technol. 2011 8:197-206; Musacchio and Torchilin, Front Biosci. 2011 16:1388-1412; Yu et al., Mol Membr Biol. 2010 27:286-298; Patil et al., Crit Rev Ther Drug Carrier Syst. 2008 25:1-61 ; Benoit et al., Biomacromolecules. 2011 12:2708-2714; Zhao et al., Expert Opin Drug Deliv. 2008 5:309-319; Akinc et al., Mol Ther. 2010 18:1357-1364; Srinivasan et al., Methods Mol Biol. 2012 820:105-116; Ben-Arie et al., Methods Mol Biol. 2012 757:497-507; Peer 2010 J Control Release. 20:63-68; Peer et al., Proc Natl Acad Sci U S A. 2007 104:4095-4100; Kim et al., Methods Mol Biol. 2011 721:339-353; Subramanya et al., Mol Ther. 2010 18:2028-2037; Song et al., Nat Biotechnol. 2005 23:709-717; Peer et al., Science. 2008 319:627-630; and Peer and Lieberman, Gene Ther. 2011 18:1127-1133.

In some embodiments, LNPs are selected for tissue-specific activity by the addition of a Selective ORgan Targeting (SORT) molecule to a formulation comprising traditional components, such as ionizable cationic lipids, amphipathic phospholipids, cholesterol and poly(ethylene glycol) (PEG) lipids. The teachings of Cheng et al. Nat Nanotechnol 15(4):313-320 (2020) demonstrate that the addition of a supplemental "SORT" component precisely alters the in vivo RNA delivery profile and mediates tissue-specific (e.g., lungs, liver, spleen) gene delivery and editing as a function of the percentage and biophysical property of the SORT molecule.

In some embodiments, the LNPs comprise biodegradable, ionizable lipids. In some embodiments, the LNPs comprise (9Z,l2Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,l2-dienoate, also called 3- ((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,l2Z)-octadeca-9,l2-dienoate) or another ionizable lipid. See, e.g, lipids of WO2019/067992, WO/2017/173054, WO2015/095340, and WO2014/136086, as well as references provided

therein. In some embodiments, the term cationic and ionizable in the context of LNP lipids is interchangeable, e.g., wherein ionizable lipids are cationic depending on the pH.

In some embodiments, the average LNP diameter of the LNP formulation may be between 10s of nm and 100s of nm, e.g., measured by dynamic light scattering (DLS). In some embodiments, the average LNP diameter of the LNP formulation may be from about 40 nm to about 150 nm, such as about 40 nm, 45 nm, 50 nm, 55 nm, 60 nm, 65 nm, 70 nm, 75 nm, 80 nm, 85 nm, 90 nm, 95 nm, 100 nm, 105 nm, 110 nm, 115 nm, 120 nm, 125 nm, 130 nm, 135 nm, 140 nm, 145 nm, or 150 nm. In some embodiments, the average LNP diameter of the LNP formulation may be from about 50 nm to about 100 nm, from about 50 nm to about 90 nm, from about 50 nm to about 80 nm, from about 50 nm to about 70 nm, from about 50 nm to about 60 nm, from about 60 nm to about 100 nm, from about 60 nm to about 90 nm, from about 60 nm to about 80 nm, from about 60 nm to about 70 nm, from about 70 nm to about 100 nm, from about 70 nm to about 90 nm, from about 70 nm to about 80 nm, from about 80 nm to about 100 nm, from about 80 nm to about 90 nm, or from about 90 nm to about 100 nm. In some embodiments, the average LNP diameter of the LNP formulation may be from about 70 nm to about 100 nm. In a particular embodiment, the average LNP diameter of the LNP formulation may be about 80 nm. In some embodiments, the average LNP diameter of the LNP formulation may be about 100 nm. In some embodiments, the average LNP diameter of the LNP formulation ranges from about l mm to about 500 mm, from about 5 mm to about 200 mm, from about 10 mm to about 100 mm, from about 20 mm to about 80 mm, from about 25 mm to about 60 mm, from about 30 mm to about 55 mm, from about 35 mm to about 50 mm, or from about 38 mm to about 42 mm.

A LNP may, in some instances, be relatively homogenous. A polydispersity index may be used to indicate the homogeneity of a LNP, e.g., the particle size distribution of the lipid nanoparticles. A small (e.g., less than 0.3) polydispersity index generally indicates a narrow particle size distribution. A LNP may have a polydispersity index from about 0 to about 0.25, such as 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20, 0.21, 0.22, 0.23, 0.24, or 0.25. In some embodiments, the polydispersity index of a LNP may be from about 0.10 to about 0.20.

The zeta potential of a LNP may be used to indicate the electrokinetic potential of the composition. In some embodiments, the zeta potential may describe the surface charge of an LNP. Lipid nanoparticles with relatively low charges, positive or negative, are generally

desirable, as more highly charged species may interact undesirably with cells, tissues, and other elements in the body. In some embodiments, the zeta potential of a LNP may be from about -10 mV to about +20 mV, from about -10 mV to about +15 mV, from about -10 mV to about +10 mV, from about -10 mV to about +5 mV, from about -10 mV to about 0 mV, from about -10 mV to about -5 mV, from about -5 mV to about +20 mV, from about -5 mV to about +15 mV, from about -5 mV to about +10 mV, from about -5 mV to about +5 mV, from about -5 mV to about 0 mV, from about 0 mV to about +20 mV, from about 0 mV to about +15 mV, from about 0 mV to about +10 mV, from about 0 mV to about +5 mV, from about +5 mV to about +20 mV, from about +5 mV to about +15 mV, or from about +5 mV to about +10 mV.

The efficiency of encapsulation of a TREM describes the amount of TREM that is encapsulated or otherwise associated with a LNP after preparation, relative to the initial amount provided. The encapsulation efficiency is desirably high (e.g., close to 100%). The encapsulation efficiency may be measured, for example, by comparing the amount of TREM in a solution containing the lipid nanoparticle before and after breaking up the lipid nanoparticle with one or more organic solvents or detergents. An anion exchange resin may be used to measure the amount of free protein or nucleic acid (e.g., RNA) in a solution. Fluorescence may be used to measure the amount of free TREM in a solution. For the lipid nanoparticles described herein, the encapsulation efficiency of a TREM may be at least 50%, for example 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%. In some embodiments, the encapsulation efficiency may be at least 80%. In some embodiments, the encapsulation efficiency may be at least 90%. In some embodiments, the encapsulation efficiency may be at least 95%.

A LNP may optionally comprise one or more coatings. In some embodiments, a LNP may be formulated in a capsule, film, or table having a coating. A capsule, film, or tablet including a composition described herein may have any useful size, tensile strength, hardness or density.

Additional exemplary lipids, formulations, methods, and characterization of LNPs are taught by WO2020061457, which is incorporated herein by reference in its entirety.

In some embodiments, in vitro or ex vivo cell lipofections are performed using Lipofectamine MessengerMax (Thermo Fisher) or TransIT-mRNA Transfection Reagent (Mirus Bio). In certain embodiments, LNPs are formulated using the GenVoy_ILM ionizable lipid mix

(Precision NanoSystems). In certain embodiments, LNPs are formulated using 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA) or dilinoleylmethyl-4-dimethylaminobutyrate (DLin-MC3-DMA or MC3), the formulation and in vivo use of which are taught in Jayaraman et al. Angew Chem Int Ed Engl 51(34):8529-8533 (2012), incorporated herein by reference in its entirety.

LNP formulations optimized for the delivery of CRISPR-Cas systems, e.g., Cas9-gRNA RNP, gRNA, Cas9 mRNA, are described in WO2019067992 and WO2019067910, both incorporated by reference.

Additional specific LNP formulations useful for delivery of nucleic acids are described in US8158601 and US8168775, both incorporated by reference, which include formulations used in patisiran, sold under the name ONPATTRO.

Exosomes can also be used as drug delivery vehicles for the TREM, TREM core fragment, TREM fragment, or TREM compositions or pharmaceutical TREM composition described herein. For a review, see Ha et al. July 2016. Acta Pharmaceutica Sinica B. Volume 6, Issue 4, Pages 287-296; https://doi.org/10.1016/j.apsb.2016.02.001.

Ex vivo differentiated red blood cells can also be used as a carrier for a TREM, TREM core fragment, TREM fragment, or TREM composition, or pharmaceutical TREM composition described herein. See, *e.g.*, WO2015073587; WO2017123646; WO2017123644; WO2018102740; wO2016183482; WO2015153102; WO2018151829; WO2018009838; Shi et al. 2014. Proc Natl Acad Sci USA. 111(28): 10131–10136; US Patent 9,644,180; Huang et al. 2017. Nature Communications 8: 423; Shi et al. 2014. Proc Natl Acad Sci USA. 111(28): 10131–10136.

Fusosome compositions, *e.g.*, as described in WO2018208728, can also be used as carriers to deliver the TREM, TREM core fragment, TREM fragment, or TREM composition, or pharmaceutical TREM composition described herein.

Virosomes and virus-like particles (VLPs) can also be used as carriers to deliver a TREM, TREM core fragment, TREM fragment, or TREM composition, or pharmaceutical TREM composition described herein to targeted cells.

Plant nanovesicles, e.g., as described in WO2011097480A1, WO2013070324A1, or WO2017004526A1 can also be used as carriers to deliver the TREM, TREM core fragment,

TREM fragment, or TREM composition, or pharmaceutical TREM composition described herein.

Delivery without a carrier

A TREM, a TREM core fragment or a TREM fragment, a TREM composition or a pharmaceutical TREM composition described herein can be administered to a cell without a carrier, e.g., via naked delivery of the TREM, a TREM core fragment or a TREM fragment, a TREM composition or a pharmaceutical TREM composition.

In some embodiments, naked delivery as used herein refers to delivery without a carrier. In some embodiments, delivery without a carrier, e.g., naked delivery, comprises delivery with a moiety, e.g., a targeting peptide.

In some embodiments, a TREM, a TREM core fragment or a TREM fragment, or TREM composition, or pharmaceutical TREM composition described herein is delivered to a cell without a carrier, e.g., via naked delivery. In some embodiments, the delivery without a carrier, e.g., naked delivery, comprises delivery with a moiety, e.g., a targeting peptide.

Use of TREMs

A TREM composition (*e.g.*, a pharmaceutical TREM composition described herein) can modulate a function in a cell, tissue or subject. In embodiments, a TREM composition (*e.g.*, a pharmaceutical TREM composition) described herein is contacted with a cell or tissue, or administered to a subject in need thereof, in an amount and for a time sufficient to modulate (increase or decrease) one or more of the following parameters: adaptor function (*e.g.*, cognate or non-cognate adaptor function), *e.g.*, the rate, efficiency, robustness, and/or specificity of initiation or elongation of a polypeptide chain; ribosome binding and/or occupancy; regulatory function (*e.g.*, gene silencing or signaling); cell fate; mRNA stability; protein stability; protein transduction; protein compartmentalization. A parameter may be modulated, *e.g.*, by at least 5% (*e.g.*, at least 10%, 15%, 20%, 25%, 30%, 40%. 50%. 60%. 70%, 80%, 90%, 100%, 150%, 200% or more) compared to a reference tissue, cell or subject (*e.g.*, a healthy, wild-type or control cell, tissue or subject).

All references and publications cited herein are hereby incorporated by reference.

The following examples are provided to further illustrate some embodiments of the present invention, but are not intended to limit the scope of the invention; it will be understood by their exemplary nature that other procedures, methodologies, or techniques known to those skilled in the art may alternatively be used.

EXAMPLES

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Example 1: Synthesis of a Modified TREM

Generally, TREM molecules (e.g., modified TREMs) may be chemically synthesized and purified by HPLC according to standard solid phase synthesis methods using phosphoramidite chemistry. (see, e.g., Scaringe S. et al. (2004) *Curr Protoc Nucleic Acid Chem*, 2.10.1-2.10.16; Usman N. et al. (1987) *J. Am. Chem. Soc*, 109, 7845-7854). Individually modified TREM

molecules containing one or more 2'-methoxy (2'OMe), 2'fluoro (2'F), 2'-methoxyethyl (2'-MOE), or phosphorothioate (PS) modifications were prepared using either TREM-Arg-TGA, TREM-Ser-TAG, or TREM-Gln-TAA sequences as a framework according to phosphoramidite technology on solid phase used in oligonucleotide synthesis. For clarity, the arginine non-cognate TREM molecule named TREM-Arg-TGA contains the sequence of ARG-UCU-TREM body but with the anticodon sequence corresponding to UCA instead of UCU (i.e., SEQ ID NO: 622). Simlarly, a serine non-cognate TREM molecule named TREM-Ser-TAG contains the sequence of SER-GCU-TREM body but with the anticodon sequence corresponding to CUA instead of GCU (i.e., SEQ ID NO: 993). A glutamine non-cognate TREM molecule named TREM-Gln-TAA contains the sequence of GLN-CUG-TREM body but with the anticodon sequence corresponding to UUA instead of CUG (i.e., SEQ ID NO: 1079).

To make the 2'OMe modified TREMs, the following 2'-O-methyl phosphoramidites were used: (5'-O-dimethoxytrityl-N6-(benzoyl)-2'-O-methyl-adenosine-3'-O-(2-cyanoethyl-N,N-diisopropy-lamino) phosphoramidite, 5'-O-dimethoxy-trityl-N4-(acetyl)-2'-O-methyl-cytidine-3'-O-(2-cyanoethyl-N,N-diisopropyl-amino) phosphoramidite, (5'- O -dimethoxytrityl-N2-(isobutyryl)-2'-O-methyl-guanosine-3'-O-(2-cyano-ethyl-N,N-diisopropylamino)-phosphoramidite, and 5'-O-dimethoxy-trityl-2'-O-methyluridine-3'- O -(2-cyanoethyl-N,N-diisopropylamino)phosphoramidite. To make the 2'-deoxy and 2'-F modified TREMs, analogous 2'-deoxy and 2'-fluoro-phosphoramidites with the same protecting groups as the 2'-O-methyl RNA amidites were used. To make the 2'-MOE modified TREMs, the following 2'-MOE-phosphoramidites were used: 5'-O-(4,4'-Dimethoxytrityl)-2'-O-methoxyethyl-N6-benzoyl-adenosine -3'-O-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite, 5'-O-(4,4'-Dimethoxytrityl)-2'-O-methoxyethyl-5-methyl-N4-benzoyl- cytidine-3'-O-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite, 5'-O-(4,4'-Dimethoxytrityl)-2'-O-methoxyethyl-N2-isobutyryl-guanosine-3'-O-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite, 5'-O-(4,4'-Dimethoxytrityl)-2'-O-methoxyethyl-5-methyl-uridine-3'-O-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite.

During the oligonucleotide synthesis via this phosphoramidites approach, the phosphorothioate was introduced by oxidizing the phosphite triester using a sulfur transfer reagent, such as tetraethylthiuram disulfide (TETD), bis(O,O-diisopropoxy phosphinothioyl) disulfide (Stec's reagent), 3H-1,2-benzodithiol-3-one-1,1,-dioxide (Beaucage reagent),

phenylacetyl disulfide (PADS), 3-ethoxy-1,2,4-dithiazoline-5-one (EDITH), 1,2-dithiazole-5-thione (xanthane hydride or ADTT), 3-((dimethylamino-methylidene)amino)-3H-1,2,4-dithiazole-3-thione (DDTT), dimethylthiuram disulfide (DTD), 3-phenyl-1,2,4-dithiazoline-5-one (PolyOrg Sulfa or POS).

Tables 15-22 below describe a series of singly and multiply modified TREMs synthesized according to this procedure. The sequences of each of these TREMs are provided in the table, wherein r: ribonucleotide; m: 2'-OMe; *: PS linkage; f: 2'-fluoro; moe: 2'-moe; d: deoxyribonucleotide; 5MeC: 5-methylcytosine. Thus, for example, mA represents 2'-O-methyl adenosine, moe5MeC represents 2'-MOE nucleotide with 5-methylcytosine nucleobase, and dA represents an adenosine deoxyribonucleotide.

Example 2: Synthesis of guanosine 2'-O-MOE phosphoramidite

This example describes the synthesis of guanosine 2'-O-MOE phosphoramidite. Guanosine 2'-O-MOE phosphoramidite is prepared and purified according to previously published procedures (Wen K. et al. (2002) *The Journal of Organic Chemistry*, 67(22), 7887–7889).

Briefly, guanosine and imidazole are dried by co-evaporation with pyridine, dissolved in dry DMF, and treated with bis(diisopropylchlorosilyl) methane added dropwise at 0 °C. The temperature is gradually increased to 25 °C and then held for 5 h. The reaction mixture is poured into ice water, and the precipitated white solid filtered to afford compound 1. To a solution of compound 1, BrCH2CH2OCH3, and TBAI in DMF at -20 °C is added with sodium bis (trimethylsilyl)amide, and the mixture is stirred for 4 hours under argon. After the reaction is quenched with methanol, the THF is evaporated and the residue is precipitated in ice to furnish compound 2. TBAF is added to a solution of compound 2 at 25 °C and then the mixture is stirred at 35 °C for 5 hours. The solvent is then evaporated under reduced pressure, and the residue is filtered in a short pad of silica gel using 10% methanol in dichloromethane to afford guanosine 2'-O-MOE phosphoramidite.

Example 3: Synthesis of 5,6 dihydrouridine

This example describes the synthesis of 5,6 dihydrouridine. 5,6 dihydrouridine phosphoramidite is prepared and purified according to previously published procedures (Hanze AR et al., (1967) *Journal of the American Chemical Society*, 89(25), 6720–6725). Briefly, oxygen is bubbled through a solution uridine in the presence of platinum black. The reaction is

followed by spotting the reaction mixture on silica gel thin layer chromatographic plates and developing in methanol-chloroform (1:1). After 1 hour, the mixture is cooled and centrifuged and the clear liquid lyophilized to yield the 5,6 dihydrouridine product.

Example 4: Synthesis of a TREM via 5'-Silyl-2'-Orthoester (2'- ACE) Chemistry

This example describes the synthesis of a TREM via 5'-Silyl-2'-Orthoester (2'- ACE) Chemistry summarized from (Hartsel SA et al., (2005) *Oligonucleotide Synthesis*, 033–050).

Protected Ribonucleoside Monomers

5'-O-silyl-2'-O-ACE protected phosphoramidites are prepared and purified according to previously published procedures (Hartsel SA et al., (2005) *Oligonucleotide Synthesis*, 033–050). Briefly, monomer synthesis begins from standard base-protected ribonucleosides [rA(ibu), rC(acetyl), rG(ibu) and U]. Orthogonal, 5'-silyl-2'-ACE protection and amidite preparation is then accomplished in five general steps:

1. Simultaneous transient protection of the 5'- and 3'-hydroxyl groups with 1,1,3,3tetraispropyldisiloxane (TIPS).
2. Regiospecific conversion of the 2'-hydroxyl to the 2'-O-orthoester using tris(acetoxyethyl)orthoformate (ACE orthoformate).
3. Removal of the 5',3'-TIPS protection.
4. Introduction of the 5'-O-silyl ether protecting group using benzhydryloxybis-(trimethylsilyloxy)-chlorosilane (BzH-Cl).
5. Phosphitylation of the 3'-OH with bis(N,N'-diisopropylamino)methoxyphosphine.

The fully protected, phosphitylated monomer is an oil. For ease of handling and dissolution, the phosphoramidite solution is evaporated to dryness in a tared flask to enable quantitation of yields. The phosphoramidite oil is then dissolved in anhydrous acetonitrile, distributed into synthesis vials in 1.0-mmol aliquots, and evaporated to dryness under vacuum in the presence of potassium hydroxide (KOH) and P2O5.

Synthesis of Oligoribonucleosides

Table 12

Synthesis Step	**Reagent**	**Delivery Time**	**Reaction Time**
Deblock	3% DCA in DCM	35	
Activator	0.5M S-ethyl-tetrazole	6	

Coupling	0.1M amidite8.0	30	
	0.5M S-ethyl-tetrazole	8	30
Repeat Coupling			
Oxidation	t-Butyl hydroperoxide	20	10
Repeat Oxidation Delivery			
Capping	1-methylimidazole and acetic anhydride	12	10
Desilylation	TEAHF	35	

5'-silyl-2'-ACE oligoribonucleotide synthesis begins with the appropriately modified 3'-terminal nucleoside attached through the 3'-hydroxyl to a polystyrene support. The solid support contained in an appropriate reaction cartridge is then placed on the appropriate column position on the instrument. A synthesis cycle is created using the delivery times and wait steps outlined in Table 12.

1. Initial detritylation: The first step in the synthesis cycle is the removal of the 5' O-DMT from the nucleoside-bound polystyrene support using 3% DCA in DCM.
2. Coupling: The 5-ethylthio-1H-tetrazole solution is delivered to the solid support, followed by simultaneous delivery of an equal quantity of activator and phosphoramidite solution. Depending on the desired sequence and synthesis scale, excess activator and activator plus amidite are alternately delivered repeatedly to increase coupling efficiency, which is typically in excess of 99% per coupling reaction. The 5-ethylthio-1H-tetrazole activates coupling by protonating the diisopropyl amine attached to the trivalent phosphorous. Nucleophilic attack of the 5-ethylthio-1H-tetrazole leads to the formation of the tetrazolide intermediate that reacts with the free 5'-OH of the support-bound nucleoside forming the internucleotide phosphite linkage.
3. Oxidation: In the next step of chain elongation, the phosphorous(III) linkage is oxidized for 10-20s to the more stable and ultimately desired P(V) linkage using t-butylhydroperoxide.
4. Capping: Although delivery of excess activator and phosphoramidite increases coupling efficiency, a small percentage of unreacted nucleoside may remain support-bound. To

prevent the introduction of mixed sequences, the unreacted 5'-OH are "capped" or blocked by acetylating the primary hydroxyl. This acetylation is achieved through simultaneous delivery of 1-methylimidazole and acetic anhydride.

5. 5'-Desilylation: Before the next nucleoside in the sequence can be added to the growing oligonucleotide chain, the 5'-silyl group is removed with fluoride ion. This requires the delivery of triethylamine trihydrogenfluoride for 45 s. The desilylation is rapid and quantitative and no wait step is required.

Steps 2-5 are repeated for each subsequent nucleotide until the desired sequence is constructed.

Oligonucleotide Deprotection

A two-stage rapid deprotection strategy is employed to remove phosphate backbone protection, release the oligonucleotide from the solid support, and remove the exocyclic amine protecting groups on A, G, and C. The treatment also removes the acetyl moiety from the acetoxyethyl orthoester, resulting in the 2'-bis-hydroxyethyl protected intermediate that is now 10 times more labile to final acid deprotection. In the first deprotection step, S2Na2 is used to selectively remove the methyl protection from the internucleotide phosphate, leaving the oligoribonucleotide attached to the polystyrene support. This configuration allows any residual reagent to be thoroughly washed away before proceeding. Alternatively, a multicolumn, manifold approach can also be used.

1. A syringe barrel is attached to one of the two luer fittings on the synthesis column. 2 mL of the S2Na2 reagent is drawn into a second syringe and attached to the opposite side of the synthesis column. The S2Na2 reagent is gently pushed through the column and into the empty syringe barrel continuing back and forth several times. The column, filled with reagent is allowed to sit at room temperature for 10 min.
2. S2Na2 reagent is removed from the column. Using a clean syringe, the column is washed thoroughly with water. In the second deprotection step, 40% 1-methylamine in water is used to free the oligoribonucleotide from the solid support, deprotect the exocyclic base amines, and deacylate the 2'-orthoester leaving the deprotected species.

N-Methylamine Deprotection

1. The solid support resin is transferred from the column into a 4-mL vial
2. 2 mL 40% methylamine is added and heated for 12 min at 60°C.
3. The methylamine is removed and is transferred into a fresh vial.

4. The oligonucleotide solution is evaporated to dryness in a SpeedVac or similar device. Oligonucleotide yields are measured using an ultraviolet (UV) spectrophotometer (absorbance at 260 nm).

Example 5: Synthesis of an arginine TREM having a 2'-*O*-MOE modification

This example describes the synthesis of an Arg TREM having one 2'-*O*-MOE modification. The 2'-*O*-MOE modification can be placed on a nucleotide on any domain or linker of the Arg TREM, or at any position in said domain or linker.

A 2'-ACE RNA oligoribonucleotide synthesis is performed on a modified Applied Biosystems 394 DNA/RNA synthesizer or similar instrument. 2'-*O*-MOE amidites are synthesized as in Example 2. An oligonucleotide sequence: GGCUCCGUGGCGCAAUGGAUAGCGCAUUGGACUUCUAAUUCAAAGGUUCCGGGUUCG(A-MOE)GUCCCGGCGGAGUCG is synthesized following the protocol described in example 4. A similar method can be used to add a 2'-*O*-MOE modification on a TREM specifying any one of the other 19 amino acids.

Example 6: Synthesis of a glutamine TREM having a pseudouridine modification

This example describes the synthesis of a Gln TREM having a pseudouridine modification. The modification can be placed on a nucleotide on any domain or linker of the Gln TREM, or at any position in said domain or linker.

A 2'-ACE RNA oligoribonucleotide synthesis is performed on a modified Applied Biosystems 394 DNA/RNA synthesizer or similar instrument. Pseudouridine (P) amidites are obtained from Glen Research or similar provider. An oligonucleotide sequence: GGUUCCAUGGUG**P**AAUGGUAAGCACUCUGGACUCTGAAUCCAGCGAUCCGAGUUCGAGUCUCGGUGGAACCUCCA is synthesized following the protocol described in example 4.

A similar method can be used to add a pseudouridine modification on a TREM specifying any one of the other 19 amino acids.

Example 7: HPLC and MS analysis of modified TREMs

Chemically modified TREM molecules may be analyzed by HPLC, for example, to evaluate the purity and homogeneity of the compositions. A Waters Aquity UPLC system using a Waters BEH C18 column (2.1 mm x 50 mm x 1.7 μm) may be used for this analysis. Samples may be prepared by dissolving 0.5 nmol of the TREM in 75 μL of water and injecting 2 μL of the solution. The buffers used may be 50 mM dimethylhexylammonium acetate with 10%

CH_3CN (acetonitrile) as buffer A and 50 mM dimethylhexylammonium acetate with 75% CH_3CN as buffer B (gradient 25-75% buffer B over 5 mins), with a flow rate of 0.5 mL/min at 60 °C. ESI-LCMS data for the chemically modified TREMs may be acquired on a Thermo Ultimate 3000-LTQ-XL mass spectrometer.

Tables 15-22 below describe a series of singly and multiply modified TREMs synthesized according to the protocol outlined in Example 1. The calculated and detected molecular weights for each sequence were determined as outlined herein.

Example 8: Analysis of modified TREMs via anion-exchange HPLC

This example describes the quality control of a synthesized TREM via anion-exchange HPLC. Using the Dionex DNA-Pac–PA-100 column, a gradient is employed using HPLC buffer A and HPLC buffer B. 0.5 ODUs of a sample that has been dissolved in H2O or Tris buffer, pH 7.5 is injected onto the gradient. The gradient employed is based on oligonucleotide length and can be applied according to Table 13. The parameters provided in Table 14 can be used to program a linear gradient on the HPLC analyzer.

Table 13: Oligonucleotide length and gradient percentages

Length (bases)	**Gradient (%B)**
0–5	0–30
6–10	10–40
11–16	20–50
17–32	30–60
33–50	40–70
>50	50–80

Table 14: Parameters for a linear gradient on HPLC analyzer

Time (min)	**Flow (mL/min)**	**% Buffer A**	**% Buffer B**
0	1.5	100	0
1	1.5	100	0
3	1.5	70a	30a

15	1.5	40a	60a
15.5	2.5	0	100
17	2.5	0	100
17.25	2.5	100	0
23	2.5	100	0
s23.1	1.5	100	0
24	1.5	100	0
25	0.1	100	0

Example 9: Analysis of TREMs via PAGE Purification and Analysis

This example describes the quality control of a synthesized TREM via PAGE Purification and Analysis. Gel purification and analysis of 2'-ACE protected RNA follows standard protocols for denaturing PAGE (Ellington and Pollard (1998) *In Current Protocols in Molecular Biology*, Chanda, V). Briefly, the 2'-ACE protected oligo is resuspended in 200 mL of gel loading buffer. Invitrogen™ NuPAGE™ 4-12% Bis-Tris Gels or similar gel is prepared in gel apparatus. Samples are loaded and gel ran at 50-120 W, maintaining the apparatus at 40°C. When complete, the gel is exposed to ultraviolet (UV) light at 254 nm to visualize the purity of the RNA using UV shadowing. If necessary, the desired gel band is excised with a clean razor blade. The gel slice is crushed and 0.3M NaOAc elution buffer is added to the gel particles, and soaked overnight. The mixture is decanted and filtered through a Sephadex column such as Nap-10 or Nap-25.

Example 10: Deprotection of synthesized TREM

This example describes the deprotection of a TREM made according to an in vitro synthesis method. The 2'-protecting groups are removed using 100 mM acetic acid, pH 3.8. The formic acid and ethylene glycol byproducts are removed by incubating at 60°C for 30 min followed by lyophilization or SpeedVac-ing to dryness. After this final deprotection step, the oligonucleotides are ready for use.

Example 11. Characterization of chemically modified TREMs for readthrough of a premature termination codon (PTC) in a reporter protein

This example describes an assay to test the ability of a non-cognate chemically modified TREM to readthrough a PTC in a cell line expressing a reporter protein having a PTC. This

Example describes analysis of chemically modified arginine, serine, and glutamine non-cognate TREM (i.e., Arg-TGA, Ser-TAG, and Gln-TAA), though a non-cognate TREM specifying any one of the othe amino acids can also be used.

A cell line engineered to stably express the NanoLuc reporter construct containing a premature termination codon (PTC) may be generated using the FlpIn system according to the manufacturer's instructions. Delivery of the chemically modified TREMs into the NanoLuc reporter cells is carried out via a reverse transfection reaction using lipofectamine RNAiMAX (ThermoFisher Scientific, USA) according to manufacturer instructions. Briefly, 5 uL of a 2.5uM solution of chemically modified TREM sample are diluted in a 20uL RNAiMAX/OptiMEM mixture. After 30min gentle mixing at room temperature, the 25uL TREM/transfection mixture is added to a 96-well plate and kept still for 20-30min before adding the cells. The NanoLuc reporter cells are harvested and diluted to 4×10^5 cells/mL in complete growth medium, and 100uL of the diluted cell suspension is added and mixed to the plate containing the TREM. After 24h, 100uL complete growth medium is added to the 96-well plate for cell health.

To monitor the efficacy of the chemically modified TREM to read through the PTC in the reporter construct 48 hours after TREM delivery into cells, a NanoGlo bioluminescent assay (Promega, USA) may be performed according to manufacturer instruction. Briefly, cell media is replaced and allowed to equilibrate to room temperature. NanoGlo reagent is prepared by mixing the buffer with substrate in a 50:1 ratio. 50uL of mixed NanoGlo reagent is added to the 96-well plate and mixed on the shaker at 600rpm for 10min. After 2min, the plate is centrifuged at 1000g, followed by a 5min incubation step at room temperature before measuring sample bioluminescence. As a positive control, a host cell expressing the NanoLuc reporter construct without a PTC is used. As a negative control, a host cell expressing the NanoLuc reporter construct with a PTC is used, but no TREM is transfected. The efficacy of the chemically modified TREMs are measured as a ratio of the NanoLuc luminescence in the experimental sample to the NanoLuc luminescence of the positive control or as a ratio of the NanoLuc luminescence in the experimental sample to the NanoLuc luminescence of the negative control. It is expected that if the sample TREM is functional, it may be able to read-through the stop mutation in the NanoLuc reporter and produce a luminescent reading higher than the luminescent reading measured in the negative control. If the sample TREM is not functional, the stop mutation is not rescued, and luminescence less or equal to the negative control is detected.

The impacts of chemical modification type and position were evaluated in singly and multiply modified TREM sequences as outlined in Table 15-22 below. Tables 15-19 describe the activity of an exemplary chemically modified TREM-Arg-TGA sequence, in which 2'-OMe (Table 15), 2'-F (Table 16), 2'-MOE (Table 17), 2'-deoxy (Table 18), and PS (Table 19) modifications were installed at every position in the TREM sequence. Additional TREM sequences were also modified at every position with a 2'-OMe modification, namely Ser-TAG (Table 20) and Gln-TAA (Table 21). In addition, a selection of multiply modified TREM sequences were prepared according to Examples 1 and 9 and tested as outlined herein; these data are summarized in Table 22. In these tables, the sequences are annotated as follows: r: ribonucleotide; m: 2'-OMe; *: PS linkage; f: 2'-fluoro; moe: 2'-moe; d: deoxyribonucleotide; 5MeC: 5-methylcytosine. Thus, for example, mA represents 2'-O-methyl adenosine, moe5MeC represents 2'-MOE nucleotide with 5-methylcytosine nucleobase, and dA represents an adenosine deoxyribonucleotide.

In addition, in these tables, the results of the activity screen are reported as log2 fold changes compared with the appropriate unmodified TREM, wherein "1" indicates less than a -0.05 log2 fold change; "2" indicates greater than or equal to -0.05 and less than 0.55 log2 fold change; and "3" indicates greater than or equal to 0.55 log2 fold change. The results for the all the singly modified TREM-Arg-TGA screens is compared in FIG. 1. The results show that certain modifications were tolerated at many positions, but particular sites were sensitive to modification or exhibited improved activity when modified. For example, neither 2'-OMe and 2'-MOE were tolerated at positions 33 in the Arg-TGA sequence, yet 2'-F and 2'-deoxy (DNA) improved the activity at positions 33. 2'OMe was particularly active at positions 1 and 73. 2'-deoxy (DNA) was also well tolerated at position 31. PS modification improved activity when incorporated in-between positions 35 and 36, in-between 37 and 38, in-between 38 and 39, in-between 54 and 55, and in-between positions 55 and 56.

Table 15: 2'OMe-Modified TREMs (TREM-Arg-TGA) and related data

SEQ ID NO.	Mod	Sequence	Calculated MW	Detected MW	Results
622		rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGr	24509.24	24508	2

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
623	OME 1	mGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24526.4	3
624	OME 2	rGmGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24516.6	3
625	OME 3	rGrGmCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24526.6	2
626	OME 4	rGrGrCmUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24517.6	3
627	OME 5	rGrGrCrUmCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24516.5	2
628	OME 6	rGrGrCrUrCmCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24511	3
629	OME 7	rGrGrCrUrCrCmGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24516.5	1
630	OME 8	rGrGrCrUrCrCrGmUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24523.21	24511.6	1

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
631	OME 9	rGrGrCrUrCrCrGrUmGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24514.9	1
632	OME 10	rGrGrCrUrCrCrGrUrGmGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24535.3	3
633	OME 11	rGrGrCrUrCrCrGrUrGrGmCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24532.9	2
634	OME 12	rGrGrCrUrCrCrGrUrGrGrCmGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24530.5	3
635	OME 13	rGrGrCrUrCrCrGrUrGrGrCrGmCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.9	3
636	OME 14	rGrGrCrUrCrCrGrUrGrGrCrGrCm ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24530	2
637	OME 15	rGrGrCrUrCrCrGrUrGrGrCrGrCr AmArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24531.3	2

638	OME 16	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArAmUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24530.2	2
639	OME 17	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUmGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24530	3
640	OME 18	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGmGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24530.3	3
641	OME 19	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGmArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24531	1
642	OME 20	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrAmUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24531.5	3
643	OME 21	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUmArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24521.2	1
644	OME 22	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrAmGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.8	3
645	OME 23	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGmCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24523.24	24529.9	2

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
646	OME 24	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCmGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.7	2
647	OME 25	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGmCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.9	2
648	OME 26	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCmAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.3	1
649	OME 27	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAm UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24529.7	2
650	OME 28	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UmUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24529.9	2
651	OME 29	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUmGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.8	3
652	OME 30	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGmGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24530	3
653	OME 31	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24523.24	24529.8	1

		UrUrGrGmArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
654	OME 32	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrAmCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24522.68	24524.9	1
655	OME 33	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCmUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24529.9	1
656	OME 34	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUmUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24529.8	1
657	OME 35	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUmCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24522.68	24530	1
658	OME 36	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCmArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.8	1
659	OME 37	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrAmArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24530	1
660	OME 38	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArAmArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.7	1

661	OME 39	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArAmUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24529.7	1
662	OME 40	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUm UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24529.5	1
663	OME 41	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UmCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24531.3	2
664	OME 42	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCmArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.9	3
665	OME 43	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrAmArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24531.9	3
666	OME 44	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArAmArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24529.6	2
667	OME 45	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArAmGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24531	3
668	OME 46	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGmGrUrUrCrCrGrGr	24523.24	24531.6	1

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
669	OME 47	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGmUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24530.5	1
670	OME 48	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUmUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.21	24511.6	2
671	OME 49	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUmCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24514.6	2
672	OME 50	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCmCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24512.7	3
673	OME 51	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCmGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24519.7	2
674	OME 52	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGmGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24517.3	3
675	OME 53	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGm GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24523.24	24520.5	2
676	OME 54	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24523.21	24516.7	2

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GmUrUrCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA			
677	OME 55	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUmUrCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.21	24521.6	1
678	OME 56	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUmCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24515.3	3
679	OME 57	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCmGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24523.7	2
680	OME 58	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGmArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24516.6	1
681	OME 59	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrAmGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24532.2	3
682	OME 60	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGmUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.21	24516.5	1
683	OME 61	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUmCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24520.7	3

684	OME 62	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCmCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24516.8	2
685	OME 63	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCmCrGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24523.2	1
686	OME 64	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCmGrGr CrGrGrArGrUrCrGrCrCrA	24523.24	24529.6	2
687	OME 65	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGmGr CrGrGrArGrUrCrGrCrCrA	24523.24	24530.9	3
688	OME 66	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGm CrGrGrArGrUrCrGrCrCrA	24523.24	24523.2	3
689	OME 67	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC mGrGrArGrUrCrGrCrCrA	24523.24	24530	2
690	OME 68	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGmGrArGrUrCrGrCrCrA	24523.24	24521.2	3
691	OME 69	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24523.24	24530.4	3

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGmArGrUrCrGrCrCrA			
692	OME 70	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrAmGrUrCrGrCrCrA	24523.24	24521.1	1
693	OME 71	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGmUrCrGrCrCrA	24523.21	24530.5	3
694	OME 72	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUmCrGrCrCrA	24523.24	24520.2	3
695	OME 73	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCmGrCrCrA	24523.24	24530.6	3
696	OME 74	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGmCrCrA	24523.24	24519.1	2
697	OME 75	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCmCrA	24523.24	24531.5	2
698	OME 76	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCmA	24523.24	24520.2	2

Table 16: 2'F-Modified TREMs (TREM-Arg-TGA) and related data

SEQ ID NO.	Mod	Sequence	Calculated MW	Detected MW	Results
699	F 1	fGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24513.3	2
700	F 2	rGfGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.7	2
701	F 3	rGrGfCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24509.1	1
702	F 4	rGrGrCfUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24514	1
703	F 5	rGrGrCrUfCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24515	1
704	F 6	rGrGrCrUrCfCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24513.8	1
705	F 7	rGrGrCrUrCrCfGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24516.7	1

706	F 8	rGrGrCrUrCrCrGfUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24517	1
707	F 9	rGrGrCrUrCrCrGrUfGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.4	1
708	F 10	rGrGrCrUrCrCrGrUrGfGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.2	2
709	F 11	rGrGrCrUrCrCrGrUrGrGfCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24517.6	2
710	F 12	rGrGrCrUrCrCrGrUrGrGrCfGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.1	2
711	F 13	rGrGrCrUrCrCrGrUrGrGrCrGfCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.3	2
712	F 14	rGrGrCrUrCrCrGrUrGrGrCrGrCf ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.1	2
713	F 15	rGrGrCrUrCrCrGrUrGrGrCrGrCr AfArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24510.68	24519.2	2

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
714	F 16	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArAfUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.5	2
715	F 17	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUfGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519.3	1
716	F 18	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGfGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.6	2
717	F 19	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGfArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24517.5	2
718	F 20	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrAfUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.4	3
719	F 21	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUfArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24519	1
720	F 22	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrAfGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24517.5	2
721	F 23	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGfCrGrCrAr	24510.67	24517.2	2

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
722	F 24	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCfGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519.3	1
723	F 25	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGfCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.6	2
724	F 26	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCfAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24514.8	1
725	F 27	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAf UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24519.2	1
726	F 28	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UfUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.5	2
727	F 29	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUfGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.3	3
728	F 30	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGfGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24517.9	2

729	F 31	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGfArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24517.4	1
730	F 32	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrAfCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.1	1
731	F 33	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCfUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24517.7	3
732	F 34	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUfUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.8	1
733	F 35	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUfCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519	1
734	F 36	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCfArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.7	1
735	F 37	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrAfArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24517.6	1
736	F 38	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArAfArUr UrCrArArArGrGrUrUrCrCrGrGr	24510.68	24518.4	1

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
737	F 39	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArAfUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24519.8	1
738	F 40	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUf UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24508.1	3
739	F 41	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UfCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519.7	3
740	F 42	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCfArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24519.8	2
741	F 43	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrAfArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.5	2
742	F 44	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArAfArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24519	3
743	F 45	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArAfGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24517.7	3
744	F 46	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24510.67	24518.8	2

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGfGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
745	F 47	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGfUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.6	2
746	F 48	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGrUfUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.5	3
747	F 49	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGrUrUfCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519.4	3
748	F 50	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGrUrUrCfCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.6	3
749	F 51	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGrUrUrCrCfGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.2	1
750	F 52	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGrUrUrCrCrGfGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519.1	3
751	F 53	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrGrUrUrCrCrGrGf GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.7	3

752	F 54	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GfUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.9	3
753	F 55	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUfUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24520.3	1
754	F 56	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUfCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.6	3
755	F 57	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCfGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.2	2
756	F 58	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGfArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518	1
757	F 59	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrAfGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.5	3
758	F 60	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGfUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.68	24518.2	2
759	F 61	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24510.67	24517.7	3

		GrUrUrCrGrArGrUfCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
760	F 62	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCfCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519.8	3
761	F 63	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCfCrGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.4	3
762	F 64	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCfGrGrC rGrGrArGrUrCrGrCrCrA	24510.67	24519	2
763	F 65	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGfGrC rGrGrArGrUrCrGrCrCrA	24510.67	24518.2	3
764	F 66	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGfC rGrGrArGrUrCrGrCrCrA	24510.67	24519.1	2
765	F 67	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC fGrGrArGrUrCrGrCrCrA	24510.67	24518.5	3
766	F 68	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGfGrArGrUrCrGrCrCrA	24510.67	24518.2	3
767	F 69	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24510.68	24519.4	3

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGfArGrUrCrGrCrCrA			
768	F 70	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrAfGrUrCrGrCrCrA	24510.67	24518.4	2
769	F 71	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGfUrCrGrCrCrA	24510.68	24520.2	3
770	F 72	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUfCrGrCrCrA	24510.67	24518.4	3
771	F 73	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCfGrCrCrA	24510.67	24517.9	1
772	F 74	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGfCrCrA	24510.67	24518.2	2
773	F 75	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCfCrA	24510.67	24518.2	3
774	F 76	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCfA	24510.68	24518.3	3

Table 17: 2'MOE-Modified TREMs (TREM-Arg-TGA) and related data

SEQ ID NO.	Mod	Sequence	Calculated MW	Detected MW	Results
775	MOE 1	moeGrGrCrUrCrCrGrUrGrGrCrGr CrArArUrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24565.5	3
776	MOE 2	rGmoeGrCrUrCrCrGrUrGrGrCrGr CrArArUrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24565.4	2
777	MOE 3	rGrGmoe5MeCrUrCrCrGrUrGrGr CrGrCrArArUrGrGrArUrArGrCr GrCrArUrUrGrGrArCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24580.5	2
778	MOE 4	rGrGrCmoeTrCrCrGrUrGrGrCrGr CrArArUrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24579.3	3
779	MOE 5	rGrGrCrUmoe5MeCrCrGrUrGrGr CrGrCrArArUrGrGrArUrArGrCr GrCrArUrUrGrGrArCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24579.6	1
780	MOE 6	rGrGrCrUrCmoe5MeCrGrUrGrGr CrGrCrArArUrGrGrArUrArGrCr GrCrArUrUrGrGrArCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24579.6	2
781	MOE 10	rGrGrCrUrCrCrGrUrGmoeGrCrGr CrArArUrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr	24566.69	24568.3	2

		GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA			
782	MOE 11	rGrGrCrUrCrCrGrUrGrGmoe5Me CrGrCrArArUrGrGrArUrArGrCr GrCrArUrUrGrGrArCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24579	1
783	MOE 12	rGrGrCrUrCrCrGrUrGrGrCmoeGr CrArArUrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.6	2
784	MOE 13	rGrGrCrUrCrCrGrUrGrGrCrGmoe 5MeCrArArUrGrGrArUrArGrCrG rCrArUrUrGrGrArCrUrUrCrArAr ArUrUrCrArArArGrGrUrUrCrCr GrGrGrUrUrCrGrArGrUrCrCrCrG rGrCrGrGrArGrUrCrGrCrCrA	24580.68	24580	2
785	MOE 14	rGrGrCrUrCrCrGrUrGrGrCrGrCm oeArArUrGrGrArUrArGrCrGrCrA rUrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24566.69	24567.7	3
786	MOE 15	rGrGrCrUrCrCrGrUrGrGrCrGrCr AmoeArUrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24561.7	3
787	MOE 16	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArAmoeTrGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24581.7	3
788	MOE 17	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUmoeGrGrArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.4	3
789	MOE 18	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGmoeGrArUrArGrCrGrCr	24566.69	24568.6	2

		ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA			
790	MOE 19	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGmoeArUrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24563.8	1
791	MOE 20	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrAmoeTrArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24580.2	3
792	MOE 21	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUmoeArGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24565.4	1
793	MOE 22	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrAmoeGrCrGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.2	1
794	MOE 23	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGmoe5MeCr GrCrArUrUrGrGrArCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24579.5	1
795	MOE 24	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCmoeGrCr ArUrUrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24567.3	1
796	MOE 25	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGmoe5 MeCrArUrUrGrGrArCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24578.8	2

797	MOE 27	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAm oeTrUrGrGrArCrUrUrCrArArArU rUrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24580.69	24580.3	2
798	MOE 28	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UmoeTrGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24582.9	1
799	MOE 29	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUmoeGrGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24568.3	3
800	MOE 30	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGmoeGrArCrUrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24567.7	2
801	MOE 32	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrAmoe5MeCrUrUrCrAr ArArUrUrCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24580.4	1
802	MOE 33	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCmoeTrUrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24574.5	1
803	MOE 34	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUmoeTrCrArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24581.3	1
804	MOE 35	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUmoe5MeCrAr ArArUrUrCrArArArGrGrUrUrCr	24580.68	24581	1

		CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA			
805	MOE 36	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCmoeArArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.6	1
806	MOE 37	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrAmoeArAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24572.4	1
807	MOE 38	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArAmoeAr UrUrCrArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24561.6	1
808	MOE 41	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr Umoe5MeCrArArArGrGrUrUrCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24583.5	1
809	MOE 42	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCmoeArArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.9	1
810	MOE 43	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrAmoeArArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.9	2
811	MOE 44	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArAmoeArGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.9	3
812	MOE 45	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24566.69	24561	3

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArAmoeGrGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA			
813	MOE 46	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGmoeGrUrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24560.1	1
814	MOE 47	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGmoeTrUrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24575.8	3
815	MOE 48	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUmoeTrCrCrGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24580.69	24580.5	1
816	MOE 49	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUmoe5MeCr CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24578.4	3
817	MOE 50	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCmoe5Me CrGrGrGrUrUrCrGrArGrUrCrCrC rGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24578.8	3
818	MOE 51	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCmoeGr GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24567.5	1
819	MOE 52	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGmoe GrGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24567.2	3

820	MOE 53	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGm oeGrUrUrCrGrArGrUrCrCrCrGrG rCrGrGrArGrUrCrGrCrCrA	24566.69	24566.8	2
821	MOE 54	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GmoeTrUrCrGrArGrUrCrCrCrGr GrCrGrGrArGrUrCrGrCrCrA	24580.69	24582.3	3
822	MOE 55	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUmoeTrCrGrArGrUrCrCrCrGr GrCrGrGrArGrUrCrGrCrCrA	24580.69	24575.3	1
823	MOE 56	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUmoe5MeCrGrArGrUrCrCr CrGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24581.5	3
824	MOE 57	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCmoeGrArGrUrCrCrCrGr GrCrGrGrArGrUrCrGrCrCrA	24566.69	24565.3	3
825	MOE 58	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGmoeArGrUrCrCrCrGr GrCrGrGrArGrUrCrGrCrCrA	24566.69	24570.7	1
826	MOE 59	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrAmoeGrUrCrCrCrGr GrCrGrGrArGrUrCrGrCrCrA	24566.69	24562.1	3
827	MOE 60	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24580.69	24581	1

		GrUrUrCrGrArGmoeTrCrCrCrGr GrCrGrGrArGrUrCrGrCrCrA			
828	MOE 61	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUmoe5MeCrCr CrGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24579.7	1
829	MOE 62	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCmoe5MeCr CrGrGrCrGrGrArGrUrCrGrCrCrA	24580.68	24579.3	1
830	MOE 64	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCmoeGr GrCrGrGrArGrUrCrGrCrCrA	24566.69	24567.3	1
831	MOE 65	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGmoe GrCrGrGrArGrUrCrGrCrCrA	24566.69	24563.6	3
832	MOE 66	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGm oe5MeCrGrGrArGrUrCrGrCrCrA	24580.68	24577.9	1
833	MOE 67	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC moeGrGrArGrUrCrGrCrCrA	24566.69	24566.7	1
834	MOE 68	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGmoeGrArGrUrCrGrCrCrA	24566.69	24567.3	2
835	MOE 69	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24566.69	24565.9	1

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGmoeArGrUrCrGrCrCrA			
836	MOE 71	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGmoeTrCrGrCrCrA	24580.69	24579.5	1
837	MOE 72	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUmoe5MeCrGrCrCrA	24580.68	24583.5	3
838	MOE 73	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCmoeGrCrCrA	24566.69	24569.6	3
839	MOE 74	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGmoe5MeCrCrA	24580.68	24580.9	1
840	MOE 75	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCmoe5MeCrA	24580.68	24579.7	2
841	MOE 76	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCmoeA	24566.69	24568.2	2

Table 18: 2'-Deoxy-Modified TREMs (TREM-Arg-TGA) and related data

SEQ ID NO.	**Mod**	**Sequence**	**Calculated MW**	**Detected MW**	**Results**

842	DNA 1	dGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24493.1	2
843	DNA 2	rGdGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24493	2
844	DNA 3	rGrGdCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24491.8	3
845	DNA 4	rGrGrCdUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24490.9	3
846	DNA 5	rGrGrCrUdCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24492.5	3
847	DNA 6	rGrGrCrUrCdCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24491.4	3
848	DNA 7	rGrGrCrUrCrCdGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24492.4	1
849	DNA 8	rGrGrCrUrCrCrGdUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24492.69	24493.5	1

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
850	DNA 9	rGrGrCrUrCrCrGrUdGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.2	1
851	DNA 10	rGrGrCrUrCrCrGrUrGdGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.9	1
852	DNA 11	rGrGrCrUrCrCrGrUrGrGdCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24491.5	2
853	DNA 12	rGrGrCrUrCrCrGrUrGrGrCdGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.4	2
854	DNA 13	rGrGrCrUrCrCrGrUrGrGrCrGdCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24491.6	2
855	DNA 14	rGrGrCrUrCrCrGrUrGrGrCrGrCd ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24497.4	3
856	DNA 15	rGrGrCrUrCrCrGrUrGrGrCrGrCr AdArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24497.3	3
857	DNA 16	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArAdUrGrGrArUrArGrCrGrCrAr	24492.69	24497.3	3

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
858	DNA 17	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUdGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24497.3	2
859	DNA 18	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGdGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24492.7	2
860	DNA 19	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGdArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24497.3	1
861	DNA 20	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrAdUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24497.8	3
862	DNA 21	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUdArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24494.8	1
863	DNA 22	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrAdGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.2	3
864	DNA 23	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGdCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24491.7	3

865	DNA 24	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCdGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24490.7	1
866	DNA 25	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGdCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24491.8	2
867	DNA 26	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCdAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24494.3	2
868	DNA 27	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAd UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24504.9	2
869	DNA 28	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UdUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24493.8	1
870	DNA 29	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUdGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24494.2	2
871	DNA 30	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGdGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24492.6	2
872	DNA 31	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGdArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24492.69	24492.2	1

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
873	DNA 32	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrAdCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24490.7	2
874	DNA 33	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCdUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24490.5	3
875	DNA 34	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUdUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24490.7	1
876	DNA 35	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUdCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24494.9	1
877	DNA 36	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCdArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491	1
878	DNA 37	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrAdArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24495.2	1
879	DNA 38	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArAdArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24494.4	2
880	DNA 39	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24492.69	24490.5	1

		UrUrGrGrArCrUrUrCrArArAdUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
881	DNA 40	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUd UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24490.2	2
882	DNA 41	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UdCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24494.2	2
883	DNA 42	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCdArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.6	2
884	DNA 43	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrAdArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24493.7	1
885	DNA 44	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArAdArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.4	2
886	DNA 45	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArAdGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24493.1	1
887	DNA 46	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGdGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24494	1

888	DNA 47	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGdUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.1	2
889	DNA 48	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUdUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24490	2
890	DNA 49	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUdCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24494.4	2
891	DNA 50	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCdCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.71	24494	1
892	DNA 51	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCdGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24497.3	1
893	DNA 52	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGdGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.9	1
894	DNA 53	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGd GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24492.69	24491.3	1
895	DNA 54	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24492.69	24489.7	3

		GdUrUrCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA			
896	DNA 55	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUdUrCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.69	24490.8	1
897	DNA 56	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUdCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.71	24493	2
898	DNA 57	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCdGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.69	24494.9	1
899	DNA 58	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGdArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.69	24493.4	2
900	DNA 59	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrAdGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.69	24491.3	3
901	DNA 60	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGdUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.69	24490.3	2
902	DNA 61	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUdCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.71	24493.3	2
903	DNA 62	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24492.71	24494.6	3

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCdCrCrGrGr CrGrGrArGrUrCrGrCrCrA			
904	DNA 63	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCdCrGrGr CrGrGrArGrUrCrGrCrCrA	24492.71	24491.7	3
905	DNA 64	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCdGrGr CrGrGrArGrUrCrGrCrCrA	24492.69	24491.8	2
906	DNA 65	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGdGr CrGrGrArGrUrCrGrCrCrA	24492.69	24491.9	2
907	DNA 66	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGd CrGrGrArGrUrCrGrCrCrA	24492.71	24491.5	2
908	DNA 67	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC dGrGrArGrUrCrGrCrCrA	24492.69	24491.5	2
909	DNA 68	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGdGrArGrUrCrGrCrCrA	24492.69	24490.5	1
910		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGdArGrUrCrGrCrCrA	24492.69	24494.2	

911	DNA 70	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrAdGrUrCrGrCrCrA	24492.69	24500.8	2
912	DNA 71	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGdUrCrGrCrCrA	24492.69	24491.1	2
913	DNA 72	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUdCrGrCrCrA	24492.71	24501.2	3
914	DNA 73	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCdGrCrCrA	24492.69	24501.4	1
915	DNA 74	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGdCrCrA	24492.71	24499.8	2
916	DNA 75	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCdCrA	24492.71	24501.9	2
917	DNA 76	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCdA	24492.69	24501.9	3

Table 19: Phosphorothioate-Modified TREMs (TREM-Arg-TGA) and related data

SEQ ID NO.	Mod	Sequence	Calculated MW	Detected MW	Results
918	PS 1	rG*rGrCrUrCrCrGrUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24525.3	24528.7	3
919	PS 2	rGrG*rCrUrCrCrGrUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24525.3	24532.7	3
920	PS 3	rGrGrC*rUrCrCrGrUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24525.3	24521.1	3
921		rGrGrCrU*rCrCrGrUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24532.3	
922		rGrGrCrUrC*rCrGrUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24532.4	
923	PS 6	rGrGrCrUrCrC*rGrUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.8	1
924		rGrGrCrUrCrCrG*rUrGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.4	
925	PS 8	rGrGrCrUrCrCrGrU*rGrGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr	24524.68	24529.8	1

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
926	PS 9	rGrGrCrUrCrCrGrUrG*rGrCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24531.1	3
927	PS 10	rGrGrCrUrCrCrGrUrGrG*rCrGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.8	2
928	PS 11	rGrGrCrUrCrCrGrUrGrGrC*rGrC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24532.4	1
929	PS 12	rGrGrCrUrCrCrGrUrGrGrCrG*rC rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24531.2	1
930	PS 13	rGrGrCrUrCrCrGrUrGrGrCrGrC* rArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.9	1
931	PS 14	rGrGrCrUrCrCrGrUrGrGrCrGrCr A*rArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530	3
932	PS 15	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArA*rUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24531.5	3

933	PS 16	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArU*rGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530	3
934	PS 17	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrG*rGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530	3
935	PS 18	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrG*rArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530	3
936	PS 19	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrA*rUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24525.3	24519.6	3
937	PS 20	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArU*rArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530	3
938	PS 21	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrA*rGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530	3
939	PS 22	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArG*rCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24531.5	2
940		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrC*rGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24524.68	24530.5	

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
941	PS 24	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrG*rCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24531.9	2
942	PS 25	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrC*rAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24528.8	2
943	PS 26	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrA*r UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24531.4	2
944	PS 27	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr U*rUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.8	2
945	PS 28	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrU*rGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.4	1
946	PS 29	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrG*rGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.6	2
947	PS 30	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrG*rArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.6	2
948	PS 31	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24524.68	24529.3	2

		UrUrGrGrA*rCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
949	PS 32	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArC*rUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24523.9	1
950	PS 33	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrU*rUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24518.8	2
951	PS 34	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrU*rCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24524.9	1
952	PS 35	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrC*rArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24524.8	3
953	PS 36	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrA*rArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24518.4	1
954	PS 37	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArA*rArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24524.7	3
955	PS 38	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArA*rUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24519.4	3

956	PS 39	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArU*r UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.7	1
957		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr U*rCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.8	
958	PS 41	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrC*rArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.9	2
959		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrA*rArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.8	
960	PS 43	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArA*rArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.4	2
961	PS 44	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArA*rGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24518.4	3
962	PS 45	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArG*rGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.7	3
963	PS 46	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrG*rUrUrCrCrGrGr	24524.68	24520.2	3

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA			
964	PS 47	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrU*rUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24528.3	2
965	PS 48	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrU*rCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24518.7	1
966	PS 49	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrC*rCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24529.6	2
967		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrC*rGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24530.4	
968		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrG*rGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24528.8	
969	PS 52	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrG*r GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrCrA	24524.68	24526	3
970		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr G*rUrUrCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24530.7	
971	PS 54	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr	24524.68	24528.5	3

		UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrU*rUrCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA			
972	PS 55	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrU*rCrGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24529.7	3
973	PS 56	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrC*rGrArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24529.4	3
974	PS 57	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrG*rArGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24529.5	3
975	PS 58	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrA*rGrUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24525.3	24520.8	3
976	PS 59	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArG*rUrCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24529.8	2
977	PS 60	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrU*rCrCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24528.3	2
978	PS 61	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrC*rCrCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24529.4	2

979	PS 62	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrC*rCrGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24530.7	2
980	PS 63	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrC*rGrGr CrGrGrArGrUrCrGrCrCrA	24524.68	24528.3	1
981	PS 64	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrG*rGr CrGrGrArGrUrCrGrCrCrA	24524.68	24524.9	1
982	PS 65	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrG*r CrGrGrArGrUrCrGrCrCrA	24524.68	24523.8	2
983	PS 66	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC *rGrGrArGrUrCrGrCrCrA	24524.68	24524.4	1
984		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rG*rGrArGrUrCrGrCrCrA	24524.68	24524.7	
985		rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrG*rArGrUrCrGrCrCrA	24524.68	24524.3	
986	PS 69	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr	24524.68	24522.6	2

		GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrA*rGrUrCrGrCrCrA			
987	PS 70	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArG*rUrCrGrCrCrA	24524.68	24524.9	2
988	PS 71	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrU*rCrGrCrCrA	24524.68	24525.1	2
989	PS 72	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrC*rGrCrCrA	24524.68	24525.3	2
990	PS 73	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrG*rCrCrA	24525.3	24520.4	3
991	PS 74	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrC*rCrA	24525.3	24533.1	3
992	PS 75	rGrGrCrUrCrCrGrUrGrGrCrGrCr ArArUrGrGrArUrArGrCrGrCrAr UrUrGrGrArCrUrUrCrArArArUr UrCrArArArGrGrUrUrCrCrGrGr GrUrUrCrGrArGrUrCrCrCrGrGrC rGrGrArGrUrCrGrCrC*rA	24525.3	24533.2	2

Table 20: 2'OMe-Modified TREMs (TREM-Ser-TAG) and related data

SEQ ID NO.	**Mod**	**Sequence**	**Calculated MW**	**Detected MW**	**Results**
993		rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr	27323.32	27329.5	2

		CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA			
994	OME 1	mGrArCrGrArGrGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27343.3	3
995	OME 2	rGmArCrGrArGrGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27342.9	2
996	OME 3	rGrAmCrGrArGrGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27342.3	1
997	OME 4	rGrArCmGrArGrGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27339.3	3
998	OME 5	rGrArCrGmArGrGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.7	3
999	OME 6	rGrArCrGrAmGrGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.8	1

1000	OME 7	rGrArCrGrArGmGrUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27341.2	1
1001	OME 8	rGrArCrGrArGrGmUrGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27341.4	1
1002	OME 9	rGrArCrGrArGrGrUmGrGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.5	1
1003	OME 10	rGrArCrGrArGrGrUrGmGrCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.4	2
1004	OME 11	rGrArCrGrArGrGrUrGrGmCrCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27339.3	1
1005	OME 12	rGrArCrGrArGrGrUrGrGrCmCrG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27336.2	1
1006	OME 13	rGrArCrGrArGrGrUrGrGrCrCmG rArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC	27337.32	27344.3	1

		rArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA			
1007	OME 14	rGrArCrGrArGrGrUrGrGrCrCrGmArGrUrGrGrUrUrArArGrGrCrGrArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27332.8	1
1008	OME 15	rGrArCrGrArGrGrUrGrGrCrCrGrAmGrUrGrGrUrUrArArGrGrCrGrArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337.7	1
1009	OME 16	rGrArCrGrArGrGrUrGrGrCrCrGrArGmUrGrGrUrUrArArGrGrCrGrArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27338.7	1
1010	OME 17	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUmGrGrUrUrArArGrGrCrGrArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27338	2
1011	OME 18	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGmGrUrUrArArGrGrCrGrArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27339	2
1012	OME 19	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGmUrUrArArGrGrCrGrArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27338.1	1

1013	OME 20	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUmUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.2	1
1014	OME 21	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUmArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27337.3	1
1015	OME 22	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrAmArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27337	1
1016	OME 23	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArAmGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.3	1
1017	OME 24	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGmGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27340.9	2
1018	OME 25	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGmCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27337.8	1
1019	OME 26	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCmGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC	27337.32	27336.8	1

		rArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA			
1020	OME 27	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGmArUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27339.7	2
1021	OME 28	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrAmUrGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337.9	1
1022	OME 29	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUmGrGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337.8	2
1023	OME 30	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGmGrArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337.5	2
1024	OME 31	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGmArCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337.7	1
1025	OME 32	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrAmCrUrCrUrArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27340.4	2

1026	OME 33	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCmUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27336.2	1
1027	OME 34	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUmCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.4	3
1028	OME 35	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCmUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.8	1
1029	OME 36	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUmArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338.1	1
1030	OME 37	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrAmArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27338	1
1031	OME 38	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArAmArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCrA	27337.32	27340.8	3
1032	OME 39	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArAmUr CrCrArUrUrGrUrGrCrUrCrUrGrC	27337.32	27337.7	3

		rArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA			
1033	OME 40	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArCrUrCrUrArArArArUmCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27336.6	2
1034	OME 41	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArCrUrCrUrArArArArUrCmCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337	2
1035		rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArCrUrCrUrArArArArUrCrCmArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27337.7	
1036	OME 43	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArCrUrCrUrArArArArUrCrCrAmUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27338.3	2
1037	OME 44	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArCrUrCrUrArArArArUrCrCrArUmUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27338.3	1
1038	OME 45	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArCrUrCrUrArArArArUrCrCrArUrUmGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGrCrCrA	27337.32	27338.1	1

1039	OME 46	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGmUrGrCrUrCrUrGr CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.3	2
1040	OME 47	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUmGrCrUrCrUrGr CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.2	2
1041	OME 48	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGmCrUrCrUrGr CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338	1
1042	OME 49	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCmUrCrUrGr CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.6	1
1043	OME 50	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUmCrUrGr CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.8	1
1044	OME 51	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCmUrGr CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.4	1
1045	OME 52	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUmGr	27337.32	27336.7	1

		CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA			
1046	OME 53	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGm CrArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27341.4	1
1047	OME 54	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC mArCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27341.3	1
1048	OME 55	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rAmCrGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.6	1
1049	OME 56	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCmGrCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.7	1
1050	OME 57	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGmCrGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.1	1
1051	OME 58	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCmGrUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.6	1

1052	OME 59	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGmUrGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.6	2
1053	OME 60	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUmGrGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.7	1
1054	OME 61	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGmGrGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.4	3
1055	OME 62	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGmGrUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.2	1
1056	OME 63	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGmUrUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.3	1
1057	OME 64	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUmUrCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.9	1
1058	OME 65	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC	27337.32	27338.2	1

		rArCrGrCrGrUrGrGrGrUrUmCrG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA			
1059	OME 66	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCmG rArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336	1
1060	OME 67	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrG mArArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.5	1
1061	OME 68	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr AmArUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.9	1
1062	OME 69	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArAmUrCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27341.1	1
1063	OME 70	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUmCrCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.9	1
1064	OME 71	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCmCrCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.1	1

1065	OME 72	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCmCrArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27338.7	1
1066	OME 73	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCmArUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27336.4	2
1067	OME 74	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrAmUrCrCrUrCrGr UrCrGrCrCrA	27337.32	27337.8	1
1068	OME 75	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUmCrCrUrCrGr UrCrGrCrCrA	27337.32	27338	1
1069	OME 76	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCmCrUrCrGr UrCrGrCrCrA	27337.32	27337.6	1
1070	OME 77	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCmUrCrGr UrCrGrCrCrA	27337.32	27335.9	1
1071	OME 78	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC	27337.32	27337.9	1

		rArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUmCrGrUrCrGrCrCrA			
1072	OME 79	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArArCrUrCrUrArArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCmGrUrCrGrCrCrA	27337.32	27336.1	3
1073	OME 80	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArArCrUrCrUrArArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGmUrCrGrCrCrA	27337.32	27337.1	3
1074	OME 81	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArArCrUrCrUrArArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUmCrGrCrCrA	27337.32	27336.5	2
1075	OME 82	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArArCrUrCrUrArArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCmGrCrCrA	27337.32	27336	3
1076	OME 83	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArArCrUrCrUrArArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGmCrCrA	27337.32	27337.4	1
1077	OME 84	rGrArCrGrArGrGrUrGrGrCrCrGrArGrUrGrGrUrUrArArArGrGrCrGrArUrGrGrArArCrUrCrUrArArArArUrCrCrArUrUrGrUrGrCrUrCrUrGrCrArCrGrCrGrUrGrGrGrUrUrCrGrArArUrCrCrCrArUrCrCrUrCrGrUrCrGmCrA	27337.32	27338.7	1

1078	OME 85	rGrArCrGrArGrGrUrGrGrCrCrGr ArGrUrGrGrUrUrArArGrGrCrGr ArUrGrGrArCrUrCrUrArArArUr CrCrArUrUrGrUrGrCrUrCrUrGrC rArCrGrCrGrUrGrGrGrUrUrCrGr ArArUrCrCrCrArUrCrCrUrCrGrU rCrGrCrCmA	27337.32	27337.9	1

Table 21: 2'OMe-Modified TREMs (TREM-Gln-TAA) and related data

SEQ ID NO.	Mod	Sequence	Calculated MW	Detected MW	Results
1079		rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24055.37	24059.2	2
1080	OME 1	mGrGrUrUrCrCrArUrGrGrUrGrU rArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24071.7	3
1081	OME 2	rGmGrUrUrCrCrArUrGrGrUrGrU rArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.8	2
1082	OME 3	rGrGmUrUrCrCrArUrGrGrUrGrU rArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24069.7	1
1083	OME 4	rGrGrUmUrCrCrArUrGrGrUrGrU rArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073	3
1084	OME 5	rGrGrUrUmCrCrArUrGrGrUrGrU rArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU	24069.37	24071.3	2

		rUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA			
1085	OME 6	rGrGrUrUrCmCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24074.2	1
1086	OME 7	rGrGrUrUrCrCmArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24074	1
1087	OME 8	rGrGrUrUrCrCrAmUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24069	1
1088	OME 9	rGrGrUrUrCrCrArUmGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24070.3	1
1089	OME 10	rGrGrUrUrCrCrArUrGmGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24069.2	2
1090	OME 11	rGrGrUrUrCrCrArUrGrGmUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24069.4	1
1091	OME 12	rGrGrUrUrCrCrArUrGrGrUmGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24068.5	3
1092	OME 13	rGrGrUrUrCrCrArUrGrGrUrGmUrArArUrGrGrUrArArGrCrArCrUr	24069.37	24068.4	3

		CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA			
1093	OME 14	rGrGrUrUrCrCrArUrGrGrUrGrU mArArUrGrGrUrArArGrCrArCrU rCrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24070.9	2
1094	OME 15	rGrGrUrUrCrCrArUrGrGrUrGrUr AmArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24068.3	2
1095	OME 16	rGrGrUrUrCrCrArUrGrGrUrGrUr ArAmUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24067.5	2
1096	OME 17	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUmGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24067.6	3
1097	OME 18	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGmGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24067.4	3
1098	OME 19	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGmUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24067.3	1
1099	OME 20	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUmArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24074	1

1100	OME 21	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrAmArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24074.8	1
1101		rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArAmGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.9	
1102	OME 23	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGmCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.8	3
1103	OME 24	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCmArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24075.6	1
1104	OME 25	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrAmCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.4	1
1105	OME 26	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCmUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.8	1
1106	OME 27	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUm CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.8	2
1107	OME 28	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CmUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU	24069.37	24073.8	3

		rUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA			
1108	OME 29	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUmGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24073.7	3
1109	OME 30	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGmGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24073.5	3
1110	OME 31	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGmArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24073.2	1
1111	OME 32	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrAmCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24074.1	1
1112	OME 33	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCmUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24073.7	1
1113	OME 34	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUmUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24074.4	2
1114	OME 35	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUmUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCrA	24069.37	24073.7	1
1115	OME 36	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUr	24069.37	24073.3	1

		CrUrGrGrArCrUrUrUmArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA			
1116	OME 37	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrAmArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.3	1
1117	OME 38	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArAmArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.8	3
1118	OME 39	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArAmUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.6	3
1119	OME 40	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUm CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUrCrCrA	24069.37	24073.3	2
1120	OME 41	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CmCrArGrCrGrArUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24074	3
1121	OME 42	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCmArGrCrGrArUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24073.6	2
1122	OME 43	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrAmGrCrGrArUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24074.3	1

1123	OME 44	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGmCrGrArUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24074.6	3
1124	OME 45	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCmGrArUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24074.5	1
1125	OME 46	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGmArUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24073.5	1
1126	OME 47	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrAmUrCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24073.8	1
1127	OME 48	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUmCrCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24074.2	3
1128	OME 49	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCmCrGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24074.5	3
1129	OME 50	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCmGrArGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24073.5	2
1130	OME 51	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGmArGr	24069.37	24074.5	3

		UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA			
1131	OME 52	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrAmGr UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24072.4	3
1132	OME 53	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGm UrUrCrGrArGrUrCrUrCrGrGrUr GrGrArArCrCrUrCrCrA	24069.37	24069.5	3
1133	OME 54	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU mUrCrGrArGrUrCrUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24068.7	1
1134	OME 55	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUmCrGrArGrUrCrUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24068.3	2
1135	OME 56	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCmGrArGrUrCrUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24069.5	2
1136	OME 57	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGmArGrUrCrUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24068.2	1
1137	OME 58	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrAmGrUrCrUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24067.8	3
1138	OME 59	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr	24069.37	24068.2	1

		CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGmUrCrUrCrGrGrUrG rGrArArCrCrUrCrCrA			
1139	OME 60	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUmCrUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24068	3
1140	OME 61	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCmUrCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24068.1	3
1141	OME 62	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUmCrGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24068.1	1
1142	OME 63	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCmGrGrUrG rGrArArCrCrUrCrCrA	24069.37	24067.6	3
1143	OME 64	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGmGrUrG rGrArArCrCrUrCrCrA	24069.37	24069.3	3
1144	OME 65	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGmUrG rGrArArCrCrUrCrCrA	24069.37	24067.3	3
1145	OME 66	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUmG rGrArArCrCrUrCrCrA	24069.37	24068.7	3

1146	OME 67	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrG mGrArArCrCrUrCrCrA	24069.37	24067	2
1147	OME 68	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GmArArCrCrUrCrCrA	24069.37	24068.3	3
1148	OME 69	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrAmArCrCrUrCrCrA	24069.37	24067.6	3
1149	OME 70	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArAmCrCrUrCrCrA	24069.37	24067	1
1150	OME 71	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCmCrUrCrCrA	24069.37	24067.2	3
1151	OME 72	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCmUrCrCrA	24069.37	24066.9	3
1152	OME 73	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU rUrCrGrArGrUrCrUrCrGrGrUrGr GrArArCrCrUmCrCrA	24069.37	24067	3
1153	OME 74	rGrGrUrUrCrCrArUrGrGrUrGrUr ArArUrGrGrUrArArGrCrArCrUr CrUrGrGrArCrUrUrUrArArArUr CrCrArGrCrGrArUrCrCrGrArGrU	24069.37	24067.6	3

		rUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCmCrA			
1154	OME 75	rGrGrUrUrCrCrArUrGrGrUrGrUrArArUrGrGrUrArArGrCrArCrUrCrUrGrGrArCrUrUrUrArArArUrCrCrArGrCrGrArUrCrCrGrArGrUrUrCrGrArGrUrCrUrCrGrGrUrGrGrArArCrCrUrCrCmA	24069.37	24067.3	3

Table 22: Additional modified TREMs (TREM-Arg-TGA) and related data

SEQ ID NO.	Mod	Sequence	Calculated MW	Detected MW	Results
1155	CCA	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrG	23569.11	23574.5	3
1156	m1,m73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrCrA	24536.69	24536.1	3
1157	m1,m52,m73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrGmGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrCrA	24550.69	24548.1	3
1158	m1,m50,m52,m73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCmCrGmGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrCrA	24564.69	24564.3	3
1159	m1,m18,m50,m52,m73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGmGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCmCrGmGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrCrA	24578.69	24585.7	3
1160	m8,m52	rGrGrCrUrCrCrGmUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrGmGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrGrCrCrA	24536.69	24536.7	3

1161	m1,m17,m18,m50,m52,m73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUmGmGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCmCrGmGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrCrA	24592.7	24591.3	3
1162	m39,m52	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArAmUrUrCrArArArGrGrUrUrCrCrGmGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrGrCrCrA	24536.69	24539.1	2
1163	m52,m62	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGmGrGrUrUrCrGrArGrUrCmCrCrGrGrCrGrGrArGrUrCrGrCrCrA	24536.68	24535.5	3
1164	moe (1); PS (1)	moeG*rGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrCrGrGrArGrUrCrGrCrCrA	24582.69	24581.7	3
1165	m (1); PS (1)	mG*rGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrCrGrGrArGrUrCrGrCrCrA	24538.69	24545.5	3
1166	m (1); PS (1, 2, 74, 75)	mG*rG*rCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrCrGrGrArGrUrCrGrC*rC*rA	24586.69	24594.9	3
1167	m (1, 2); PS (1, 2, 74, 75)	mG*mG*rCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrCrGrGrArGrUrCrGrC*rC*rA	24600.69	24603.5	3
1168	m (1, 2, 74, 75); PS (1, 2, 74, 75)	mG*mG*rCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrCrGrGrArGrUrCrGmC*mC*rA	24628.68	24632.7	3
1169	m (1, 2, 74, 75,	mG*mG*rCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUr	24642.69	24646.2	3

	76); PS (1, 2, 74, 75)	UrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrGmC*mC*mA			
1170		mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUmGmGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCmCrGmGrGrUrUmCrGrArGrUrCrCrCrGmGrCrGrGrArGmUrCmGrCrCrA	24634.7	24632.6	3
1171		mGrGrCmUrCrCrGrUrGrGrCrGrCrArArUrGrGrAmUrArGrCrGrCrArUrUmGmGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCmCrGmGrGrUrUmCrGrArGrUrCrCrCrGmGrCrGrGrArGmUrCmGrCrCrA	24662.7	24667.1	2
1172		mGrGrCmUrCrCrGrUrGrGrCrGmCrArArUmGmGrAmUrArGrCrGmCrArUrUmGmGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCmCrGmGrGrUrUmCrGrAmGrUrCrCrCrGmGrCrGrGmArGmUmCmGrCrCrA	24774.7	24779.4	3
1173		mGrGrCmUrCrCrGrUrGmGmCmGmCrArArUmGmGrAmUrArGrCrGmCrArUrUmGmGrArCrUrUrCrArArArUrUrCrArArAmGrGrUrUmCmCrGmGrGrUrUmCrGrAmGrUmCrCrCrGmGmCrGmGmArGmUmCmGrCrCrA	24872.7	24881.5	1
1174		mGrGrCmUrCmCrGrUrGmGmCmGmCrArArUmGmGrAmUrAmGrCrGmCrArUrUmGmGrArCrUrUrCrArArArArUrUmCmAmArAmGrGrUrUmCmCrGmGrGrUrUmCrGrAmGrUmCmCrCrGmGmCmGmGmArGmUmCmGrCrCmA	24984.71	24992.1	1
1175	N-1; m73	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrC	24193.48	24197.4	
1176	N-2; m73	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArArArGrGrUrUrCrCrCrGrGrCrGrGrArGrUrCmGrC	23888.3	23889.2	3
1177	N-3; m73	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArUrUrCrArAr	23583.11	23583.8	1

		ArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmG			
1178	N-3, m1, 73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmG	23597.12	23598.2	1
1179	N-2; m1, 73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrC	23902.3	23904.4	3
1180	N-1; m1, 73	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrC	24207.48	24208.3	3
1181	m1-6, DS1, DS2, TS1	mGmGmCmUmCmCrGrUrGmGmCmGmCrArArUrGrGrArUrAmGmCmGmCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUmCmCmGmGmGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrGrCrCrA	24774.69	24779.6	3
1182	m1-6,DS1, DS2, TS1, m73	mGmGmCmUmCmCrGrUrGmGmCmGmCrArArUrGrGrArUrAmGmCmGmCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUmCmCmGmGmGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmGrCrCrA	24788.69	24782.3	3
1183	N-3, m1-6,DS1, DS2, TS1, m73	mGmGmCmUmCmCrGrUrGmGmCmGmCrArArUrGrGrArUrAmGmCmGmCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUmCmCmGmGmGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCmG	23849.11	23854.6	1
1184	N-3, m1	mGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrG	23583.11	23587.8	3
1185	N-3, m1-6	mGmGmCmUmCmCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrUrUrC	23653.11	23646.8	3

		rGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrG			
1186	N-3, PS 54	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrCrU*rUrCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrCrG	23585.11	23589.6	3
1187	N-3, PS 55	rGrGrCrUrCrCrGrUrGrGrCrGrCrArArUrGrGrArUrArGrCrGrCrArUrUrGrGrArArCrUrUrCrArArArArUrUrCrArArArGrGrUrUrCrCrGrGrGrCrU*rCrGrArGrUrCrCrCrGrGrCrGrGrArGrUrCrCrG	23585.11	23589.9	

Example 12: Correction of a missense mutation in an ORF with administration of a TREM

This example describes the administration of a TREM to correct a missense mutation. In this example, a TREM translates a reporter with a missense mutation into a wild type (WT) protein by incorporation of the WT amino acid (at the missense position) in the protein.

Host cell modification

A cell line stably expressing a GFP reporter construct containing a missense mutation, for example T203I or E222G, which prevent GFP excitation at the 470 nm and 390 nm wavelengths, is generated using the FlpIn system according to manufacturer's instructions. Briefly, HEK293T (293T ATCC ® CRL-3216) cells are co-transfected with an expression vector containing a GFP reporter with a missense mutation, such as pcDNA5/FRT-NanoLuc-TAA and a pOG44 Flp-Recombinase expression vector using Lipofectamine2000 according to manufacturer's instructions. After 24 hours, the media is replaced with fresh media. The next day, the cells are split 1:2 and selected with 100ug/mL Hygromycin for 5 days. The remaining cells are expanded and tested for reporter construct expression.

Synthesis and preparation of TREM

The TREM is synthesized as described in Example 1 and quality control methods as described in Examples 7-9 are performed. To ensure proper folding, the TREM is heated at 85°C for 2 minutes and then snap cooled at 4°C for 5 minutes.

Transfection of non-cognate TREM into host cells

To deliver the TREM to mammalian cells, 100 nM of TREM is transfected into cells expressing the ORF having a missense mutation using lipofectamine 2000 reagents according to

the manufacturer's instructions. After 6-18 hours, the transfection media is removed and replaced with fresh complete media.

Missense mutation correction assay

To monitor the efficacy of the TREM to correct the missense mutation in the reporter construct, 24-48 hours after TREM transfection, cell media is replaced, and cell fluorescence is measured. As a negative control, no TREM is transfected in the cells and as a positive control, cells expressing WT GFP are used for this assay. If the TREM is functional, it is expected that the GFP protein produced fluoresces when illuminated with a 390 nm excitation wavelength using a fluorimeter, as observed in the positive control. If the TREM is not functional, the GFP protein produced fluoresces only when excited with a 470 nm wavelength, as is observed in the negative control.

Example 13: Evaluation of protein expression levels of SMC-containing ORF with administration of a TREM

This example describes administration of a TREM to alter expression levels of an SMC-containing ORF.

To create a system in which to study the effects of TREM administration on protein expression levels of an SMC-containing protein, in this example, from the PNPL3A gene coding for adiponutrin, a plasmid containing the PNPL3A rs738408 ORF sequence is transfected in the normal human hepatocyte cell line THLE-3, edited by CRISPR/Cas to contain a frameshift mutation in a coding exon of PNPLA3 to knock out endogenous PNPLA3 (THLE-3_PNPLA3KO cells). As a control, an aliquot of THLE-3_PNPLA3KO cells are transfected with a plasmid containing the wildtype PNPL3A ORF sequence.

Synthesis and preparation of TREM

An arginine TREM is synthesized as described in Example 1 and quality control methods as described in Examples 7-9 are performed. To ensure proper folding, the TREM is heated at 85°C for 2 minutes and then snap cooled at 4°C for 5 minutes.

Evaluation of protein level of SMC-containing ORF

A TREM is delivered to the THLE-3_PNPLA3KO cells containing the rs738408 ORF sequence as well as to the THLE-3_PNPLA3KO cells containing the wildtype PNPL3A ORF sequence. In this example, the TREM contains a proline isoacceptor containing an AGG anticodon, that base pairs to the CCT codon, i.e. with the sequence

GGCUCGUUGGUCUAGGGGUAUGAUUCUCGCUUAGGGUGCGAGAGGUCCCGGGUU CAAAUCCCGGACGAGCCC. A time course is performed ranging from 30 minutes to 6 hours with hour-long interval time points. At each time point, cells are trypsinized, washed and lysed. Cell lysates are analyzed by Western blotting and blots are probed with antibodies against the adiponutrin protein. A total protein loading control, such as GAPDH, actin or tubulin, is also probed as a loading control.

The methods described in this example can be adopted for use to evaluate the expression levels of the adiponutrin protein in rs738408 ORF containing cells.

Example 14: Modulation of protein translation rate of SMC-containing ORF with TREM administration

This example describes administration of a TREM to alter the rate of protein translation of an SMC-containing ORF.

To monitor the effects of TREM addition on translation elongation rates, an in vitro translation system, in this example the RRL system from Promega, is used in which the fluorescence change over time of a reporter gene, in this example GFP, is a surrogate for translation rates.

Synthesis and preparation of TREM

An arginine TREM is synthesized as described in Example 1 and quality control methods as described in Examples 7-9 are performed. To ensure proper folding, the TREM is heated at 85°C for 2 minutes and then snap cooled at 4°C for 5 minutes.

Evaluation of protein translation rate of SMC-containing ORF

First, a rabbit reticulocyte lysate that is depleted of the endogenous tRNA using an antisense oligonucleotide targeting the sequence between the anticodon and variable loop is generated (see, e.g., Cui et al. 2018. Nucleic Acids Res. 46(12):6387–6400). In this example, a TREM comprising an alanine isoacceptor containing an UGC anticodon, that base pairs to the GCA codon, i.e. with the sequence GGGGAUGUAGCUCAGUGGUAGAGCGCAUGCUUUGCAUGUAUGAGGUCCCGGGUU CGAUCCCCGGCAUCUCCA is added to the in vitro translation assay lysate in addition to 0.1-0.5 ug/uL of mRNA coding for the wildtype TERT ORF fused to the GFP ORF by a linker or an mRNA coding for the rs2736098 TERT ORF fused to the GFP ORF by a linker. The progress of GFP mRNA translation is monitored by fluorescence increase on a microplate reader at 37 °C

using $\lambda_{ex}485/\lambda_{em}528$ with data points collected every 30 seconds over a period of 1hour. The amount of fluorescence change over time is plotted to determine the rate of translation elongation of the wildtype ORF compared to the rs2736098 ORF with and without TREM addition. The methods described in this example can be adopted for use to evaluate the translation rate of the rs2736098 ORF and the wildtype ORF in the presence or absence of TREM.

What is claimed is:

1. A TREM comprising a sequence of Formula A:

[L1]-[ASt Domain1]-[L2]-[DH Domain]-[L3]-[ACH Domain] -[VL Domain]-[TH Domain]-[L4]-[ASt Domain2], wherein:

independently, [L1] and [VL Domain], are optional;

one of [L1], [ASt Domain1], [L2]-[DH Domain], [L3], [ACH Domain], [VL Domain], [TH Domain], [L4], and [ASt Domain2] comprises a nucleotide having a non-naturally occurring modification, and

the non-naturally occurring modification is present on a nucleotide (e.g., a modified nucleotide) at a position corresponding to a modified position in a row of any of Table 15-22, e.g., described herein.

2. The TREM of claim 1, wherein the non-naturally occurring modification is present on the 2'-position of a nucleotide sugar or within the internucleotide region (e.g., a backbone modification).

3. The TREM of claim 2, wherein the non-naturally occurring modification is selected from a 2-O-methyl (2-OMe), 2'-halo (e.g., 2'F or 2'Cl), 2'-O-methoxyethyl (2'MOE), or 2'deoxy modification.

4. The TREM of claim 3, wherein the non-naturally occurring modification is a 2'OMe modification.

5. The TREM of claim 3, wherein the non-naturally occurring modification is a 2'halo (e.g., 2'F or 2'Cl) modification.

6. The TREM of claim 3, wherein the non-naturally occurring modification is a 2'MOE modification.

7. The TREM of claim 3, wherein the non-naturally occurring modification is a 2'-deoxy modification.

8. The TREM of claim 2, wherein the non-naturally occurring modification is present in the internucleotide region (e.g., a backbone modification).

9. The TREM of claim 8, wherein the non-naturally occurring modification is a phosphorothioate modification.

10. The TREM of claim 2, wherein the non-naturally occurring modification is present on or within any one of nucleotides 1-76 of SEQ ID NO: 622, nucleotides 1-85 of SEQ ID NO: 993, or nucleotides 1-75 of SEQ ID NO: 1079.

11. The TREM of claim 2, wherein the non-naturally occurring modification is present on or within any one of nucleotides 1-76 of SEQ ID NO: 622.

12. The TREM of claim 10, wherein the non-naturally occurring modification is present on or within a nucleotide in the [ASt Domain1] or [ASt Domain2].

13. The TREM of claim 10, wherein the non-naturally occurring modification is present on or within a nucleotide in the [DH Domain], [ACH Domain], [VL Domain], or [TH Domain].

14. The TREM of claim 10, wherein the non-naturally occurring modification is present within a linker domain (e.g., [L1], [L2], [L3], or [L4]).

15. The TREM of claim 1, wherein the non-naturally occurring modification is present on or within any one of nucleotides 1, 2, 4, 6, 10, 12, 13, 17, 18, 20, 22, 29, 30, 42, 43, 45, 50, 52, 56, 59, 61, 65, 66, 68, 69, 71, 72, and 73 of SEQ ID NO: 622.

16. The TREM of claim 1, wherein the non-naturally occurring modification is present on or within any one of nucleotides 20, 29, 33, 40, 41, 44, 45, 48, 49, 50, 52, 53, 54, 56, 59, 61, 62, 63, 65, 67, 68, 69, 71, 72, 75, and 76 of SEQ ID NO: 622.

17. The TREM of claim 1, wherein the non-naturally occurring modification is present on or within any one of nucleotides 1, 4, 14, 15, 16, 17, 20, 29, 44, 45, 47, 49, 50, 52, 54, 56, 57, 59, 65, 72, and 73 of SEQ ID NO: 622.

18. The TREM of claim 1, wherein the non-naturally occurring modification is present on or within any one of nucleotides 3, 4, 5, 6, 14, 15, 16, 20, 22, 23, 33, 54, 59, 62, 63, 72, and 76 of SEQ ID NO: 622.

19. The TREM of claim 1, wherein the non-naturally occurring modification is present on or within any one of nucleotides 1, 2, 3, 9, 14, 15, 16, 17, 18, 19, 20, 21, 35, 37, 38, 44, 45, 46, 52, 54, 55, 56, 57, 58, 73, and 74 of SEQ ID NO: 622.

20. The TREM of claim 1, wherein the non-naturally occurring modification is present on or within any one of nucleotides 1, 17, 18, 20, 29, 30, 50, 52, and 73 of SEQ ID NO: 622.

21. A pharmaceutical composition comprising a TREM of claim 1.

22. The pharmaceutical composition of claim 21, further comprising a pharmaceutically acceptable component, e.g., an excipient.

23. A lipid nanoparticle formulation comprising a TREM of claim 1.

24. A lipid nanoparticle formulatin comprising a pharmaceutical composition of claim 21.