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(54) **CONDITIONAL-SIRNAS AND USES THEREOF IN TREATING CARDIAC HYPERTROPHY**

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(57) **ABSTRACT**

Disclosed herein are conditional siRNAs activatable by pro-hypertrophic RNA sequences and use thereof for treating conditions such as cardiac hypertrophy. The conditional siRNAs target calcineurin or HDAC2.

21 Claims, 230 Drawing Sheets
(80 of 230 Drawing Sheet(s) Filed in Color)

Specification includes a Sequence Listing.

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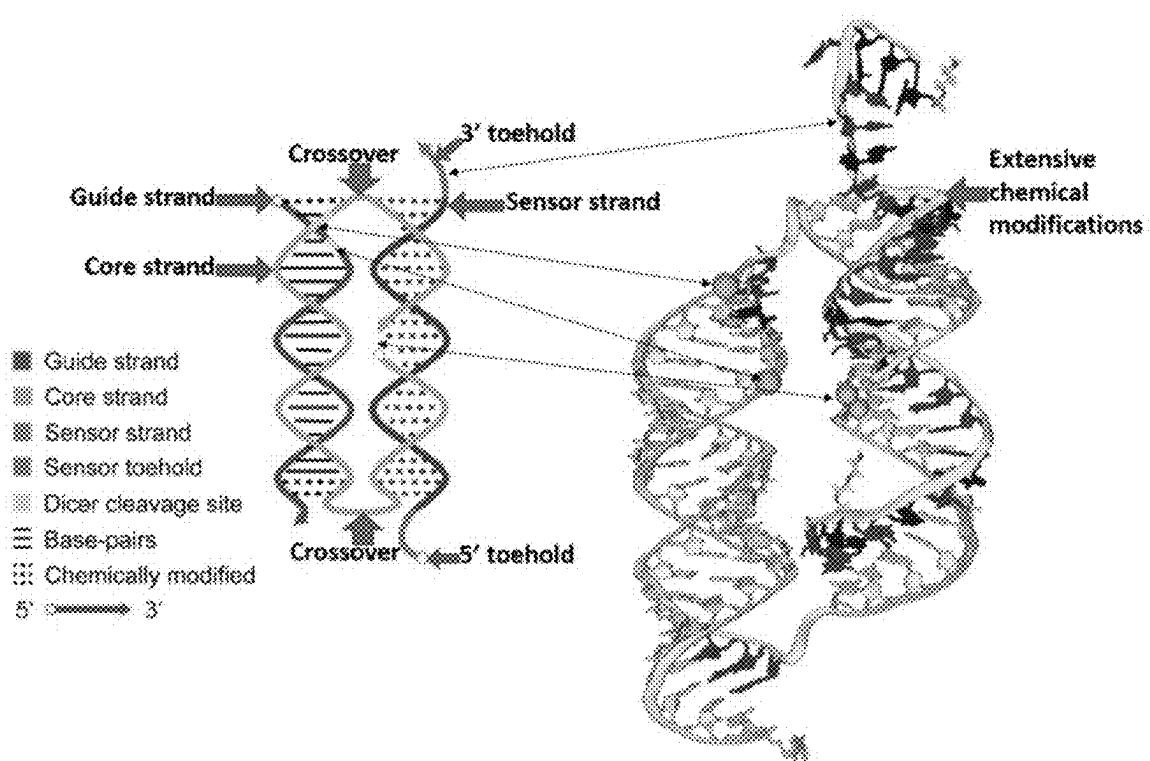
FIG. 1

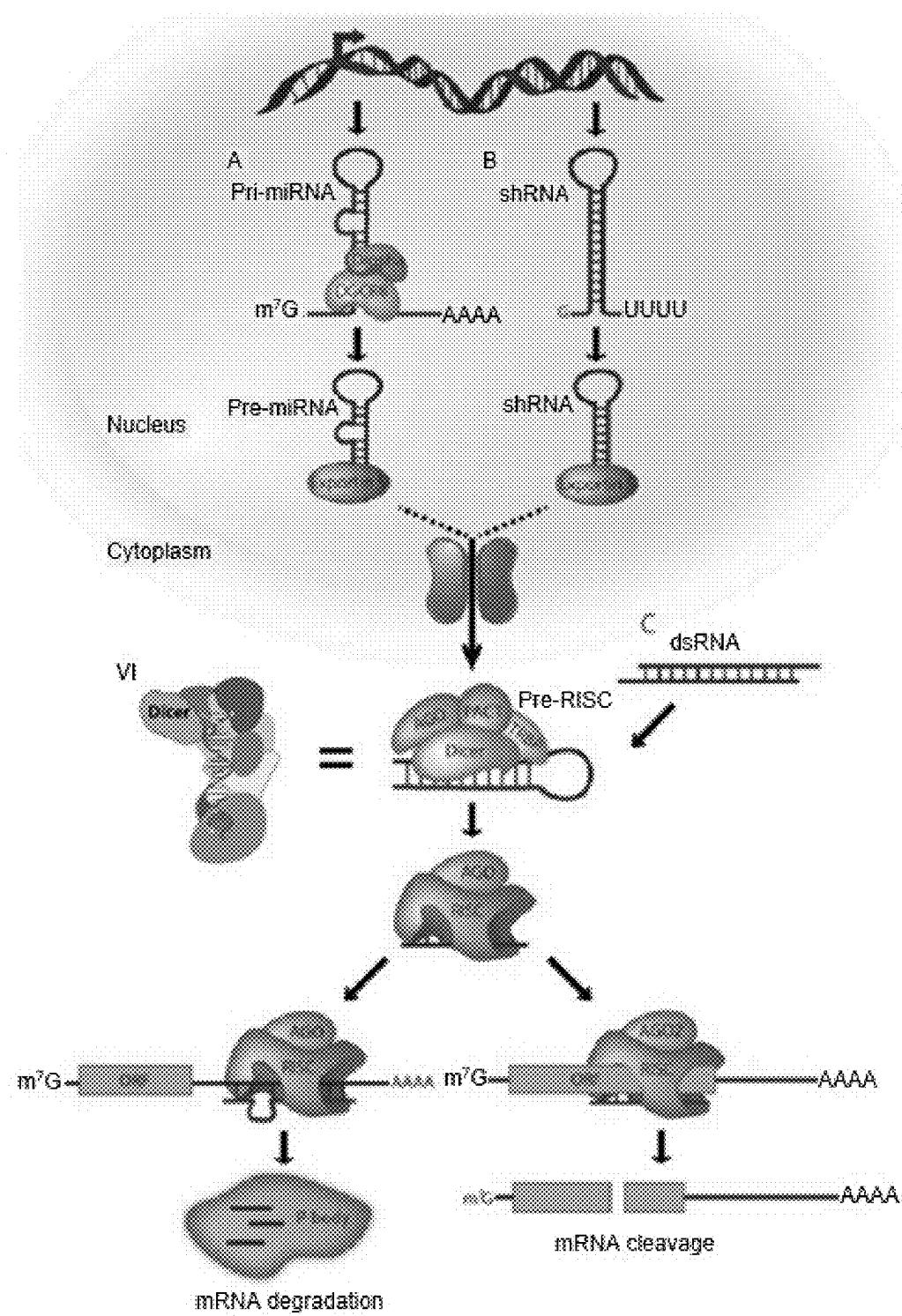
FIG. 2

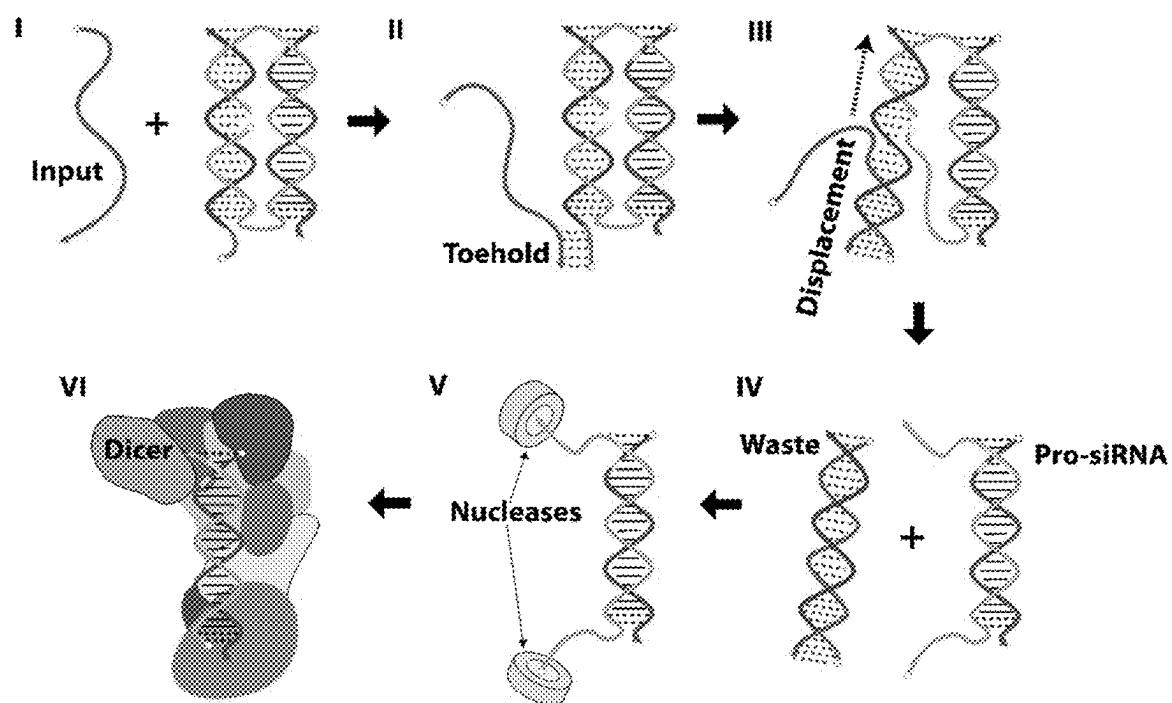
FIG. 3

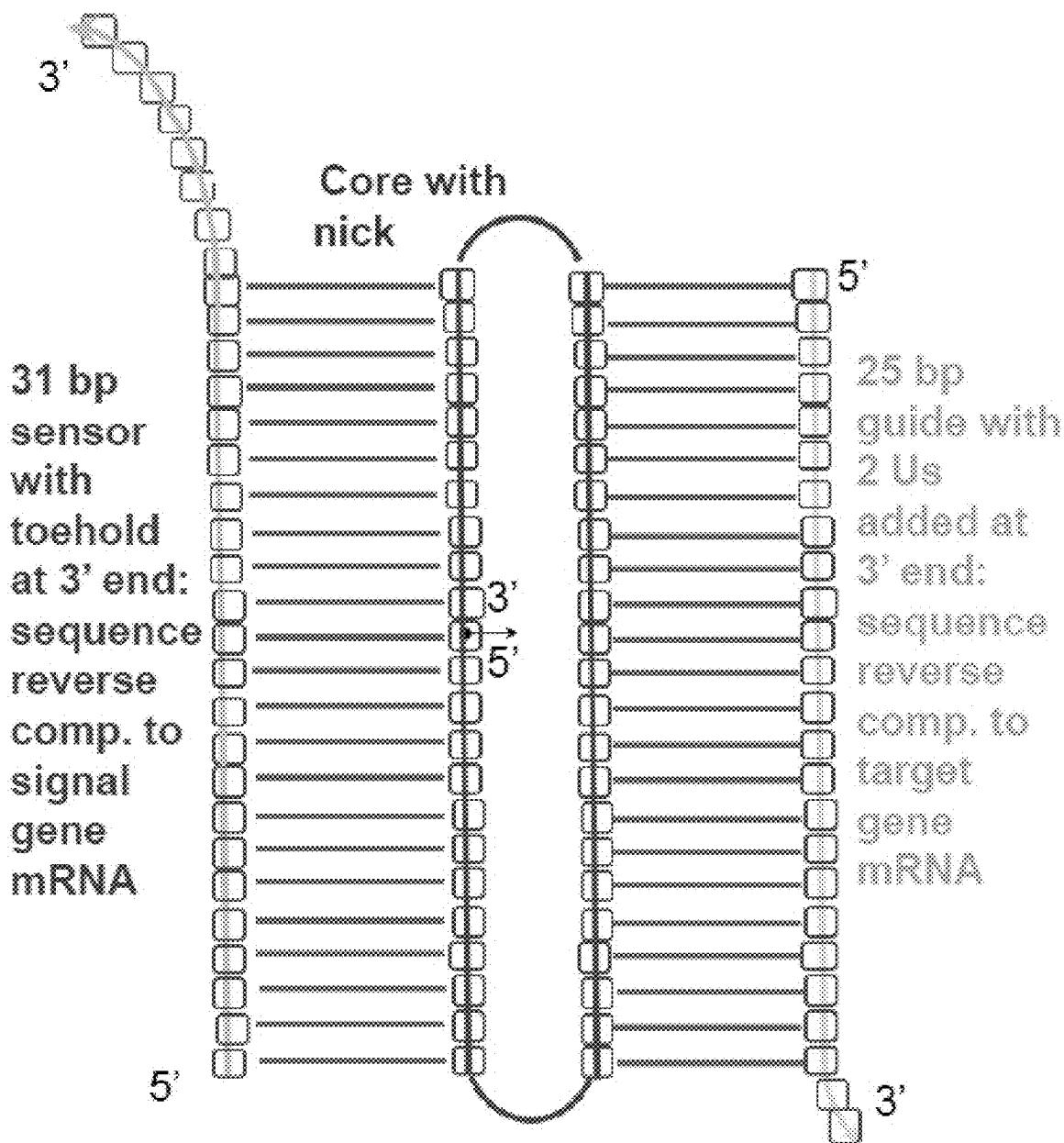
FIG. 4A

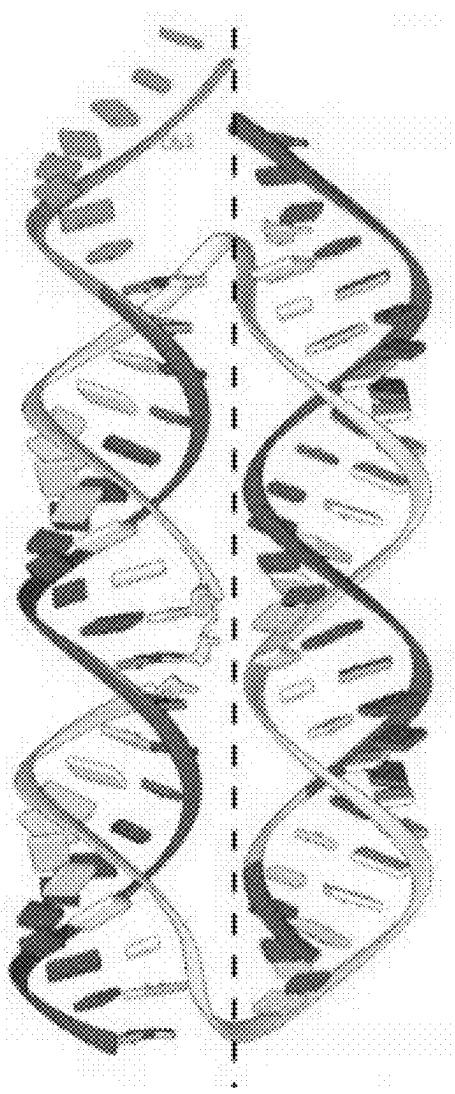
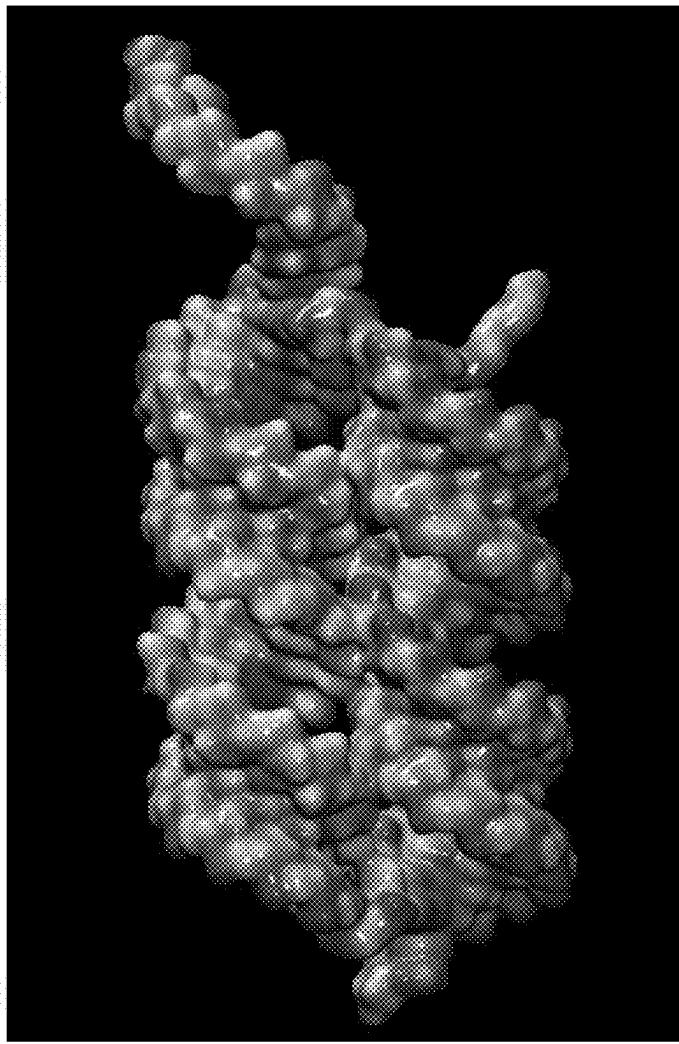
FIG. 4B**FIG. 4C**

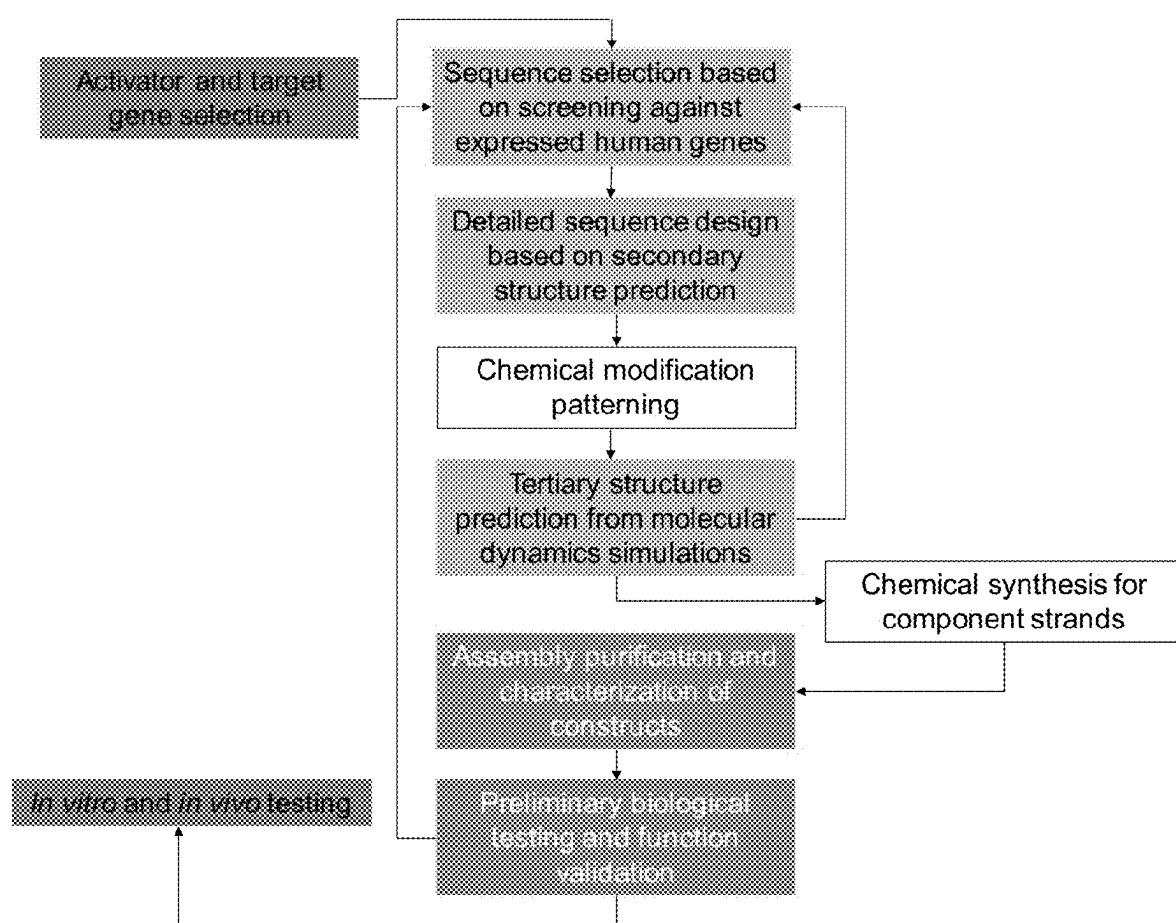
FIG. 5

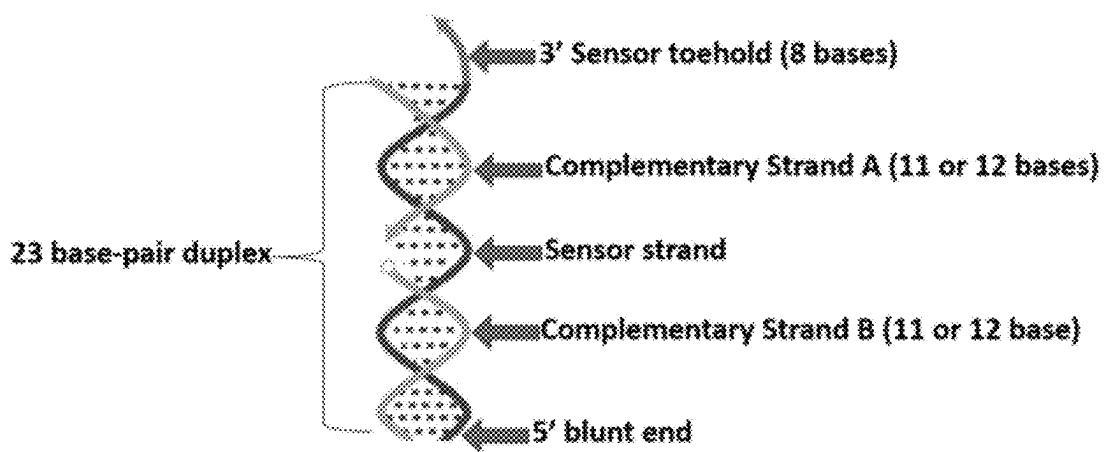
FIG. 6

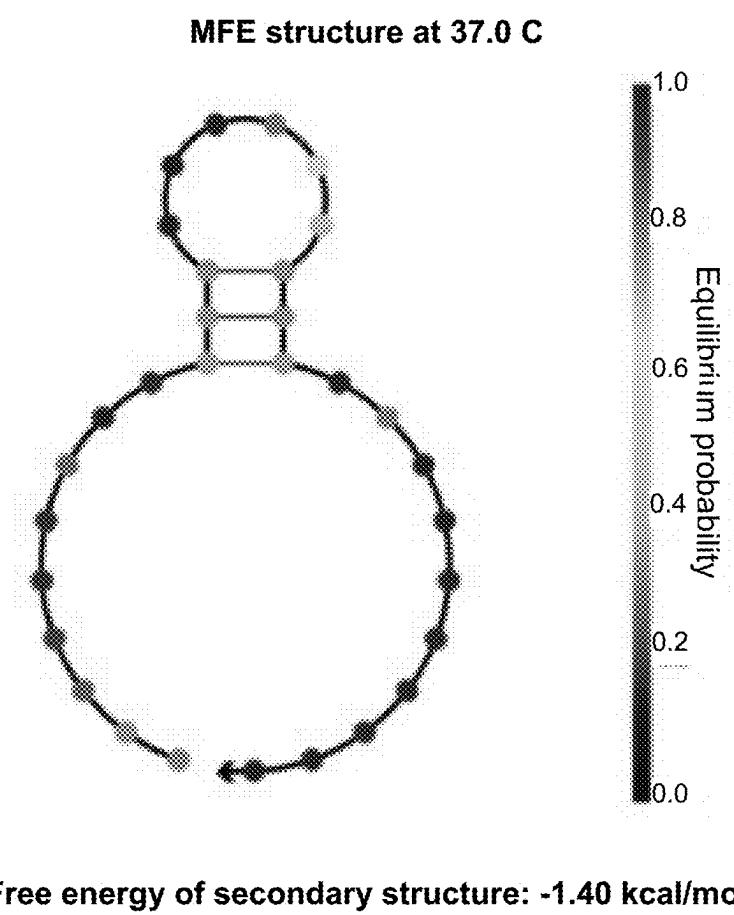
FIG. 7

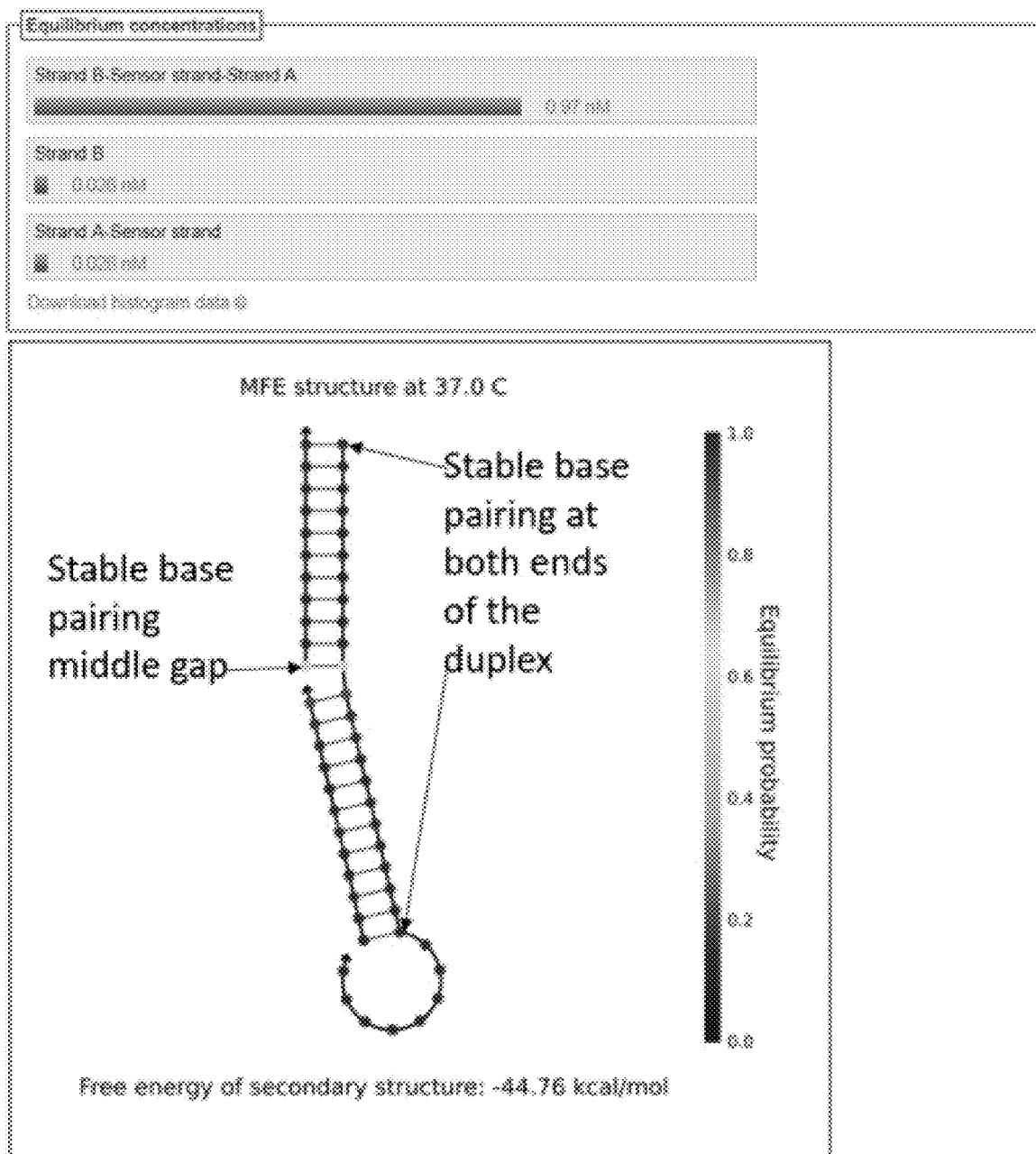
FIG. 8

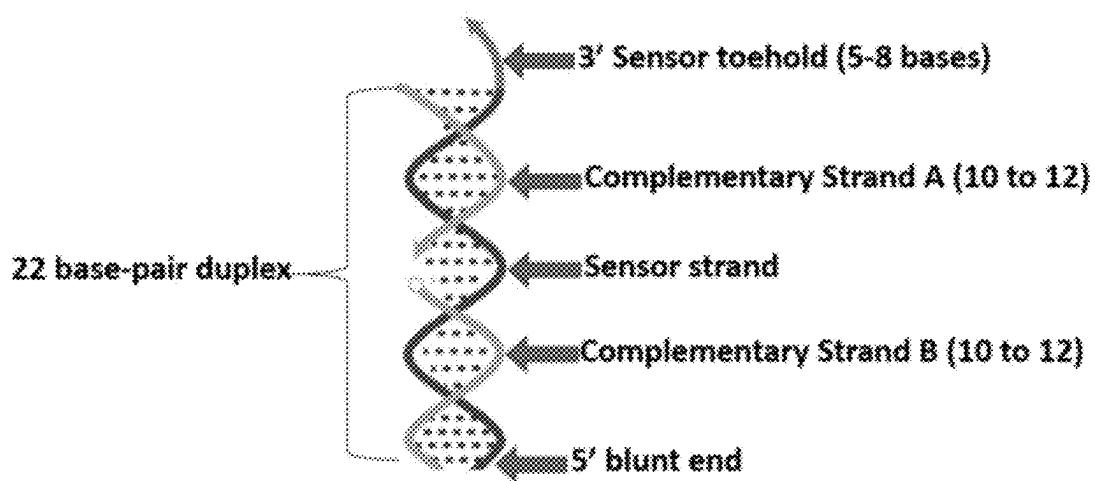
FIG. 9

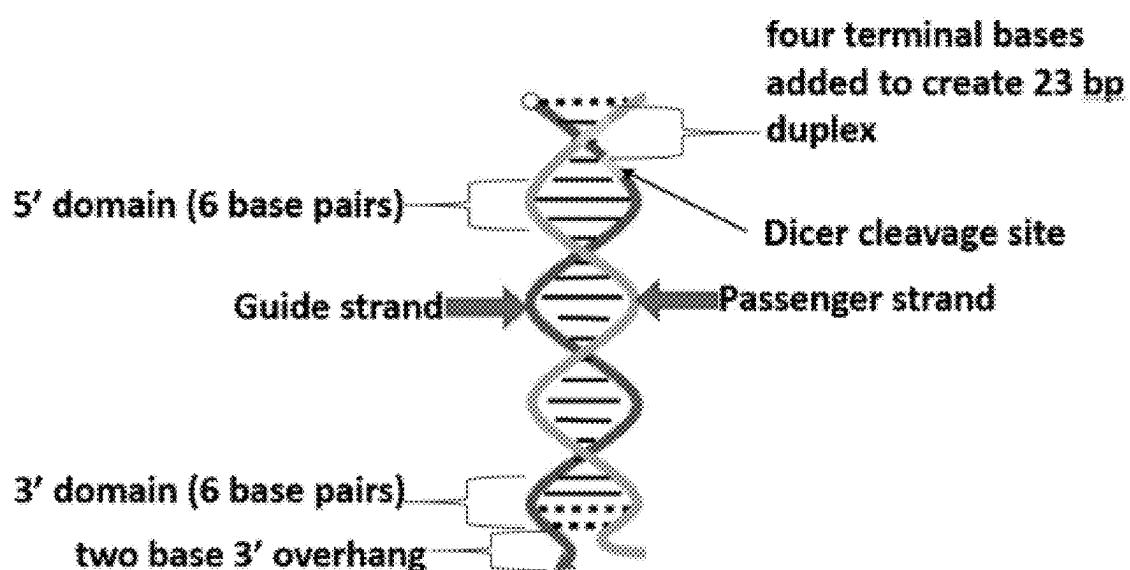
FIG. 10

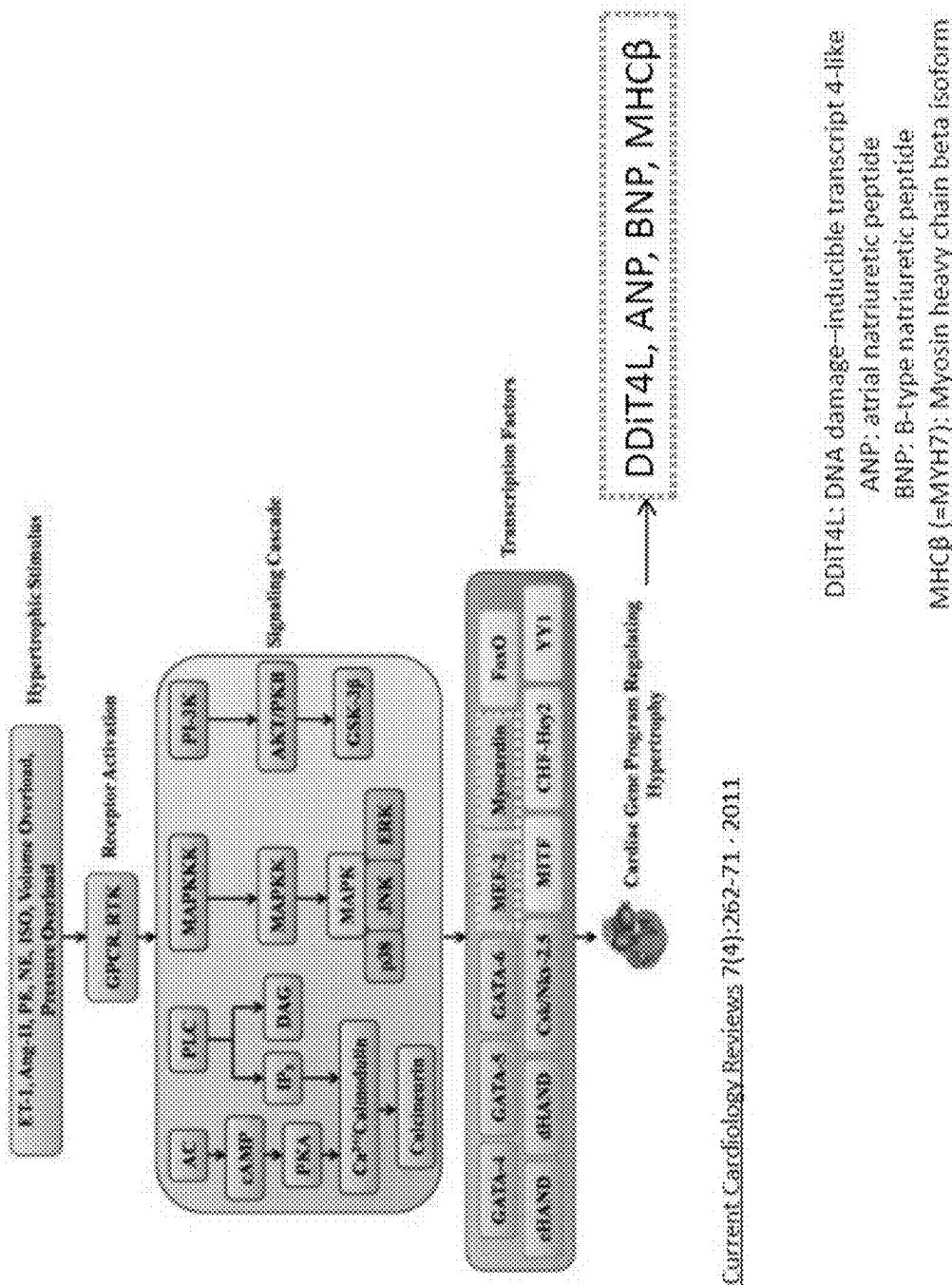
FIG. 11

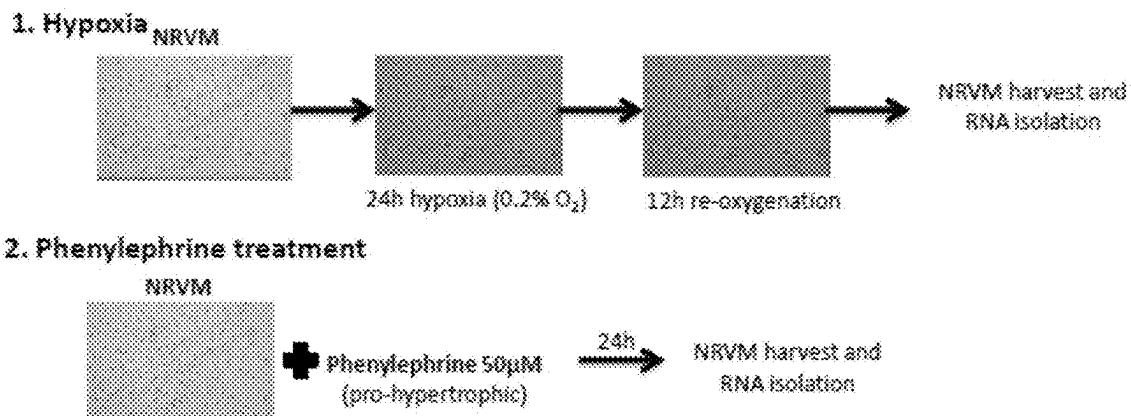
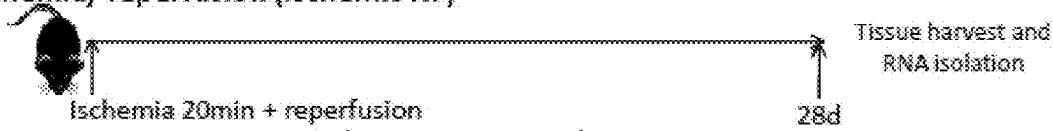
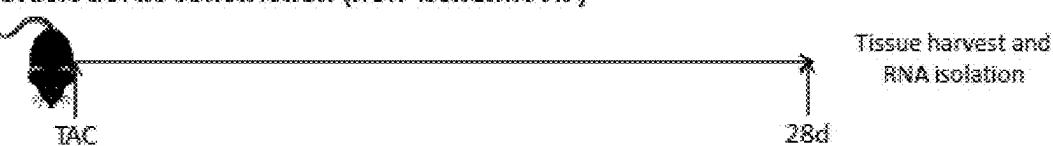
FIG. 12A*In vitro:***FIG. 12B***In vivo:***1. Ischemia/ reperfusion (ischemic HF)****2. Thoracic aortic constriction (non-ischemic HF)**

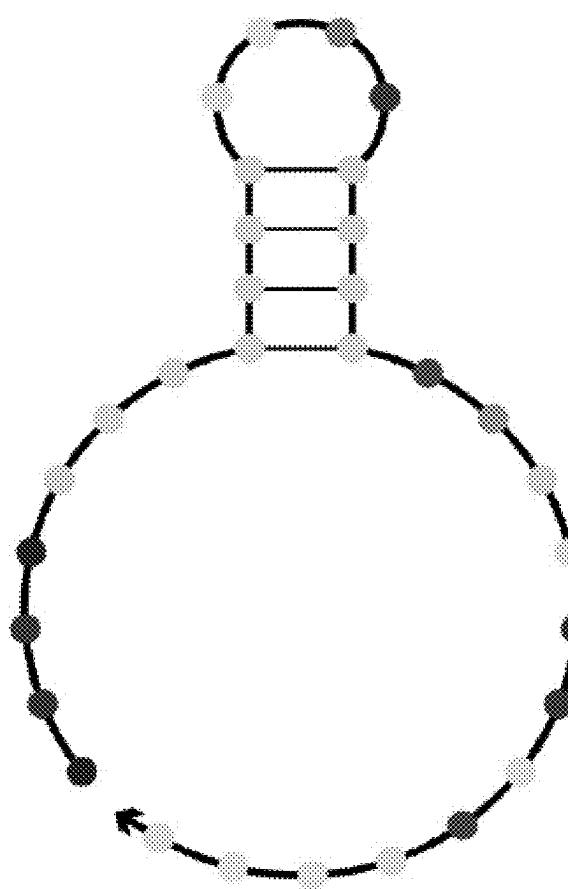
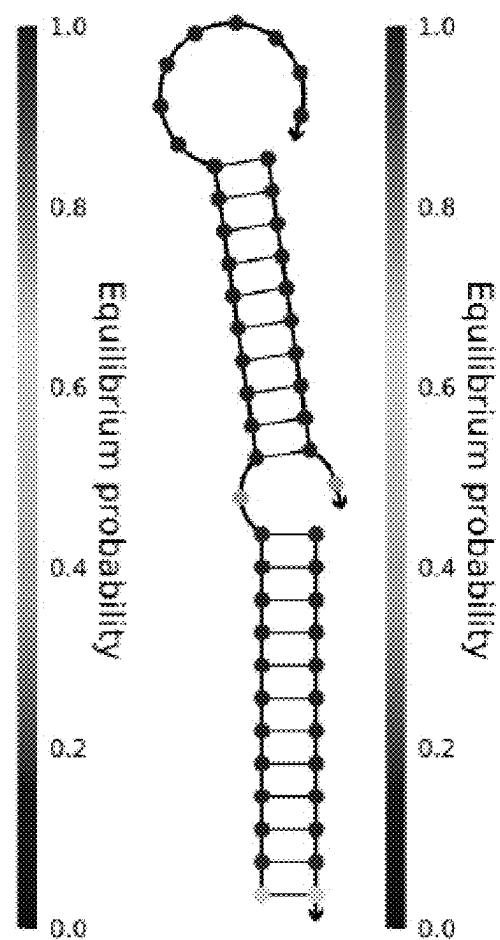
FIG. 13A**FIG. 13B**

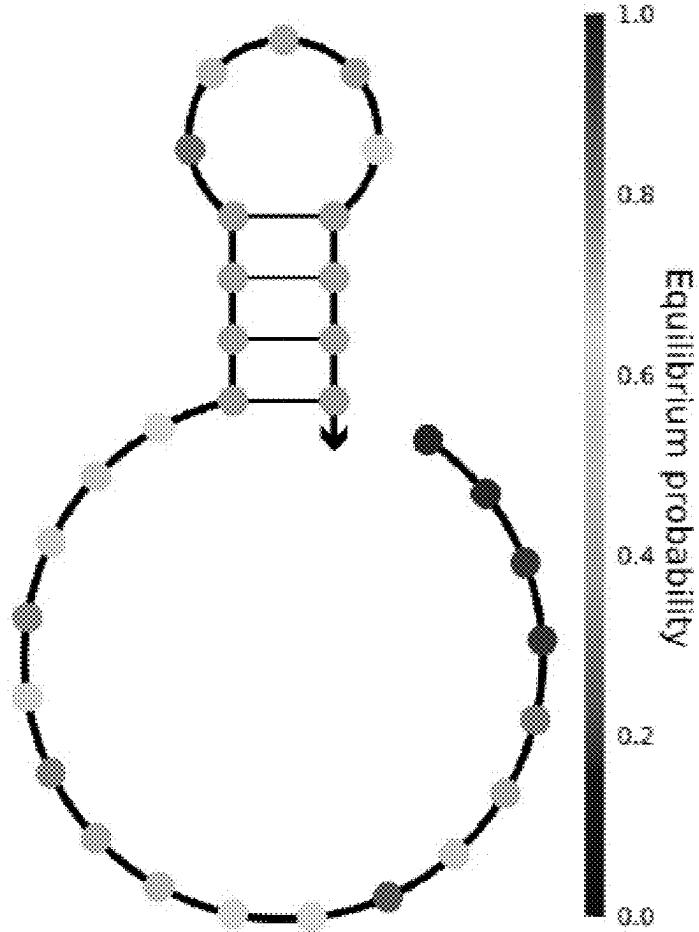
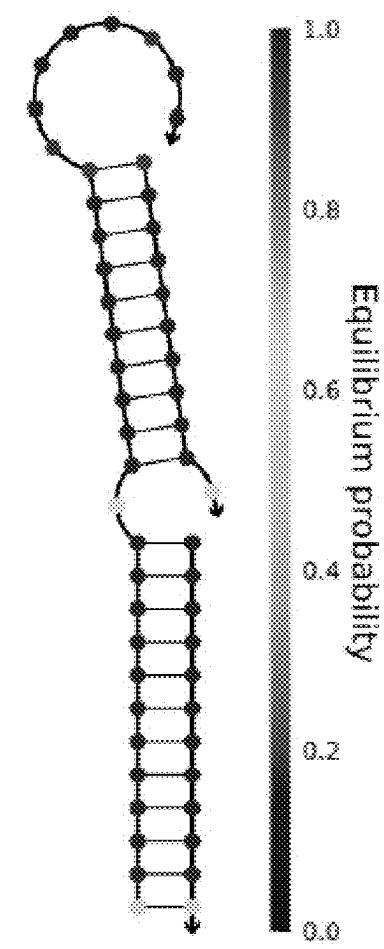
FIG. 14A**FIG. 14B**

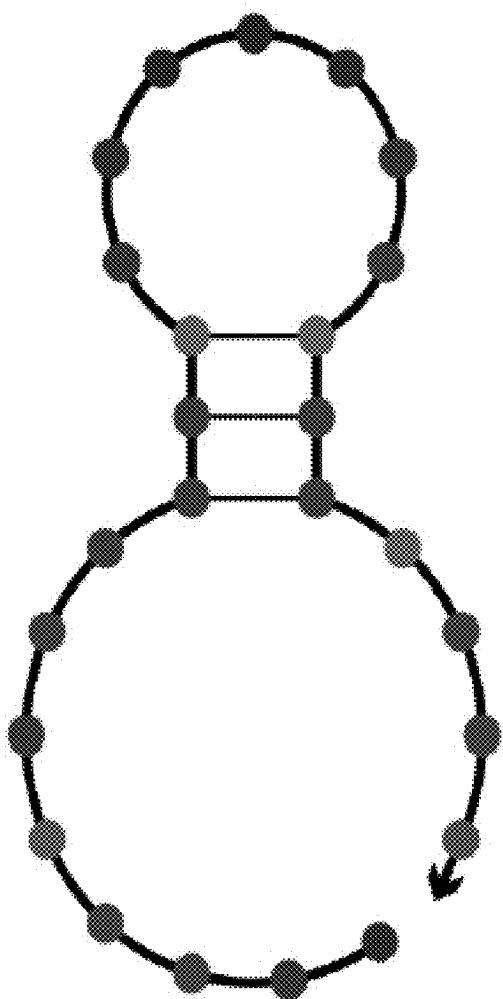
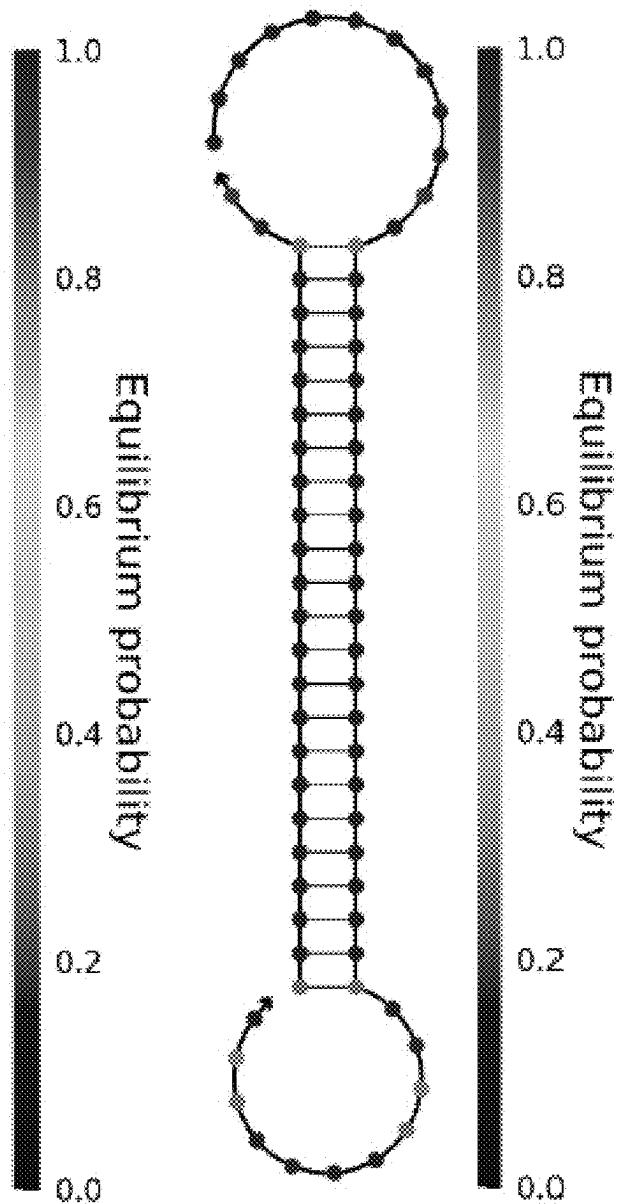
FIG. 15A**FIG. 15B**

FIG. 16

Original ANP : Calcineurin

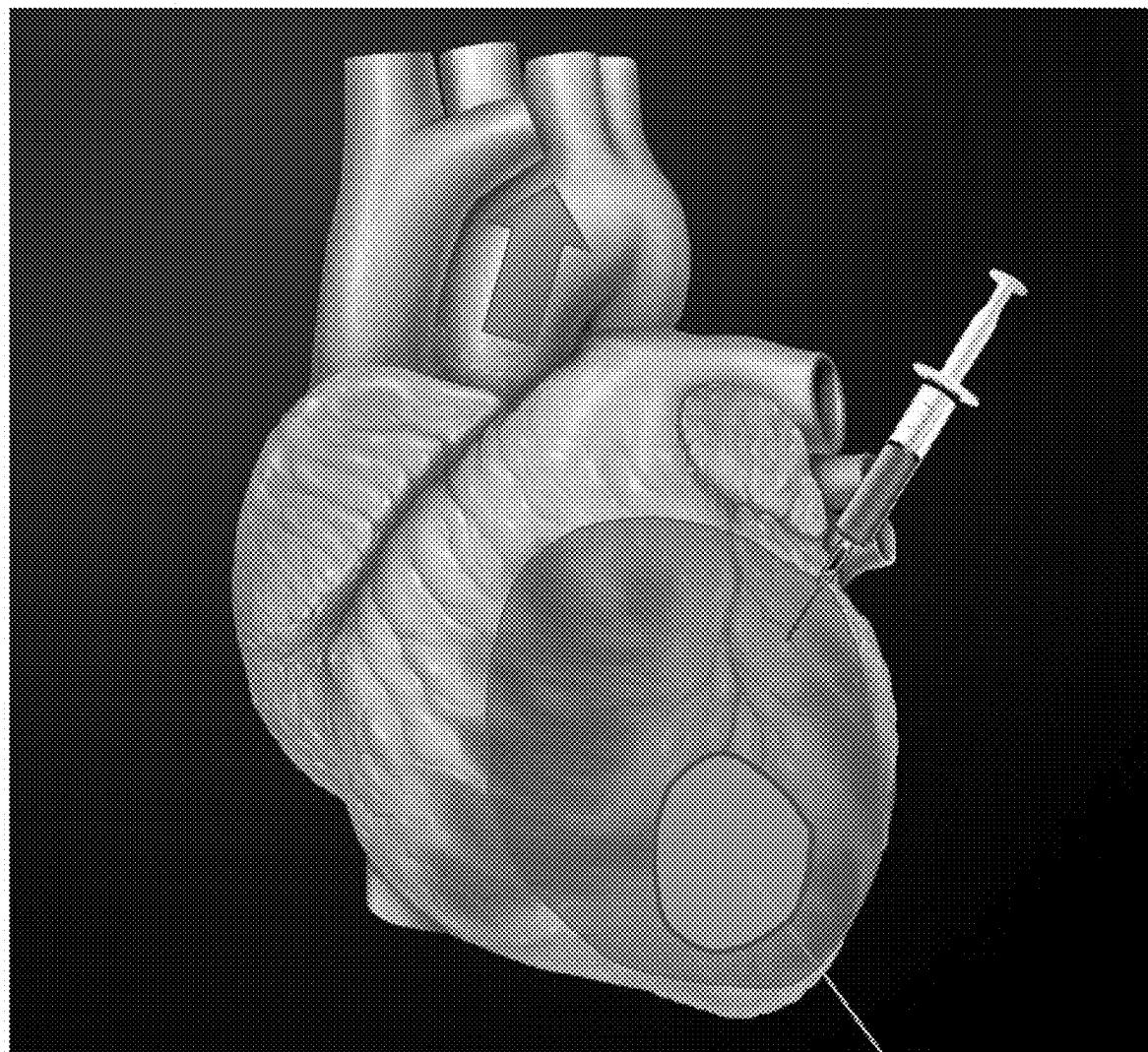
New sensor with less PS and one more LNA (middle C) in toehold

New sensor plus modified guide

New sensor with Cholesterol*TEG, modified quide

■ = LNA; ■ = 2'-O-methyl; ■ = RNA; . = phosphodiester; * = phosphorothioate; ↑ = Dicer cleavage site; □ = Exonuclease blocking domain; C3 = C₃ spacer; TEG = triethylene glycol; NH₂ = primary amine linker

FIG. 18



Site of injury

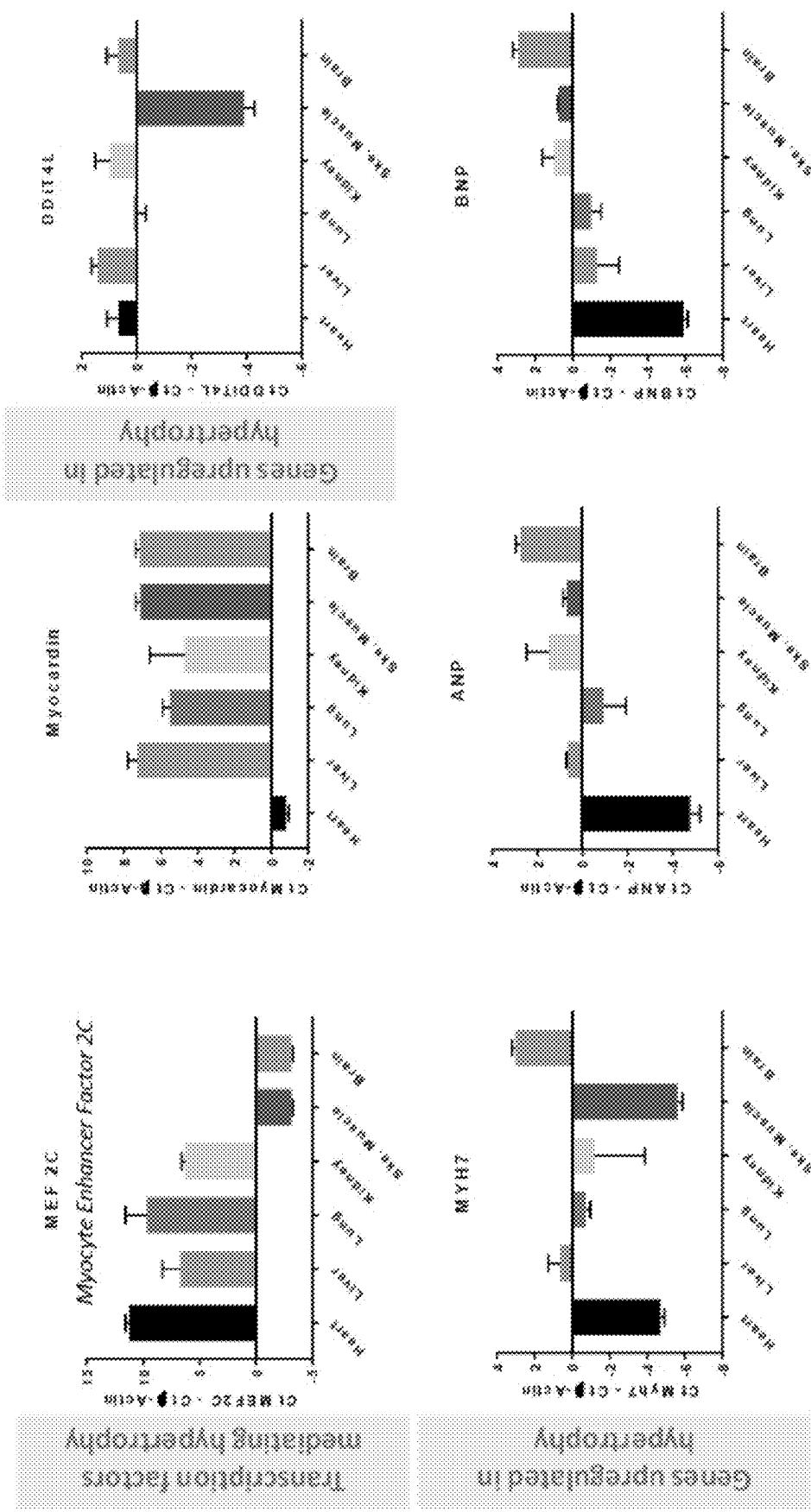
FIG. 19

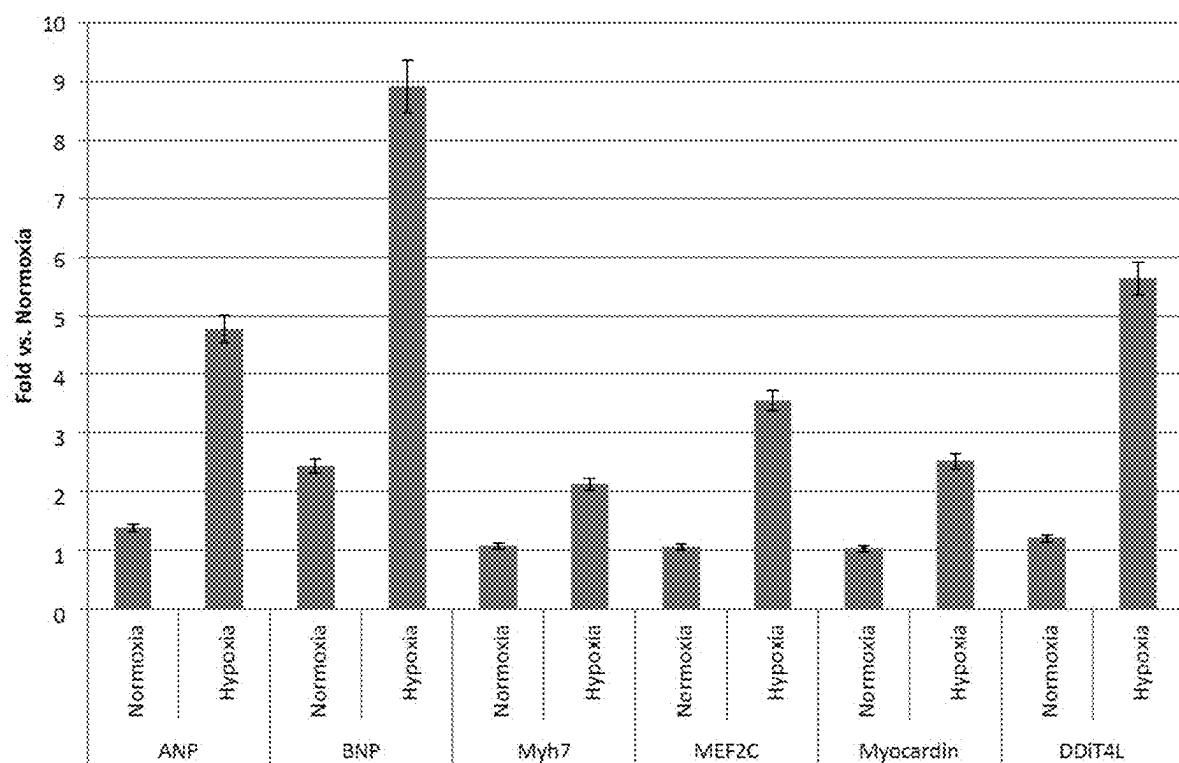
FIG. 20

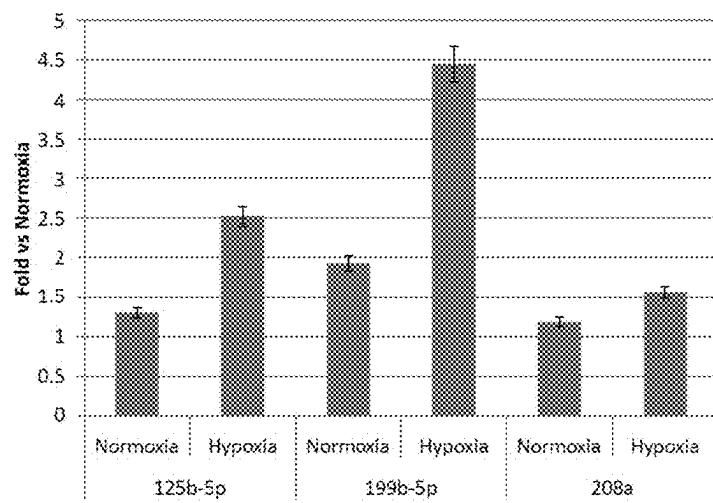
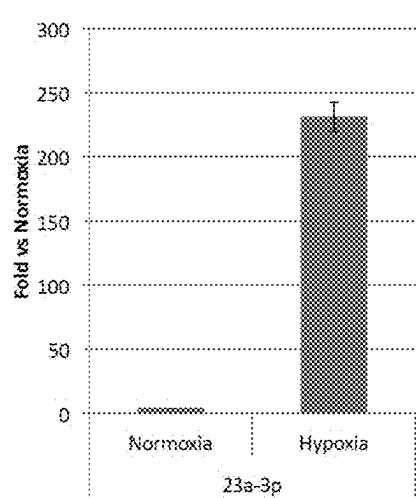
FIG. 21

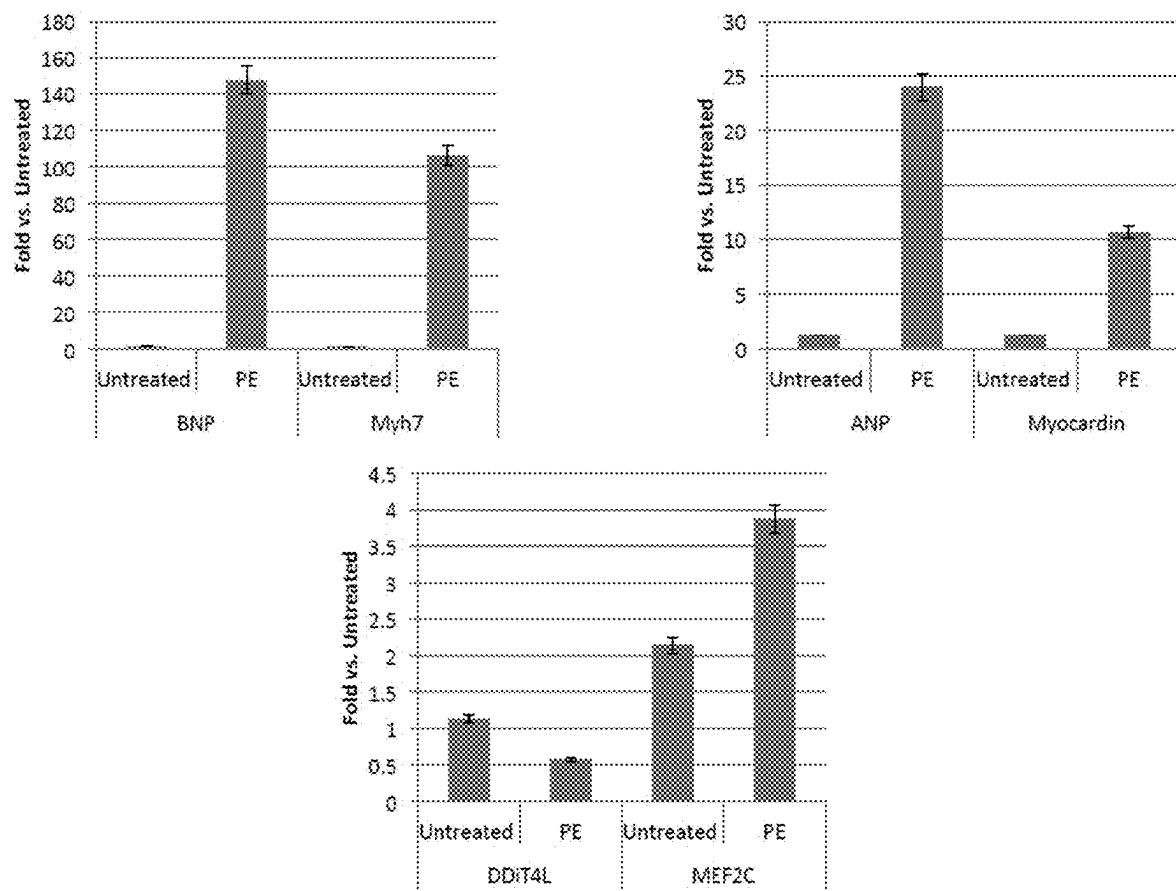
FIG. 22

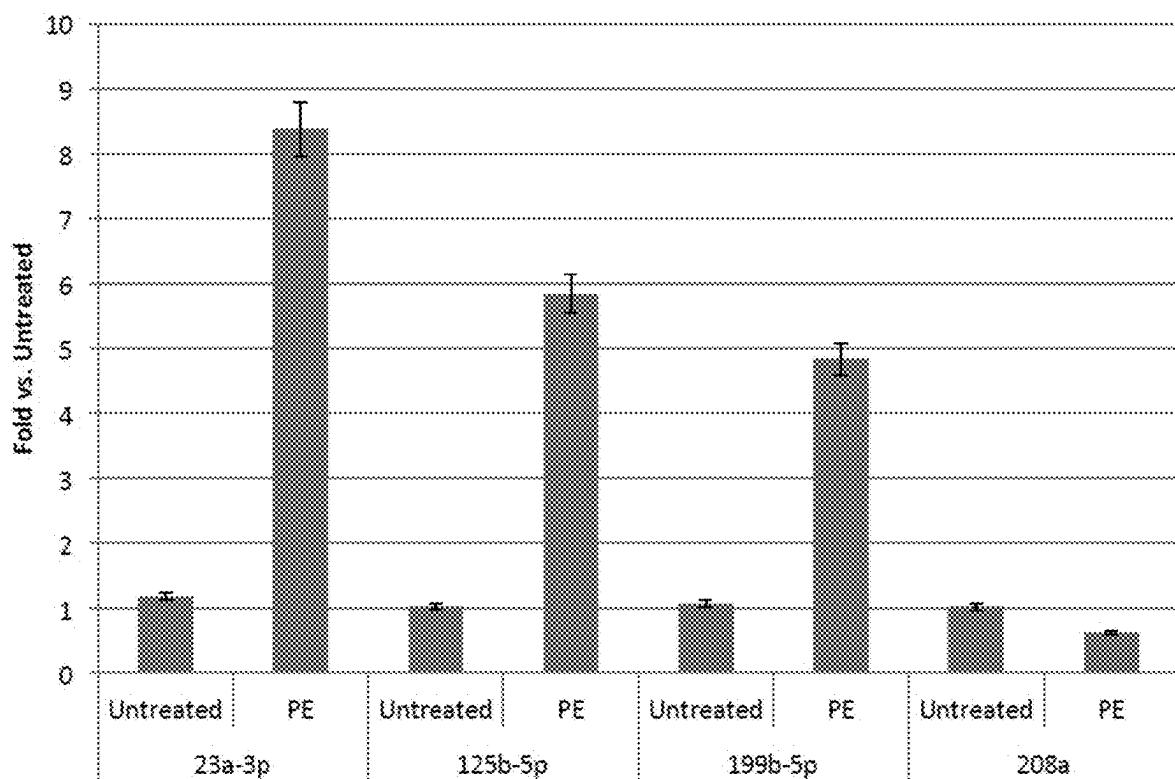
FIG. 23

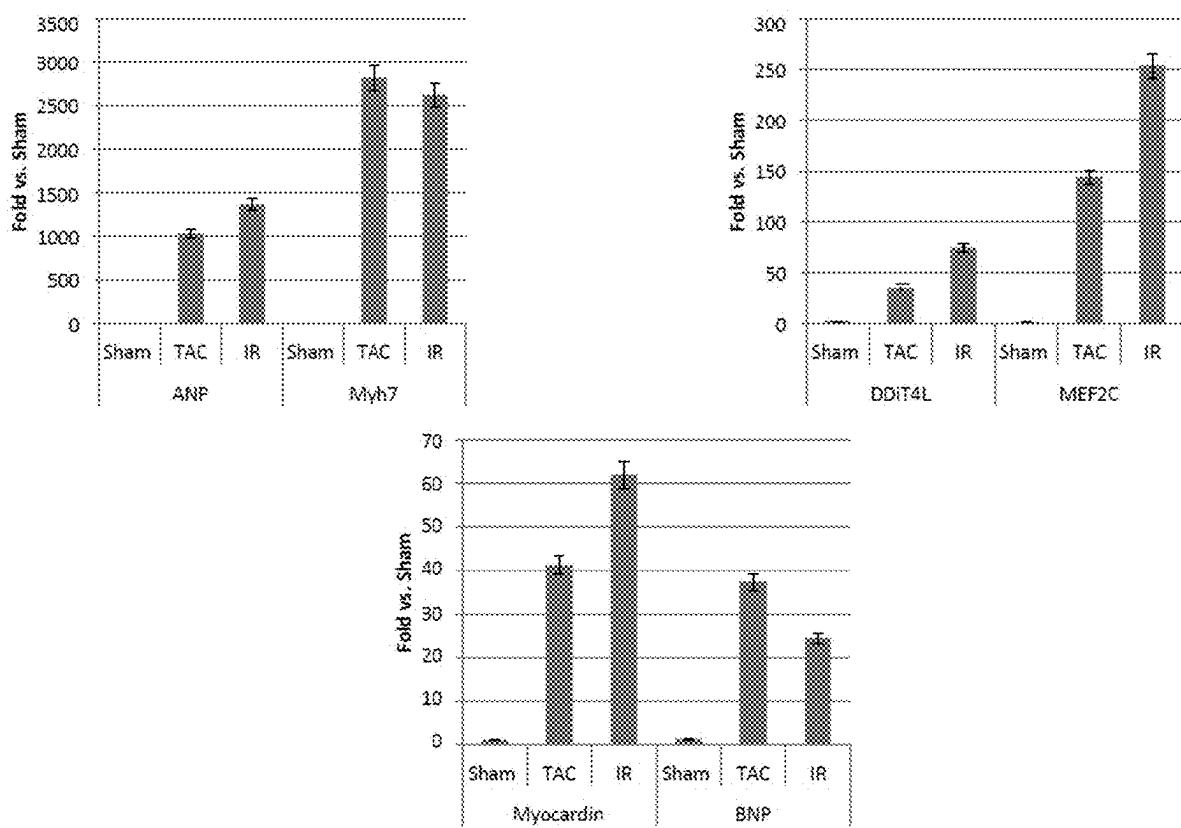
FIG. 24

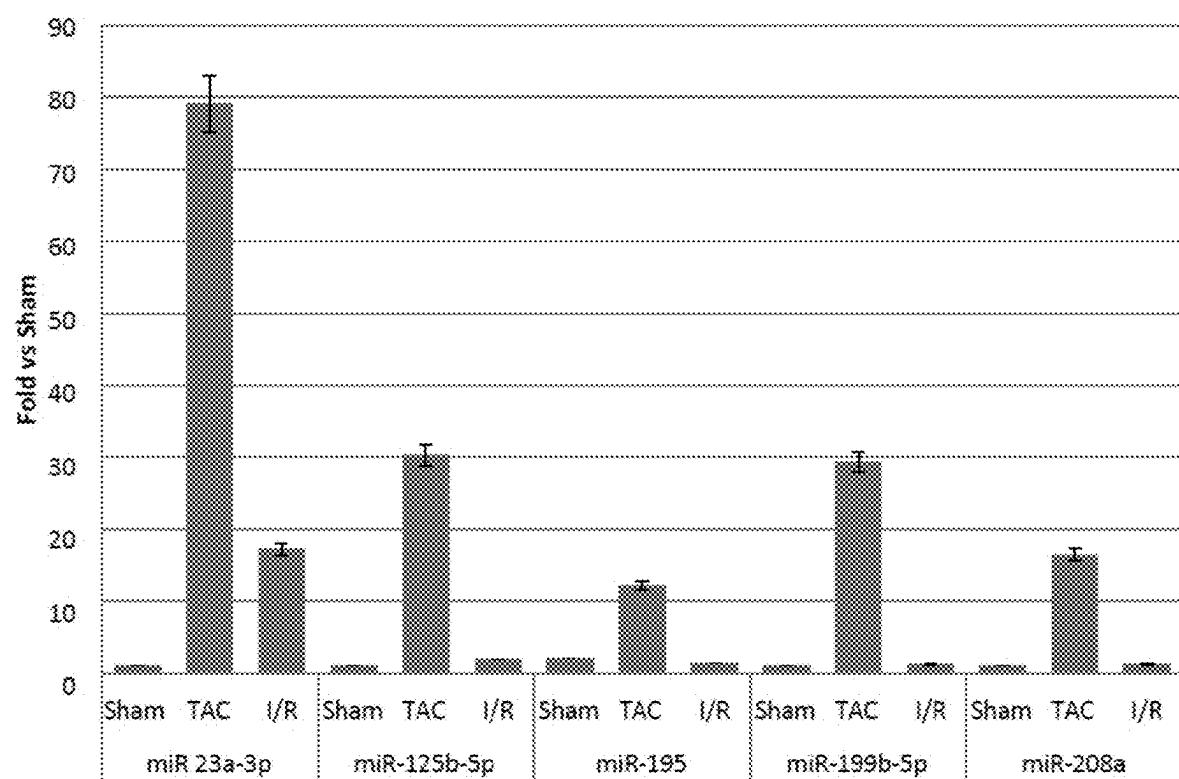
FIG. 25

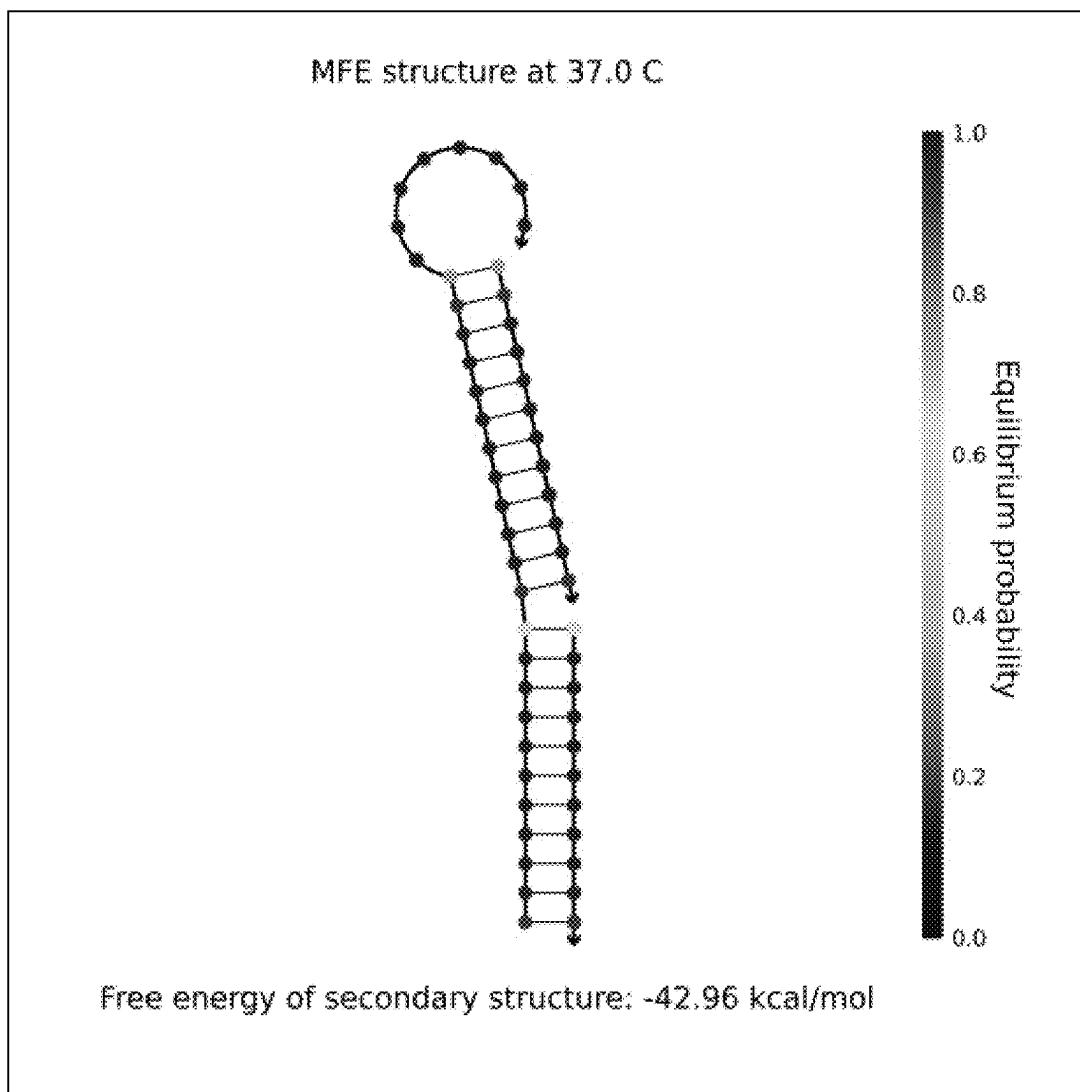
FIG. 26

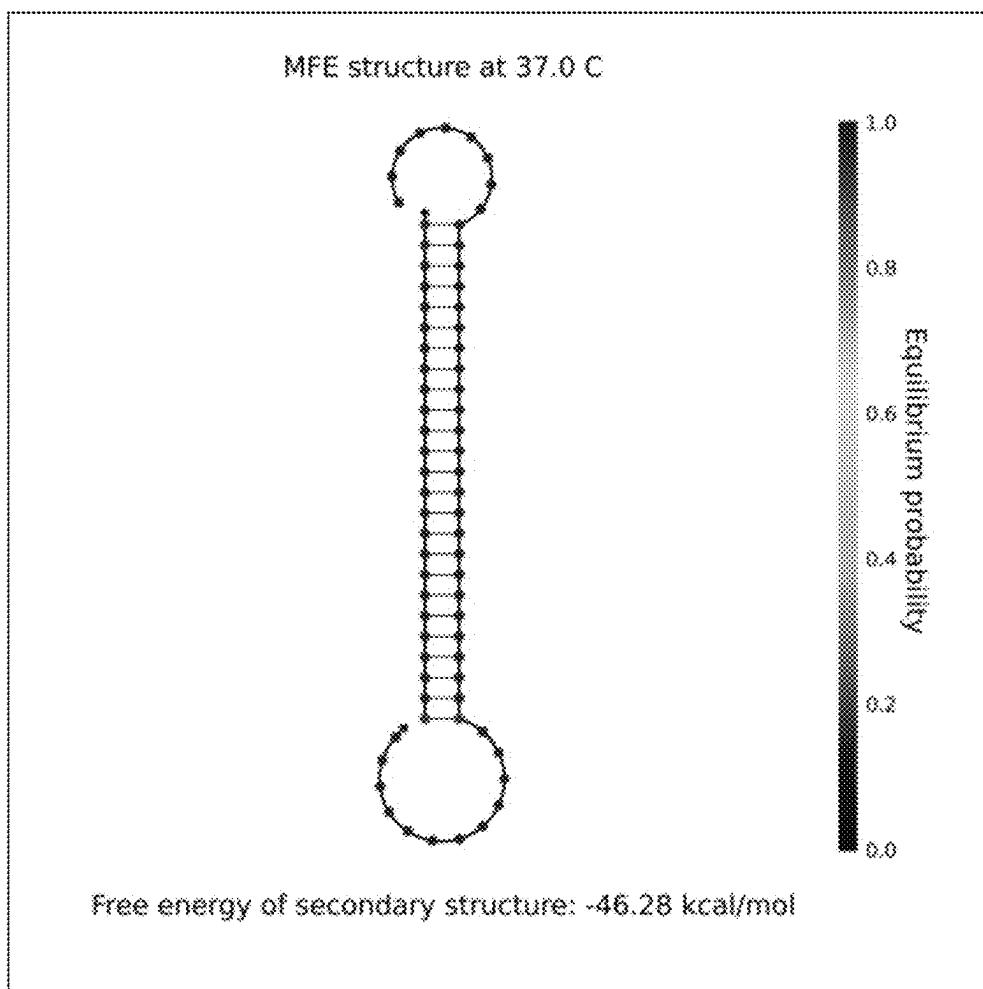
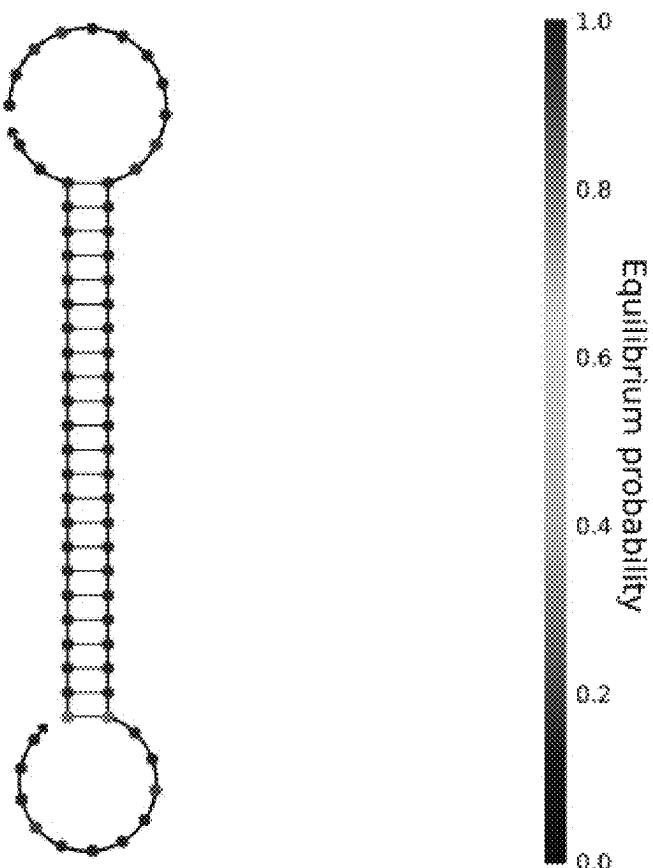
FIG. 27

FIG. 28

MFE structure at 37.0 °C



Free energy of secondary structure: -43.68 kcal/mol

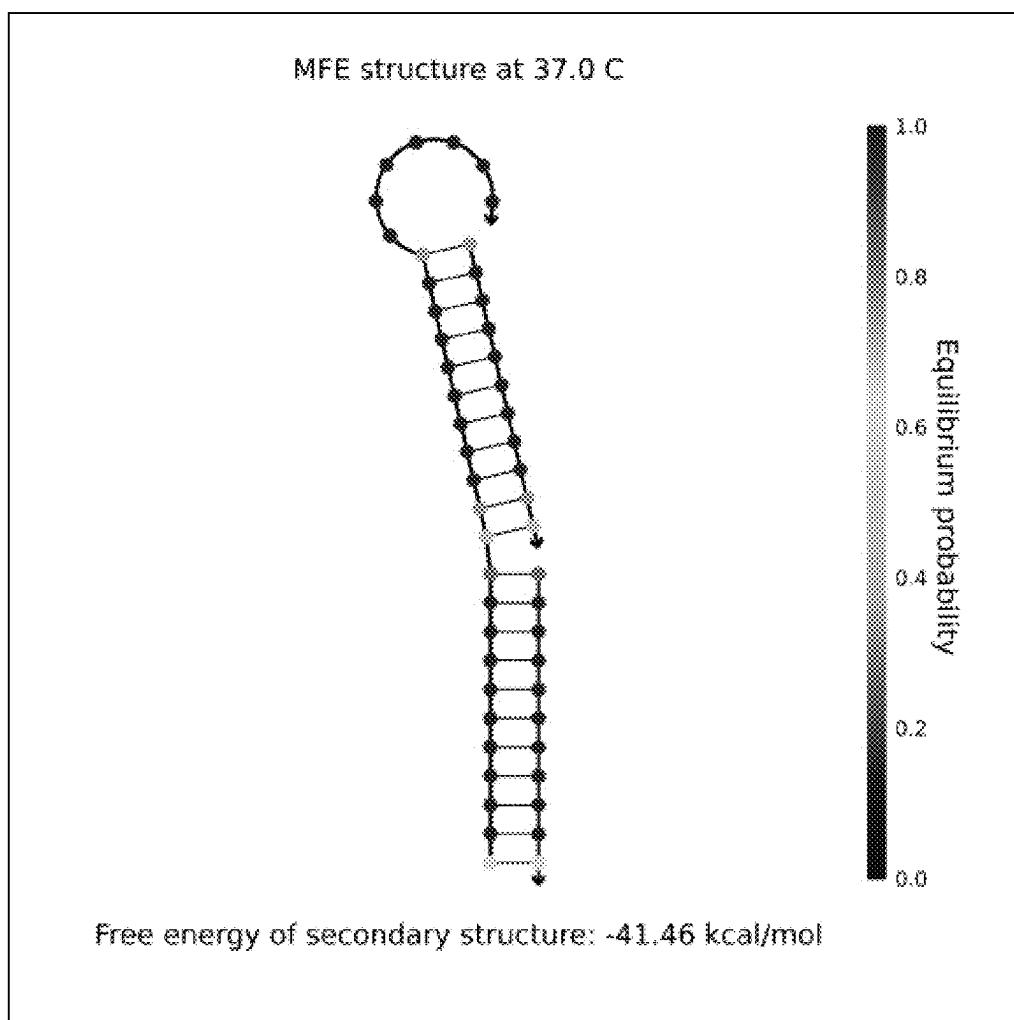
FIG. 29

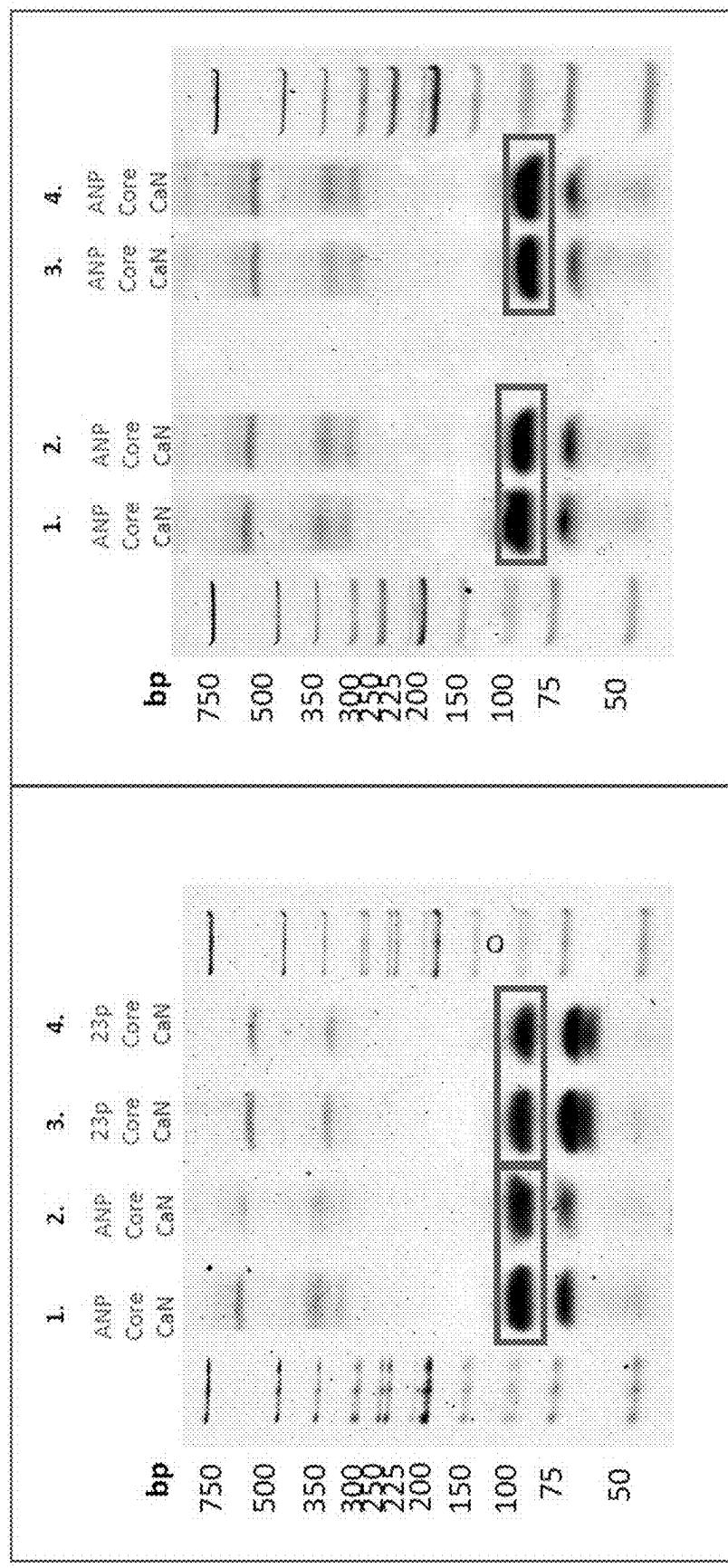
FIG. 30

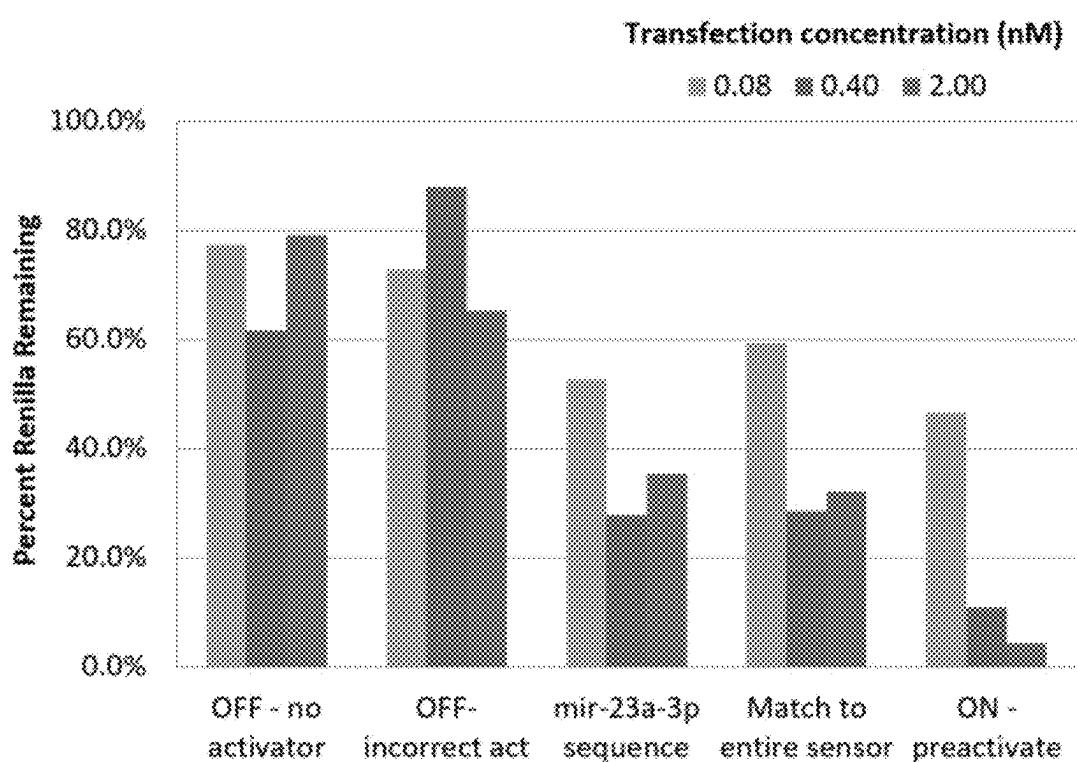
FIG. 31

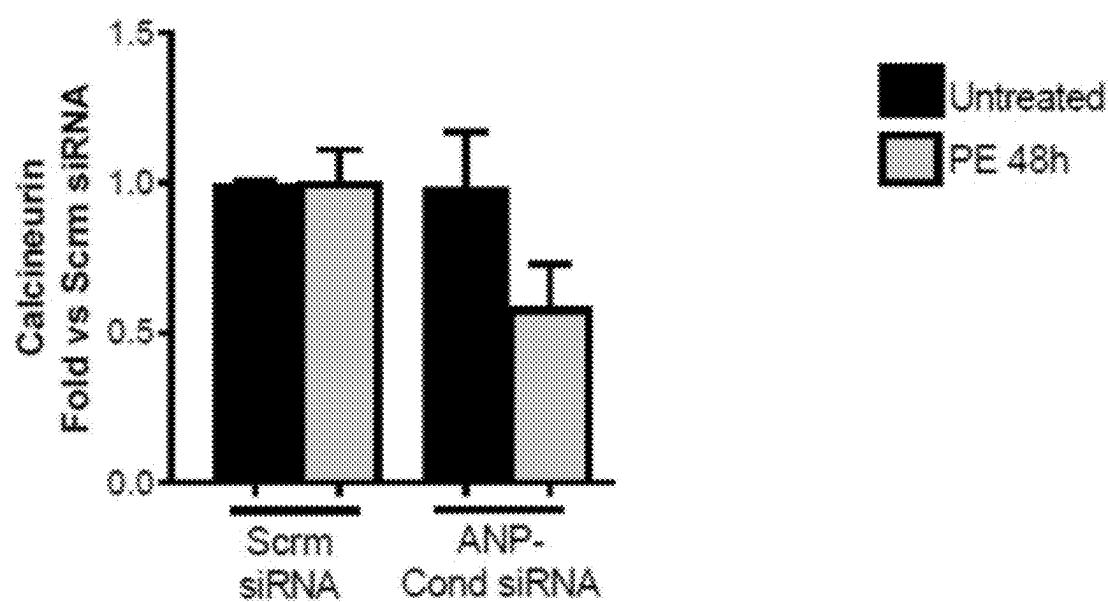
FIG. 32

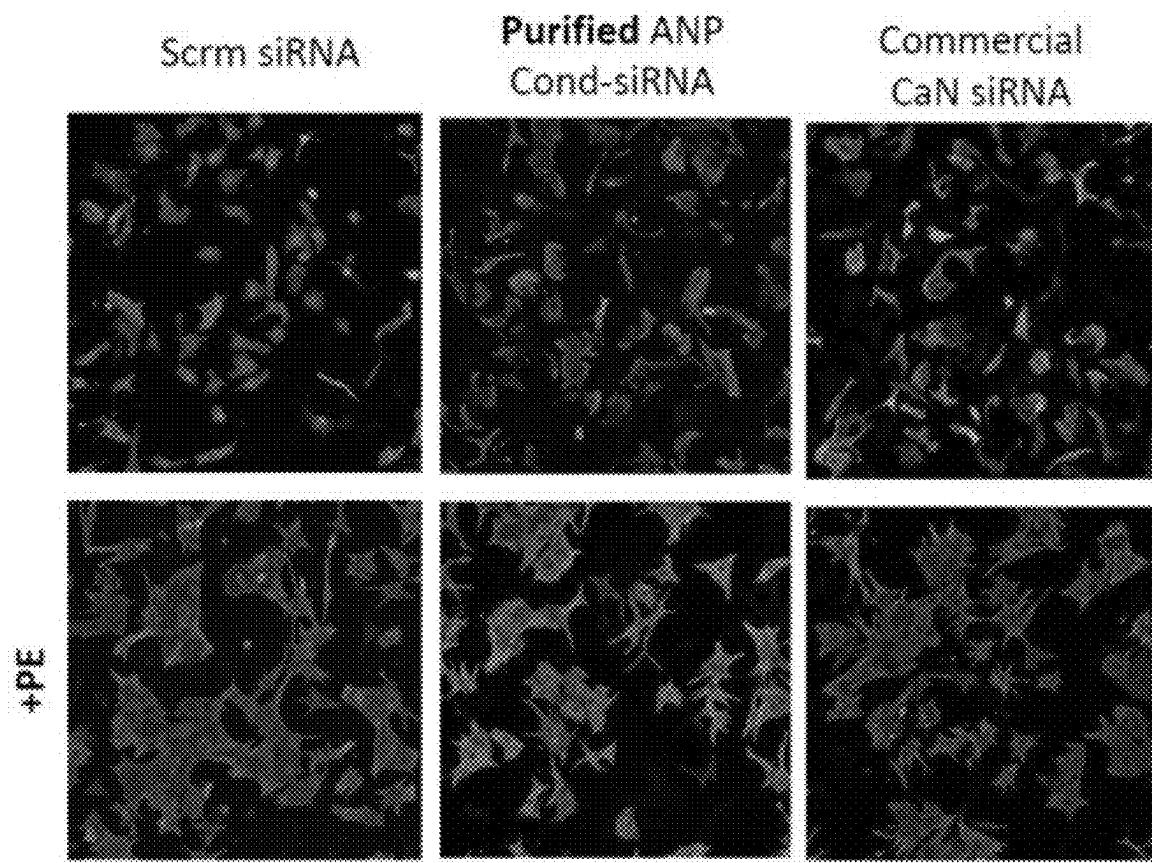
FIG. 33

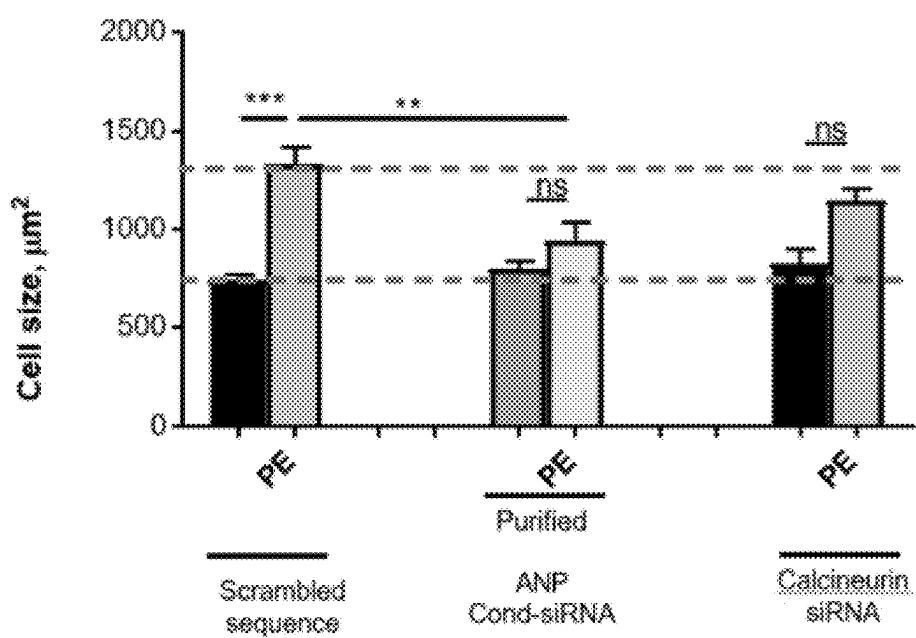
FIG. 34

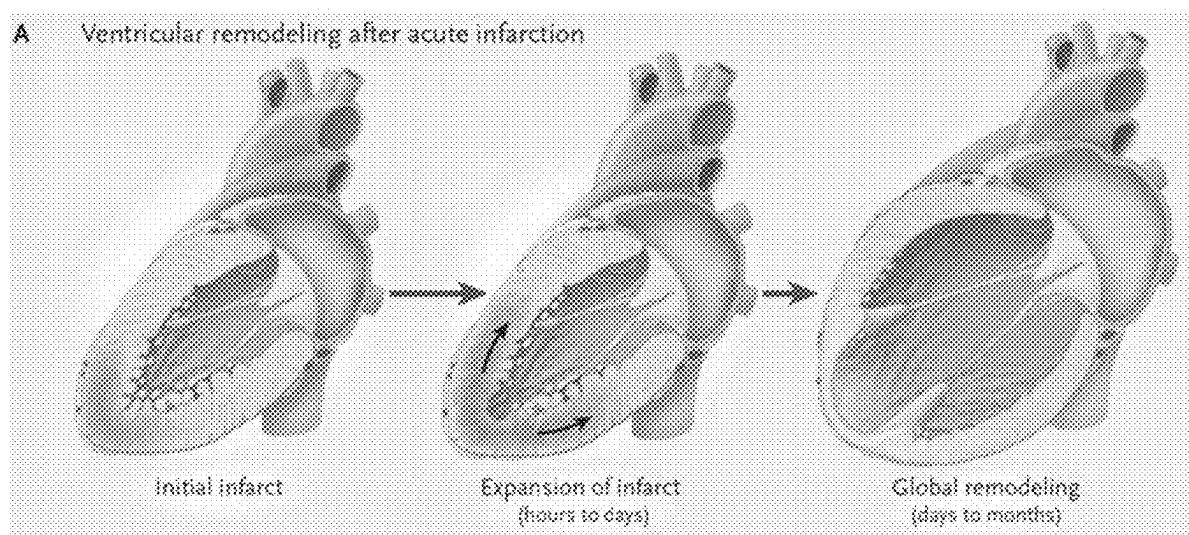
FIG. 35A

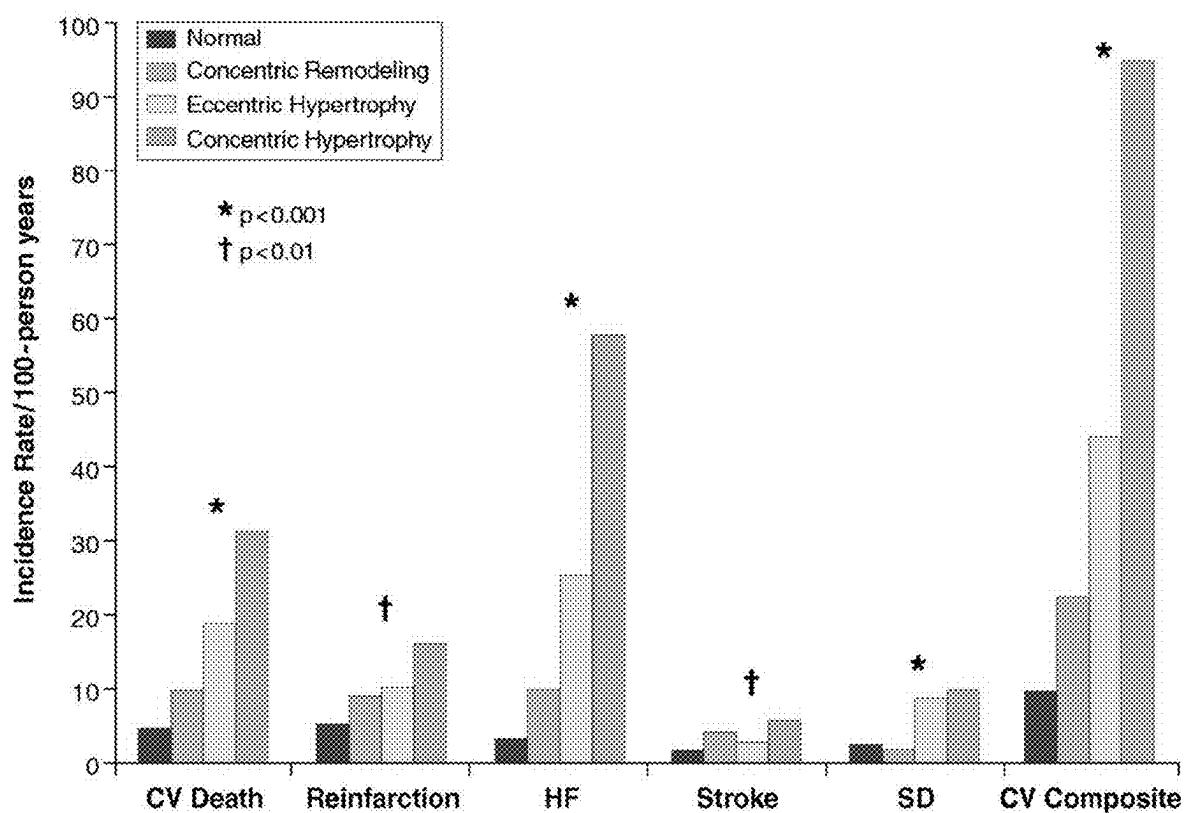
FIG. 35B

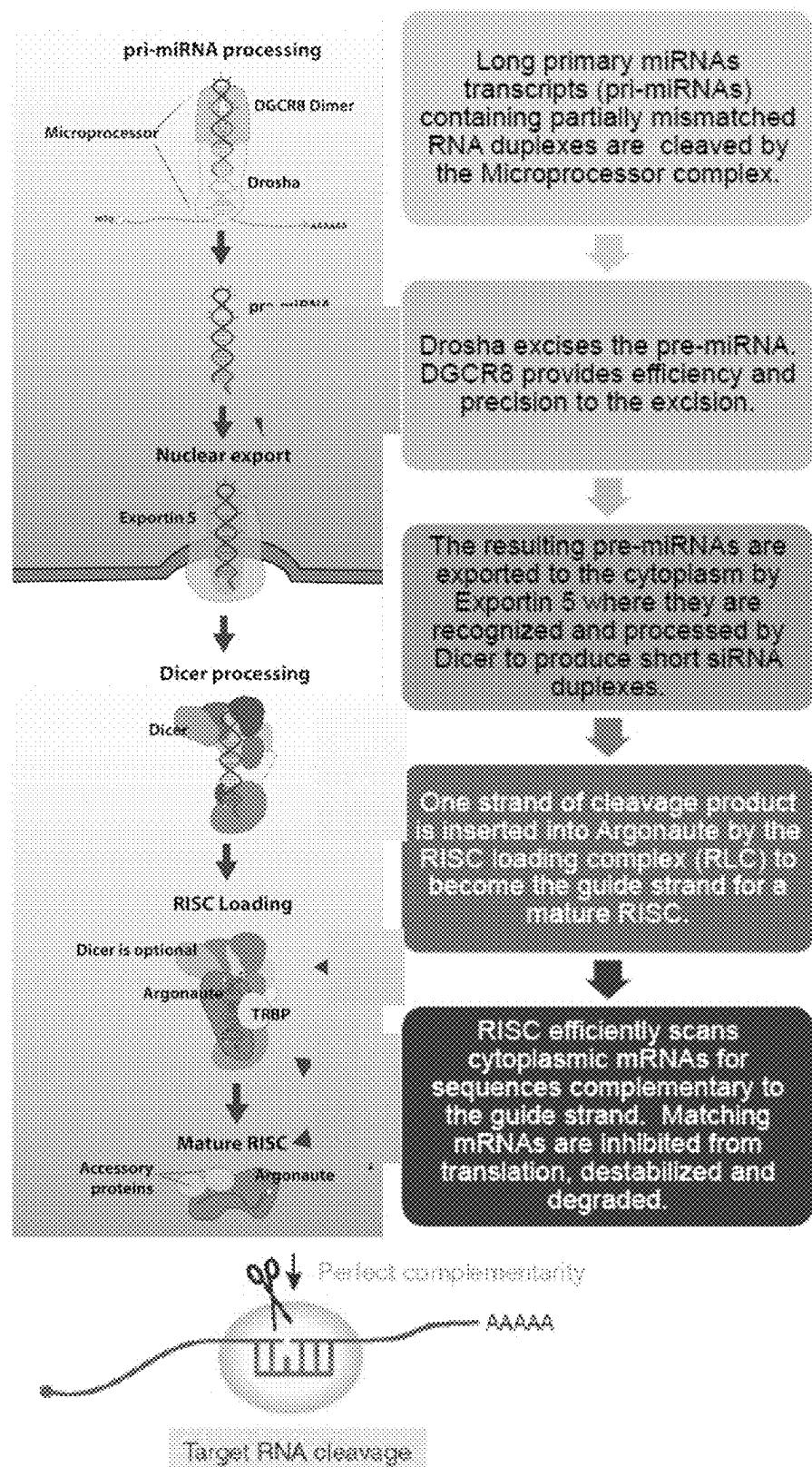
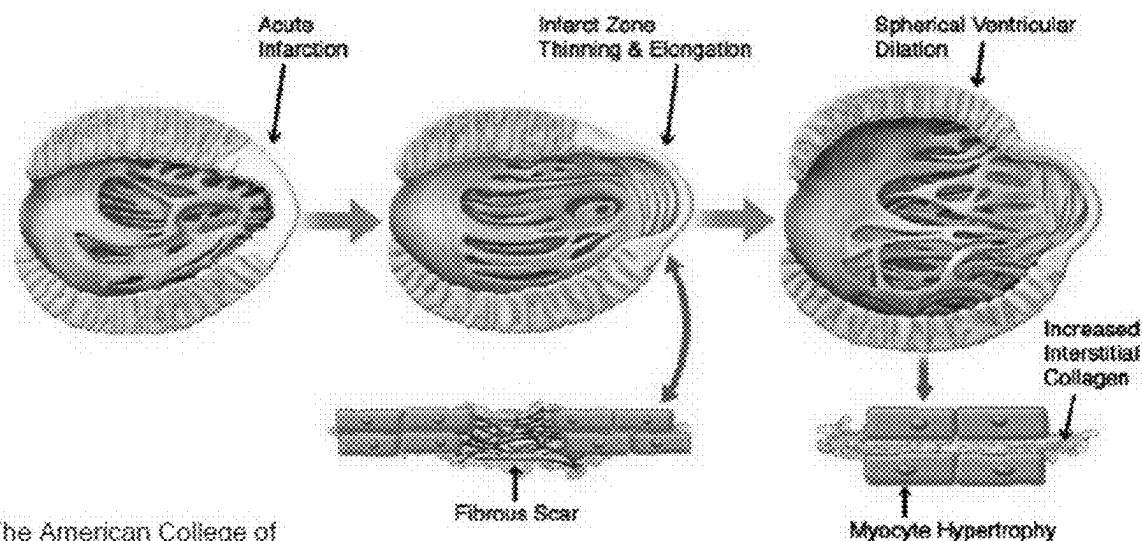
FIG. 36

FIG. 37**POST-MI REMODELING**

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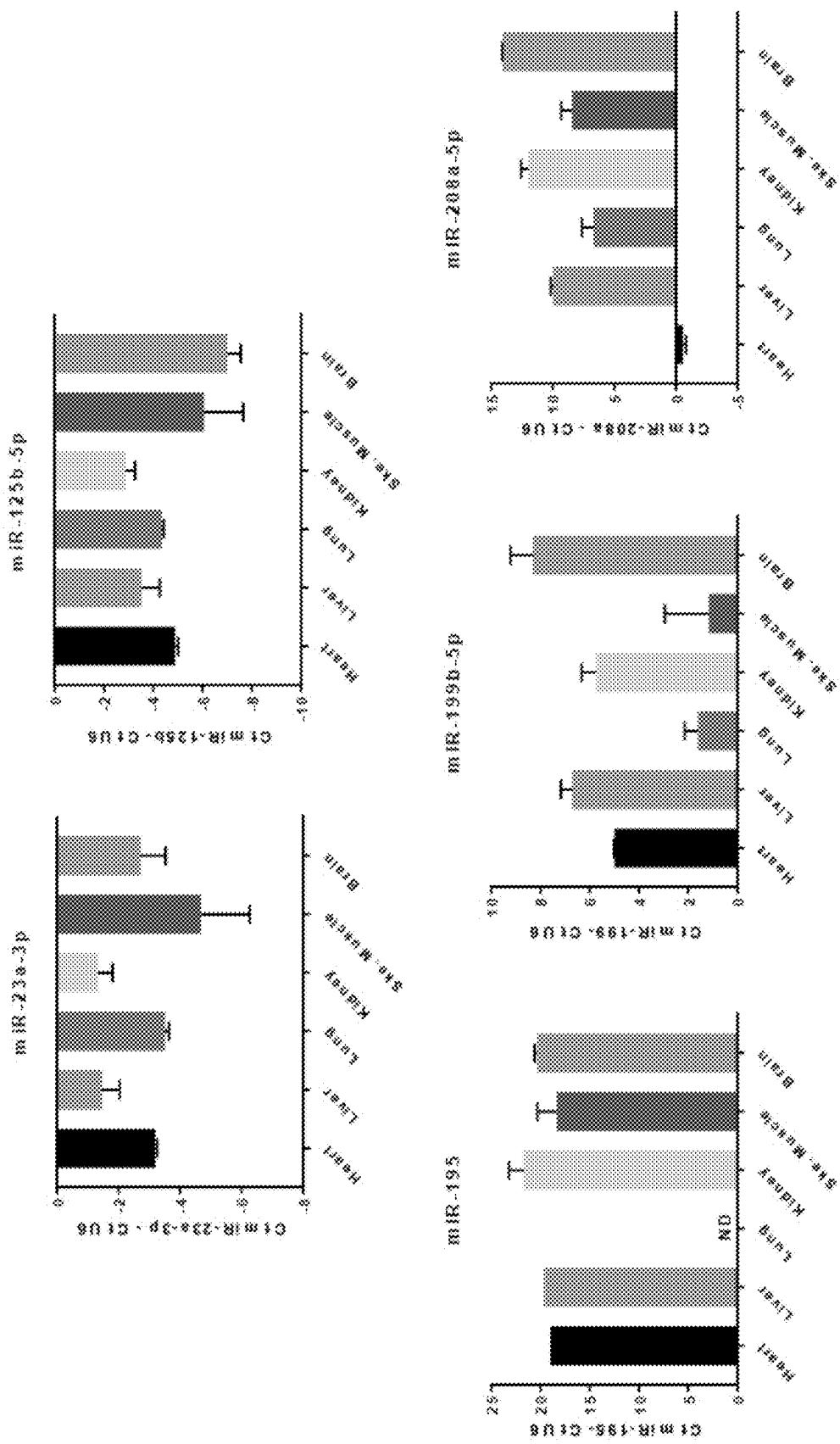
FIG. 38

FIG. 39

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCAAGGGAGCUGUUACAC AGGCUCCAGCAUGG' (SEQ ID NO:50)	[], [], []	0.580645	0.83871	0	37
'GGCUCCAGCAUGGGGC UUUGCUGGCACCUCC' (SEQ ID NO:168)	[], ['GGG'], []	0.677419	0.903226	1	55
'CCAGGGCUGAGCAGAUC AAGAUGUGGCAAAG' (SEQ ID NO:169)	[], ['GGG'], []	0.548387	0.870968	1	84
'CAGGGCUGAGCAGAUCA AGAUGUGGCAAAGC' (SEQ ID NO:170)	[], ['GGG'], []	0.548387	0.870968	1	85
'GCUGGCACCUCCAGGG CUGAGCAGAUCAAGA' (SEQ ID NO:171)	[], ['GGG'], []	0.612903	0.870968	1	74
'CAGGCCUCCAGCAUGGG GCUUUGCUGGCACCU' (SEQ ID NO:172)	[], ['GGG'], []	0.645161	0.870968	1	53
'AGGCUCCAGCAUGGGG CUUUGCUGGCACCUC' (SEQ ID NO:173)	[], ['GGG'], []	0.645161	0.870968	1	54
'GCUCCAGCAUGGGGU UUGCUGGCACCUCCA' (SEQ ID NO:174)	[], ['GGG'], []	0.645161	0.870968	1	56

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CUCCAGCAUGGGGCUUU GCUGGCACCUCCAG' (SEQ ID NO:175)	[], ['GGG'], []	0.645161	0.870968	1	57
'UCCAGCAUGGGGCUUU GCUGGCACCUCCAGG' (SEQ ID NO:176)	[], ['GGG'], []	0.645161	0.870968	1	58
'AUUCUGCUUCCUCCAA GGAGCUGUUACACA' (SEQ ID NO:177)	[['CCC'], [], []]	0.483871	0.83871	1	24
'UCCAGGGCUGAGCAGAU CAAGAUGUGGGCAA' (SEQ ID NO:178)	[], ['GGG'], []	0.516129	0.83871	1	83
'UGUUACACAGGCCUCCAG CAUGGGGCUUUGC' (SEQ ID NO:179)	[], ['GGG'], []	0.548387	0.83871	1	46
'CUCCAGGGCUGAGCAGA UCAAGAUGUGGGCAA' (SEQ ID NO:180)	[], ['GGG'], []	0.548387	0.83871	1	82
'CUCCCAAGGAGCUGUUA CACAGGCCUCCAGCA' (SEQ ID NO:181)	[['CCC'], [], []]	0.580645	0.83871	1	34
'CCCAAGGAGCUGUUACA CAGGCCUCCAGCAUG' (SEQ ID NO:182)	[['CCC'], [], []]	0.580645	0.83871	1	36

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CAAGGAGCUGUUACACA GGCUCCAGCAUGGG' (SEQ ID NO:183)	[], ['GGG'], []	0.580645	0.83871	1	38
'AAGGAGCUGUUACACAG GCUCCAGCAUGGGG' (SEQ ID NO:184)	[], ['GGG'], []	0.580645	0.83871	1	39
'GCUGUUACACAGGUCC AGCAUGGGGCCUUUG' (SEQ ID NO:185)	[], ['GGG'], []	0.580645	0.83871	1	44
'CUGUUACACAGGCCUCCA GCAUGGGGCCUUUGC' (SEQ ID NO:186)	[], ['GGG'], []	0.580645	0.83871	1	45
'GUUACACAGGCCUCCAGC AUGGGGCCUUUGCUG' (SEQ ID NO:187)	[], ['GGG'], []	0.580645	0.83871	1	47
'UUACACAGGCCUCCAGCA UGGGGCCUUUGCUGG' (SEQ ID NO:188)	[], ['GGG'], []	0.580645	0.83871	1	48
'CUGGCACCUCCAGGGCU GAGCAGAUCAAGAU' (SEQ ID NO:189)	[], ['GGG'], []	0.580645	0.83871	1	75
'UGGCACCUCCAGGGCU GAGCAGAUCAAGAUG' (SEQ ID NO:190)	[], ['GGG'], []	0.580645	0.83871	1	76

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GGCACCUCCAGGGCUGA GCAGAUCAAGAUGU' (SEQ ID NO:191)	[], ['GGG'], []	0.580645	0.83871	1	77
'GCACCUCCAGGGCUGAG CAGAUCAAGAUGUG' (SEQ ID NO:192)	[], ['GGG'], []	0.580645	0.83871	1	78
'CACCUCCAGGGCUGAGC AGAUCAAGAUGUGG' (SEQ ID NO:193)	[], ['GGG'], []	0.580645	0.83871	1	79
'ACCUCCAGGGCUGAGCA GAUCAAGAUGUGGC' (SEQ ID NO:194)	[], ['GGG'], []	0.580645	0.83871	1	80
'CCUCCAGGGCUGAGCAG AUCAAGAUGUGGC'A (SEQ ID NO:195)	[], ['GGG'], []	0.580645	0.83871	1	81
'CCUCCCAAGGAGCUGUU ACACAGGCCUCCAGC' (SEQ ID NO:196)	[["CCC"], [], []]	0.612903	0.83871	1	33
'AGGAGCUGUUACACAGG CUCCAGCAUGGGGC' (SEQ ID NO:197)	[], ['GGG'], []	0.612903	0.83871	1	40
'UACACAGGCCUCCAGCAU GGGGCUUUGCUGGC' (SEQ ID NO:198)	[], ['GGG'], []	0.612903	0.83871	1	49

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GCUUUGCUGGCACCUCC AGGGCUGAGCAGAU' (SEQ ID NO:199)	[], ['GGG'], []	0.612903	0.83871	1	69
'CUUUGCUGGCACCUCCA GGGCUGAGCAGAUC' (SEQ ID NO:200)	[], ['GGG'], []	0.612903	0.83871	1	70
'UGCUGGCACCUCCAGG GCUGAGCAGAUCAAG' (SEQ ID NO:201)	[], ['GGG'], []	0.612903	0.83871	1	73
'CACAGGCCUCCAGCAUGG GGCUUUGCUGGCAC' (SEQ ID NO:202)	[], ['GGG'], []	0.645161	0.83871	1	51
'ACAGGCCUCCAGCAUGGG GCUUUGCUGGCACC' (SEQ ID NO:203)	[], ['GGG'], []	0.645161	0.83871	1	52
'GGCUUUGCUGGCACCU CCAGGGCUGAGCAGA' (SEQ ID NO:204)	[], ['GGG'], []	0.645161	0.83871	1	68
'UUCUGCUUCCUCCCAAG GAGCUGUUACACAG' (SEQ ID NO:205)	['CCC'], [], []	0.516129	0.806452	1	25
'UCUGCUUCCUCCCAAGG AGCUGUUACACAGG' (SEQ ID NO:206)	['CCC'], [], []	0.548387	0.806452	1	26

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGCUUCCUCCCAAGGAG CUGUUACACAGGCU' (SEQ ID NO:207)	[['CCC'], [], []]	0.548387	0.806452	1	28
'UUCCUCCCAAGGAGCUG UUACACAGGCUCCA' (SEQ ID NO:208)	[['CCC'], [], []]	0.548387	0.806452	1	31
'UCCCAAGGAGCUGUUAC ACAGGCCUCCAGCAU' (SEQ ID NO:209)	[['CCC'], [], []]	0.548387	0.806452	1	35
'AGCUGUUACACAGGCUC CAGCAUGGGGUUU' (SEQ ID NO:210)	[[], [GGG], []]	0.548387	0.806452	1	43
'CUGCUUCCUCCCAAGGA GCUGUUACACAGGC' (SEQ ID NO:211)	[['CCC'], [], []]	0.580645	0.806452	1	27
'GCUUCCUCCCAAGGAGC UGUUACACAGGCUC' (SEQ ID NO:212)	[['CCC'], [], []]	0.580645	0.806452	1	29
'CUUCCUCCCAAGGAGCU GUUACACAGGCUCC' (SEQ ID NO:213)	[['CCC'], [], []]	0.580645	0.806452	1	30
'UCCUCCCAAGGAGCUGU UACACAGGCUCCAG' (SEQ ID NO:214)	[['CCC'], [], []]	0.580645	0.806452	1	32

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GAGCUGUUACACAGGCC CCAGCAUGGGCUU' (SEQ ID NO:215)	[], ['GGG'], []	0.580645	0.806452	1	42
'UUUGCUGGCACCUCCAG GGCUGAGCAGAUCA' (SEQ ID NO:216)	[], ['GGG'], []	0.580645	0.806452	1	71
'UUGCUGGCACCUCCAGG GCUGAGCAGAUCAA' (SEQ ID NO:217)	[], ['GGG'], []	0.580645	0.806452	1	72
'GGAGCUGUUACACAGGC UCCAGCAUGGGCU' (SEQ ID NO:218)	[], ['GGG'], []	0.612903	0.806452	1	41
'ACACAGGCCUCCAGCAUG GGGCUUUGCUGGCA' (SEQ ID NO:219)	[], ['GGG'], []	0.612903	0.806452	1	50
'GCAUGGGCUUUGCUG GCACCUCCAGGGCUG' (SEQ ID NO:220)	[], ['GGG', 'GGG'], []	0.677419	0.903226	2	62
'UGGGGCUUUGCUGGCA CCUCCAGGGCUGAGC' (SEQ ID NO:221)	[], ['GGG', 'GGG'], []	0.677419	0.903226	2	65
'CUUCAAGGAAAAUUGC UUAUUCUGCUUCCU' (SEQ ID NO:222)	[], [], ['AAAA', 'UUUA']]	0.354839	0.870968	2	5

FIG. 39 (Cont'd)

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUCAAGGAAAAUUGCUU UAUUCUGCUUCCUC' (SEQ ID NO:223)	[[],[], ['AAAAA', 'UUUA']]	0.354839	0.870968	2	6
'UCAAGGAAAAUUGCUUU AUUCUGCUUCCUCC' (SEQ ID NO:224)	[[],[], ['AAAAA', 'UUUA']]	0.387097	0.870968	2	7
'UUGCUUUAUUCUGCUUC CUCCCAAGGAGCUG' (SEQ ID NO:225)	[['CCC'], [], ['UUUA']]	0.483871	0.870968	2	17
'UGCUUUAUUCUGCUUCC UCCCAAGGAGCUGU' (SEQ ID NO:226)	[['CCC'], [], ['UUUA']]	0.483871	0.870968	2	18
'GCUUUUAUUCUGCUUCCU CCCAAGGAGCUGUU' (SEQ ID NO:227)	[['CCC'], [], ['UUUA']]	0.483871	0.870968	2	19
'AGCAUGGGCUUUGC GGCACCUCCAGGGCU' (SEQ ID NO:228)	[[], ['GGG', 'GGG'], []]	0.645161	0.870968	2	61
'CAUGGGCUUUGCUGG CACCUCCAGGGCUGA' (SEQ ID NO:229)	[[], ['GGG', 'GGG'], []]	0.645161	0.870968	2	63
'AUGGGGCUUUGCUGGC ACCUCCAGGGCUGAG' (SEQ ID NO:230)	[[], ['GGG', 'GGG'], []]	0.645161	0.870968	2	64

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCAGCAUGGGGCUUUG CUGGCACCUCCAGGG' (SEQ ID NO:231)	[], ['GGG', 'GGG'], []	0.677419	0.870968	2	59
'CAGCAUGGGGCUUUGC UGGCACCUCCAGGGC' (SEQ ID NO:232)	[], ['GGG', 'GGG'], []	0.677419	0.870968	2	60
'GGGCCUUUGCUGGCAC CUCCAGGGCUGAGCA' (SEQ ID NO:233)	[], ['GGG', 'GGG'], []	0.677419	0.870968	2	66
'GGGCUUUGCUGGCACC UCCAGGGCUGAGCAG' (SEQ ID NO:234)	[], ['GGG', 'GGG'], []	0.677419	0.870968	2	67
'GCUUCAAGGAAAAUUGC UUUAUUCUGCUUCC' (SEQ ID NO:235)	[], [], ['AAAA', 'UUUA']]	0.387097	0.83871	2	4
'AUUGCUUUAUUCUGCUU CCUCCCAAGGAGCU' (SEQ ID NO:236)	[['CCC'], [], ['UUUA']]	0.451613	0.83871	2	16
'CUUUAUUCUGCUUCCUC CCAAGGAGCUGUUA' (SEQ ID NO:237)	[['CCC'], [], ['UUUA']]	0.451613	0.83871	2	20

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUUAUUCUGCUUCCUCC CAAGGAGCUGUUAC' (SEQ ID NO:238)	[['CCC'], [], ['UUUA']]	0.451613	0.83871	2	21
'UUAUUCUGCUUCCUCCC AAGGAGCUGUUACAC' (SEQ ID NO:239)	[['CCC'], [], ['UUAU']]	0.451613	0.83871	2	22
'UAUUCUGCUUCCUCCCA AGGAGCUGUUACAC' (SEQ ID NO:240)	[['CCC'], [], ['UAUU']]	0.483871	0.83871	2	23
'UCGGCUUCAAGGAAAAAU UGCUUUAUUCUGCU' (SEQ ID NO:241)	[], [], ['AAAA', 'UUUA']]	0.387097	0.806452	2	1
'CGGCUUCAAGGAAAAUU GCUUUAUUCUGCUU' (SEQ ID NO:242)	[], [], ['AAAA', 'UUUA']]	0.387097	0.806452	2	2
'GGCUUCAAGGAAAAUUG CUUUAUUCUGCUUC' (SEQ ID NO:243)	[], [], ['AAAA', 'UUUA']]	0.387097	0.806452	2	3
'CUCGGCUUCAAGGAAAA UUGCUUUAUUCUGC' (SEQ ID NO:244)	[], [], ['AAAA', 'UUUA']]	0.419355	0.806452	2	0
'AAGGAAAAUUGCUUUAU UCUGCUUCCUCCCA' (SEQ ID NO:245)	[['CCC'], [], ['AAAA', 'UUUA']]	0.387097	0.870968	3	9

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGGAAAAAUUGCUUUAUU CUGCUUCCUCCCAA' (SEQ ID NO:246)	[["CCC"], [], ['AAAA', 'UUUA']]	0.387097	0.870968	3	10
'AAAAAUUGCUUUAUUCUG CUUCCUCCCAAGGA' (SEQ ID NO:247)	[["CCC"], [], ['AAAA', 'UUUA']]	0.387097	0.870968	3	13
'CAAGGAAAAUUGCUUUA UUCUGCUUCCUCCC' (SEQ ID NO:248)	[["CCC"], [], ['AAAA', 'UUUA']]	0.419355	0.870968	3	8
'GGAAAAAUUGCUUUAUUC UGCUUCCUCCCAAG' (SEQ ID NO:249)	[["CCC"], [], ['AAAA', 'UUUA']]	0.419355	0.83871	3	11
'GAAAAAUUGCUUUAUUCU GCUUCCUCCCAAGG' (SEQ ID NO:250)	[["CCC"], [], ['AAAA', 'UUUA']]	0.419355	0.83871	3	12
'AAAUAUGCUUUAUUCUGC UUCCUCCCAAGGAG' (SEQ ID NO:251)	[["CCC"], [], ['AAAU', 'UUUA']]	0.419355	0.83871	3	14

FIG. 39 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AAUUGCUUUAUUCUGCU UCCUCCCCAAGGGAGC' (SEQ ID NO:252)	[['CCC'], [], ['AAUU', 'UUUA']]	0.451613	0.83871	3	15

FIG. 39 (Cont'd)

FIG. 40

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GUGUUUCUGCCUAAGG UGCUGUUCAAAGGC' (SEQ ID NO:253)	[], [], []	0.483871	0.83871	0	24
'GUUCUGCCUAAGGUG CUGUUCAAAGGCUC' (SEQ ID NO:254)	[], [], []	0.483871	0.83871	0	26
'UUUCUGCCUAAGGUGC UGUUUCAAAGGCUCC' (SEQ ID NO:255)	[], [], []	0.483871	0.83871	0	27
'UGUGUUUCUGCCUAAG GUGCUGUUCAAAGG' (SEQ ID NO:256)	[], [], []	0.451613	0.83871	0	23
'UGUUUCUGCCUAAGGU GCUGUUCAAAGGCU' (SEQ ID NO:257)	[], [], []	0.451613	0.83871	0	25
'UUGUGUUUCUGCCUA GGUGCUGUUCAAAG' (SEQ ID NO:258)	[], [], []	0.419355	0.83871	0	22
'AUUGUGUUUCUGCCUA AGGUGCUGUUCAAA' (SEQ ID NO:259)	[], [], []	0.387097	0.83871	0	21
'CUGCCUAAGGUGCUGU UUCAAAGGCUCCAGG' (SEQ ID NO:260)	[], [], []	0.548387	0.806452	0	30

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GCCUAAGGUGCUGUUU CAAAGGCUCCAGGUC' (SEQ ID NO:261)	[], [], []	0.548387	0.806452	0	32
'AGGUGCUGUUUCAAAG GCUCCAGGUCUCAGG' (SEQ ID NO:262)	[], [], []	0.548387	0.806452	0	37
'UCUGCCUAAGGUGCUG UUUCAAAGGCUCCAG' (SEQ ID NO:263)	[], [], []	0.516129	0.806452	0	29
'UGCCUAAGGUGCUGUU UCAAAGGCUCCAGGU' (SEQ ID NO:264)	[], [], []	0.516129	0.806452	0	31
'CCUAAGGUGCUGUUUC AAAGGCUCCAGGUCU' (SEQ ID NO:265)	[], [], []	0.516129	0.806452	0	33
'CUAAGGUGCUGUUUCA AAGGCUCCAGGUCUC' (SEQ ID NO:266)	[], [], []	0.516129	0.806452	0	34
'UUCUGCCUAAGGUGCU GUUUCAAAGGCUCCA' (SEQ ID NO:267)	[], [], []	0.483871	0.806452	0	28
'AAGGUGCUGUUUCAAA GGCUCCAGGUCUCAG' (SEQ ID NO:268)	[], [], []	0.516129	0.774194	0	36

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'UAAGGUGCUGUUUCAA AGGCUCCAGGUCUCA' (SEQ ID NO:269)	[], [], []	0.483871	0.774194	0	35
'UUGCUUUAUUGUGUUU CUGCCUAAGGUGCUG' (SEQ ID NO:270)	[], [], ['UUUA']]	0.419355	0.903226	1	14
'UGCUUUAUUGUGUUUC UGCCUAAGGUGCUGU' (SEQ ID NO:271)	[], [], ['UUUA']]	0.419355	0.903226	1	15
'GCUUUAUUGUGUUUCU GCCUAAGGUGCUGUU' (SEQ ID NO:272)	[], [], ['UUUA']]	0.419355	0.903226	1	16
'CUUUAUUGUGUUUCUG CCUAAGGUGCUGUUU' (SEQ ID NO:273)	[], [], ['UUUA']]	0.387097	0.903226	1	17
'UUUAUUGUGUUUCUGC CUAAGGUGCUGUUUC' (SEQ ID NO:274)	[], [], ['UUUA']]	0.387097	0.903226	1	18
'AUUGCUUUAUUGUGUU UCUGCCUAAGGUGCU' (SEQ ID NO:275)	[], [], ['UUUA']]	0.387097	0.870968	1	13
'UUAUUUGUGUUUCUGCC UAAGGUGCUGUUUCA' (SEQ ID NO:276)	[], [], ['UUAU']]	0.387097	0.870968	1	19

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GGCUCCAGGUCUCAGG GCUUCACAGGCAUCC' (SEQ ID NO:277)	[], ['GGG'], []	0.645161	0.83871	1	52
'CAAAGGCUCCAGGUCU CAGGGCUUCACAGGC' (SEQ ID NO:278)	[], ['GGG'], []	0.612903	0.83871	1	48
'GCUCCAGGUCUCAGGG CUUCACAGGCAUCCU' (SEQ ID NO:279)	[], ['GGG'], []	0.612903	0.83871	1	53
'GGUGCUGUUUCAAAGG CUCCAGGUCUCAGGG' (SEQ ID NO:280)	[], ['GGG'], []	0.580645	0.83871	1	38
'GUGCUGUUUCAAAGGC UCCAGGUCUCAGGGC' (SEQ ID NO:281)	[], ['GGG'], []	0.580645	0.83871	1	39
'AAAGGCUCCAGGUCUC AGGGCUUCACAGGCA' (SEQ ID NO:282)	[], ['GGG'], []	0.580645	0.83871	1	49
'CUCCAGGUCUCAGGGC UUCACAGGCAUCCUU' (SEQ ID NO:283)	[], ['GGG'], []	0.580645	0.83871	1	54
'UGCUGUUUCAAAGGCU CCAGGUCUCAGGGCU' (SEQ ID NO:284)	[], ['GGG'], []	0.548387	0.83871	1	40

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GCUGUUUCAAAGGCUC CAGGUCUCAGGGCUU' (SEQ ID NO:285)	[], ['GGG'], []	0.548387	0.83871	1	41
'CUGUUUCAAAGGCUCC AGGUCUCAGGGCUUC' (SEQ ID NO:286)	[], ['GGG'], []	0.548387	0.83871	1	42
'UAUUGUGUUUCUGCCU AAGGUGCUGUUUCAA' (SEQ ID NO:287)	[], [], ['UAUU']]	0.387097	0.83871	1	20
'AGGCUCCAGGUCUCAG GGCUUCACAGGCAUC' (SEQ ID NO:288)	[], ['GGG'], []	0.612903	0.806452	1	51
'UCAAAGGCCUCCAGGUC UCAGGGCUUCACAGG' (SEQ ID NO:289)	[], ['GGG'], []	0.580645	0.806452	1	47
'AAGGCUCCAGGUCUCA GGGCUUCACAGGCAU' (SEQ ID NO:290)	[], ['GGG'], []	0.580645	0.806452	1	50
'CCAGGUCUCAGGGCUU CACAGGCAUCCUUAG' (SEQ ID NO:291)	[], ['GGG'], []	0.580645	0.806452	1	56
'CAGGUCUCAGGGCUUC ACAGGCAUCCUUAGG' (SEQ ID NO:292)	[], ['GGG'], []	0.580645	0.806452	1	57

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GUUCAAAGGCUCCAG GUCUCAGGGCUUCAC' (SEQ ID NO:293)	[], ['GGG'], []	0.548387	0.806452	1	44
'UCCAGGUCUCAGGGCU UCACAGGCAUCCUUA' (SEQ ID NO:294)	[], ['GGG'], []	0.548387	0.806452	1	55
'UGUUUCAAAGGCUCCA GGUCUCAGGGCUUCA' (SEQ ID NO:295)	[], ['GGG'], []	0.516129	0.806452	1	43
'UUCAAAGGCUCCAGGU CUCAGGGCUUCACAG' (SEQ ID NO:296)	[], ['GGG'], []	0.548387	0.774194	1	46
'UUUCAAAGGCUCCAGG UCUCAGGGCUUCACA' (SEQ ID NO:297)	[], ['GGG'], []	0.516129	0.774194	1	45
'GGCUUGAAGGAAAAUU GCUUUAUUGUGUUUC'	[], [], ['AAAA', 'UUUA']]	0.354839	0.903226	2	0
'GCUUGAAGGAAAAUUG CUUUAUUGUGUUUCU'	[], [], ['AAAA', 'UUUA']]	0.322581	0.903226	2	1
'CUUGAAGGAAAAUUGC UUUAUUGUGUUUCUG'	[], [], ['AAAA', 'UUUA']]	0.322581	0.903226	2	2

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'UGAAGGAAAAUUGCUC UUAUUGUGUUUCUGC' (SEQ ID NO:301)	[], [], ['AAAA', 'UUUA']]	0.322581	0.903226	2	3
'UGAAGGAAAAUUGCUU UAUUGUGUUUCUGCC' (SEQ ID NO:302)	[], [], ['AAAA', 'UUUA']]	0.354839	0.870968	2	4
'GAAGGAAAAUUGCUUU AUUGUGUUUCUGCCU' (SEQ ID NO:303)	[], [], ['AAAA', 'UUUA']]	0.354839	0.870968	2	5
'GGAAAAUUGCUUUAUU GUGUUUCUGCCUAAG' (SEQ ID NO:304)	[], [], ['AAAA', 'UUUA']]	0.354839	0.870968	2	8
'GAAAAAUUGCUUUAUUG UGUUUCUGCCUAAGG' (SEQ ID NO:305)	[], [], ['AAAA', 'UUUA']]	0.354839	0.870968	2	9
'AAAUUGCUUUAUUGUG UUUCUGCCUAAGGUG' (SEQ ID NO:306)	[], [], ['AAAU', 'UUUA']]	0.354839	0.870968	2	11
'AAGGAAAAUUGCUUUAU UGUGUUUCUGCCUA' (SEQ ID NO:307)	[], [], ['AAAA', 'UUUA']]	0.322581	0.870968	2	6
'AGGAAAAAUUGCUUUAU UGUGUUUCUGCCUA' (SEQ ID NO:308)	[], [], ['AAAA', 'UUUA']]	0.322581	0.870968	2	7

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'AAAAUUGCUUUAUUGU GUUCUGCCUAAGGU' (SEQ ID NO:309)	[[], [], ['AAAA', 'UUUA']]	0.322581	0.870968	2	10
'GGUCUCAGGGCUUCAC AGGCAUCCUUAGGGU' (SEQ ID NO:310)	[[], ['GGG', 'GGG'], []]	0.580645	0.83871	2	59
'CUCAGGGCUUCACAGG CAUCCUUAGGGUUGG' (SEQ ID NO:311)	[[], ['GGG', 'GGG'], []]	0.580645	0.83871	2	62
'GGCUUCACAGGCAUCC UUAGGGUUGGGUAGC' (SEQ ID NO:312)	[[], ['GGG', 'GGG'], []]	0.580645	0.83871	2	67
'GUCUCAGGGCUUCACA GGCAUCCUUAGGGUU' (SEQ ID NO:313)	[[], ['GGG', 'GGG'], []]	0.548387	0.83871	2	60
'UCUCAGGGCUUCACAG GCAUCCUUAGGGUUG' (SEQ ID NO:314)	[[], ['GGG', 'GGG'], []]	0.548387	0.83871	2	61
'AAUUGCUUUAUUGUGU UUCUGCCUAAGGUGC' (SEQ ID NO:315)	[[], [], ['AAUU', 'UUUA']]	0.387097	0.83871	2	12
'AGGUCUCAGGGCUUCA CAGGCAUCCUUAGGG' (SEQ ID NO:316)	[[], ['GGG', 'GGG'], []]	0.580645	0.806452	2	58

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GCUUCACAGGCAUCCU UAGGGUUGGGUAGCA' (SEQ ID NO:317)	[], ['GGG', 'GGG'], []]	0.548387	0.806452	2	68
'CUUCACAGGCAUCCUU AGGGUUGGGUAGCAC' (SEQ ID NO:318)	[], ['GGG', 'GGG'], []]	0.548387	0.806452	2	69
'CACAGGCAUCCUUAGG GUUGGGUAGCACAAG' (SEQ ID NO:319)	[], ['GGG', 'GGG'], []]	0.548387	0.806452	2	72
'ACAGGCAUCCUUAGGG UUGGGUAGCACAAGA' (SEQ ID NO:320)	[], ['GGG', 'GGG'], []]	0.516129	0.806452	2	73
'CAGGCAUCCUUAGGGU UGGGUAGCACAAGAU' (SEQ ID NO:321)	[], ['GGG', 'GGG'], []]	0.516129	0.806452	2	74
'UUCACAGGCAUCCUUA GGGUUGGGUAGCACA' (SEQ ID NO:322)	[], ['GGG', 'GGG'], []]	0.516129	0.774194	2	70
'UCACAGGCAUCCUAG GGUUGGGUAGCACAA' (SEQ ID NO:323)	[], ['GGG', 'GGG'], []]	0.516129	0.774194	2	71
'UCAGGGCUUCACAGGC AUCCUUAGGGUUGGG' (SEQ ID NO:324)	[], ['GGG', 'GGG', 'GGG'], []]	0.580645	0.83871	3	63

FIG. 40 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'CAGGGCUUCACAGGCA UCCUUAGGGUUGGGU' (SEQ ID NO:325)	[[], ['GGG', 'GGG', 'GGG'], []]	0.580645	0.83871	3	64
'GGGCUUCACAGGCAUC CUUAGGGUUGGGUAG' (SEQ ID NO:326)	[[], ['GGG', 'GGG', 'GGG'], []]	0.580645	0.83871	3	66
'AGGGCUUCACAGGCAU CCUUAGGGUUGGGUA' (SEQ ID NO:327)	[[], ['GGG', 'GGG', 'GGG'], []]	0.548387	0.806452	3	65

FIG. 40 (Cont'd)

FIG. 41

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGAGAGGCGAGGAAGU CACCAUCAAACCCACU' (SEQ ID NO:328)	[], [], []	0.548387	0.903226	0	90
'AGAUGUGAGAAGUGUUG ACAGGAAGCUGGCAG' (SEQ ID NO:329)	[], [], []	0.483871	0.903226	0	139
'UAAGAUGUGAGAAGUGU UGACAGGAAGCUGC' (SEQ ID NO:330)	[], [], []	0.451613	0.903226	0	137
'AAGAUGUGAGAAGUGUU GACAGGAAGCUGCA' (SEQ ID NO:331)	[], [], []	0.451613	0.903226	0	138
'AUUCACUUUCAAACAC UUUCAGUAACAGGU' (SEQ ID NO:332)	[], [], []	0.354839	0.903226	0	26
'GAGAGGCGAGGAAGUCA CCAUCAAACCCACUU' (SEQ ID NO:333)	[], [], []	0.516129	0.870968	0	91
'GAUGUGAGAAGUGUUGA CAGGAAGCUGCAGC' (SEQ ID NO:334)	[], [], []	0.516129	0.870968	0	140
'AUGUGAGAAGUGUUGAC AGGAAGCUGCAGCU' (SEQ ID NO:335)	[], [], []	0.483871	0.870968	0	141

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGUGAGAAGUGUUGACA GGAAGCUGCAGCUU' (SEQ ID NO:336)	[], [], []	0.483871	0.870968	0	142
'GUGAGAAGUGUUGACAG GAAGCUGCAGCUUA' (SEQ ID NO:337)	[], [], []	0.483871	0.870968	0	143
'UGAGAAGUGUUGACAGG AAGCUGCAGCUUAG' (SEQ ID NO:338)	[], [], []	0.483871	0.870968	0	144
'GAGAAGUGUUGACAGGA AGCUGCAGCUUAGA' (SEQ ID NO:339)	[], [], []	0.483871	0.870968	0	145
'GAAGUGUUGACAGGAAG CUGCAGCUUAGAUG' (SEQ ID NO:340)	[], [], []	0.483871	0.870968	0	147
'AAGUGUUGACAGGAAGC UGCAGCUUAGAUGG' (SEQ ID NO:341)	[], [], []	0.483871	0.870968	0	148
'AGAAGUGUUGACAGGAA GCUGCAGCUUAGAU' (SEQ ID NO:342)	[], [], []	0.451613	0.870968	0	146
'GAUCACAACUCCAUGGC AACAAAGAUGACACA' (SEQ ID NO:343)	[], [], []	0.451613	0.870968	0	182

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUCACAAACUCCAUGGCA ACAAGAUGACACAA' (SEQ ID NO:344)	[], [], []	0.419355	0.870968	0	183
'UCACAAACUCCAUGGCAA CAAGAUGACACAAA' (SEQ ID NO:345)	[], [], []	0.419355	0.870968	0	184
'UUCACUUUCAAACCACU UUCAGUAACAGGUG' (SEQ ID NO:346)	[], [], []	0.387097	0.870968	0	27
'UCACUUUCAAACCACUU UCAGUAACAGGUGA' (SEQ ID NO:347)	[], [], []	0.387097	0.870968	0	28
'AGAGGCGAGGAAGUCAC CAUCAAACCACUUU' (SEQ ID NO:348)	[], [], []	0.483871	0.83871	0	92
'GGAUGAUCACAACUCCA UGGCAACAAAGAUGA' (SEQ ID NO:349)	[], [], []	0.451613	0.83871	0	178
'GAUGAUCACAACUCCAU GGCAACAAGAUGAC' (SEQ ID NO:350)	[], [], []	0.451613	0.83871	0	179
'UGAUCACAACUCCAUGG CAACAAAGAUGACAC' (SEQ ID NO:351)	[], [], []	0.451613	0.83871	0	181

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CACUUUCAAACCACUUU CAGUAACAGGUGAG' (SEQ ID NO:352)	[], [], []	0.419355	0.83871	0	29
'AUGAUCACAACUCCAUG GCAACAAGAUGACA' (SEQ ID NO:353)	[], [], []	0.419355	0.83871	0	180
'AACCACUUUCAGUAACA GGUGAGGUUCUACC'	[], [], []	0.451613	0.806452	0	37
'ACCACUUUCAGUAACAG GUGAGGUUCUACCU'	[], [], []	0.451613	0.806452	0	38
'CCACUUUCAGUAACAGG UGAGGUUCUACCUU'	[], [], []	0.451613	0.806452	0	39
'ACUUUCAAACCACUUUC AGUAACAGGUGAGG'	[], [], []	0.419355	0.806452	0	30
'CUUUCAAACCACUUUCA GUAACAGGUGAGGU'	[], [], []	0.419355	0.806452	0	31
'UUCAAACCACUUUCAGU AACAGGUGAGGUUC'	[], [], []	0.419355	0.806452	0	33

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCAAACCACUUUCAGUA ACAGGUGAGGUUCU' (SEQ ID NO:360)	[], [], []	0.419355	0.806452	0	34
'CAAACCACUUUCAGUAA CAGGUGAGGUUCUA' (SEQ ID NO:361)	[], [], []	0.419355	0.806452	0	35
'AAACCACUUUCAGUAAC AGGUGAGGUUCUAC' (SEQ ID NO:362)	[], [], []	0.419355	0.806452	0	36
'CACUUUCAGUAACAGGU GAGGUUCUACCUUA' (SEQ ID NO:363)	[], [], []	0.419355	0.806452	0	40
'UUUCAAACCACUUUCAG UAACAGGUGAGGUU' (SEQ ID NO:364)	[], [], []	0.387097	0.806452	0	32
'UUUAUUCACUUUCAAAC CACUUUCAGUAACA' (SEQ ID NO:365)	[], [], ['UUUA']]	0.290323	0.967742	1	23
'GGGAGAGGCGAGGAAG UCACCAUCAAACCAC' (SEQ ID NO:366)	[], ['GGG'], []	0.580645	0.935484	1	89
'GGCAACAAAGAUGACACA AAUGCAGCAGAGAC' (SEQ ID NO:367)	[], [], ['AAAU']]	0.483871	0.935484	1	196

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GCAACAAGAUGACACAA AUGCAGCAGAGACC' (SEQ ID NO:368)	[], [], ['AAAU']]	0.483871	0.935484	1	197
'GUUAGCAUAAGAUGUGA GAAGUGUUGACAGG' (SEQ ID NO:369)	[], [], ['AUAA']]	0.419355	0.935484	1	130
'AGCAUAAGAUGUGAGAA GUGUUGACAGGAAG' (SEQ ID NO:370)	[], [], ['AUAA']]	0.419355	0.935484	1	133
'AUAAGAUGUGAGAAGUG UUGACAGGAAGCUG' (SEQ ID NO:371)	[], [], ['AUAA']]	0.419355	0.935484	1	136
'UCACCAUCAAACCAACUU UAUCUACAGUUAGC' (SEQ ID NO:372)	[], [], ['UUUA']]	0.387097	0.935484	1	105
'CACCAUCAAACCAACUUU AUCUACAGUUAGCA' (SEQ ID NO:373)	[], [], ['UUUA']]	0.387097	0.935484	1	106
'AGUUAGCAUAAGAUGUG AGAAGUGUUGACAG' (SEQ ID NO:374)	[], [], ['AUAA']]	0.387097	0.935484	1	129
'UUAGCAUAAGAUGUGAG AAGUGUUGACAGGA' (SEQ ID NO:375)	[], [], ['AUAA']]	0.387097	0.935484	1	131

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UAGCAUAAGAUGUGAGA AGUGUUGACAGGAA' (SEQ ID NO:376)	[], [], ['AUAA']]	0.387097	0.935484	1	132
'AAGUCACCAUCAAACCA CUUUAUCUACAGUU' (SEQ ID NO:377)	[], [], ['UUUA']]	0.354839	0.935484	1	102
'AGUCACCAUCAAACCAC UUUAUCUACAGUU' (SEQ ID NO:378)	[], [], ['UUUA']]	0.354839	0.935484	1	103
'ACCAUCAAACCAUCUUUA UCUACAGUUAGCAU' (SEQ ID NO:379)	[], [], ['UUUA']]	0.354839	0.935484	1	107
'CCAUCAAACCAUCUUUAU CUACAGUUAGCAU' (SEQ ID NO:380)	[], [], ['UUUA']]	0.354839	0.935484	1	108
'UACAGUUAGCAUAAGAU GUGAGAAGUGUUGA' (SEQ ID NO:381)	[], [], ['AUAA']]	0.354839	0.935484	1	126
'CUGAACGUUUAUUCACUU UCAAACCAUCUUCA' (SEQ ID NO:382)	[], [], ['UUUA']]	0.322581	0.935484	1	17
'GUUUAUUCACUUUCAA CCACUUUCAGUAAC' (SEQ ID NO:383)	[], [], ['UUUA']]	0.322581	0.935484	1	22

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUAAUCACUUCAAACC ACUUUCAGUAACAG' (SEQ ID NO:384)	[], [], ['UUAU']]	0.322581	0.935484	1	24
'AAGUUUUAUUCACUUUCA AACCACUUUCAGUA' (SEQ ID NO:385)	[], [], ['UUUA']]	0.290323	0.935484	1	20
'AGUUUUAUUCACUUCAA ACCACUUUCAGUAA' (SEQ ID NO:386)	[], [], ['UUUA']]	0.290323	0.935484	1	21
'GGUGGGAGAGGCGAGG AAGUCACCAUCAAAC' (SEQ ID NO:387)	[], ['GGG'], []	0.580645	0.903226	1	86
'GUGGGAGAGGCGAGGA AGUCACCAUCAAACC' (SEQ ID NO:388)	[], ['GGG'], []	0.580645	0.903226	1	87
'UGGGAGAGGCGAGGAA GUCACCAUCAAACCA' (SEQ ID NO:389)	[], ['GGG'], []	0.548387	0.903226	1	88
'CCAUGGCAACAAGAUGA CACAAAUGCAGCAG' (SEQ ID NO:390)	[], [], ['AAAU']]	0.483871	0.903226	1	192
'GCAUAAGAUGUGAGAAG UGUUGACAGGAAGC' (SEQ ID NO:391)	[], [], ['AUAA']]	0.451613	0.903226	1	134

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CAUGGCAACAAGAUGAC ACAAAUGCAGCAGA' (SEQ ID NO:392)	[], [], ['AAAU']]	0.451613	0.903226	1	193
'AUGGCAACAAGAUGACA CAAAUGCAGCAGAG' (SEQ ID NO:393)	[], [], ['AAAU']]	0.451613	0.903226	1	194
'UGGCAACAAGAUGACAC AAAUGCAGCAGAGA' (SEQ ID NO:394)	[], [], ['AAAU']]	0.451613	0.903226	1	195
'CAUAAGAUGUGAGAAGU GUUGACAGGAAGCU' (SEQ ID NO:395)	[], [], ['AUAA']]	0.419355	0.903226	1	135
'AGGAAGUCACCAUCAAA CCACUUUAUCUACA' (SEQ ID NO:396)	[], [], ['UUUA']]	0.387097	0.903226	1	99
'GAAGUCACCAUCAAACC ACUUUAUCUACAGU' (SEQ ID NO:397)	[], [], ['UUUA']]	0.387097	0.903226	1	101
'GUCACCAUCAAACCACU UUAUCUACAGUUAG' (SEQ ID NO:398)	[], [], ['UUUA']]	0.387097	0.903226	1	104
'CUACAGUUAGCAUAAGA UGUGAGAAGUGUUG' (SEQ ID NO:399)	[], [], ['AUAA']]	0.387097	0.903226	1	125

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACAGUUAGCAUAAGAUG UGAGAAAGUGUUGAC' (SEQ ID NO:400)	[], [], ['AUAA']]	0.387097	0.903226	1	127
'CAGUUAGCAUAAGAUGU GAGAAGUGUUGACA' (SEQ ID NO:401)	[], [], ['AUAA']]	0.387097	0.903226	1	128
'GCUGAACGUUUAUUCACU UUCAAACCACUUUC' (SEQ ID NO:402)	[], [], ['UUUA']]	0.354839	0.903226	1	16
'UAUUCACUUUCAAACCA CUUUCAGUAACAGG' (SEQ ID NO:403)	[], [], ['UAUU']]	0.354839	0.903226	1	25
'UAUCUACAGUUAGCAUA AGAUGUGAGAAGUG' (SEQ ID NO:404)	[], [], ['AUAA']]	0.354839	0.903226	1	122
'AUCUACAGUUAGCAUAA GAUGUGAGAAGUGU' (SEQ ID NO:405)	[], [], ['AUAA']]	0.354839	0.903226	1	123
'UCUACAGUUAGCAUAAG AUGUGAGAAGUGUU' (SEQ ID NO:406)	[], [], ['AUAA']]	0.354839	0.903226	1	124
'UGCUGAACGUUUAUUCAC UUUCAAACCACUUU' (SEQ ID NO:407)	[], [], ['UUUA']]	0.322581	0.903226	1	15

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGAAGUUUAUUCACUUU CAAACCACUUUCAG' (SEQ ID NO:408)	[], [], ['UUUA']]	0.322581	0.903226	1	18
'GAAGUUUAUUCACUUUC AAACCACUUUCAGU' (SEQ ID NO:409)	[], [], ['UUUA']]	0.322581	0.903226	1	19
'AGUGUUGACAGGAAGCU GCAGCUUAGAUGGG' (SEQ ID NO:410)	[], ['GGG'], []	0.516129	0.870968	1	149
'GUGUUGACAGGAAGCUG CAGCUUAGAUGGGA' (SEQ ID NO:411)	[], ['GGG'], []	0.516129	0.870968	1	150
'GUUGACAGGAAGCUGCA GCUUAGAUGGGAUG' (SEQ ID NO:412)	[], ['GGG'], []	0.516129	0.870968	1	152
'UGUUGACAGGAAGCUGC AGCUUAGAUGGGAU' (SEQ ID NO:413)	[], ['GGG'], []	0.483871	0.870968	1	151
'UUGACAGGAAGCUGCAG CUUAGAUGGGAUGA' (SEQ ID NO:414)	[], ['GGG'], []	0.483871	0.870968	1	153
'UGACAGGAAGCUGCAGC UUAGAUGGGGAUGAU' (SEQ ID NO:415)	[], ['GGG'], []	0.483871	0.870968	1	154

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CUCCAUGGCAACAAAGAU GACACAAAUGCAGC' (SEQ ID NO:416)	[], [], ['AAAU']]	0.483871	0.870968	1	190
'CAACUCCAUGGCAACAA GAUGACACAAAUGC' (SEQ ID NO:417)	[], [], ['AAAU']]	0.451613	0.870968	1	187
'ACUCCAUGGCAACAAAGA UGACACAAAUGCAG' (SEQ ID NO:418)	[], [], ['AAAU']]	0.451613	0.870968	1	189
'UCCAUGGCAACAAAGAUG ACACAAAUGCAGCA' (SEQ ID NO:419)	[], [], ['AAAU']]	0.451613	0.870968	1	191
'CGAGGAAGUCACCAUCA AACCACUUUAUCUA' (SEQ ID NO:420)	[], [], ['UUUA']]	0.419355	0.870968	1	97
'GAGGAAGUCACCAUCAA ACCACUUUAUCUAC' (SEQ ID NO:421)	[], [], ['UUUA']]	0.419355	0.870968	1	98
'GGAAGUCACCAUCAAAC CACUUUAUCUACAG' (SEQ ID NO:422)	[], [], ['UUUA']]	0.419355	0.870968	1	100
'CACACUCCAUGGCAAC AAGAUGACACAAU' (SEQ ID NO:423)	[], [], ['AAAU']]	0.419355	0.870968	1	185

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACAACUCCAUGGCAACA AGAUGACACAAAUG' (SEQ ID NO:424)	[], [], ['AAAU']]	0.419355	0.870968	1	186
'AACUCCAUGGCAACAAG AUGACACAAAUGCA' (SEQ ID NO:425)	[], [], ['AAAU']]	0.419355	0.870968	1	188
'GUGCUGAAGUUUAUUCA CUUUCAAACCACUU' (SEQ ID NO:426)	[], [], ['UUUA']]	0.354839	0.870968	1	14
'CCAGGGGACAGGAGCCU CUUGCAGUCUGUCC' (SEQ ID NO:427)	[], ['GGG'], []	0.645161	0.83871	1	228
'GGACAGGAGGCCUCUUGC AGUCUGUCCCAGG' (SEQ ID NO:428)	[["CCC"], [], []]	0.612903	0.83871	1	233
'GACAGGAGGCCUCUUGCA GUCUGUCCCAGG' (SEQ ID NO:429)	[["CCC"], [], []]	0.612903	0.83871	1	234
'ACAGGAGGCCUCUUGCAG UCUGUCCCAGG' (SEQ ID NO:430)	[["CCC"], [], []]	0.612903	0.83871	1	235
'GACAGGAAGCUGCAGCU UAGAUGGGAUGAUC' (SEQ ID NO:431)	[], ['GGG'], []	0.516129	0.83871	1	155

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GAGGCAGGAAGUCACC AUCAAACCACUUUA' (SEQ ID NO:432)	[], [], ['UUUA']]	0.483871	0.83871	1	93
'ACAGGAAGCUGCAGCUU AGAUGGGAUGAUCA' (SEQ ID NO:433)	[], ['GGG'], []	0.483871	0.83871	1	156
'AGGAAGCUGCAGCUUAG AUGGGAUGAUCACA' (SEQ ID NO:434)	[], ['GGG'], []	0.483871	0.83871	1	158
'GGAAGCUGCAGCUUAGA UGGGAUGAUCAACAA' (SEQ ID NO:435)	[], ['GGG'], []	0.483871	0.83871	1	159
'GAUGGGAUGAUCAACAA UCCAUGGCAACAAAG' (SEQ ID NO:436)	[], ['GGG'], []	0.483871	0.83871	1	174
'GGGAUGAUCAACACUCC AUGGCAACAAAGAUG' (SEQ ID NO:437)	[], ['GGG'], []	0.483871	0.83871	1	177
'GCGAGGAAGUCACCAUC AAACCACUUUAUCU' (SEQ ID NO:438)	[], [], ['UUUA']]	0.451613	0.83871	1	96
'AGAUGGGAUGAUCAACAA CUCCAUGGCAACAA' (SEQ ID NO:439)	[], ['GGG'], []	0.451613	0.83871	1	173

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUGGGAUGAUCACAACU CCAUGGCAACAAGA' (SEQ ID NO:440)	[[], ['GGG'], []]	0.451613	0.83871	1	175
'GCUUCUGGUCCAUGGU GCUGAAGUUUAUUCA' (SEQ ID NO:441)	[[], [], ['UUUA']]	0.419355	0.83871	1	0
'UCUUCUGGUCCAUGGUGC UGAAGUUUAUUCAC' (SEQ ID NO:442)	[[], [], ['UUUA']]	0.419355	0.83871	1	1
'CUUCUGGUCCAUGGUGCU GAAGUUUAUUCACU' (SEQ ID NO:443)	[[], [], ['UUUA']]	0.419355	0.83871	1	2
'CUGUCCAUGGUGCUGAA GUUUAUUCACUUUC' (SEQ ID NO:444)	[[], [], ['UUUA']]	0.419355	0.83871	1	5
'UUCUGGUCCAUGGUGCU GAAGUUUAUUCACUU' (SEQ ID NO:445)	[[], [], ['UUUA']]	0.387097	0.83871	1	3
'UCUGGUCCAUGGUGCUGA AGUUUAUUCACUUU' (SEQ ID NO:446)	[[], [], ['UUUA']]	0.387097	0.83871	1	4
'CCAUGGUGCUGAAGUUU AUUCACUUUCAAAC' (SEQ ID NO:447)	[[], [], ['UUUA']]	0.387097	0.83871	1	9

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CAUGGUGCUGAAGUUUA UUCACUUUCAAACC' (SEQ ID NO:448)	[], [], ['UUUA']]	0.387097	0.83871	1	10
'UGGUGCUGAAGUUUAUU CACUUUCAAACCAC' (SEQ ID NO:449)	[], [], ['UUUA']]	0.387097	0.83871	1	12
'GGUGCUGAAGUUUAUUC ACUUUCAAACCACU' (SEQ ID NO:450)	[], [], ['UUUA']]	0.387097	0.83871	1	13
'UCCAUGGUGCUGAAGUU UAUUCACUUUCAAA' (SEQ ID NO:451)	[], [], ['UUUA']]	0.354839	0.83871	1	8
'AUGGUGCUGAAGUUUAU UCACUUUCAAACCA' (SEQ ID NO:452)	[], [], ['UUUA']]	0.354839	0.83871	1	11
'UUUCAGUAACAGGUGAG GUUCUACCUUAAAAA' (SEQ ID NO:453)	[], [], ['UUAA']]	0.354839	0.83871	1	43
'UUCAGUAACAGGUGAGG UUCUACCUUAAAAAU' (SEQ ID NO:454)	[], [], ['UUAA']]	0.354839	0.83871	1	44
'CAGGAAGCUGCAGCUUA GAUGGGAUGAUCAC' (SEQ ID NO:455)	[], ['GGG'], []	0.516129	0.806452	1	157

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGCGAGGAAGUCACCAU CAAACCACUUUAUC' (SEQ ID NO:456)	[], [], ['UUUA']]	0.483871	0.806452	1	95
'GAAGCUGCAGCUUAGAU GGGAUGAUCACAAC' (SEQ ID NO:457)	[], ['GGG'], []	0.483871	0.806452	1	160
'AGGCGAGGAAGUCACCA UCAAACCACUUUAU' (SEQ ID NO:458)	[], [], ['UUUA']]	0.451613	0.806452	1	94
'AAGCUGCAGCUUAGAUG GGAUGAUCACAACU' (SEQ ID NO:459)	[], ['GGG'], []	0.451613	0.806452	1	161
'UAGAUGGGAUGAUCACA ACUCCAUGGCAACA' (SEQ ID NO:460)	[], ['GGG'], []	0.451613	0.806452	1	172
'UGGGAUGAUCACAACUC CAUGGCAACAAGAU' (SEQ ID NO:461)	[], ['GGG'], []	0.451613	0.806452	1	176
'UGUCCAUGGUGCUGAAG UUUAUUCACUUUCA' (SEQ ID NO:462)	[], [], ['UUUA']]	0.387097	0.806452	1	6
'GUCCAUGGUGCUGAAGU UUAUUCACUUUCAA' (SEQ ID NO:463)	[], [], ['UUUA']]	0.387097	0.806452	1	7

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACUUUCAGUAACAGGUG AGGUUCUACCUUAA' (SEQ ID NO:464)	[], [], ['UUAA']]	0.387097	0.806452	1	41
'CUUUCAGUAACAGGUGA GGUUCUACCUAAA' (SEQ ID NO:465)	[], [], ['UUAA']]	0.387097	0.806452	1	42
'GCUGCAGCUUAGAUGG GAUGAUCACAACUCC' (SEQ ID NO:466)	[], ['GGG'], []	0.516129	0.774194	1	163
'AGCUGCAGCUUAGAUGG GAUGAUCACAACUC' (SEQ ID NO:467)	[], ['GGG'], []	0.483871	0.774194	1	162
'CUGCAGCUUAGAUGGGA UGAUCACAACUCCA' (SEQ ID NO:468)	[], ['GGG'], []	0.483871	0.774194	1	164
'GCAGCUUAGAUGGGAUG AUCACAACUCCAUG' (SEQ ID NO:469)	[], ['GGG'], []	0.483871	0.774194	1	166
'CAGCUUAGAUGGGAUGA UCACAACUCCAUGG' (SEQ ID NO:470)	[], ['GGG'], []	0.483871	0.774194	1	167
'AGCUUAGAUGGGAUGAU CACAAACUCCAUGGC' (SEQ ID NO:471)	[], ['GGG'], []	0.483871	0.774194	1	168

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GCUUAGAUGGGAUGAUC ACAAACUCCAUGGCA' (SEQ ID NO:472)	[], ['GGG'], []	0.483871	0.774194	1	169
'UGCAGCUUAGAUGGGAU GAUCACAACUCCAU' (SEQ ID NO:473)	[], ['GGG'], []	0.451613	0.774194	1	165
'CUUAGAUGGGAUGAUCA CAACUCCAUGGCAA' (SEQ ID NO:474)	[], ['GGG'], []	0.451613	0.774194	1	170
'UUAGAUGGGAUGAUCAC AACUCCAUGGCAAC' (SEQ ID NO:475)	[], ['GGG'], []	0.451613	0.774194	1	171
'AAUGCAGCAGAGACCCC AGGGGACAGGAGGCC' (SEQ ID NO:476)	[["CCC"], ['GGG'], []]	0.645161	0.967742	2	213
'UGCAGCAGAGACCCCAG GGGACAGGAGGCCUC' (SEQ ID NO:477)	[["CCC"], ['GGG'], []]	0.677419	0.935484	2	215
'GCAGCAGAGACCCCAGG GGACAGGAGGCCUCU' (SEQ ID NO:478)	[["CCC"], ['GGG'], []]	0.677419	0.935484	2	216
'AUGCAGCAGAGACCCCA GGGGACAGGAGGCCU' (SEQ ID NO:479)	[["CCC"], ['GGG'], []]	0.645161	0.935484	2	214

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CAAGAUGACACAAUUGC AGCAGAGACCCAG' (SEQ ID NO:480)	[["CCC"], [], ['AAAU']]	0.516129	0.935484	2	201
'AAGAUGACACAAUUGCA GCAGAGACCCAGG' (SEQ ID NO:481)	[["CCC"], [], ['AAAU']]	0.516129	0.935484	2	202
'CAACAAGAUGACACAAA UGCAGCAGAGACCC' (SEQ ID NO:482)	[["CCC"], [], ['AAAU']]	0.483871	0.935484	2	198
'AACAAAGAUGACACAAU GCAGCAGAGACCC' (SEQ ID NO:483)	[["CCC"], [], ['AAAU']]	0.483871	0.935484	2	199
'ACAAGAUGACACAAUUG CAGCAGAGACCCA' (SEQ ID NO:484)	[["CCC"], [], ['AAAU']]	0.483871	0.935484	2	200
'CAUCAAACCACUUUAUC UACAGUUAGCAUAA' (SEQ ID NO:485)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.935484	2	109
'GCAGAGACCCAGGGGA CAGGAGCCUCUUGC' (SEQ ID NO:486)	[["CCC"], ['GGG'], []]	0.677419	0.903226	2	219
'GCAUGGGGUGGGAGAG GCGAGGAAGUCACCA' (SEQ ID NO:487)	[[], ['GGG', 'GGG'], []]	0.645161	0.903226	2	80

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CAGCAGAGACCCCAGGG GACAGGAGGCCUCUU' (SEQ ID NO:488)	[["CCC"], ['GGG'], []]	0.645161	0.903226	2	217
'AGCAGAGACCCCAGGGGG ACAGGAGGCCUCUUG' (SEQ ID NO:489)	[["CCC"], ['GGG'], []]	0.645161	0.903226	2	218
'CAGAGACCCCAGGGGAC AGGAGCCUCUUGCA' (SEQ ID NO:490)	[["CCC"], ['GGG'], []]	0.645161	0.903226	2	220
'AGAGACCCCAGGGGACA GGAGCCUCUUGCAG' (SEQ ID NO:491)	[["CCC"], ['GGG'], []]	0.645161	0.903226	2	221
'GGGUUGGGAGAGGGCGA GGAAGUCACCAUCAA' (SEQ ID NO:492)	[[], ['GGG', 'GGG'], []]	0.612903	0.903226	2	84
'AAUGCAUGGGGUGGGA GAGGCGAGGAAGUCA' (SEQ ID NO:493)	[[], ['GGG', 'GGG'], []]	0.580645	0.903226	2	77
'GGGUUGGGAGAGGGCGAG GAAGUCACCAUCAAA' (SEQ ID NO:494)	[[], ['GGG', 'GGG'], []]	0.580645	0.903226	2	85
'AUCAAACCACUUUAUCU ACAGUUAGCAUAAG' (SEQ ID NO:495)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.903226	2	110

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCAAACCACUUUAUCUA CAGUUAGCAUAAGA' (SEQ ID NO:496)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.903226	2	111
'CAAACCACUUUAUCUAC AGUUAGCAUAAGAU' (SEQ ID NO:497)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.903226	2	112
'UUUAUCUACAGUUAGCA UAAGAUGUGAGAAG' (SEQ ID NO:498)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.903226	2	120
'UUAUCUACAGUUAGCAU AAGAUGUGAGAAGU' (SEQ ID NO:499)	[[], [], ['UUAU', 'AUAA']]	0.322581	0.903226	2	121
'UGCAUGGGGUGGGAGA GGCGAGGAAGUCACC' (SEQ ID NO:500)	[[], ['GGG', 'GGG'], []]	0.645161	0.870968	2	79
'GAGACCCCAGGGGACAG GAGCCUCUUGCAGU' (SEQ ID NO:501)	[['CCC'], ['GGG'], []]	0.645161	0.870968	2	222
'AGACCCCAGGGGACAGG AGCCUCUUGCAGUC' (SEQ ID NO:502)	[['CCC'], ['GGG'], []]	0.645161	0.870968	2	223
'CAGGAGCCUCUUGCAGU CUGUCCCUAGGCC' (SEQ ID NO:503)	[['CCC', 'CCC'], [], []]	0.645161	0.870968	2	236

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGAGCCUCUUGCAGUCU GUCCCUAGGCCAG' (SEQ ID NO:504)	[["CCC", 'CCC'],[], []]]	0.645161	0.870968	2	238
'GAGCCUCUUGCAGUCUG UCCCUAGGCCAGC' (SEQ ID NO:505)	[["CCC", 'CCC'],[], []]]	0.645161	0.870968	2	239
'AGCCUCUUGCAGUCUGU CCCUAGGCCAGCC' (SEQ ID NO:506)	[["CCC", 'CCC'],[], []]]	0.645161	0.870968	2	240
'AUGCAUGGGGUGGGAG AGGCGAGGAAGUCAC' (SEQ ID NO:507)	[[],['GGG', 'GGG'],[]]]	0.612903	0.870968	2	78
'CAUGGGGUGGGAGAGGG CGAGGAAGUCACCAU' (SEQ ID NO:508)	[[],['GGG', 'GGG'],[]]]	0.612903	0.870968	2	81
'AUGGGGUGGGAGAGGC GAGGAAGUCACCAUC' (SEQ ID NO:509)	[[],['GGG', 'GGG'],[]]]	0.612903	0.870968	2	82
'UGGGGGUGGGAGAGGCG AGGAAGUCACCAUCA' (SEQ ID NO:510)	[[],['GGG', 'GGG'],[]]]	0.612903	0.870968	2	83
'AGUAACAGGUGAGGUUC UACCUUAAAAUUUA' (SEQ ID NO:511)	[[],[], [['UUAA', 'AAUU']]]	0.322581	0.870968	2	47

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GUAACAGGUGAGGUUCU ACCUUAAAUUUUA' (SEQ ID NO:512)	[[], [], ['UUAA', 'AAUU']]	0.322581	0.870968	2	48
'AAACCACUUUAUCUACA GUUAGCAUAAGAUG' (SEQ ID NO:513)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.870968	2	113
'AACCCACUUUAUCUACAG UUAGCAUAAGAUGU' (SEQ ID NO:514)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.870968	2	114
'ACUUUAUCUACAGUUAG CAUAAGAUGUGAGA' (SEQ ID NO:515)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.870968	2	118
'CUUUUAUCUACAGUUAGC AUAAGAUGUGAGAA' (SEQ ID NO:516)	[[], [], ['UUUA', 'AUAA']]	0.322581	0.870968	2	119
'GACCCCAGGGGACAGGA GCCUCUUGCAGUCU' (SEQ ID NO:517)	[["CCC"], ["GGG"], []]	0.645161	0.83871	2	224
'ACCCCAGGGGACAGGAG CCUCUUGCAGUCUG' (SEQ ID NO:518)	[["CCC"], ["GGG"], []]	0.645161	0.83871	2	225
'CCCCAGGGGACAGGAGC CUCUUGCAGUCUGU' (SEQ ID NO:519)	[["CCC"], ["GGG"], []]	0.645161	0.83871	2	226

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCCAGGGGACAGGAGCC UCUUGCAGUCUGUC' (SEQ ID NO:520)	[["CCC"], ['GGG'], []]	0.645161	0.83871	2	227
'CAGGGGACAGGAGGCCUC UUGCAGUCUGUCCCC' (SEQ ID NO:521)	[["CCC"], ['GGG'], []]	0.645161	0.83871	2	229
'AGGGGACAGGAGGCCUCU UGCAGUCUGUCCCCU' (SEQ ID NO:522)	[["CCC"], ['GGG'], []]	0.612903	0.83871	2	230
'GGGGACAGGAGGCCUCU UGCAGUCUGUCCCCUA' (SEQ ID NO:523)	[["CCC"], ['GGG'], []]	0.612903	0.83871	2	231
'GGGACAGGAGGCCUCUU GCAGUCUGUCCCCUAG' (SEQ ID NO:524)	[["CCC"], ['GGG'], []]	0.612903	0.83871	2	232
'AGGAGCCUCUUGCAGUC UGUCCCUAGGCCCA' (SEQ ID NO:525)	[["CCC", 'CCC'], [], []]	0.612903	0.83871	2	237
'UCAGUAACAGGUGAGGU UCUACCUAAAAAUU' (SEQ ID NO:526)	[[], [], ['UUAA', 'AAUU']]	0.354839	0.83871	2	45
'CAGUAACAGGUGAGGUU CUACCUAAAAUUU' (SEQ ID NO:527)	[[], [], ['UUAA', 'AAUU']]	0.354839	0.83871	2	46

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACCACUUUAUCUACAGU UAGCAUAAGAUGUG' (SEQ ID NO:528)	[[], [], ['UUUA', 'AUAA']]	0.354839	0.83871	2	115
'CCACUUUAUCUACAGUU AGCAUAAGAUGUGA' (SEQ ID NO:529)	[[], [], ['UUUA', 'AUAA']]	0.354839	0.83871	2	116
'CACUUUAUCUACAGUUA GCAUAAGAUGUGAG' (SEQ ID NO:530)	[[], [], ['UUUA', 'AUAA']]	0.354839	0.83871	2	117
'GGCCCAGCCUGCUUG UCCUCCCUGGCUGUU' (SEQ ID NO:531)	[["CCC", 'CCC', 'CCC'], [], []]	0.677419	0.967742	3	262
'CACAAAUGCAGCAGAGA CCCCAGGGGACAGGG' (SEQ ID NO:532)	[["CCC"], ['GGG'], ['AAAU']]	0.612903	0.967742	3	209
'CAAAUGCAGCAGAGACC CCAGGGGACAGGGAG' (SEQ ID NO:533)	[["CCC"], ['GGG'], ['AAAU']]	0.612903	0.967742	3	211
'AAAUGCAGCAGAGACCC CAGGGGACAGGGAGC' (SEQ ID NO:534)	[["CCC"], ['GGG'], ['AAAU']]	0.612903	0.967742	3	212
'GACACAAAUGCAGCAGA GACCCCAGGGGACA' (SEQ ID NO:535)	[["CCC"], ['GGG'], ['AAAU']]	0.580645	0.967742	3	207

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACACAAAUGCAGCAGAG ACCCCAGGGGACAG' (SEQ ID NO:536)	[['CCC'], ['GGG'], ['AAAU']]	0.580645	0.967742	3	208
'ACAAAUGCAGCAGAGAC CCCAGGGGACAGGA' (SEQ ID NO:537)	[['CCC'], ['GGG'], ['AAAU']]	0.580645	0.967742	3	210
'CCUAGGCCAGCCCUGC UUGUCCUCCCUGGC' (SEQ ID NO:538)	[['CCC', 'CCC', 'CCC'],[], []]	0.709677	0.935484	3	258
'CUGUCCCUAGGCCAGC CCUGCUUGGUCCUCC' (SEQ ID NO:539)	[['CCC', 'CCC', 'CCC'],[], []]	0.677419	0.935484	3	253
'CUAGGCCAGCCCUGCU UGUCCUCCCUGGCU' (SEQ ID NO:540)	[['CCC', 'CCC', 'CCC'],[], []]	0.677419	0.935484	3	259
'UAGGCCAGCCCUGCUU GUCCUCCCUGGCUG' (SEQ ID NO:541)	[['CCC', 'CCC', 'CCC'],[], []]	0.677419	0.935484	3	260
'AGGCCAGCCCUGCUUG UCCUCCCUGGCUGU' (SEQ ID NO:542)	[['CCC', 'CCC', 'CCC'],[], []]	0.677419	0.935484	3	261

FIG. 41 (Cont'd)

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GUCUGUCCUAGGCCA GCCUGCUUGGUCCU' (SEQ ID NO:543)	[['CCC', 'CCC', 'CCC'],[], []]	0.645161	0.935484	3	251
'UCUGUCCUAGGCCAG CCCUGCUUGGUCCUC' (SEQ ID NO:544)	[['CCC', 'CCC', 'CCC'],[], []]	0.645161	0.935484	3	252
'GCCAGCCCUGCUUGUC CUCCCUGGCUGUUA' (SEQ ID NO:545)	[['CCC', 'CCC', 'CCC'],[], []]	0.645161	0.935484	3	263
'CCAGCCCUGCUUGUCCU CCUGGGCUGUUAUC' (SEQ ID NO:546)	[['CCC', 'CCC'],[], ['UUAU']]	0.612903	0.935484	3	265
'GAUGACACAAAUGCAGC AGAGACCCCAGGGG' (SEQ ID NO:547)	[['CCC'], ['GGG'], ['AAAU']]	0.580645	0.935484	3	204
'UGACACACAAAUGCAGCAG AGACCCCCAGGGGAC' (SEQ ID NO:548)	[['CCC'], ['GGG'], ['AAAU']]	0.580645	0.935484	3	206
'CAGCCCUGCUUGUCCUC CCUGGGCUGUUAUCU' (SEQ ID NO:549)	[['CCC', 'CCC'],[], ['UUAU']]	0.580645	0.935484	3	266
'UUUAAUGCAUGGGGUG GGAGAGGGCGAGGAAG' (SEQ ID NO:550)	[[],['GGG', 'GGG'], ['UUUA']]	0.548387	0.935484	3	74

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUAAUGCAUGGGGUGG GAGAGGCGAGGAAGU' (SEQ ID NO:551)	[[], ['GGG', 'GGG'], ["UUAA"]]	0.548387	0.935484	3	75
'AGAUGACACAAAUGCAG CAGAGACCCCAGGG' (SEQ ID NO:552)	[['CCC'], ['GGG'], ['AAAU']]	0.548387	0.935484	3	203
'AUGACACACAAAUGCAGCA GAGACCCCCAGGGGA' (SEQ ID NO:553)	[['CCC'], ['GGG'], ['AAAU']]	0.548387	0.935484	3	205
'AUUUAAUGCAUGGGGUG GGAGAGGCGAGGAA' (SEQ ID NO:554)	[[], ['GGG', 'GGG'], ['AUUU']]	0.516129	0.935484	3	73
'GCCUCUUGCAGUCUGUC CCUAGGCCAGCCC' (SEQ ID NO:555)	[['CCC', 'CCC', 'CCC'], [], []]	0.677419	0.903226	3	241
'CCUCUUGCAGUCUGUCC CUAGGCCAGCCCU' (SEQ ID NO:556)	[['CCC', 'CCC', 'CCC'], [], []]	0.645161	0.903226	3	242
'CUCUUGCAGUCUGUCCC UAGGCCAGCCUG' (SEQ ID NO:557)	[['CCC', 'CCC', 'CCC'], [], []]	0.645161	0.903226	3	243

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCUUGCAGUCUGUCCCC AGGCCAGCCCUGC' (SEQ ID NO:558)	[["CCC", 'CCC', 'CCC'],[], []]	0.645161	0.903226	3	244
'CUUGCAGUCUGUCCCCUA GGCCCAGCCCUGCU' (SEQ ID NO:559)	[["CCC", 'CCC', 'CCC'],[], []]	0.645161	0.903226	3	245
'UGCAGUCUGUCCCCUAGG CCCAGCCCUGCUUG' (SEQ ID NO:560)	[["CCC", 'CCC', 'CCC'],[], []]	0.645161	0.903226	3	247
'GCAGUCUGUCCCCUAGGC CCAGCCCUGCUUGU' (SEQ ID NO:561)	[["CCC", 'CCC', 'CCC'],[], []]	0.645161	0.903226	3	248
'CAGUCUGUCCCCUAGGCC CAGCCCUGCUUGUC' (SEQ ID NO:562)	[["CCC", 'CCC', 'CCC'],[], []]	0.645161	0.903226	3	249
'AGUCUGUCCCCUAGGCC AGCCCUGCUUGUCC' (SEQ ID NO:563)	[["CCC", 'CCC', 'CCC'],[], []]	0.645161	0.903226	3	250

FIG. 41 (Cont'd)

FIG. 41 (Cont'd)

SEQUENCE	ES	CGNESS	SLN	NBP	P
'UUGCAGUCUGUCCCCUAG GCCCGAGCCCUGCUU' (SEQ ID NO:564)	[['CCC', 'CCC', 'CCC'],[], []]	0.612903	0.903226	3	246
'UAAUGCAUGGGGUGGG AGAGGCGAGGAAGUC' (SEQ ID NO:565)	[],['GGG', 'GGG'], [['UAAU']]	0.580645	0.903226	3	76
'GGUGAGGUUCUACCUUA AAAUUUAAUGCAUG' (SEQ ID NO:566)	[],[], [['UUAA', 'AAUU', 'UAAU']]	0.354839	0.870968	3	54
'GUGAGGUUCUACCUAA AAUUUAAUGCAUGG' (SEQ ID NO:567)	[],[], [['UUAA', 'AAUU', 'UAAU']]	0.354839	0.870968	3	55
'AACAGGUGAGGUUCUAC CUUAAAAUUUAAUG' (SEQ ID NO:568)	[],[], [['UUAA', 'AAUU', 'UAAU']]	0.322581	0.870968	3	50
'AGGUGAGGUUCUACCUU AAAAUUUAAUGCAU' (SEQ ID NO:569)	[],[], [['UUAA', 'AAUU', 'UAAU']]	0.322581	0.870968	3	53
'UAACAGGUGAGGUUCUA CCUUAAAAUUUAAU' (SEQ ID NO:570)	[],[], [['UUAA', 'AAUU', 'UAAU']]	0.290323	0.870968	3	49

FIG. 41 (Cont'd)

SEQUENCE	BS	CGNESS	SLN	NBP	P
'ACAGGUGAGGUUCUACC UUAAAAUUUAUGC' (SEQ ID NO:571)	[], [], 'UUAA', 'AAUU', 'UAAU']]	0.354839	0.83871	3	51
'CAGGUGAGGUUCUACCU UAAAAUUUAUGCA' (SEQ ID NO:572)	[], [], 'UUAA', 'AAUU', 'UAAU']]	0.354839	0.83871	3	52
'CCCUAGGCCAGCCCUG CUUGGUCCUCCCCUGG' (SEQ ID NO:573)	[["CCC", 'CCC', 'CCC', 'CCC'], [], []]	0.709677	0.935484	4	257
'UGUCCCUAGGCCAGGCC CUGCUUGGUCCUCCCC' (SEQ ID NO:574)	[["CCC", 'CCC', 'CCC', 'CCC'], [], []]	0.677419	0.935484	4	254
'GUCCCUAGGCCAGCCC UGCUUGGUCCUCCCCU' (SEQ ID NO:575)	[["CCC", 'CCC', 'CCC', 'CCC'], [], []]	0.677419	0.935484	4	255
'UCCCUAGGCCAGCCCU GCUUGGUCCUCCCCUG' (SEQ ID NO:576)	[["CCC", 'CCC', 'CCC', 'CCC'], [], []]	0.677419	0.935484	4	256

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCCAGCCCUGCUUGUCC UCCCUGGCUGUUAU' (SEQ ID NO:577)	[['CCC', 'CCC', 'CCC'], [], ['UUAU']]	0.612903	0.935484	4	264
'AAAUUUUAUGCAUGGGG UGGGAGAGGGCGAGG' (SEQ ID NO:578)	[[], ['GGG', 'GGG'], ['AAAU', 'UUAA']]	0.516129	0.935484	4	71
'AAUUUUUAUGCAUGGGGU GGGAGAGGGCGAGGA' (SEQ ID NO:579)	[[], ['GGG', 'GGG'], ['AAUU', 'UAAU']]	0.516129	0.935484	4	72
'AAAAUUUUUAUGCAUGGG GUGGGAGAGGGCGAG' (SEQ ID NO:580)	[[], ['GGG', 'GGG'], ['AAAA', 'UUUA']]	0.483871	0.935484	4	70
'AAAAAAUUUUUAUGCAUGG GGUGGGAGAGGCGA' (SEQ ID NO:581)	[[], ['GGG', 'GGG'], ['AAAA', 'AUUU']]	0.451613	0.935484	4	69
'GAGGUUCUACCUUAAA UUUUAUGCAUGGGG' (SEQ ID NO:582)	[[], ['GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.387097	0.870968	4	57

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGUUCUACCUAAAAUU UAAUGCAUGGGGUG' (SEQ ID NO:583)	[[], ['GGG'], ['UUAA'], 'AAUU', 'UAAU']]	0.387097	0.870968	4	59
'GUUCUACCUAAAAUU AAUGCAUGGGGUGG' (SEQ ID NO:584)	[[], ['GGG'], ['UUAA'], 'AAUU', 'UAAU']]	0.387097	0.870968	4	60
'UGAGGUUCUACCUAAA AUUUAAUGCAUGGG' (SEQ ID NO:585)	[[], ['GGG'], ['UUAA'], 'AAUU', 'UAAU']]	0.354839	0.870968	4	56
'AGGUUCUACCUAAAAU UUAUGCAUGGGGU' (SEQ ID NO:586)	[[], ['GGG'], ['UUAA'], 'AAUU', 'UAAU']]	0.354839	0.870968	4	58
'UUAAAAUUUAUGCAUG GGGUGGGAGAGGCG' (SEQ ID NO:587)	[[], ['GGG', 'GGG'], ['UUAA'], 'AAUU', 'UAAU']]	0.451613	0.935484	5	68

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCUUAAAUAUUUAUGCA UGGGGUGGGAGAGG' (SEQ ID NO:588)	[[], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.451613	0.903226	5	66
'CUUAAAUAUUUAUGCAU GGGGUGGGAGAGGC' (SEQ ID NO:589)	[[], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.451613	0.903226	5	67
'ACCUAAAUAUUUAUGC AUGGGGUGGGAGAG' (SEQ ID NO:590)	[[], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.419355	0.903226	5	65
'UACCUAAAUAUUUAUG CAUGGGGUGGGAGA' (SEQ ID NO:591)	[[], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.387097	0.903226	5	64
'CUACCUAAAUAUUAAU GCAUGGGGUGGGAG' (SEQ ID NO:592)	[[], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.419355	0.870968	5	63

FIG. 41 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUCUACCUAAAAUUUA AUGCAUGGGGUGGG' (SEQ ID NO:593)	[]], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.387097	0.870968	5	61
'UCUACCUAAAAUUUA UGCAUGGGGUGGGA' (SEQ ID NO:594)	[]], ['GGG', 'GGG'], ['UUAA', 'AAUU', 'UAAU']]	0.387097	0.870968	5	62

FIG. 41 (Cont'd)

FIG. 42

SEQUENCE	BS	GCNESS	SLN	NEP	P
'GGCCUCAGCGUCUGUC CGUGGUGCUGAAGUU' (SEQ ID NO:595)	[], [], []	0.612903	0.903226	0	2
'GCCUCAGCGUCUGUCC GUUGGUGCUGAAGUUU' (SEQ ID NO:596)	[], [], []	0.580645	0.903226	0	3
'GAUGAAGACAGGAAGC UGCAGCUCCAGGAGG' (SEQ ID NO:597)	[], [], []	0.580645	0.903226	0	154
'AGAUGAAGACAGGAAG CUGCAGCUCCAGGAG' (SEQ ID NO:598)	[], [], []	0.548387	0.903226	0	153
'CAGGCCUCAGCGUCUG UCCGUGGUGCUGAAG' (SEQ ID NO:599)	[], [], []	0.645161	0.870968	0	0
'AGGCCUCAGCGUCUGU CCGUGGUGCUGAAGU' (SEQ ID NO:600)	[], [], []	0.612903	0.870968	0	1
'GGCAAUGCGACCAAGC UGUGUGACACACCGC' (SEQ ID NO:601)	[], [], []	0.612903	0.870968	0	204
'GCAAUGCGACCAAGCU GUGUGACACACCGCA' (SEQ ID NO:602)	[], [], []	0.580645	0.870968	0	205

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUGCGACCAAGCUGUG UGACACACCCGCAAGG' (SEQ ID NO:603)	[], [], []	0.580645	0.870968	0	208
'CAAUGCGACCAAGCUG UGUGACACACCCGCAA' (SEQ ID NO:604)	[], [], []	0.548387	0.870968	0	206
'AAUGCGACCAAGCUGU GUGACACACCCGCAAG' (SEQ ID NO:605)	[], [], []	0.548387	0.870968	0	207
'GAUAGAUGAAGACAGG AAGCUGCAGCUCCAG' (SEQ ID NO:606)	[], [], []	0.516129	0.870968	0	150
'AUAGAUGAAGACAGGAA GCUGCAGCUCCAGG' (SEQ ID NO:607)	[], [], []	0.516129	0.870968	0	151
'UAGAUGAAGACAGGAA GCUGCAGCUCCAGGA' (SEQ ID NO:608)	[], [], []	0.516129	0.870968	0	152
'GAUCGUGAUAGAUGAA GACAGGAAGCUGCAG' (SEQ ID NO:609)	[], [], []	0.483871	0.870968	0	144
'AUCGAUCGUGAUAGAU GAAGACAGGAAGCUG' (SEQ ID NO:610)	[], [], []	0.451613	0.870968	0	141

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AACAUCAUCGUGAUA GAUGAAGACAGGAAG' (SEQ ID NO:611)	[], [], []	0.419355	0.870968	0	138
'UAACAUCAUCGUGAU AGAUGAAGACAGGAA' (SEQ ID NO:612)	[], [], []	0.387097	0.870968	0	137
'UCACCACCUUCAGUG GCAAUGCGACCAAGC' (SEQ ID NO:613)	[], [], []	0.580645	0.83871	0	189
'CACCAACCUCUCAGUGG CAAUGCGACCAAGCU' (SEQ ID NO:614)	[], [], []	0.580645	0.83871	0	190
'ACCACCUCUCAGUGGC AAUGCGACCAAGCUG' (SEQ ID NO:615)	[], [], []	0.580645	0.83871	0	191
'GUGGCAAUGCGACCAA GCUGUGUGACACACC'	[], [], []	0.580645	0.83871	0	202
'UGGCAAUGCGACCAAG CUGUGUGACACACCG'	[], [], []	0.580645	0.83871	0	203
'CAGUGGCAAUGCGACC AAGCUGUGUGACACA'	[], [], []	0.548387	0.83871	0	200

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGUGGCAAUGCACCA AGCUGUGUGACACAC' (SEQ ID NO:619)	[], [], []	0.548387	0.83871	0	201
'CGUGAUAGAUGAAGAC AGGAAGCUGCAGCUC' (SEQ ID NO:620)	[], [], []	0.516129	0.83871	0	147
'GUGAUAGAUGAAGACA GGAAGCUGCAGCUCC' (SEQ ID NO:621)	[], [], []	0.516129	0.83871	0	148
'AUUCACCACCUUCUCAG UGGCAAUGCACCAA' (SEQ ID NO:622)	[], [], []	0.516129	0.83871	0	187
'UCGAUCGUGAUAGAUG AAGACAGGAAGCUGC' (SEQ ID NO:623)	[], [], []	0.483871	0.83871	0	142
'CGAUCGUGAUAGAUGA AGACAGGAAGCUGCA' (SEQ ID NO:624)	[], [], []	0.483871	0.83871	0	143
'AUCGUGAUAGAUGAAG ACAGGAAGCUGCAGC' (SEQ ID NO:625)	[], [], []	0.483871	0.83871	0	145
'UCGUGAUAGAUGAAGA CAGGAAGCUGCAGCU' (SEQ ID NO:626)	[], [], []	0.483871	0.83871	0	146

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGAUAGAUGAAGACAG GAAGCUGCAGCUCCA' (SEQ ID NO:627)	[], [], []	0.483871	0.83871	0	149
'ACAUCGAUCGUGAUAG AUGAAGACAGGAAGC' (SEQ ID NO:628)	[], [], []	0.451613	0.83871	0	139
'CAUCGAUCGUGAUAGA UGAAGACAGGAAGCU' (SEQ ID NO:629)	[], [], []	0.451613	0.83871	0	140
'CCACCUCUCAGUGGCA AUGCGACCAAGCUGU' (SEQ ID NO:630)	[], [], []	0.580645	0.806452	0	192
'CACCUCUCAGUGGCAA UGCGACCAAGCUGUG' (SEQ ID NO:631)	[], [], []	0.580645	0.806452	0	193
'CCUCUCAGUGGCAAUG CGACCAAGCUGUGUG' (SEQ ID NO:632)	[], [], []	0.580645	0.806452	0	195
'UUCACCACCUCUCAGU GGCAAUGCGACCAAG' (SEQ ID NO:633)	[], [], []	0.548387	0.806452	0	188
'CUCAGUGGCAAUGCAG CCAAGCUGUGUGACA' (SEQ ID NO:634)	[], [], []	0.548387	0.806452	0	198

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCAGUGGCAAUGCAC CAAGCUGUGUGACAC' (SEQ ID NO:635)	[], [], []	0.548387	0.806452	0	199
'ACCUCUCAGUGGCAAU GCGACCAAGCUGUGU' (SEQ ID NO:636)	[], [], []	0.548387	0.774194	0	194
'CUCUCAGUGGCAAUGC GACCAAGCUGUGUGA' (SEQ ID NO:637)	[], [], []	0.548387	0.774194	0	196
'UCUCAGUGGCAAUGCG ACCAAGCUGUGUGAC' (SEQ ID NO:638)	[], [], []	0.548387	0.774194	0	197
'UAAGGCCUCACUAAACC ACUCAUCUACACUU' (SEQ ID NO:639)	[], [], ['UAAA']]	0.419355	0.935484	1	107
'AAGGCCUCACUAAACCA CUCAUCUACACUU' (SEQ ID NO:640)	[], [], ['UAAA']]	0.419355	0.935484	1	108
'AAACCACUCAUCAUCAC UUAACAUCGAUCGU' (SEQ ID NO:641)	[], [], ['UUAA']]	0.387097	0.935484	1	119
'GCGACCAAGCUGUGUG ACACACCGCAAGGGC' (SEQ ID NO:642)	[], ['GGG'], []	0.645161	0.903226	1	210

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUGAACAGACAGGAAGCU GCAGCUCCAGGAGGG' (SEQ ID NO:643)	[], ['GGG'], []	0.580645	0.903226	1	155
'GAAGACAGGAAGCUGC AGCUCCAGGAGGGUA' (SEQ ID NO:644)	[], ['GGG'], []	0.580645	0.903226	1	157
'GCGUCUGUCCGUGGUG CUGAACGUUUAUUCGG' (SEQ ID NO:645)	[], [], ['UUUA']	0.548387	0.903226	1	9
'GUAAGGCCUCACUAAA CCACUCAUCUACACU' (SEQ ID NO:646)	[], [], ['UAAA']	0.451613	0.903226	1	106
'AACCACUCAUCUACACU UAACAUCGAUCGUG' (SEQ ID NO:647)	[], [], ['UUAA']	0.419355	0.903226	1	120
'ACCACUCAUCUACACUU AACAUCAUCGAUCGUGA' (SEQ ID NO:648)	[], [], ['UUAA']	0.419355	0.903226	1	121
'CCACUCAUCUACACUUA ACAUCAUCGAUCGUGAU' (SEQ ID NO:649)	[], [], ['UUAA']	0.419355	0.903226	1	122
'CACUCAUCUACACUUAA CAUCGAUCGUGUA' (SEQ ID NO:650)	[], [], ['UUAA']	0.387097	0.903226	1	123

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGCGACCAAGCUGUGU GACACACCGCAAGGG' (SEQ ID NO:651)	[[], ['GGG'], []]	0.612903	0.870968	1	209
'CGACCAAGCUGUGUGA CACACCGCAAGGGCU' (SEQ ID NO:652)	[[], ['GGG'], []]	0.612903	0.870968	1	211
'UGAAGACAGGAAGCUG CAGCUCCAGGAGGGU' (SEQ ID NO:653)	[[], ['GGG'], []]	0.580645	0.870968	1	156
'CCUCAGCGUCUGUCCG UGGUGCUGAAGUUUA' (SEQ ID NO:654)	[[], [], ['UUUA']]	0.548387	0.870968	1	4
'AAGACAGGAAGCUGCA GCUCCAGGAGGGUAU' (SEQ ID NO:655)	[[], ['GGG'], []]	0.548387	0.870968	1	158
'CUCAGCGUCUGUCCGU GGUGCUGAAGUUUAU' (SEQ ID NO:656)	[[], [], ['UUUA']]	0.516129	0.870968	1	5
'CAGCGUCUGUCCGUGG UGCUGAAGUUUAUUC' (SEQ ID NO:657)	[[], [], ['UUUA']]	0.516129	0.870968	1	7
'AGCGUCUGUCCGUGGU GCUGAAGUUUAUUCG' (SEQ ID NO:658)	[[], [], ['UUUA']]	0.516129	0.870968	1	8

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CGUCUGUCCGUGGUGC UGAAGUUUAUUCGGA' (SEQ ID NO:659)	[], [], ['UUUA'])	0.516129	0.870968	1	10
'UCAGCGUCUGUCCGUG GUGCUGAAGUUUAUU' (SEQ ID NO:660)	[], [], ['UUUA'])	0.483871	0.870968	1	6
'GUCUGUCCGUGGUGCU GAAGUUUAUUCGGAU' (SEQ ID NO:661)	[], [], ['UUUA'])	0.483871	0.870968	1	11
'GGUAAGGCCUCACUAA ACCACUCAUCUACAC' (SEQ ID NO:662)	[], [], ['UAAA'])	0.483871	0.870968	1	105
'UCUGUCCGUGGUGCUG AAGUUUAUUCGGAUU' (SEQ ID NO:663)	[], [], ['UUUA'])	0.451613	0.870968	1	12
'AGGUUAAGGCCUCACUA AACCAUCUCAUCUACA' (SEQ ID NO:664)	[], [], ['UAAA'])	0.451613	0.870968	1	104
'ACUCAUCUACACUUAAC AUCGAUCGUGAUAG' (SEQ ID NO:665)	[], [], ['UUAA'])	0.387097	0.870968	1	124
'CUCAUCUACACUUAACA UCGAUCGUGAUAGA' (SEQ ID NO:666)	[], [], ['UUAA'])	0.387097	0.870968	1	125

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUAACAUCAUCGAUCGUGA UAGAUGAAGACAGGA' (SEQ ID NO:667)	[], [], ['UUAA']]	0.387097	0.870968	1	136
'UCAUCUACACUUACAU CGAUCGUGAUAGAU' (SEQ ID NO:668)	[], [], ['UUAA']]	0.354839	0.870968	1	126
'CCAAGCUGUGUGACAC ACCGCAAGGGCUUGG' (SEQ ID NO:669)	[], ['GGG'], []]	0.612903	0.83871	1	214
'GACCAAGCUGUGUGAC ACACCGCAAGGGCUU' (SEQ ID NO:670)	[], ['GGG'], []]	0.580645	0.83871	1	212
'ACCAAGCUGUGUGACA CACCGCAAGGGCUUG' (SEQ ID NO:671)	[], ['GGG'], []]	0.580645	0.83871	1	213
'UAUGCAGAGUGGGAGAG GGUAAGGCCUCACUA' (SEQ ID NO:672)	[], ['GGG'], []]	0.516129	0.83871	1	89
'AUGCAGAGUGGGAGAG GUAAGGCCUCACUAA' (SEQ ID NO:673)	[], ['GGG'], []]	0.516129	0.83871	1	90
'GGAGAGGUAGGCCUC ACUAAAACCACUCAUC' (SEQ ID NO:674)	[], [], ['UAAA']]	0.516129	0.83871	1	100

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UAUUCACCACCUCUA GUGGCAAUGCGACCA' (SEQ ID NO:675)	[[], [], ['UAUU']]	0.516129	0.83871	1	186
'GAGGUAAGGCCUCACU AAACCACUCAUCAUCUAC' (SEQ ID NO:676)	[[], [], ['UAAA']]	0.483871	0.83871	1	103
'UUUCCAACUGCUUUCU GAAAGGGGUGAGGAU' (SEQ ID NO:677)	[[], ['GGG'], []]	0.451613	0.83871	1	49
'UGCUUUCUGAAAGGGG UGAGGAUCUACCUUA' (SEQ ID NO:678)	[[], ['GGG'], []]	0.451613	0.83871	1	57
'AGAGGUAAGGCCUCAC UAAACCACUCAUCAUCUA' (SEQ ID NO:679)	[[], [], ['UAAA']]	0.451613	0.83871	1	102
'CUUAACAUCAUCGUG AUAGAUGAAGACAGG' (SEQ ID NO:680)	[[], [], ['UUAA']]	0.419355	0.83871	1	135
'CAUCUACACUUACAUC GAUCGUGAUAGAUG' (SEQ ID NO:681)	[[], [], ['UUAA']]	0.387097	0.83871	1	127
'ACUUAAACAUCAUCGU GAUAGAUGAAGACAG' (SEQ ID NO:682)	[[], [], ['UUAA']]	0.387097	0.83871	1	134

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUCUACACUUAAACAUCG AUCGUGAUAGAUGA' (SEQ ID NO:683)	[[], [], ['UUAA']]	0.354839	0.83871	1	128
'UCUACACUUAAACAUCGA UCGUGAUAGAUGAA' (SEQ ID NO:684)	[[], [], ['UUAA']]	0.354839	0.83871	1	129
'UACACUUAAACAUCGAUC GUGAUAGAUGAAGA' (SEQ ID NO:685)	[[], [], ['UUAA']]	0.354839	0.83871	1	131
'GUUUUCACCACCUUCUC AGUGGCAAUGCGACC' (SEQ ID NO:686)	[[], [], ['UAUU']]	0.548387	0.806452	1	185
'UUCCAACUGCUUUCUG AAAGGGGUGAGGAUC' (SEQ ID NO:687)	[[], ['GGG'], []]	0.483871	0.806452	1	50
'UCCAACUGCUUUCUGA AAGGGGUGAGGAUCU' (SEQ ID NO:688)	[[], ['GGG'], []]	0.483871	0.806452	1	51
'CCAACUGCUUUCUGAA AGGGGUGAGGAUCUA' (SEQ ID NO:689)	[[], ['GGG'], []]	0.483871	0.806452	1	52
'CAACUGCUUUCUGAAA GGGGUGAGGAUCUAC' (SEQ ID NO:690)	[[], ['GGG'], []]	0.483871	0.806452	1	53

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AACUGCUUUCUGAAAG GGGUGAGGAUCUACC' (SEQ ID NO:691)	[[], ['GGG'], []]	0.483871	0.806452	1	54
'ACUGCUUUCUGAAAGG GGUGAGGAUCUACCU' (SEQ ID NO:692)	[[], ['GGG'], []]	0.483871	0.806452	1	55
'CUGCUUUCUGAAAGGG GUGAGGAUCUACCUU' (SEQ ID NO:693)	[[], ['GGG'], []]	0.483871	0.806452	1	56
'GAGAGGUAGGCCUCA CUAAACCACUCUCAUCU' (SEQ ID NO:694)	[[], [], ['UAAA']]	0.483871	0.806452	1	101
'CUACACUUACAUCGAU CGUGAUAGAUGAAG' (SEQ ID NO:695)	[[], [], ['UUAA']]	0.387097	0.806452	1	130
'ACACUUACAUCGAUCG UGAUAGAUGAAGAC' (SEQ ID NO:696)	[[], [], ['UUAA']]	0.387097	0.806452	1	132
'CACUUACAUCGAUCG UGAUAGAUGAAGACA' (SEQ ID NO:697)	[[], [], ['UUAA']]	0.387097	0.806452	1	133
'GGUAUUCACCACCUU CAGUGGCAAUGCGAC' (SEQ ID NO:698)	[[], [], ['UAUU']]	0.548387	0.774194	1	184

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCUCACUAAACCACUCA UCUACACUUACAU' (SEQ ID NO:699)	[[], [], ['UAAA', 'UUAA']]	0.387097	1	2	112
'CUCACUAAACCACUCAU CUACACUUACACUCAUC' (SEQ ID NO:700)	[[], [], ['UAAA', 'UUAA']]	0.387097	1	2	113
'GCCUCACUAAACCACUC AUCUACACUUACA (SEQ ID NO:701)	[[], [], ['UAAA', 'UUAA']]	0.419355	0.967742	2	111
'UCACUAAACCACUCAUC UACACUUACACUCAUCG' (SEQ ID NO:702)	[[], [], ['UAAA', 'UUAA']]	0.387097	0.967742	2	114
'CACUAAACCACUCAUCU ACACUUACACUCAUCGA' (SEQ ID NO:703)	[[], [], ['UAAA', 'UUAA']]	0.387097	0.967742	2	115
'CUAAACCACUCAUCUAC ACUUACACUCAUCGAUC' (SEQ ID NO:704)	[[], [], ['UAAA', 'UUAA']]	0.387097	0.967742	2	117
'ACUAAACCACUCAUCUA CACUUACACUCAUCGAU' (SEQ ID NO:705)	[[], [], ['UAAA', 'UUAA']]	0.354839	0.967742	2	116
'GGCCUCACUAAACCAC UCAUCUACACUUAC' (SEQ ID NO:706)	[[], [], ['UAAA', 'UUAA']]	0.451613	0.935484	2	110

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGGCCUCACUAAACCAC UCAUCUACACUUAA' (SEQ ID NO:707)	[[], [], ['UAAA', 'UUAA']]	0.419355	0.935484	2	109
'UAAACCACUCAUCAUCACA CUUAACAUCAUCGAUCG' (SEQ ID NO:708)	[[], [], ['UAAA', 'UUAA']]	0.387097	0.935484	2	118
'UACCUUAAUAUGCAGA GUUAGAGAGGUAGG' (SEQ ID NO:709)	[[], ['GGG'], ['UUAA']]	0.451613	0.903226	2	81
'GCAGAGUGGGAGAGGU AAGGCCUCACUAAAC' (SEQ ID NO:710)	[[], ['GGG'], ['UAAA']]	0.548387	0.870968	2	92
'CAGAGUGGGAGAGGU AGGCCUCACUAAACC' (SEQ ID NO:711)	[[], ['GGG'], ['UAAA']]	0.548387	0.870968	2	93
'GAGUGGGAGAGGUAG GCCUCACUAAACCAC' (SEQ ID NO:712)	[[], ['GGG'], ['UAAA']]	0.548387	0.870968	2	95
'GGCUUGGGAUCUUUUG CGAUCUGGCUCGAGCA' (SEQ ID NO:713)	[[], ['GGG'], ['UUUU']]	0.548387	0.870968	2	238
'GCUUGGGAUCUUUUGC GAUCUGCUCGAGCAG' (SEQ ID NO:714)	[[], ['GGG'], ['UUUU']]	0.548387	0.870968	2	239

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGAGUGGGAGAGGUAA GGCCUCACUAACCA' (SEQ ID NO:715)	[[], ['GGG'], ['UAAA']]	0.516129	0.870968	2	94
'CUUUUGCGAUCUGCUC GAGCAGAUUUGGCUG' (SEQ ID NO:716)	[[], [], ['UUUU', 'AUUU']]	0.516129	0.870968	2	248
'GGGGUGAGGAUCUACC UUAAUAUGCAGAGUG' (SEQ ID NO:717)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	69
'GGGUGAGGAUCUACCU UAAUAUGCAGAGUGGG' (SEQ ID NO:718)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	70
'GGUGAGGAUCUACCUU AAUAUGCAGAGUGGG' (SEQ ID NO:719)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	71
'GGAUCUACCUUAAAU GCAGAGUGGGAGAGG' (SEQ ID NO:720)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	76
'ACCUUAAUAUGCAGAG UGGGAGAGGUAGGC' (SEQ ID NO:721)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	82
'CUUAAUAUGCAGAGUG GGAGAGGUAGGCCU' (SEQ ID NO:722)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	84

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUAAUAUGCAGAGUGG GAGAGGUAGGCCUC' (SEQ ID NO:723)	[[], ['GGG'], ['UUAA']]	0.483871	0.870968	2	85
'UAAUAUGCAGAGUGGG AGAGGUAGGCCUCA' (SEQ ID NO:724)	[[], ['GGG'], ['UAAU']]	0.483871	0.870968	2	86
'UCUUUUGCGAUCUGCU CGAGCAGAUUUGGCU' (SEQ ID NO:725)	[[], [], ['UUUU', 'AUUU']]	0.483871	0.870968	2	247
'CUGUCCGUGGUGCUGA AGUUUAUUCGGAUUU' (SEQ ID NO:726)	[[], [], ['UUUA', 'AUUU']]	0.451613	0.870968	2	13
'GAAAGGGGUGAGGAUC UACCUUAAUAUGCAG' (SEQ ID NO:727)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	65
'AAGGGGUGAGGAUCUA CCUUAUAUGCAGAG' (SEQ ID NO:728)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	67
'AGGGGUGAGGAUCUAC CUUAAUAUGCAGAGU' (SEQ ID NO:729)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	68
'GUGAGGAUCUACCUUA AUAUGCAGAGUGGGA' (SEQ ID NO:730)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	72

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGAGGAUCUACCUUAA UAUGCAGAGUGGGAG' (SEQ ID NO:731)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	73
'GAGGAUCUACCUUAAU AUGCAGAGUGGGAGA' (SEQ ID NO:732)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	74
'AGGAUCUACCUUAAUAU GCAGAGUGGGAGAGAG' (SEQ ID NO:733)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	75
'GAUCUACCUUAAUUAUG CAGAGUGGGAGAGGU' (SEQ ID NO:734)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	77
'CUACCUUAAUUAUGCAGA GUUGGAGAGGUAAG' (SEQ ID NO:735)	[[], ['GGG'], ['UUAA']]	0.451613	0.870968	2	80
'UGUCCGUGGUGCUGAA GUUUAUUCGGAUUUA' (SEQ ID NO:736)	[[], [], ['UUUA', 'AUUU']]	0.419355	0.870968	2	14
'GUCCGUGGUGCUGAAG UUUAAUUCGGAUUUAU' (SEQ ID NO:737)	[[], [], ['UUUA', 'AUUU']]	0.419355	0.870968	2	15
'UCUGAAAGGGGUGAGG AUCUACCUUAAUUAUG' (SEQ ID NO:738)	[[], ['GGG'], ['UUAA']]	0.419355	0.870968	2	62

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGAAAGGGUGAGGAU CUACCUUAUAUGCA' (SEQ ID NO:739)	[], ['GGG'], ['UUAA']]	0.419355	0.870968	2	64
'AAAGGGUGAGGAUCU ACCUUAUAUGCAGA' (SEQ ID NO:740)	[], ['GGG'], ['UUAA']]	0.419355	0.870968	2	66
'AUCUACCUUAUAUGCA GAGUGGGAGAGGU'A (SEQ ID NO:741)	[], ['GGG'], ['UUAA']]	0.419355	0.870968	2	78
'UCUACCUUAUAUGCA GAGUGGGAGAGGUAA' (SEQ ID NO:742)	[], ['GGG'], ['UUAA']]	0.419355	0.870968	2	79
'UCCGUGGGUGCUGAAGU UUAUUCGGAUUUUUU' (SEQ ID NO:743)	[], [], ['UUUA', 'AUUU']]	0.387097	0.870968	2	16
'UUUCUGAAAGGGUGA GGAUCUACCUUAUA' (SEQ ID NO:744)	[], ['GGG'], ['UUAA']]	0.387097	0.870968	2	60
'UUCUGAAAGGGUGAG GAUCUACCUUAUAU' (SEQ ID NO:745)	[], ['GGG'], ['UUAA']]	0.387097	0.870968	2	61
'CAAGCUGUGUGACACA CCGCAAGGGCUUGGG' (SEQ ID NO:746)	[], ['GGG'], ['GGG'], []	0.612903	0.83871	2	215

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GACAGGAAGCUGCAGC UCCAGGAGGGUAUUC' (SEQ ID NO:747)	[], ['GGG'], ['UAUU']]	0.580645	0.83871	2	160
'CAGGAAGCUGCAGCUC CAGGAGGGUAUUCAC' (SEQ ID NO:748)	[], ['GGG'], ['UAUU']]	0.580645	0.83871	2	162
'AGGAAGCUGCAGCUCC AGGAGGGUAUUCACC' (SEQ ID NO:749)	[], ['GGG'], ['UAUU']]	0.580645	0.83871	2	163
'GGAAGCUGCAGCUCCA GGAGGGUAUUCACCA' (SEQ ID NO:750)	[], ['GGG'], ['UAUU']]	0.580645	0.83871	2	164
'GAAGCUGCAGCUCCAG GAGGGUAUUCACCAC' (SEQ ID NO:751)	[], ['GGG'], ['UAUU']]	0.580645	0.83871	2	165
'AAGCUGCAGCUCCAGG AGGGUAUUCACCACC' (SEQ ID NO:752)	[], ['GGG'], ['UAUU']]	0.580645	0.83871	2	166
'AAGCUGUGUGACACAC CGCAAGGGCUUGGGA' (SEQ ID NO:753)	[], ['GGG'], ['GGG'], []	0.580645	0.83871	2	216
'GUGGGAGAGGUAGGC CUCACUAAACCACUC' (SEQ ID NO:754)	[], ['GGG'], ['UAUA']]	0.548387	0.83871	2	97

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGACAGGAAGCUGCAG CUCCAGGAGGGUAUU' (SEQ ID NO:755)	[], ['GGG'], ['UAUU'])	0.548387	0.83871	2	159
'ACAGGAAGCUGCAGCU CCAGGAGGGUAUUCA' (SEQ ID NO:756)	[], ['GGG'], ['UAUU'])	0.548387	0.83871	2	161
'CCUUAAUAUGCAGAGU GGGAGAGGUAGGCC' (SEQ ID NO:757)	[], ['GGG'], ['UUAA'])	0.516129	0.83871	2	83
'AAUAUGCAGAGUGGGAG GAGGUAGGCCUCACU' (SEQ ID NO:758)	[], ['GGG'], ['AAUA'])	0.516129	0.83871	2	87
'AU AUGCAGAGUGGGAG AGGUAGGCCUCACU' (SEQ ID NO:759)	[], ['GGG'], ['AU AU'])	0.516129	0.83871	2	88
'UGCAGAGUGGGAGAGG UAAGGCCUCACUAAA' (SEQ ID NO:760)	[], ['GGG'], ['UAAA'])	0.516129	0.83871	2	91
'AGUGGGAGAGGUAGG CCUCACUAAACCACU' (SEQ ID NO:761)	[], ['GGG'], ['UAAA'])	0.516129	0.83871	2	96
'UGGGAGAGGUAGGCC UCACUAAACCACUCA' (SEQ ID NO:762)	[], ['GGG'], ['UAAA'])	0.516129	0.83871	2	98

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGGAGAGGUAGGCCU CACUAAACCACUCAU' (SEQ ID NO:763)	[[], ['GGG'], ['UAAA']]	0.516129	0.83871	2	99
'CUUGGGAUCUUUUGCG AUCUGCUCGAGCAGA' (SEQ ID NO:764)	[[], ['GGG'], ['UUUU']]	0.516129	0.83871	2	240
'UUGGGAUCUUUUGCGA UCUGCUCGAGCAGAU' (SEQ ID NO:765)	[[], ['GGG'], ['UUUU']]	0.483871	0.83871	2	241
'UGGGGAUCUUUUGCGAU CUGCUCGAGCAGAUU' (SEQ ID NO:766)	[[], ['GGG'], ['UUUU']]	0.483871	0.83871	2	242
'GGAUCUUUUGCGAUCU GCUCGAGCAGAUUUG' (SEQ ID NO:767)	[[], [], ['UUUU', 'AUUU']]	0.483871	0.83871	2	244
'GAUCUUUUGCGAUCUG CUCGAGCAGAUUUGG' (SEQ ID NO:768)	[[], [], ['UUUU', 'AUUU']]	0.483871	0.83871	2	245
'AUCUUUUGCGAUCUGC UCGAGCAGAUUUGGC' (SEQ ID NO:769)	[[], [], ['UUUU', 'AUUU']]	0.483871	0.83871	2	246
'UUUUUCCAACUGCUUU CUGAAAGGGGUGAGG' (SEQ ID NO:770)	[[], ['GGG'], ['UUUU']]	0.451613	0.83871	2	47

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUUUCCAACUGCUUUC UGAAAGGGGUGAGGA' (SEQ ID NO:771)	[], ['GGG'], ['UUUU'])	0.451613	0.83871	2	48
'GCUUUCUGAAAGGGGU GAGGAUCUACCUUAA' (SEQ ID NO:772)	[], ['GGG'], ['UUAA'])	0.451613	0.83871	2	58
'CUGAAAGGGGUGAGGA UCUACCUUAAUAUGC' (SEQ ID NO:773)	[], ['GGG'], ['UUAA'])	0.451613	0.83871	2	63
'UUUUUUCCAACUGCUU UCUGAAAGGGGUGAG' (SEQ ID NO:774)	[], ['GGG'], ['UUUU'])	0.419355	0.83871	2	46
'CUUUCUGAAAGGGGUG AGGAUCUACCUUAAU' (SEQ ID NO:775)	[], ['GGG'], ['UUAA'])	0.419355	0.83871	2	59
'UUUUUUUUCCAACUGCU UUCUGAAAGGGGUGA' (SEQ ID NO:776)	[], ['GGG'], ['UUUU'])	0.387097	0.83871	2	45
'GCUGCAGCUCCAGGAG GGUAUUCACCACCUUC' (SEQ ID NO:777)	[], ['GGG'], ['UAUU'])	0.612903	0.806452	2	168
'GCUGUGUGACACACCG CAAGGGCUUGGGAUC' (SEQ ID NO:778)	[], ['GGG'], ['GGG'], [])	0.612903	0.806452	2	218

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGCUGCAGCUCCAGGA GGGUUUUCACCACCU' (SEQ ID NO:779)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	167
'CUGCAGCUCCAGGAGG GUUUUCACCACCUUCU' (SEQ ID NO:780)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	169
'UGCAGCUCCAGGAGGG UAUUUCACCACCUUCU' (SEQ ID NO:781)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	170
'GCAGCUCCAGGAGGGU AUUCACCACCUUCUCA' (SEQ ID NO:782)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	171
'CAGCUCCAGGAGGGUA UUCACCACCUUCUCAG' (SEQ ID NO:783)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	172
'GCUCCAGGAGGGUAUU CACCAACCUCUCAGUGG' (SEQ ID NO:784)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	174
'CUCCAGGAGGGUAUUC ACCACCUCUCAGUGG' (SEQ ID NO:785)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	175
'UCCAGGAGGGUAUUC CCACCUCUCAGUGGC' (SEQ ID NO:786)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	176

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CCAGGAGGGUAUUCAC CACCUCUCAGUGGCA' (SEQ ID NO:787)	[], ['GGG'], ['UAUU'])	0.580645	0.806452	2	177
'AGCUGUGUGACACACC GCAAGGGCUUGGGAU' (SEQ ID NO:788)	[], ['GGG', 'GGG'], [])	0.580645	0.806452	2	217
'CUGUGUGACACACCGC AAGGGCUUGGGGAUCU' (SEQ ID NO:789)	[], ['GGG', 'GGG'], [])	0.580645	0.806452	2	219
'CAGGAGGGUAUUCACC ACCUUCUCAGUGGCAA' (SEQ ID NO:790)	[], ['GGG'], ['UAUU'])	0.548387	0.806452	2	178
'UGUGUGACACACCGCA AGGGCUUGGGGAUCUU' (SEQ ID NO:791)	[], ['GGG', 'GGG'], [])	0.548387	0.806452	2	220
'GUGUGACACACCGCAA GGGCUUGGGGAUCUUU' (SEQ ID NO:792)	[], ['GGG', 'GGG'], [])	0.548387	0.806452	2	221
'AGCUCCAGGAGGGUAU UCACCACCUUCAGU' (SEQ ID NO:793)	[], ['GGG'], ['UAUU'])	0.548387	0.774194	2	173

FIG. 42 (Cont'd)

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGAGGGUAUUCACCA CUCUCAGUGGCAAUG' (SEQ ID NO:794)	[[], ['GGG'], ['UAUU']]	0.548387	0.774194	2	180
'GAGGGUAUUCACCACC UCUCAGUGGCAAUGC' (SEQ ID NO:795)	[[], ['GGG'], ['UAUU']]	0.548387	0.774194	2	181
'AGGGUAUUCACCACCU CUCAGUGGCAAUGCG' (SEQ ID NO:796)	[[], ['GGG'], ['UAUU']]	0.548387	0.774194	2	182
'GGGUAUUCACCACCU UCAGUGGCAAUGCGA' (SEQ ID NO:797)	[[], ['GGG'], ['UAUU']]	0.548387	0.774194	2	183
'AGGAGGGUAUUCACCA CCUCUCAGUGGCAAU' (SEQ ID NO:798)	[[], ['GGG'], ['UAUU']]	0.516129	0.774194	2	179
'GUGGUGCUGAAGUUUA UUCGGAUUUAUUUUUU' (SEQ ID NO:799)	[[],[], ['UUUA', 'AUUU', 'AUUU']]	0.322581	0.935484	3	19
'UGGUGCUGAAGUUUAU UCGGAUUUAUUUUUU' (SEQ ID NO:800)	[[],[], ['UUUA', 'AUUU', 'AUUU']]	0.290323	0.935484	3	20
'GGCUUGGGAUCUUU GCGAUCUGCUCGAGC' (SEQ ID NO:801)	[[], ['GGG', 'GGG'], ['UUUU']]	0.580645	0.903226	3	237

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CGUGGGUGCUGAAGUUU AUUCGGAUUUUUUUU' (SEQ ID NO:802)	[[], [], ['UUUA', 'UUUU', 'UUUU']]	0.354839	0.903226	3	18
'AUUCGGAUUUUUUUU UUCCAACUGCUUUCU' (SEQ ID NO:803)	[[], [], ['AUUU', 'AUUU', 'UUUU']]	0.290323	0.903226	3	34
'CCGCAAGGGCUUGGGA UCUUUUGCGAUCUGC' (SEQ ID NO:804)	[[], ['GGG', 'GGG'], ['UUUU']]	0.580645	0.870968	3	231
'CGCAAGGGCUUGGGAU CUUUUGCGAUCUGCU' (SEQ ID NO:805)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.870968	3	232
'GCAAGGGCUUGGGAUC UUUUGCGAUCUGCUC' (SEQ ID NO:806)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.870968	3	233
'CAAGGGCUUGGGAUCU UUUGCGAUCUGCUCG' (SEQ ID NO:807)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.870968	3	234

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGGGCUUGGGAUCUUU UGCGAUCUGCUCGAG' (SEQ ID NO:808)	[[], 'GGG', 'GGG'], 'UUUU']]	0.548387	0.870968	3	236
'CCGUGGGUGCUGAAGUU UAUUCGGAUUUUUUUU' (SEQ ID NO:809)	[[], [], 'UUUA', 'AUUU', 'AUUU']]	0.387097	0.870968	3	17
'UUCGGAUUUUUUUUUU UCCAACUGCUUUCUG' (SEQ ID NO:810)	[[], [], 'AUUU', 'AUUU', 'UUUU']]	0.322581	0.870968	3	35
'UCGGAUUUUUUUUUU CCAACUGCUUUCUGA' (SEQ ID NO:811)	[[], [], 'AUUU', 'AUUU', 'UUUU']]	0.322581	0.870968	3	36
'CGGAUUUUUUUUUUUC CAACUGCUUUCUGAA' (SEQ ID NO:812)	[[], [], 'AUUU', 'AUUU', 'UUUU']]	0.322581	0.870968	3	37
'GGAUUUUUUUUUUCC AACUGCUUUCUGAAA' (SEQ ID NO:813)	[[], [], 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	3	38

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GAUUUAUUUUUUUCCA ACUGCUUUCUGAAAG' (SEQ ID NO:814)	[[], [], 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	3	39
'AUUUAUUUUUUUUCCAAC UGCUUUCUGAAAGG' (SEQ ID NO:815)	[[], [], 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	3	40
'CACCGCAAGGGCUUGG GAUCUUUUGCGAUCU' (SEQ ID NO:816)	[[], 'GGG', 'GGG'], 'UUUU']]	0.548387	0.83871	3	229
'ACCGCAAGGGCUUGGG AUCUUUUGCGAUCUG' (SEQ ID NO:817)	[[], 'GGG', 'GGG'], 'UUUU']]	0.548387	0.83871	3	230
'AAGGGCUUGGGAUCUU UUGCGAUCUGCUCGA' (SEQ ID NO:818)	[[], 'GGG', 'GGG'], 'UUUU']]	0.516129	0.83871	3	235
'GGGAUCUUUUGCGAUC UGCUCGAGCAGAUUU' (SEQ ID NO:819)	[[], 'GGG'], 'UUUU', 'AUUU']]	0.483871	0.83871	3	243

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUUUUUUUUCCAACUGC UUUCUGAAAGGGGUG' (SEQ ID NO:820)	[], ['GGG'], ['AUUU', 'UUUU']]	0.387097	0.83871	3	44
'UUAUUUUUUUCCACU GCUUUCUGAAAGGGG' (SEQ ID NO:821)	[], ['GGG'], ['UUAU', 'UUUU']]	0.354839	0.83871	3	42
'UAUUUUUUUCCACUG CUUUCUGAAAGGGU' (SEQ ID NO:822)	[], ['GGG'], ['UAUU', 'UUUU']]	0.354839	0.83871	3	43
'UUUAUUUUUUUCCAAC UGCUUUCUGAAAGGG' (SEQ ID NO:823)	[], ['GGG'], ['UUUA', 'UUUU']]	0.322581	0.83871	3	41
'GACACACCGCAAGGGC UUGGGAUCUUUGCG' (SEQ ID NO:824)	[], ['GGG', 'GGG'], ['UUUU']]	0.580645	0.806452	3	225
'GUGACACACCGCAAGG GCUUGGGAUCUUUG' (SEQ ID NO:825)	[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.806452	3	223

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGACACACCCGCAAGGG CUUGGGAUCUUUUGC' (SEQ ID NO:826)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.806452	3	224
'CACACCGCAAGGGCUU GGGAUCUUUUGCGAU' (SEQ ID NO:827)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.806452	3	227
'ACACCGCAAGGGCUUG GGAUCUUUUGCGAUC' (SEQ ID NO:828)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.806452	3	228
'UGUGACACACCGCAAG GGCUUGGGAUCUUUU' (SEQ ID NO:829)	[[], ['GGG', 'GGG'], ['UUUU']]	0.516129	0.806452	3	222
'ACACACCGCAAGGGCU UGGGGAUCUUUUGCGA' (SEQ ID NO:830)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387	0.774194	3	226
'GGUGCUGAAGUUUAUU CGGAUUUAUUUUUUU' (SEQ ID NO:831)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.935484	4	21

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GUGCUGAAGUUUAUUC GGAUUUAUUUUUUUUC' (SEQ ID NO:832)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.903226	4	22
'UAUUCGGAUUUAUUUU UUUCCAACUGCUUUC' (SEQ ID NO:833)	[[], [], ['UAUU', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.903226	4	33
'UUUAUUCGGAUUUAUU UUUUUCCAACUGCUU' (SEQ ID NO:834)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258065	0.903226	4	31
'UUUAUUCGGAUUUAUU UUUUUCCAACUGCUUU' (SEQ ID NO:835)	[[], [], ['UUAU', 'AUUU', 'AUUU', 'UUUU']]	0.258065	0.903226	4	32
'UGCUGAAGUUUAUUCG GAUUUAUUUUUUUCC' (SEQ ID NO:836)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	4	23

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GCUGAAGUUUAUUCGG AUUUAUUUUUUUCCA' (SEQ ID NO:837)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	4	24
'AGUUUAUUCGGAUUA UUUUUUUCCAACUGGC' (SEQ ID NO:838)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	4	29
'GUUUAUUCGGAUUAU UUUUUUUCCAACUGCU' (SEQ ID NO:839)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290323	0.870968	4	30
'CUGAAGUUUAUUCGGA UUUAUUUUUUUUCCAA' (SEQ ID NO:840)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258065	0.870968	4	25
'UGAAGUUUAUUCGGAU UUUAUUUUUUUUCCAAC' (SEQ ID NO:841)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258065	0.870968	4	26

FIG. 42 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GAAGUUUAUUCGGAUU UAUUUUUUUCCAACU' (SEQ ID NO:842)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258065	0.870968	4	27
'AAGUUUAUUCGGAUU AUUUUUUUCCAACUG' (SEQ ID NO:843)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258065	0.870968	4	28

FIG. 42 (Cont'd)

FIG. 43

SEQUENCE	BS	GCNESS	3LN	NEP	P
'GGAAUCAGAAGCAGGU GUCUGCAGCCAGGAC' (SEQ ID NO:844)	[], [], []	0.580645	0.87 096 8	0	153
'GUGGAAUCAGAAGCAG GUGUCUGCAGCCAGG' (SEQ ID NO:845)	[], [], []	0.580645	0.83 871	0	151
'UGGAAUCAGAAGCAGG UGUCUGCAGCCAGGA' (SEQ ID NO:846)	[], [], []	0.548387	0.83 871	0	152
'GAAUCAGAAGCAGGUG UCUGCAGCCAGGACU' (SEQ ID NO:847)	[], [], []	0.548387	0.83 871	0	154
'UCAGAACAGGUGUCU GCAGCCAGGACUUCC' (SEQ ID NO:848)	[], [], []	0.580645	0.80 645 2	0	157
'CAGAACAGGUGUCUG CAGCCAGGACUUCCU' (SEQ ID NO:849)	[], [], []	0.580645	0.80 645 2	0	158
'AGAACAGGUGUCUGC AGCCAGGACUUCCUC' (SEQ ID NO:850)	[], [], []	0.580645	0.80 645 2	0	159
'UGUGGAAUCAGAAGCA GGUGUCUGCAGCCAG' (SEQ ID NO:851)	[], [], []	0.548387	0.80 645 2	0	150

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUCAGAAGCAGGUGUC UGCAGCCAGGACUUC' (SEQ ID NO:852)	[], [], []	0.548387	0.80 645 2	0	156
'UUGUGGAAUCAGAAC AGGUGUCUGCAGCCA' (SEQ ID NO:853)	[], [], []	0.516129	0.80 645 2	0	149
'AAUCAGAAGCAGGUGU CUGCAGCCAGGACUU' (SEQ ID NO:854)	[], [], []	0.516129	0.80 645 2	0	155
'CCUUGUGGAAUCAGAA GCAGGUGUCUGCAGC' (SEQ ID NO:855)	[], [], []	0.548387	0.77 419 4	0	147
'CUUGUGGAAUCAGAAC CAGGUGUCUGCAGCC' (SEQ ID NO:856)	[], [], []	0.548387	0.77 419 4	0	148
'CACUUCAAAGGCGGCC ACAGGGUUGAGGAAA' (SEQ ID NO:857)	[], ['GGG'], []	0.548387	0.87 096 8	1	111
'AAAAAAUGAGUCACUUC AAAGGCGGCCACAGG' (SEQ ID NO:858)	[], [], ['AAAA']]	0.483871	0.87 096 8	1	101
'AAAAAAUAUGAGUCACUU CAAAGGCGGCCACAG' (SEQ ID NO:859)	[], [], ['AAAA']]	0.451613	0.87 096 8	1	100

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACCGUGGAAAUUUUGU GCUAAAGGUAGAA' (SEQ ID NO:860)	[], [], ['AAAU']]	0.387097	0.87 096 8	1	26
'CCGUGGAAAUUUUGUG CUCAAAGGUAGAAA' (SEQ ID NO:861)	[], [], ['AAAU']]	0.387097	0.87 096 8	1	27
'CGUGGAAAUUUUGUGC UCAAAGGUAGAAAC' (SEQ ID NO:862)	[], [], ['AAAU']]	0.387097	0.87 096 8	1	28
'GUGGAAAUUUUGUGCU CAAAGGUAGAAACC' (SEQ ID NO:863)	[], [], ['AAAU']]	0.387097	0.87 096 8	1	29
'UGGAAAUUUUGUGCUC AAAGGUAGAAACCA' (SEQ ID NO:864)	[], [], ['AAAU']]	0.354839	0.87 096 8	1	30
'GGAAAUUUUGUGCUA AAGGUAGAAACCAU' (SEQ ID NO:865)	[], [], ['AAAU']]	0.354839	0.87 096 8	1	31
'GAGUCACUUCAAAGGC GGCCACAGGGUUGAG' (SEQ ID NO:866)	[], ['GGG'], []]	0.580645	0.83 871	1	107
'AGUCACUUCAAAGGCG GCCACAGGGUUGAGG' (SEQ ID NO:867)	[], ['GGG'], []]	0.580645	0.83 871	1	108

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GUCACUUCAAAGGCCGG CCACAGGGUUGAGGA' (SEQ ID NO:868)	[], ['GGG'], []	0.580645	0.83 871	1	109
'UCACUUCAAAGGCGGC CACAGGGUUGAGGAA' (SEQ ID NO:869)	[], ['GGG'], []	0.548387	0.83 871	1	110
'UCACCGUGGAAAUUUU GUGCUAAAGGUAGA' (SEQ ID NO:870)	[], [], ['AAAU']]	0.419355	0.83 871	1	24
'CACCGUGGAAAUUUUG UGCUCAAAGGUAGA' (SEQ ID NO:871)	[], [], ['AAAU']]	0.419355	0.83 871	1	25
'UUUCACCGUGGAAAUU UUGUGCUCAAAGGUAA' (SEQ ID NO:872)	[], [], ['AAAU']]	0.387097	0.83 871	1	22
'UUCACCGUGGAAAUU UGUGCUCAAAGGUAA' (SEQ ID NO:873)	[], [], ['AAAU']]	0.387097	0.83 871	1	23
'GAAAUUUUGUGCUCAA AGGUAGAAACCAUC' (SEQ ID NO:874)	[], [], ['AAAU']]	0.354839	0.83 871	1	32
'AAAUUUUGUGCUCAAA GGUAAGAAACCAUCU' (SEQ ID NO:875)	[], [], ['AAAU']]	0.322581	0.83 871	1	33

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AAUUUUGUGCUCAAAG GUAAGAAACCAUCUU' (SEQ ID NO:876)	[], [], ['AAUU'])	0.322581	0.83 871	1	34
'AUUUUGUGCUCAAAGG UAAGAAACCAUCUUA' (SEQ ID NO:877)	[], [], ['AUUU'])	0.322581	0.83 871	1	35
'UUUGUGCUCAAAGGUA AGAAACCAUCUUUAUA' (SEQ ID NO:878)	[], [], ['UUAU'])	0.322581	0.83 871	1	37
'UUGUGCUCAAAGGUAA GAAACCAUCUUUAUAU' (SEQ ID NO:879)	[], [], ['UUAU'])	0.322581	0.83 871	1	38
'UGUGCUCAAAGGUAG AACCAUCUUUAUAU' (SEQ ID NO:880)	[], [], ['UUAU'])	0.322581	0.83 871	1	39
'GCCCUUGUGGAAUCA GAAGCAGGUGUCUGC' (SEQ ID NO:881)	['CCC'], [], []]	0.580645	0.80 645 2	1	144
'AUGAGUCACUUCAAAG GCGGCCACAGGGUUG' (SEQ ID NO:882)	[], ['GGG'], []]	0.548387	0.80 645 2	1	105
'UGAGUCACUUCAAAGG CGGCCACAGGGUUGA' (SEQ ID NO:883)	[], ['GGG'], []]	0.548387	0.80 645 2	1	106

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AAUGAGUCACUUCAAA GGCGGCCACAGGGUU' (SEQ ID NO:884)	[], ['GGG'], []	0.516129	0.80 645 2	1	104
'AAAGCCCCUUGUGGAA UCAGAAGCAGGUGUC' (SEQ ID NO:885)	[['CCC'], [], []]	0.516129	0.80 645 2	1	141
'AGCCCCUUGUGGAAUC AGAACCGAGGUGUCUG' (SEQ ID NO:886)	[['CCC'], [], []]	0.548387	0.77 419 4	1	143
'CCCCUUGUGGAAUCAGA AAGCAGGUGUCUGCA' (SEQ ID NO:887)	[['CCC'], [], []]	0.548387	0.77 419 4	1	145
'CCCUUGUGGAAUCAGA AGCAGGUGUCUGCAG' (SEQ ID NO:888)	[['CCC'], [], []]	0.548387	0.77 419 4	1	146
'AAGCCCCUUGUGGAAU CAGAACCGAGGUGUCU' (SEQ ID NO:889)	[['CCC'], [], []]	0.516129	0.77 419 4	1	142
'CAAAGGCGGCCACAGG GUUGAGGAAAAAGCC' (SEQ ID NO:890)	[], ['GGG'], ['AAAA']]	0.580645	0.93 548 4	2	116
'GUAAGAAACCAUCUUA UAUAAAACAAUCAAA' (SEQ ID NO:891)	[], [], ['UUAU', 'AUAA']]	0.225806	0.93 548 4	2	50

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCAAAGGCGGCCACAG GGUUGAGGAAAAAGC' (SEQ ID NO:892)	[[], ['GGG'], ['AAAA']]	0.548387	0.90 322 6	2	115
'CUAAAGGUAGAAC CAUCUUUAUAAAAC' (SEQ ID NO:893)	[[], [], ['UUAU', 'AUAA']]	0.290323	0.90 322 6	2	43
'UCAAAGGUAGAACCC AUCUUUAUAAAACA' (SEQ ID NO:894)	[[], [], ['UUAU', 'AUAA']]	0.258065	0.90 322 6	2	44
'CAAAGGUAGAACCA UCUUUAUAAAACAA' (SEQ ID NO:895)	[[], [], ['UUAU', 'AUAA']]	0.258065	0.90 322 6	2	45
'AAGGUAGAACCAUC UUUAUAAAACAAUC' (SEQ ID NO:896)	[[], [], ['UUAU', 'AUAA']]	0.258065	0.90 322 6	2	47
'AGGUAGAACCAUCU UUAUAAAACAAUCA' (SEQ ID NO:897)	[[], [], ['UUAU', 'AUAA']]	0.258065	0.90 322 6	2	48
'GGUAAGAACCAUCUU AUUAUAAAACAAUCA' (SEQ ID NO:898)	[[], [], ['UUAU', 'AUAA']]	0.258065	0.90 322 6	2	49
'AAAGGUAGAACCAU CUUAUUAACAAU' (SEQ ID NO:899)	[[], [], ['UUAU', 'AUAA']]	0.225806	0.90 322 6	2	46

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AAAAAUGAGUCACUUCA AAGGCAGGCCACAGGG' (SEQ ID NO:900)	[], ['GGG'], ['AAAA'])	0.516129	0.87 096 8	2	102
'ACUUCAAAGGCGGCCA CAGGGUUGAGGAAAA' (SEQ ID NO:901)	[], ['GGG'], ['AAAA'])	0.516129	0.87 096 8	2	112
'CUUCAAAGGCGGCCAC AGGGUUGAGGAAAAAA' (SEQ ID NO:902)	[], ['GGG'], ['AAAA'])	0.516129	0.87 096 8	2	113
'UUCAAAGGCGGCCACA GGGUUGAGGAAAAAG' (SEQ ID NO:903)	[], ['GGG'], ['AAAA'])	0.516129	0.87 096 8	2	114
'GGAAAAAAGCCCCUUGU GGAAUCAGAAGCAGG' (SEQ ID NO:904)	[['CCC'], [], ['AAAA'])	0.516129	0.87 096 8	2	137
'GAGGAAAAAAGCCCCUU GUGGAAUCAGAAGCA' (SEQ ID NO:905)	[['CCC'], [], ['AAAA'])	0.483871	0.87 096 8	2	135
'AGGAAAAAAGCCCCUUG UGGAAUCAGAAGCAG' (SEQ ID NO:906)	[['CCC'], [], ['AAAA'])	0.483871	0.87 096 8	2	136
'AAAAAAAAUGAGUCACU UCAAAGGCGGCCACA' (SEQ ID NO:907)	[], [], ['AAAA', 'AAAU'])	0.419355	0.87 096 8	2	99

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GUUGACUUUAUUUCAC CGUGGAAAUUUUGUG' (SEQ ID NO:908)	[[], [], ['UUUA', 'AAAU']]	0.354839	0.87 096 8	2	12
'AUGUUGACUUUAUUUC ACCGUGGAAAUUUUG' (SEQ ID NO:909)	[[], [], ['UUUA', 'AAAU']]	0.322581	0.87 096 8	2	10
'UGUUGACUUUAUUUCA CCGUGGAAAUUUUGU' (SEQ ID NO:910)	[[], [], ['UUUA', 'AAAU']]	0.322581	0.87 096 8	2	11
'AAAGCUUUAUAUGUUG ACUUUAUUUCACCGU' (SEQ ID NO:911)	[[], [], ['UUAU', 'UUUA']]	0.290323	0.87 096 8	2	0
'UUUAUAUGUUGACUUU AUUUCACCGUGGAAA' (SEQ ID NO:912)	[[], [], ['UUAU', 'UUUA']]	0.290323	0.87 096 8	2	5
'AAUGUUGACUUUAUUU CACCGUGGAAAUUUU' (SEQ ID NO:913)	[[], [], ['UUUA', 'AAAU']]	0.290323	0.87 096 8	2	9
'UGCUCAAAGGUAAGAA ACCAUCUUUAUAUAAA' (SEQ ID NO:914)	[[], [], ['UUAU', 'AUAA']]	0.290323	0.87 096 8	2	41
'GCUCAAAGGUAAGAAA CCAUCUUUAUAUAAAA' (SEQ ID NO:915)	[[], [], ['UUAU', 'AUAA']]	0.290323	0.87 096 8	2	42

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUACAUUAAAAAAAUGA GUCACUUCAAAGGC' (SEQ ID NO:916)	[[], [], ['AUUA', 'AAAA']]	0.290323	0.87 096 8	2	92
'AAAUGAGUCACUCAA AGGCGGCCACAGGGU' (SEQ ID NO:917)	[[], ['GGG'], ['AAAU']]	0.516129	0.83 871	2	103
'GGUUGAGGAAAAAGCC CCUUGUGGAAUCAGA' (SEQ ID NO:918)	[['CCC'], [], ['AAAA']]	0.483871	0.83 871	2	131
'UGAGGAAAAAGCCCCU UGUGGAAUCAGAACG' (SEQ ID NO:919)	[['CCC'], [], ['AAAA']]	0.483871	0.83 871	2	134
'GAAAAAGCCCCUUGUG GAAUCAGAACGCAGGU' (SEQ ID NO:920)	[['CCC'], [], ['AAAA']]	0.483871	0.83 871	2	138
'AAAAAGCCCCUUGUGG AAUCAGAACGCAGGUG' (SEQ ID NO:921)	[['CCC'], [], ['AAAA']]	0.483871	0.83 871	2	139
'GUUGAGGAAAAAGCCC CUUGUGGAAUCAGAA' (SEQ ID NO:922)	[['CCC'], [], ['AAAA']]	0.451613	0.83 871	2	132
'UUGAGGAAAAAGCCCC UUGUGGAAUCAGAACG' (SEQ ID NO:923)	[['CCC'], [], ['AAAA']]	0.451613	0.83 871	2	133

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUUUUUUUUAUGAGAGUCAC UUCAAAGGCGGCCAC' (SEQ ID NO:924)	[[], [], ['UAAA', 'AAAA']]	0.419355	0.83 871	2	98
'UAUUUCACCGUGGAAA UUUUGUGCUCAAAGG' (SEQ ID NO:925)	[[], [], ['UAUU', 'AAAU']]	0.387097	0.83 871	2	20
'AUUUCACCGUGGAAAU UUUGUGCUCAAAGGU' (SEQ ID NO:926)	[[], [], ['AUUU', 'AAAU']]	0.387097	0.83 871	2	21
'AGCUUUAUAUGUUGAC UUUAAAUCACCGUGG' (SEQ ID NO:927)	[[], [], ['UUAU', 'UUUA']]	0.354839	0.83 871	2	2
'GCUUUAUAUGUUGACU UUUUUCACCGUGGA' (SEQ ID NO:928)	[[], [], ['UUAU', 'UUUA']]	0.354839	0.83 871	2	3
'UUGACUUUAUUUCACC GUGGAAAUUUUGUGC' (SEQ ID NO:929)	[[], [], ['UUUA', 'AAAU']]	0.354839	0.83 871	2	13
'UGACUUUAUUUCACCG UGGAAAUUUUGUGC' (SEQ ID NO:930)	[[], [], ['UUUA', 'AAAU']]	0.354839	0.83 871	2	14
'ACUUUAUUUCACCGUG GAAAUUUUGUGCUC' (SEQ ID NO:931)	[[], [], ['UUUA', 'AAAU']]	0.354839	0.83 871	2	16

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CUUUAUUUUCACCGUGG AAUUUUUGUGCUCAA' (SEQ ID NO:932)	[], [], ['UUUA', 'AAAU']]	0.354839	0.83 871	2	17
'UUAUUUUCACCGUGGAA AUUUUGUGCUCAAAG' (SEQ ID NO:933)	[], [], ['UUAU', 'AAAU']]	0.354839	0.83 871	2	19
'ACAUUAAAAAAAUGAG UCACUUCAAAGGCGG' (SEQ ID NO:934)	[], [], ['AUUA', 'AAAA']]	0.354839	0.83 871	2	94
'AAGCUUUAUAUGUUGA CUUUAUUUUCACCGUG' (SEQ ID NO:935)	[], [], ['UUAU', 'UUUA']]	0.322581	0.83 871	2	1
'CUUAUAAUGUUGACUU UAUUUCACCGUGGAA' (SEQ ID NO:936)	[], [], ['UUAU', 'UUUA']]	0.322581	0.83 871	2	4
'UUUAUUUUCACCGUGGA AAUUUUUGUGCUAAA' (SEQ ID NO:937)	[], [], ['UUUA', 'AAAU']]	0.322581	0.83 871	2	18
'UUUUGUGCUCAAAGGU AAGAAACCAUCUUAU' (SEQ ID NO:938)	[], [], ['UUUU', 'UUAU']]	0.322581	0.83 871	2	36
'GUGCUCAAAGGUAGA AACCAUCUUUAUAAA' (SEQ ID NO:939)	[], [], ['UUAU', 'AUAA']]	0.322581	0.83 871	2	40

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UACAUUUAAAAAAAUGA GUCACUUCAAAGGCG' (SEQ ID NO:940)	[[], [], ['AUUA', 'AAAA']]	0.322581	0.83 871	2	93
'AAAAGCCCCUUGUGGA AUCAGAACGAGGUGU' (SEQ ID NO:941)	[['CCC'], [], ['AAAA']]	0.483871	0.80 645 2	2	140
'GACUUUUUUUCACCGU GGAAAUUUUGUGGUUC' (SEQ ID NO:942)	[[], [], ['UUUA', 'AAAU']]	0.387097	0.80 645 2	2	15
'CAUUAAAAAAUAGAGU CACUUCAAAGGCGGC' (SEQ ID NO:943)	[[], [], ['AUUA', 'AAAA']]	0.387097	0.80 645 2	2	95
'AUUAAAAAAUAGAGUC ACUUCAAAGGCGGCC' (SEQ ID NO:944)	[[], [], ['AUUA', 'AAAA']]	0.387097	0.80 645 2	2	96
'UUAAAAAAUAGAGUCA CUUCAAAGGCGGCCA' (SEQ ID NO:945)	[[], [], ['UUAA', 'AAAA']]	0.387097	0.80 645 2	2	97
'UAAGAAACCAUCUUAU AUAAAACAAUCAAAU' (SEQ ID NO:946)	[[], [], ['UUAU', 'AUAA', 'AAAU']]	0.193548	0.96 774 2	3	51
'AAGAAACCAUCUUAU UAAAACAAUCAAAU' (SEQ ID NO:947)	[[], [], ['UUAU', 'AUAA', 'AAAU']]	0.193548	0.96 774 2	3	52

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGAAACCAUCUUUAU AAAACAAUCAAAUAA' (SEQ ID NO:948)	[[], [], ['UUAU', 'AUAA', 'AAAU']]	0.193548	0.96 774 2	3	53
'GAAACCAUCUUUAU AAACAAUCAAAUAAA' (SEQ ID NO:949)	[[], [], ['UUAU', 'AUAA', 'AAAU']]	0.193548	0.96 774 2	3	54
'AAGGCGGCCACAGGGU UGAGGAAAAAGCCCC' (SEQ ID NO:950)	[['CCC'], ['GGG'], ['AAAA']]	0.612903	0.93 548 4	3	118
'AAAGGCGGCCACAGGG UUGAGGAAAAAGCCC' (SEQ ID NO:951)	[['CCC'], ['GGG'], ['AAAA']]	0.580645	0.93 548 4	3	117
'ACAUAUUACAUUAAA AAAUGAGUCACUUC' (SEQ ID NO:952)	[[], [], ['AUAA', 'AUUA', 'AAAA']]	0.225806	0.93 548 4	3	86
'CAUAAAUAACAUUAAAA AAUGAGUCACUCA' (SEQ ID NO:953)	[[], [], ['AUAA', 'AUUA', 'AAAA']]	0.225806	0.93 548 4	3	87
'AUACAUAAAUAACAUUAA AAAAAUGAGUCACU' (SEQ ID NO:954)	[[], [], ['AUAA', 'AUUA', 'AAAA']]	0.193548	0.93 548 4	3	84
'UACAUAAAUAACAUUAAA AAAAAUGAGUCACUU' (SEQ ID NO:955)	[[], [], ['AUAA', 'AUUA', 'AAAA']]	0.193548	0.93 548 4	3	85

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUAAAUCAUUAAAAAA AUGAGUCACUUCAA' (SEQ ID NO:956)	[[], [], ['AUAA', 'AUUA', 'AAAA']]	0.193548	0.93 548 4	3	88
'UAAAUCAUUAAAAAA UGAGUCACUUCAAA' (SEQ ID NO:957)	[[], [], ['UAAA', 'AUUA', 'AAAA']]	0.193548	0.93 548 4	3	89
'AGGCGGCCACAGGGU UGAGGAAAAAGCCCCU' (SEQ ID NO:958)	[['CCC'], ['GGG'], ['AAAA']]	0.612903	0.90 322 6	3	119
'AAAUCAUUAAAAAAU GAGUCACUUCAAAG' (SEQ ID NO:959)	[[], [], ['AAAU', 'AUUA', 'AAAA']]	0.225806	0.90 322 6	3	90
'GGCGGCCACAGGGUU GAGGAAAAAGCCCCUU' (SEQ ID NO:960)	[['CCC'], ['GGG'], ['AAAA']]	0.612903	0.87 096 8	3	120
'GCGGCCACAGGUUG AGGAAAAAGCCCCUUG' (SEQ ID NO:961)	[['CCC'], ['GGG'], ['AAAA']]	0.612903	0.87 096 8	3	121
'UAUAAUGUUGACUUUA UUUCACCGUGGAAAU' (SEQ ID NO:962)	[[], [], ['UAUA', 'UUUA', 'AAAU']]	0.290323	0.87 096 8	3	6
'AUAAUGUUGACUUUAU UUCACCGUGGAAAUU' (SEQ ID NO:963)	[[], [], ['AUAA', 'UUUA', 'AAAU']]	0.290323	0.87 096 8	3	7

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UAAUGUUGACUUUAUU UCACCGUGGAAAUU' (SEQ ID NO:964)	[], [], ['UAAU', 'UUUA', 'AAAU']]	0.290323	0.87 096 8	3	8
'AAUACAUUAAAAAAAUG AGUCACUUCAAAGG' (SEQ ID NO:965)	[], [], ['AAUA', 'AUUA', 'AAAA']]	0.258065	0.87 096 8	3	91
'CGGCCACAGGGUUGA GGAAAAAGCCCCUUGU' (SEQ ID NO:966)	[['CCC'], ['GGG'], ['AAAA']]	0.580645	0.83 871	3	122
'GGCCACAGGGUUGAG GAAAAAGCCCCUUGUG' (SEQ ID NO:967)	[['CCC'], ['GGG'], ['AAAA']]	0.580645	0.83 871	3	123
'GCCACAGGGUUGAGGA AAAAGCCCCUUGUGGG' (SEQ ID NO:968)	[['CCC'], ['GGG'], ['AAAA']]	0.580645	0.83 871	3	124
'CCACAGGGUUGAGGAA AAAGCCCCUUGUGGAA' (SEQ ID NO:969)	[['CCC'], ['GGG'], ['AAAA']]	0.548387	0.83 871	3	125
'CACAGGGUUGAGGAAA AAGCCCCUUGUGGAA' (SEQ ID NO:970)	[['CCC'], ['GGG'], ['AAAA']]	0.516129	0.83 871	3	126
'GGGUUGAGGAAAAAGC CCCUUGUGGAAUCAG' (SEQ ID NO:971)	[['CCC'], ['GGG'], ['AAAA']]	0.516129	0.83 871	3	130

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'ACAGGGUUGAGGAAAA AGCCCCUUGUGGAAU' (SEQ ID NO:972)	[['CCC'], ['GGG'], ['AAAA']]	0.483871	0.83 871	3	127
'AGGGUUGAGGAAAAAG CCCCUUGUGGAAUCA' (SEQ ID NO:973)	[['CCC'], ['GGG'], ['AAAA']]	0.483871	0.83 871	3	129
'CAGGGUUGAGGAAAAAA GCCCUUGUGGAAUC' (SEQ ID NO:974)	[['CCC'], ['GGG'], ['AAAA']]	0.516129	0.80 645 2	3	128
'ACCAUCUUUAUAAAAA CAAUCAAAUAAAUAAC' (SEQ ID NO:975)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU']]	0.193548	1	4	57
'CCAUCUUUAUAAAAAC AAUCAAAUAAAUACA' (SEQ ID NO:976)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU']]	0.193548	1	4	58
'AAACCAUCUUUAUAA AACAAUCAAAUAAAUA' (SEQ ID NO:977)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU']]	0.16129	1	4	55
'AACCAUCUUUAUAAA ACAAUCAAAUAAAUA' (SEQ ID NO:978)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU']]	0.16129	1	4	56
'CAUCUUUAUAAAACA AUCAAAUAAAUAUACAU' (SEQ ID NO:979)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU']]	0.16129	1	4	59

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUCUUUAUAAAACAA UCAAAUAAAUCAU'A (SEQ ID NO:980)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU']]	0.129032	1	4	60
'UAUAAAACAAUCAAAUA AAUACAUAAAUCACA' (SEQ ID NO:981)	[[], [], ['UAUA', 'AAAU', 'AAAU', 'AUAA']]	0.129032	1	4	66
'AUAAAACAAUCAAAUAA AUACAUAAAUCACAU' (SEQ ID NO:982)	[[], [], ['AUAA', 'AAAU', 'AAAU', 'AUAA']]	0.129032	1	4	67
'UAAAACAAUCAAAUAAA UACAUAAAUCACUU' (SEQ ID NO:983)	[[], [], ['UAAA', 'AAAU', 'AAAU', 'AUAA']]	0.129032	1	4	68
'AACAAUCAAAUAAAUA CAUAAAUCACUUAA' (SEQ ID NO:984)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA']]	0.129032	1	4	70
'AACAAUCAAAUAAAUC AUAAAUCACUUAAA' (SEQ ID NO:985)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA']]	0.129032	1	4	71
'ACAAUCAAAUAAAUCAC UAAAAUACACUUAAAA' (SEQ ID NO:986)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA']]	0.129032	1	4	72
'AAUACAUAAAUCACUUA AAAAAAUGAGUCAC' (SEQ ID NO:987)	[[], [], ['AAUA', 'AUAA', 'AUUA', 'AAAA']]	0.193548	0.93 548 4	4	83

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUUUUACAUAAAUCAU AAAAAAAAUGAGUC' (SEQ ID NO:988)	[[], [], ['UAAA', 'AUAA', 'AUUA', 'AAAA']]	0.16129	0.93 548 4	4	81
'AAAUACAUAAAUCAUU AAAAAAAAUGAGUCA' (SEQ ID NO:989)	[[], [], ['AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.16129	0.93 548 4	4	82
'AUAAAUCAUAAAACA UUAAAAAAAAUGAGU' (SEQ ID NO:990)	[[], [], ['AUAA', 'AUAA', 'AUUA', 'AAAA']]	0.129032	0.93 548 4	4	80
'UCUUUAUAAAACAAU CAAAUAAAUCAUAA' (SEQ ID NO:991)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU', 'AUAA']]	0.129032	1	5	61
'CUUUAUAAAACAAUC AAAUAAAUCAUAAA' (SEQ ID NO:992)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AAAU', 'AUAA']]	0.129032	1	5	62
'AUAUAAAACAAUCAAAU AAAUACAUAAAUCAC' (SEQ ID NO:993)	[[], [], ['AUAU', 'AAAA', 'AAAU', 'AAAU', 'AUAA']]	0.129032	1	5	65
'AAAACAAUCAAAUAAA ACAUAAAUCAUUA' (SEQ ID NO:994)	[[], [], ['AAAA', 'AAAU', 'AAAU', 'AUAA', 'AUUA']]	0.129032	1	5	69
'CAAUCAAAUAAAUCAU AAAUACAUUAAAAA' (SEQ ID NO:995)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.129032	1	5	73

FIG. 43 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUUAUAAAACAAUCAA AUAAAUCAUAAA'U (SEQ ID NO:996)	[[], [], ['UUAU', 'AUAA', 'AAAU', 'AUAA']]	0.096774	1	5	63
'UAUUAUAAAACAAUCAAA UAAAUCAUAAAUA' (SEQ ID NO:997)	[[], [], ['UAUA', 'UAAA', 'AAAU', 'AUAA']]	0.096774	1	5	64
'AAUCAAAUAAAUAACAUA AAUACAUUAAAAAAA' (SEQ ID NO:998)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.096774	1	5	74
'AUCAAAUAAAUAACAUA AUACAUUAAAAAAA' (SEQ ID NO:999)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.096774	1	5	75
'UCAAAUAAAUAACAUA UACAUUAAAAAAAUA' (SEQ ID NO:1000)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.096774	1	5	76
'CAAAUAAAUAACAUA ACAUUAAAAAAAUG' (SEQ ID NO:1001)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.129032	0.96 774 2	5	77
'AAAUAAAUAACAUA CAUUAAAAAAAUGA' (SEQ ID NO:1002)	[[], [], ['AAAU', 'AAAU', 'AUAA', 'AUUA', 'AAAA']]	0.096774	0.96 774 2	5	78
'AAUAAAUAACAUA AUUAAAAAAAUGAG' (SEQ ID NO:1003)	[[], [], ['AAUA', 'AAUA', 'AUAA', 'AUUA', 'AAAA']]	0.129032	0.93 548 4	5	79

FIG. 43 (Cont'd)

FIG. 44

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGCCUCAGCGUCUG UCCGUGGUGGCUGAA GUU' (SEQ ID NO:1004)	[], [], []	0.612903226	0.903225806	0	2
'GCCUCAGCGUCUGU CCGUGGUGGCUGAAG UUU' (SEQ ID NO:1005)	[], [], []	0.580645161	0.903225806	0	3
'GAUGAAGACAGGAA GCUGCAGCUCCAGG AGG' (SEQ ID NO:1006)	[], [], []	0.580645161	0.903225806	0	154
'AGAUGAAGACAGGA AGCUGCAGCUCCAG GAG' (SEQ ID NO:1007)	[], [], []	0.548387097	0.903225806	0	153
'CAGGCCUCAGCGUC UGUCCGUGGUGGCUG AAG' (SEQ ID NO:1008)	[], [], []	0.64516129	0.870967742	0	0
'AGGCCUCAGCGUCU GUCCGUGGUGGCUGA AGU' (SEQ ID NO:1009)	[], [], []	0.612903226	0.870967742	0	1

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GGCAAUGCGACCAA GCUGUGUGACACAC CGC' (SEQ ID NO:1010)	[], [], []	0.612903226	0.870967742	0	204
'GCAAUGCGACCAAG CUGUGUGACACACC GCA' (SEQ ID NO:1011)	[], [], []	0.580645161	0.870967742	0	205
'AUGCGACCAAGCUG UGUGACACACCGCAA GG' (SEQ ID NO:1012)	[], [], []	0.580645161	0.870967742	0	208
'CAAUGCGACCAAGC UGUGUGACACACCG CAA' (SEQ ID NO:1013)	[], [], []	0.548387097	0.870967742	0	206
'AAUGCGACCAAGCU GUGUGACACACCGC AAG' (SEQ ID NO:1014)	[], [], []	0.548387097	0.870967742	0	207
'GAUAGAUGAAGACA GGAAGCUGCAGCUC CAG' (SEQ ID NO:1015)	[], [], []	0.516129032	0.870967742	0	150
'AUAGAUGAAGACAG GAAGCUGCAGCUCC AGG' (SEQ ID NO:1016)	[], [], []	0.516129032	0.870967742	0	151

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NEP	P
'UAGAUGAAGACAGG AAGCUGCAGCUCCA GGA' (SEQ ID NO:1017)	[], [], []	0.516129032	0.870967742	0	152
'GAUCGUGAUAGAUG AAGACAGGAAGCUGC AG' (SEQ ID NO:1018)	[], [], []	0.483870968	0.870967742	0	144
'AUCGAUCGUGAUAG AUGAAGACAGGAAGC UG' (SEQ ID NO:1019)	[], [], []	0.451612903	0.870967742	0	141
'AACAUCAUCGAUCGUGA UAGAUGAAGACAGGA AG' (SEQ ID NO:1020)	[], [], []	0.419354839	0.870967742	0	138
'UAACAUCAUCGAUCGUG AUAGAUGAAGACAGG AA' (SEQ ID NO:1021)	[], [], []	0.387096774	0.870967742	0	137
'UCACCACCUCUCAG UGGCAAUGCGACCAA GC' (SEQ ID NO:1022)	[], [], []	0.580645161	0.838709677	0	189
'CACCAACCUCUCAGU GGCAAUGCGACCAA GCU' (SEQ ID NO:1023)	[], [], []	0.580645161	0.838709677	0	190
'ACCACCUCUCAGUG GCAAUGCGACCAAGC UG' (SEQ ID NO:1024)	[], [], []	0.580645161	0.838709677	0	191

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'GUGGCAAUGCAGACC AAGCUGUGUGACACA CC' (SEQ ID NO:1025)	[], [], []	0.580645161	0.838709677	0	202
'UGGCAAUGCAGCCA AGCUGUGUGACACA CCG' (SEQ ID NO:1026)	[], [], []	0.580645161	0.838709677	0	203
'CAGUGGCAAUGCAGA CCAAGCUGUGUGAC ACA' (SEQ ID NO:1027)	[], [], []	0.548387097	0.838709677	0	200
'AGUGGCAAUGCAGAC CAAGCUGUGUGAC CAC' (SEQ ID NO:1028)	[], [], []	0.548387097	0.838709677	0	201
'CGUGAUAGAUGAAG ACAGGAAGCUGGCAG CUC' (SEQ ID NO:1029)	[], [], []	0.516129032	0.838709677	0	147
'GUGAUAGAUGAAGA CAGGAAGCUGGCAGC UCC' (SEQ ID NO:1030)	[], [], []	0.516129032	0.838709677	0	148
'AUUCACCACCUCUC AGUGGCAAUGCAGAC CAA' (SEQ ID NO:1031)	[], [], []	0.516129032	0.838709677	0	187

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'UCGAUCGUGAUAGA UGAAGACAGGAAGCU GC' (SEQ ID NO:1032)	[], [], []	0.483870968	0.838709677	0	142
'CGAUCGUGAUAGAU GAAGACAGGAAGCU GCA' (SEQ ID NO:1033)	[], [], []	0.483870968	0.838709677	0	143
'AUCGUGAUAGAUGA AGACAGGAAGCUGCA GC' (SEQ ID NO:1034)	[], [], []	0.483870968	0.838709677	0	145
'UCGUGAUAGAUGAA GACAGGAAGCUGCA GCU' (SEQ ID NO:1035)	[], [], []	0.483870968	0.838709677	0	146
'UGAUAGAUGAAGAC AGGAAGCUGCAGCU CCA' (SEQ ID NO:1036)	[], [], []	0.483870968	0.838709677	0	149
'ACAUCGAUCGUGAU AGAUGAAGACAGGAA GC' (SEQ ID NO:1037)	[], [], []	0.451612903	0.838709677	0	139
'CAUCGAUCGUGUA GAUGAAGACAGGAAG CU' (SEQ ID NO:1038)	[], [], []	0.451612903	0.838709677	0	140
'CCACCUCUCAGUGG CAAUGCGACCAAGCU GU' (SEQ ID NO:1039)	[], [], []	0.580645161	0.806451613	0	192

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'CACCUCUCAGUGGC AAUGCGACCAAGCUG UG' (SEQ ID NO:1040)	[], [], []	0.580645161	0.806451613	0	193
'CCUCUCAGUGGCAA UGCGACCAAGCUGU GUG' (SEQ ID NO:1041)	[], [], []	0.580645161	0.806451613	0	195
'UUCACCACCUCUCA GUGGCAAUGCGACC AAG' (SEQ ID NO:1042)	[], [], []	0.548387097	0.806451613	0	188
'CUCAGUGGCAAUGC GACCAAGCUGUGUG ACA' (SEQ ID NO:1043)	[], [], []	0.548387097	0.806451613	0	198
'UCAGUGGCAAUGCG ACCAAGCUGUGUGA CAC' (SEQ ID NO:1044)	[], [], []	0.548387097	0.806451613	0	199
'ACCUCUCAGUGGCA AUGCGACCAAGCUG UGU' (SEQ ID NO:1045)	[], [], []	0.548387097	0.774193548	0	194
'CUCUCAGUGGCAAU GCGACCAAGCUGUG UGA' (SEQ ID NO:1046)	[], [], []	0.548387097	0.774193548	0	196

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCUCAGUGGCAAUG CGACCAAGCUGUGU GAC' (SEQ ID NO:1047)	[], [], []	0.548387097	0.774193548	0	197
'UAAGGCCUCACUAA ACCACUCAUCUACAC UU' (SEQ ID NO:1048)	[], [], ['UAAA']]	0.419354839	0.935483871	1	107
'AAGGCCUCACUAAA CCACUCAUCUACACU UA' (SEQ ID NO:1049)	[], [], ['UAAA']]	0.419354839	0.935483871	1	108
'AAACCACUCAUCUAC ACUUAAACAUCGAUCG U' (SEQ ID NO:1050)	[], [], ['UUAA']]	0.387096774	0.935483871	1	119
'GCGACCAAGCUGUG UGACACACCGCAAGG GC' (SEQ ID NO:1051)	[], ['GGG'], []	0.64516129	0.903225806	1	210
'AUGAAGACAGGAAG CUGCAGCUCCAGGA GGG' (SEQ ID NO:1052)	[], ['GGG'], []	0.580645161	0.903225806	1	155
'GAAGACAGGAAGCU GCAGCUCCAGGAGG GUA' (SEQ ID NO:1053)	[], ['GGG'], []	0.580645161	0.903225806	1	157

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NEP	P
'GCGUCUGUCCGUGG UGCUGAAGUUUAUU CGG' (SEQ ID NO:1054)	[], [], ['UUUA'])	0.548387097	0.903225806	1	9
'GUAAGGCCUCACUA AACACACUCAUCUACA CU' (SEQ ID NO:1055)	[], [], ['UAAA'])	0.451612903	0.903225806	1	106
'AACCAACUCAUCUACA CUUAACAUCAUCGU G' (SEQ ID NO:1056)	[], [], ['UUAA'])	0.419354839	0.903225806	1	120
'ACCACACUCAUCUACAC UUAACAUCAUCGAUCGUG A' (SEQ ID NO:1057)	[], [], ['UUAA'])	0.419354839	0.903225806	1	121
'CCACUCAUCUACAC UUAACAUCAUCGAUCGUG AU' (SEQ ID NO:1058)	[], [], ['UUAA'])	0.419354839	0.903225806	1	122
'CACUCAUCUACACU UAACAUCAUCGAUCGUGA UA' (SEQ ID NO:1059)	[], [], ['UUAA'])	0.387096774	0.903225806	1	123
'UGCGACCAAGCUGU GUGACACACCGCAAG GG' (SEQ ID NO:1060)	[], ['GGG'], [])	0.612903226	0.870967742	1	209
'CGACCAAGCUGUGU GACACACCGCAAGG GCU' (SEQ ID NO:1061)	[], ['GGG'], [])	0.612903226	0.870967742	1	211

SEQUENCE	BS	GCNESS	SLN	NBP	P
'UGAAGACAGGAAGC UGCAGCUCCAGGAG GGU' (SEQ ID NO:1062)	[], [GGG], []	0.580645161	0.870967742	1	156
'CCUCAGCGUCUGUC CGUGGUGCUGAAGU UUA' (SEQ ID NO:1063)	[], [], [UUUA']]	0.548387097	0.870967742	1	4
'AAGACAGGAAGCUG CAGCUCCAGGAGGG UAU' (SEQ ID NO:1064)	[], [GGG], []	0.548387097	0.870967742	1	158
'CUCAGCGUCUGUCC GUGGUGCUGAAGUU UAU' (SEQ ID NO:1065)	[], [], [UUUA']]	0.516129032	0.870967742	1	5
'CAGCGUCUGUCCGU GGUGCUGAAGUUUA UUC' (SEQ ID NO:1066)	[], [], [UUUA']]	0.516129032	0.870967742	1	7
'AGCGUCUGUCCGUG GUGCUGAAGUUUAU UCG' (SEQ ID NO:1067)	[], [], [UUUA']]	0.516129032	0.870967742	1	8

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CGUCUGUCCGUGGU GCUGAAGUUUAUUC GGA' (SEQ ID NO:1068)	[], [], ['UUUA'])	0.516129032	0.870967742	1	10
'UCAGCGUCUGUCCG UGGUGCUGAAGUUU AUU' (SEQ ID NO:1069)	[], [], ['UUUA'])	0.483870968	0.870967742	1	6
'GUCUGUCCGUGGUG CUGAAGUUUAUUCG GAU' (SEQ ID NO:1070)	[], [], ['UUUA'])	0.483870968	0.870967742	1	11
'GGUAAGGCCUCACU AAACCACUCAUCAUC AC' (SEQ ID NO:1071)	[], [], ['UAAA'])	0.483870968	0.870967742	1	105
'UCUGUCCGUGGUGC UGAAGUUUAUUCGG AUU' (SEQ ID NO:1072)	[], [], ['UUUA'])	0.451612903	0.870967742	1	12
'AGGUAGGCCUCAC UAAACCACUCAUCAUC CA' (SEQ ID NO:1073)	[], [], ['UAAA'])	0.451612903	0.870967742	1	104
'ACUCAUCUACACUUA ACAUCGAUCGUGAUA G' (SEQ ID NO:1074)	[], [], ['UUAA'])	0.387096774	0.870967742	1	124

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CUCAUCUACACUUAA CAUCGAUCGUGUA GA' (SEQ ID NO:1075)	[], [], ['UUAA'])]	0.387096774	0.870967742	1	125
'UUAACAUCAUCGU GAUAGAUGAAGACAG GA' (SEQ ID NO:1076)	[], [], ['UUAA'])]	0.387096774	0.870967742	1	136
'UCAUCUACACUUAC AUCGAUCGUGAUAGA U' (SEQ ID NO:1077)	[], [], ['UUAA'])]	0.35483871	0.870967742	1	126
'CCAAGCUGUGUGAC ACACCGCAAGGGCU UGG' (SEQ ID NO:1078)	[], ['GGG'], [])	0.612903226	0.838709677	1	214
'GACCAAGCUGUGUG ACACACCGCAAGGGC UU' (SEQ ID NO:1079)	[], ['GGG'], [])	0.580645161	0.838709677	1	212
'ACCAAGCUGUGUGA CACACCGCAAGGGC UUG' (SEQ ID NO:1080)	[], ['GGG'], [])	0.580645161	0.838709677	1	213
'UAUGCAGAGUGGGA GAGGUAGGCCUCA CUA' (SEQ ID NO:1081)	[], ['GGG'], [])	0.516129032	0.838709677	1	89

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUGCAGAGUGGGAG AGGUAAAGGCCUCAC UAA' (SEQ ID NO:1082)	[], ['GGG'], []	0.516129032	0.838709677	1	90
'GGAGAGGUAGGCC UCACUAAACCACCUA UC' (SEQ ID NO:1083)	[], [], ['UAAA']]	0.516129032	0.838709677	1	100
'UAUUCACCACCUCU CAGUGGCAAUGCGA CCA' (SEQ ID NO:1084)	[], [], ['UAUU']]	0.516129032	0.838709677	1	186
'GAGGUAGGCCUCA CUAAACCACUCAUCU AC' (SEQ ID NO:1085)	[], [], ['UAAA']]	0.483870968	0.838709677	1	103
'UUUCCAACUGCUUU CUGAAAGGGGUGAG GAU' (SEQ ID NO:1086)	[], ['GGG'], []	0.451612903	0.838709677	1	49
'UGCUUUCUGAAAGG GGUGAGGAUCUACC UUA' (SEQ ID NO:1087)	[], ['GGG'], []	0.451612903	0.838709677	1	57
'AGAGGUAGGCCUC ACUAAACCACUCAUC UA' (SEQ ID NO:1088)	[], [], ['UAAA']]	0.451612903	0.838709677	1	102

FIG. 44 (Cont'd)

FIG. 44 (Cont'd)

SEQUENCE	ES	GCNESS	3LN	NBP	P
'CUUAACAUCAUCG UGAUAGAUGAAGACA GG' (SEQ ID NO:1089)	[], [], ['UUAA'])	0.419354839	0.838709677	1	135
'CAUCUACACUUACA UCGAUCGUGAUAGA UG' (SEQ ID NO:1090)	[], [], ['UUAA'])	0.387096774	0.838709677	1	127
'ACUUAACAUCAUC GUGAUAGAUGAAGAC AG' (SEQ ID NO:1091)	[], [], ['UUAA'])	0.387096774	0.838709677	1	134
'AUCUACACUUACAU CGAUCGUGAUAGAU GA' (SEQ ID NO:1092)	[], [], ['UUAA'])	0.35483871	0.838709677	1	128
'UCUACACUUACACA GAUCGUGAUAGAUG AA' (SEQ ID NO:1093)	[], [], ['UUAA'])	0.35483871	0.838709677	1	129
'UACACUUACAUCA UCGUGAUAGAUGAA GA' (SEQ ID NO:1094)	[], [], ['UUAA'])	0.35483871	0.838709677	1	131
'GUAUUCACCACCUC UCAGUGGCCAUGC ACC' (SEQ ID NO:1095)	[], [], ['UAUU'])	0.548387097	0.806451613	1	185
'UUCCAACUGCUUUC UGAAAGGGUGAGG AUC' (SEQ ID NO:1096)	[], ['GGG'], [])	0.483870968	0.806451613	1	50

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UCCAACUGCUUUCU GAAAGGGGUGAGGA UCU' (SEQ ID NO:1097)	[], ['GGG'], []	0.483870968	0.806451613	1	51
'CCAACUGCUUUCUG AAAGGGGUGAGGAU CUA' (SEQ ID NO:1098)	[], ['GGG'], []	0.483870968	0.806451613	1	52
'CAACUGCUUUCUGA AAGGGGUGAGGAUC UAC' (SEQ ID NO:1099)	[], ['GGG'], []	0.483870968	0.806451613	1	53
'AACUGCUUUCUGAA AGGGGUGAGGAUCU ACC' (SEQ ID NO:1100)	[], ['GGG'], []	0.483870968	0.806451613	1	54
'ACUGCUUUCUGAAA GGGGUGAGGAUCUA CCU' (SEQ ID NO:1101)	[], ['GGG'], []	0.483870968	0.806451613	1	55
'CUGCUUUCUGAAAG GGGUGAGGAUCUAC CUU' (SEQ ID NO:1102)	[], ['GGG'], []	0.483870968	0.806451613	1	56
'GAGAGGUAGGCCU CACUAAACCACUCAU CU' (SEQ ID NO:1103)	[], [], ['UAAA']]	0.483870968	0.806451613	1	101

FIG. 44 (Cont'd)

SEQUENCE	ES	GCNESS	3LN	NBP	P
'CUACACUUAAACAUC GAUCGUGAUAGAUG AAG' (SEQ ID NO:1104)	[], [], ['UUAA']]	0.387096774	0.806451613	1	130
'ACACUUAAACAUCGAU CGUGAUAGAUGAAGA C' (SEQ ID NO:1105)	[], [], ['UUAA']]	0.387096774	0.806451613	1	132
'CACUUAAACAUCGAU CGUGAUAGAUGAAGA CA' (SEQ ID NO:1106)	[], [], ['UUAA']]	0.387096774	0.806451613	1	133
'GGUAUUCACCACCU CUCAGUGGCAAUGC GAC' (SEQ ID NO:1107)	[], [], ['UAUU']]	0.548387097	0.774193548	1	184
'CCUCACUAAACCACU CAUCUACACUUACA U' (SEQ ID NO:1108)	[], [], ['UAAA', 'UUAA']]	0.387096774	1	2	112
'CUCACUAAACCACUC AUCUACACUUACAU C' (SEQ ID NO:1109)	[], [], ['UAAA', 'UUAA']]	0.387096774	1	2	113
'GCCUCACUAAACCA CUCAUCUACACUUAA CA' (SEQ ID NO:1110)	[], [], ['UAAA', 'UUAA']]	0.419354839	0.967741935	2	111
'UCACUAAACCACUCA UCUACACUUACAU G' (SEQ ID NO:1111)	[], [], ['UAAA', 'UUAA']]	0.387096774	0.967741935	2	114

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CACUAAACCACUCAU CUACACUUACAUCAUCG A' (SEQ ID NO:1112)	[], [], ['UAAA', 'UUAA']]	0.387096774	0.967741935	2	115
'CUAAACCACUCAUCU ACACUUACAUCAUCGAU C' (SEQ ID NO:1113)	[], [], ['UAAA', 'UUAA']]	0.387096774	0.967741935	2	117
'ACUAAACCACUCAUC UACACUUACAUCAUCGA U' (SEQ ID NO:1114)	[], [], ['UAAA', 'UUAA']]	0.35483871	0.967741935	2	116
'GGCCUCACUAAACC ACUCAUCUACACUUA AC' (SEQ ID NO:1115)	[], [], ['UAAA', 'UUAA']]	0.451612903	0.935483871	2	110
'AGGCCUCACUAAAC CACUCAUCUACACUU AA' (SEQ ID NO:1116)	[], [], ['UAAA', 'UUAA']]	0.419354839	0.935483871	2	109
'UAAACCACUCAUCUA CACUUACAUCAUCGAUC G' (SEQ ID NO:1117)	[], [], ['UAAA', 'UUAA']]	0.387096774	0.935483871	2	118
'UACCUUAAUAUGCA GAGUGGGAGAGGUAA AGG' (SEQ ID NO:1118)	[], ['GGG'], ['UUAA']]	0.451612903	0.903225806	2	81
'GCAGAGUGGGAGAG GUAAGGCCUCACUAA AC' (SEQ ID NO:1119)	[], ['GGG'], ['UAAA']]	0.548387097	0.870967742	2	92

FIG. 44 (Cont'd)

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	SLN	NBP	P
'CAGAGUGGGAGAGG UAAGGCCUCACUAAA CC' (SEQ ID NO:1120)	[], ['GGG'], ['UAAA']]	0.548387097	0.870967742	2	93
'GAGUGGGAGAGGU AGGCCUCACUAAACC AC' (SEQ ID NO:1121)	[], ['GGG'], ['UAAA']]	0.548387097	0.870967742	2	95
'GGCUUGGGAUCUUU UGCGAUCUGCUCGA GCA' (SEQ ID NO:1122)	[], ['GGG'], ['UUUU']]	0.548387097	0.870967742	2	238
'GCUUGGGAUCUUUU GCGAUCUGCUCGAG CAG' (SEQ ID NO:1123)	[], ['GGG'], ['UUUU']]	0.548387097	0.870967742	2	239
'AGAGUGGGAGAGGU AAGGCCUCACUAAAC CA' (SEQ ID NO:1124)	[], ['GGG'], ['UAAA']]	0.516129032	0.870967742	2	94
'CUUUUGCGAUCUGC UCGAGCAGAUUUGG CUG' (SEQ ID NO:1125)	[], [], ['UUUU', 'AUUU']]	0.516129032	0.870967742	2	248
'GGGGUGAGGAUCUA CCUUAUAUGCAGAG UG' (SEQ ID NO:1126)	[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	69
'GGGUGAGGAUCUAC CUUAAUAUGCAGAGU GG' (SEQ ID NO:1127)	[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	70

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGUGAGGAUCUACC UUAAUAUGCAGAGUG GG' (SEQ ID NO:1128)	[[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	71
'GGAUCUACCUUAU AUGCAGAGUGGGAG AGG' (SEQ ID NO:1129)	[[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	76
'ACCUUAAUAUGCAG AGUGGGAGAGGUAA GGC' (SEQ ID NO:1130)	[[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	82
'CUUAAUAUGCAGAG UGGGAGAGGUAGG CCU' (SEQ ID NO:1131)	[[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	84
'UUAAUAUGCAGAGU GGGAGAGGUAGGC CUC' (SEQ ID NO:1132)	[[], ['GGG'], ['UUAA']]	0.483870968	0.870967742	2	85
'UAAUAUGCAGAGUG GGAGAGGUAGGCC UCA' (SEQ ID NO:1133)	[[], ['GGG'], ['UAAU']]	0.483870968	0.870967742	2	86
'UCUUUUGCGAUCUG CUCGAGCAGAUUUG GCU' (SEQ ID NO:1134)	[[], [], ['UUUU', 'AUUU']]	0.483870968	0.870967742	2	247

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CUGUCCGUGGGUGCU GAAGUUUAUUCGGA UUU' (SEQ ID NO:1135)	[], [], ['UUUA', 'AUUU']]	0.451612903	0.870967742	2	13
'GAAAGGGGUGAGGA UCUACCUUAAUAUGC AG' (SEQ ID NO:1136)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	65
'AAGGGGUGAGGAUC UACCUUAAUAUGCAG AG' (SEQ ID NO:1137)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	67
'AGGGGUGAGGAUCU ACCUUAAUAUGCAGA GU' (SEQ ID NO:1138)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	68
'GUGAGGAUCUACCU UAAAUGCAGAGUG GGA' (SEQ ID NO:1139)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	72
'UGAGGAUCUACCUU AAUAUGCAGAGUGG GAG' (SEQ ID NO:1140)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	73
'GAGGAUCUACCUA AUAUGCAGAGUGGG AGA' (SEQ ID NO:1141)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	74

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGGAUCUACCUUAA UAUGCAGAGUGGGGA GAG' (SEQ ID NO:1142)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	75
'GAUCUACCUUAAA UGCAGAGUGGGAGA GGU' (SEQ ID NO:1143)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	77
'CUACCUUAAAUGC AGAGUGGGAGAGGU AAG' (SEQ ID NO:1144)	[], ['GGG'], ['UUAA']]	0.451612903	0.870967742	2	80
'UGUCCGUGGGUGCUG AAGUUUAAUCGGAUU UA' (SEQ ID NO:1145)	[], [], ['UUUA', 'AUUU']]	0.419354839	0.870967742	2	14
'GUCCGUGGGUGCUGA AGUUUAAUCGGAUU UAU' (SEQ ID NO:1146)	[], [], ['UUUA', 'AUUU']]	0.419354839	0.870967742	2	15
'UCUGAAAGGGGUGA GGAUCUACCUUAAA UG' (SEQ ID NO:1147)	[], ['GGG'], ['UUAA']]	0.419354839	0.870967742	2	62
'UGAAAGGGGUGAGG AUCUACCUUAAAUG CA' (SEQ ID NO:1148)	[], ['GGG'], ['UUAA']]	0.419354839	0.870967742	2	64

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AAAGGGGUGAGGAU CUACCUUAUAUAGCA GA' (SEQ ID NO:1149)	[], ['GGG'], ['UUAA']]	0.419354839	0.870967742	2	66
'AUCUACCUUAUAU GCAGAGUGGGAGAG GUA' (SEQ ID NO:1150)	[], ['GGG'], ['UUAA']]	0.419354839	0.870967742	2	78
'UCUACCUUAUAUG CAGAGUGGGAGAGG UAA' (SEQ ID NO:1151)	[], ['GGG'], ['UUAA']]	0.419354839	0.870967742	2	79
'UCCGUGGGUGCUGAA GUUUAUUCGGAUUU AUU' (SEQ ID NO:1152)	[], [], ['UUUA', 'AUUU']]	0.387096774	0.870967742	2	16
'UUUCUGAAAGGGGU GAGGAUCUACCUUAA UA' (SEQ ID NO:1153)	[], ['GGG'], ['UUAA']]	0.387096774	0.870967742	2	60
'UUCUGAAAGGGUG AGGAUCUACCUUAAU AU' (SEQ ID NO:1154)	[], ['GGG'], ['UUAA']]	0.387096774	0.870967742	2	61
'CAAGCUGUGUGACA CACCGCAAGGGCUU GGG' (SEQ ID NO:1155)	[], ['GGG', 'GGG'], []	0.612903226	0.838709677	2	215

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GACAGGAAGCUGCA GCUCCAGGAGGGUA UUC' (SEQ ID NO:1156)	[], ['GGG'], ['UAUU'])	0.580645161	0.838709677	2	160
'CAGGAAGCUGCAGC UCCAGGAGGGUAUU CAC' (SEQ ID NO:1157)	[], ['GGG'], ['UAUU'])	0.580645161	0.838709677	2	162
'AGGAAGCUGCAGCU CCAGGAGGGUAUUC ACC' (SEQ ID NO:1158)	[], ['GGG'], ['UAUU'])	0.580645161	0.838709677	2	163
'GGAAGCUGCAGCUC CAGGAGGGUAUUCA CCA' (SEQ ID NO:1159)	[], ['GGG'], ['UAUU'])	0.580645161	0.838709677	2	164
'GAAGCUGCAGCUCC AGGAGGGUAUUCAC CAC' (SEQ ID NO:1160)	[], ['GGG'], ['UAUU'])	0.580645161	0.838709677	2	165
'AAGCUGCAGCUCCA GGAGGGUAUUCACC ACC' (SEQ ID NO:1161)	[], ['GGG'], ['UAUU'])	0.580645161	0.838709677	2	166

FIG. 44 (Cont'd)

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AAGCUGUGUGACAC ACCGCAAGGGCUUG GGA' (SEQ ID NO:1162)	[], ['GGG', 'GGG'], []	0.580645161	0.838709677	2	216
'GUGGGAGAGGUAG GCCUCACUAACCAC UC' (SEQ ID NO:1163)	[], ['GGG'], ['UAAA']]	0.548387097	0.838709677	2	97
'AGACAGGAAGCUGC AGCUCCAGGAGGGU AUU' (SEQ ID NO:1164)	[], ['GGG'], ['UAUU']]	0.548387097	0.838709677	2	159
'ACAGGAAGCUGCAG CUCCAGGAGGGUAU UCA' (SEQ ID NO:1165)	[], ['GGG'], ['UAUU']]	0.548387097	0.838709677	2	161
'CCUUAAUAUGCAGA GUGGGAGAGGUAG GCC' (SEQ ID NO:1166)	[], ['GGG'], ['UUAA']]	0.516129032	0.838709677	2	83
'AAUAUGCAGAGUGG GAGAGGUAGGCCU CAC' (SEQ ID NO:1167)	[], ['GGG'], ['AAUA']]	0.516129032	0.838709677	2	87
'AUAUGCAGAGUGGG AGAGGUAGGCCUC ACU' (SEQ ID NO:1168)	[], ['GGG'], ['AUAU']]	0.516129032	0.838709677	2	88

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGCAGAGUGGGAGA GGUAAGGCCUCACU AAA' (SEQ ID NO:1169)	[], ['GGG'], ['UAAA']]	0.516129032	0.838709677	2	91
'AGUGGGAGAGGUAA GGCCUCACUAAACCA CU' (SEQ ID NO:1170)	[], ['GGG'], ['UAAA']]	0.516129032	0.838709677	2	96
'UGGGAGAGGUAGG CCUCACUAAACCACU CA' (SEQ ID NO:1171)	[], ['GGG'], ['UAAA']]	0.516129032	0.838709677	2	98
'GGGAGAGGUAGGC CUCACUAAACCACUC AU' (SEQ ID NO:1172)	[], ['GGG'], ['UAAA']]	0.516129032	0.838709677	2	99
'CUUGGGAUCUUUG CGAUCUGCUCGAGC AGA' (SEQ ID NO:1173)	[], ['GGG'], ['UUUU']]	0.516129032	0.838709677	2	240
'UUGGGAUCUUUGC GAUCUGCUCCGAGCA GAU' (SEQ ID NO:1174)	[], ['GGG'], ['UUUU']]	0.483870968	0.838709677	2	241
'UGGGAUCUUUGCG AUCUGCUCGAGCAG AUU' (SEQ ID NO:1175)	[], ['GGG'], ['UUUU']]	0.483870968	0.838709677	2	242

FIG. 44 (Cont'd)

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GGAUCUUUUGCGAU CUGCUCGAGCAGAU UUG' (SEQ ID NO:1176)	[], [], ['UUUU', 'AUUU']]	0.483870968	0.838709677	2	244
'GAUCUUUUGCGAUC UGCUCGAGCAGAUU UGG' (SEQ ID NO:1177)	[], [], ['UUUU', 'AUUU']]	0.483870968	0.838709677	2	245
'AUCUUUUGCGAUCU GCUCGAGCAGAUUU GGC' (SEQ ID NO:1178)	[], [], ['UUUU', 'AUUU']]	0.483870968	0.838709677	2	246
'UUUUUCCAACUGCU UUCUGAAAGGGGUG AGG' (SEQ ID NO:1179)	[], ['GGG'], ['UUUU']]	0.451612903	0.838709677	2	47
'UUUUUCCAACUGCUU UCUGAAAGGGGUGA GGA' (SEQ ID NO:1180)	[], ['GGG'], ['UUUU']]	0.451612903	0.838709677	2	48
'GCUUUCUGAAAGGG GUGAGGAUCUACCU UAA' (SEQ ID NO:1181)	[], ['GGG'], ['UUAA']]	0.451612903	0.838709677	2	58
'CUGAAAGGGGUGAG GAUCUACCUUAUAU GC' (SEQ ID NO:1182)	[], ['GGG'], ['UUAA']]	0.451612903	0.838709677	2	63

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UUUUUUUCCAACUGC UUUCUGAAAGGGGU GAG' (SEQ ID NO:1183)	[], ['GGG'], ['UUUU'])	0.419354839	0.838709677	2	46
'CUUUCUGAAAGGGG UGAGGAUCUACCUUA AU' (SEQ ID NO:1184)	[], ['GGG'], ['UUAA'])	0.419354839	0.838709677	2	59
'UUUUUUUCCAACUG CUUUCUGAAAGGGG UGA' (SEQ ID NO:1185)	[], ['GGG'], ['UUUU'])	0.387096774	0.838709677	2	45
'GCUGCAGCUCCAGG AGGGUAUUCACCACC UC' (SEQ ID NO:1186)	[], ['GGG'], ['UAUU'])	0.612903226	0.806451613	2	168
'GCUGUGUGACACAC CGCAAGGGCUUGGG AUC' (SEQ ID NO:1187)	[], ['GGG', 'GGG'], [])	0.612903226	0.806451613	2	218
'AGCUGCAGCUCCAG GAGGGUAUUCACCA CCU' (SEQ ID NO:1188)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	167
'CUGCAGCUCCAGGA GGGUUAUUCACCACC UCU' (SEQ ID NO:1189)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	169

FIG. 44 (Cont'd)

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGCAGCUCCAGGAG GGUAUUCACCACCUUC UC' (SEQ ID NO:1190)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	170
'GCAGCUCCAGGAGG GUAUUCACCACCUUCU CA' (SEQ ID NO:1191)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	171
'CAGCUCCAGGAGGG UAUUCACCACCUUCUC AG' (SEQ ID NO:1192)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	172
'GCUCCAGGAGGGUA UUCACCACCUUCUCAG UG' (SEQ ID NO:1193)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	174
'CUCCAGGAGGGUAU UCACCACCUUCUCAGU GG' (SEQ ID NO:1194)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	175
'UCCAGGAGGGUAUU CACCAACCUCUCAGUG GC' (SEQ ID NO:1195)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	176
'CCAGGAGGGUAUUC ACCACCUUCUCAGUG GCA' (SEQ ID NO:1196)	[], ['GGG'], ['UAUU'])	0.580645161	0.806451613	2	177
'AGCUGUGUGACACA CCGCAAGGGCUUGG GAU' (SEQ ID NO:1197)	[], ['GGG', 'GGG'], [])	0.580645161	0.806451613	2	217

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CUGUGUGACACACC GCAAGGGCUUGGGA UCU' (SEQ ID NO:1198)	[], ['GGG', 'GGG'], []	0.580645161	0.806451613	2	219
'CAGGAGGGUAUUCA CCACCUCUCAGUGG CAA' (SEQ ID NO:1199)	[], ['GGG'], ['UAUU']]	0.548387097	0.806451613	2	178
'UGUGUGACACACCG CAAGGGCUUGGGAU CUU' (SEQ ID NO:1200)	[], ['GGG', 'GGG'], []	0.548387097	0.806451613	2	220
'GUGUGACACACCGC AAGGGCUUGGGAUC UUU' (SEQ ID NO:1201)	[], ['GGG', 'GGG'], []	0.548387097	0.806451613	2	221
'AGCUCCAGGAGGGU AUUCACCACCUCUCA GU' (SEQ ID NO:1202)	[], ['GGG'], ['UAUU']]	0.548387097	0.774193548	2	173
'GGAGGGUAUUCACC ACCUCUCAGUGGCAA UG' (SEQ ID NO:1203)	[], ['GGG'], ['UAUU']]	0.548387097	0.774193548	2	180
'GAGGGUAUUCACCA CCUCUCAGUGGCAA UGC' (SEQ ID NO:1204)	[], ['GGG'], ['UAUU']]	0.548387097	0.774193548	2	181

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGGGUAUUCACCAC CUCUCAGUGGCAAU GCG' (SEQ ID NO:1205)	[], ['GGG'], ['UAUU'])	0.548387097	0.774193548	2	182
'GGGUAUUCACCACC UCUCAGUGGCAAUG CGA' (SEQ ID NO:1206)	[], ['GGG'], ['UAUU'])	0.548387097	0.774193548	2	183
'AGGAGGGUAUUCAC CACCUUCUCAGUGGC AAU' (SEQ ID NO:1207)	[], ['GGG'], ['UAUU'])	0.516129032	0.774193548	2	179
'GUGGUGCUGAAGUU UAUUCGGAUUUUUUU UU' (SEQ ID NO:1208)	[], [], ['UUUA', 'AUUU', 'AUUU'])	0.322580645	0.935483871	3	19
'UGGUGCUGAAGUUU AUUCGGAUUUUUUUU UU' (SEQ ID NO:1209)	[], [], ['UUUA', 'AUUU', 'AUUU'])	0.290322581	0.935483871	3	20
'GGGCUUGGGGAUCUU UUGCGAUCUGCUCG AGC' (SEQ ID NO:1210)	[] ['GGG', 'GGG'], ['UUUU'])	0.580645161	0.903225806	3	237

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'CGUGGGUGCUGAAGU UUAUUCGGAUUUUU UU' (SEQ ID NO:1211)	[[], [], ['UUUA', 'AUUU', 'AUUU']]	0.35483871	0.903225806	3	18
'AUUCGGAUUUUU UUUUCCAACUGCUUU CU' (SEQ ID NO:1212)	[[], [], ['AUUU', 'AUUU', 'UUUU']]	0.290322581	0.903225806	3	34
'CCGCAAGGGCUUGG GAUCUUUUGCGAUC UGC' (SEQ ID NO:1213)	[[], ['GGG', 'GGG'], ['UUUU']]	0.580645161	0.870967742	3	231
'CGCAAGGGCUUGGG AUCUUUUGCGAUCU GCU' (SEQ ID NO:1214)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.870967742	3	232
'GCAAGGGCUUGGG UCUUUUGCGAUCUG CUC' (SEQ ID NO:1215)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.870967742	3	233
'CAAGGGCUUGGGAU CUUUUGCGAUCUGC UCG' (SEQ ID NO:1216)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.870967742	3	234

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AGGGCUUGGGAUCU UUUGCGAUCUGCUC GAG' (SEQ ID NO:1217)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.870967742	3	236
'CCGUGGGUGCGUGAAG UUUAUUCGGAUUUUAU UU' (SEQ ID NO:1218)	[[],[], ['UUUA', 'AUUU', 'AUUU']]	0.387096774	0.870967742	3	17
'UUCGGAUUUAUUUU UUUCCAACUGCUUUC UG' (SEQ ID NO:1219)	[[],[], ['AUUU', 'AUUU', 'UUUU']]	0.322580645	0.870967742	3	35
'UCGGAUUUAUUUUU UUCCAACUGCUUUCU GA' (SEQ ID NO:1220)	[[],[], ['AUUU', 'AUUU', 'UUUU']]	0.322580645	0.870967742	3	36
'CGGAUUUAUUUUUU UCCAACUGCUUUCU GAA' (SEQ ID NO:1221)	[[],[], ['AUUU', 'AUUU', 'UUUU']]	0.322580645	0.870967742	3	37
'GGAUUUAUUUUUUU CCAACUGCUUUCUGA AA' (SEQ ID NO:1222)	[[],[], ['AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	3	38

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GAUUUUAUUUUUUUUC CAACUGCUUUCUGAA AG' (SEQ ID NO:1223)	[[], [], ['AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	3	39
'AUUUAUUUUUUUUCC AACUGCUUUCUGAAA GG' (SEQ ID NO:1224)	[[], [], ['AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	3	40
'CACCGCAAGGGCUU GGGAUCUUUUGCGA UCU' (SEQ ID NO:1225)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.838709677	3	229
'ACCGCAAGGGCUUG GGAUCUUUUGCGAU CUG' (SEQ ID NO:1226)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.838709677	3	230
'AAGGGCUUGGGAUC UUUUGCGAUCUGCU CGA' (SEQ ID NO:1227)	[[], ['GGG', 'GGG'], ['UUUU']]	0.516129032	0.838709677	3	235
'GGGAUCUUUUGCGA UCUGCUCGAGCAGA UUU' (SEQ ID NO:1228)	[[], ['GGG'], ['UUUU', 'AUUU']]	0.483870968	0.838709677	3	243

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'AUUUUUUUUCCAACU GCUUUCUGAAAGGG GUG' (SEQ ID NO:1229)	[[], ['GGG'], ['AUUU'], ['UUUU']]	0.387096774	0.838709677	3	44
'UUAUUUUUUUUCCAA CUGCUUUCUGAAAG GGG' (SEQ ID NO:1230)	[[], ['GGG'], ['UUAU'], ['UUUU']]	0.35483871	0.838709677	3	42
'UAUUUUUUUCCAAC UGCUUUCUGAAAGG GGU' (SEQ ID NO:1231)	[[], ['GGG'], ['UAUU'], ['UUUU']]	0.35483871	0.838709677	3	43
'UUUAUUUUUUUCCA ACUGCUUUCUGAAAG GG' (SEQ ID NO:1232)	[[], ['GGG'], ['UUUA'], ['UUUU']]	0.322580645	0.838709677	3	41
'GACACACCGCAAGG GCUUGGGGAUCUUU GCG' (SEQ ID NO:1233)	[[], ['GGG', 'GGG'], ['UUUU']]	0.580645161	0.806451613	3	225
'GUGACACACCGCAA GGGCUUGGGGAUCUU UUG' (SEQ ID NO:1234)	[[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.806451613	3	223

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'UGACACACACCGCAAG GGCUUGGGAUCUUU UGC' (SEQ ID NO:1235)	[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.806451613	3	224
'CACACCGCAAGGGC UUGGGAUCUUUUGC GAU' (SEQ ID NO:1236)	[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.806451613	3	227
'ACACCGCAAGGGCU UGGGGAUCUUUUGCG AUC' (SEQ ID NO:1237)	[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.806451613	3	228
'UGUGACACACCGCA AGGGCUUGGGAUCU UUU' (SEQ ID NO:1238)	[], ['GGG', 'GGG'], ['UUUU']]	0.516129032	0.806451613	3	222
'ACACACCGCAAGGG CUUGGGAUCUUUUG CGA' (SEQ ID NO:1239)	[], ['GGG', 'GGG'], ['UUUU']]	0.548387097	0.774193548	3	226
'GGUGCUGAAGUUUA UUCGGAUUUAUUUU UUU' (SEQ ID NO:1240)	[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.935483871	4	21

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GUGCUGAAGUUUAU UCGGAUUUAUUUUU UUC' (SEQ ID NO:1241)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.903225806	4	22
'UAUUCGGAUUUAUU UUUUUCCAACUGCUU UC' (SEQ ID NO:1242)	[[], [], ['UAUU', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.903225806	4	33
'UUUAUUCGGAUUUUA UUUUUUUCCAACUGC UU' (SEQ ID NO:1243)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258064516	0.903225806	4	31
'UUUAUUCGGAUUUAU UUUUUUUCCAACUGCU UU' (SEQ ID NO:1244)	[[], [], ['UUAU', 'AUUU', 'AUUU', 'UUUU']]	0.258064516	0.903225806	4	32
'UGCUGAAGUUUAU CGGAUUUAUUUUUU UCC' (SEQ ID NO:1245)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	4	23

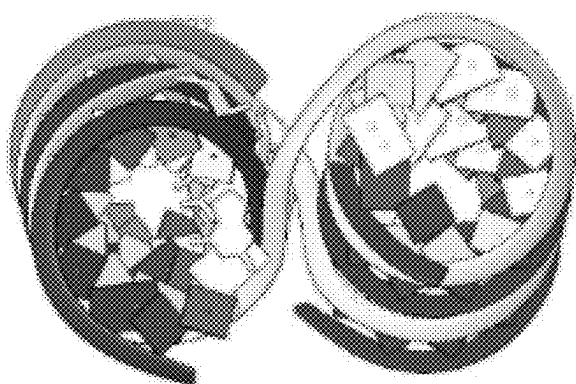
FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GCUGAAGUUUAUUC GGAUUUAUUUUUUUU CCA' (SEQ ID NO:1246)	[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	4	24
'AGUUUAUUCGGAUU UAUUUUUUUCCAACU GC' (SEQ ID NO:1247)	[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	4	29
'GUUUAUUCGGAUUU AUUUUUUUCCAACUG CU' (SEQ ID NO:1248)	[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.290322581	0.870967742	4	30
'CUGAAGUUUAUUCG GAUUUAUUUUUUUUCC AA' (SEQ ID NO:1249)	[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258064516	0.870967742	4	25
'UGAAGUUUAUUCGG AUUUAUUUUUUUCCA AC' (SEQ ID NO:1250)	[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258064516	0.870967742	4	26

FIG. 44 (Cont'd)

SEQUENCE	BS	GCNESS	3LN	NBP	P
'GAAGUUUAUUCGGA UUUAUUUUUUUCCAA CU' (SEQ ID NO:1251)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258064516	0.870967742	4	27
'AAGUUUAUUCGGAU UUAUUUUUUUUCCAAC UG' (SEQ ID NO:1252)	[[], [], ['UUUA', 'AUUU', 'AUUU', 'UUUU']]	0.258064516	0.870967742	4	28

FIG. 44 (Cont'd)

FIG. 45

- Guide strand
- Core strand
- Sensor strand
- Sensor toehold
- Dicer cleavage site

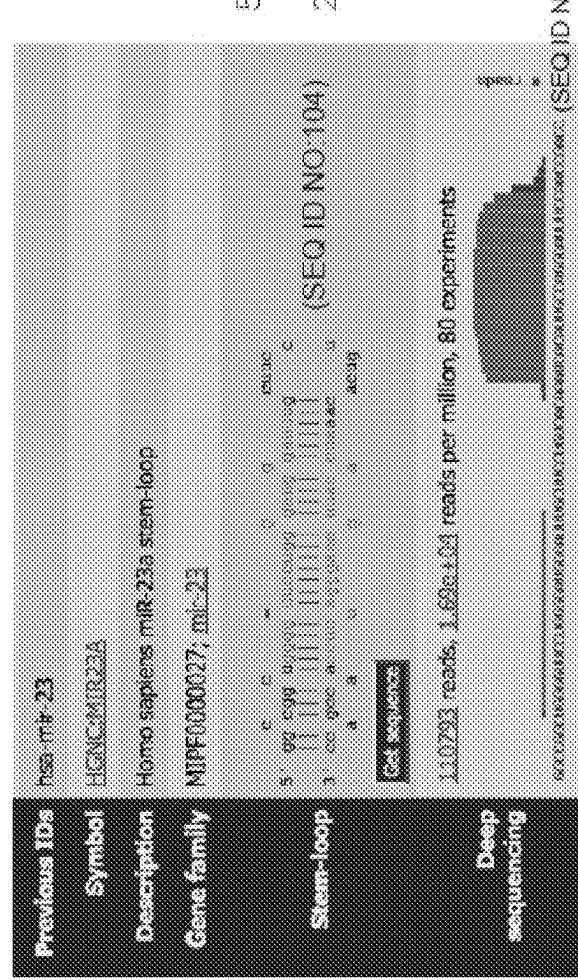
FIG. 46

FIG. 47

- NCBI Check for sensor strand
- miR-23a-3p match and match of primary concern:

• <https://blast.ncbi.nlm.nih.gov/Blast.cgi>

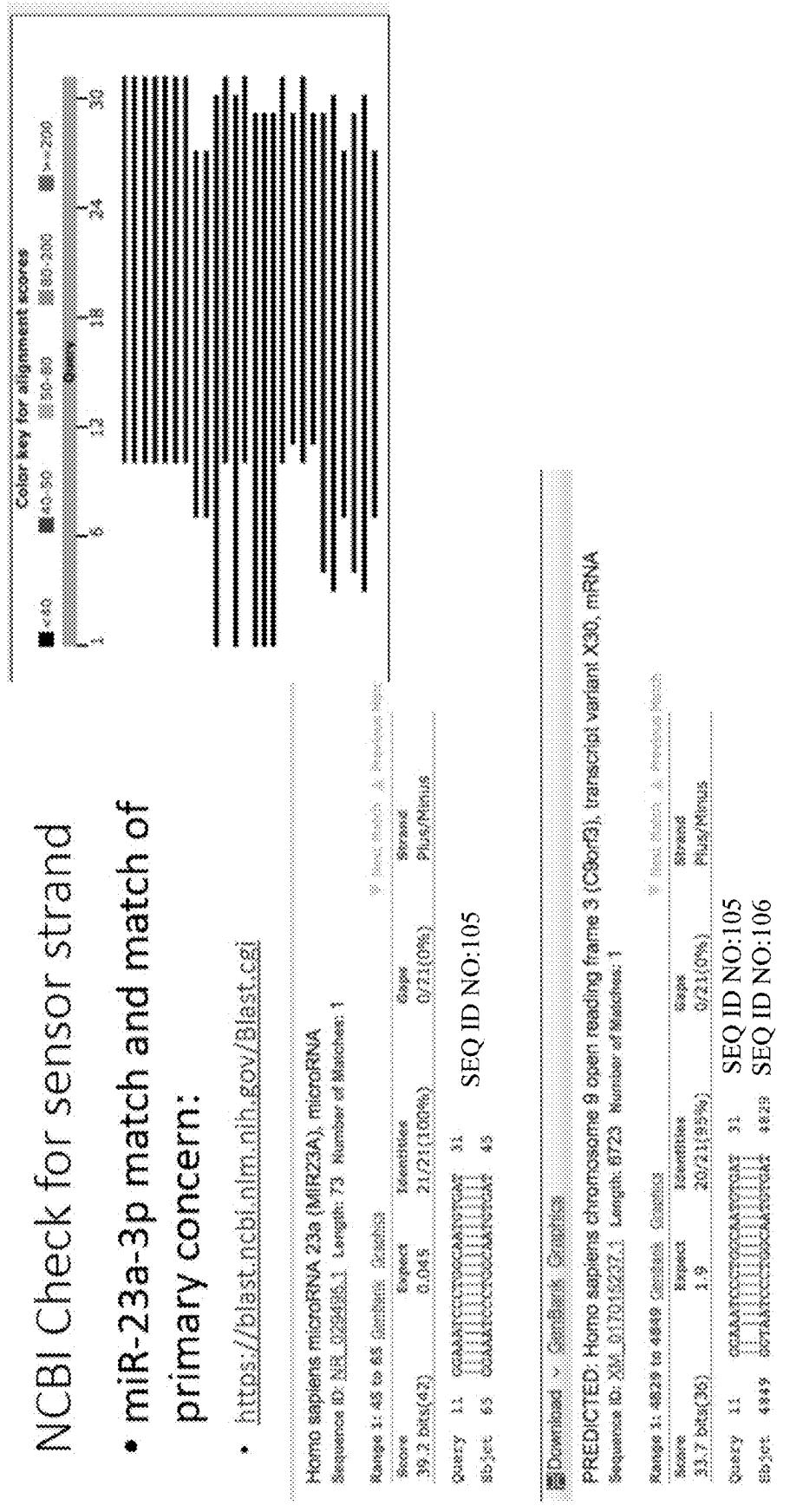


FIG. 48

- Calcineurin (PPP3CA) guide check: 5' CGAG UGUUG UUUGG Cuuuu CCUG uu 3' (SEQ ID NO:11)
<https://blast.ncbi.nlm.nih.gov/Blast.cgi>
Homo sapiens protein phosphatase 3 catalytic subunit alpha (PPP3CA), transcript variant 3, mRNA
Sequence ID: NM_001130822.1 Length: 45220 Number of Matches: 1
- Range 1: 1847 to 1888 Scores: Scores
Score: 0.040 Expect: 20.20(100%) Identical: 0/20(0%)
40.1 bits(20) Subject: 1866 Target: transcriptfactor 1347
- Query 3 TTTTTTTCCTTTCCTT 24 (SEQ ID NO:107)
Scores: Scores
Score: 0.040 Expect: 20.20(100%) Identical: 0/20(0%)
Plus/Minus: -----
- HDAC2 check guide: 5' GCACUUA GAUUG AAACA ACCCA GUU 3' (25 bp) (SEQ ID NO: 13)
<https://blast.ncbi.nlm.nih.gov/Blast.cgi>
PREDICTED: Homo sapiens histone deacetylase 2 (HDAC2), transcript variant X2, mRNA
Sequence ID: XM_017010732.1 Length: 2072 Number of Matches: 1
- Range 1: 1874 to 1893 Scores: Scores
Score: 0.040 Expect: 20.20(100%) Identical: 0/20(0%)
40.1 bits(20) Subject: 1893 Target: transcriptfactor 1374
- Query 5 TTAATTTAACCACT 24 (SEQ ID NO: 108)
Scores: Scores
Score: 0.040 Expect: 20.20(100%) Identical: 0/20(0%)
Plus/Minus: -----

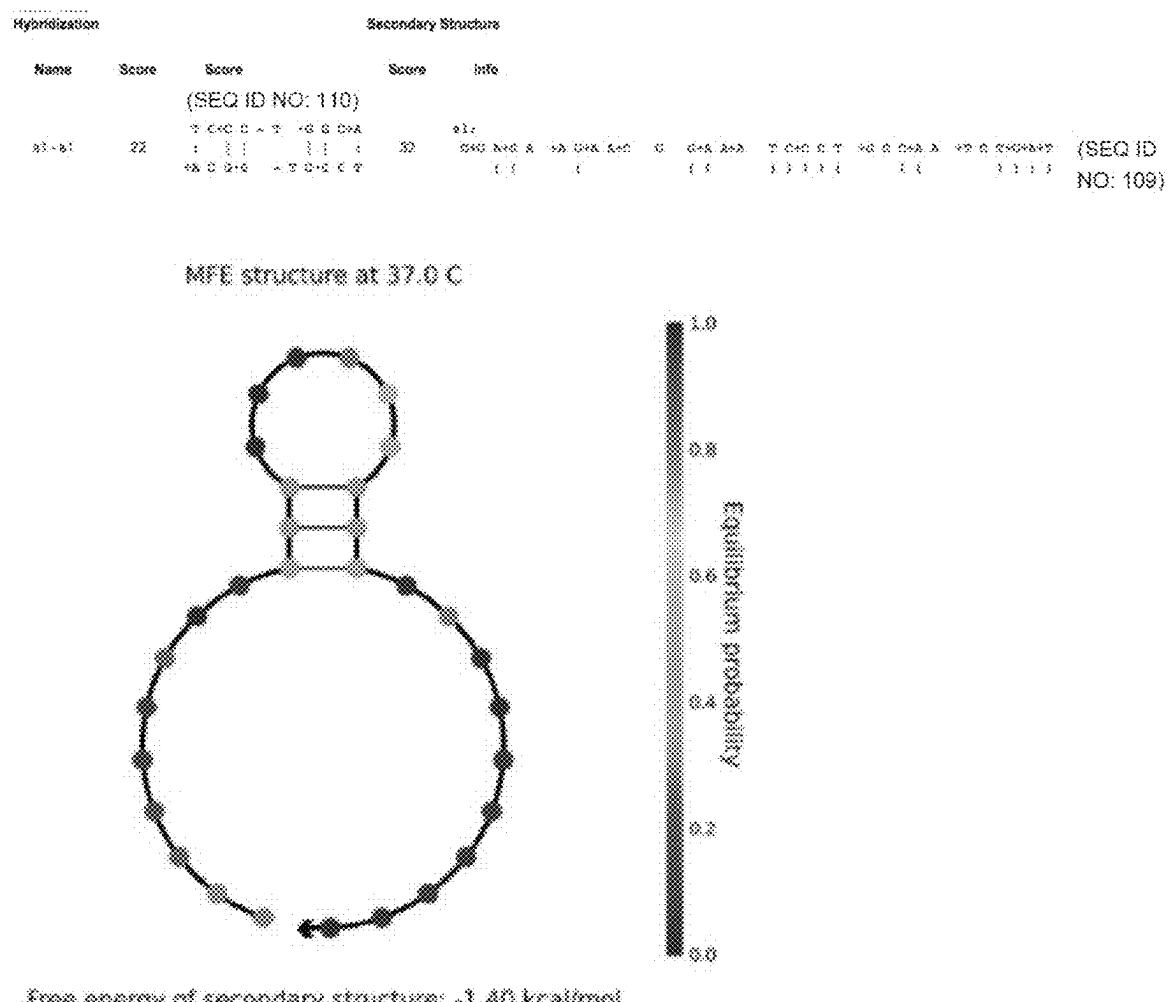
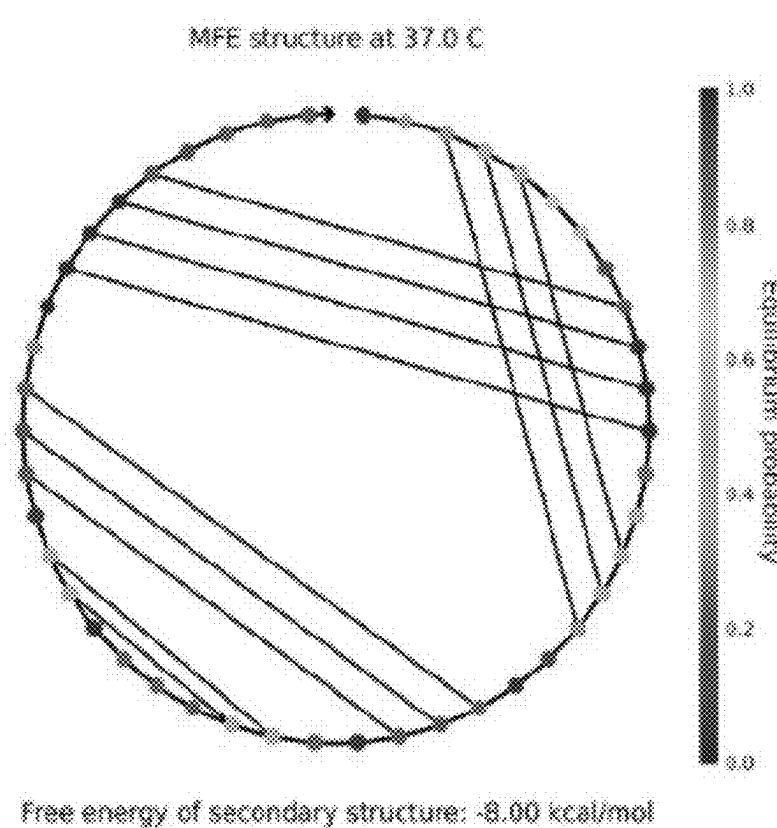
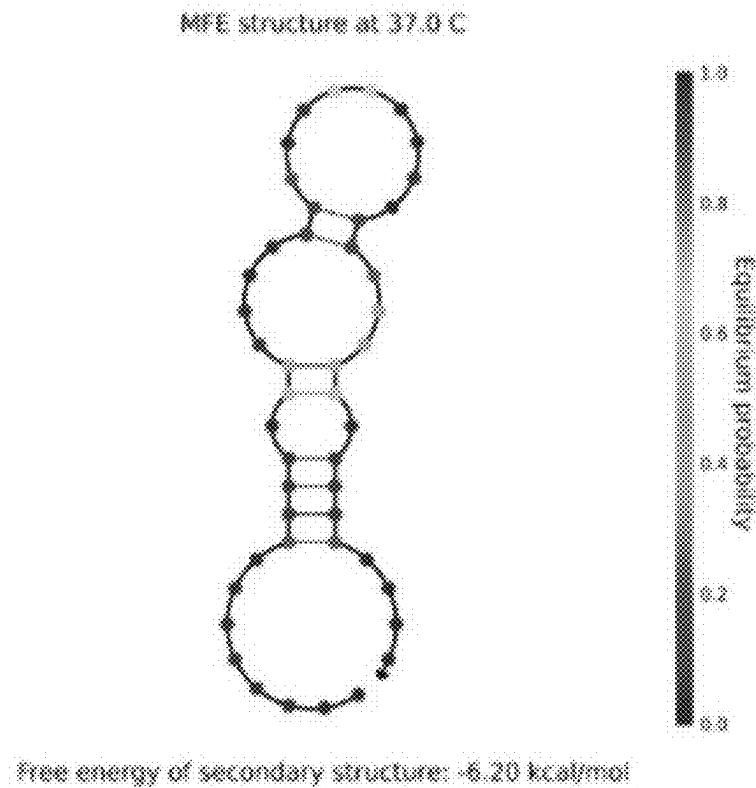
FIG. 49

FIG. 50A

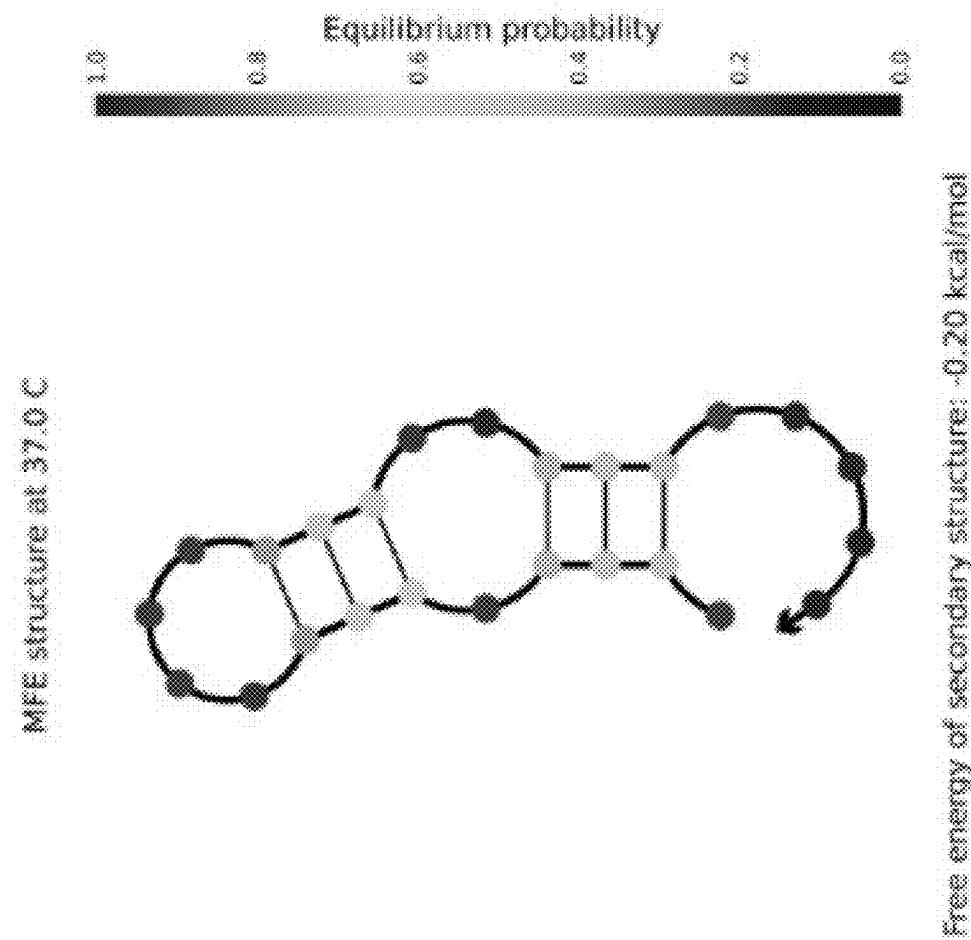
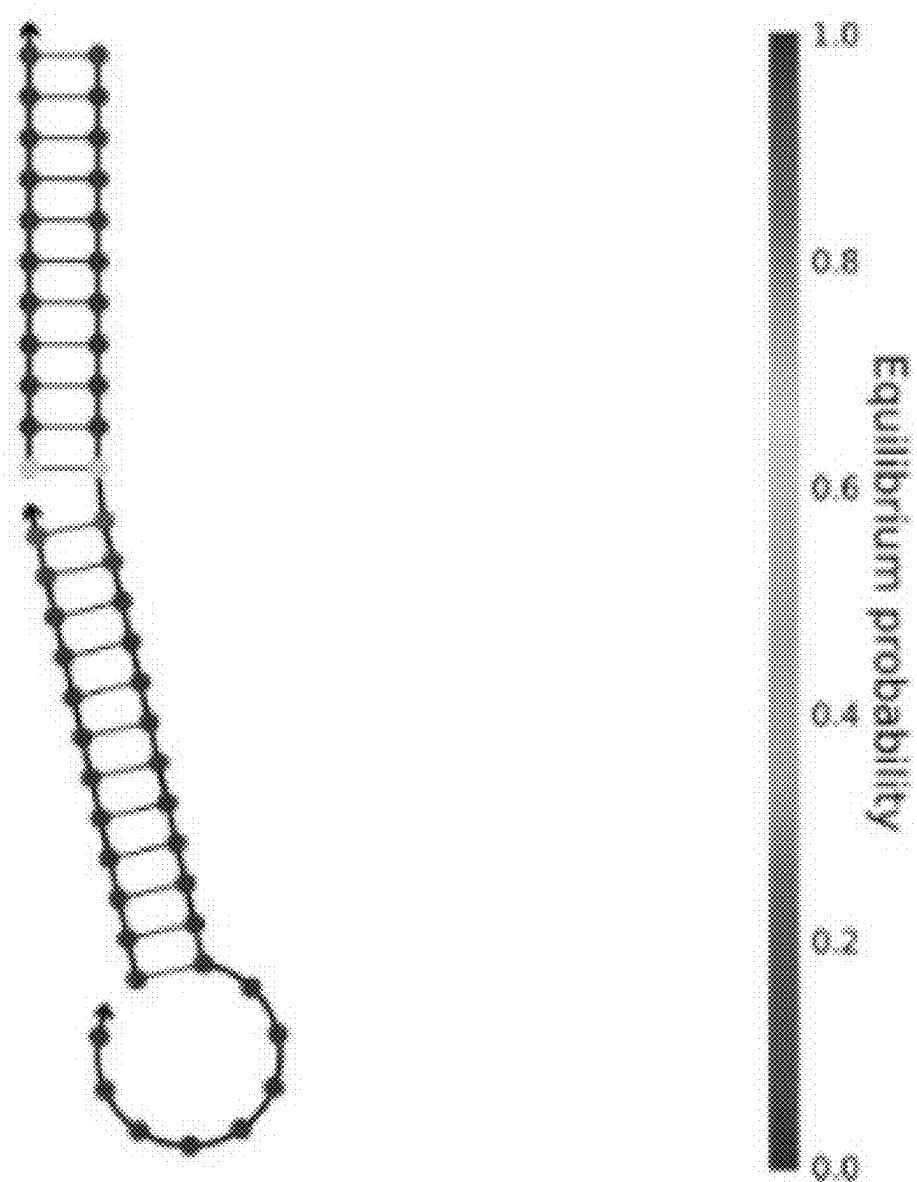


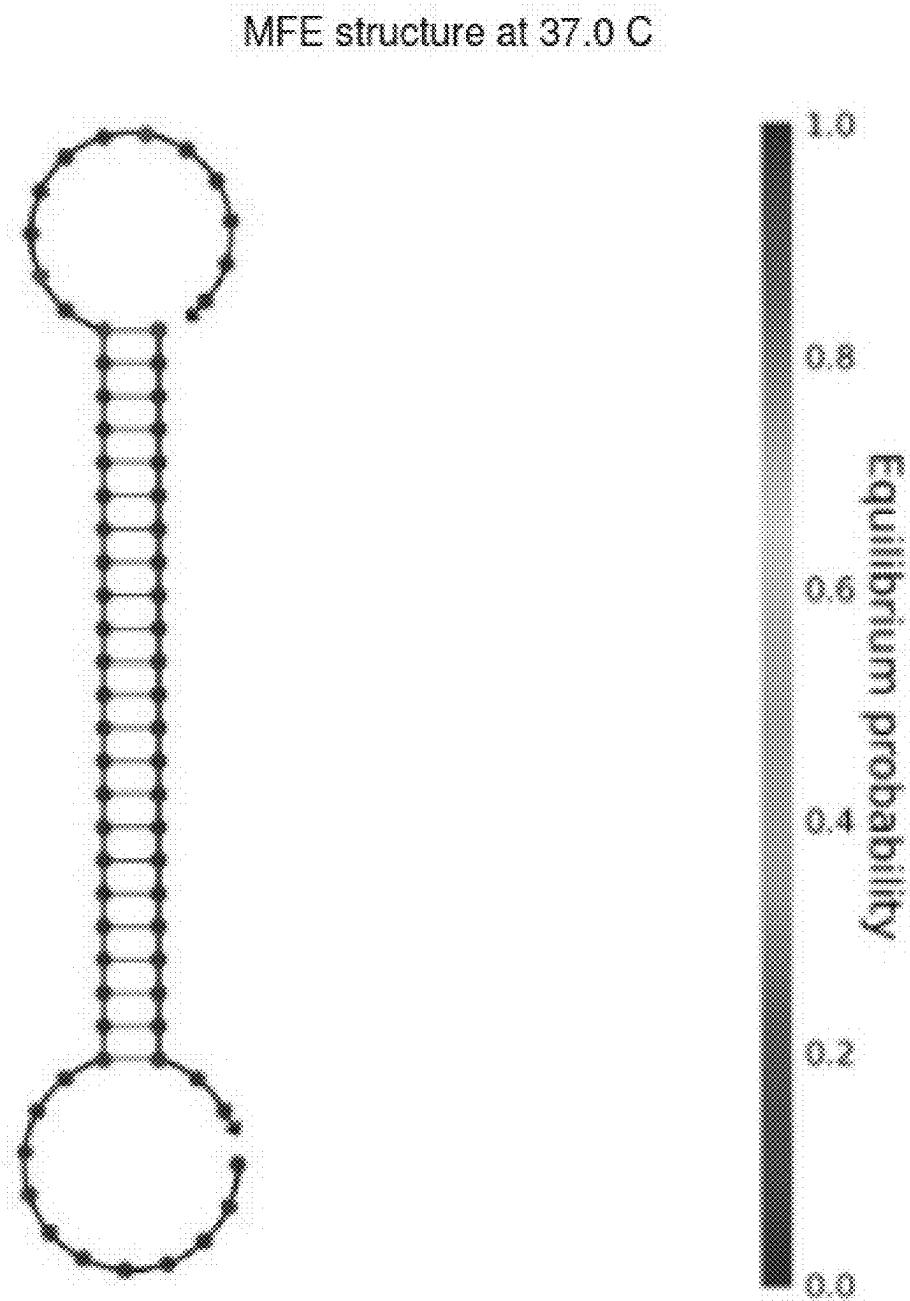
FIG. 50B

FIG. 50C

MFE structure at 37.0 C



Free energy of secondary structure: -44.76 kcal/mol

FIG. 50D

Free energy of secondary structure: -44.48 kcal/mol

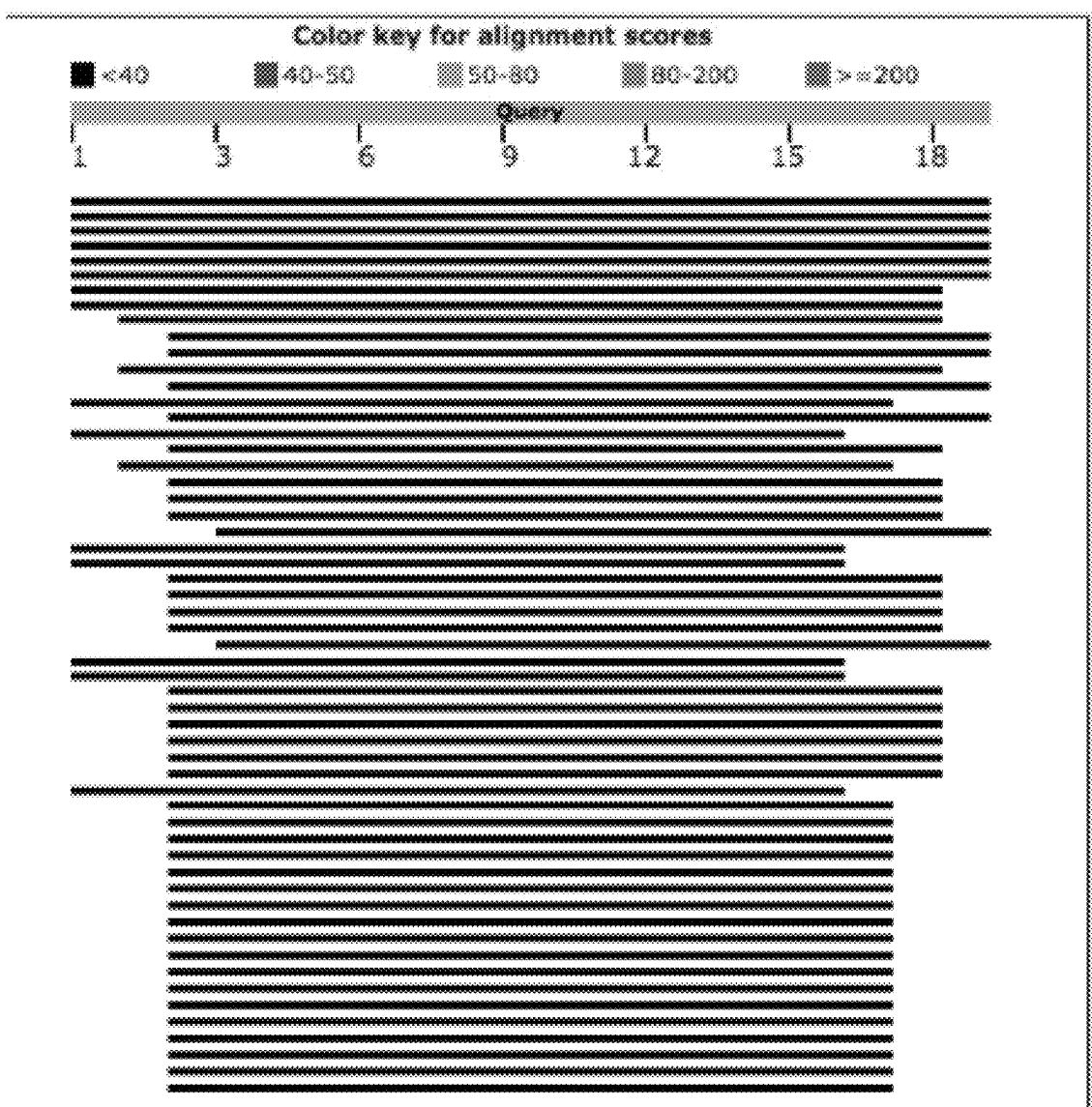
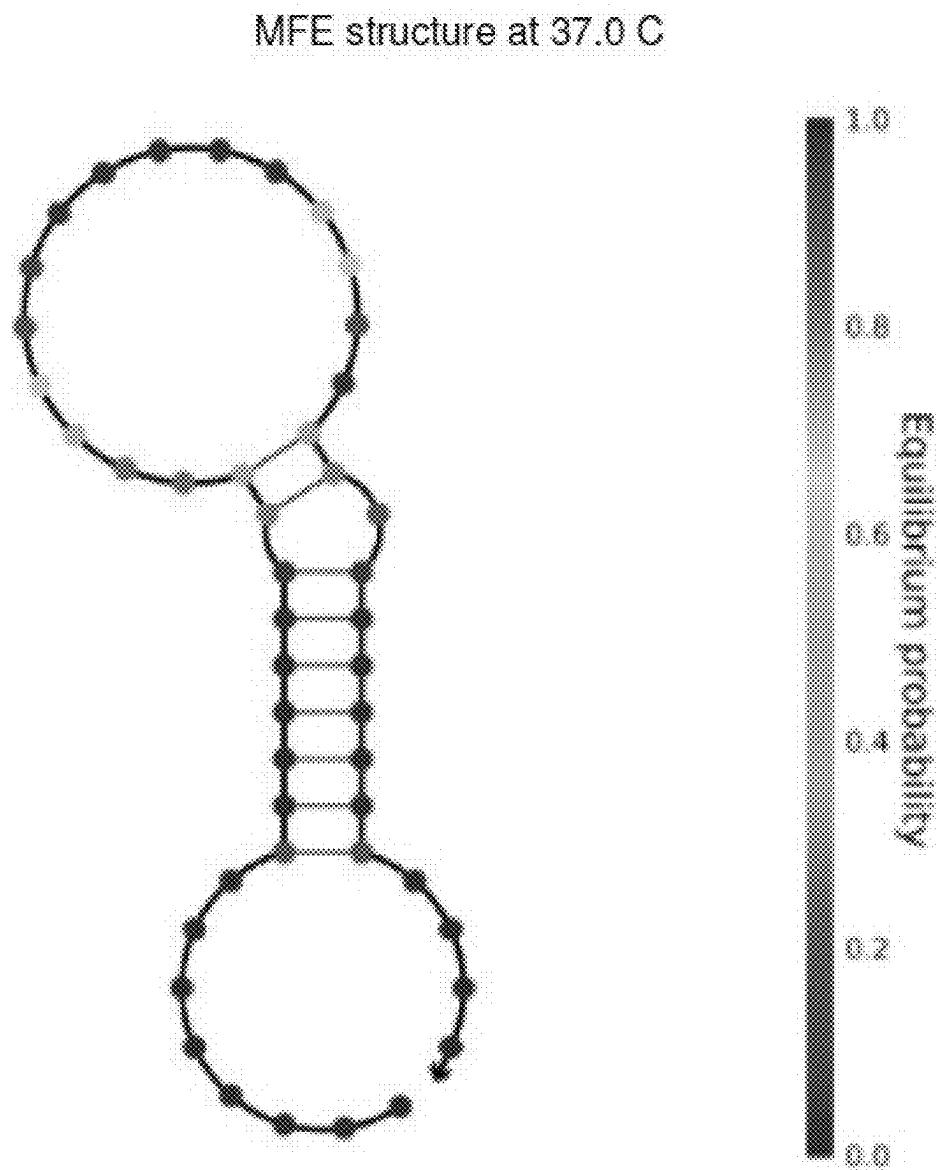
FIG. 51

FIG. 52A

Free energy of secondary structure: -12.60 kcal/mol

FIG. 52B

MFE structure at 37.0 °C

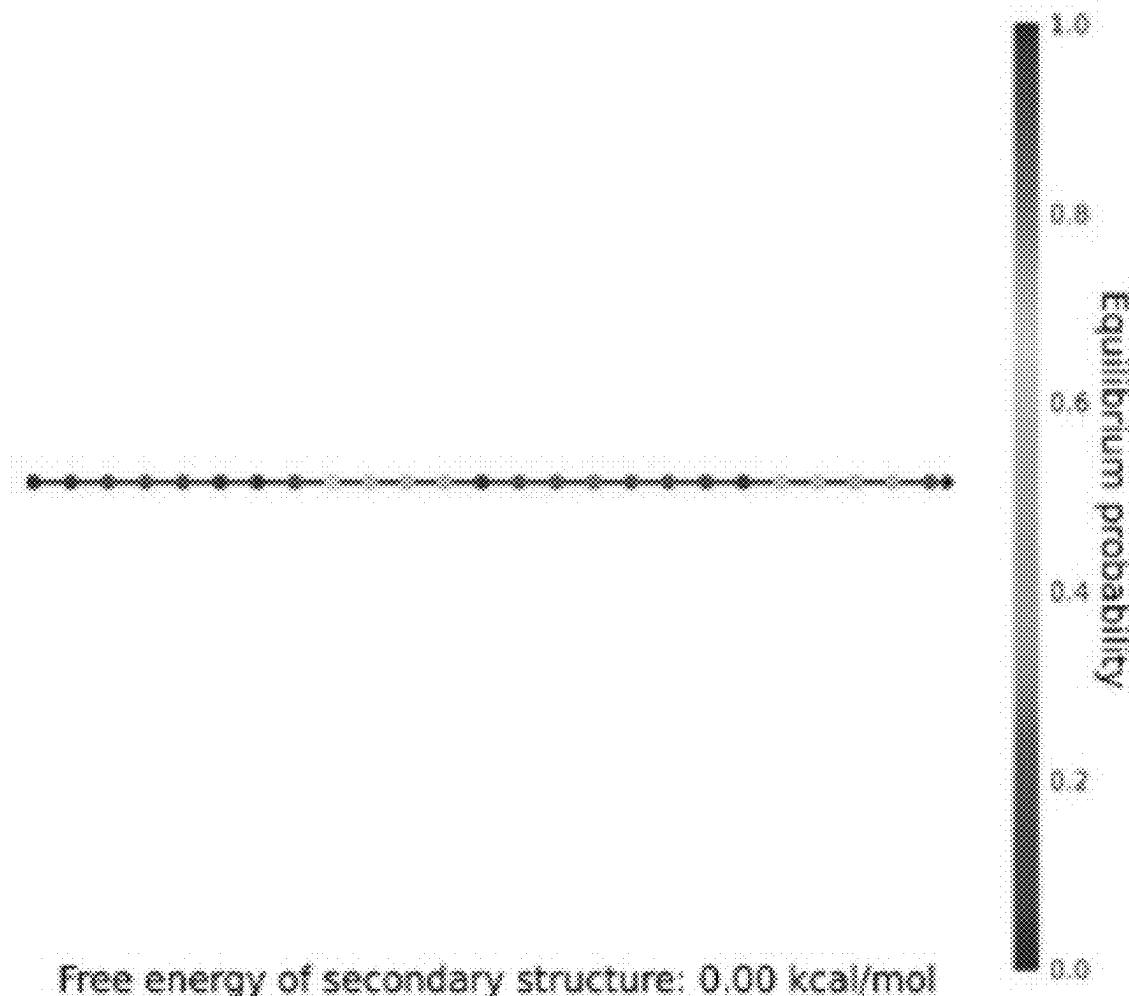
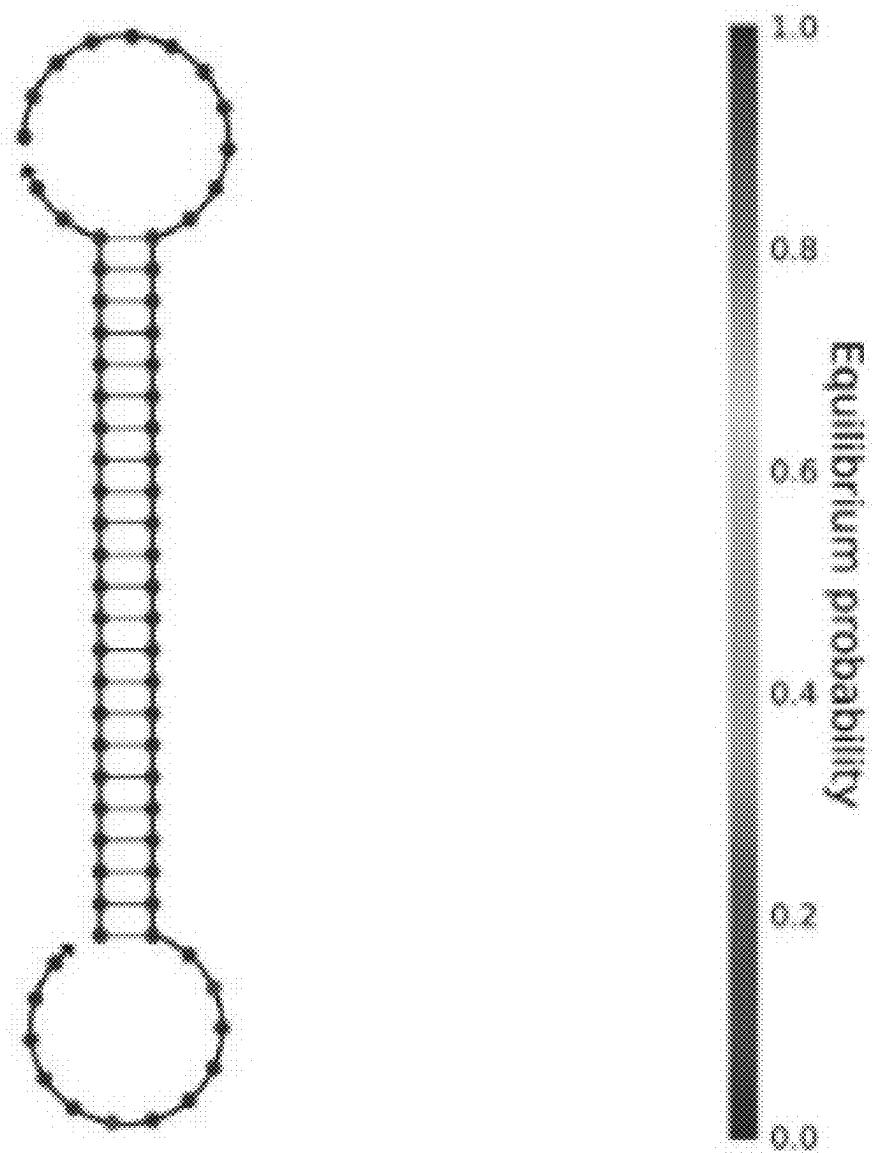


FIG. 52C

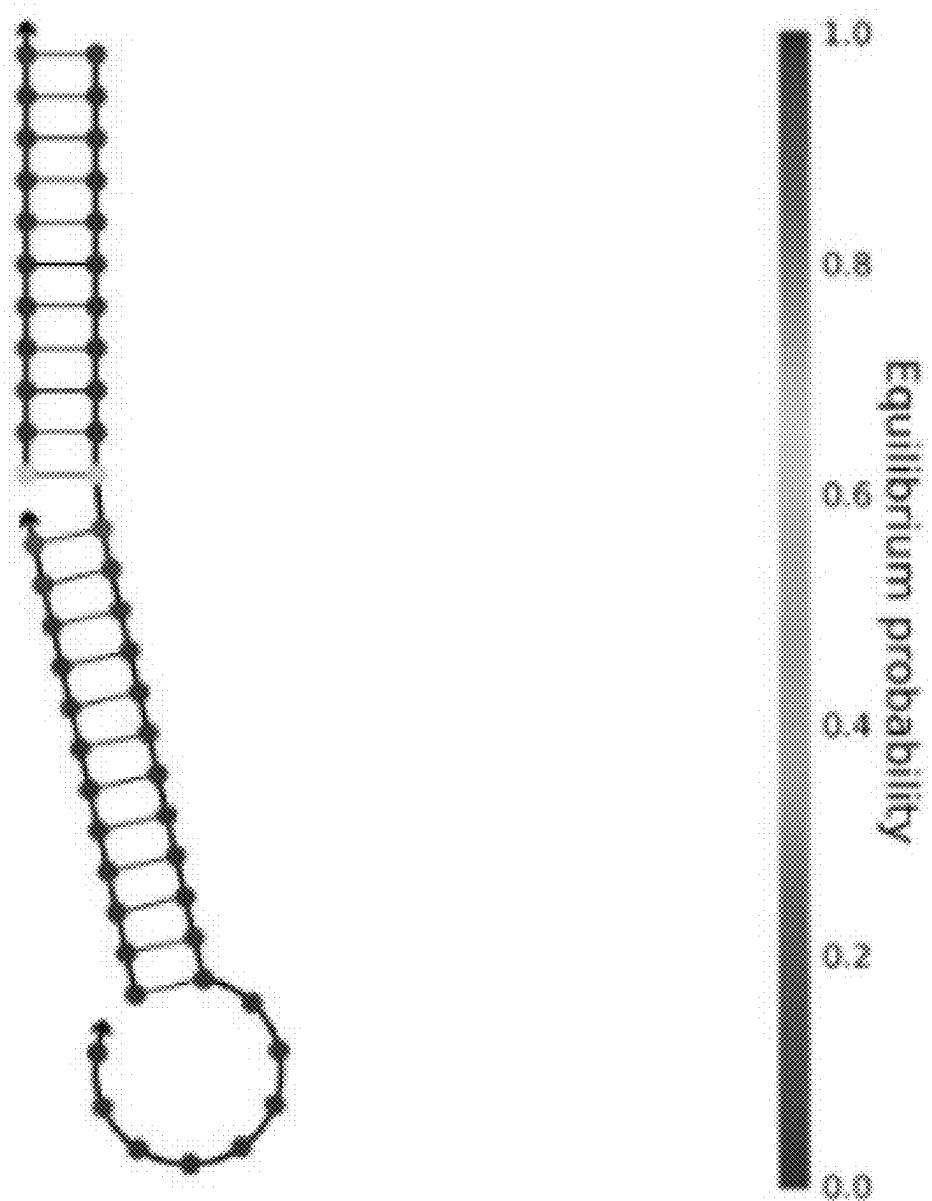
MFE structure at 37.0 °C



Free energy of secondary structure: -43.98 kcal/mol

FIG. 52D

MFE structure at 37.0 C



Free energy of secondary structure: -44.76 kcal/mol

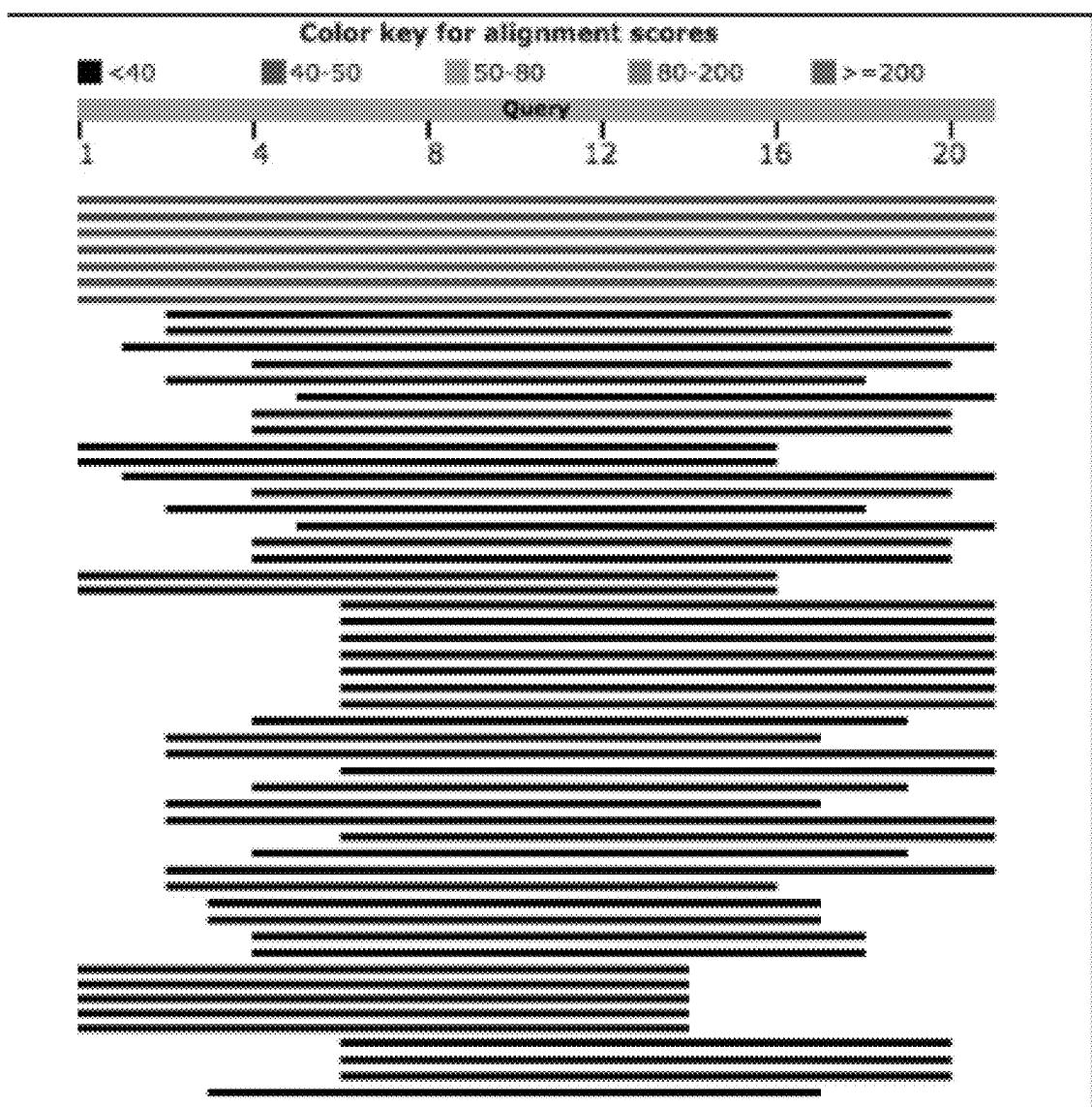
FIG. 53

FIG. 54A

PREDICTED: Homo sapiens lysine acetyltransferase 2A (KAT2A), transcript variant X1, mRNA Sequence ID: NC_000018.1.3 Length: 3143 Number of Nucleotides: 1	Source: 6 3886 to 8722 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 8723 3886(13) 283 SEQ ID NO:113 Source: 5 8723 3886(13) 3986 3886 SEQ ID NO:114	Source: 6 3886 to 8722 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 8723 3886(13) 283 SEQ ID NO:119
PREDICTED: Homo sapiens acetyl-CoA acetyltransferase beta (ACACB), transcript variant X3, mRNA Sequence ID: NM_001003353.2 Length: 8093 Number of Nucleotides: 1	Source: 6 3886 to 8722 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 8723 3886(13) 283 SEQ ID NO:115 Source: 5 8723 3886(13) 3986 3886 SEQ ID NO:120	Source: 6 3886 to 8722 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 8723 3886(13) 283 SEQ ID NO:115 Source: 5 8723 3886(13) 3986 3886 SEQ ID NO:120
PREDICTED: Homo sapiens acetyl-CoA acetyltransferase alpha (ACACB), transcript variant X4, mRNA Sequence ID: NM_001003353.2 Length: 8093 Number of Nucleotides: 1	Source: 6 3886 to 8722 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 8723 3886(13) 283 SEQ ID NO:116 Source: 5 8723 3886(13) 3986 3886 SEQ ID NO:117	Source: 6 3886 to 8722 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 8723 3886(13) 283 SEQ ID NO:116 Source: 5 8723 3886(13) 3986 3886 SEQ ID NO:117
Homo sapiens ADAM metallopeptidase with thrombospondin type 1 motif 12 (ADAMTS12), mRNA Sequence ID: NM_001003353.2 Length: 4935 Number of Nucleotides: 1	Source: 6 3886 to 3798 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 400 3886(13) 283 SEQ ID NO:118 Source: 5 400 3886(13) 3986 3886 SEQ ID NO:119	Source: 6 3886 to 3798 Sequence: GCGGGG Query: 283 3886(13) 3986 3886 Source: 5 400 3886(13) 283 SEQ ID NO:118 Source: 5 400 3886(13) 3986 3886 SEQ ID NO:119

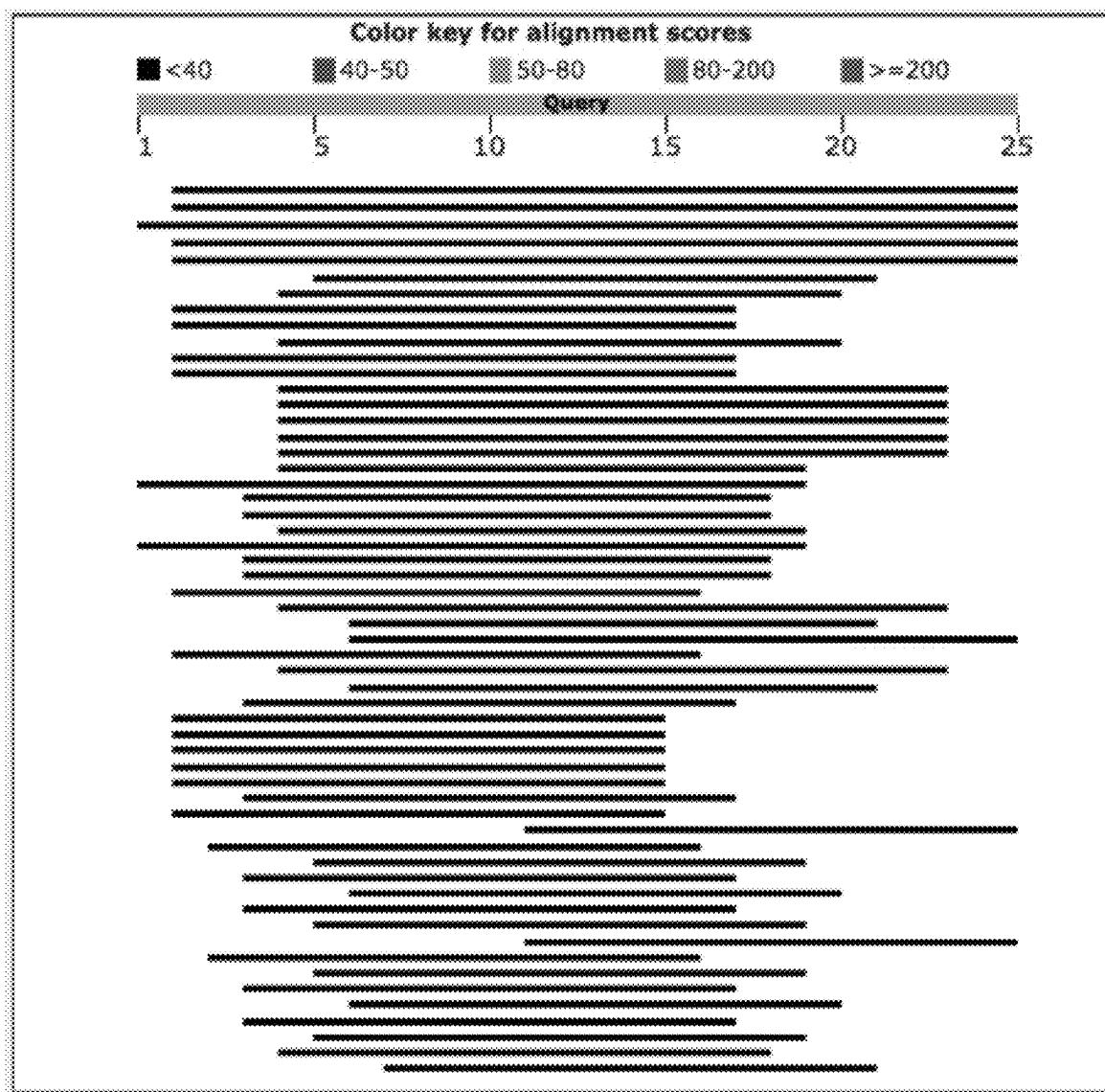
FIG. 54B

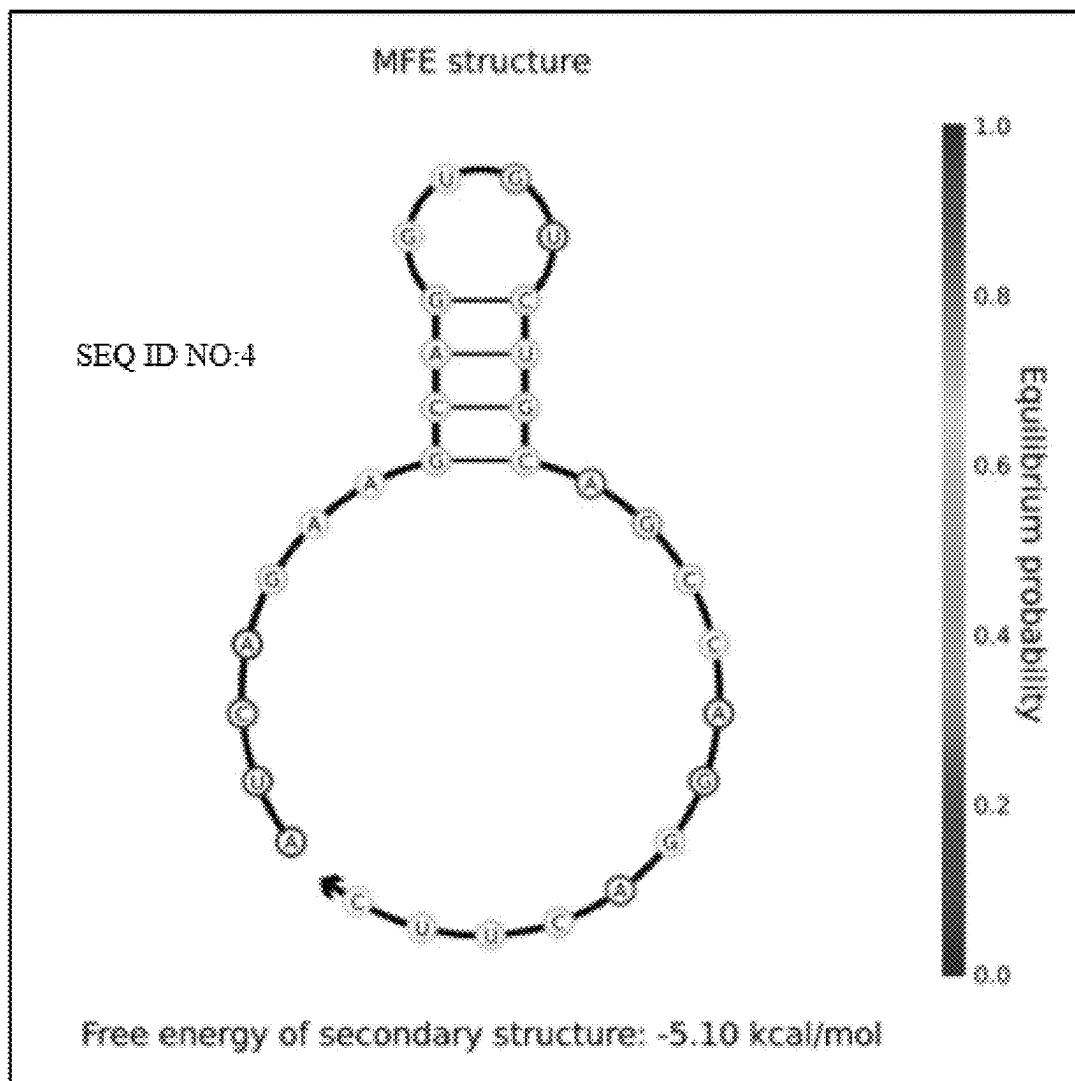
FIG. 55

FIG. 56

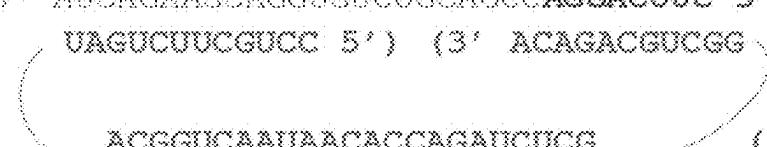
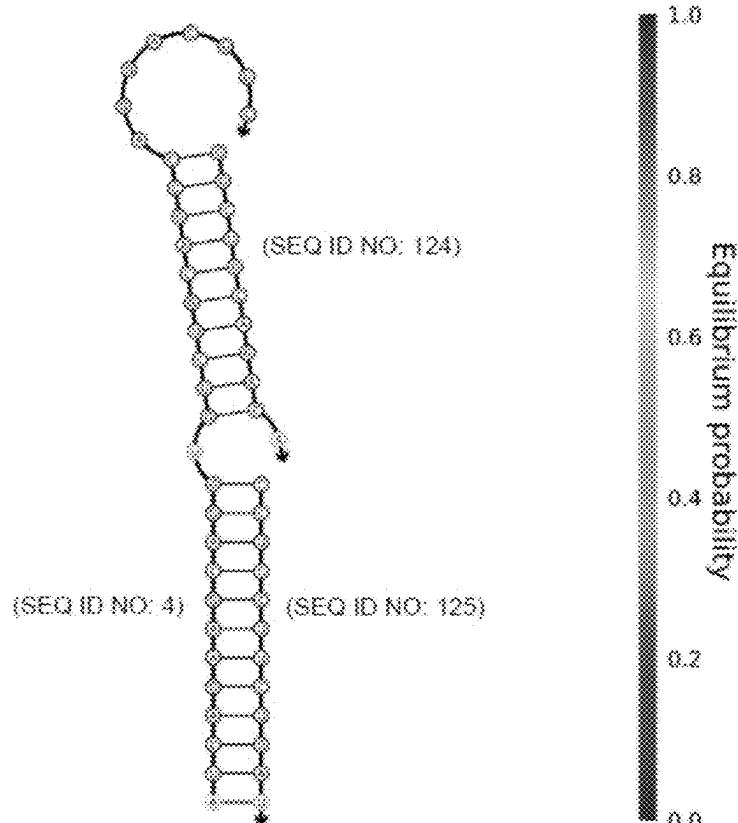
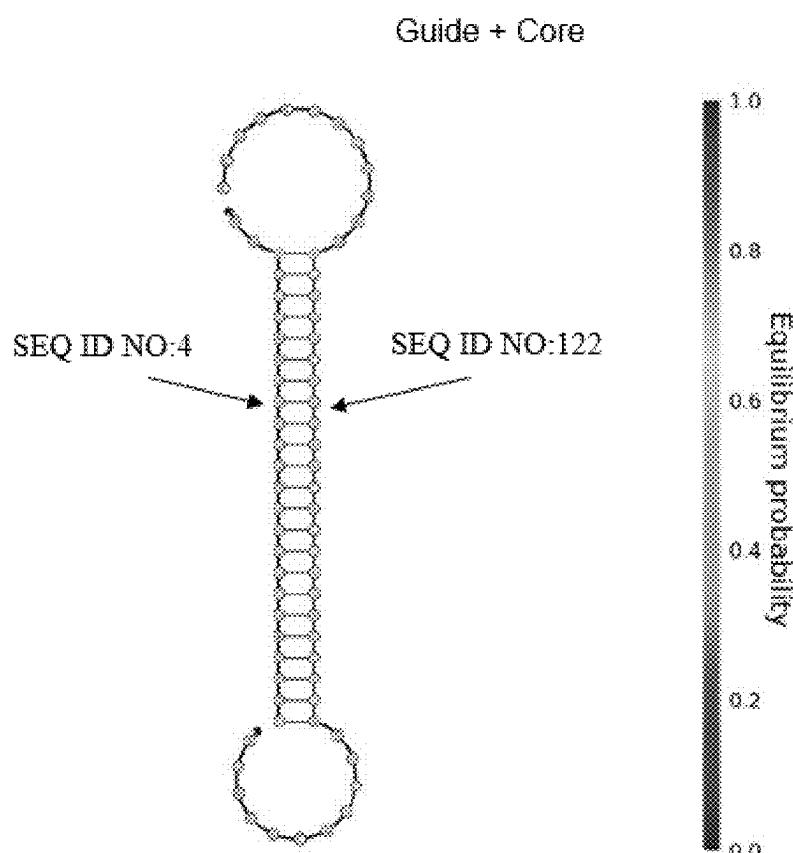
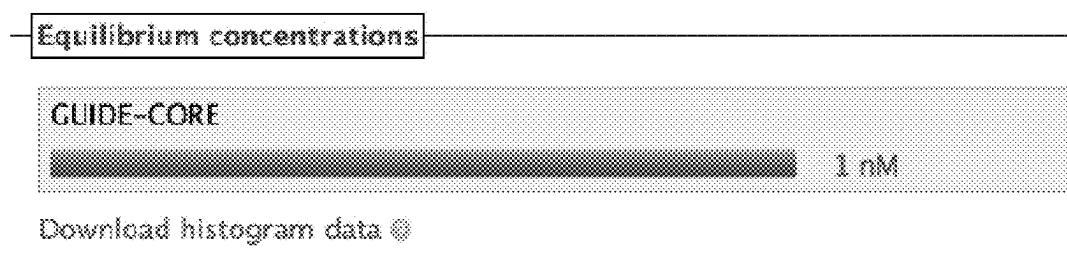
5' AUCAGAAGCAGGUGUCUGGCCAGGACUUC 3' (SENSOR) (SEQ ID NO: 2)
UAGUCUUUCGUCC 5') (3' ACAGACGUCGG (CORE NICK)

ACGGGUCAAUACACCAGAUCUCC (CORE GUIDE) (SEQ ID NO: 122)
3' UUUGCAGUUUUGUGGUUCUAGAGC 5' (GUIDE +2 U) (SEQ ID NO: 122)

FIG. 57A

Equilibrium concentrations	
SENSOR-CORE1-CORE2	0.99 nM
CORE1	0.0045 nM
SENSOR-CORE2	0.0041 nM
CORE2	0.003 nM
SENSOR-CORE1	0.0026 nM

SENSOR WITH CORE OVERHANGS

Free energy of secondary structure: -47.36 kcal/mol

FIG. 57B

Free energy of secondary structure: -45.08 kcal/mol

FIG. 58

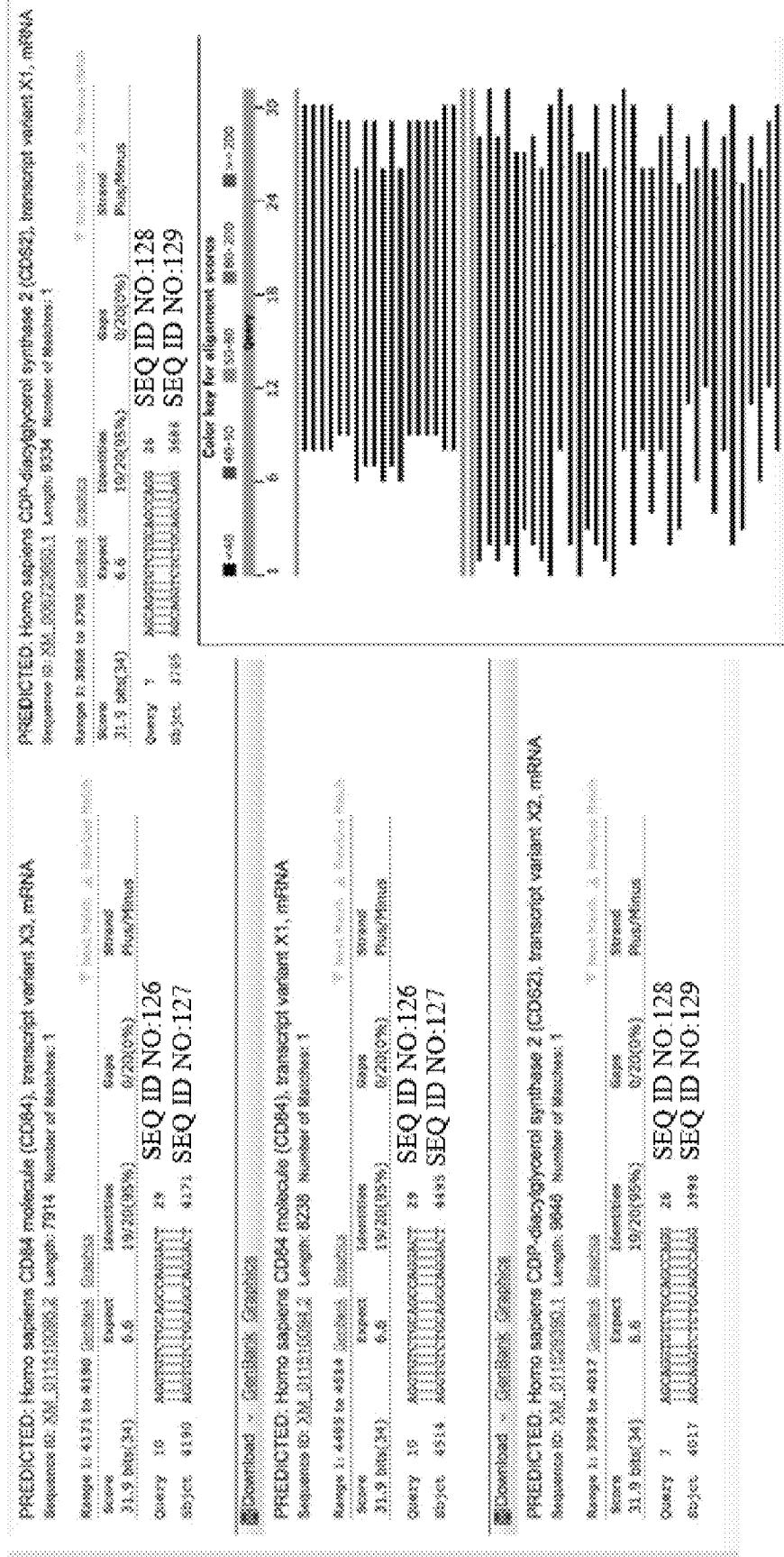


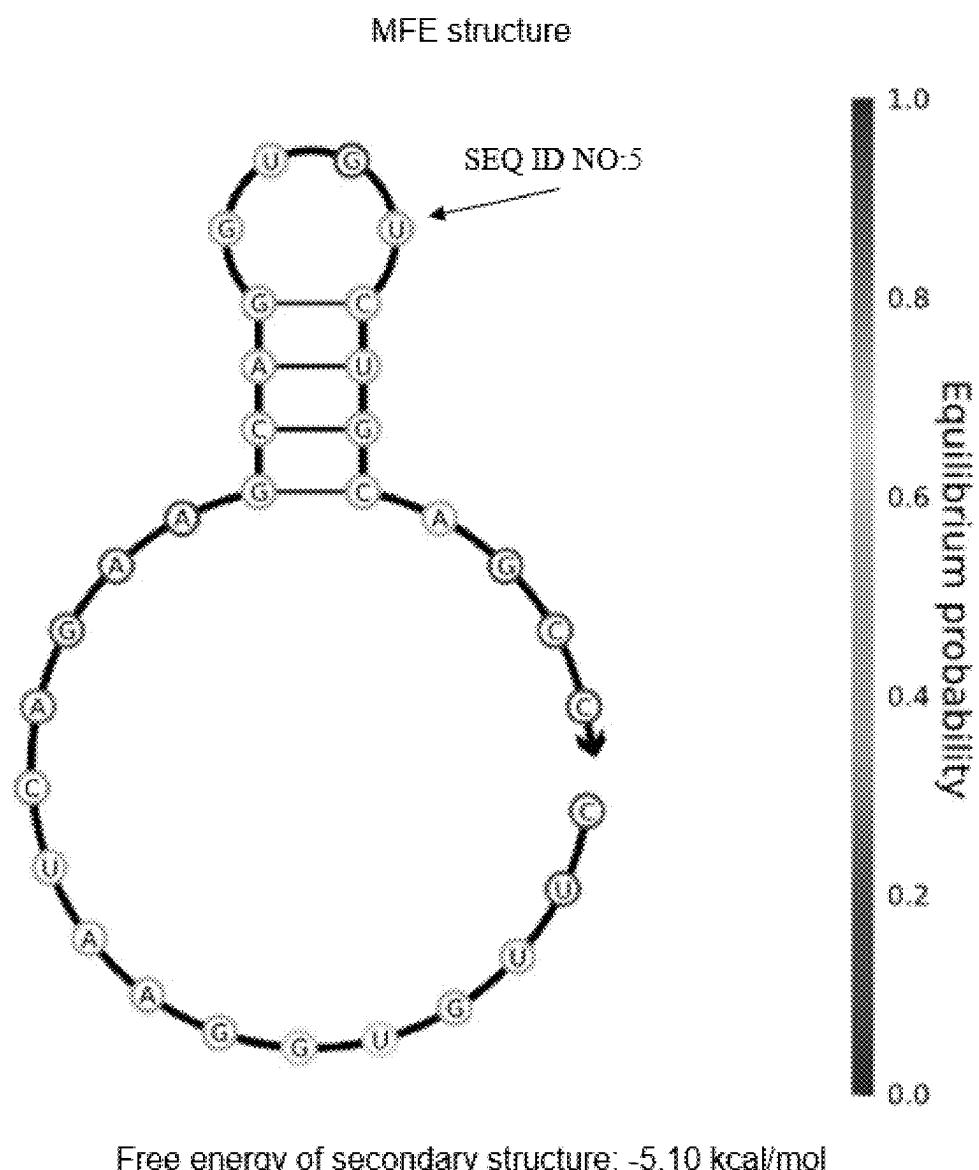
FIG. 59

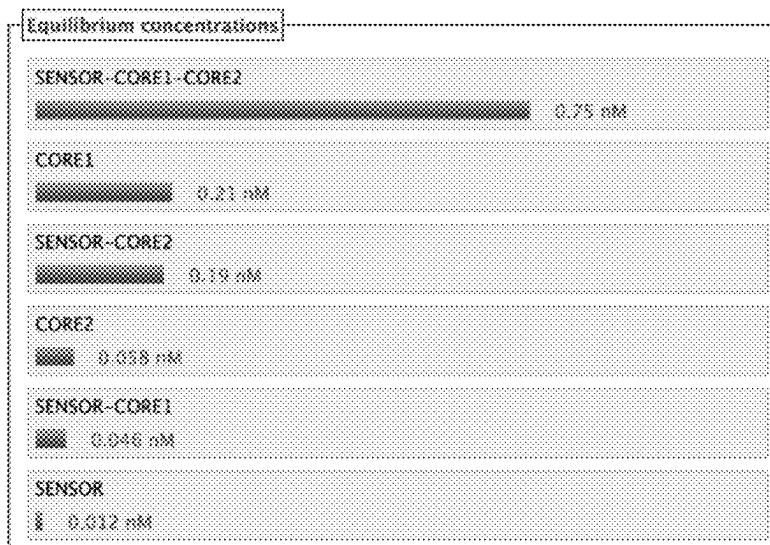
FIG. 60

5' CUUGUGGAAUCAGAACCAAGCAGGUGUCUGCAGCC 3' (SENSOR) (SEQ ID NO: 5)
GAACACCUUAG 5') (3' UCUUCGUCCACA) (CORE W/NICK 12 BP FROM
TOP)

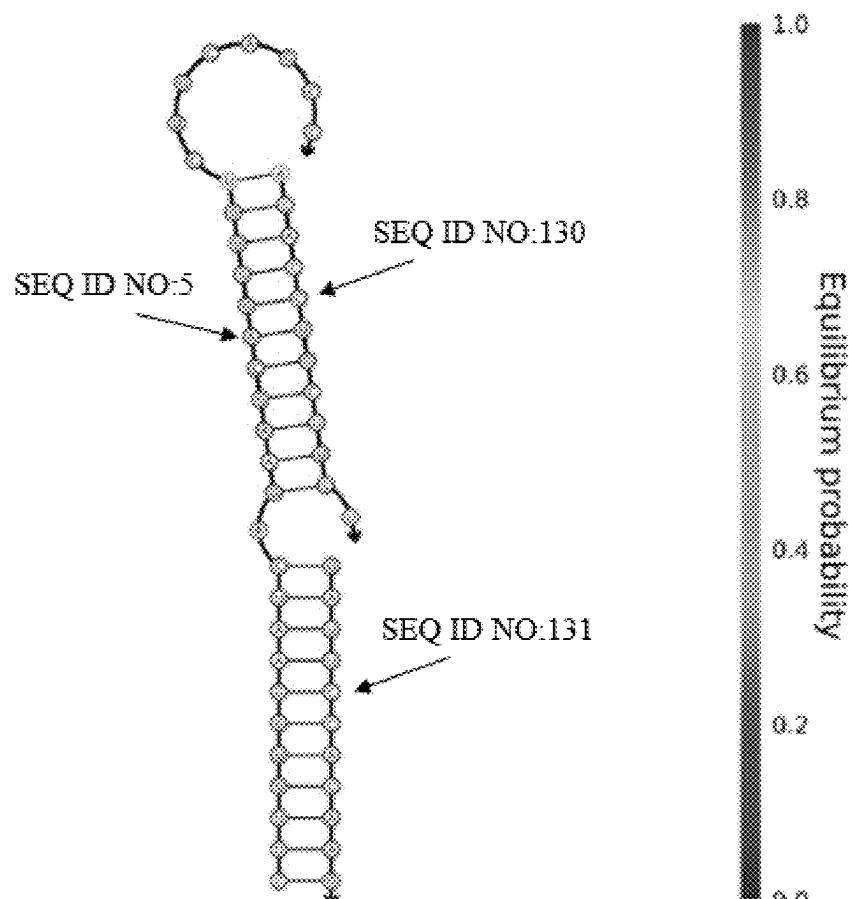
ACGGGUCAAUAACACCAGAUCUCC (CORE GUIDE) (SEQ ID NO: 22)

3' UUUGCCAGUUAUUGUGGUUCUAGAGC 5' (GUIDE +2 U) (SEQ ID NO: 132)

FIG. 61A



MFE structure



Free energy of secondary structure: -41.56 kcal/mol

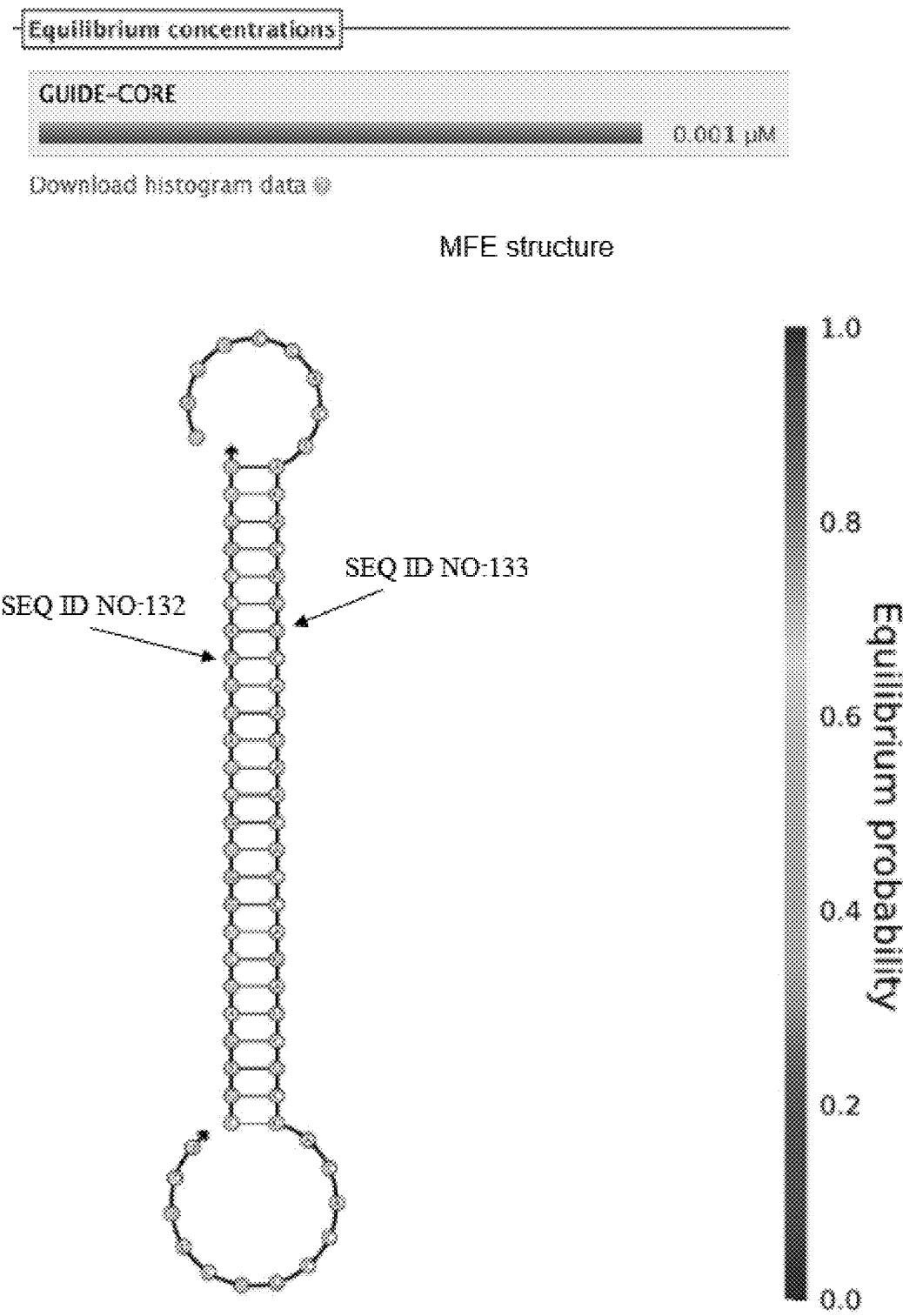
FIG. 61B

FIG. 62

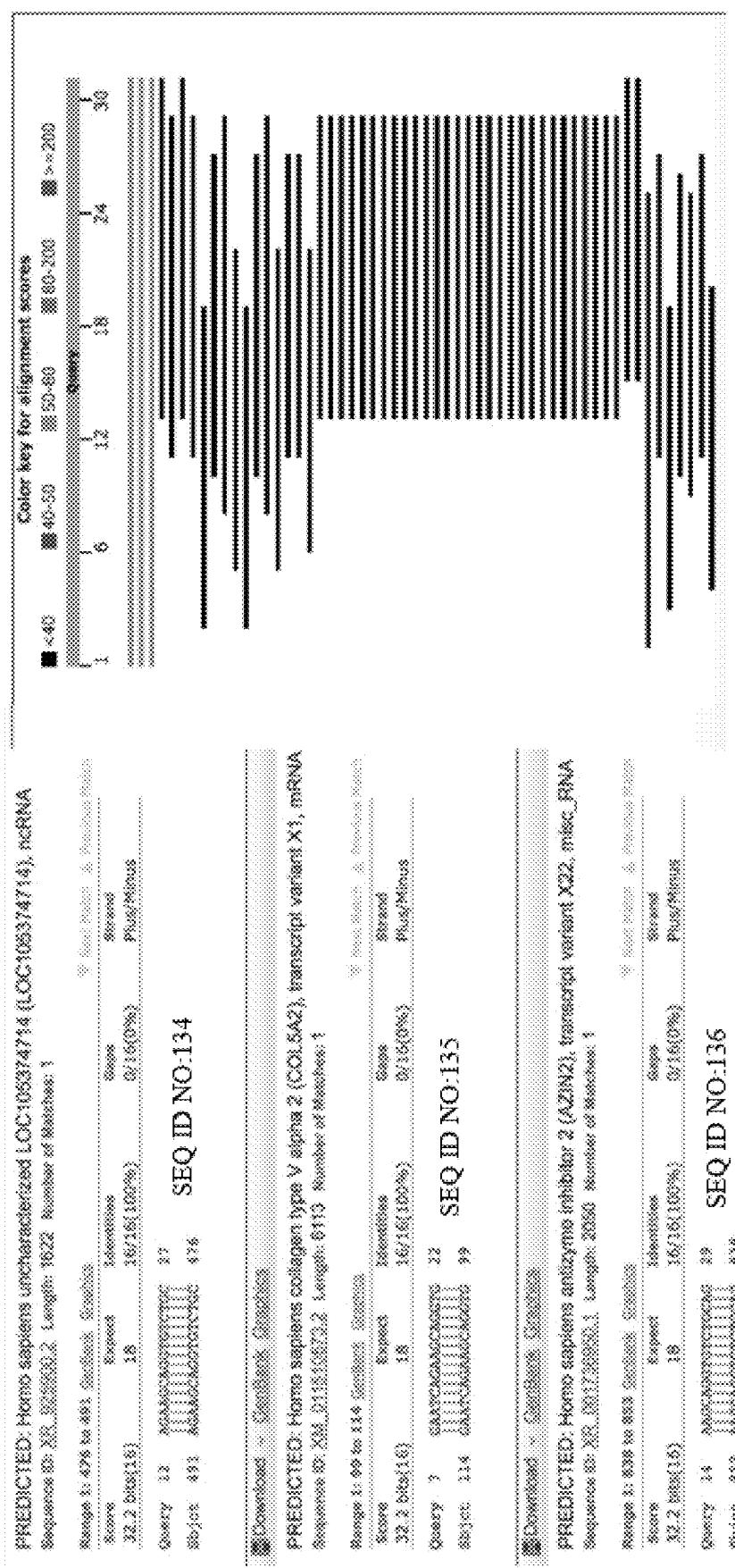


FIG. 62 (Cont'd)

Sensor VS NCBI human transcripts

PREDICTED: Homo sapiens tissue factor pathway inhibitor (TFPI), transcript variant X1, mRNA Sequence ID: XM_011511107.2 Length: 4075 Number of Matches: 1				
Range: 11 18865 to 18828 GenBank Statistics				
Score:	Request	Identical	Same	Y Recent Search & Previous Results
30.2 bits(1%)	71	15/15(100%)	0/15(0%)	<input type="checkbox"/> Shared
Query 9	ATCGAGCTTTCCTTTT	23	SEQ ID NO:137	Plus/Minus
Subject 1820	ATCGAGCTTTCCTTTT	1808		
PREDICTED: Homo sapiens zinc finger CCCH-type containing 2 (ZCCHC2), transcript variant X1, misc_RNA Sequence ID: XR_001151525.1 Length: 4636 Number of Matches: 1				
Range: 11 43118 to 43228 GenBank Statistics				
Score:	Request	Identical	Same	Y Recent Search & Previous Results
30.2 bits(1%)	71	18/18(100%)	0/18(0%)	<input type="checkbox"/> Shared
Query 13	CACGCCGTTCTTGCC	31	SEQ ID NO:138	Plus/Minus
Subject 4320	CACGCCGTTCTTGCC	4310	SEQ ID NO:139	
PREDICTED: Homo sapiens LIG1, scutella cell polarity complex component (LIG1), transcript variant X12, mRNA Sequence ID: XM_011521832.1 Length: 3660 Number of Matches: 1				
Range: 12 497 to 493 GenBank Statistics				
Score:	Request	Identical	Same	Y Recent Search & Previous Results
30.3 bits(1%)	71	13/15(100%)	0/15(0%)	<input type="checkbox"/> Shared
Query 13	TTCCTTGTGTTT	13	SEQ ID NO:140	Plus/Minus
Subject 490	TTCCTTGTGTTT	479		

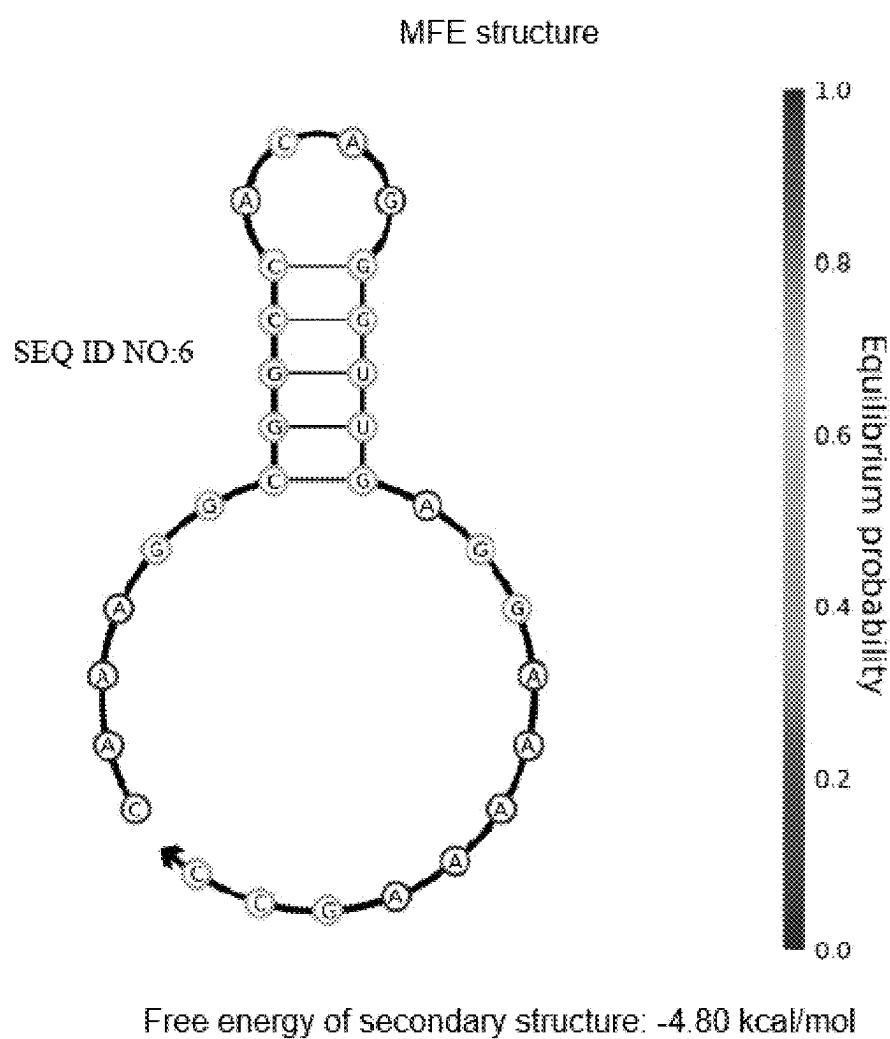
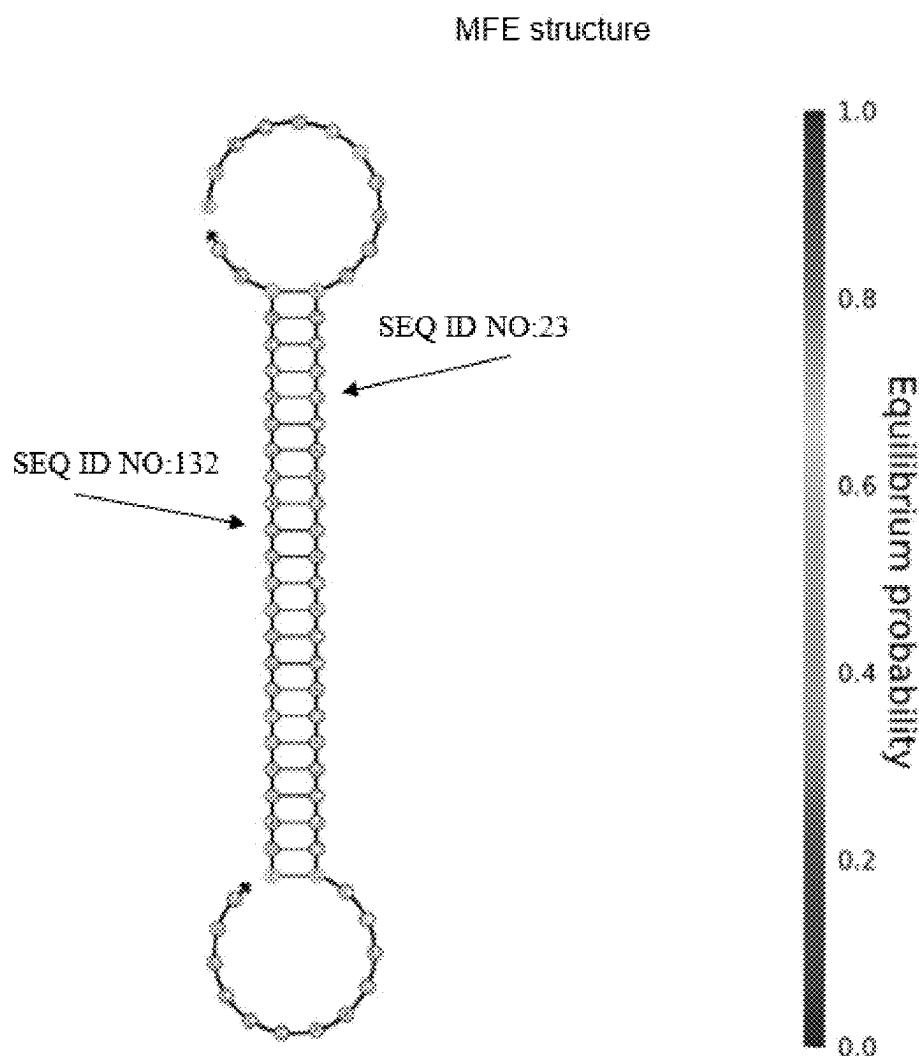
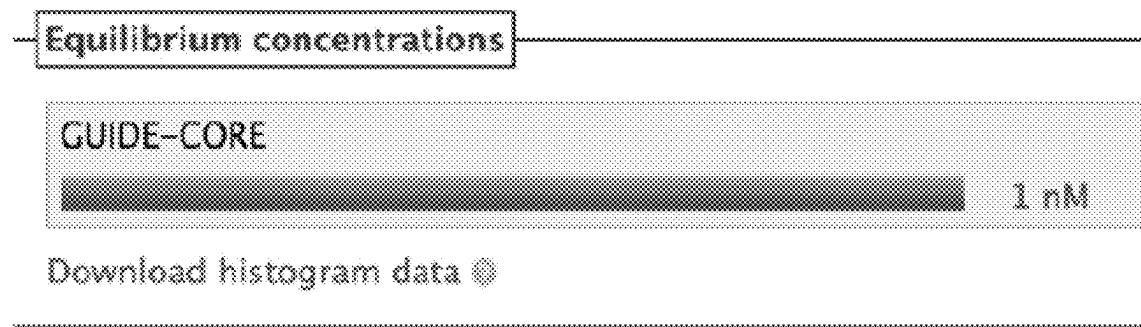
FIG. 63

FIG. 64

5' CAAAGCCGGCCACAGGGUUGAGGAAAAAGCC 3' (SENSOR) (SEQ ID NO: 6)
GUUUCCCCCGG 5') (3' UGUCCCCAACUCC (CORE NICK)

ACGGGUCAAUAACACCAGAUCUCC (CORE GUIDE) (SEQ ID NO: 23)

3' UUUGCCCAGUUUAUUGUGGGUCUAGAGC 5' (GUIDE +2 U) (SEQ ID NO: 132)

FIG. 65

Free energy of secondary structure: -44.38 kcal/mol

FIG. 66

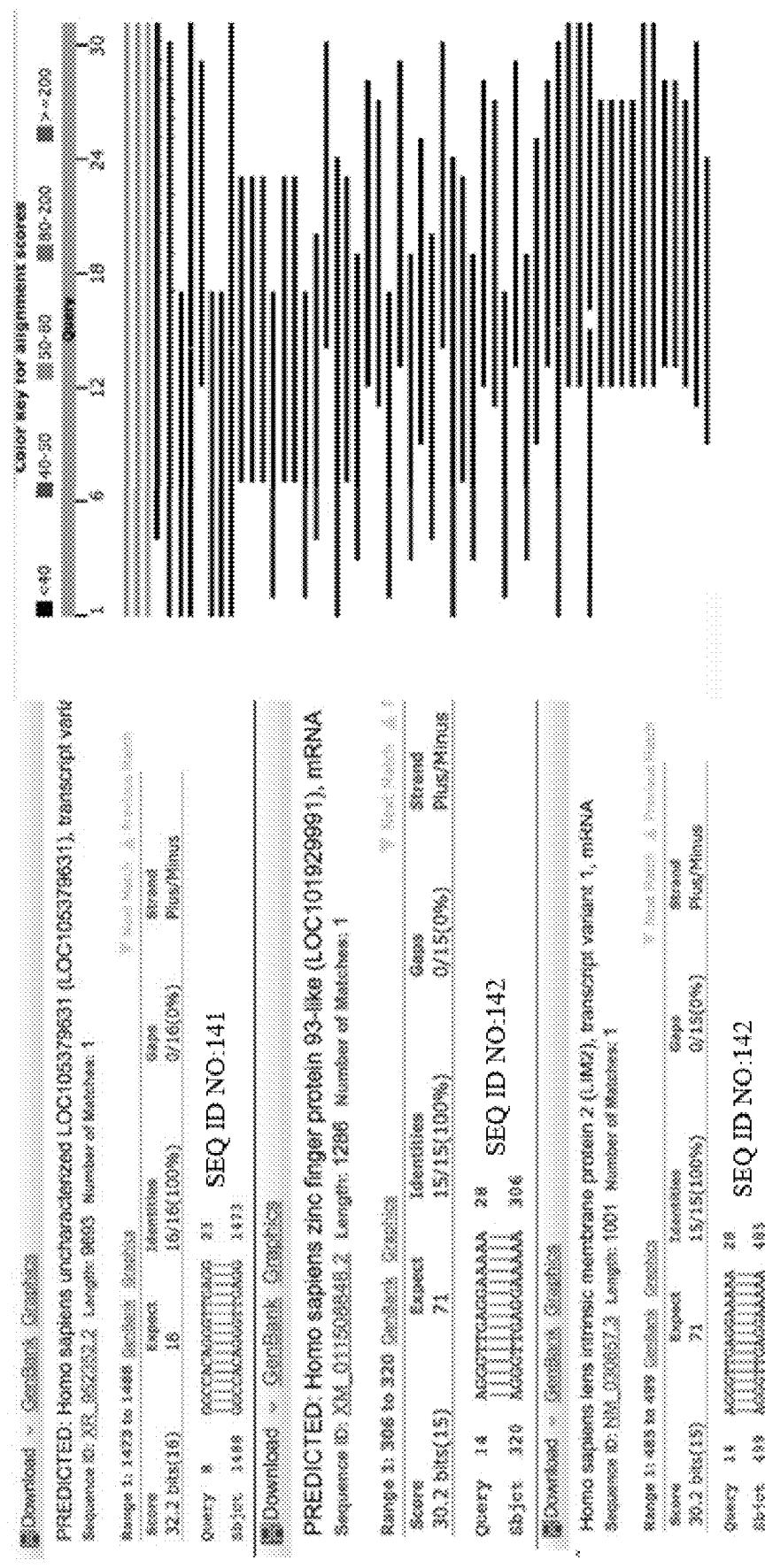
Sensor vs NCBI human transcripts

FIG. 66 (Cont'd)

Sensor vs NCBI human transcripts

PREDICTED: Homo sapiens tissue factor pathway inhibitor (TFPI), transcript variant X1, mRNA Sequence ID: XM_011511707.2 Length: 4075 Number of matches: 1					
Range: 11:18088 to 18280 Identifies: 0 matches					
Score:	Expect	Identifies	Gaps	Strand	
30.2 bits(15)	71	15/15(100%)	0/15(0%)	Plus/Minus	
Query: 9 ATCACACCCAGCTT	23	SEQ ID NO:137			
Subject: 1838 ACGGAAACGGGTT	1806				
Download GenBank Graphics					
PREDICTED: Homo sapiens zinc finger CCHC-type containing 2 (ZCCHC2), transcript variant X1, misc_RNA Sequence ID: XR_001763206.1 Length: 4636 Number of matches: 1					
Range: 1:4318 to 4328 Identifies: 0 matches					
Score:	Expect	Identifies	Gaps	Strand	
30.2 bits(15)	71	18/19(95%)	0/19(0%)	Plus/Minus	
Query: 13 CAGGCAAGTCCTTCTTCTT	31	SEQ ID NO:138			
Subject: 4328 TTTTTTTTTTTTTTTTTTT	4318				
PREDICTED: Homo sapiens LLGL2, scribble cell polarity complex component (LLGL2), transcript variant X12, mRNA Sequence ID: XM_013246321 Length: 2300 Number of matches: 1					
Range: 1:477 to 943 Identifies: 0 matches					
Score:	Expect	Identifies	Gaps	Strand	
30.2 bits(15)	71	13/18(100%)	0/18(0%)	Plus/Minus	
Query: 3 TGTGGAATCTTCTTCTT	18	SEQ ID NO:140			
Subject: 491 TTTTTTTTTTTTTTT	477				

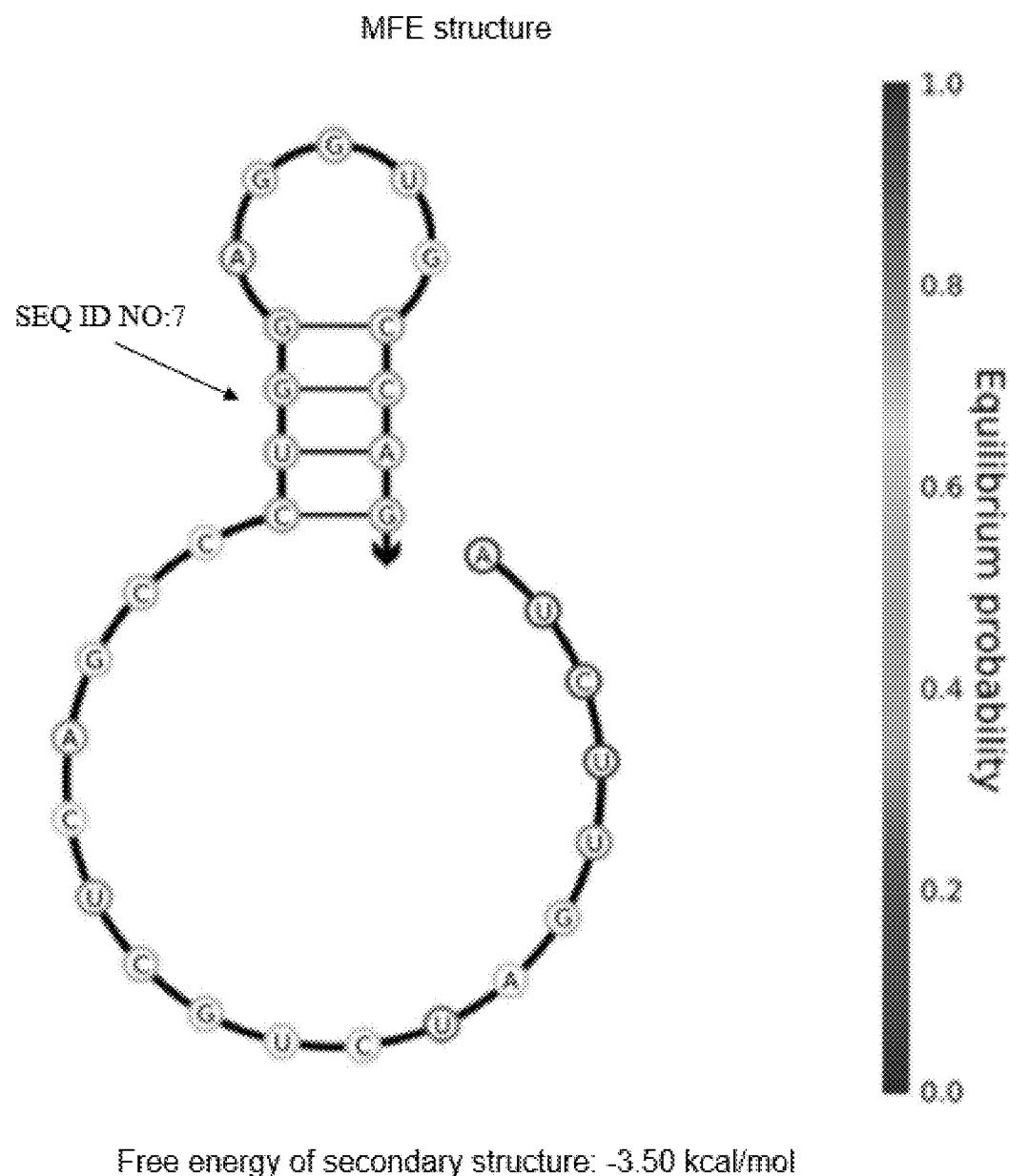
FIG. 67

FIG. 68

5' AUCUUGAUCUGCUAGCCCUGGAGGGUGCCAG 3' (SENSOR) (SEQ ID NO: 7)
UAGAACURGACCG 5') (3' ACUCGGGACCU (CORE NICK)
ACGGGUCAAUAACACCAGAUUCUCG (CORE GUIDE) (SEQ ID NO: 24)
3' UUUGGCCAGUUAUUGUGGUUCUAGAGC 5' (GUIDE +2 U) (SEQ ID NO: 132)

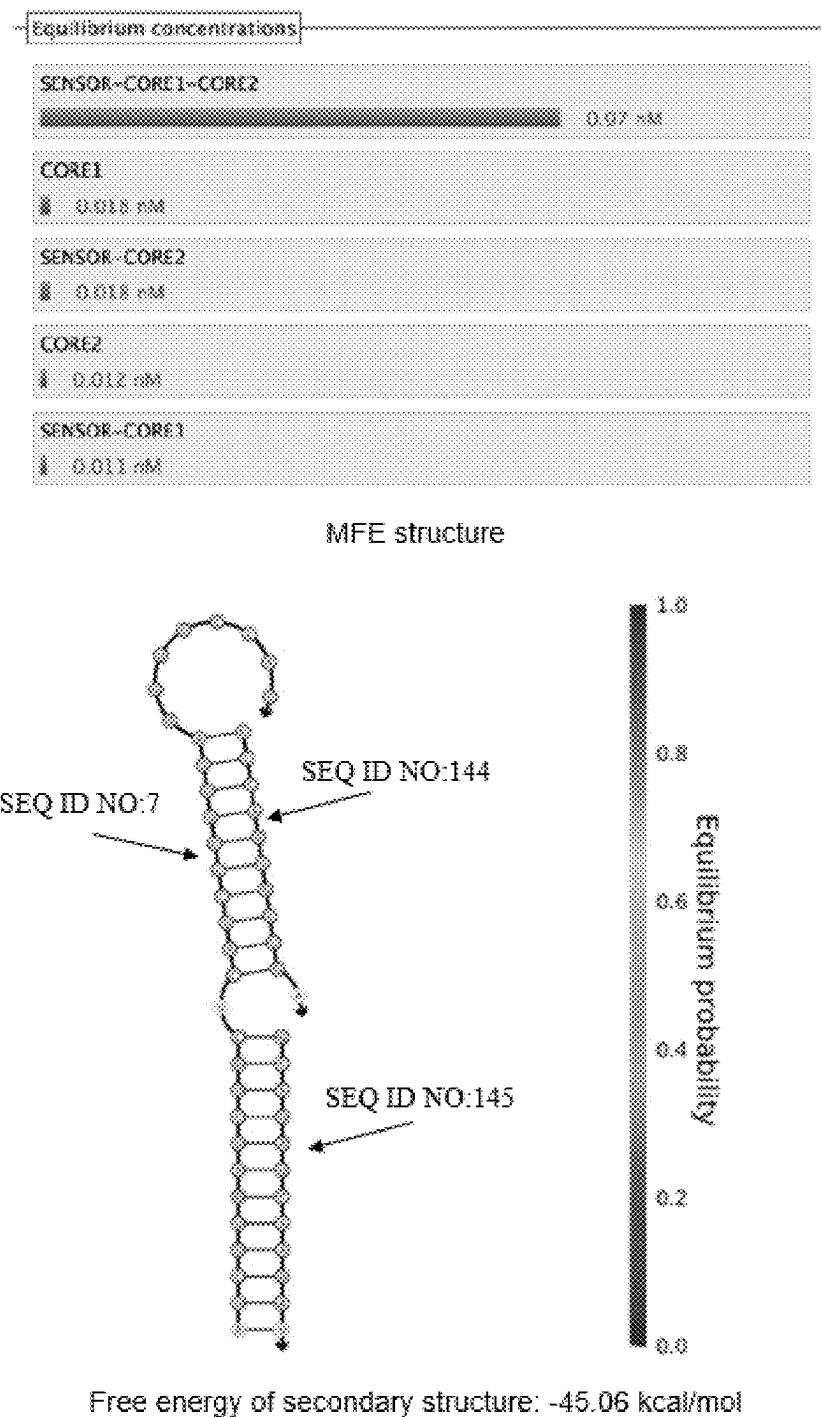
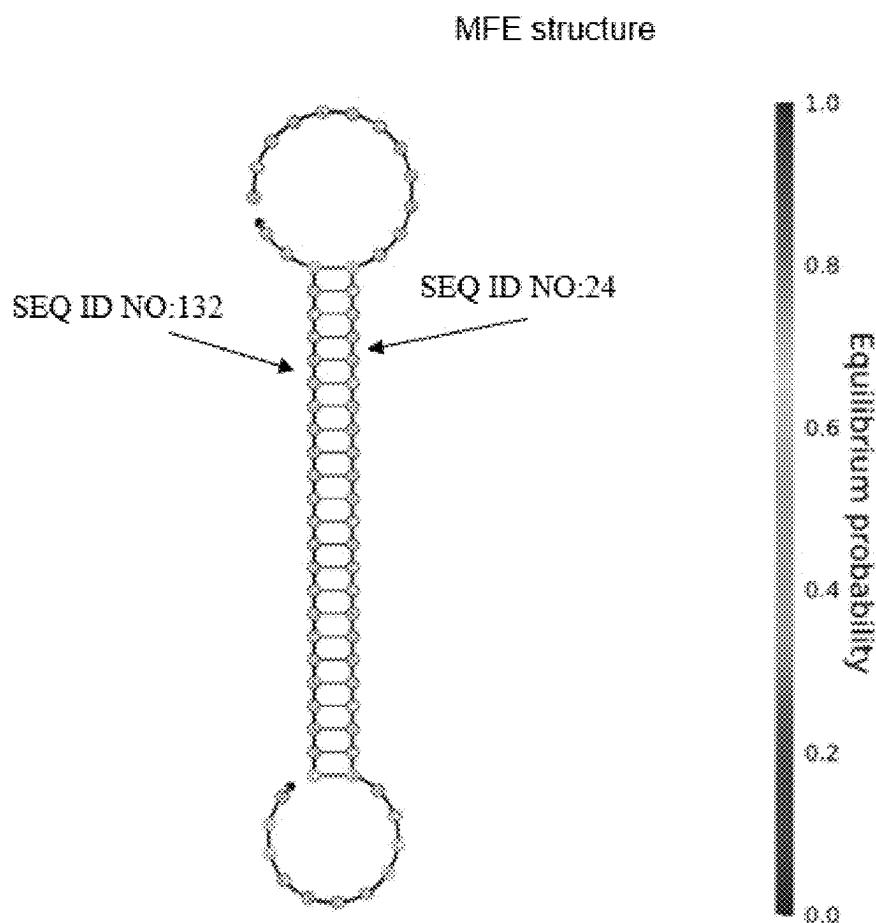
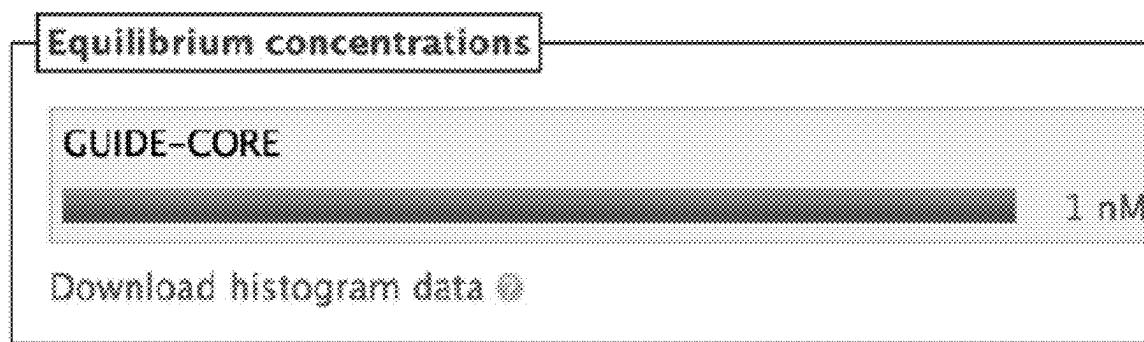
FIG. 69A

FIG. 69B

Free energy of secondary structure: -44.38 kcal/mol

FIG. 70

Sensor vs NCBI human transcripts

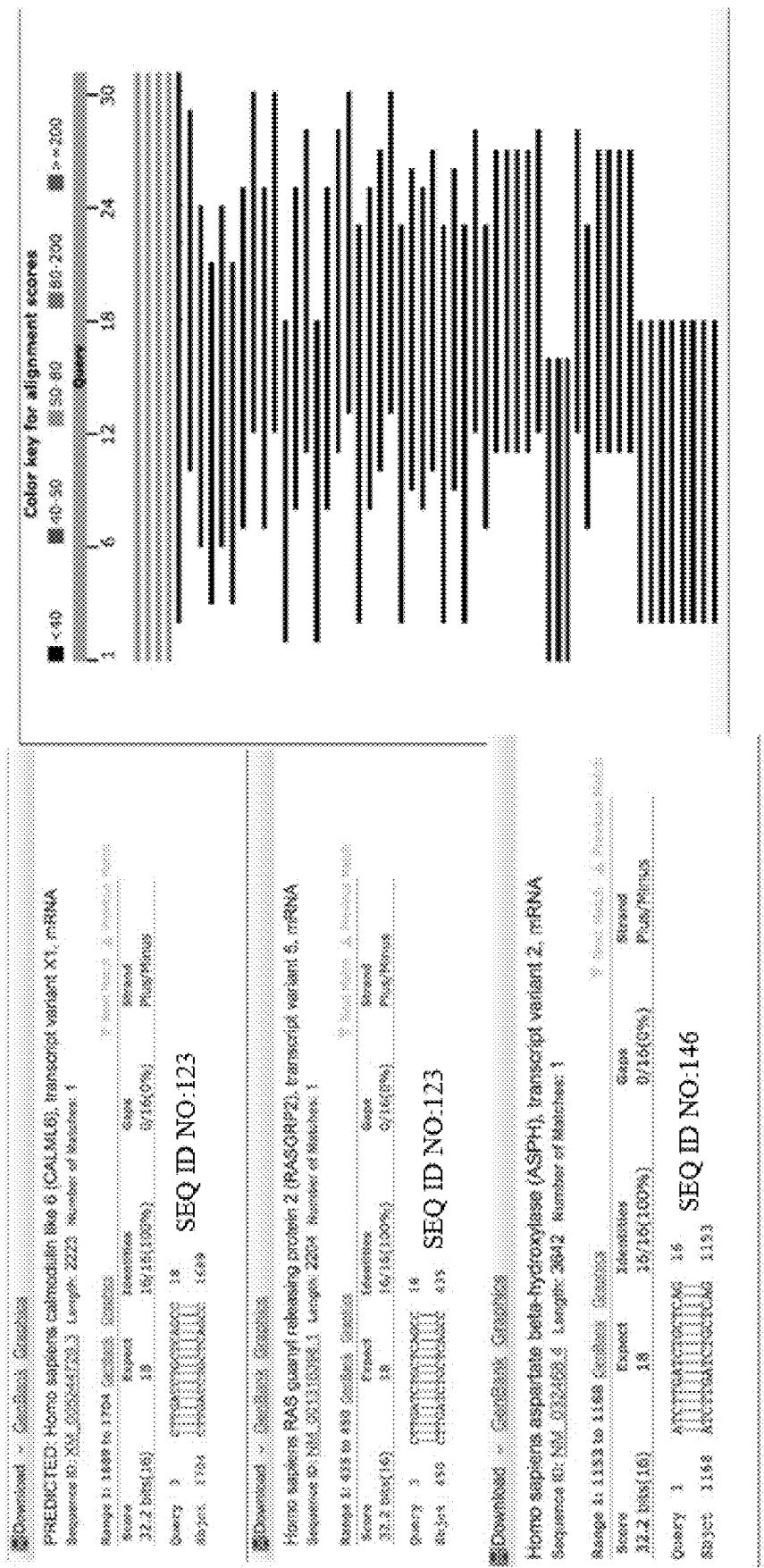


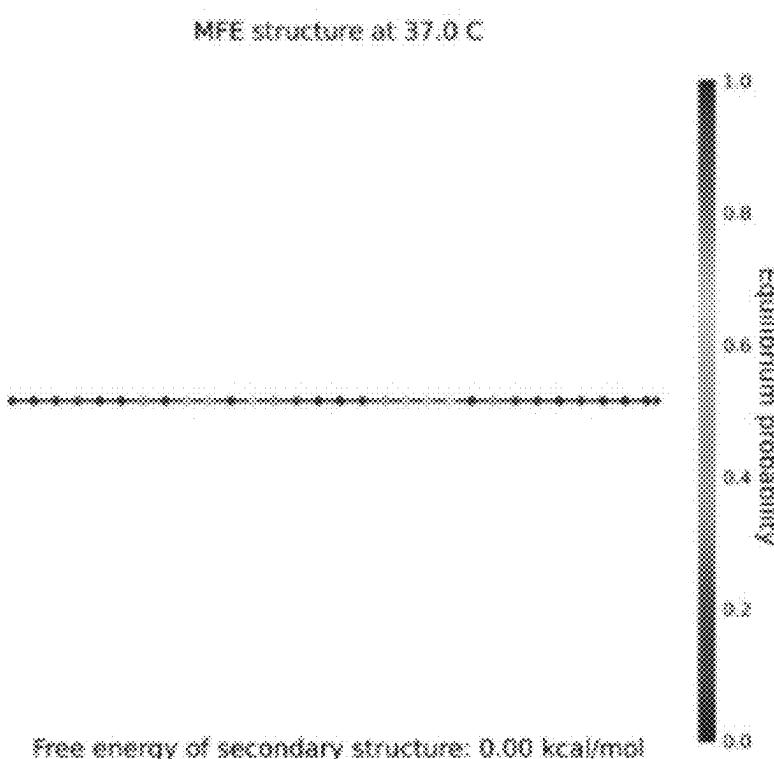
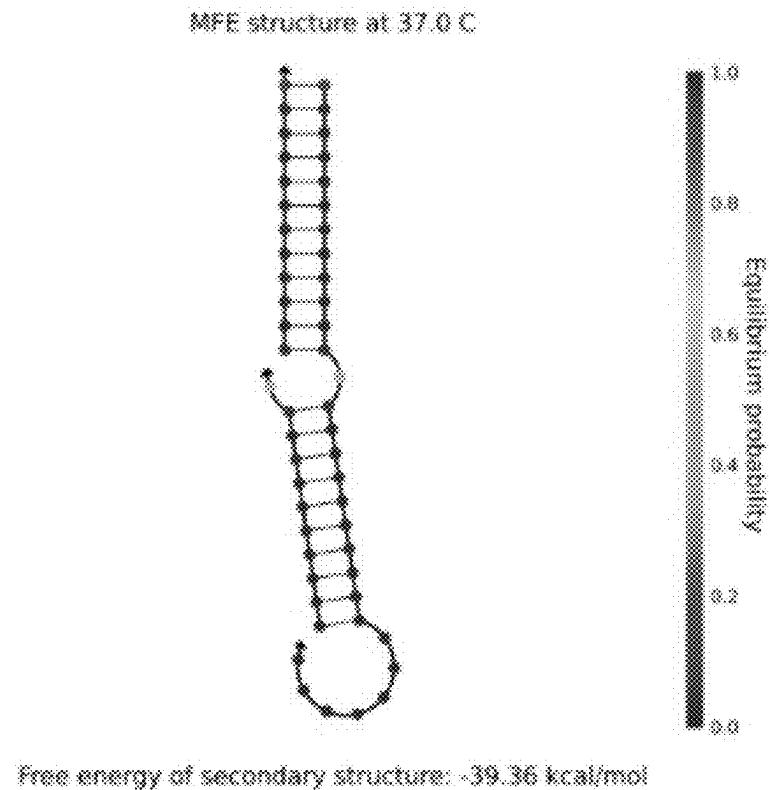
FIG. 71

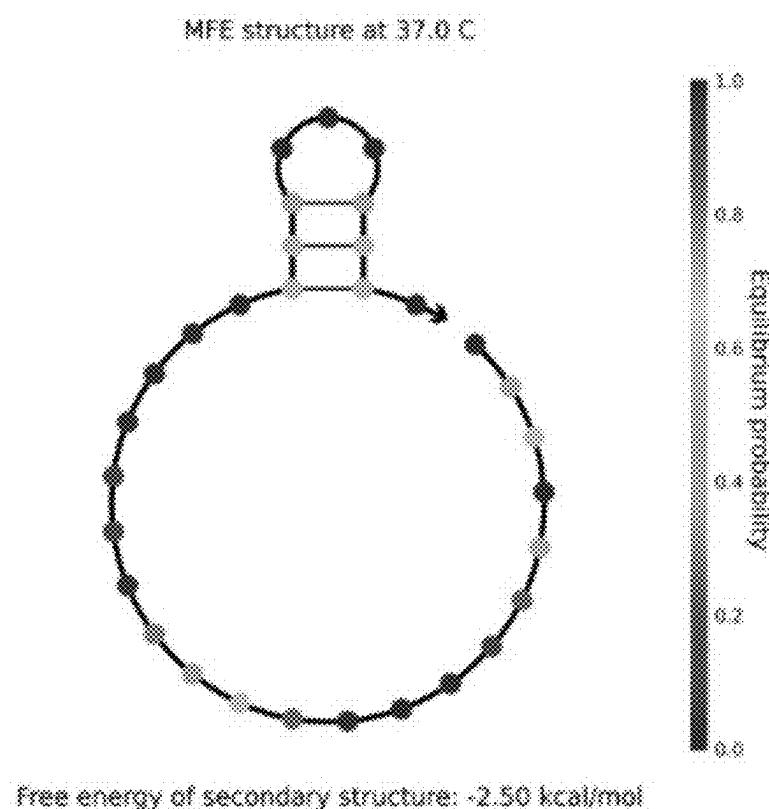
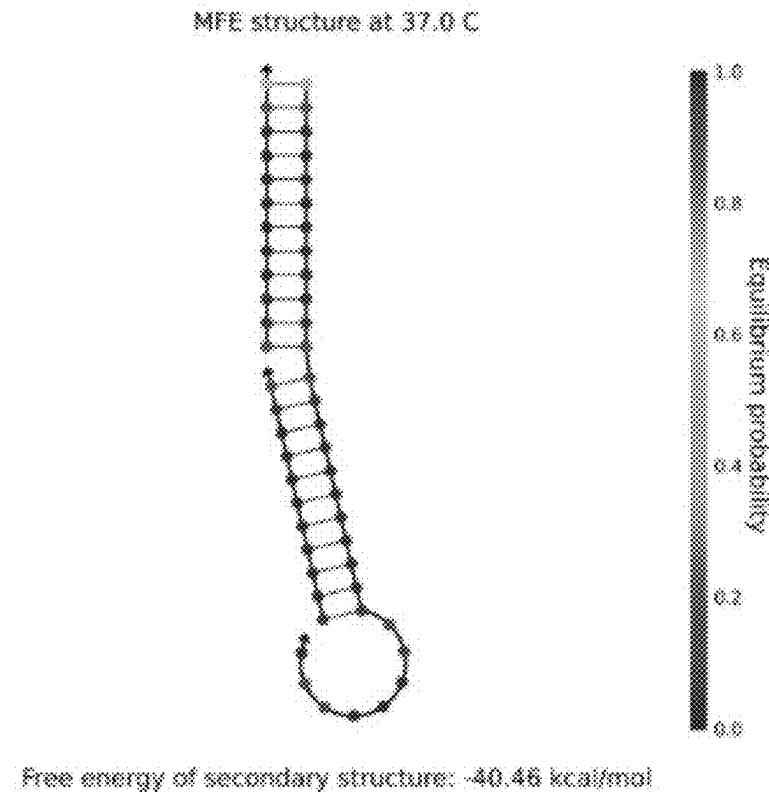
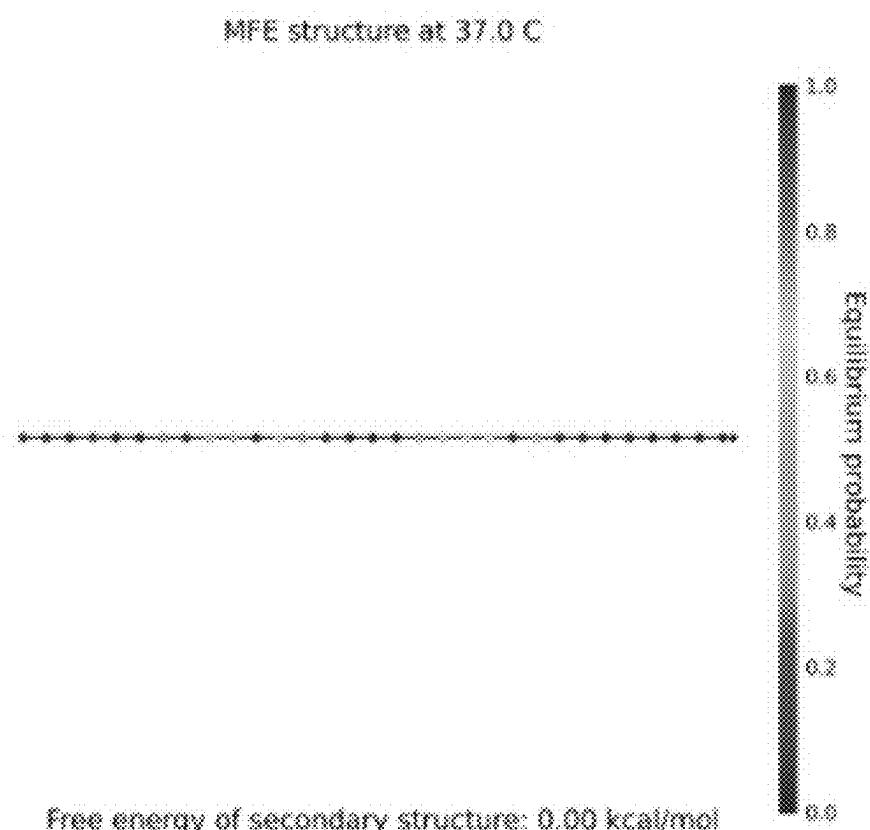
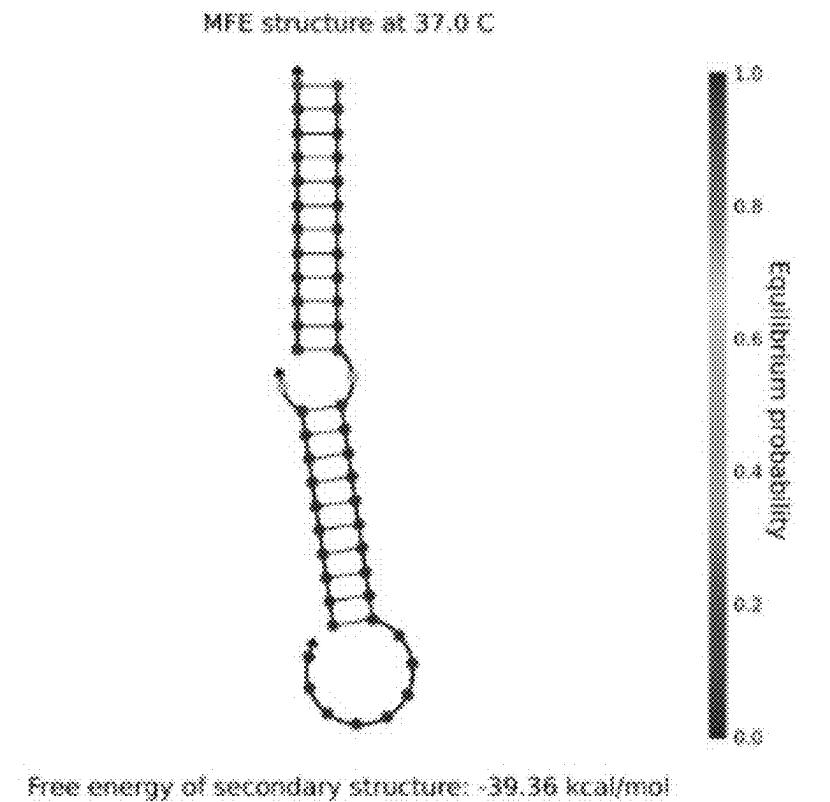
FIG. 72

FIG. 73

1

**CONDITIONAL-SIRNAS AND USES
THEREOF IN TREATING CARDIAC
HYPERTROPHY**

PRIORITY CLAIM

This application is a U.S. National Phase Application of International Application No. PCT/US2018/046379, filed Aug. 10, 2018, which claims priority to U.S. Provisional Patent Application No. 62/543,882, filed Aug. 10, 2017, the subject matter of which is hereby incorporated by reference in its entirety, as if fully set forth herein.

**STATEMENT REGARDING FEDERALLY
SPONSORED RESEARCH**

This invention was made with government support under Grant Number 1332411, awarded by National Science Foundation through the Emerging Frontiers in Research and Innovation, Origami Design for Integration of Self-assembling Systems for Engineering Innovation (EFRI-ODIS-SEI), and Grant Number A1029329, awarded by National Institutes of Health (NIH). The government has certain rights to the invention.

SEQUENCE LISTING

This disclosure includes a sequence listing, which is submitted in ASCII format via EFS-Web, and is hereby incorporated by reference in its entirety. The ASCII copy, created Nov. 29, 2021, is named SubstituteSequenceListing.txt and is 252 kilobytes in size.

BACKGROUND

RNA interference (RNAi) is a sequence-specific mRNA degradation pathway mediated by siRNA duplexes, key for cellular immunity and developmental regulation. Researchers have utilized synthetic RNAi triggers for therapeutics by inhibiting a specific gene product found to be essential in disease driving pathways but non-essential for normal functioning.

Consider however that some genes essential in disease progression may have vital functions in normal cells and are dangerous to target. Meanwhile other upregulated genes are not essential for disease progression, but serve as effective indicators. Therefore, there is a need in the art to develop effective therapies to exploit this differential expression in various indications. The conditionally active siRNA complexes described below are candidates for investigation of treatments for those indications, such as cardiac hypertrophy.

Heart Failure (HF) is a chronic cardiac condition, affecting millions of people worldwide, and considered a major contributor to healthcare expenditure in the US. Compensatory cardiac hypertrophy is one of the initial hallmarks of pathological ventricular remodeling, which is characterized by an upregulation of a variety of genes and miRNA that mediate and regulate myocardial hypertrophy, and ultimately HF. Even though important advances have been done in the treatment of HF, no cardiac specific therapies with lack of adverse effects have been developed to date. Therefore, there is a need in the art to develop an effective therapy for HF.

BRIEF DESCRIPTION OF THE DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application

2

publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

FIG. 1 shows a comparison of secondary and tertiary structure (from full atomistic MD simulations) of a Cond-siRNA construct according to one embodiment. Black arrows show corresponding features between the 2D and 3D representations.

FIG. 2 is a diagram showing the RNAi pathway.

FIG. 3 shows toehold mediated strand displacement process of conditional siRNA. In step I, c-siRNA meets RNA transcript with correct activation sequence (Input). In step II, an Input RNA binds to the toehold. Step III shows toehold mediated strand displacement. Step IV shows the sensor strand and input forming a waste duplex that separates from the pro-siRNA. In step V, XRN1, exosome and other cytosolic RNases rapidly degrade unprotected overhangs, turning pro-siRNA into efficient Dicer substrate. In step VI, siRNA is processed by Dicer for incorporation into RISC. The basic biophysical process of toehold mediated strand displacement includes a fast 1D random walk: uS to mS for each of N² steps. This results in sequence specificity from both toehold and duplexes. Thermodynamically stable chemical modifications are confined to sensor strand to avoid kinetic traps.

FIGS. 4A-C: A) General construct design of cond-siRNA with green sensor strand designed reverse comp. to signal gene mRNA, red core strand with nick either 11 or 12 bp from toehold end on sensor side designed comp. to sensor and guide, and yellow guide strand designed reverse comp. to target gene mRNA. B) Model of cond-siRNA. C) Molecular simulation of cond-siRNA.

FIG. 5 shows an overview of the design process for Cond-siRNAs according to one embodiment.

FIG. 6 shows a hypothetical sensor duplex for mRNA used to check for thermodynamic stability of the sensor according to one embodiment.

FIG. 7 shows a structure calculation showing sensor strand with low internal secondary structure according to one embodiment.

FIG. 8 shows a histogram showing a 97% predicted formation of the hypothetical sensor duplex and correct secondary structure according to one embodiment.

FIG. 9 shows a hypothetical sensor duplex for miRNA used to check for thermodynamic stability of the sensor according to one embodiment.

FIG. 10 shows a structure of the RNAi targeting duplex according to one embodiment.

FIG. 11 is a schematic diagram of a signaling pathway involved in cardiac gene program regulating hypertrophy.

FIGS. 12A-B show schematic depicting in vivo and in vitro screening approaches.

FIGS. 13A-B: A) NuPack generated secondary structure of selected NPPB 31 bp sensor strand. Minimal secondary structure with approximately 40-50% probability of folding onto itself. B) NPPB sensor strand bound to 5' and 3' core overhangs 99% of the time.

FIGS. 14A-B: A) NuPack generated secondary structure of selected MYH7 31 bp sensor strand. Minimal secondary structure with approximately 30% probability folding onto itself. B) NPPB sensor strand bound to 5' and 3' core overhangs 97% of the time.

FIGS. 15A-B: A) NuPack generated secondary structure of HDAC2 25 bp guide strand. Significant secondary structure indicated by the equilibrium probabilities of binding. B)

NuPack generated secondary structure of HDAC2 guide bound to core strand with the 5' and 3' overhangs that bind to the appropriate sensor strand. Although guide strand has

significant and strong secondary structure, when placed with core strand, guide binds to core 100%.

FIG. 16 shows test constructs detecting murine ANP mRNA and targeting murine Calcineurin according to certain embodiments.

FIG. 17 shows test constructs detecting murine and human mir-23a-3p and targeting murine Calcineurin according to certain embodiments.

FIG. 18 is a schematic depicting a site of injury that can be targeted for treatment according to methods of the present invention.

FIG. 19 is a series of bar graphs depicting experimental results of differential gene expression in tissues of wild-type mice in homeostasis.

FIG. 20: Gene expression in NRVM under hypoxia.

FIG. 21: Differential miRNA expression in NRVM under hypoxia.

FIG. 22: Gene expression in NRVM after PE treatment.

FIG. 23: Differential miRNA expression in NRVM after treatment with PE.

FIG. 24: Gene expression in mice with non-ischemic (TAC) and ischemic (I/R) HF.

FIG. 25: miRNA expression in mice with non-ischemic (TAC) and ischemic (I/R) HF.

FIG. 26 shows an equilibrium probability for an MFE structure.

FIG. 27 shows an equilibrium probability for an MFE structure.

FIG. 28 shows an equilibrium probability for an MFE structure.

FIG. 29 shows an equilibrium probability for an MFE structure.

FIG. 30 shows (ANP:calcineurin) and (mir-23a-3p:calcineurin) Cond-siRNAs on 10% non-denaturing PAGE gel in TBE. The correct assemblies are indicated in the green boxes.

FIG. 31 shows results of a dual luciferase assay of mir-23a-3p calcineurin Cond-siRNA according to certain embodiments.

FIG. 32 is a bar graph showing RNAi activity against Calcineurin in NRVM cells under PE stimulation according to one embodiment.

FIG. 33 shows images of NRVM cells with and without PE stimulation when treated with scrambled siRNA (negative control), (ANP:calcineurin) Cond-siRNA, and commercial calcineurin siRNA (positive control) according to one embodiment.

FIG. 34 shows results of cell size quantitation according to one embodiment.

FIG. 35A shows Post-MI cardiac remodeling and left ventricular enlargement.

FIG. 35B is a bar graph showing experimental results where patients with any of the patterns of LV remodeling post-MI had a greater risk of the composite of cardiovascular (CV) death, MI, heart failure (HF), stroke, or resuscitated cardiac arrest.

FIG. 36 is a flowchart accompanied by a corresponding schematic showing the RNA interference pathway starting with pri-miRNA processing in the nucleus.

FIG. 37 is a schematic showing post-MI remodeling.

FIG. 38 is a series of bar graphs depicting experimental results of differential miRNA expression in tissues of wild-type mice in homeostasis.

FIG. 39 is a table including candidate sensor strands for the 3' UTR of the human myh7 gene. Column abbreviations are as follows: BS is Bad Segments; 3LN is 3-Letteredness; NBP is Number Bad Points; P is Position.

FIG. 40 is a table including candidate sensor strands for the 3' UTR of the rat myh7 gene. Column abbreviations are as follows: BS is Bad Segments; 3LN is 3-Letteredness; NBP is Number Bad Points; P is Position.

FIG. 41 is a table including candidate sensor strands for the 3' UTR of the human nppa gene. Column abbreviations are as follows: BS is Bad Segments; 3LN is 3-Letteredness; NBP is Number Bad Points; P is Position.

FIG. 42 is a table including candidate sensor strands for the 3' UTR of the rat nppa gene. Column abbreviations are as follows: BS is Bad Segments; 3LN is 3-Letteredness; NBP is Number Bad Points; P is Position.

FIG. 43 is a table including candidate sensor strands for the 3' UTR of the human nppb gene. Column abbreviations are as follows: BS is Bad Segments; 3LN is 3-Letteredness; NBP is Number Bad Points; P is Position.

FIG. 44 is a table including candidate sensor strands for the 3' UTR of the rat nppb gene. Column abbreviations are as follows: BS is Bad Segments; 3LN is 3-Letteredness; NBP is Number Bad Points; P is Position.

FIG. 45 shows a top view of a 3D schematic of a Cond-siRNA construct according to one embodiment.

FIG. 46 shows the design of sensor miR-23-a-3p gene sequence.

FIG. 47 illustrates NCBI check for sensor strand.

FIG. 48 illustrates NCBI check for calcineurin and HDAC2 guide strand sequences.

FIG. 49 shows the secondary structure and MFE structure at 37° C. of the full miR-23a-3p sensor strand with toehold for calcineurin.

Figs. 50A-50D show that NuPack analyses were performed on core (FIG. 50A), guide (FIG. 50B), Sensor with two small overhangs of core: 97% (FIG. 50C), and calcineurin guide with core: 100% (FIG. 50D).

FIG. 51 shows NCBI check for calcineurin guide strand vs. human constructs.

Figs. 52A-52D show that NuPack analyses of miR-23a-3p sensor strand for HDAC2 were performed on core (FIG. 52A), guide (FIG. 52B), HDAC2 guide with core: 100% (FIG. 52C), and sensor with core overhangs: 97% (FIG. 52D).

FIG. 53 shows NCBI check for HDAC2 guide strand vs. human transcripts.

Figs. 54A-54B illustrate the check of guide vs. NCBI human transcripts and sequence alignment, respectively.

FIG. 55 shows the MFE structure of SEQ ID NO: 4.

FIG. 56 shows the BNP sensor sequence (SEQ ID NO: 4) together with core and guide sequences.

Figs. 57A and 57B show Nupack analyses of BNP sensor (SEQ ID NO: 4) with overhangs, and guide with core, respectively.

FIG. 58 shows NCBI check of BNP sensor first candidate vs. human transcripts.

FIG. 59 shows the MFE structure of SEQ ID NO: 5.

FIG. 60 shows the BNP sensor sequence (SEQ ID NO: 5) together with core and guide sequences.

Figs. 61A and 61B show Nupack analyses of BNP sensor (SEQ ID NO: 5) with overhangs, and guide with core, respectively.

FIG. 62 shows NCBI check of BNP sensor second candidate vs. human transcripts.

FIG. 63 shows the MFE structure of SEQ ID NO: 6.

FIG. 64 shows the BNP sensor sequence (SEQ ID NO: 6) together with core and guide sequences.

FIG. 65 shows Nupack analysis of guide with core for the third BNP candidate.

FIG. 66 shows NCBI check of BNP sensor third candidate vs. human transcripts.

FIG. 67 shows the MFE structure of SEQ ID NO: 7.

FIG. 68 shows the MYH7 sensor sequence (SEQ ID NO: 7) together with core and guide sequences.

FIGS. 69A and 69B show Nupack analyses of MYH7 sensor (SEQ ID NO: 7) with overhangs, and guide with core, respectively.

FIG. 70 shows NCBI check of MYH7 sensor vs. human transcripts.

FIG. 71 shows the MFE structure of NPPA HDAC2 construct #1.

FIG. 72 shows the MFE structure of NPPA HDAC2 construct #3.

FIG. 73 shows the MFE structure of NPPA calcineurin construct #1.

DETAILED DESCRIPTION

Overview of Conditional-siRNA

Described herein are conditional siRNA complexes (also referred to herein as Cond-siRNA, a conditional RNA-sensor, or an RNA-sensor) that include a therapeutic component (e.g., siRNA molecule) associated with a molecular sensor via a core molecule. The conditional siRNA complexes are inactive under normal conditions, but are activated upon interaction between the molecular sensor and a biomarker. Such molecules are synthetic riboswitch molecules that allow an input gene or RNA molecule to “switch on” an RNAi pathway against a target output gene.

An RNA-sensor molecule or complex includes sensor strand, a guide strand, and a core strand that bind to each other to form a multi-strand molecular complex having a dual duplex structure shown in FIGS. 1, 45. In certain embodiments, those three strands (core, sensor and guide) form two parallel oligonucleotide duplexes connected in a double crossover configuration. [14] (See FIG. 1). In some aspects, the length of each of the oligonucleotide duplexes is sufficient to operate within the RNA interference (RNAi) pathway (See FIGS. 2, 36). For example, the duplexes may be between about 15 and 30 base pairs in length. In some embodiments, the duplexes are between 15 and 20 base pairs in length, between 20 and 25 base pairs in length, between 25 and 30 base pairs in length. In other embodiments, the duplexes are about 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 25, 26, 27, 28, 29, 30, or more than 30 base pairs in length.

The double crossover configuration as shown in FIG. 1 represents the inactive or “OFF” state of the RNA-sensor complex wherein the sensor duplex inhibits RNAi loading of the siRNA duplex, serving as a “lock” on RNAi activity. In the OFF state, the guide strand binds a first portion (or “passenger” segment) of the core strand to form an siRNA duplex that serves as a pro-RNA molecule. The pro-RNA molecule operates in the RNAi pathway of a target cell to alter expression of a target gene or target RNA molecule associated with a pathological condition (i.e., the “therapeutic target molecule”). The second duplex is formed by the sensor strand binding to a second portion (or “protection” segment) of the core strand to form the sensor duplex. In some embodiments, the core strand has a third portion (or “protection” segment) that binds the sensor strand. In certain such embodiments, the core strand includes the passenger strand (P) that is joined to first and second protection segments (A, B) at each end by a linker (L1, L2) in the following configuration:

5' B-L2-P-L1-A 3'

The sequence of the core strand is determined by the sequences of the sensor and guide strands, and may be fully or complementary to the sensor strand, the guide strand, or both. Any suitable linker can be used in accordance with the 5 embodiments described herein, including, but not limited to, an internal C3 spacer, a C6 linker, a tri-ethylene glycol linker.

The RNA-sensor complex is activated to the “ON” state upon interaction with a biomarker in the cell expressing a 10 phenotype associated with the pathological condition targeted by the guide strand of the siRNA duplex. This activation is primarily due to the design of the sensor strand, which serves as the activation signal for RNAi activity. When this is the case, the RNA-sensor complex is said to detect the biomarker.

The sensor strand includes a nucleotide sequence 15 designed to bind the biomarker associated with the pathological condition (i.e., “pathological biomarker”). Binding to the biomarker is initiated by the binding of at least one 20 toehold segment (single stranded) to an input RNA strand that encodes at least a portion of the pathological biomarker, as shown in FIG. 3. Upon displacement of the sensor strand, the sensor and input strands from a waste duplex that separates from the pro-siRNA molecule, allowing the pro-siRNA to be processed by the target cell’s RNAi system. The structure and binding dynamics of the conditional-siRNAs described herein is explained further in U.S. Pat. No. 9,725, 715, the content of which is incorporated herein by reference in its entirety.

The sequence of the sensor strand can be fully or partially 30 complementary to an RNA sequence present in the pathological biomarker. In certain embodiments, the sensor strand is 100% complementary to the RNA sequence present in the pathological biomarker. Other embodiments may include a 35 sensor strand that is largely complementary to the RNA sequence present in the pathological biomarker, for example, the sensor strand may be greater than 70% complementary, greater than 75% complementary, greater than 80% complementary, greater than 85% complementary, greater than 90% complementary, greater than 95% complementary, greater than 96% complementary, greater than 97% complementary, greater than 98% complementary, or greater than 99% complementary to the RNA sequence present in the pathological biomarker.

In some embodiments, the pathological biomarker is an 40 RNA sequence that forms or encodes a molecule that is associated with the pathologic condition. In some aspects, the pathological biomarker is an RNA sequence that is present in the target cell under pathological conditions, but 45 is substantially absent under normal conditions. Alternatively, the pathological biomarker is an RNA sequence that is upregulated in the target cell under pathological conditions as compared to normal conditions.

The guide strand includes a Dicer cleavage site near the 50 3' end. The sequence between the Dicer cleavage site and the 3' terminus of the guide strand is either fully or partially complementary to a nucleotide sequence found in the therapeutic target molecule (e.g., target gene, target mRNA or target miRNA). When this is the case, the Cond-siRNA is 55 said to target the gene or RNA molecule. In certain embodiments, the guide strand is 100% complementary to the nucleotide sequence found in the therapeutic target molecule. Other embodiments may include a guide strand that is 60 largely complementary to the nucleotide sequence found in the therapeutic target molecule, for example, the guide strand may be greater than 70% complementary, greater than 75% complementary, greater than 80% complementary,

greater than 85% complementary, greater than 90% complementary, greater than 95% complementary, greater than 96% complementary, greater than 97% complementary, greater than 98% complementary, or greater than 99% complementary to the nucleotide sequence found in the therapeutic target molecule.

A challenge of using oligonucleotides *in vivo* lies in preventing nuclease degradation of RNA nucleotides. Several chemical modifications in the sensor strand can be used to overcome this challenge. For example, Locked Nucleic Acids (LNAs) include a modification of RNA nucleotides with an extra bridge between the 2' O and 4' C increases thermal stability of RNA duplexes and allows for resistance to nucleases. 2'-O-Methyl modifications confer stability, increase binding affinity to RNA nucleotides and prevent degradation by nucleases. And, phosphorothioate: modification by replacing one of the non-bridging oxygens in the phosphate linkage between bases with a sulfur that reduces nucleolytic degradation; however also lowers binding affinity.

Thus, in certain embodiments, the RNA-sensor complex includes one or more modifications to the nucleotide sequence of the sensor strand, the core strand, and/or the guide strand. Exemplary modifications that may be used include, but are not limited to, locked nucleic acids (LNA), peptide nucleic acids (PNA), 2'-O-methyl modifications, morpholino modifications, phosphorothioate modifications, terminal modifications, and other linker or backbone modifications or connections. Additional chemical modifications may be chosen according to methods described in U.S. Pat. No. 9,725,715B2, the disclosure of which is hereby fully incorporated herein.

The approach of designing a cond-siRNA sensor complex for use in treating a disease or other pathological condition using the cond-siRNA sensor complexes is advantageous in that it allows the complex to become biologically active only in diseased cells AND remain OFF in healthy cells. In addition, the approach allows for increased disease cell specificity and prevents toxicity from delivery to unintended off-targets. Further, the approach combines disease specificity from one gene with treatment efficacy from a second gene to create therapeutics that are precisely tailored to specific gene expression patterns. Still further, the approach is advantageous due to steric hindrance of the two RNA duplexes positioned in a parallel configuration (FIG. 4). The sensor strand inhibits RNAi loading of siRNA and will only displace when activated in disease cells.

Overview of Methods for Designing a Conditional siRNA Complex

An siRNA complex is designed based on biomarkers and therapeutic target molecules that are specific to each cell type, pathological condition, and/or indication. According to certain embodiments, methods for designing and testing each conditional siRNA complex includes several steps, as described below.

FIG. 5 shows an overview of the design process. In certain embodiments methods for designing a conditional siRNA complex (the “design method”) includes a step of determining a biomarker that will serve as an input for activation and a therapeutic target for RNAi inhibition. This step may include a determining one or more factors that are differentially expressed (i.e., upregulated or present in a diseased cell as compared to a normal cell) using methods known in the art.

The design method further includes a step of generating a list of candidate target segments of the biomarker (i.e., target mRNA sequence or target miRNA sequence) that can serve

as a biomarker segment for binding the sensor strand, and then designing sensor strands for each biomarker.

The design method further includes a step of estimating the thermodynamic stability of the resulting sensor strand-biomarker duplexes (the sensor duplex) generated by the target segments and sensor strands by using secondary structure prediction tools used in the art [15].

The design method further includes a step of checking for the uniqueness of the binding site for the most stable sensor duplexes against the known transcriptome of the animal to which the conditional siRNA complex will be tested against.

The design method further includes a step of generating a list of guide strand sequences by using a protocol that may include, but is not limited to, standard siRNA design tools, literature references, or heuristic rules.

The design method further includes a step of creating a Dicer substrate from the chosen guide strand sequences.

The design method further includes a step of generating sequences for the core strand that connect the sensor strands to the guide strands.

The design method further includes a step of checking that the sensor: guide pairing does not create unwanted interactions.

The design method further includes a step of selecting a pattern of suitable chemical modifications as described herein, and optionally simulating the constructs using molecular simulation methods used in the art [16] to simulate the constructs (optional).

The design method may also include a method of synthesizing or purchasing the sensor, core, and guide strands from commercial vendors such as Qiagen, Dharmacaon, or IDT, the constructs of which are then assembled, characterized, and purified using gel electrophoresis.

The design method further includes a step of conducting preliminary biological testing and validation of the construct function, and then optionally test in *in vitro* and *in vivo* models of pathological conditions, including, but not limited to, MI induced maladaptive hypertrophy as described below.

Additional embodiments related to designing the guide, the sensor and the core strands are explained below.

Method for Designing Sensor Strands for mRNA Biomarker

According to certain embodiments, methods for designing and testing sensor strands that target an mRNA biomarker includes an algorithm that includes several steps, as described below.

In certain embodiments, a method for designing a sensor strand for an mRNA biomarker (the “mRNA sensor design method”) includes a step of identifying the 3' UTR for each messenger RNA biomarker.

The mRNA sensor design method further includes a step of generating all possible consecutive 31 base sequences for each 3' UTR identified above.

The mRNA sensor design method further includes a step of obtaining the prospective sensor strand sequence for each sequence segment from the previous step by identifying the reverse complement (full or partial) of each sequence

The mRNA sensor design method further includes a step of checking each sensor strand sequence for the following undesirable features: (i) three or more consecutive Gs, and (ii) four or more consecutive A or U bases.

The mRNA sensor design method further includes a step of checking each sensor strand sequence for the following desirable features: (i) higher than 50% G/C bases—this correlates with thermodynamic stability, (ii) “three letteredness,” (iii) The first base at the 5' end of the sensor strand is a C or a G; and (iv) the 9th base from the 3' end of the sensor strand is a C or a G. According to the embodiments

described herein, “three letteredness” is defined as the proportion of the sequence comprising of the three most numerous bases (e.g., the extent to which sequence is mostly made of A, U, C; or C, G, A; or A, U, G). A higher three letteredness score correlates with lower internal secondary structure. Exemplar ranking tables can be seen in FIGS. 39-44, which correspond to the genes or nucleotide sequences in Appendices C-H, submitted herewith.

The mRNA sensor design method further includes a step of ranking all possible sensor strands. Strands with the least number of features from 4 and the highest scores from 5 are ranked highest

The mRNA sensor design method further includes a step of generating hypothetical sensor duplexes using the pattern shown in FIG. 6, starting from the highest ranked strands.

The RNA sensor design method further includes a step of using Nupack or similar secondary structure prediction codes to calculate the following, starting from the highest ranked strands: (i) the internal secondary structure of the sensor strand (lower amounts of internal secondary structure are desirable (FIG. 7), (ii) the thermodynamic stability of the hypothetical duplex from 7. Ideally, at 1 nM strand concentration, Nupack should predict that >90% or >95% of component strands should form the hypothetical sensor duplex (FIG. 8); and (iii) if sensor duplex is not stable, can adjust 1 to 5 bases at the 5' terminus of the sensor sequence to increase stability at the cost of reducing complementarity to the corresponding binding site on the putative biomarker.

The RNA sensor design method further includes a step of screening the sensor strand for thermodynamically stable duplexes using NCBI BLAST according to the following parameters: (i) use the “somewhat similar” search option, (ii) for sensor sequences, the 8 bases at the 3' terminus (constituting the 3' toehold) should have no more than 5 bases complementary to known transcripts in the target animal (eg, human or mouse) other than the intended biomarker, and (iii) if the first two criteria not met, broaden sequences considered in 1 to the coding region or the entirety of the mRNA.

Method for Designing Sensors for miRNA Biomarker

According to certain embodiments, methods for designing and testing sensor strands that target an miRNA biomarker includes an algorithm that includes several steps, as described below.

In certain embodiments, a method for designing a sensor strand for an miRNA biomarker (the “miRNA sensor design method”) includes a step of identifying a guide sequence for each miRNA biomarker, to which the sensor strand is designed to bind (typically approximately 21 bases according to one aspect)

The miRNA sensor design method further includes a step of obtaining the reverse complement (full or partial) of the miRNA guide sequence.

The miRNA sensor design method further includes a step of adding 8 more bases to the 5' end of the sequence from the prior step.

The miRNA sensor design method further includes a step of generating hypothetical sensor duplexes using the pattern shown in FIG. 9, starting from the sequence developed in the prior step.

The miRNA sensor design method further includes a step of using Nupack or similar secondary structure prediction codes to calculate the following: (i) the thermodynamic stability of the hypothetical duplex from the prior step. Ideally, at 1 nM strand concentration, Nupack should predict that >90% or >95% of component strands should form the hypothetical sensor duplex. (ii) if sensor duplex is not stable

or the secondary structure is incorrect, determine whether the 8 terminal bases at the 5' end of the sensor strand, or the length of strand A or strand B can be altered or modified to optimize thermodynamic stability.

The miRNA sensor design method further includes a step of screening the sensor strand for thermodynamically stable duplexes in NCBI BLAST according to the following parameters: (i) use the “somewhat similar” search option, (ii) for sensor sequences, the 8 bases added at the 5' end of the sensor should not increase complementarity to transcripts other than the intended miRNA. If they do, adjust the sequence and start over from 4.

Methods for Designing a Guide Strand Sequence Against a Therapeutic Target Molecule

According to certain embodiments, methods for designing a guide strand sequence against a therapeutic target gene or RNA molecule (e.g., mRNA or miRNA) includes several steps, as described below.

In certain embodiments, a method for designing a guide strand sequence against a therapeutic target (the “guide strand design method”) includes a step of obtaining one or more prospective guide strand sequences using at least one of the following methods: (i) find a published guide strand sequence for the intended target; (ii) find a known miRNA target site on the target gene, or (iii) use a published algorithm or design tool known in the art [17, 18].

The guide strand design method further includes a step of checking the guide sequence to make sure that the 6 bases at the 5' domain (FIG. 10) is more AU rich than the 6 bases in the 3' domain (FIG. 10). This will improve probability for correct strand loading [19]. Ideally, the 3' domain should be CG rich, and terminate in a CG base-pair.

The guide strand design method further includes a step of adding four terminal bases to the 5' end of the guide strand to complete the duplex. Those should be CG rich to improve thermodynamic stability.

The guide strand design method further includes a step of constructing the hypothetical RNAi targeting duplex as shown in FIG. 10.

The guide strand design method further includes a step of checking that the guide strand has weak internal secondary structure and minimal tendency to bind to itself (no more than 10% at 1 nM strand concentration) using Nupack or similar standard secondary structure calculation tool. Adjust bases added in 3 as necessary.

Methods for Designing a Core Strand Sequence and Checking Compatibility of Pairing Sensor to Guide

According to certain embodiments, methods for designing a core strand sequence and checking compatibility of pairing sensor to guide includes several steps, as described below.

In certain embodiments, a method for designing a guide strand sequence against a therapeutic target (the “core strand design method”) includes a step of choosing a suitable combination of sensor and guide strands, methods for designing those strands are discussed above and in the working examples, according to the embodiments described herein.

The core strand design method further includes a step of constructing the core strand by constructing a strand of the form 5'-B-C3-P-C3 A-3' where A and B are the sequence of complementary strand B from the hypothetical sensor duplex (FIG. 6 or 9), P is the sequence of the passenger strand from the hypothetical RNAi duplex (FIG. 10) and C3 are C3 linkers.

The core strand design method further includes a step of using Nupack or similar standard secondary structure calculation tool to check that the guide strand and core strand

11

base-pairing has the following properties: (i) >95% of strands are base-paired in the correct duplex at 1 nM strand concentration, (ii) the guide strand duplex has the correct conformation, with a ~23 base-pair duplex, a two base 3' guide strand overhang, and 10-12 base 5' and 3' core overhangs with minimal secondary structures, and (iii) If above criteria not met, choose new sensor or guide pairing.

Conditional siRNA Complexes for Treating Cardiac Hypertrophy

Disclosed herein is a therapeutic strategy that targets molecular pathways involved in cardiac hypertrophy (that often results after a myocardial infarction), with minimal off-target effects. A myocardial infarction (MI) is a heart attack. MIs can occur when a blood clot blocks a coronary artery, interrupting blood flow to the heart—a condition known as cardiac ischemia.

Heart muscles downstream of the blockage lose oxygen, leading to injury and death of the muscle cells. Post-MI, the hypoxia and tissue damage induces left ventricular remodeling (FIGS. 35A, 37). Cardiac reperfusion results in inflammation and oxidative damage. The injuries to cardiomyocytes during MI can cause a cascade of biological signaling events that leads cardiomyocytes to increase in volume and undergo proliferation in a specific way that compromises the functioning of the heart. This hypertrophic response is driven by a complex interplay of factors including a maladaptive regeneration gene program. During maladaptive regeneration, the heart undergoes changes that induce detrimental conditions to the patient (FIG. 35B). The affected ventricle increases its volume, but the walls of the ventricle become thinner, and the ability of the heart to pump blood decreases over time. This can lead to a variety of serious problems, including heart failure, a second heart attack, or sudden death. Thus, this process is called maladaptive hypertrophy (as opposed to adaptive hypertrophy, which strengthens the heart in reaction to stimuli such as exercise).

Maladaptive cardiac hypertrophy can be ameliorated by drugs that inhibit calcineurin and histone deacetylase 2 (HDAC2), for example. However, these drugs can cause serious side effects in non-cardiac tissues. Therefore, it's necessary to have a method to restrict drug activity to the heart.

The specificity and versatility of the conditional small interfering RNAs (cond-siRNA) described herein offers a new class of therapeutics for a variety of diseases and cancers by hijacking the RNA interference (RNAi) pathway. Although current treatment options for post-MI cardiac hypertrophy alleviate the severity of the condition, it is necessary to target the internal maladaptive gene program that drives the hypertrophic responses. In particular, cond-siRNAs (FIG. 4) are sequenced with a signal and target strand that due to steric hindrance, will only activate when the appropriate cardiac hypertrophy signal is present—thus only targeting disease cells through toehold-mediated strand displacement.

The Cond-siRNAs described herein can achieve this by using cardiac RNA biomarkers of MI as activation signals to switch ON RNAi silencing against calcineurin or HDAC2. Using this approach, RNAi silencing of the target genes are restricted to cardiomyocytes that express MI associated RNA biomarkers. This means that RNAi activity will NOT occur in other organs and tissues where inhibition of the targets can cause serious side effects. In one aspect, disclosed herein is a strand-displacement operated, programmable conditional-siRNA complex that can be activated by specific mRNA and miRNA transcripts expressed in the

12

hypertrophied myocardium, to target unrelated pro-hypertrophic pathways by RNAi knockdown.

To design an effective Cond-siRNA for treating Cardiac Hypertrophy, in vivo and/or in vitro screening approaches for measuring relevant gene expression may be used in accordance with the embodiments described herein.

Certain genes are upregulated under pathological cardiac hypertrophic conditions, which may be candidate pathological biomarkers to guide a Cond-siRNA molecule to a population of target cells, and which can be used to displace the sensor strand of the Cond-siRNA. For example, certain signaling cascades are activated under hypertrophic stimulating conditions (see FIG. 11). For example, genes and miRNAs that are upregulated in pathological cardiac hypertrophy were screened for differential gene expression in wild type (wt) mice as well as under various hypertrophic conditions to determine which genes are suitable candidates for use as a target for designing a sensor strand. See working examples below

In vitro screening approaches may include the use of a cardiomyocyte cell line (e.g., neonatal rat ventricular myocytes (NRVM), human cardiac myocytes (HCM)) cultured under hypoxic conditions or treated with phenylephrine. FIG. 12A. In vivo approaches may also be used including, but not limited to, rat models for ischemic heart failure (HF) (e.g., ischemia/reperfusion model), or rat models for non-ischemic HF (e.g., thoracic aortic constriction (TAC) model). See FIG. 12B.

Selection of RNA pathological biomarkers (input signals) for activation of Cond-siRNAs an important process for designing the cond-siRNA complexes described herein. The purpose of using pathological RNA biomarkers specific to the condition of cardiac hypertrophy for conditional RNAi activation is to ensure that RNAi activity is only active in cardiac tissues. Ideally, these biomarkers should be highly overexpressed in cardiac tissues affected by MI and not expressed in other tissues of the body. By comparing data gathered from in vitro and in vivo experiments on NRVM cell cultures and mice models with known organism wide expression patterns for the tested mRNAs and miRNAs (see working examples below), it was determined that at least three mRNAs and three miRNAs fit the criteria, including mRNAs that encode atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), and myosin heavy chain β (MHCP), and miRNAs that encode mir-23a-3p, mir-125-5p, and mir-199b-5p.

Thus therapeutic biomarkers that may be used to activate the conditional siRNA complexes in accordance with the embodiments described herein include, but are not limited to, mRNA biomarkers for MI affected cardiomyocytes, such as those described below.

In certain embodiments, a Cond-siRNA for treating cardiac hypertrophy includes a sensor strand designed to target a biomarker that is present and/or upregulated in heart cells (e.g., cardiac myocytes). Such biomarkers may include, but are not limited to, atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), myosin heavy chain β (MHCP), mir-23a-3p, mir-125-5p, and mir-199b-5p. In some aspects, the sensor strand detects an mRNA or an miRNA sequence that encodes the biomarker. And, in certain aspects, the sensor strand detects an mRNA sequence that encodes the biomarker by binding to the 3' UTR of the mRNA. Additional information regarding exemplary biomarkers is discussed below.

ANP (nppa) signal sensor strands. nppa (Natriuretic Peptide A) encodes for ANP protein that is overexpressed in hypertrophic conditions, thus is suitable as a biomarker for hypertrophy.

BNP (nppb) signal sensor strands. nppb (Natriuretic Peptide B) encodes for BNP protein that functions as a cardiac hormone and regulates natriuresis, diuresis, vasorelaxation and cardiovascular homeostasis. Low levels of BNP naturally found in the bloodstream in healthy individuals; high levels from cardiac ventricles. High concentrations of BNP in bloodstream indicates heart failure, and is a biomarker for hypertrophy. Thus, significant upregulation of BNP in induced cardiac hypertrophic conditions is indicative of effective sensor strand gene selection.

In some embodiments, a NPPB RH SSS v2.0 sensor was designed, wherein 31 bp sequence windows checked by hand through screening in entire 3' UTR of *Homo sapiens* mRNA based on A-U richness, hairpins, poly G tracts, and 8 bp toehold region. Three areas were found; NCBI Blast check for matches with other mRNAs and % yield of binding narrowed down options to chosen sensor (see NPPB sensor structures, FIG. 13).

MHC3 (myh7) signal sensor strands. MYH7 (myosin heavy chain 7) encodes for the p-heavy chain subunit of cardiac myosin. Varying amounts of the encoded protein correlate with cardiac muscle fiber contractile velocity. myh7 is predominantly expressed in the ventricle and type I muscle fibers. Gene mutations are associated with hypertrophic cardiomyopathy, and myh7 is upregulated in pathological cardiac hypertrophy. A significant upregulation of myh7 is seen in induced cardiac hypertrophic conditions, indicating that myh7 is another potential sensor strand gene selection.

In some embodiments, a myh7 RH SSS v2.0 sensor was designed, wherein 31 bp sequence windows checked by hand through screening of entire *Homo sapiens* mRNA. Because 3' UTR of mRNA is short with numerous poly G tracts, screening went into the coding region; however those contained secondary structure. Only 1 area found and chosen; checked NCBI Blast for matches with other mRNAs (see, e.g., myh7 sensor structures, FIG. 14).

In some embodiments, the sensor strand is fully complementary to any of the biomarkers discussed above (i.e., 100% complementary). In some embodiments the sensor strand is partially complementary to any of the biomarkers discussed above. For example, the sensor strand may be at least 70% complementary to the biomarker, at least 70% complementary to the biomarker, at least 75% complementary to the biomarker, at least 80% complementary to the biomarker, at least 85% complementary to the biomarker, at least 90% complementary to the biomarker, at least 95% complementary to the biomarker, at least 96% complementary to the biomarker, at least 97% complementary to the biomarker, at least 98% complementary to the biomarker, or at least 99% complementary to the biomarker.

Further, the complementarity of the sensor strand to the biomarker may be matched to any 19-40 base segment of any variant of the mRNA sequence that encodes ANP (nppa), BNP (nppb), or MHC β (myh7).

In other embodiments, the sensor strand includes one of the sequences in Table 1 below:

SEQ ID	BIO- NO STRAND MARKER SEQUENCE
1 SENSOR MIR- 23A- 3P	5' CGAAGAACGGAAUCCUGGCAAUGTGAT 3' 3P
2 SENSOR MIR- 23A- 3P	5' CGAAGAACGGAAUCCCTGGCAATGTGAU 3' 3P
3 SENSOR MIR- 23A- 3P	5' GGAGAAGAACGGAAUCCUGGC <u>AAUGUGAU</u> 3' 3P
4 SENSOR BNP	5' AUCAGAACCGAGUGUCUGCAGCC <u>AGGACUUC</u> 3' (used with HDAC2 - 2) + 2 U
5 SENSOR BNP	5' CUUGUGGAAUCAGAACGCAGGUGUC <u>UGCAGCC</u> 3'
6 SENSOR BNP	5' CAAAGGCCGCCACAGGGUUGAGG <u>AAAAAGCC</u> 3'
7 SENSOR MHC β / myh7	5' AUCUUGAACUGCUAGCCCUGG <u>GGUGCCAG</u> 3'
8 SENSOR ANP	5' CAACAAGAUGACACAAUUGCAGCAGAGACCC 3'
9 SENSOR ANP	5' AUGACACAAAUGCAGCAGAGACCCAGGGGA 3'
10 SENSOR ANP	5' CTUCACCACCUUCAGTGGCAAUGCGACCAA 3'

In certain embodiments, a Cond-siRNA for treating cardiac hypertrophy includes a guide strand designed to target a therapeutic RNAi target that is present and/or upregulated in heart cells (e.g., cardiac myocytes) and known to the field to ameliorate post-MI maladaptive hypertrophy, but whose systemic inhibition or expression may lead to unwanted side effects. In certain embodiments, therapeutic targets that may be used to design guide strands of Cond-siRNAs include, but are not limited to, Calcineurin [7-10] (or a subunit thereof, e.g., PPP3Ca, PPP3CB, PPP3CC, PPP3R1, PPP3R2), and HDAC2 [11, 12] or HDAC2 [11, 12]. In some aspects, the guide strand binds to an mRNA or an miRNA sequence that encodes the therapeutic target.

HDAC2 guide strands. HDAC2 (Histone deacetylase 2) functions as a central regulator in transcriptional regulation, cell cycle progression and developmental pathways by modifying chromatin structure. HDAC2 inhibition represses the maladaptive regeneration program through a pathway involving GSK3 β , inhibiting the hypertrophic response. HDAC2 serves as a key cardiac hypertrophic regulator and a potential therapeutic target.

In some embodiments, an HDAC2 RH TGS v2.1 guide strand was designed, wherein a 23 base-pair sequence was taken from the HDAC2 *Homo sapiens* mRNA based on past research utilizing HDAC2-targeted siRNAs. Two U base pairs added to the 3' end. Four base pairs at 5' end purposefully changed to mismatch the mRNA in order to prevent potential improper Dicer cleavage and RISC complex loading incorporation. An NCBI Blast check was also done to check for matches with other mRNAs. See HDAC2 guide strand structures, FIG. 15

Calcineurin guide strands. Calcineurin is a major promoter of cardiac hypertrophy, and inhibition of Calcineurin has been found to reduce hypertrophy. And, since it's always

15

present in ischemic cells, calcineurin is a good therapeutic target for the present invention.

In some aspects, the RNAi targeting segment of the guide strand (i.e., bases 1-21 from the 3' terminus) is fully complementary to any of the therapeutic targets discussed above (i.e., 100% complementary). In some aspects, the RNAi targeting segment of the guide strand (i.e., bases 1-21 from the 3' terminus) is partially complementary to any of the therapeutic targets discussed above. For example, the sensor strand may be at least 70% complementary to the biomarker, at least 70% complementary to the biomarker, at least 75% complementary to the biomarker, at least 80% complementary to the biomarker, at least 85% complementary to the biomarker, at least 90% complementary to the biomarker, at least 95% complementary to the biomarker, at least 96% complementary to the biomarker, at least 97% complementary to the biomarker, at least 98% complementary to the biomarker, or at least 99% complementary to any of the therapeutic targets discussed above. In other embodiments, bases 14-20 from the 3' terminus (the putative seed region of the guide strand) has at least 90% complementarity to the 3' UTR of an mRNA sequence that encodes at least a portion of a subunit of calcineurin (e.g., PPP3Ca, PPP3CB, PPP3CC, PPP3R1, PPP3R2) or HDAC2.

In certain embodiments, Cond-siRNAs that inhibit maladaptive hypertrophy are Cond-siRNAs that detect any biomarker from list A and target any member of list B in Table 2 below

TABLE 2

List A-cardiomyocytes biomarkers	List B-anti-maladaptive hypertrophy targets
ANP (nppa)	Calcineurin
BNP (nppb)	HDAC2
MHC β (myh7)	
mir-23a-3p	
mir-125-5p	
mir-199b-5p	

16

Thus, according to some embodiments, the Cond-siRNA described herein may have a sensor strand that is mostly or completely complementary to a sequence of the RNA transcripts corresponding to biomarkers listed in A, and a guide strand that targets a member of list B in the manner described above.

In other embodiments, the sensor strand includes one of the sequences in Table 3 below:

SEQ	THERA-		
ID	PEUTIC		
NO	STRAND	TARGET	SEQUENCE
11	GUIDE	CALCI- NEURIN	5' CGAGUGUUGUUUGCUUUCCUGUU 3' (green: change from C to G)
12	GUIDE	CALCI- NEURIN	5' CGAGUGUUGUUUGCUUUCCUGUU 3'
13	GUIDE	HDAC2	5' GCACUUAGAUUGAAACAACCCAGUU 3'
14	GUIDE	HDAC2	5' UGUUAUCUGGUGU UAUUGACCGU 3'
15	GUIDE	HDAC2	5' CGAGAUCUGGUGU UAUUGACCGU 3' (4 bp of 5' guide purposefully mismatched?) (used with BNP Sensor)
16	GUIDE	HDAC2	5' GCUCUUAGAUUGAAACAACCCAGUU 3'

In other embodiments, a Cond-siRNA for treating cardiac hypertrophy includes a core strand designed to connect the sensor to the guide strand according a method described above. IN certain aspects the core strand includes one of the sequences in Table 4 below:

SEQ	THERA-		
ID	PEUTIC		
NO	STRAND	TARGET	SEQUENCE
17	CORE	CALCINEURIN	5' CGUUCUUCUC C-linker- CAGGAAAAGCAAACACACUCG-linker-GCCAGGGAUU UC 3'
18	CORE	CALCINEURIN	5' GUCAUCUUGUUG-linker- CAGGAAAAGCAAACACACUCG-linker-GCUGCAUUUGU 3'
19	CORE	CALCINEURIN	5' AGGUGGUGAAG-linker- CAGGAAAAGCAAACACACUCG-linker- AUUGCACUGAG 3'
20	CORE	HDAC2	5' CGUUC UUCUC C CUGGGUUGUUUCAAUCUAAGUGC GCCAG GGAU UC 3'
21	CORE	HDAC2	5' CCUGCUCUGAU-linker- ACGGUCAAAACACCCAGAUUCUG-linker- GGCUGCAGACA 3' (used with BNP Sensor)
22	CORE	HDAC2	5' GAUUCACAAAG-linker- ACGGUCAAAACACCCAGAUUCUG-linker- ACACCUGCUUCU 3'
23	CORE	HDAC2	5' GGCGGCCUUUG-linker- ACGGUCAAAACACCCAGAUUCUG-linker- CCUCAACCCUGU 3'

-continued

SEQ ID NO	STRAND	THERAPEUTIC TARGET	SEQUENCE
24	CORE	HDAC2	5' GCAGAUCAAGAU-linker- ACGGUCAAUAACACCAGAUCUCG-linker- UCCAGGGCUGA 3'
25	CORE	HDAC2	5' GUCAUCUUGUUGCUGGGUUGUUUCAAUCUAAGAGCGC UGCAUUUGU 3'
26	CORE	HDAC2	5' CAUUGUGCUAUUGUUAGAUUGAAACAACCCAGGGUCU CUGCUG 3'

In some embodiments, the core strands above include 03 spacer linkers, where indicated, but any suitable linker may be used.

In certain embodiments, a Cond-siRNA for treating cardiac hypertrophy is a construct that includes a guide strand, core strand, and sensor strand as indicated in Table 5 below (also see FIGS. 16-17):

	SENSOR	CORE	GUIDE
CONSTRUCT 1	BNP (SEQ ID NO: 4)	HDAC2 (SEQ ID NO 21)	HDAC2 (SEQ ID NO 15)
CONSTRUCT 2	BNP (SEQ ID NO: 5)	HDAC2 (SEQ ID NO 22)	HDAC2 (SEQ ID NO 15)
CONSTRUCT 3	BNP (SEQ ID NO 6)	HDAC2 (SEQ ID NO 23)	HDAC2 (SEQ ID NO 15)
CONSTRUCT 4	MHCp/myh7 (SEQ ID NO 7)	HDAC2 (SEQ ID NO 24)	HDAC2 (SEQ ID NO 15)
CONSTRUCT 5	ANP (SEQ ID NO 8)	HDAC2 (SEQ ID NO 25)	HDAC2 (SEQ ID NO 16)
CONSTRUCT 6	ANP (SEQ ID NO 9)	HDAC2 (SEQ ID NO 26)	HDAC2 (SEQ ID NO 16)
CONSTRUCT 7	ANP (SEQ ID NO 8)	Calcineurin (SEQ ID NO 18)	Calcineurin (SEQ ID NO 11)
CONSTRUCT 8	ANP (SEQ ID NO 10)	Calcineurin (SEQ ID NO 19)	Calcineurin (SEQ ID NO 12)
CONSTRUCT 9	MIR-23A-3P (SEQ ID NO: 1)	Calcineurin (SEQ ID NO 19)	Calcineurin (SEQ ID NO 12)
CONSTRUCT 10	MIR-23A-3P (SEQ ID NO. 2)	Calcineurin (SEQ ID NO 19)	Calcineurin (SEQ ID NO 12))

In other embodiments, the conditional siRNA complex may comprise any combination of one sensor strand, one guide strand, and one core strand selected from Tables 1, 3, and 4, respectively. Additional embodiments of the conditional siRNA complex showing the full complex may be found in Appendix A, which is attached hereto.

Further, as described in the examples below, several mRNA and miRNA transcripts were screened under different pro-hypertrophic conditions both *in vivo* and *in vitro*, to assist with designing cond-siRNA complex strands.

Methods of Treatment

The cond-siRNA complexes described above may be used in methods to treat cardiac hypertrophy. Thus, in some embodiments, a method for treating cardiac hypertrophy

disclosed herein, wherein the method includes a step of administering to a subject a therapeutically effective amount of one or more of the cardiac hypertrophy-related cond-siRNAs described above. As disclosed herein, the subject may be any human or other animal suffering from post-MI cardiac hypertrophy, or any other type of cardiac hypertrophy.

"Treating" or "treatment" of a condition may refer to preventing the condition, slowing the onset or rate of development of the condition, reducing the risk of developing the condition, preventing or delaying the development of symptoms associated with the condition, reducing or ending symptoms associated with the condition, generating a complete or partial regression of the condition, or some combination thereof.

The methods for treating cardiac hypertrophy include administering a therapeutically effective amount of a therapeutic composition. An "effective amount," "therapeutically effective amount" or "effective dose" is an amount of a composition (e.g., a therapeutic composition or agent) that produces a desired therapeutic effect in a subject, such as preventing or treating a target condition or alleviating symptoms associated with the condition. The precise therapeutically effective amount is an amount of the composition that will yield the most effective results in terms of efficacy of treatment in a given subject. This amount will vary depending upon a variety of factors, including but not limited to the characteristics of the therapeutic compound (including activity, pharmacokinetics, pharmacodynamics, and bioavailability), the physiological condition of the subject (including age, sex, disease type and stage, general physical condition, responsiveness to a given dosage, and type of medication), the nature of the pharmaceutically acceptable carrier or carriers in the formulation, and the route of administration. One skilled in the clinical and pharmaceutical arts will be able to determine a therapeutically effective amount through routine experimentation, namely by monitoring a subject's response to administration of a compound and adjusting the dosage accordingly. For additional guidance, see Remington: The Science and Practice of Pharmacy 21st Edition, Univ. of Sciences in Philadelphia (USIP), Lippincott Williams & Wilkins, Philadelphia, PA, 2005.

In some embodiments, one or more cond-siRNAs may be used alone or as part of a pharmaceutical composition for treating cardiac hypertrophy. Thus, in some embodiments, a pharmaceutical composition comprising any one or more of the cardiac hypertrophy-related Cond-siRNAs described above is disclosed. The therapeutic compositions may also include one or more pharmaceutically acceptable carriers. A

"pharmaceutically acceptable carrier" refers to a pharmaceutically acceptable material, composition, or vehicle that is involved in carrying or transporting a compound of interest from one tissue, organ, or portion of the body to another tissue, organ, or portion of the body. For example, the carrier may be a liquid or solid filler, diluent, excipient, solvent, or encapsulating material, or some combination thereof. Each component of the carrier must be "pharmaceutically acceptable" in that it must be compatible with the other ingredients of the formulation. It also must be suitable for contact with any tissue, organ, or portion of the body that it may encounter, meaning that it must not carry a risk of toxicity, irritation, allergic response, immunogenicity, or any other complication that excessively outweighs its therapeutic benefits.

The therapeutic compositions described herein may be administered by any suitable route of administration. A route of administration may refer to any administration pathway known in the art, including but not limited to aerosol, enteral, nasal, ophthalmic, oral, parenteral, rectal, transdermal (e.g., topical cream or ointment, patch), or vaginal. "Transdermal" administration may be accomplished using a topical cream or ointment or by means of a transdermal patch. "Parenteral" refers to a route of administration that is generally associated with injection, including intraorbital, infusion, intraarterial, intracapsular, intracardiac, intradermal, intramuscular, intraperitoneal, intrapulmonary, intraspinal, intrasternal, intrathecal, intrauterine, intravenous, subarachnoid, subcapsular, subcutaneous, transmucosal, or transtracheal. In one embodiment the cardiac hypertrophy-related cond-siRNAs or therapeutic compositions thereof is administered by intracardial injection (FIG. 18) to ensure local delivery to the heart tissue.

Having described the invention with reference to the embodiments and illustrative examples, those in the art may appreciate modifications to the invention as described and illustrated that do not depart from the spirit and scope of the invention as disclosed in the specification. The examples are set forth to aid in understanding the invention but are not intended to, and should not be construed to limit its scope in any way. The examples do not include detailed descriptions of conventional methods. Such methods are well known to those of ordinary skill in the art and are described in numerous publications. Further, all references cited above and in the examples below are hereby incorporated by reference in their entirety, as if fully set forth herein. All appendices A-E submitted herewith constitute part of the complete disclosure.

EXAMPLES

Example 1: Prohypertrophic Gene and miRNA Expression Screening for Selection of Sensor Candidates for Treatment of Cardiac Hypertrophy

Genes and miRNA that are upregulated under pathological cardiac hypertrophic conditions were screened for differential expression in mice and in NRVM under various conditions to determine which molecules are suitable candidates for use as a biomarker target for designing a sensor strand.

Differential gene expression in tissues of wild type mice in homeostasis. Suitable pathological biomarker candidates should be differentially expressed in the heart as compared to other tissues to minimize off target effects. Several genes that are upregulated in pathological cardiac hypertrophy (DDiT4L, MYH7, ANP, BNP), as well as transcription

factors that control their expression (MEF2C, Myocardin), were measured in normal heart, liver, lung, kidney, skeletal muscle, and brains of wt mice. FIG. 19. Several miRNA were also measured, as shown in 38

5 Differential gene and miRNA expression in NRVM under hypoxic conditions. Suitable pathological biomarker candidates (ANP, BNP, MYH7, MEF2C, Myocardin, DDiT4L, and miRNAs) were screened in NRVM for differential expression under hypoxic conditions as shown in FIGS. 10-21.

10 This experiment mimics oxygen deprivation (hypoxia) during myocardial infarction (MI). NRVM cells were prepared cultured on standard petri dish substrates using techniques known to those who are skilled in the art [1,2].

15 Cultured NRVM cells are then exposed to hypoxic conditions (0.2% O₂ atmosphere) for 24 hours at 37 C. This was followed by incubation for 12 hours under normal oxygen conditions (95% ambient air/5% CO₂).

Following incubation, NRVM cells were harvested and 20 total RNA was extracted using protocols and kits standard in the art [3]. The messenger RNAs ANP, BNP, Myh7, MEF2C, Myocardin, DDiT4L, and the microRNAs mir-23a-3p, mir-125b-5p, mir-199b-5p, mir-208 and mir-195 were quantified by quantitative RT-PCR using standard methods 25 appropriate for mRNAs and miRNAs [5].

Results are presented in FIGS. 20-21 as fold change in copy numbers of mRNA or miRNA present in NRVM cells exposed to hypoxia compared to those incubated for 36 hours under normal oxygen conditions.

30 The results of this experiment show that ANP, BNP, DDiT4L, mir-23a-3p, and mir-199b-5p, were overexpressed by more than 4x under hypoxic conditions.

Differential gene and miRNA expression in NRVM after 35 phenylephrine treatment. Expression of miRNAs, and of ANP, BNP, MYH7, MEF2C, Myocardin, DDiT4L was measured in phenylephrine (PE) treated as compared to untreated NRVM.

Phenylephrine stimulation is a standard method for studying hypertrophy in cardiomyocytes [6,7]. In this experiment, 40 NRVM cells were prepared by standard protocols. Phenylephrine was then added to the culture media to 50 μM concentration for 24 hours. After 24 hours, cells were harvested for RNA isolation and analysis as described above.

45 The results of the experiment show that ANP, BNP, Myh7, myocardin mRNA were overexpressed by more than 10x after PE stimulation (FIG. 22), and that miRNAs, mir-23a-3p, mir-125b-5p, and mir-199b-5p were overexpressed by more than 4x after PE stimulation (FIG. 23).

50 Differential gene expression in mouse models of heart failure. Expression of ANP, BNP, MYH7, MEF2C, Myocardin, DDiT4L was measured in heart tissue of mice with non-ischemic heart failure in a thoracic aortic constriction (TAC) model and of mice with ischemic heart failure in an 55 ischemia/reperfusion (I/R) model as compared to sham-treated mice.

In experiments related to the ischemia/reperfusion (I/R) model, mice underwent procedures to simulate ischemic (deprivation of blood flow) heart failure. At day zero, mice 60 were subject to ischemic heart failure via surgical clamping of a coronary artery for 20 min, followed by reperfusion. After 28 days, the experimental mice were sacrificed. Heart tissue was harvested and RNA was isolated using standard protocols as described above. mRNA and miRNAs were 65 quantified using RT-PCR as described above. The mRNA and miRNA in the treated mice were compared with those found in control mice who were subjected to a sham

21

procedure that did not involve clamping of the coronary artery to induce ischemia/reperfusion.

The results show that all mRNAs tested were overexpressed by more than 10 \times in mice with ischemic HF (FIG. 24). ANP and myh7 were overexpressed by more than 1000 \times (FIG. 24). And for miRNAs, only mir-23a-3p was significantly overexpressed, by ~15 \times (FIG. 25).

In experiments related to the non-ischemic HF model (TAC), mice underwent thoracic aortic constriction (TAC) procedures to induce non-ischemic heart failure. Briefly the upper thorax of mice constricted to reduce blood flow through the aorta for 28 days. This induced non-ischemic heart failure. After 28 days, the animals were sacrificed and heart tissue was harvested. RNA was isolated using standard protocols as described above. mRNA and miRNAs were quantified using RT-PCR as described above. The mRNA and miRNA in the treated mice were compared with those found in control mice who were subjected to a sham procedure that did not involve aortic constriction.

The results show that all mRNAs tested were overexpressed by more than 20 \times in the constricted mice (FIG. 24). ANP and myh7 were overexpressed by more than 1000 \times (FIG. 24). For miRNAs, all tested miRNAs were overexpressed by more than 10 \times . (FIG. 25). And, mir-23a-3p was overexpressed by ~80 \times (FIG. 25).

Example 2: Design of ANP:Calcineurin Cond-siRNA

The 5' UTR and coding sequences of messenger RNAs are frequently occupied by mRNA binding proteins or transiting ribosomes. In mammals, miRNAs commonly bind at 3' UTR sites to regulate mRNAs. Thus, binding sites in the 3' UTR may be more accessible than sites in the 5' UTR and the coding sequence of region of mRNAs.

When designing sensors to detect mRNAs, it is desirable to start with sites in the 3' UTR. If such sites cannot be found or there are other reasons (such as the need to detect a particular important sequence in the coding region or the 5' UTR), then sensors can be designed to those sites.

ANP 3'UTR sequencing results. Murine models were used to test the ability of ANP:Calcineurin Cond-siRNAs to inhibit phenylephrine induced cardiomyocytes hypertrophy. Thus, an ANP sensor was designed to target rat ANP.

To design the ANP sensor, the 3' UTR of ANP mRNA found in neonatal rat ventricular cardiomyocytes cells was sequenced by extracting RNA using standard procedures, amplifying the 3' UTR via RT-PCR, and submitting the amplified DNA for sequencing by the Massachusetts General Hospital's DNA sequencing core.

The sequenced DNA is as follows (N indicates indetermined base)

ANP 3'UTR sequencing results from CCIB DNA Core (MGH)
293387-293389_D10_1_074_nppa_3_UTR_Ane.seq
this is the forward sequence:

22

-continued

TAGATGAGTGGTTAGTGAGGCCCTAACCTCTCCACTCTGCATATTAAGG

TAGATCCTCACCCNNNNANNANNNNNNNNNNNNNNNNNNNNNNNNNN

5 NNNNNNNNN

Using NCBI BLAST, it was determined that the central sequence

10

(SEQ ID NO: 28)
GAGCAGATCGAAAAGATCCAAGGCCTTGCGGTGTGTCACACAGC**TGG****TCCGCATTGCCACTGAGAGCTGGTGAATACCCCTCTGGAGCTGCAGCTTCC**

15

TGTCTTCATCTATCACGATCGATGTTAAGTGTAGATGAGTGGTTAGTGA
GCCCTTACCTCTCCCACTCTGCATATTAAGGTAGATCCTCACCC

20

Is 99% homologous to *Rattus norvegicus* nppa mRNA 3' UTR and 92% homologous to *Mus musculus* nppa mRNA 3' UTR.

25

Generation of Sensor Candidates:

To generate candidate sensor strands, the reverse complement of the above sequence was determined.

25

(SEQ ID NO: 29)
NNNTNNNNNGGTGAG

30

GATCTACCTTAATATGCAGAGTGGGAGAGGTAAAGCCTCACTAAACCAC
CATCTACACTAACATCGATCGTGATAGATGAAGACAGGAAGCTGCAGCT
CCAGGAGGGTATTCAACACCTCTCAGGGCAATGCGACCAAGCTGTGTA
CACACCGCAAGGCCTGGGATCTTTCGATCTGCTCNNNNNNNNNTGGC
35 TGA

35

Then, a Python script was used to generate all possible consecutive 31 nt segments (8 nt for toehold, plus 23 nt for duplex region) of the central bold sequence (rat nppa 3 prime utr sensor.xlsx). These are the initial possible sensor sequences for this region (T needs to be converted to U). The python script is attached herewith as Appendix B.

45

The Python code that was generated performed following analyses for each sensor sequence: (i) add one demerit point for each occurrence of three or more consecutive Gs (eg: GGG, GGGG, GGGGG); (ii) add one demerit point for each occurrence of four or more consecutive A/Ts (eg: ATAT, AAAA, TTTT, TTAT, etc), (iii) calculate the percent of the sequence composed of G or Cs; and (iv) calculate the percent of the sequence accounted for by the most numerous three bases (e.g., out of A, G, C, T, if A, G and T are the most numerous in the sequence, what percent of bases are A, G or T).

55

Then the list of possible sensors were ranked by the following criteria, in order of importance: (i) least number of demerit points, preferably 0'; (ii) highest 3 letteredness; and (iii) highest GC content (see, e.g., FIGS. 41-42)

60

The sequences on the ranked list were screened one by one for two qualities: (i) the hypothetical sensor duplex has high stability and correctness according to standard RNA secondary structure prediction codes; and (ii) the sensor strand has few significant matches to RNA transcripts other than nppa mRNA in rats and mice that extends from the toehold region (8 bases at 3') into more than 50% of the duplex region (bases 9 to 31 from the 3').

(SEQ ID NO: 27)
TCAGCCANNNNNNNNAGCAGATCGAAAAGATCCAAGGCCTTGCG
GTGTGTACACAGCTGGTGCATTGCCACTGAGAGGTGGTAATACCC
TCCTGGAGCTGCAGCTTCTGTCTCATCACGATCGATGTTAAGTG

23

The following sensor sequence was identified as favorable:

(SEQ ID NO: 30)
ATTCACCACCTCTCAGTGGCAATGCGACCAA

To further improve the thermodynamic stability of the sensor, the first base was changed at the 5' from an A to a C. This gives the following sensor sequence:

Sensor (mutated base underlined):
(SEQ ID NO: 31)
CUCUACCACCUUCAGUGGCCAUGCACCAA

On nupack, the hypothetical sensor duplex constructed from this sequence showed 8 thermodynamic stability, with an equilibrium concentration of 0.97 nM. Also see FIG. 26.

NCBI BLAST of the sensor sequence using “somewhat similar” settings showed no significant sequence matches other than to mouse and rat ANP (nppa) mRNA.

Calcineurin is a heterodimer composed of one of three catalytic isoforms (PPP3CA, PPP3CB, PPP3CC) and one of two regulatory subunits (PPP3R1 and PPP3R2). To target Calcineurin, a guide sequence against the PPP3CA subunit of Calcineurin was identified that targets a widely conserved target site present in human, rat, and mice: UGUUGU UGGCUU UUCCUG UU (SEQ ID NO:32)

The segment CGAG was then added to the 5' end to create a 23 nt guide strand, and then generated the core strand according to the previous stated rules. Those sequences are shown below:

Guide:
(SEQ ID NO: 11)
CG AG UGUUGU UGGCUU UU UUCCUG UU

Sensor (mutated base underlined):
(SEQ ID NO: 33)
CUUCACCACCU CUCAGUGGCCAAU GCGACCAA

Core:
(SEQ ID NO: 19)
AGGUGGUGAAG-linker-CAGGAAAAGCCAACACACUCG-linker-
AUUGGCCACUGAG

The guide strand plus the core strand showed good thermodynamic stability as predicted by Nupack (FIG. 27)

Then, chemical modifications were added according to schemes previously disclosed in U.S. Pat. No. 9,725,715, the subject matter of which is incorporated by reference herein. The final sequences are shown below:

Sensor:
(SEQ ID NO: 34)
/5Sp9/mC*+T*mU*mC*+A*mC*mC*+A*mC*+C*mU*mC*mU*+C*mA/
mG+T*mG*+G*mC*mA*+A*mU*mG*mC*+G*mA*mC*mC*+A*mA*/

3AmMO/

Guide:
(SEQ ID NO: 35)
/5AmMC6/+C*+G rArG rUrGrUrUrGrU rUrUrGrCrC rUrU
rUrUrCrCrUrG rUrU

24

-continued

Core:
(SEQ ID NO: 36)
mArGmGrUrGrGrUrGrArArg/iSpC3/mC*+A*mGrGrArArArGr
5 CrCrArArArCrArArCrArCrUrC*mG/iSpC3/rArUrUrGrCrCrAr
CrUrGrAmG

The nucleotides and modifications are indicated as follows: (1)+A, +T, +C, +G are LNA; (2) mA, mU, mC, mG are 2'-O-methyl; (3) rA, rU, rC, rG are RNA; (4) * denotes phosphorothioate backbone connection; (5) /5Sp9/ is a triethylene glycol linker; (6) /iSpC3/ is an internal C3 spacer; (7) /5AmMC6/ is a 5' primary amine modification on a C6 linker; (8) /3AmMO/ is a 3' primary amine modification.

15 Example 3: Design of mir-23a-3p:Calcineurin Cond-siRNA

An mir-23a-3p sensor was designed as follows. The mir-23a entry for miRbase is found at the following URL: 20 http://www.mirbase.org/cgi-bin/mirna_entry.pl?acc=M10000079

The sequence of mir-23a-3P sequence, 5'-3' is:

25 >hsa-miR-23a-3p MIMAT0000078
(SEQ ID NO: 37)
AUCACAUUGCCAGGGAUUCC

The reverse complement of mir-23a-3p is GGAAAUCC-CUGGCAAUGUGAU (SEQ ID NO:38)

30 The Cond-siRNA sensor to sense a microRNA input is that the microRNA guide strand is usually only 21 nt long, whereas the Cond-siRNA sensor's duplex region is usually 23 nucleotides long and the toehold is usually 5 to 8 nucleotides long. This means that a microRNA guide strand is not long enough to completely displace the sensor strand from the core strand.

35 This issue was solved by configuring the sensor strand so that the guide strand will displace the sensor from base-pairing with the 3' overhang of the core strand and the last few bases at the 5' terminus of 5' overhang of the core strand.

This way, the 3' overhang of the core strand becomes unprotected and is degraded. The 5' terminus of the 5' overhang also becomes unprotected and subject to degradation, leading to eventual degradation of the entire 5' overhang. This then allows the sensor strand to completely dissociate from the RNAi region.

40 Thus, assuming a 21 nt miRNA guide strand, some of the possible geometries for the sensor strand, starting from the 3' end, are shown in Table 6 below:

50 Scheme	Toehold length	Length bound to 3' core strand overhang	Length bound to 5' core strand overhang
55 A	6	11	12
B	7	11	12
C	7	10	13
D	6	10	13
E	6	10	12
F	7	11	11

60 In Table 6, scheme A gives a 23 bp sensor duplex and allows the miRNA to displace up to 4 terminal bases of the 5' core strand segment, scheme B, 23 bp sensor, 3 terminal bases displaced, scheme C, 23 bp sensor, 4 terminal bases displaced, scheme D, 23 bp sensor, 5 terminal bases displaced, scheme E, 22 bp sensor, 5 terminal bases displaced, and scheme F, 22 bp sensor, 3 terminal bases displaced

Calcineurin Sensor Design:

Scheme F from Table 6 was used to design the following calcineurin sensor:

(SEQ ID NO: 39)
5' CGAAGAACGGAAAUCCCUGGCAAUGUGAU 3'

A sequence: CGAAGAAC (SEQ ID NO:40) is added to the 5' of the sensor. This sequence is designed to improve thermodynamic stability of the sensor duplex, minimize secondary structure in the sensor strand, and minimize overlap with non-mir23a-3p transcripts.

According to NCBI BLAST, the sensor has no significant unintended matches to human RNA transcripts, and there are only a few significant unintended matches to mouse RNA transcripts.

The same Calcineurin PPP3CA siRNA guide identified for the ANP: Calcineurin construct above was used and the core strand sequence was generated using the algorithms described herein.

Core:

(SEQ ID NO: 41)
UCCGUUCUUCG-linker-CAGGAAAGCCAACACACUCG-linker-
UGCCAGGGAUU

The guide strand plus the core strand showed good thermodynamic stability as predicted by Nupack (FIG. 28), as did the hypothetical sensor duplex (FIG. 29).

Thus, the final fully modified sequences are as follows:

Calcineurin guide:

(SEQ ID NO: 42)
C6Amine+C*+GrArG rUrGrUrUrGrU rUrUrGrGrC rUrU
rUrUrCrCrUrG rUrU

Mir-23a-3p sensor using a 22 bp sensor duplex with LNA pattern:

(SEQ ID NO: 43)
/5Sp9/mC*+G*mA*+A*mG*mA+A*mC *+G*mG*mA*+A*mA*mU*
mC*mC*+C*mU*mG*+G*mC*mA*+A*mU*mG*+T*mG*+A*T*/

3AmMO/

Core strand:

(SEQ ID NO: 44)
mUrCrCrGrUrUrCrUrCrG/iSpC3/mC*+A*mGrGrArArArGr
CrCrArArArCrArCrArCrUrC*mG/iSpC3/rUrGrCrCrArGrGr
G mA rU mU

The nucleotides and modifications are indicated as follows: (1)+A, +T, +C, +G are LNA; (2) mA, mU, mC, mG are 2'-O-methyl; (3) rA, rU, rC, rG are RNA; (3) * denotes phosphorothioate backbone connection; (4) /5Sp9/ is a triethylene glycol linker; (5) /iSpC3/ is an internal C3 spacer; (6) /5AmMC6/ is a 5' primary amine modification on a C6 linker; (7) /3AmMO/ is a 3' primary amine modification.

Example 4: Synthesis and Testing of Cond-siRNA Constructs

To demonstrate use of Cond-siRNAs to inhibit hypertrophy of cardiomyocytes, Cond-siRNAs were designed and synthesized to detect murine ANP or mir-23a-3p and inhibit calcineurin. The constructs are shown in FIGS. 16 and 17.

All strands were purchased from a commercial oligonucleotide vendor (Exiqon Inc, now a part of Qiagen).

Assembly and purification. Sensor, core, and guide strands were mixed at 1.0:1.1:1.0 ratios at 50 nM to 1 uM strand concentrations and underwent thermal annealing in 1xPBS buffer (80 C for 30 seconds followed by constant temperature incubation at 50 C to 60 C for -1 hour followed by cooling to room temperature).

Where purification was desired, constructs were annealed at 500 nM, loaded at 20 uL per well in 10% non-denaturing PAGE. Run in 1xTBE buffer at 120V for 90 min. The correct bands were excised. The Cond-siRNA constructs were then extracted via the crush and soak method using standard RNA isolation kits.

15 FIG. 30 shows an example gel where Cond-siRNAs were assembled and purified.

Dual luciferase assays of mir-23a-3p:calcineurin Cond-siRNA (FIG. 31). For this assay, the Cond-siRNA described above was assessed for its ability of to keep RNAi activity OFF in the absence of the correct biomarker and switching RNAi ON in the presence of RNA transcripts bearing the mir-23a-3p sequence. For this test, unpurified mir-23a-3p: calcineurin Cond-siRNAs was co-transfected at the indicated concentrations into human Hek 293 cells, along activator and dual luciferase plasmids.

The activator plasmids expressed either a null transcript, a transcript with an incorrect activator, the 21 base mir-23a-3p sequence, or a longer sequence that was complementary to the entire sensor strand.

20 The dual luciferase plasmid encoded Firefly luciferase as the control and a Renilla luciferase with the calcineurin target site in its 3' UTR as the target of RNAi.

The results show that this Cond-siRNA had significantly increased RNAi activity against the calcineurin target when either the mir-23a-3p sequence or the fully matching sequence was expressed. FIG. 31. Thus, this construct should be able to activation RNAi activity against calcineurin in the presence of mir-23a-3p.

25 in vitro experiment for purified ANP:calcineurin Cond-siRNA in NRVM cells under PE stimulation. For this experiment, it was tested whether the murine ANP calcineurin Cond-siRNA could detect overexpression of ANP upon phenylephrine (PE) stimulation, and activate RNAi knock-down against calcineurin.

30 The biological effects of ANP:calcineurin against murine biomarkers and targets is tested because there are no suitable human models to test against. The biological effect of this murine oriented Cond-siRNA should be representative of biological effects that Cond-siRNA configured for humans would have.

For this experiment, NRVM cells were incubated using standard protocols under normal conditions (95% air, 5% CO2, 37 C). The purified ANP: calcineurin Cond-siRNA was transfected at 20 nM concentration into NRVM cells 35 using RNAiMax. The transfected cells were incubated for 24 hours. PE was then added to the media to 50 uM final concentration. After a further 48 hours, cells were harvested and stained or processed for RNA isolation.

The results for RT-PCR quantitation of calcineurin mRNA are shown in FIG. 32. For each cohort (untreated and PE treated cells), the level of calcineurin mRNA observed in cells transfected with scrambled siRNA (negative control) was normalized to 1.0. In the untreated cohort, cells transfected with ANP:Calcineurin Cond-siRNA had no detectable knockdown of calcineurin. This means that, as intended, the Cond-siRNA has very little RNAi activity in normal cells.

27

In cells treated with PE, the Cond-siRNA activated RNAi, and reduced calcineurin mRNA levels by ~ 50% compared with levels seen in cells transfected with the scrambled siRNA control. This shows that the ANP:calcineurin Cond-siRNA can detect overexpression of ANP mRNA, and respond with RNAi inhibition of calcineurin as intended.

The results of imaging of the treated and untreated cells by fluorescence microscopy are shown in FIG. 33. The results show that cells treated with purified ANP:calcineurin Cond-siRNAs underwent less hypertrophy than cells treated with scrambled siRNA. Furthermore, the effects of treatment with Cond-siRNAs was similar to treatment with the positive control (commercial, non-conditional calcineurin siRNA).

The results of cell size quantitation using fluorescence microscopy are shown in FIG. 34. The results show that PE stimulation resulting in the increase in the average cell size from ~750 μm^2 to ~1300 μm^2 in cells treated with the negative control scrambled siRNA. However, in cells treated with the Cond-siRNA, average cell size increased from ~750 μm^2 to ~900 μm^2 , and was not statistically significant. This result is similar to the non-conditional, commercial calcineurin siRNA.

The above results show that the ANP:Calcineurin Cond-siRNA has low background RNAi activity, can detect and respond to PE stimulation of NRVM cells, and has significant biological effects on reducing hypertrophy of NRVM cells.

Example 5: Exemplary Guide and Sensor Strand Sequences

Below are examples of automatically generating core strand sequences from guide and sensor strand sequences. These have 23 bp sensor duplexes with 8 base toeholds

Example 5a, randomly chosen human/rat PPP3CA mRNA guide paired with randomly chosen human NPPA sensor

Cond-siRNA Guide: (SEQ ID NO: 45)
CCAC UUUACCAGCAUCUCAGUCAUU

Cond-siRNA Sensor: (SEQ ID NO: 46)
GGAGAGGCGAGGAAGUCACCAUAAACCACU

Core is: (SEQ ID NO: 47)
CUCGCCUCUCC UGACUGAGAUGCUGGUAAAGUGGGAUUGGACUUC

Example 5b, human/rat PPP3CA mRNA guide above paired with randomly chosen human NPPB sensor

Cond-siRNA Guide: (SEQ ID NO: 45)
CCAC UUUACCAGCAUCUCAGUCAUU

Cond-siRNA Sensor: (SEQ ID NO: 48)
GGAAUCAGAACAGGUGUCUGCAGCCAGGAC

Core is: (SEQ ID NO: 49)
CUUCUGAUUCC UGACUGAGAUGCUGGUAAAGUGGGUGACACCCUG

28

Example 5c, human/rat PPP3CA mRNA guide above paired with randomly chosen human Myh7 sensor

Cond-siRNA Guide:

(SEQ ID NO: 45)

CCAC UUUACCAGCAUCUCAGUCAUU

Cond-siRNA Sensor:

(SEQ ID NO: 50)

CCAAGGAGCUGUUACACAGGCUCAGCAUGG

Core is:

(SEQ ID NO: 51)

CAGCUCCUUGG UGACUGAGAUGCUGGUAAAGUGGGAGCCUGUGUAA

Example 5d, randomly chosen human/rat HDAC2 mRNA guide paired with human NPPA sensor from example 1

Cond-siRNA Guide:

(SEQ ID NO: 52)

CCAC UUCAUCACAAGCUAUCCGUU

Cond-siRNA Sensor:

(SEQ ID NO: 46)

GGAGAGGCGAGGAAGUCACCAUAAACCACU

Core is:

(SEQ ID NO: 53)

CUCGCCUCUCC GCGGAUAGCUUGUGAUGAAGUGGGAUUGGACUUC

Example 5e, randomly chosen human/rat HDAC2 mRNA guide above paired with human NPPB sensor from example 1

2

Cond-siRNA Guide:

(SEQ ID NO: 52)

CCAC UUCAUCACAAGCUAUCCGUU

Cond-siRNA Sensor:

(SEQ ID NO: 48)

GGAAUCAGAACAGGUGUCUGCAGCCAGGAC

Core is:

(SEQ ID NO: 54)

CUUCUGAUUCC GCGGAUAGCUUGUGAUGAAGUGGGUGACACCCUG

Example 5f, randomly chosen human/rat HDAC2 mRNA guide above paired with human Myh7 sensor from example 3

3

Cond-siRNA Guide:

(SEQ ID NO: 52)

CCAC UUCAUCACAAGCUAUCCGUU

Cond-siRNA Sensor:

(SEQ ID NO: 50)

CCAAGGAGCUGUUACACAGGCUCAGCAUGG

Core is:

(SEQ ID NO: 55)

CAGCUCCUUGG GCGGAUAGCUUGUGAUGAAGUGG

GAGCCUGUGUAA

In the next examples, we reuse the guide from examples 1-6, but choose miRNA sensors. The sensors are configured as 22 bp duplexes with 7 base overhangs and symmetric 11 base core strand overhangs

US 12,385,041 B2

29

Example 5g, randomly chosen human/rat PPP3CA mRNA guide paired with mir-23a-3p sensor

Cond-siRNA Guide: (SEQ ID NO: 45)

CCAC UUUACCAGCAUCUCAGUCAUU

Cond-siRNA Sensor: (SEQ ID NO: 39)

CGAAGAAC GGAAAUCCCUGGCAAUGUGAU

Core is: (SEQ ID NO: 56)

UCCGUUUCUUCG UGACUGAGAUGCUGGUAAAGUGG

UGCCAGGGAUU

Example 5h, human/rat PPP3CA mRNA guide above paired with mir-125b-5p sensor

Cond-siRNA Guide: (SEQ ID NO: 45)

CCAC UUUACCAGCAUCUCAGUCAUU

Cond-siRNA Sensor: (SEQ ID NO: 57)

CGACAGU UCACAAAGGUAGGGUCACAGGGAA

Core is: (SEQ ID NO: 58)

GUGAACUGUCG UGACUGAGAUGCUGGUAAAGUGG

GACCCUAACUU

Example 5i, human/rat PPP3CA mRNA guide above paired with mir-195b-5p sensor

Cond-siRNA Guide: (SEQ ID NO: 45)

CCAC UUUACCAGCAUCUCAGUCAUU

Cond-siRNA Sensor: (SEQ ID NO: 59)

CCUGAA GAACAGAUAGCUAAACACUGGG

Core is: (SEQ ID NO: 60)

UGUUCUUCAGG UGACUGAGAUGCUGGUAAAGUGG

UUUAGACUAUC

Example 5j, randomly chosen human/rat HDAC2 mRNA guide paired with mir-23a-3p sensor

Cond-siRNA Guide: (SEQ ID NO: 52)

CCAC UUCAUCACAAGCUAUCCGCUU

Cond-siRNA Sensor: (SEQ ID NO: 39)

CGAAGAAC GGAAAUCCCUGGCAAUGUGAU

Core is: (SEQ ID NO: 61)

AACAGCUCCUUGG GCGGAUAGCUUUGUGAUGAAGUGG

GGAGCCUGUGU

30

Example 5k, randomly chosen human/rat HDAC2 mRNA guide above paired with mir-125b-5p sensor

Cond-siRNA Guide: (SEQ ID NO: 52)

CCAC UUCAUCACAAGCUAUCCGCUU

Cond-siRNA Sensor: (SEQ ID NO: 57)

CGACAGU UCACAAAGGUAGGGUCACAGGGAA

Core is: (SEQ ID NO: 62)

UCCGUUUCUUCG GCGGAUAGCUUUGUGAUGAAGUGG

UGCCAGGGAUU

Example 5l, randomly chosen human/rat HDAC2 mRNA guide above paired with mir-195b-5p sensor

Cond-siRNA Guide: (SEQ ID NO: 52)

CCAC UUCAUCACAAGCUAUCCGCUU

Cond-siRNA Sensor: (SEQ ID NO: 59)

CCUGAA GAACAGAUAGCUAAACACUGGG

Core is: (SEQ ID NO: 63)

UGUUCUUCAGG GCGGAUAGCUUUGUGAUGAAGUGG

UUUAGACUAUC

Example 6: Exemplar siRNAs Designed by a Commercial siRNA Automated Design Website

From: <http://dharmacon.horizondiscovery.com/design-center/>

For each category below, the design tool was tasked with designing siRNAs targeting the protein coding region of both the human and the rat mRNA. The top three candidates are shown. Cond-siRNA guides are made by adding 4 G/C rich bases to the 5' of the antisense strand.

Candidate siRNA guide strands sequences (antisense) and corresponding target sites (sense) targeting both Human (NM_000944) and Rat (NM_017041) PPP3CA mRNA

Sense: (SEQ ID NO: 64)
5' G.A.A.C.A.A.G.A.U.C.C.G.A.G.C.A.A.U.U 3'

Antisense: (SEQ ID NO: 65)
5' U.A.U.U.G.C.U.C.G.G.A.U.C.U.U.G.U.U.C.U.U 3'

Cond-siRNA Guide: (SEQ ID NO: 66)
5' CGACU.A.U.U.G.C.U.C.G.G.A.U.C.U.U.G.U.U.C.U.U 3'

Sense: (SEQ ID NO: 67)
5' U.G.A.C.U.G.A.G.A.U.G.C.U.G.G.U.A.A.U.U 3'

Antisense: (SEQ ID NO: 68)
5' U.U.U.A.C.C.A.G.C.A.U.C.U.G.C.A.U.U 3'

US 12,385,041 B2

31

-continued

Cond-siRNA Guide:

(SEQ ID NO: 69)

5' CGACU.U.U.A.C.C.A.G.C.A.U.C.U.C.A.G.U.C.A.U.U
3'

Sense:

(SEQ ID NO: 70)

5' G.G.U.C.A.G.A.A.G.A.A.U.G.G.A.U.U.U.U 3'

Antisense:

(SEQ ID NO: 71)

5' A.A.U.C.C.A.U.C.U.U.C.U.C.U.G.A.C.C.U.U 3'

Cond-siRNA Guide:

(SEQ ID NO: 72)

5' CCACA.A.U.C.C.A.U.C.U.U.C.U.C.U.G.A.C.C.U.U
15

3'

Candidate siRNA guide strands sequences (antisense) and corresponding target sites (sense) targeting both Human (NM_001142353) and Rat (NM_017042) PPP3CB mRNA

Sense:

(SEQ ID NO: 73)

5' G.C.U.A.U.A.G.A.A.U.G.U.A.C.A.G.A.A.A.U.U 3'

Antisense:

(SEQ ID NO: 74)

5' U.U.U.C.U.G.U.A.C.A.U.U.C.U.A.U.A.G.C.U.U 3'

Cond-siRNA Guide:

(SEQ ID NO: 75)

5' CGACU.U.U.C.U.G.U.A.C.A.U.U.C.U.A.U.A.G.C.U.U
30

Sense:

(SEQ ID NO: 76)

5' C.C.U.U.U.A.A.G.C.A.G.G.A.A.U.G.U.A.A.U.U 3'

Antisense:

(SEQ ID NO: 77)

5' U.U.A.C.A.U.U.C.C.U.G.C.U.U.A.A.A.G.G.U.U 3'

Cond-siRNA Guide:

(SEQ ID NO: 78)

5' GGACU.U.A.C.A.U.U.C.C.U.G.C.U.U.A.A.A.G.G.U.U
35

Sense:

(SEQ ID NO: 79)

5' G.C.A.A.U.U.G.G.C.A.A.G.A.U.G.G.C.A.A.U.U 3'

Antisense:

(SEQ ID NO: 80)

5' U.U.G.C.C.A.U.C.U.U.G.C.C.A.A.U.U.G.C.U.U 3'

Cond-siRNA Guide:

(SEQ ID NO: 81)

5' CCACU.U.G.C.C.A.U.C.U.U.G.C.C.A.A.U.U.G.C.U.U
40

Candidate siRNA guide strands sequences (antisense) and corresponding target sites (sense) targeting both Human (NM_001243974) and Rat (NM_134367) PPP3CB mRNA

Sense:

(SEQ ID NO: 82)

5' G.U.A.U.A.G.A.G.U.G.U.G.U.G.C.U.G.U.A.U.U 3'

Antisense:

(SEQ ID NO: 83)

5' U.A.C.A.G.C.A.C.A.C.U.C.U.A.U.A.C.U.U 3'

Cond-siRNA Guide:

(SEQ ID NO: 84)

5' CCACU.A.C.A.G.C.A.C.A.C.U.C.U.A.U.A.C.U.U
45

3'

32

-continued

Sense:

(SEQ ID NO: 85)

5' A.G.U.A.U.U.U.G.A.G.A.A.U.G.G.G.A.A.A.U.U 3'

Antisense:

(SEQ ID NO: 86)

5' U.U.U.C.C.C.A.U.U.C.U.C.A.A.A.U.A.C.U.U 3'

10 Cond-siRNA Guide:

(SEQ ID NO: 87)

5' CCACU.U.U.C.C.C.A.U.U.C.U.C.A.A.A.U.A.C.U.U
15

3'

Sense:

(SEQ ID NO: 88)

5' C.U.A.U.G.U.G.G.A.C.A.G.A.G.G.C.U.A.U.U 3'

Antisense:

(SEQ ID NO: 89)

5' A.U.A.G.C.C.U.C.U.G.U.C.C.A.C.A.U.A.G.U.U
20

Cond-siRNA Guide:

(SEQ ID NO: 90)

5' CCACA.U.A.G.C.C.U.C.U.G.U.C.C.A.C.A.U.A.G.U.U
25

3'

Candidate siRNA guide strands sequences (antisense) and corresponding target sites (sense) targeting both Human (NM_001527) and Rat (NM_053447) HDAC2 mRNA

Sense:

(SEQ ID NO: 91)

5' G.C.G.G.A.U.A.G.C.U.U.G.U.G.A.U.G.A.A.U.U 3'

Antisense:

(SEQ ID NO: 92)

5' U.U.C.A.U.C.A.C.A.G.C.U.A.U.C.C.G.C.U.U
30

Cond-siRNA Guide:

(SEQ ID NO: 52)

5' CCACU.U.C.A.U.C.A.C.A.G.C.U.A.U.C.C.G.C.U.U
35

3'

Sense:

(SEQ ID NO: 93)

5' G.G.A.U.A.U.U.G.G.U.G.C.U.G.G.A.A.A.U.U 3'

Antisense:

(SEQ ID NO: 94)

5' U.U.U.C.C.A.G.C.A.C.C.A.A.U.A.U.C.C.U.U
40

Cond-siRNA Guide:

(SEQ ID NO: 95)

5' CCACU.U.U.U.C.C.A.G.C.A.C.C.A.A.U.A.U.C.C.U.U
45

3'

Sense:

(SEQ ID NO: 96)

5' A.A.G.C.A.G.A.U.G.C.A.G.A.G.A.U.U.A.U.U 3'

Antisense:

(SEQ ID NO: 97)

5' U.A.A.A.U.C.U.C.U.G.C.A.U.C.U.G.C.U.U.U.U 3'

Cond-siRNA Guide:

(SEQ ID NO: 98)

5' CCACU.A.A.A.U.C.U.C.U.G.C.A.U.C.U.G.C.U.U.U.U
55

3'

33

Example 7: Example Designs for miRNA Sensor Strands

Example designs for miRNA sensor strands are shown below.

miRNAs have highly conserved sequences across mammalian species. Therefore, we can design a single miRNA sensor for all test animals, including humans.

For each sequence, we first take the reverse complement of the guide sequence, then add 8 bases to create a 29 nt sensor.

```
>hsa-miR-23a-3p MIMAT0000078
                           (SEQ ID NO: 37) 15
AUCACAUUGCCAGGGAUUCC

> reverse complement
                           (SEQ ID NO: 38)
GGAAAUCCCUGGCAAUGUGAU

> Sensor, add 8 bases to make 29 mer
                           (SEQ ID NO: 39)
CGAGAAC GGAAUCCCUGGCAAUGUGAU
```

Nupack shows minimum secondary structure and no self-self base-pairing accept

```
>hsa-miR-125b-5p MIMAT0000423
                           (SEQ ID NO: 99)
UCCCCUGAGACCCUAACUUGUGA

> reverse complement
                           (SEQ ID NO: 100)
UCACAAGUUAGGGUCUCAGGGA

> Sensor, add 7 bases to make 29 mer,
                           (SEQ ID NO: 57) 35
CGACAGU UCACAAGUUAGGGUCUCAGGGA
```

Use secondary structure prediction codes make sure that the secondary structure is relatively open. If not, change the added bases and try again

```
>hsa-miR-199b-5p MIMAT0000263
                           (SEQ ID NO: 101)
CCCAGUGUUUAGACUAUCUGUUC

> reverse complement
                           (SEQ ID NO: 102)
GAACAGAUAGUCUAAACACUGGG

> Sensor, add 6 bases to make 29 mer,
                           (SEQ ID NO: 59) 50
CCUGAA GAACAGAUAGUCUAAACACUGGG
```

Acceptably Low Secondary Structure

Example 8: miRNAs

Additional miRNAs are shown below:

```
>rno-miR-23a-3p MIMAT0000792
                           (SEQ ID NO: 37)
AUCACAUUGCCAGGGAUUCC

>hsa-miR-23a-3p MIMAT0000078
                           (SEQ ID NO: 37)
AUCACAUUGCCAGGGAUUCC
```

60
65

34

-continued
>rno-miR-23a-3p MIMAT0000792
(SEQ ID NO: 37)

```
AUCACAUUGCCAGGGAUUCC

>mmu-miR-125b-5p MIMAT0000136
                           (SEQ ID NO: 99)
UCCCCUGAGACCCUAACUUGUGA

>hsa-miR-125b-5p MIMAT0000423
                           (SEQ ID NO: 99)
UCCCCUGAGACCCUAACUUGUGA

>rno-miR-125b-5p MIMAT0000830
                           (SEQ ID NO: 99)
UCCCCUGAGACCCUAACUUGUGA

>hsa-miR-199b-5p MIMAT0000263
                           (SEQ ID NO: 101)
CCCAGUGUUUAGACUAUCUGUUC

>mmu-miR-199b-5p MIMAT0000672
                           (SEQ ID NO: 103)
CCCAGUGUUUAGACUACCUGUUC
```

Example 9: Design Review for Sensor Strand miR-23a-3p with Calcineurin and HDAC2 Targets

FIG. 46 illustrates the design of sensor miR-23a-3p. FIG. 47 illustrates that the sequence of the sensor strand was checked against NCBI by blast. FIG. 48 illustrates that calcineurin and HDAC2 guide strand sequences are checked against NCBI by blast as well. FIG. 49 illustrates the secondary structure and MFE structure at 37° C. of the full miR-23a-3p sensor strand with toehold for calcineurin or HDAC2. The sensor has the following sequence, with toe hold shown in bold and underlined:

```
5' GGAGA AGAAC G (nick) GAAA UCCU GGCAA UGUGAU 3'  
(31 bp).
```

The Nupack analysis was performed on the sensor strand. The exon code with LNA modifications is shown as follows:

```
5' G + GA + GA + AG + AA + C G G + AA + A TC +
CCT + GGC + AA + TGT + G + A + T 3'.
```

Calcineurin is a protein phosphatase and is composed of two subunits: PPP3CA (catalytic) and PPP3R1 (regulatory). Thermo Fisher has an siRNA for this protein (PPP3CA) beginning at base pair 1549 (www.thermofisher.com/order/genome-database/browse/sirna/keyword/s72075). The guide and core strand sequences are as follows:

55 Guide (calcineurin target of 19 bp), starting from 1549: 5' CGAG UGUUG UUUGG CUUUU CCUG UU 3' (SEQ ID NO: 11, mutation from C to G is shown in bold and underlined);

```
Core strand:
5' CGUUC UUCUC C CAGGA AAAGC CAAAC AACAC UCG GCCAG
GGAUU UC 3'.
```

FIG. 50 shows that NuPack analyses of miR-23a-3p sensor strand for calcineurin were performed on core (FIG.

50A), guide (FIG. **50B**), Sensor with two small overhangs of core: 97% (FIG. **50C**), and calcineurin guide with core: 100% (FIG. **50D**).

FIG. **51** shows NCBI check for calcineurin guide strand vs. human constructs. The matches of primary concern include: *Homo sapiens* poly(ADP-ribose) polymerase family member 14 (PARP14), transcript variant X2, mRNA (20/21 plus/minus match); *Homo sapiens* uncharacterized LOC105374732 (LOC105374732), ncRNA (15 bp plus/minus match); *Homo sapiens* zinc finger FYVE-type containing 16 (ZFYVE16), transcript variant X19, mRNA (15 bp plus/minus match); and *Homo sapiens* GC-rich promoter binding protein 1 (GPBP1), transcript variant X11, misc_RNA (15 bp plus/minus match).

The guide of HDAC2 was from S100434959 (www.qiagen.com/us/shop/rnai/flexitube-sirna/?catno=S100434952#orderinginformation), having the following sequence: 5' GC ACUUA GAUUG AAACA ACCCA GUU 3' (25 bp) (SEQ ID NO: 13). The core with HDAC2 target has the following sequence, with short overhangs shown in bold and underlined: 5' CGUUC UUCUC C CUGGGUU-GUUUCAAUCUAAGUGC GCCAG GGAUU UC 3' (SEQ ID NO: 20).

FIG. **52** shows that NuPack analyses of miR-23a-3p sensor strand for HDAC2 were performed on core (FIG. **52A**), guide (FIG. **52B**), HDAC2 guide with core: 100% (FIG. **52C**), and sensor with core overhangs: 97% (FIG. **52D**).

FIG. **53** shows NCBI check for HDAC2 guide strand vs. human transcripts. The matches of primary concern include: *Homo sapiens* solute carrier family 35 member F5 (SLC35F5), transcript variant X6, mRNA (15 bp plus/minus match); and PREDICTED: *Homo sapiens* aquaporin 12B (AQP12B), transcript variant X16, misc_RNA (14 bp plus/minus match).

Example 10: Design Review for HDAC2 Targeted Conditional siRNA Constructs with Signals of BNP and MYH7

HDAC2 target guide sequence was designed as follows. HDAC2 siRNA was disclosed in published literature: www.nature.com/cddis/journal/v8/n3/extref/cddis201749x1.docx. The sequence was checked against the HDAC2 mRNA sequence from NCBI: www.ncbi.nlm.nih.gov/nuccore/NM_001527.3. A given DNA sequence was made into an RNA sequence, and then taken the reverse complement for the guide strand, starting at bp 518 on HDAC2 mRNA:

(SEQ ID NO: 111)
5' ACG GTCAATAAGA CCAGATAACA 3';
(SEQ ID NO: 112)
5' ACG GUCAAAUACA CCAGAUACA 3';

Guide target HDAC2: 5' UGU UAUCUGGUGU UAUUGACCGU 3' (SEQ ID NO: 14); and then 4 bp of 5' guide were purposefully mismatched: 5' CGAG AUCUG-GUGU UAUUGACCGU 3' (SEQ ID NO: 15).

FIG. **54** illustrates the check of guide vs. NCBI human transcripts and sequence alignment.

Three BNP candidates were selected. The first BNP candidate had an mRNA sequence source from www.ncbi.nlm.nih.gov/nuccore/83700236. The sequence starting from 3' UTR of BNP mRNA is as follows, with the 31 bp sequence used for reference for sensor strand shown in bold and underlined:

(SEQ ID NO: 121)
GAGGAAGUCCUGGCUGCAGACACUGCUUCUGAUUCCACAAGGGCUUUU
CCUCAACCCUGGCCGUUUGAAGUGACUCAUUUUUUAUGUAUUUAU
GAUUUAUUUGAUUUGUUUUAUAAGAUGGUUUCUACCUCUUGAGCACAAA
AUUCCACGGGAAUAAAGUCAACAUUA AAGCUUUAAAAAAAAAA.

The BNP sensor was designed by taking the reverse complement of the bold and underlined portion of SEQ ID NO: 121. The sequence is as follows, with the 8 bp toehold shown in bold and underlined:

(SEQ ID NO: 4)
AUCAGAACGAGGUGUCUGCAGCCAGGACUUC.

The Nupack assessment was performed (www.nupack.org/partition/histogram_detail/1166536?token=PcTqQEaZRt&strand_id=0) and the MFE structure of SEQ ID NO: 4 is shown in FIG. **55**.

FIG. **56** shows the BNP sensor sequence (SEQ ID NO: 4) together with core and guide sequences. FIGS. **57A** and **57B** show Nupack analyses of BNP sensor (SEQ ID NO: 4) with overhangs, and guide with core, respectively. The revised guide strand with the first 4 bp of 5' end with CGAG to provide mismatching in case of incorrect Dicer cleavage and RISC complex loading. The modified guide has 2 U overhang: 5' CGAG AUCUGGUGUU AUUGACCGUUU 3' (SEQ ID NO: 4). The modified core has the following sequence: CCUGCUUCUGAUACGGUCAAAACACCAGAUUCUGGGCUGCAGACA (SEQ ID NO: 122). FIG. **58** shows NCBI check of BNP sensor vs. human transcripts.

The design of the second BNP candidate was similar to the first except that the 31 bp sequence used for reference for sensor strand was a different portion from SEQ ID NO: 121 shown in bold and underlined:

(SEQ ID NO: 121)
GAGGAAGUCCUGGCUGCAGACACUGCUUCUGAUUCCACAAGGGCUUUU
CCUCAACCCUGGCCGUUUGAAGUGACUCAUUUUUUAUGUAUUUAU
GAUUUAUUUGAUUUGUUUUAUAAGAUGGUUUCUACCUCUUGAGCACAAA
AUUCCACGGGAAUAAAGUCAACAUUA AAGCUUUAAAAAAAAAA.

The sequence of the second BNP sensor is as follows, with the 8 bp toehold shown in bold and underlined:

(SEQ ID NO: 5)
CUUGUGGAAUCAGAACGAGGUGUCUGGCAGCC.

The Nupack assessment was performed (www.nupack.org/partition/histogram_detail/1166628?token=wqLsVGJxBN&strand_id=0) and the MFE structure of SEQ ID NO: 5 is shown in FIG. **59**. FIG. **60** shows the BNP sensor sequence (SEQ ID NO: 5) together with core and guide sequences. FIGS. **61A** and **61B** show Nupack analyses of BNP sensor (SEQ ID NO: 5) with overhangs, and guide with core, respectively. FIG. **62** shows NCBI check of BNP sensor second candidate vs. human transcripts.

Likewise, the design of the third BNP candidate was similar to the first and second except that the 31 bp sequence used for reference for sensor strand was a different portion from SEQ ID NO: 121 shown in bold and underlined:

(SEQ ID NO: 121)
GAGGAAGUCCUGGCUGCAGACACUGCUUCUGAUUCCACAAGGGGGCUUUUU

CCUCAACCCUGUGGCCGCCUUUGAAGUGACUCAUUUUUUUAUGUAUUA
 UGAUUUAUUUGAUUGUUUUUAUAAGAUGGUUUCCUACCUUUGAGCACAA
 AAUUCACGGAAAAGUCAACAUUA AAGCUUAAAAAAAAAA.

The sequence of the third BNP sensor is as follows, with the 8 bp toehold shown in bold and underlined:

(SEQ ID NO: 6)
CAAAGGCGGCCACAGGGUUGAGGAAAAAGCC.

The Nupack assessment was performed (www.nupack.org/partition/histogram_detail/1166638?token=wZSopNPdDt&strand_id=0) and the MFE structure of SEQ ID NO: 6 is shown in FIG. 63. FIG. 64 shows the BNP sensor sequence (SEQ ID NO: 6) together with core and guide sequences. FIG. 65 shows Nupack analysis of guide with core for the third BNP candidate. FIG. 66 shows NCBI check of BNP sensor third candidate vs. human transcripts.

Myosin heavy chain 7 (MYH7) encodes for a heavy chain subunit of cardiac myosin-contractile velocity of cardiac muscle. Myosin has 2 heavy chains, 2 alkali light chains, and 2 regulatory light chains. It is expressed in normal human ventricles as well as type 1 (slow twitch) muscle fibers. Mutations in this gene result in hypertrophic cardiomyopathy, myosin storage myopathy, and numerous other cardiac diseases. See www.genecards.org/cgi-bin/carddisp.pl?gene=MYH7.

The MYH7 candidate had an mRNA sequence source from www.ncbi.nlm.nih.gov/nuccore/NM_000257.3. The sequence starting from 3' UTR of MYH7 mRNA is as follows, with the 31 bp sequence used for reference for sensor strand shown in bold and underlined:

Core: 5' GUCAUCUUGUUGCUGGGUUGUUCAACUAAGAGCGCUGCAUUUGU
 3' (SEQ ID NO: 25);
 Sensor: 5' CAACAAAGAUGACACAAUGCAGCAGAGACCC 3' (SEQ ID NO: 8)
 Modified sensor (SEQ ID NO: 147):
 CA + ACA + AG + ATG + AC + ACA + AA + TGC + AGC + AG + AGA + C + C + C
 s1-s1: 28 S1: 24 DNA ™: 87 RNA ™: 92;
 and
 Guide: 5' GCUCUUAGAUUGAAACAACCCAGUU 3' (SEQ ID NO: 16)

Construct #3 (MPE structure shown in FIG. 72) (www.nupack.org/partition/show/1169058?time_refresh=1.0&token=OXLbgX6bBo) was designed with the following sequences:

Core: 5' CAUUGUGUCAUUGUAGAUUGAAACAACCCAGGGUCUGCUG 3'
 (SEQ ID NO: 26);
 Sensor: 5' AUGACACAAUGCAGCAGAGACCCAGGG 3' (SEQ ID NO: 9)

(SEQ ID NO: 143)
 UUUUUUUUUU UUUUUCUGG CUUCAAGGAA AAUUGC
 UUCUGCUUCC UCCCAAGGAG CUGUACACA GGCUC
 5 UGGGGCUUUG **CUGGCACCUC CAGGGCUGAG CAGAUCAAGA**
UGGGCAAAG.

The MYH7 sensor was designed by taking the reverse complement of the bold and underlined portion of SEQ ID NO: 143. The sequence is as follows, with the 8 bp toehold shown in bold and underlined:

(SEQ ID NO: 7)
AUCUUGAUCUGCUAGCCUGGAGGUGCCAG.

The Nupack assessment was performed (www.nupack.org/partition/histogram_detail/1167009?token=OyDl4ywh0J&strand_id=0) and the MFE structure of SEQ ID NO: 7 is shown in FIG. 67.

FIG. 68 shows the MYH7 sensor sequence (SEQ ID NO: 7) together with core and guide sequences. FIGS. 69A and 69B show Nupack analyses of MYH7 sensor (SEQ ID NO: 7) with overhangs, and guide with core, respectively. FIG. 70 shows NCBI check of MYH7 sensor vs. human transcripts.

Example 11: Design Review of Conditional siRNAs in Cardiac Ischemia

30 NPPA (aka: ANP, ANF, ANH, or CDD), if overexpressed in heart cells, inhibits maladaptive cardiac hypertrophy. High levels of NPPB (aka: BNP) serve as a biomarker for heart failure in ischemic patients. Overexpression or mutation of MYH7 (aka: CMD1S, C1, MYHCB, SPMD, or SPMM) can cause cells to die prematurely and increase cardiac fibrosis. This design uses NPPA, NPPB or MYH7 as sensor, and HDAC2 and calcineurin as targets. Inhibition of HDAC2 or calcineurin causes reduced cardiac hypertrophy.

Examples of NPPA HDAC2 designs are illustrated as follows. Construct #1 (best, MPE structure shown in FIG. 71) (www.nupack.org/partition/histogram_detail/1157307?temperature=37.0&token=gYZWv2FATz&permutation_id=2&complex_id=23) was designed with the following sequences:

- continued

Modified sensor (SEQ ID NO: 148):

A + TG + AC + ACA + AA + TGC + AGC + A + G + A + G + ACCCC + AG + GGG + A
 s1-s1: 40 s1: 33 DNA " : 95 RNA " : 100
 and

Guide: 5' GCUCUUAGAUUGAAACAACCCAGUU 3' (SEQ ID NO: 16) .

An example of NPPA calcineurin design is illustrated as follows. Construct #1 (best, MPE structure shown in FIG. 10 73) (www.nupack.org/partition/show/1169063?time_refresh=1.0&to肯=RnEIROmvsz) was designed with the following sequences:

Core: 5' GUCAUCUUGUUGCAGGAAAAGCCAAACAACACUCGGCUGCAUUUGU

3' (SEQ ID NO: 149) ;

Sensor: 5' CAACAAGAUGACACAAUUGCAGCAGAGACCC 3' (SEQ ID NO: 8)

Modified sensor (SEQ ID NO: 147):

Modified sensor: CA + ACA + AG + ATG + AC + ACA + AA + TGC +
 AGC + AG + AGA + C + C + C
 s1-s1: 28 s1: 24 DNA " : 87 RNA " : 92
 and

Guide: 5' CGAGUGUUGUUGGUCCUUUCCUGUU 3' (SEQ ID NO: 12) .

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APPENDIX B

```

import re
def check_sequence(seq, n, filename, exclude = ['CCC', 'GGG', '[A, U, T]{4}']):
    '''This will check through a sequence and see if it meets a set of requirements'''
    nseq = len(seq)
    assert nseq >= n
    excludereg = [ ]
    for i in exclude:
        exclude_reg.append(re.compile(i))
    # make everything upper case
    seq = seq.upper()
    lines = [ ]
    for i in range(nseq-n+1):
        bad=0
        excluded = [ ]
        seg = seq[i:i+n]
        gcau = (seg.count('G'), seg.count('C'), seg.count('A'), seg.count('U')+seg.count('T'))
        assert (gcau[0]+gcau[1]+ gcau[2] + gcau[3]) == n
        gc_percent = float((gcau[0]+gcau[1]))/n
        for pat in exclude reg:
            x = pat.findall(seg)
            bad += len(x)
            excluded.append(x)
        threeletter = 1-float(min(gcau))/n
        lines.append((seg, excluded, gc_percent, threeletter, bad, i))
    f = open(filename, 'w')
    f.write('Sequence \t Bad Segments\t GCness\t 3-letteredness\t Number bad points\t
position\n')
    for i in lines:
        for j in i:
            f.write(repr(j)+'\f')
    f.write('\n')
    f.close()
    return lines
def reverse_complement_RNA(input):
    output =""
    input=input.upper()
    for i in range(len(input)):
        x = input[i]
        if x== 'A':
            output += U
        elif x == 'a':
            output += 'u'
        elif x == U or x=T':
            output += 'A'
        elif x == 'u':
            output += 'a'
        elif x == 'G':
            output += 'C'
        elif x == 'C':
            output += 'G'
        elif x == 'g':
            output += 'c'
        elif x == 'c':
            output += 'g'
    return output[::-1]
# generate 31 nt sensor candidates for human myh7 3' utr
hmyh7 =
'gcttgccacatcttgatctgctcagccctggagggtgccagcaa

```

- continued

```

agccccatgctggagcctgtgtaacagctccttggaggaagca
gaataaaagcaatttccttgaagccgag' (SEQ ID NO: 150)

chmyh7 = reverse_complement_RNA(hmyh7)
print(chmyh7)
print('\n')
check_sequence(chmyh7, 31, 'myh7 human.tsv')
# generate 31 nt sensor candidates for human nppa 3' utr
hnppa = "agata acagccagg aggacaagca gggctggcc tagggacaga ctgcgaagg ctccctgtccc

ctggggtctc tgctgcattt gtgtcatttt gttgccatgg agtttgtatc atcccatcta
agctgcagtc ttctgtcaac acttctcaca tcttatgtca acttgtatc aagtggtttgc
atggtgactt cctcgccctt cccacccat gcattaaattt ttaaggtaga acctcacctg
ttactgaaag tgggttggaaa gtgataaaac ttccagcacca tggacagaag ac'' (SEQ ID NO: 151)

chnppa = reverse_complement_RNA(hnppa)
print(chnppa)
printin'
check_sequence(chnppa, 31, 'nppa human.tsv')
# generate 31 nt sensor candidates for human nppb 3' utr
hnppb = 'gag aaaggccctgg ctgcagacac ctgcatttgc ttccacaagg

ggcttttcc tcaaccctgt ggccgcctttt gaagtgtactt atttttttaa tggatgtttat
tatttttttg attgttttat ataagatgtt ttcttacattt tgagcacaaa atttccacgg
tgaataaaag tcaacattt aagcttf'' (SEQ ID NO: 152)

chnppb = reversecomplementRNA(hnppb)
print(chnppb)
print('\n')
check_sequence(chnppb, 31, 'nppb human.tsv')
# generate 31 nt sensor candidates for rat myh7 3' utr
rmyh7 = 'atct

tggcttacc acccctaagg atgcctgtga agccctgaga cctggagctt ttgaaacagc
accttaggca gaaacacaat aaagcaattt tccttcaagc c'' (SEQ ID NO: 153)

crmyh7 = reverse_complement_RNA(rmyh7)
print(crmyh7)
print('\n')
check_sequence(crmyh7, 31, 'myh7 rat.tsv')
# generate 31 nt sensor candidates for rat nppa 3' utr
rnppa = 'cagcc
aaatctgtca gaggcagatcg caaaaatgc caagcccttg cggtgtgtca cacagctgg

tcgcattgcc actgagaggt ggtgaataacc ctctggagc tgcagttcc tggatgtttatc
tatcacgtatc gatgttaagt gtatgtatgtt gggttagtgc ggccttacactt ctccactt
gcatattaag gtatgttgc accccattca gaaagcgtt ggaaaaaaat aaatccgaat
aaacctcagc accacggaca gacgttgagg cctg'' (SEQ ID NO: 154)

crnppa = reversecomplementRNA(rnppa)
print(crnppa)
print('\n')
check_sequence(crnppa, 31, 'nppa rat.tsv')
# generate 31 nt sensor candidates for rat nppa 3' utr
rnppb = 'gaagacc tcctggctgc agactccggc ttctgactctt ggcctgggtt cttttttttt

cagctctggg accacccatc aagtgtatctt gtttattttt ttgtttatattt atttattttt
atgttgctga ttttctacaa gactgtttctt tatcttccatc cacaacttgc ccacagtgtatc
ataaacatag ctttatttgc gctttttgg'' (SEQ ID NO: 155)

crnppb = reversecomplementRNA(rnppb)
print(crnppb)
print('\n')
check_sequence(crnppa, 31, 'nppb rat.tsv')

```

Homo sapiens myosin heavy chain 7 (MYH7), mRNA
NCBI Reference Sequence: NM_000257.3
FASTA Graphics
Go to:
LOCUS NM_0002576069 bp mRNA linear PRI 17-JUN-2018
DEFINITION *Homo sapiens* myosin heavy chain 7 (MYH7), mRNA.
ACCESSION NM_000257 XM_005267696
VERSION NM_000257.3
KEYWORDS RefSeq.
SOURCE *Homo sapiens* (human)

ORGANISM *Homo sapiens*
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 6069)
AUTHORS Feng X, He T, Wang JG and Zhao P.
TITLE Asn391Thr Mutation of beta-Myosin Heavy Chain in a Hypertrophic Cardiomyopathy Family
JOURNAL Int Heart J 59 (3), 596-600 (2018)
PUBMED 29743414
REMARK GeneRIF: Asn391Thr mutation of MYH7 is a malignant mutation for hypertrophic cardiomyopathy and that mutation carriers should get effective treatment to prevent sudden death.

REFERENCE 2 (bases 1 to 6069)
AUTHORS Viswanathan SK, Sanders HK, McNamara JW, Jagadeesan A, Jahangir A, Tajik AJ and Sadyappan S.
TITLE Hypertrophic cardiomyopathy clinical phenotype is independent of gene mutation and mutation dosage
JOURNAL PLoS ONE 12 (11), e0187948 (2017)
PUBMED 29121657
REMARK GeneRIF: Data provide evidence that MYH7 mutations contributed to 24.4% MYBPC3 mutations of hypertrophic cardiomyopathy (HCM) cases, that MYBPC3 constitute the preeminent cause of HCM and that both mutations are phenotypically indistinguishable.
Publication Status: Online-Only

REFERENCE 3 (bases 1 to 6069)
AUTHORS Wang B, Guo R, Zuo L, Shao H, Liu Y, Wang Y, Ju Y, Sun C, Wang L, Zhang Y and Liu L.
TITLE [Analysis of genotype and phenotype correlation of MYH7-V878A mutation among ethnic Han Chinese pedigrees affected with hypertrophic cardiomyopathy]
JOURNAL Zhonghua Yi Xue Zi Za Chuan Xue Za Zhi 34 (4), 514-518 (2017)
PUBMED 28777849
REMARK GeneRIF: MYH7-V878A is a hot spot among ethnic Han Chinese with a high penetrance.

REFERENCE 4 (bases 1 to 6069)
AUTHORS Oldfors A.
TITLE Hereditary myosin myopathies
JOURNAL Neuromuscul. Disord. 17 (5), 355-367 (2007)
PUBMED 17434305
REMARK Review article

REFERENCE 5 (bases 1 to 6069)
AUTHORS Cirino, A.L. and Ho, C.
TITLE Hypertrophic Cardiomyopathy Overview
JOURNAL (in) Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K and Amemiya A (Eds.); GENEREVIEW S((R)); (1993)
PUBMED 20301725

REFERENCE 6 (bases 1 to 6069)
AUTHORS Lamont, P. and Laing, N.G.
TITLE Laing Distal Myopathy
JOURNAL (in) Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K and Amemiya A (Eds.); GENEREVIEW S((R)); (1993)
PUBMED 20301606

REFERENCE 7 (bases 1 to 6069)
AUTHORS Hershberger, R.E. and Morales, A.
TITLE Dilated Cardiomyopathy Overview
JOURNAL (in) Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens

-continued

K and Amemiya A (Eds.) ;
GENEREVIEW S((R)) ;
(1993)
PUBMED 20301486

REFERENCE 8 (bases 1 to 6069)
AUTHORS DeChene, E.T., Kang, P.B. and Beggs, A.H.
TITLE Congenital Fiber-Type Disproportion
JOURNAL (in) Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K and Amemiya A (Eds.) ;
GENEREVIEW S((R)) ;
(1993)
PUBMED 20301436

REFERENCE 9 (bases 1 to 6069)
AUTHORS Warlick CA, Ramachandra S, Mishra S and Donis-Keller H.
TITLE Dinucleotide repeat polymorphism at the human cardiac beta-myosin heavy chain gene (HMSYHCO1) locus
JOURNAL Hum. Mol. Genet. 1 (2), 136 (1992)
PUBMED 1301151

REFERENCE 10 (bases 1 to 6069)
AUTHORS Fougerousse F, Dufour C, Roudaut C and Beckmann JS.
TITLE Dinucleotide repeat polymorphism at the human gene for cardiac beta-myosin heavy chain (MYH6)
JOURNAL Hum. Mol. Genet. 1 (1), 64 (1992)
PUBMED 1301139

COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from BF834726.1, EU747717.1, M58018.1 and BC112173.L
On or before Jun. 20, 2014 this sequence version replaced XM_005267696.1, NM_000257.2.

Summary: Muscle myosin is a hexameric protein containing 2 heavy chain subunits, 2 alkali light chain subunits, and 2 regulatory light chain subunits. This gene encodes the beta (or slow) heavy chain subunit of cardiac myosin. It is expressed predominantly in normal human ventricle. It is also expressed in skeletal muscle tissues rich in slow-twitch type I muscle fibers. Changes in the relative abundance of this protein and the alpha (or fast) heavy subunit of cardiac myosin correlate with the contractile velocity of cardiac muscle. Its expression is also altered during thyroid hormone depletion and hemodynamic overloading. Mutations in this gene are associated with familial hypertrophic cardiomyopathy, myosin storage myopathy, dilated cardiomyopathy, and Laing early-onset distal myopathy, [provided by RefSeq, Jul 2008].

Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Gene record to access additional publications.

```
##Evidence-Data-START ##
Transcript exon combination :: EU747717.1, M58018.1 [ECO:0000332]
RNAseq introns:: mixed/partial sample support
SAMEA1965299, SAMEA1968540
[ECO:0000350]
##Evidence-Data-END##
COMPLETENESS: complete on the 3' end.
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PRIMARY COMP	REFSEQ_SPAN	PRIMARY IDENTIFIER PRIMARY SPAN
1-25	BF834726.1	60-84
26-320	EU747717.1	1-295
321-1831	M58018.1	276-1786
1832-3501	BC112173.1	1756-3425
3502-6053	M58018.1	3457-6008
6054-6069	EU747717.1	6029-6044
FEATURES	Location/Qualifiers	
source	1 . . . 6069 /organism="Homo sapiens" /mol_type="mRNA" /db_xref="taxon:9606" /chromosome="14" /map="14q11.2"	

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gene 1 . . . 6069
 /gene="MYH7"
 /gene_synonym="CMD1S; CMH1; MPD1; MYHCB; SPMD; SPMM"
 /note="myosin heavy chain 7"
 /db_xref="GeneID:4625"

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 myhc-slow; myopathy, distal 1; cardiac muscle myosin heavy
 chain 7 beta; rhabdomyosarcoma antigen MU-RMS-40.7A;
 myHC-beta; myosin heavy chain slow isoform; myosin heavy
 chain, cardiac muscle beta isoform; myosin 7; myosin,
 heavy chain 7, cardiac muscle, beta; myosin heavy chain
 beta-subunit"
 /codon_start=1
 /product="myosin-7"
 /protein_id="NP_000248.2"
 /db_xref="CCDS:CCDS9601.1"
 /db_xref="GeneID:4625"
 /db_xref="HGNC:HGNC:7577"
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 /gene_synonym="CMD 1S; CMH1; MPDI; MYHCB; SPMD; SPMM"
 /note="myosin, heavy polypeptide 7, cardiac muscle, beta;
 myhc-slow; myopathy, distal 1; cardiac muscle myosin heavy
 chain 7 beta; rhabdomyosarcoma antigen MU-RMS-40.7A;
 myHC-beta; myosin heavy chain slow isoform; myosin heavy
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 heavy chain 7, cardiac muscle, beta; myosin heavy chain
 beta-subunit"
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 DNSSRFG KFIRIH PGATGKLASADIETYLL EKSRVIFQLKAERDYHI
 FYQI LS NKKP ELLDMLL ITNNYD YAFISQGETTVA S IDDAEELM
 ATD NAF DV LGFT SEE KNSMYKLT GAIMH FGNM KFKL KQREE
 QAE PDGTE EADKS SAYLM GLNSADL LKGLC HPRV KV
 GNEY VTKG QNVQV IYAT GALAKA VY ERMP NMV TRINA
 TLET KQP RQY FIGV LDIAG FEI FDF NS FE QLC IN FTNE
 KLO QFF NHMFV LEQE EY KKEGI EWT FID FGMD LQAC
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 HGK SAN FQ KPRNI KGK PEA HFS LIHYAGI VD YNI IGWLQ
 KNKDP LNETVV GLY QKSSL KLL STL FANYAGAD API EKG
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 II PNET KSPG VM DNPL VMH QLRC NGVLEG
 IRICRKGF PN RILY GDGR QRY RIL NP A PIE PGQF
 IDSRK GAE KL LSSLDIDHNQYKEGH TKVFFF
 KAGLL GLL EEMR DERLSRIITRIQA SRGV LARMEY
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 PLL KSAER EKEMAS MKEE FTRL KEALEK SEARR KELE
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 /gene_synonym="CMD1S; CMH1; MPD1; MYHCB; SPMD; SPMM"
 /experiment="experimental evidence, no additional details recorded"
 /note="Phosphothreonine. {ECO:0000250 UniProtKB:P02563}; propagated from UniProtKB/Swiss-Prot (P12883.5); phosphorylation site"

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 /experiment="experimental evidence, no additional details recorded"
 /note="propagated from UniProtKB/Swiss-Prot (P12883.5); Region: Actin-binding"

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phosphorylation site"

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phosphorylation site"

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phosphorylation site"

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/experiment-'experimental evidence, no additional details
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phosphorylation site"

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exon        477 . . . 633
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exon      5691 . . . 5786
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STS	5814 . . . 5971 /gene="MYH7" /gene_synonym="CMD1S; CMH1; MPD1; MYHCB; SPMD; SPMM" /standard_name="RH66825" /db_xref="UniSTS:5241"
exon	5922 . . . 6055 /gene="MYH7" /gene_synonym="CMD1S; CMH1; MPD1; MYHCB; SPMD; SPMM" /inference="alignment: Spalign:2.1.0"
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ORIGIN

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 2881 ccaaggatggaa gggatgtcc ctttgcatttgcacccatc cccacttttgcatttgcatttgc
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APPENDIX D

Homo sapiens natriuretic peptide A (NPPA), mRNA
 NCBI Reference Sequence: NM_006172.3
 FASTA Graphics
 Go to:
 LOCUS NM_006172 858 bp mRNA linear PRI 29-JUL-2018
 DEFINITION *Homo sapiens natriuretic peptide A (NPPA), mRNA.*
 ACCESSION NM_006172
 VERSION NM_006172.3
 KEYWORDS RefSeq.
 SOURCE *Homo sapiens* (human)
 ORGANISM *Homo sapiens*
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
 Catarrhini; Hominidae; Homo.

 REFERENCE 1 (bases 1 to 858)
 AUTHORS Cannone V., Scott C. G., Decker P. A., Larson N. B., Palmas W., Taylor K. D.,
 Wang T. J., Gupta D. K., Bielinski S. J. and Burnett J. C. Jr.
 TITLE A favorable cardiometabolic profile is associated with the G allele
 of the genetic variant rs5068 in African Americans: The
 Multi-Ethnic Study of Atherosclerosis (MESA)
 JOURNAL PLoS ONE 12 (12), e0189858 (2017)
 PUBMED 29253899
 REMARK GeneRIF: the G allele of the genetic variant rs5068 in African
 Americans is associated with lower prevalence of metabolic syndrome

-continued

and lower triglycerides values
Publication Status: Online-Only

REFERENCE 2 (bases 1 to 858)

AUTHORS Salo, P. P., Havulinna, A. S., Tukiainen, T., Raitakari, O., Lehtimaki, T., Kahonen, M., Kettunen, J., Mannikko, M., Eriksson, J. G., Jula, A., Blankenberg, S., Zeller, T., Salomaa, V., Kristiansson, K. and Perola, M.

TITLE Genome-Wide Association Study Implicates Atrial Natriuretic Peptide Rather Than B-Type Natriuretic Peptide in the Regulation of Blood Pressure in the General Population

JOURNAL Circ Cardiovasc Genet 10 (6) (2017)

PUBMED 29237677

REMARK GeneRIF: Data indicate the blood pressure-lowering effect of atrial natriuretic peptide (ANP) in the general population.

REFERENCE 3 (bases 1 to 858)

AUTHORS Wakula P., Neumann B., Kienemund J., Thon-Gutschi E., Stojakovic T., Manninger M., Scherr D., Schamagl H., Kapi M., Pieske B. and Henzel F. R.

TITLE CHA2DS2-VASc score and blood biomarkers to identify patients with atrial high-rate episodes and paroxysmal atrial fibrillation

JOURNAL Europace 19 (4), 544-551 (2017)

PUBMED 28431065

REMARK GeneRIF: TIMP-4, NT-proANP, NT-proBNP were strongest associated with PAF and AHRE. The discriminatory performance of CHADS2-VASc for PAF was increased by addition of selected biomarkers.

REFERENCE 4 (bases 1 to 858)

AUTHORS Bartus K., Podolec J., Lee R. J., Kapelak B., Sadowski J., Bartus M., Oles K., Ceranowicz P., Trabka R. and Litwinowicz R.

TITLE Atrial natriuretic peptide and brain natriuretic peptide changes after epicardial percutaneous left atrial appendage suture ligation using LARIAT device

JOURNAL J. Physiol. Pharmacol. 68 (1), 117-123 (2017)

PUBMED 28456775

REMARK GeneRIF: In summary, there were no significant differences in ANP and BNP levels after percutaneous epicardial left atrial appendage suture ligation using LARIAT device 3 months after procedure.

REFERENCE 5 (bases 1 to 858)

AUTHORS Suga S., Nakao K., Hosoda K., Mukoyama M., Ogawa Y., Shirakami G., Arai H., Saito Y., Kambayashi Y., Inouye K. et al.

TITLE Receptor selectivity of natriuretic peptide family, atrial natriuretic peptide, brain natriuretic peptide, and C-type natriuretic peptide

JOURNAL Endocrinology 130 (1), 229-239 (1992)

PUBMED 1309330

REFERENCE 6 (bases 1 to 858)

AUTHORS Bennett B. D., Bennett G. L., Vitangcol R. V., Jewett J. R., Burnier J., Henzel W. and Lowe D. G.

TITLE Extracellular domain-IgG fusion proteins for three human natriuretic peptide receptors. Hormone pharmacology and application to solid phase screening of synthetic peptide antisera

JOURNAL J. Biol. Chern. 266 (34), 23060-23067 (1991)

PUBMED 1660465

REFERENCE 7 (bases 1 to 858)

AUTHORS Koller K. J., Lowe D. G., Bennett G. L., Minamino N., Kangawa K., Matsuo H. and Goeddel D. V.

TITLE Selective activation of the B natriuretic peptide receptor by C-type natriuretic peptide (CNP)

JOURNAL Science 252 (5002), 120-123 (1991)

PUBMED 1672777

REFERENCE 8 (bases 1 to 858)

AUTHORS Yang-Feng, T. L., Floyd-Smith, G., Nemer, M., Drouin, J. and Francke, U.

TITLE The pronatriodilatin gene is located on the distal short arm of human chromosome 1 and on mouse chromosome 4

JOURNAL Am. J. Hum. Genet. 37 (6), 1117-1128 (1985)

PUBMED 2934979

REFERENCE 9 (bases 1 to 858)

AUTHORS Zivin, R. A., Condra, J. H., Dixon, R. A., Seidah, N. G., Chretien, M., Nemer, M., Chamberland, M. and Drouin, J.

TITLE Molecular cloning and characterization of DNA sequences encoding rat and human atrial natriuretic factors

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 81 (20), 6325-6329 (1984)

-continued

PUBMED 6238331

REFERENCE 10 (bases 1 to 858)
 AUTHORS Oikawa, S., Imai, M., Ueno, A., Tanaka, S., Noguchi, T., Nakazato, H.,
 Kangawa, K., Fukuda, A. and Matsuo, H.
 TITLE Cloning and sequence analysis of cDNA encoding a precursor for
 human atrial natriuretic polypeptide
 JOURNAL Nature 309 (5970), 724-726 (1984)
 PUBMED 6203042

COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from BC005893.1 and AA779538.1. This sequence is a reference standard in the RefSeqGene project. On Jun. 13, 2009 this sequence version replaced NM_006172.2.

Summary: The protein encoded by this gene belongs to the natriuretic peptide family. Natriuretic peptides are implicated in the control of extracellular fluid volume and electrolyte homeostasis. This protein is synthesized as a large precursor (containing a signal peptide), which is processed to release a peptide from the N-terminus with similarity to vasoactive peptide, cardiodilatin, and another peptide from the C-terminus with natriuretic-diuretic activity. Mutations in this gene have been associated with atrial fibrillation familial type 6. This gene is located adjacent to another member of the natriuretic family of peptides on chromosome 1. [provided by RefSeq, October 2015].

Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Gene record to access additional publications.

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RNAseq introns :: single sample supports all introns
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[ECO: 0000348]
##Evidence-Data-END##
COMPLETENESS: complete on the 3'end.
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/note = "Cleavage, by CORIN. {ECO: 0000269|PubMed: 10880574};
propagated from UniProtKB/Swiss-Prot (P01160.1); cleavage
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{ECO: 0000269|PubMed: 10880574, ECO: 0000269|PubMed:6230082}"
/experiment = "experimental evidence, no additional details
recorded"
/note = "propagated from UniProtKB/Swiss-Prot (P01160.1)"

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/experiment = "experimental evidence, no additional details
recorded"
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/inference = "alignment: Splign: 2.1.0"

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/gene_synonym = "ANF; ANP; ATFB6; ATRST2; CDD; CDD-ANF; CDP;
PND"

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/gene_synonym = "ANF; ANP; ATFB6; ATRST2; CDD; CDD-ANF; CDP;
PND"

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APPENDIX E

Homo sapiens natriuretic peptide B (NPPB), mRNA
 NCBI Reference Sequence: NM_002521.2
 FASTA Graphics
 Go to:
 LOCUS NM_002521 708 bp mRNA linear PRI 22-JUL-2018
 DEFINITION *Homo sapiens* natriuretic peptide B (NPPB), mRNA.
 ACCESSION NM_002521
 VERSION NM_002521.2
 KEYWORDS RefSeq.
 SOURCE *Homo sapiens* (human)
 ORGANISM *Homo sapiens*
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
 Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 708)
 AUTHORS Hex C., Smeets M., Penders J., Van Hoof V., Verbakel J., Buntinx F. and
 Vaes B.
 TITLE Accuracy, user-friendliness and usefulness of the Cobas h232
 point-of-care test for NT-proBNP in primary care
 JOURNAL J. Clin. Pathol. 71 (6), 539-545 (2018)
 PUBMED 29263170
 REMARK GeneRIF: Report usefulness of point-of-care test for NT-proBNP in
 primary care for the diagnosis of heart failure.
 REFERENCE 2 (bases 1 to 708)
 AUTHORS Drozdz T., Kwinta P., Kordon Z., Sztefko K., Rudzinski A., Zachwieja K.,
 Miklaszewska M., Czarnecka D. and Drozdz D.
 TITLE [B-type natriuretic peptide as a marker of cardiac dysfunction in
 children with chronic kidney disease]
 JOURNAL Pol. Merkur. Lekarski 44 (262), 171-176 (2018)
 PUBMED 29775443
 REMARK GeneRIF: In children with chronic kidney disease, BNP is an
 indicator of heart failure correlating with renal function
 parameters and left ventricular mass index.

-continued

REFERENCE 3 (bases 1 to 708)
 AUTHORS Fernandez-Susavila H., Rodriguez-Yanez M., Dopico-Lopez A., Arias S., Santamaria M., Avila-Gomez P., Doval-Garcia J. M., Sobrino T., Iglesias-Rey R., Castillo J. and Campos F.
 TITLE Heads and Tails of Natriuretic Peptides: Neuroprotective Role of Brain Natriuretic Peptide
 JOURNAL J Am Heart Assoc 6 (12), e007329 (2017)
 PUBMED 29203579
 REMARK GeneRIF: Suggest potential role for BNP as a protective endogenous factor against cerebral ischemia.
 Publication Status: Online-Only

REFERENCE 4 (bases 1 to 708)
 AUTHORS Legaz-Arrese A., Carranza-Garcia L. E., Navarro-Orocio R., Valadez-Lira A., Mayolas-Pi C., Munguia-Izquierdo D., Reverter-Masia J. and George K.
 TITLE Cardiac Biomarker Release after Endurance Exercise in Male and Female Adults and Adolescents
 JOURNAL J. Pediatr. 191, 96-102 (2017)
 PUBMED 29173327
 REMARK GeneRIF: An exercise-associated increase in hs-cTnT and NT-proBNP occurred in response to a 60-minute maximal swimming test that was independent of pubertal status/adolescent vs adults. The present data also suggests that baseline and postexercise hs-cTnT values are higher in male compared with female, with no sex differences in NT-proBNP values.

REFERENCE 5 (bases 1 to 708)
 AUTHORS Krause A., Liepke C., Meyer M., Adermann K., Forssmann W. G. and Maronde E.
 TITLE Human natriuretic peptides exhibit antimicrobial activity
 JOURNAL Eur. J. Med. Res. 6 (5), 215-218 (2001)
 PUBMED 11410403
 REMARK GeneRIF: Brain-type natriuretic peptide (hBNP-32) is an antimicrobial peptide active against Gram-positive and Gram-negative bacteria and yeast.

REFERENCE 6 (bases 1 to 708)
 AUTHORS Arden K. C., Viards C. S., Weiss S., Argentin S. and Nemer M.
 TITLE Localization of the human B-type natriuretic peptide precursor (NPBP) gene to chromosome 1p36
 JOURNAL Genomics 26 (2), 385-389 (1995)
 PUBMED 7601467
 REFERENCE 7 (bases 1 to 708)
 AUTHORS Suga S., Nakao K., Hosoda K., Mukoyama M., Ogawa Y., Shirakami G., Arai H., Saito Y., Kambayashi Y., Inouye K. et al.
 TITLE Receptor selectivity of natriuretic peptide family, atrial natriuretic peptide, brain natriuretic peptide, and C-type natriuretic peptide
 JOURNAL Endocrinology 130 (1), 229-239 (1992)
 PUBMED 1309330

REFERENCE 8 (bases 1 to 708)
 AUTHORS Bennett B. D., Bennett G. L., Vitangcol R. V., Jewett J. R., Burnier J., Henzel W. and Lowe D. G..
 TITLE Extracellular domain-IgG fusion proteins for three human natriuretic peptide receptors. Hormone pharmacology and application to solid phase screening of synthetic peptide antisera
 JOURNAL J. Biol. Chern. 266 (34), 23060-23067 (1991)
 PUBMED 1660465

REFERENCE 9 (bases 1 to 708)
 AUTHORS Koller K. J., Lowe D. G., Bennett G. L., Minamino N., Kangawa K., Matsuo H. and Goeddel D. V..
 TITLE Selective activation of the B natriuretic peptide receptor by C-type natriuretic peptide (CNP)
 JOURNAL Science 252 (5002), 120-123 (1991)
 PUBMED 1672777

REFERENCE 10 (bases 1 to 708)
 AUTHORS Sudoh T., Maekawa K., Kojima M., Minamino N., Kangawa K. and Matsuo H.
 TITLE Cloning and sequence analysis of cDNA encoding a precursor for human brain natriuretic peptide
 JOURNAL Biochem. Biophys. Res. Commun. 159 (3), 1427-1434 (1989)
 PUBMED 2522777

COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from AJ708502.1, M25296.1 and BC025785.1.

-continued

On Dec. 16, 2005 this sequence version replaced NM_002521.1.

Summary: This gene is a member of the natriuretic peptide family and encodes a secreted protein which functions as a cardiac hormone. The protein undergoes two cleavage events, one within the cell and a second after secretion into the blood. The protein's biological actions include natriuresis, diuresis, vasorelaxation, inhibition of renin and aldosterone secretion, and a key role in cardiovascular homeostasis. A high concentration of this protein in the bloodstream is indicative of heart failure. The protein also acts as an antimicrobial peptide with antibacterial and antifungal activity. Mutations in this gene have been associated with postmenopausal osteoporosis, [provided by RefSeq, November 2014].

Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Gene record to access additional publications.

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##Evidence-Data-START##
Transcript exon combination :: BC025785.1, ERR279856.3578.1
[ECO: 0000332]
RNAseq introns :: single sample supports all introns
SAMEA2148093, SAMEA2151741
[ECO: 0000348]
##Evidence-Data-END##
##RefSeq-Attributes-START##
Protein has antimicrobial activity :: PMID: 11410403
##RefSeq-Attributes-END##
COMPLETENESS: complete on the 3' end.
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PRIMARY COMP	REFSEQ_SPAN	PRIMARY_IDENTIFIER	PRIMARY_SPAN
1-4	AJ708502.1		19-22
5-695	M25296.1		2-692
696-708	BC025785.1		683-695
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source	1 . . . 708 /organism = "Homo sapiens" /mol_type = "mRNA" /db_xref = "taxon: 9606" /chromosome = "1" /map = "1p36.22"		
gene	1 . . . 708 /gene = "NPPB" /gene_synonym = "BNP" /note = "natriuretic peptide B" /db_xref = "GeneID: 4879" /db_xref = "HGNC: HGNC: 7940" /db_xref = "MIM: 600295"		
exon	1 . . . 234 /gene = "NPPB" /gene_synonym = "BNP" /inference = "alignment: Splign: 2.1.0"		
CDS	103 . . . 507 /gene = "NPPB" /gene_sy_nony_m = "BNP" /note = "natriuretic peptide precursor B; brain type natriuretic peptide; natriuretic peptides B; natriuretic protein; gamma-brain natriuretic peptide" /codon_start = 1 /product = "natriuretic peptides B preproprotein" /protein_id = "NP_002512.1" /db_xref = "CCDS: CCDS140.1" /db_xref = "GeneID: 4879" /db_xref = "HGNC HGNC: 7940" /db_xref = "MIM: 600295"		
	/translation = "MDPQTAPS RALLLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQ EQRNHLQGKLSELQVEQTSLEPLQESPRPTGVWKSREVATEGIRGHKRKMVLYTLRAP R SPKMWQGS GCFGRKMDRISSSSLGCKVLRRH" (SEQ_ID NO: 160)		
	sig_peptide 103 . . . 180		

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/gene_synonym = "BNP"
/inference = "COORDINATES: ab initio prediction: SignalP: 4.0"

proprotein 181 . . . 5 04
/gene = "NPPB"
/gene_synonym = "BNP"
/product = "natriuretic peptides B proprotein"
/note = "proBNP; gamma-brain natriuretic peptide"

mat_peptide 409 . . . 504
/gene = "NPPB"
/gene_synonym = "BNP"
/product = "natriuretic peptides B"
/experiment = "DESCRIPTION: antimicrobial
peptide[PMID: 11410403]"
/note = "brain natriuretic peptide 32"

exon 235 . . . 490
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/gene_synonym = "BNP"
/inference = "alignment: Salign: 2.1.0"

exon 491 . . . 698
/gene = "NPPB"
/gene_synonym = "BNP"
/inference = "alignment: Salign: 2.1.0"

regulatory 674 . . . 679
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/gene = "NPPB"
/gene_synonym = "BNP"

polyA_site 698
/gene = "NPPB"
/gene_synonym = "BNP"


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 121 ccttcccggg cgctcctgtc cctgcgtttc ttgcattctgg ctttcctggg aggtcggtcc
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 541 ttccacaagg gggttttttc tcaaccctgt ggccgcctt gaatgttgc atttttttaa
 601 tgtatatttg tatatttttg attgttttat ataagatgtt ttcttacatt tgagcacaaa
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Rattus norvegicus myosin heavy chain 7 (Myh7), mRNA
 NCBI Reference Sequence: NM_017240.2
 FASTA Graphics
 Go to:
 LOCUS NM_0172405923 bp mRNA linear ROD 31-MAY-2018
 DEFINITION Rattus norvegicus myosin heavy chain 7 (Myh7), mRNA.
 ACCESSION NM_017240
 VERSION NM_017240.2
 KEYWORDS RefSeq.
 SOURCE Rattus norvegicus (Norway rat)
 ORGANISM Rattus norvegicus
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha;
 Muroidea; Muridae; Murinae; Rattus.

REFERENCE 1 (bases 1 to 5923)
 AUTHORS Tomita-Mitchell A., Stamm K. D., Mahnke D. K., Kim M. S., Hidestrand P. M.,
 Liang H. L., Goetsch M. A., Hidestrand M., Simpson P., Pelech A. N., Tweddell
 J. S., Benson D. W., Lough J. W. and Mitchell M.E.
 TITLE Impact of MYH6 variants in hypoplastic left heart syndrome
 JOURNAL Physiol. Genomics 48 (12), 912-921 (2016)
 PUBMED 27789736

-continued

REFERENCE 2 (bases 1 to 5923)

AUTHORS Chandra V., Gollapudi S. K. and Chandra M.
 TITLE Rat cardiac troponin T mutation (F72L)-mediated impact on thin filament cooperativity is divergently modulated by alpha- and beta-myosin heavy chain isoforms
 JOURNAL Am. J. Physiol. Heart Circ. Physiol. 309 (8), H1260-H1270 (2015)
 PUBMED 26342069
 REMARK GenoRIF: TnT mutation F72L leads to contractile changes that are linked to dilated cardiomyopathy in the presence of MYH6 and hypertrophic cardiomyopathy in the presence of MYH7.

REFERENCE 3 (bases 1 to 5923)

AUTHORS Kralova E., Doka G., Pivackova L., Sránkova J., Kuracinova K., Janega P., Babal P., Klímaš J. and Krenel P.
 TITLE 1-Arginine Attenuates Cardiac Dysfunction, But Further Down-Regulates alpha-Myosin Heavy Chain Expression in Isoproterenol-Induced Cardiomyopathy
 JOURNAL Basic Clin. Pharmacol. Toxicol. 117 (4), 251-260 (2015)
 PUBMED 25865156

REFERENCE 4 (bases 1 to 5923)

AUTHORS Taylor K. C., Buvoli M., Korkmaz E. N., Buvoli A., Zheng Y., Heinze N. T., Cui Q., Leinwand L. A. and Rayment I.
 TITLE Skip residues modulate the structural properties of the myosin rod and guide thick filament assembly
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 112 (29), E3806-E3815 (2015)
 PUBMED 26150528

REFERENCE 5 (bases 1 to 5923)

AUTHORS Zhang P., Shan T., Liang X., Deng C. and Kuang S.
 TITLE Mammalian target of rapamycin is essential for cardiomyocyte survival and heart development in mice
 JOURNAL Biochem. Biophys. Res. Commun. 452 (1), 53-59 (2014)
 PUBMED 25139234

REFERENCE 6 (bases 1 to 5923)

AUTHORS O'Neill L., Holbrook N. J., Farnol J. and Lakatta E. G.
 TITLE Progressive changes from young adult age to senescence in mRNA for rat cardiac myosin heavy chain genes
 JOURNAL Cardioscience 2 (1), 1-5 (1991)
 PUBMED 1888877

REFERENCE 7 (bases 1 to 5923)

AUTHORS Schuyler G. T. and Yarbrough L. R.
 TITLE Changes in myosin and creatine kinase mRNA levels with cardiac hypertrophy and hypothyroidism
 JOURNAL Basic Res. Cardiol. 85 (5), 481-494 (1990)
 PUBMED 1703406

REFERENCE 8 (bases 1 to 5923)

AUTHORS McNally E. M., Kraft R., Bravo-Zehnder M., Taylor D. A. and Leinwand L. A.
 TITLE Full-length rat alpha and beta cardiac myosin heavy chain sequences. Comparisons suggest a molecular basis for functional differences
 JOURNAL J. Mol. Biol. 210 (3), 665-671 (1989)
 PUBMED 2614840

REFERENCE 9 (bases 1 to 5923)

AUTHORS Kraft R., Bravo-Zehnder M., Taylor D. A. and Leinwand L. A.
 TITLE Complete nucleotide sequence of full length cDNA for rat beta cardiac myosin heavy chain
 JOURNAL Nucleic Acids Res. 17 (18), 7529-7530 (1989)
 PUBMED 2798112

REFERENCE 10 (bases 1 to 5923)

AUTHORS Izumo, S., Lompre, A. M., Matsuoka, R., Koren, G., Schwartz, K., Nadal-Ginard, B. and Mahdavi, V.
 TITLE Myosin heavy chain messenger RNA and protein isoform transitions during cardiac hypertrophy. Interaction between hemodynamic and thyroid hormone-induced signals
 JOURNAL J. Clin. Invest. 79 (3), 970-977 (1987)
 PUBMED 2950137

COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final NCBI review. The reference sequence was derived from X15939.1. On Feb. 21, 2013 this sequence version replaced NM_017240.1.

Summary: heavy chain of myosin; involved in muscle contraction

-continued

[RGD, February 2006].

Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Gene record to access additional publications.

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##Evidence-Data-START##
Transcript exon combination :: X15939.1 [ECO: 0000332]
RNaseq introns :: mixed/partial sample support
SAMD00052296, SAMD00052297
[ECO: 0000350]
##Evidence-Data-END##
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exon	1 . . . 209 /gene = "Myh7" /gene_synonym = "Bmyo; myHC-beta; myHC-slow; Myhcb" /inference = "alignment: Salign: 2.0.8"			
CDS	9 . . . 5816 /gene = "Myh7" /gene_synonym = "Bmyo; myHC-beta; myHC-slow; Myhcb" /note = "myosin heavy chain, cardiac muscle, fetal; beta myosin heavy chain; myosin heavy chain slow isoform; myosin heavy chain, cardiac muscle beta isoform; myosin, heavy polypeptide 7, cardiac muscle, beta; myosin heavy chain, polypeptide 7; myosin heavy chain polypeptide 7 cardiac muscle fetal; myosin, heavy chain 7, cardiac muscle, beta" /codon_start = 1 /product = "myosin-7" /protein_id = "NP_058936.1" /db_xref = "GeneID: 29557" /db_xref = "RGD: 62030"			
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 /gene_synonym = "Bmyo; myHC-beta; myHC-slow; Myhcb"
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 /note = "N6,N6,N6-trimethyllysine. {ECO: 0000255}; propagated from UniProtKB/Swiss-Prot (P02564.2); methylation site"

misc_feature 1140 . . . 1142
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 /experiment = "experimental evidence, no additional details recorded"
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 /experiment = "experimental evidence, no additional details recorded"
 /note = "propagated from UniProtKB/Swiss-Prot (P02564.2); Region: Actin-binding"

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 /experiment = "experimental evidence, no additional details recorded"
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 /experiment = "experimental evidence, no additional details recorded"
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misc_feature 3813 . . . 3815
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/gene_synonym = "Bmyo; myHC-beta; myHC-slow; Myhcb"
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phosphorylation site"

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/experiment = "experimental evidence, no additional details
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/note = "Phosphothreonine. {ECO: 0000250|UniProtKB: P02563};
propagated from UniProtKB/Swiss-Prot (P02564.2);
phosphorylation site"

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/experiment = "experimental evidence, no additional details
recorded"
/note = "Phosphotyrosine. {ECO: 0000250|UniProtKB: P02563};
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phosphorylation site"

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/gene_synonym = "Bmyo; myHC-beta; myHC-slow; Myhcb"
/experiment = "experimental evidence, no additional details
recorded"
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propagated from UniProtKB/Swiss-Prot (P02564.2);
phosphorylation site"

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/note = "Phosphothreonine. {ECO: 0000250|UniProtKB: P02563};
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phosphorylation site"

exon      210 . . . 353
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/gene_synonym = "Bmyo; myHC-beta; myHC-slow; Myhcb"
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exon      1008 . . . 1146
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exon      1147 . . . 1265
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exon      1416 . . . 1586
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exon      1587 . . . 1896
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exon      1897 . . . 1964
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exon      2053 . . . 2170
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exon      2171 . . . 2294
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exon      2432 . . . 2687
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exon      2931 . . . 3107
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exon      4178 . . . 4361
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/inference = "alignment: Salign: 2.0.8"

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/inference = "alignment: Salign: 2.0.8"

exon      4653 . . . 4961
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/inference = "alignment: Salign: 2.0.8"

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APPENDIX G

Rattus norvegicus natriuretic peptide A (Nppa), mRNA
NCBI Reference Sequence: NM_012612.2

FASTA Graphics
Go to:
LOCUS NM_012612831 bp mRNA linear ROD 10-JUN-2018
DEFINITION Rattus norvegicus natriuretic peptide A (Nppa), mRNA.
ACCESSION NM_012612
VERSION NM_012612.2
KEYWORDS RefSeq.
SOURCE Rattus norvegicus (Norway rat)
ORGANISM Rattus norvegicus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha;
Muroidea; Muridae; Murinae; Rattus.
REFERENCE 1 (bases 1 to 831)
AUTHORS Barallobre-Barreiro J, Gupta SK, Zoccarato A, Kitazume-Taneike R,
Fava M, Yin X, Werner T, Hirt MN, Zampetaki A, Viviano A, Chong M,
Bern M, Kourliouros A, Domenech N, Willeit P, Shah AM, Jahangiri M,
Schaefer L, Fischer JW, Iozzo RV, Viner R, Thum T, Heineke J,
Kicherer A, Otsu K and Mayr M.
TITLE Glycoproteomics Reveals Decorin Peptides With Anti-Myostatin
Activity in Human Atrial Fibrillation
JOURNAL Circulation 134 (11), 817-832 (2016)

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PUBMED	27559042
REFERENCE	2 (bases 1 to 831)
AUTHORS	Yuan K, Park BM, Choi YT, Kim JH, Cho KW and Kim SH.
TITLE	Effects of endothelin family on ANP secretion
JOURNAL	Peptides 82, 12-19 (2016)
PUBMED	27208702
REMARK	GeneRIF: we suggest that the order of secretagogue effect of ET family on ANP secretion was ET-1>/ = ET-2>>ET-3>s6C and ET-1-induced atrial natriuretic peptide secretion negatively regulates the pressor effect of ET-1.
REFERENCE	3 (bases 1 to 831)
AUTHORS	Lee CH, Ha GW, Kim JH and Kim SH.
TITLE	Modulation in Natriuretic Peptides System in Experimental Colitis in Rats
JOURNAL	Dig. Dis. Sci. 61 (4), 1060-1068 (2016)
PUBMED	26660905
REMARK	GeneRIF: augmentation of inhibitory effect on basal motility by ANP in experimental colitis may be due an increased expression of colonic natriuretic peptide receptor-A mRNA
REFERENCE	4 (bases 1 to 831)
AUTHORS	Bugrova, M.L.
TITLE	[ATRIAL AND BRAIN NATRIURETIC PEPTIDES OF CARDIAC MUSCLE CELLS IN POSTREPERFUSION PERIOD IN RATS]
JOURNAL	Tsitologia 58 (2), 129-134 (2016)
PUBMED	27228659
REMARK	GeneRIF: This is due to the fact that ANP is the main hormone of the natriuretic peptide system involved in the regulation of blood pressure in normal conditions, while BNP is the principal regulator of pressure in cardiovascular pathology
REFERENCE	5 (bases 1 to 831)
AUTHORS	Pang A, Hu Y, Zhou P, Long G, Tian X, Men L, Shen Y, Liu Y and Cui Y.
TITLE	Corin is down-regulated and exerts cardioprotective action via activating pro-atrial natriuretic peptide pathway in diabetic cardiomyopathy
JOURNAL	Cardiovasc Diabetol 14, 134 (2015)
PUBMED	26446774
REMARK	GeneRIF: ANP mRNA and protein are decreased in diabetic cardiomyopathy. Publication Status: Online-Only
REFERENCE	6 (bases 1 to 831)
AUTHORS	Bennett BD, Bennett GL, Vitangcol RV, Jewett JR, Burnier J, Henzel W and Lowe DG.
TITLE	Extracellular domain-IgG fusion proteins for three human natriuretic peptide receptors. Hormone pharmacology and application to solid phase screening of synthetic peptide antisera
JOURNAL	J. Biol. Chern. 266 (34), 23060-23067 (1991)
PUBMED	1660465
REFERENCE	7 (bases 1 to 831)

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AUTHORS Levin ER and Frank HJ.

TITLE Natriuretic peptides inhibit rat astroglial proliferation: mediation by C receptor

JOURNAL Am. J. Physiol. 261 (2 Pt 2), R453-R457 (1991)

PUBMED 1652217

REFERENCE 8 (bases 1 to 831)

AUTHORS Koller KJ, Lowe DG, Bennett GL, Minamino N, Kangawa K, Matsuo H and Goeddel DV.

TITLE Selective activation of the B natriuretic peptide receptor by C-type natriuretic peptide (CNP)

JOURNAL Science 252 (5002), 120-123 (1991)

PUBMED 1672777

REFERENCE 9 (bases 1 to 831)

AUTHORS Mukoyama,M., Nakao,K., Saito,Y., Ogawa,Y., Hosoda,K., Suga,S., Shirakami,G., Jougasaki,M. and Imura,H.

TITLE Increased human brain natriuretic peptide in congestive heart failure

JOURNAL N. Engl. J. Med. 323 (11), 757-758 (1990)

PUBMED 2143809

REFERENCE 10 (bases 1 to 831)

AUTHORS Jin H, Yang RH, Chen YF, Jackson RM and Oparil S.

TITLE Atrial natriuretic peptide attenuates the development of pulmonary hypertension in rats adapted to chronic hypoxia

JOURNAL J. Clin. Invest. 85 (1), 115-120 (1990)

PUBMED 2136863

COMMENT This record has undergone validation or preliminary review. The reference sequence was derived from CB724799.1, X00665.1 and AI602287.1.

VALIDATED On Oct 17, 2007 this sequence version replaced NM_012612.1.

REFSEQ: Summary: peptide involved in the control of fluid volume and vascular function [RGD, Feb 2006].

Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Gene record to access additional publications.

##Evidence-Data-START##

Transcript exon combination:: EV765126.1, BC158590.1 [ECO:0000332]

RNAseq introns:: single sample supports all introns

SAMD00052296, SAMD00052297

[ECO:0000348]

##Evidence-Data-END##

PRIMARY COMP	REFSEQ_SPAN	PRIMARY IDENTIFIER PRIMARY SPAN
1-8	CB724799.1	128-135
9-576	X00665.1	1-568
577-831	AI602287.1	1-255 c

FEATURES Location/Qualifiers

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 /strain = "Sprague-Dawley"
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/db_xref = "RGD:3193"

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STS          518..724
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/standard_name = "RH127740"
/db_xref = "UniSTS:211050"

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/gene_synonym = "ANF; ANP; Pnd; RATANF"
/inference = "alignment: Splign: 2.0.8"

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/note = "pot. proteolytic processing site"

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APPENDIX H

Rattus norvegicus natriuretic peptide B (Nppb), mRNA
NCBI Reference Sequence: NM_031545.1

FASTA Graphics

Go to:

LOCUS NM_031545628 bp mRNA linear ROD 21-JUL-2018

DEFINITION Rattus norvegicus natriuretic peptide B (Nppb), mRNA.

ACCESSION NM_031545

VERSION NM_031545.1

KEYWORDS RefSeq.

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SOURCE	<i>Rattus norvegicus</i> (Norway rat)
ORGANISM	<i>Rattus norvegicus</i> Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; <i>Rattus</i> .
REFERENCE	1 (bases 1 to 628)
AUTHORS	Saklani R, Gupta SK, Mohanty IR, Kumar B, Srivastava S and Mathur R.
TITLE	Cardioprotective effects of rutin via alteration in TNF-alpha, CRP, and BNP levels coupled with antioxidant effect in STZ-induced diabetic rats
JOURNAL	Mol. Cell. Biochem. 420 (1-2), 65-72 (2016)
PUBMED	27443845
REMARK	GeneRIF: Cardioprotective effects of rutin via alteration in TNF-alpha, CRP, and BNP levels coupled with antioxidant effect in STZ-induced diabetic rats.
REFERENCE	2 (bases 1 to 628)
AUTHORS	Holditch SJ, Schreiber CA, Burnett JC and Ikeda Y.
TITLE	Arterial Remodeling in B-Type Natriuretic Peptide Knock-Out Females
JOURNAL	Sci Rep 6, 25623 (2016)
PUBMED	27162120
REMARK	GeneRIF: Data show that approximately 60% of natriuretic peptide precursor type B (Nppb) -/- females developed mesenteric polyarteritis-nodososa (PAN)-like vasculitis in their life span, some as early as 4 months of age. Publication Status: Online-Only
REFERENCE	3 (bases 1 to 628)
AUTHORS	Terse PS, Joshi PS, Bordelon NR, Brys AM, Patton KM, Arndt TP and Sutula TP.
TITLE	2-Deoxy-d-Glucose (2-DG)-Induced Cardiac Toxicity in Rat: NT-proBNP and BNP as Potential Early Cardiac Safety Biomarkers
JOURNAL	Int. J. Toxicol. 35 (3), 284-293 (2016)
PUBMED	26838190
REMARK	GeneRIF: NT-proBNP and BNP are potential early biomarkers for 2-DG-induced cardiac toxicity that can be useful to monitor 2-DG therapy in clinical trials.
REFERENCE	4 (bases 1 to 628)
AUTHORS	Bugrova, ML.
TITLE	[ATRIAL AND BRAIN NATRIURETIC PEPTIDES OF CARDIAC MUSCLE CELLS IN POSTREPERFUSION PERIOD IN RATS]
JOURNAL	Tsitologiya 58 (2), 129-134 (2016)
PUBMED	27228659
REMARK	GeneRIF: This is due to the fact that ANP is the main hormone of the natriuretic peptide system involved in the regulation of blood pressure in normal conditions, while BNP is the principal regulator of pressure in cardiovascular pathology
REFERENCE	5 (bases 1 to 628)
AUTHORS	Dogan H, Sarikaya S, Neijmann ST, Uysal E, Yucel N, Ozcelik DN, Okuturlar Y, Solak S, Sever N and Ayan C.
TITLE	N-terminal pro-B-type natriuretic peptide as a marker of blunt cardiac contusion in trauma

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JOURNAL	Int J Clin Exp Pathol 8 (6), 6786-6792 (2015)
PUBMED	26261563
REMARK	GeneRIF: Serum NT-proBNP levels significantly increased after 5 hours of the blunt chest trauma. Publication Status: Online-Only
REFERENCE	6 (bases 1 to 628) AUTHORS Bennett BD, Bennett GL, Vitangcol RV, Jewett JR, Burnier J, Henzel W and Lowe DG.
TITLE	Extracellular domain-IgG fusion proteins for three human natriuretic peptide receptors. Hormone pharmacology and application to solid phase screening of synthetic peptide antisera
JOURNAL	J. Biol. Chern. 266 (34), 23060-23067 (1991)
PUBMED	1660465
REFERENCE	7 (bases 1 to 628)
AUTHORS	Dagnino L, Drouin J and Nemer M.
TITLE	Differential expression of natriuretic peptide genes in cardiac and extracardiac tissues
JOURNAL	Mol. Endocrinol. 5 (9), 1292-1300 (1991)
PUBMED	1837590
REFERENCE	8 (bases 1 to 628)
AUTHORS	Levin ER and Frank HJ.
TITLE	Natriuretic peptides inhibit rat astroglial proliferation: mediation by C receptor
JOURNAL	Am. J. Physiol. 261 (2 Pt 2), R453-R457 (1991)
PUBMED	1652217
REFERENCE	9 (bases 1 to 628)
AUTHORS	Hoffman A, Grossman E and Keiser HR.
TITLE	Increased plasma levels and blunted effects of brain natriuretic peptide in rats with congestive heart failure
JOURNAL	Am. J. Hypertens. 4 (7 Pt 1), 597-601 (1991)
PUBMED	1831369
REFERENCE	10 (bases 1 to 628)
AUTHORS	Koller KJ, Lowe DG, Bennett GL, Minamino N, Kangawa K, Matsuo H and Goeddel DV.
TITLE	Selective activation of the B natriuretic peptide receptor by C-type natriuretic peptide (CNP)
JOURNAL	Science 252 (5002), 120-123 (1991)
PUBMED	1672777
COMMENT	This record has not yet been subject to final
PROVISIONAL	NCBI review. The reference sequence was derived from M25297.1.
REFSEQ:	Summary: hormone produced primarily by the atrium and ventricle of the heart [RGD, Feb 2006]. Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Gene record to access additional publications. ##Evidence-Data-START##
	Transcript exon combination:: M25297.1, FQ228997.1 [ECO:0000332] RNAseq introns:: single sample supports all introns SAMEA2689596, SAMEA2689600 [ECO:0000348] ##Evidence-Data-END##

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FEATURES	Location/Qualifiers
source	1..628 /organism = "Rattus norvegicus" /mol_type = "mRNA" /db_xref = "taxon: 10116" /chromosome = "5" /map = "5q36"
gene	1..628 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /note = "natriuretic peptide B" /db_xref = "GeneID:25105" /db_xref = "RGD:3194"
exon	1..183 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /inference = "alignment: Salign: 2.0.8"
CDS	58..423 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /note = "natriuretic peptides B; brain natriuretic peptide; natriuretic peptide precursor B; iso-ANP; gamma-brain natriuretic peptide; Brain natriuretic factor; natriuretic peptide precursor type B" /codon_start = 1 /product = "natriuretic peptides B precursor" /protein_id = "NP_1 13733.1" /db_xref = "GeneID:25105" /db_xref = "RGD:3194"
	/translation = "MDLQKVLPQMILLLFLNLSPGGHSHPLGSPSQSPSEQSTMQKL LELIREKSEEMAQRQLSKDQGPTKELLKRVLRNSQDSAFRIQERLRNSKMAHSSSCFG Q KIDRIGAVSRLGCDGLRLF" (SEQ ID NO: 166)
sig_peptide	58..135 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /inference = "COORDINATES: ab initio prediction:SignalP:4.0"
mat_peptide	136..420 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /product = "natriuretic peptides B" /note = "putative"
misc_feature	328..333 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /experiment = "experimental evidence, no additional details recorded" /note = "Cleavage, by FAP. {ECO:0000250 UniProtKB:P16860}; propagated from UniProtKB/Swiss-Prot (P13205.3); cleavage site"
exon	184..406 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /inference = "alignment: Salign: 2.0.8"
STS	280..464 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /standard_name = "RH130424" /db_xref = "UnisTS:213708"
exon	407..628 /gene = "Nppb" /gene_synonym = "Bnf; BNP" /inference = "alignment: Salign: 2.0.8"
polyA_site	628 /gene = "Nppb" /gene_synonym = "Bnf; BNP"
ORIGIN	

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121 ctggggaggc actccatcc cttggaaagt cctaggcagt ctccagaaca atccacgatc
181 cagaagctgc tggagctgat aagagaaaag tcagaggaaa tggctcagag acagctctca
241 aaggaccaag gcctcacaaa aqaacttca aaaagagtcc ttaggtctca agacagcgcc
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361 cagaagatag accggatcgg cgccagtcgt cgcttggct gtgacgggct gaggttggtt
421 taggaagacc tcctggctgc agactccggc ttctgactct gcctgcggct ttctttccc
481 cagctctggg accaccttc aagtgtactt gtttattttat ttgttattttt atttattttt
541 attttgctga ttcttacaa gactgttct tatcttccag cacaacttg ccacagtgtta
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<212> TYPE: DNA

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<220> FEATURE:

<223> OTHER INFORMATION: MIR-23A-3P Sensor

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<210> SEQ ID NO 3

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: MIR-23A-3P Sensor

<400> SEQUENCE: 3

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31

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<212> TYPE: RNA

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<220> FEATURE:

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<400> SEQUENCE: 4

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<220> FEATURE:
<223> OTHER INFORMATION: BNP sensor

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25

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<223> OTHER INFORMATION: calcineurin guide strand

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25

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<211> LENGTH: 25

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<220> FEATURE:

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23

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46

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46

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<223> OTHER INFORMATION: HDAC2 core strand

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<212> TYPE: RNA
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<223> OTHER INFORMATION: HDAC2 core strand

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<210> SEQ ID NO 24
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46

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<223> OTHER INFORMATION: HDAC2 core strand

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44

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<223> OTHER INFORMATION: synthetic polynucleotide
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<221> NAME/KEY: modified_base
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<223> OTHER INFORMATION: n is a, c, t, or g
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<223> OTHER INFORMATION: n is a, c, g, or t
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<223> OTHER INFORMATION: n is a, c, g, or t

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gcttggtcgc attgccactg agagggtgggt aataccctcc tggagctgca gttccctgtc

120

ttcatctatc acgatcgatg ttaagtgttag atgagtggtt tagtgaggcc ttacctctcc

180

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240

nnnnnnnnnn nnn

253

<210> SEQ ID NO 28

<211> LENGTH: 194

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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: central sequence

<400> SEQUENCE: 28

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actgagaggt ggtgaataacc ctcctggago tgcagcttcc tgttccatc tatcacgatc      120
gatgttaagt gtagatgagt ggtttagtga ggcttaccc ctcccactct gcataattaag      180
gtagatccctc accc                                         194

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<223> OTHER INFORMATION: n is a, c, t, or g
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<223> OTHER INFORMATION: n is a, c, t, or g
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cgtgatagat gaagacagga agctgcagct ccaggaggg attcaccacc tctcagttggc      180
aatgcgacca agctgtgtga cacaccgcaa ggcccttggga tctttgcga tctgctcnnn      240
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: sensor strand

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31

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<223> OTHER INFORMATION: a or c

<400> SEQUENCE: 31

cuucaccacc ucucaguggc aaugcgacca a

31

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<220> FEATURE:
<223> OTHER INFORMATION: guide sequence

<400> SEQUENCE: 32

uguuuguuuugg cuuuuccug u

21

<210> SEQ ID NO 33
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<212> TYPE: RNA
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<400> SEQUENCE: 33

cuucaccacc ucucaguggc aaugcgacca a

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<400> SEQUENCE: 34

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<223> OTHER INFORMATION: LNA
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<223> OTHER INFORMATION: phosphorothioate backbone connection
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26

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<210> SEQ ID NO 37
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<220> FEATURE:
<223> OTHER INFORMATION: mir-23a-3P

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<400> SEQUENCE: 37

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21

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<210> SEQ ID NO 38
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<223> OTHER INFORMATION: mir-23a-3p

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<400> SEQUENCE: 38

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21

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<210> SEQ ID NO 39
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<220> FEATURE:
<223> OTHER INFORMATION: Calcineurin sensor

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29

<210> SEQ ID NO 40

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8

<210> SEQ ID NO 41
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Calcineurin PPP3CA siRNA guide

<400> SEQUENCE: 41

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<400> SEQUENCE: 42

ccngagugu guuuggcuuu uccuguu

27

<210> SEQ ID NO 43
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<223> OTHER INFORMATION: Mir-23a-3p sensor
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (30)..(30)
<223> OTHER INFORMATION: n is a, c, g, t or u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (31)..(31)
<223> OTHER INFORMATION: primary amine modification

<400> SEQUENCE: 43

cgaagaacgg aaaucccugg caaughtgatn

30

<210> SEQ ID NO 44
<211> LENGTH: 48
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand
<220> FEATURE:
<221> NAME/KEY: misc_feature

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<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: 2'-O-methyl
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: 2'-O-methyl
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: phosphorothioate backbone connection
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: LNA
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (16)..(16)
<223> OTHER INFORMATION: phosphorothioate backbone connection
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (17)..(17)
<223> OTHER INFORMATION: 2'-O-methyl
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (36)..(36)
<223> OTHER INFORMATION: n is a, c, g, or u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (37)..(37)
<223> OTHER INFORMATION: phosphorothioate backbone connection
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (38)..(38)
<223> OTHER INFORMATION: 2'-O-methyl
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (48)..(48)
<223> OTHER INFORMATION: 2'-O-methyl
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (50)..(50)
<223> OTHER INFORMATION: 2'-O-methyl

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<400> SEQUENCE: 44

uccgguuuuc gcnanggaaa agccaaacaa cacucngugc cagggauu

48

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<210> SEQ ID NO 45
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: cond-sirNA guide

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<400> SEQUENCE: 45

ccacuuuacc agcaucucag ucauu

25

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<210> SEQ ID NO 46
<211> LENGTH: 31
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-sirNA Sensor

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<400> SEQUENCE: 46

ggagaggcga ggaagucacc aucaaaccac u

31

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<210> SEQ ID NO 47
<211> LENGTH: 46
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

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<400> SEQUENCE: 47

cucggccucuc cugacugaga ugcugguaaa gugggauggu gacuuc

46

<210> SEQ ID NO 48

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: cond-siRNA sensor

<400> SEQUENCE: 48

gaaaucagaa gcaggugucu gcagccagga c

31

<210> SEQ ID NO 49

<211> LENGTH: 46

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 49

cuucugauuc cugacugaga ugcugguaaa guggugcaga caccug

46

<210> SEQ ID NO 50

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: cond-siRNA sensor

<400> SEQUENCE: 50

ccaaggagcu guuacacagg cuccagcaug g

31

<210> SEQ ID NO 51

<211> LENGTH: 46

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 51

cagcuccuug gugacugaga ugcugguaaa gugggagccu guguua

46

<210> SEQ ID NO 52

<211> LENGTH: 25

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: cond-siRNA guide

<400> SEQUENCE: 52

ccacuucauc acaagguauc cgcuu

25

<210> SEQ ID NO 53

<211> LENGTH: 46

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 53

cucggccucuc cgcggaugc uugugaugaa gugggauggu gacuuc

46

<210> SEQ ID NO 54

<211> LENGTH: 46

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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 54

cuuucugauuc cgccgauagc uugugaugaa guggugcaga caccug

46

<210> SEQ ID NO 55
<211> LENGTH: 46
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 55

cagcuccuug ggccgauagc uugugaugaa guggagccu guguaa

46

<210> SEQ ID NO 56
<211> LENGTH: 45
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 56

uccguuuuuc gugacugaga ugcugguaaa guggugccag ggauu

45

<210> SEQ ID NO 57
<211> LENGTH: 29
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA sensor

<400> SEQUENCE: 57

cgacaguuca caaguuaggc ucucaggga

29

<210> SEQ ID NO 58
<211> LENGTH: 45
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 58

gugaacuguc gugacugaga ugcugguaaa gugggacccu aacuu

45

<210> SEQ ID NO 59
<211> LENGTH: 29
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA sensor

<400> SEQUENCE: 59

ccugaagaac agauagucua aacacuggg

29

<210> SEQ ID NO 60
<211> LENGTH: 45
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 60

US 12,385,041 B2

131

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uguucuuucag gugacugaga ugcugguaaa gugguuuaga cuauc

45

<210> SEQ ID NO 61
<211> LENGTH: 47
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 61

aacagcuccu uggcgccgaua gcuugugaua aaguggggag ccugugu

47

<210> SEQ ID NO 62
<211> LENGTH: 45
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 62

uccguucuuc ggccggaugc uugugaugaa guggugccag ggauu

45

<210> SEQ ID NO 63
<211> LENGTH: 45
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 63

uguucuuucag ggcggaua uugugaugaa gugguuuaga cuauc

45

<210> SEQ ID NO 64
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 64

gaacaagauc cgagcaauau u

21

<210> SEQ ID NO 65
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 65

uauuugcucgg aucuuguuuc u

21

<210> SEQ ID NO 66
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 66

cgacauauugc ucggauauug uucuu

25

<210> SEQ ID NO 67
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
 <223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 67

ugacugagau gcugguaaau u

21

<210> SEQ ID NO 68
 <211> LENGTH: 21
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 68

uuuaccagca ucucaguau u

21

<210> SEQ ID NO 69
 <211> LENGTH: 25
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 69

cgcacuuuacc agcaucucag ucauu

25

<210> SEQ ID NO 70
 <211> LENGTH: 21
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 70

ggucagaaga agauggauuu u

21

<210> SEQ ID NO 71
 <211> LENGTH: 21
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 71

aauccaucuu cuucugaccu u

21

<210> SEQ ID NO 72
 <211> LENGTH: 25
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 72

ccacaaucca ucuucuucug accuu

25

<210> SEQ ID NO 73
 <211> LENGTH: 21
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 73

gcuauagaau guacagaaaau u

21

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<210> SEQ ID NO 74
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 74

uuucuguaca uucuaauagcu u

21

<210> SEQ ID NO 75
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 75

cgacuuucug uacauucuau agcuu

25

<210> SEQ ID NO 76
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 76

cceuuaaggca gaauguaau u

21

<210> SEQ ID NO 77
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 77

uuacauuccu gcuuaagggu u

21

<210> SEQ ID NO 78
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 78

ggacuuacau uccugcuuaa aggua

25

<210> SEQ ID NO 79
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 79

gcaauuggca agauggcaau u

21

<210> SEQ ID NO 80
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA guide strand

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<400> SEQUENCE: 80

uugccauuu gccaauugcu u

21

<210> SEQ ID NO 81

<211> LENGTH: 25

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 81

ccacuugcca ucuuugccaa ugcuu

25

<210> SEQ ID NO 82

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 82

guauagagug ugugcuguaau u

21

<210> SEQ ID NO 83

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 83

uacagcacac acucuaauacu u

21

<210> SEQ ID NO 84

<211> LENGTH: 25

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 84

ccacuacagc acacacucua uacuu

25

<210> SEQ ID NO 85

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 85

aguauuugag aaugggaaau u

21

<210> SEQ ID NO 86

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 86

uuuucccaauuc ucaaaauacuu u

21

<210> SEQ ID NO 87

US 12,385,041 B2

139

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<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-sirNA guide

<400> SEQUENCE: 87

ccacuuuccc aaucucaaau acuuu

25

<210> SEQ ID NO 88
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sirNA target site

<400> SEQUENCE: 88

cuauguggac agaggcuauu u

21

<210> SEQ ID NO 89
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sirNA guide strand

<400> SEQUENCE: 89

auagccucug uccacauagu u

21

<210> SEQ ID NO 90
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-sirNA guide

<400> SEQUENCE: 90

ccacauagcc ucuguccaca uaguu

25

<210> SEQ ID NO 91
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sirNA target site

<400> SEQUENCE: 91

gcggauagcu ugugaugaaau u

21

<210> SEQ ID NO 92
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sirNA guide strand

<400> SEQUENCE: 92

uucaucacaa gcuauccgcu u

21

<210> SEQ ID NO 93
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sirNA target site

<400> SEQUENCE: 93

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ggauauuggu gcuggaaaaau u

21

<210> SEQ ID NO 94
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 94

uuuuuccagca ccaauauccu u

21

<210> SEQ ID NO 95
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 95

ccacuuuuucc agcaccaaaua uccuu

25

<210> SEQ ID NO 96
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA target site

<400> SEQUENCE: 96

aagcagaugc agagauuuau u

21

<210> SEQ ID NO 97
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: siRNA guide strand

<400> SEQUENCE: 97

aaaaaucucug caucugcuuu u

21

<210> SEQ ID NO 98
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Cond-siRNA guide

<400> SEQUENCE: 98

ccacuaaac ucugcaucug cuuuu

25

<210> SEQ ID NO 99
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: hsa-miR-125b-5p MIMAT0000423

<400> SEQUENCE: 99

ucccugagac ccuaacuugu ga

22

<210> SEQ ID NO 100
<211> LENGTH: 22
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: reverse complement hsa-miR-125b-5p MIMAT0000423
<400> SEQUENCE: 100

ucacaaguua gggucucagg ga

22

<210> SEQ ID NO 101
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: hsa-miR-199b-5p MIMAT0000263
<400> SEQUENCE: 101

cccaguguuu agacuaucug uuc

23

<210> SEQ ID NO 102
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: reverse complement hsa-miR-199b-5p MIMAT0000263
<400> SEQUENCE: 102

gaacagauag ucuaaacacu ggg

23

<210> SEQ ID NO 103
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: mmu-miR-199b-5p MIMAT0000672
<400> SEQUENCE: 103

cccaguguuu agacuaccug uuc

23

<210> SEQ ID NO 104
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens
<400> SEQUENCE: 104

ggccggcugg gguuccuggg gaugggauuu gcuuccuguc acaaaucaca uugccaggga

60

uuuccaaccg acc

73

<210> SEQ ID NO 105
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<400> SEQUENCE: 105

ggaaatccct ggcaatgtga t

21

<210> SEQ ID NO 106
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<400> SEQUENCE: 106

ggtaatccct ggcaatgtga t

21

<210> SEQ ID NO 107
<211> LENGTH: 20

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<212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 107

tgttgttgg ctttcctgt

20

<210> SEQ ID NO 108
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 108

tttagattgaa acaacccagt

20

<210> SEQ ID NO 109
 <211> LENGTH: 31
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: miR-23a-3p sensor strand with LNA modifications

<400> SEQUENCE: 109

ggagaagaac ggaaatccct ggcaatgtga t

31

<210> SEQ ID NO 110
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 110

tccctggcat ccctggca

18

<210> SEQ ID NO 111
 <211> LENGTH: 23
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: HDAC2 target guide

<400> SEQUENCE: 111

acggtaata agaccagata aca

23

<210> SEQ ID NO 112
 <211> LENGTH: 23
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: HDAC2 target guide

<400> SEQUENCE: 112

acgguaaua acaccagaua aca

23

<210> SEQ ID NO 113
 <211> LENGTH: 17
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 113

atctggtgtt attgacc

17

<210> SEQ ID NO 114
 <211> LENGTH: 17
 <212> TYPE: DNA

US 12,385,041 B2

147

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<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 114	
atctggtgta attgacc	17
<210> SEQ ID NO 115	
<211> LENGTH: 13	
<212> TYPE: DNA	
<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 115	
atctggtgtt att	13
<210> SEQ ID NO 116	
<211> LENGTH: 17	
<212> TYPE: DNA	
<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 116	
gagatctggt gttattg	17
<210> SEQ ID NO 117	
<211> LENGTH: 17	
<212> TYPE: DNA	
<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 117	
gagatctggt cttattg	17
<210> SEQ ID NO 118	
<211> LENGTH: 14	
<212> TYPE: DNA	
<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 118	
gagatctggt gtta	14
<210> SEQ ID NO 119	
<211> LENGTH: 13	
<212> TYPE: DNA	
<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 119	
ctgggtttat tga	13
<210> SEQ ID NO 120	
<211> LENGTH: 14	
<212> TYPE: DNA	
<213> ORGANISM: Homo sapiens	
<400> SEQUENCE: 120	
gatctggtgt tatt	14
<210> SEQ ID NO 121	
<211> LENGTH: 201	
<212> TYPE: RNA	
<213> ORGANISM: Artificial Sequence	
<220> FEATURE:	
<223> OTHER INFORMATION: BNP mRNA	
<400> SEQUENCE: 121	
aaaaaaaaaa auuucgaaaa uuacaacuga aaauaaagugg caccuuuaaa acacgaguuu	60
ccauucuuug guagaauaua uuuuguuagu uuauuuauug auuuauguaa uuuuuuuuacu	120

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cagugaaguu uccggccggug ucccaacucc uuuuuucgggg aacaccuuag ucuucgucca 180
 cagacgucgg uccugaagga g 201

<210> SEQ ID NO 122
 <211> LENGTH: 46
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: core guide strand
 <400> SEQUENCE: 122

ccugcuucug auacggucaa uaacaccaga ucucggcug cagaca 46

<210> SEQ ID NO 123
 <211> LENGTH: 16
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 123

cttgatctgc tcagcc 16

<210> SEQ ID NO 124
 <211> LENGTH: 11
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: sensor strand

<400> SEQUENCE: 124

ggcugcagac a 11

<210> SEQ ID NO 125
 <211> LENGTH: 12
 <212> TYPE: RNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: sensor strand

<400> SEQUENCE: 125

ccugcuucug au 12

<210> SEQ ID NO 126
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 126

aggtgtctgc agccaggact 20

<210> SEQ ID NO 127
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 127

aggtgtctgc aggaggact 20

<210> SEQ ID NO 128
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 128

US 12,385,041 B2

151

-continued

agcagggtgtc tgcagccagg

20

<210> SEQ ID NO 129
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 129

agcagggtctc tgcagccagg

20

<210> SEQ ID NO 130
<211> LENGTH: 12
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BNP sensor

<400> SEQUENCE: 130

acaccugcua cu

12

<210> SEQ ID NO 131
<211> LENGTH: 11
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: BNP sensor

<400> SEQUENCE: 131

gauuccacaa g

11

<210> SEQ ID NO 132
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: MFE structure

<400> SEQUENCE: 132

cgagaucugg uguuaugac cguuu

25

<210> SEQ ID NO 133
<211> LENGTH: 46
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: MFE structure

<400> SEQUENCE: 133

gauuccacaa gacggucaau aacaccagau cucgacaccu gcuucu

46

<210> SEQ ID NO 134
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 134

agaagcaggt gtctgc

16

<210> SEQ ID NO 135
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 135

gaatcagaag caggtg

16

152

-continued

<210> SEQ ID NO 136
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 136

aagcaggtgt ctgcag

16

<210> SEQ ID NO 137
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 137

atcagaagca ggtgt

15

<210> SEQ ID NO 138
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 138

gaagcaggtg tctgcagcc

19

<210> SEQ ID NO 139
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 139

gaagcaggtg cctgcagcc

19

<210> SEQ ID NO 140
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 140

tgtggaatca gaagc

15

<210> SEQ ID NO 141
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 141

ggccacaggg ttgagg

16

<210> SEQ ID NO 142
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 142

agggttgagg aaaaa

15

<210> SEQ ID NO 143
<211> LENGTH: 130
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: UTR of MYH7 mRNA

-continued

<400> SEQUENCE: 143

```
gaaaacggugu agaacuagac gagucggac cuccacgguc guuuucgggu acgaccucgg      60
acacauuguc gaggaacccu cciuucgucuu auuucguuaa aaggaacuuc ggcucuuuuu      120
uuuuuuuuuuu      130
```

<210> SEQ ID NO 144
<211> LENGTH: 11
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: MFE structure

<400> SEQUENCE: 144

```
uccagggcug a      11
```

<210> SEQ ID NO 145
<211> LENGTH: 12
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: MFE structure

<400> SEQUENCE: 145

```
gcagaucaag au      12
```

<210> SEQ ID NO 146
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 146

```
atcttgatct gtcag      16
```

<210> SEQ ID NO 147
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sensor strand

<400> SEQUENCE: 147

```
caacaagatg acacaaatgc agcagagacc c      31
```

<210> SEQ ID NO 148
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: sensor strand

<400> SEQUENCE: 148

```
atgacacaaa tgcagcagag accccagggg a      31
```

<210> SEQ ID NO 149
<211> LENGTH: 46
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: core strand

<400> SEQUENCE: 149

```
gucaucuugg ugcaggaaaa gccaaacaac acucggcugc auuugu      46
```

US 12,385,041 B2

157

-continued

158

<210> SEQ ID NO 150
<211> LENGTH: 116
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 150

```
gctttgccac atcttgatct gctcagccct ggaggtgccca gcaaagcccc atgctggagc      60
ctgtgtaca gtccttggg aggaaggaga ataaagcaat tttccttcaa gccgag      116
```

<210> SEQ ID NO 151
<211> LENGTH: 297
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 151

```
agataaacgc caggggaggac aagcagggct gggccttaggg acagactgca agaggctcct      60
gtccccctggg gtctctgctg catttgcgtc atcttgcgtc catggagttg tgatcatccc      120
atctaagctg cagcttcctg tcaacacttc tcacatctta tgctaactgt agataaaagtg      180
gtttgatggc gacttccctcg cctctccac cccatgcatt aaattttaag gtagaacctc      240
acctgttact gaaagtgggt tgaaaatgtaa taaaacttcag caccatggac agaagac      297
```

<210> SEQ ID NO 152
<211> LENGTH: 190
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 152

```
gaggaagtcc tggctgcaga cacctgcctc tgattccaca aggggcttt tcctcaaccc      60
tgtggccgc tttgaagtga ctcattttt taatgtattt atgtattttat ttgattttt      120
tatataagat ggttcttac ctggagcac aaaatttcca cggtaaaata aagtcaacat      180
tataagctt      190
```

<210> SEQ ID NO 153
<211> LENGTH: 105
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 153

```
atcttgcgtc acccaaccct aaggatgcct gtgaagccct gagacctgga gccttggaa      60
cagcacctta ggcagaaaca caataaagca atttccttc aagcc      105
```

<210> SEQ ID NO 154
<211> LENGTH: 279
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 154

```
cagccaaatc tgctcgagca gatcgaaaaa gatcccaagc cttgcgggtg tgcacacag      60
cttggctgca ttgccactga gaggtggta ataccctctt ggagctgcag cttcctgtct      120
tcatctatca cgatcgatgt taatgtaga tgagtggttt agtgaggccct tacctctccc      180
actctgcata ttaaggtaga tcctcaccctt tttcagaaag cagttggaaa aaaataaattc      240
cgaataaact tcagcaccac ggacagacgc tgaggcctg      279
```

<210> SEQ ID NO 155
<211> LENGTH: 205
<212> TYPE: DNA

US 12,385,041 B2

159

-continued

160

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 155

gaagacacctcc	tggctgcaga	ctccggcttc	tgactctgcc	tgcggtctt	ctttccccag	60
ctctgggacc	acctctcaag	tgatcctgtt	tatttatttg	tttattttat	tatTTtatG	120
ttgctgattt	tctacaagac	tgtttcttat	cTCCAGCAC	aaacttgcca	cagtgtataa	180
aacatagctt	atttcttgct	tttgg				205

<210> SEQ ID NO 156

<211> LENGTH: 1935

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 156

Met	Gly	Asp	Ser	Glu	Met	Ala	Val	Phe	Gly	Ala	Ala	Ala	Pro	Tyr	Leu
1				5				10					15		

Arg	Lys	Ser	Glu	Lys	Glu	Arg	Leu	Glu	Ala	Gln	Thr	Arg	Pro	Phe	Asp
	20				25						30				

Leu	Lys	Lys	Asp	Val	Phe	Val	Pro	Asp	Asp	Lys	Gln	Glu	Phe	Val	Lys
	35				40					45					

Ala	Lys	Ile	Val	Ser	Arg	Glu	Gly	Gly	Lys	Val	Thr	Ala	Glu	Thr	Glu
	50				55				60						

Tyr	Gly	Lys	Thr	Val	Thr	Val	Lys	Glu	Asp	Gln	Val	Met	Gln	Gln	Asn
65				70			75		80						

Pro	Pro	Lys	Phe	Asp	Lys	Ile	Glu	Asp	Met	Ala	Met	Leu	Thr	Phe	Leu
		85				90			95						

His	Glu	Pro	Ala	Val	Leu	Tyr	Asn	Leu	Lys	Asp	Arg	Tyr	Gly	Ser	Trp
	100				105				110						

Met	Ile	Tyr	Thr	Tyr	Ser	Gly	Leu	Phe	Cys	Val	Thr	Val	Asn	Pro	Tyr
	115				120			125							

Lys	Trp	Leu	Pro	Val	Tyr	Thr	Pro	Glu	Val	Val	Ala	Ala	Tyr	Arg	Gly
	130				135			140							

Lys	Lys	Arg	Ser	Glu	Ala	Pro	Pro	His	Ile	Phe	Ser	Ile	Ser	Asp	Asn
145				150				155		160					

Ala	Tyr	Gln	Tyr	Met	Leu	Thr	Asp	Arg	Glu	Asn	Gln	Ser	Ile	Leu	Ile
	165				170			175							

Thr	Gly	Glu	Ser	Gly	Ala	Gly	Lys	Thr	Val	Asn	Thr	Lys	Arg	Val	Ile
	180				185			190							

Gln	Tyr	Phe	Ala	Val	Ile	Ala	Ala	Ile	Gly	Asp	Arg	Ser	Lys	Lys	Asp
	195				200			205							

Gln	Ser	Pro	Gly	Lys	Gly	Thr	Leu	Glu	Asp	Gln	Ile	Ile	Gln	Ala	Asn
	210			215			220								

Pro	Ala	Leu	Glu	Ala	Phe	Gly	Asn	Ala	Lys	Thr	Val	Arg	Asn	Asp	Asn
225				230			235		240						

Ser	Ser	Arg	Phe	Gly	Lys	Phe	Ile	Arg	Ile	His	Phe	Gly	Ala	Thr	Gly
	245				250			255							

Lys	Leu	Ala	Ser	Ala	Asp	Ile	Glu	Thr	Tyr	Leu	Leu	Glu	Lys	Ser	Arg
	260				265			270							

Val	Ile	Phe	Gln	Leu	Lys	Ala	Glu	Arg	Asp	Tyr	His	Ile	Phe	Tyr	Gln
	275			280				285							

Ile	Leu	Ser	Asn	Lys	Lys	Pro	Glu	Leu	Leu	Asp	Met	Leu	Leu	Ile	Thr
	290			295				300							

Asn	Asn	Pro	Tyr	Asp	Tyr	Ala	Phe	Ile	Ser	Gln	Gly	Glu	Thr	Thr	Val
305				310			315			320					

US 12,385,041 B2

161

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Ala Ser Ile Asp Asp Ala Glu Glu Leu Met Ala Thr Asp Asn Ala Phe
 325 330 335

 Asp Val Leu Gly Phe Thr Ser Glu Glu Lys Asn Ser Met Tyr Lys Leu
 340 345 350

 Thr Gly Ala Ile Met His Phe Gly Asn Met Lys Phe Lys Leu Lys Gln
 355 360 365

 Arg Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Glu Ala Asp Lys Ser
 370 375 380

 Ala Tyr Leu Met Gly Leu Asn Ser Ala Asp Leu Leu Lys Gly Leu Cys
 385 390 395 400

 His Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly Gln Asn
 405 410 415

 Val Gln Gln Val Ile Tyr Ala Thr Gly Ala Leu Ala Lys Ala Val Tyr
 420 425 430

 Glu Arg Met Phe Asn Trp Met Val Thr Arg Ile Asn Ala Thr Leu Glu
 435 440 445

 Thr Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile Ala Gly
 450 455 460

 Phe Glu Ile Phe Asp Phe Asn Ser Phe Glu Gln Leu Cys Ile Asn Phe
 465 470 475 480

 Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe Val Leu
 485 490 495

 Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile Asp
 500 505 510

 Phe Gly Met Asp Leu Gln Ala Cys Ile Asp Leu Ile Glu Lys Pro Met
 515 520 525

 Gly Ile Met Ser Ile Leu Glu Glu Cys Met Phe Pro Lys Ala Thr
 530 535 540

 Asp Met Thr Phe Lys Ala Lys Leu Phe Asp Asn His Leu Gly Lys Ser
 545 550 555 560

 Ala Asn Phe Gln Lys Pro Arg Asn Ile Lys Gly Lys Pro Glu Ala His
 565 570 575

 Phe Ser Leu Ile His Tyr Ala Gly Ile Val Asp Tyr Asn Ile Ile Gly
 580 585 590

 Trp Leu Gln Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val Gly Leu
 595 600 605

 Tyr Gln Lys Ser Ser Leu Lys Leu Leu Ser Thr Leu Phe Ala Asn Tyr
 610 615 620

 Ala Gly Ala Asp Ala Pro Ile Glu Lys Gly Lys Ala Lys Lys
 625 630 635 640

 Gly Ser Ser Phe Gln Thr Val Ser Ala Leu His Arg Glu Asn Leu Asn
 645 650 655

 Lys Leu Met Thr Asn Leu Arg Ser Thr His Pro His Phe Val Arg Cys
 660 665 670

 Ile Ile Pro Asn Glu Thr Lys Ser Pro Gly Val Met Asp Asn Pro Leu
 675 680 685

 Val Met His Gln Leu Arg Cys Asn Gly Val Leu Glu Gly Ile Arg Ile
 690 695 700

 Cys Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp Phe Arg Gln
 705 710 715 720

 Arg Tyr Arg Ile Leu Asn Pro Ala Ala Ile Pro Glu Gly Gln Phe Ile
 725 730 735

162

US 12,385,041 B2

163**164**

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Asp Ser Arg Lys Gly Ala Glu Lys Leu Leu Ser Ser Leu Asp Ile Asp
 740 745 750
 His Asn Gln Tyr Lys Phe Gly His Thr Lys Val Phe Phe Lys Ala Gly
 755 760 765
 Leu Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Arg Leu Ser Arg Ile
 770 775 780
 Ile Thr Arg Ile Gln Ala Gln Ser Arg Gly Val Leu Ala Arg Met Glu
 785 790 795 800
 Tyr Lys Lys Leu Leu Glu Arg Arg Asp Ser Leu Leu Val Ile Gln Trp
 805 810 815
 Asn Ile Arg Ala Phe Met Gly Val Lys Asn Trp Pro Trp Met Lys Leu
 820 825 830
 Tyr Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu Arg Glu Lys Glu
 835 840 845
 Met Ala Ser Met Lys Glu Glu Phe Thr Arg Leu Lys Glu Ala Leu Glu
 850 855 860
 Lys Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys Met Val Ser Leu
 865 870 875 880
 Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Gln Asp
 885 890 895
 Asn Leu Ala Asp Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Asn Lys
 900 905 910
 Ile Gln Leu Glu Ala Lys Val Lys Glu Met Asn Glu Arg Leu Glu Asp
 915 920 925
 Glu Glu Glu Met Asn Ala Glu Leu Thr Ala Lys Lys Arg Lys Leu Glu
 930 935 940
 Asp Glu Cys Ser Glu Leu Lys Arg Asp Ile Asp Asp Leu Glu Leu Thr
 945 950 955 960
 Leu Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val Lys
 965 970 975
 Asn Leu Thr Glu Glu Met Ala Gly Leu Asp Glu Ile Ile Ala Lys Leu
 980 985 990
 Thr Lys Glu Lys Ala Leu Gln Glu Ala His Gln Gln Ala Leu Asp
 995 1000 1005
 Asp Leu Gln Ala Glu Glu Asp Lys Val Asn Thr Leu Thr Lys Ala
 1010 1015 1020
 Lys Val Lys Leu Glu Gln Gln Val Asp Asp Leu Glu Gly Ser Leu
 1025 1030 1035
 Glu Gln Glu Lys Lys Val Arg Met Asp Leu Glu Arg Ala Lys Arg
 1040 1045 1050
 Lys Leu Glu Gly Asp Leu Lys Leu Thr Gln Glu Ser Ile Met Asp
 1055 1060 1065
 Leu Glu Asn Asp Lys Gln Gln Leu Asp Glu Arg Leu Lys Lys Lys
 1070 1075 1080
 Asp Phe Glu Leu Asn Ala Leu Asn Ala Arg Ile Glu Asp Glu Gln
 1085 1090 1095
 Ala Leu Gly Ser Gln Leu Gln Lys Lys Leu Lys Glu Leu Gln Ala
 1100 1105 1110
 Arg Ile Glu Glu Leu Glu Glu Glu Leu Glu Ala Glu Arg Thr Ala
 1115 1120 1125
 Arg Ala Lys Val Glu Lys Leu Arg Ser Asp Leu Ser Arg Glu Leu
 1130 1135 1140
 Glu Glu Ile Ser Glu Arg Leu Glu Glu Ala Gly Gly Ala Thr Ser

US 12,385,041 B2

165**166**

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1145	1150	1155
Val Gln Ile Glu Met Asn Lys Lys Arg Glu Ala Glu Phe Gln Lys		
1160	1165	1170
Met Arg Arg Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr		
1175	1180	1185
Ala Ala Ala Leu Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu		
1190	1195	1200
Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys Gln Lys Leu Glu		
1205	1210	1215
Lys Glu Lys Ser Glu Phe Lys Leu Glu Leu Asp Asp Val Thr Ser		
1220	1225	1230
Asn Met Glu Gln Ile Ile Lys Ala Lys Ala Asn Leu Glu Lys Met		
1235	1240	1245
Cys Arg Thr Leu Glu Asp Gln Met Asn Glu His Arg Ser Lys Ala		
1250	1255	1260
Glu Glu Thr Gln Arg Ser Val Asn Asp Leu Thr Ser Gln Arg Ala		
1265	1270	1275
Lys Leu Gln Thr Glu Asn Gly Glu Leu Ser Arg Gln Leu Asp Glu		
1280	1285	1290
Lys Glu Ala Leu Ile Ser Gln Leu Thr Arg Gly Lys Leu Thr Tyr		
1295	1300	1305
Thr Gln Gln Leu Glu Asp Leu Lys Arg Gln Leu Glu Glu Glu Val		
1310	1315	1320
Lys Ala Lys Asn Ala Leu Ala His Ala Leu Gln Ser Ala Arg His		
1325	1330	1335
Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu Glu Thr Glu Ala		
1340	1345	1350
Lys Ala Glu Leu Gln Arg Val Leu Ser Lys Ala Asn Ser Glu Val		
1355	1360	1365
Ala Gln Trp Arg Thr Lys Tyr Glu Thr Asp Ala Ile Gln Arg Thr		
1370	1375	1380
Glu Glu Leu Glu Glu Ala Lys Lys Lys Leu Ala Gln Arg Leu Gln		
1385	1390	1395
Glu Ala Glu Glu Ala Val Glu Ala Val Asn Ala Lys Cys Ser Ser		
1400	1405	1410
Leu Glu Lys Thr Lys His Arg Leu Gln Asn Glu Ile Glu Asp Leu		
1415	1420	1425
Met Val Asp Val Glu Arg Ser Asn Ala Ala Ala Ala Leu Asp		
1430	1435	1440
Lys Lys Gln Arg Asn Phe Asp Lys Ile Leu Ala Glu Trp Lys Gln		
1445	1450	1455
Lys Tyr Glu Glu Ser Gln Ser Glu Leu Glu Ser Ser Gln Lys Glu		
1460	1465	1470
Ala Arg Ser Leu Ser Thr Glu Leu Phe Lys Leu Lys Asn Ala Tyr		
1475	1480	1485
Glu Glu Ser Leu Glu His Leu Glu Thr Phe Lys Arg Glu Asn Lys		
1490	1495	1500
Asn Leu Gln Glu Glu Ile Ser Asp Leu Thr Glu Gln Leu Gly Ser		
1505	1510	1515
Ser Gly Lys Thr Ile His Glu Leu Glu Lys Val Arg Lys Gln Leu		
1520	1525	1530
Glu Ala Glu Lys Met Glu Leu Gln Ser Ala Leu Glu Glu Ala Glu		
1535	1540	1545

US 12,385,041 B2

167

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Ala Ser Leu Glu His Glu Glu Gly Lys Ile Leu Arg Ala Gln Leu
 1550 1555 1560
 Glu Phe Asn Gln Ile Lys Ala Glu Ile Glu Arg Lys Leu Ala Glu
 1565 1570 1575
 Lys Asp Glu Glu Met Glu Gln Ala Lys Arg Asn His Leu Arg Val
 1580 1585 1590
 Val Asp Ser Leu Gln Thr Ser Leu Asp Ala Glu Thr Arg Ser Arg
 1595 1600 1605
 Asn Glu Ala Leu Arg Val Lys Lys Met Glu Gly Asp Leu Asn
 1610 1615 1620
 Glu Met Glu Ile Gln Leu Ser His Ala Asn Arg Met Ala Ala Glu
 1625 1630 1635
 Ala Gln Lys Gln Val Lys Ser Leu Gln Ser Leu Leu Lys Asp Thr
 1640 1645 1650
 Gln Ile Gln Leu Asp Asp Ala Val Arg Ala Asn Asp Asp Leu Lys
 1655 1660 1665
 Glu Asn Ile Ala Ile Val Glu Arg Arg Asn Asn Leu Leu Gln Ala
 1670 1675 1680
 Glu Leu Glu Glu Leu Arg Ala Val Val Glu Gln Thr Glu Arg Ser
 1685 1690 1695
 Arg Lys Leu Ala Glu Gln Glu Leu Ile Glu Thr Ser Glu Arg Val
 1700 1705 1710
 Gln Leu Leu His Ser Gln Asn Thr Ser Leu Ile Asn Gln Lys Lys
 1715 1720 1725
 Lys Met Asp Ala Asp Leu Ser Gln Leu Gln Thr Glu Val Glu Glu
 1730 1735 1740
 Ala Val Gln Glu Cys Arg Asn Ala Glu Glu Lys Ala Lys Lys Ala
 1745 1750 1755
 Ile Thr Asp Ala Ala Met Met Ala Glu Glu Leu Lys Lys Glu Gln
 1760 1765 1770
 Asp Thr Ser Ala His Leu Glu Arg Met Lys Lys Asn Met Glu Gln
 1775 1780 1785
 Thr Ile Lys Asp Leu Gln His Arg Leu Asp Glu Ala Glu Gln Ile
 1790 1795 1800
 Ala Leu Lys Gly Gly Lys Lys Gln Leu Gln Lys Leu Glu Ala Arg
 1805 1810 1815
 Val Arg Glu Leu Glu Asn Glu Leu Glu Ala Glu Gln Lys Arg Asn
 1820 1825 1830
 Ala Glu Ser Val Lys Gly Met Arg Lys Ser Glu Arg Arg Ile Lys
 1835 1840 1845
 Glu Leu Thr Tyr Gln Thr Glu Glu Asp Arg Lys Asn Leu Leu Arg
 1850 1855 1860
 Leu Gln Asp Leu Val Asp Lys Leu Gln Leu Lys Val Lys Ala Tyr
 1865 1870 1875
 Lys Arg Gln Ala Glu Glu Ala Glu Glu Gln Ala Asn Thr Asn Leu
 1880 1885 1890
 Ser Lys Phe Arg Lys Val Gln His Glu Leu Asp Glu Ala Glu Glu
 1895 1900 1905
 Arg Ala Asp Ile Ala Glu Ser Gln Val Asn Lys Leu Arg Ala Lys
 1910 1915 1920
 Ser Arg Asp Ile Gly Thr Lys Gly Leu Asn Glu Glu
 1925 1930 1935

168

US 12,385,041 B2

169**170**

-continued

<210> SEQ ID NO 157
<211> LENGTH: 6069
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 157

cagccccgtga	gaccaggctct	ggctccacag	ctctgtcttg	ctctgtgtct	ttccctgtcg	60
ctctcaggctc	ccctgcggc	cttggccctt	ttcttcatct	gttagacacac	tttagatggcc	120
caggcacacgc	catgggagat	tccggagatgg	cagtcttgg	ggctgccgccc	ccctacacctc	180
gcaaggcaga	gaaggagcgg	ctagaagcgc	agaccaggcc	ttttgaccc	aagaaggatg	240
tcttcgtgcc	tgtatgacaaa	caggagtttgc	tcaaggccaa	gatcgtgtct	cgagagggtg	300
gcaaagtca	tgcccgagacc	gagttatggca	agacagtgc	cgtgaaggag	gaccagggtg	360
tgcagcagaa	cccacccaag	ttcgacaaaa	tcgaggacat	ggccatgctg	acccctcg	420
atgagccccgc	ggtgctctac	aacctcaagg	atcgctacgg	ctccctggatg	atctacaccc	480
actcggggct	tttctgtgtc	accgtcaacc	cttacaagtgc	gctgcgggtg	tacactcctg	540
aggtgggtggc	tgcctaccgg	ggcaagaaga	ggagcggaggc	cccgccccac	atcttctcca	600
tctccgacaa	cgcctatcag	tacatgctga	cagacagaga	aaaccagtcc	atccctgatca	660
ccggagaatc	cgaggcagggg	aagacagtca	acaccaagag	ggtcatccag	tactttgctg	720
ttatttgcagc	cattttggac	cgcagcaaga	aggaccagag	cccgggcaag	ggcacccctgg	780
aggaccagat	catccaggcc	aacctgctc	tggaggcctt	tggcaatgcc	aagaccgtcc	840
ggaacgacaa	ctcccccgc	ttcgggaaat	tcatttcgaat	tcattttggg	gcaacaggaa	900
agttggcatc	tgcagacata	gagacctatc	ttctggaaaa	atccagagtt	attttccagc	960
tgaaaagcaga	gagagattat	cacattttct	accaaattct	gtctaaca	aaaggctgagc	1020
tgctggacat	gctgctgatc	accaacaacc	cctacgatta	tgcatttc	tcccaaggag	1080
agaccaccgt	ggcctccatt	gatgacgctg	aggagctcat	ggccactgat	aacgcttttg	1140
atgtgctggg	cttcacttca	gaggagaaaa	actccatgt	taagctgaca	ggcgccatca	1200
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gcactgaaga	ggctgacaag	tctgcctacc	tcatggggct	gaactcagcc	gacctgctca	1320
aggggctgtg	ccaccctcg	gtgaaagtgg	gcaatgaga	cgtcaccaag	gggcagaatg	1380
tccagcagg	gatatatgcc	actggggcac	tggccaaggc	agtgtatgag	aggatgtca	1440
actggatgg	gacgcgcata	aatgcaccc	tggagaccaa	gcagccacgc	cagtacttca	1500
taggagtcct	ggacatcgct	ggcttcgaga	tcttcgattt	caacagctt	gagcagctct	1560
gcatcaactt	caccaacgag	aagctgcgc	agttcttca	ccaccacatg	tttgtctgg	1620
agcaggagga	gtacaagaag	gagggcatcg	agtggacatt	cattgactt	ggcatggacc	1680
tgcaggcctg	cattgaccc	atcgagaagc	ccatggccat	catgtccatc	ctggaagagg	1740
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tggccaaatc	cgcacacttc	cagaagccac	gcaatata	ggggaaagcct	gaagcccact	1860
tctccctgat	ccactatgcc	ggcatcggt	actacaacat	cattggctgg	ctgcagaaga	1920
acaaggatcc	tctcaatgag	actgtcggt	gcttgtatca	gaagtcttcc	ctcaagctgc	1980
tcagcaccct	gtttgcacac	tatgttgggg	ctgtgcgc	tattgagaag	ggcaaaaggca	2040
aggccaaagaa	aggctcgcc	tttcagactg	tgtcagctct	gcacaggaa	aatctgaaca	2100
agctgatgac	caacttgcgc	tccacccatc	cccacttgc	acgttgatc	atcccta	2160

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agacaaaatgc tccaggggtg atggacaacc ccctggcat gcaccagctg cgctgcaatg	2220
gtgtgctgga gggcatccgc atctgcagga aaggcttccc caaccgcate ctctacgggg	2280
acttcggca gaggtatcgc atcctgaacc cagcgccat ccctgaggga cagttcattg	2340
atacgagaa gggggcagag aagctgctca gctccctgga cattgtatcac aaccagtaca	2400
agtttggcca caccaagggtg ttcttcaagg ccgggctgct ggggctgctg gaggaaatga	2460
gggacgagag gctgagccgc atcatcacgc gtatccaggc ccagteccga ggtgtgctcg	2520
ccagaatgga gtacaaaaag ctgctggaac gtagagactc octgctggta atccagtgga	2580
acattcgggc cttcatgggg gtcaagaatt ggccctggat gaagctctac ttcaagatca	2640
agccgctgct gaagagtgca gaaagagaga aggagatggc ctccatgaag gaggagttca	2700
cacgcctcaa agaggcgcta gagaagtcgg aggctcgccg caaggagctg gaggagaaga	2760
tggtgtccct gctgcaggag aagaatgacc tgcagctcca agtgcaggcg gaacaagaca	2820
acctggcaga tgctgaggag cgctgtgatc agctgatcaa aaacaagatt cagctggagg	2880
ccaagggtgaa ggagatgaac gagaggctgg aggtgagga ggagatgaat gctgagctca	2940
ctgccaagaa ggcgaagctg gaagatgagt gctcagagct caaaagggac atcgatgatc	3000
tggagctgac actggccaaa gtggagaagg agaaacacgc aacagagaac aaggtaaaaa	3060
acctgacaga ggagatggct gggctggatc agatcattgc caagctgacc aaggagaaga	3120
aagctctgca agaggccccac caacaggctc tggatgaccc tcagggcagag gaggacaagg	3180
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atgagcggct gaaaaaaaaa gactttgago tgaatgctct caacgcaagg attgaggatg	3420
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agctggagga ggagctggag gccgagcgca ccgccaggcc taaggtggag aagctgcgc	3540
cacacctgtc tcggggactg gaggagatca gcgagccgc ggaagggcc ggccccccca	3600
cgtccgtca gatcgagatg aacaagaago gcgaggccga gttccagaag atgcggccgg	3660
acctggagga ggccacgctg cagcacgagg ccactgcgcg ggccctgcgc aagaagcacg	3720
ccgacagcgt ggccgagctg ggcgagcaga tcgacaacct gcagcgggtg aagcagaac	3780
tggagaagga qaagagcgag ttcaagctgg agctggatc cgtcacccctt aacatggagc	3840
agatcatcaa ggccaaggct aacctggaga agatgtccgc gacctggaa gaccagatga	3900
atgagcaccg gagcaaggcg gaggagaccc agcgttctgt caacgaccc accagccac	3960
ggcccaagtt gcaaaccgag aatggtgago tgcacccggca gctggatgag aaggaggcac	4020
tgatctccca gctgacccga ggcaagctca cctacacccca gcagctggag gacctcaaga	4080
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tgcagcgcgt ctttccaaag gccaactcg aggtggccca gtggaggacc aagtatgaga	4260
cgacgcctat tcagcggact gaggagctg aggaggccaa gaagaagctg gcccagccgc	4320
tgcaggaagc tgaggaggcc gtggaggctg ttaatgccaat gtcctctcg ctggagaaga	4380
ccaagcaccg gctacagaat gagatcgagg acttgcgtt ggacgttagag cgctccaatg	4440
ctgctgctgc agccctggac aagaagcaga ggaacttcga caagatcctg gccgagtgga	4500

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agcagaagta tgaggagtcg cagtccggagc tggagtcctc gcagaaggag gctcgctccc	4560
tcagcacaga gctcttcaaa ctcaagaacg cctatgagga gtccctggaa catctggaga	4620
ccttcaagcg ggagaacaaa aacctgcagg aggagatctc cgacttgact gagcagttgg	4680
gttccagcgg aaagactatac catagactgg agaaggctcg aaagcagctg gaggccgaga	4740
agatggagct gcagtcagcc ctggaggagg ccgaggctc cctggagcac gaggaggcga	4800
agatcctccg ggcccgactg gagttcaacc agatcaaggc agagatcgag cggaaagctgg	4860
cagagaagga cgaggagatg gaacaggcca agcgcaacca cctgcgggtg gtggactcgc	4920
tgcagacctc cctggacgcgca gagacacgcg gccgcaacga ggccctgagg gtgaagaaga	4980
agatggaagg agacctaatt gagatggaga tccagcttag ccacgccaac cgcatggccg	5040
ccggggccca aagcaagtc aagagcctcc agagcttggtaa catcgccatc gtggagccgc	5100
tggacgatgc agtccgtgcc aacgacgacc tgaaggagaa catcgccatc gtggagccgc	5160
gcaacaacct gctgcaggct gagctggagg agttgcgtgc cgtgggtggag cagacagagc	5220
ggtccccggaa gctggcgagg caggagctga ttgagacttag tgagcgggtg cagctgctgc	5280
attccccagaa caccacccctc atcaaccaga agaagaagat ggatgctgac ctgtcccagc	5340
tccagactga agtggaggag gcagtgccagg agtgcaggaa tgctgaggag aaggccaaga	5400
aggccatcac ggatgcccgc atgatggcag aggagctgaa gaaggagcag gacaccagcg	5460
cccacctgga ggcgcataag aagaacatgg aacagaccat taaggaccatc cagcaccggc	5520
tggacgaaacgc cagacgatgc gcccctaagg gccggcaagaa gcagctgcag aagctggaa	5580
cgcgggtgcg ggagctggag aatgagctgg aggccgagca gaagcgcaac gcagagtcgg	5640
tgaaggccat gaggaagagc gagcggcgca tcaaggagct cacctaccag acggaggagg	5700
acaggaaaaaa cctgctgcgg ctgcaggacc ttggtagacaa gctgcagacta aaggtcaagg	5760
cctacaagcg ccaggccgag gaggccgagg agcaagccaa caccaacctg tccaagttcc	5820
gcaagggtgcg caacgagctg gatggccgcg aggagccggc ggacatcgcc gagtcccagg	5880
tcaacaagct gcccccaag agccgtgaca ttggcacgaa gggcttgaat gaggagtagc	5940
tttgccacat cttgatctgc tcagccctgg aggtgccagc aaagccccat gctggagcct	6000
gtgttaacagc tccttggag gaagcagaat aaagcaattt tccttgaagc cgagaaaaaa	6060
aaaaaaaaaa	6069

<210> SEQ ID NO 158

<211> LENGTH: 151

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 158

Met Ser Ser Phe Ser Thr Thr Val Ser Phe Leu Leu Leu Ala			
1	5	10	15

Phe Gln Leu Leu Gly Gln Thr Arg Ala Asn Pro Met Tyr Asn Ala Val			
20	25	30	

Ser Asn Ala Asp Leu Met Asp Phe Lys Asn Leu Leu Asp His Leu Glu			
35	40	45	

Glu Lys Met Pro Leu Glu Asp Glu Val Val Pro Pro Gln Val Leu Ser			
50	55	60	

Glu Pro Asn Glu Glu Ala Gly Ala Ala Leu Ser Pro Leu Pro Glu Val			
65	70	75	80

Pro Pro Trp Thr Gly Glu Val Ser Pro Ala Gln Arg Asp Gly Gly Ala			
85	90	95	

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Leu Gly Arg Gly Pro Trp Asp Ser Ser Asp Arg Ser Ala Leu Leu Lys
 100 105 110

Ser Lys Leu Arg Ala Leu Leu Thr Ala Pro Arg Ser Leu Arg Arg Ser
 115 120 125

Ser Cys Phe Gly Gly Arg Met Asp Arg Ile Gly Ala Gln Ser Gly Leu
 130 135 140

Gly Cys Asn Ser Phe Arg Tyr
 145 150

<210> SEQ ID NO 159

<211> LENGTH: 858

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 159

gagacagggaa	cagacgttagg	ccaagagagg	ggaaccagag	aggaaccaga	ggggagagac	60
agagcagcaa	gcagtggatt	gctcattgac	gacgccagca	ttagctccctt	ctccaccacc	120
acctgtgagct	tccctttttt	actggcattc	cagctcttag	gtcagaccag	agctaattccc	180
atgtacaatg	ccgtgtccaa	cgcagacctg	atggatttca	agaatttgct	ggaccatttg	240
gaagaaaaaga	tgcctttaga	agatgaggtc	gtgcccccac	aagtgtctag	tgagccgaat	300
gaagaagcg	gggctgctct	cageccccctc	cctgagggtgc	ctccctggac	cggggaaatc	360
agccccagccc	agagagatgg	agggtccctc	gggcggggcc	cctgggactc	ctctgtatcga	420
tctgcccctcc	taaaaagcaa	gctgagggeg	ctgctcaact	ccccteggag	cctgeggaga	480
tccagctgct	tcgggggcag	atggacagg	attggageccc	agagcggact	gggctgtaac	540
agcttcccggt	actgaagata	acagccaggg	aggacaagca	gggctggggcc	tagggacaga	600
ctgcaagagg	ctccctgtccc	ctggggtctc	tgtgcattt	gtgtcatctt	gttgcctatgg	660
atggtagata	aagtggttt	atggtgactt	cctcgccctc	cccacccat	gcattaaatt	720
ttaaggtaga	acctcacctg	ttactgaaag	tggttgaaa	gtgaataaac	ttcagcacca	780
tggacagaag	acaaaaaaaaa					840
						858

<210> SEQ ID NO 160

<211> LENGTH: 134

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 160

Met Asp Pro Gln Thr Ala Pro Ser Arg Ala Leu Leu Leu Leu Leu Phe
 1 5 10 15

Leu His Leu Ala Phe Leu Gly Gly Arg Ser His Pro Leu Gly Ser Pro
 20 25 30

Gly Ser Ala Ser Asp Leu Glu Thr Ser Gly Leu Gln Glu Gln Arg Asn
 35 40 45

His Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu
 50 55 60

Glu Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg
 65 70 75 80

Glu Val Ala Thr Glu Gly Ile Arg Gly His Arg Lys Met Val Leu Tyr
 85 90 95

Thr Leu Arg Ala Pro Arg Ser Pro Lys Met Val Gln Gly Ser Gly Cys
 100 105 110

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Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys
 115 120 125

Lys Val Leu Arg Arg His
 130

<210> SEQ ID NO 161

<211> LENGTH: 708

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 161

ccccgcaggc tgagggcagg tggaaagcaa acccgacgc atcgcagcag cagcagcagc	60
agcagaagca gcagcagcag cctccgcagt ccctccagag acatggatcc ccagacagca	120
ccttcccggg cgctcctgct cctgtcttc ttgcacatcg ctttcctggg aggtcggtcc	180
cacccgctgg gcagccccgg ttcagcctcg gacttgaaa cgtccgggtt acaggagcag	240
cgcAACATT tgcaggcCAA actgtcgag ctgcagggtt agcagacatc cctggagccc	300
ctccaggaga gccccgtcc cacaggtgtc tggaaagtccc gggaggttagc caccgagggc	360
atccgtgggc accgcAAAT ggtcctctac accctgcggg caccacgaag ccccaagatg	420
gtgcaagggt ctggctgtt tggagggaaat atggacccggta ctagctctc cagtggctg	480
ggctgcaaaag tgctgaggcg gcattaagag gaagtccctgg ctgcagacac ctgcttctga	540
ttoccacaagg ggcttttcc tcaaccctgt ggccgcctt gaagtgactc attttttaa	600
tgttatattt attttttat ataagatggt ttcttaccc ttgagcacaaa	660
atttccacgg tgaaataaaag tcaacattat aagtttaaa aaaaaaaaaaaaaaa	708

<210> SEQ ID NO 162

<211> LENGTH: 1935

<212> TYPE: PRT

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 162

Met Ala Asp Arg Glu Met Ala Ala Phe Gly Ala Gly Ala Pro Phe Leu	
1 5 10 15	

Arg Lys Ser Glu Lys Glu Arg Leu Glu Ala Gln Thr Arg Pro Phe Asp	
20 25 30	

Leu Lys Lys Asp Val Phe Val Pro Asp Asp Lys Glu Glu Phe Val Lys	
35 40 45	

Ala Lys Ile Val Ser Arg Glu Gly Gly Lys Val Thr Ala Glu Thr Glu	
50 55 60	

Asn Gly Lys Thr Val Thr Val Lys Glu Asp Gln Val Met Gln Gln Asn	
65 70 75 80	

Pro Pro Lys Phe Asp Lys Ile Glu Asp Met Ala Met Leu Thr Phe Leu	
85 90 95	

His Glu Pro Ala Val Leu Tyr Asn Leu Lys Glu Arg Tyr Ala Ser Trp	
100 105 110	

Met Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Thr Val Asn Pro Tyr	
115 120 125	

Lys Trp Leu Pro Val Tyr Asn Ala Gln Val Val Ala Ala Tyr Arg Gly	
130 135 140	

Lys Lys Arg Ser Glu Ala Pro Pro His Ile Phe Ser Ile Ser Asp Asn	
145 150 155 160	

Ala Tyr Gln Tyr Met Leu Thr Asp Arg Glu Asn Gln Ser Ile Leu Ile	
165 170 175	

US 12,385,041 B2

179

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Thr Gly Glu Ser Gly Ala Gly Lys Thr Val Asn Thr Lys Arg Val Ile
 180 185 190
 Gln Tyr Phe Ala Val Ile Ala Ala Ile Gly Asp Arg Ser Lys Lys Asp
 195 200 205
 Gln Thr Pro Gly Lys Gly Thr Leu Glu Asp Gln Ile Ile Gln Ala Asn
 210 215 220
 Pro Ala Leu Glu Ala Phe Gly Asn Ala Lys Thr Val Arg Asn Asp Asn
 225 230 235 240
 Ser Ser Arg Phe Gly Lys Phe Ile Arg Ile His Phe Gly Ala Thr Gly
 245 250 255
 Lys Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu Glu Lys Ser Arg
 260 265 270
 Val Ile Phe Gln Leu Lys Ala Glu Arg Asp Tyr His Ile Phe Tyr Gln
 275 280 285
 Ile Leu Ser Asn Lys Lys Pro Glu Leu Leu Asp Met Leu Leu Ile Thr
 290 295 300
 Asn Asn Pro Tyr Asp Tyr Ala Phe Phe Ser Gln Gly Glu Thr Thr Val
 305 310 315 320
 Ala Ser Ile Asp Asp Ser Glu Glu His Met Ala Thr Asp Ser Ala Phe
 325 330 335
 Asp Val Leu Gly Phe Thr Pro Glu Glu Lys Asn Ser Ile Tyr Lys Leu
 340 345 350
 Thr Gly Ala Ile Met His Phe Gly Asn Met Lys Phe Lys Gln Lys Gln
 355 360 365
 Arg Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Glu Ala Asp Lys Ser
 370 375 380
 Ala Tyr Leu Met Gly Leu Asn Ser Ala Asp Leu Leu Lys Gly Leu Cys
 385 390 395 400
 His Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly Gln Asn
 405 410 415
 Val Gln Gln Val Ala Tyr Ala Ile Gly Ala Leu Ala Lys Ser Val Tyr
 420 425 430
 Glu Lys Met Phe Asn Trp Met Val Thr Arg Ile Asn Ala Thr Leu Glu
 435 440 445
 Thr Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile Ala Gly
 450 455 460
 Phe Glu Ile Phe Asp Phe Asn Ser Phe Glu Gln Leu Cys Ile Asn Phe
 465 470 475 480
 Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe Val Leu
 485 490 495
 Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile Asp
 500 505 510
 Phe Gly Met Asp Leu Gln Ala Cys Ile Asp Leu Ile Glu Lys Pro Met
 515 520 525
 Gly Ile Met Ser Ile Leu Glu Glu Cys Met Phe Pro Lys Ala Thr
 530 535 540
 Asp Met Thr Phe Lys Ala Lys Leu Tyr Asp Asn His Leu Gly Lys Ser
 545 550 555 560
 Asn Asn Phe Gln Lys Pro Arg Asn Ile Lys Gly Lys Gln Glu Ala His
 565 570 575
 Phe Ser Leu Ile His Tyr Ala Gly Thr Val Asp Tyr Asn Ile Leu Gly
 580 585 590

180

US 12,385,041 B2

181**182**

-continued

Trp Leu Gln Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val Gly Leu
 595 600 605
 Tyr Gln Lys Ser Ser Leu Lys Leu Leu Ser Asn Leu Phe Ala Asn Tyr
 610 615 620
 Ala Gly Ala Asp Ala Pro Val Asp Lys Gly Lys Gly Lys Ala Lys Lys
 625 630 635 640
 Gly Ser Ser Phe Gln Thr Val Ser Ala Leu His Arg Glu Asn Leu Asn
 645 650 655
 Lys Leu Met Thr Asn Leu Arg Ser Thr His Pro His Phe Val Arg Cys
 660 665 670
 Ile Ile Pro Asn Glu Thr Lys Ser Pro Gly Val Met Asp Asn Pro Leu
 675 680 685
 Val Met His Gln Leu Arg Cys Asn Gly Val Leu Glu Gly Ile Arg Ile
 690 695 700
 Cys Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp Phe Arg Gln
 705 710 715 720
 Arg Tyr Arg Ile Leu Asn Pro Ala Ala Ile Pro Glu Gly Gln Phe Ile
 725 730 735
 Asp Ser Arg Lys Gly Ala Glu Lys Leu Leu Gly Ser Leu Asp Ile Asp
 740 745 750
 His Asn Gln Tyr Lys Phe Gly His Thr Lys Val Phe Phe Lys Ala Gly
 755 760 765
 Leu Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Arg Leu Ser Arg Ile
 770 775 780
 Ile Thr Arg Ile Gln Ala Gln Ser Arg Gly Val Leu Ser Arg Met Glu
 785 790 795 800
 Phe Lys Lys Leu Leu Glu Arg Arg Asp Ser Leu Leu Ile Ile Gln Trp
 805 810 815
 Asn Ile Arg Ala Phe Met Gly Val Lys Asn Trp Pro Trp Met Lys Leu
 820 825 830
 Tyr Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu Thr Glu Lys Glu
 835 840 845
 Met Ala Asn Met Lys Glu Glu Phe Gly Arg Val Lys Asp Ala Leu Glu
 850 855 860
 Lys Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys Met Val Ser Leu
 865 870 875 880
 Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Gln Asp
 885 890 895
 Asn Leu Ala Asp Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Asn Lys
 900 905 910
 Ile Gln Leu Glu Ala Lys Val Lys Glu Met Thr Glu Arg Leu Glu Asp
 915 920 925
 Glu Glu Glu Met Asn Ala Glu Leu Thr Ala Lys Lys Arg Lys Leu Glu
 930 935 940
 Asp Glu Cys Ser Glu Leu Lys Arg Asp Ile Asp Asp Leu Glu Leu Thr
 945 950 955 960
 Leu Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val Lys
 965 970 975
 Asn Leu Thr Glu Glu Met Ala Gly Leu Asp Glu Ile Ile Val Lys Leu
 980 985 990
 Thr Lys Glu Lys Lys Ala Leu Gln Glu Ala His Gln Gln Ala Leu Asp
 995 1000 1005
 Asp Leu Gln Ala Glu Glu Asp Lys Val Asn Thr Leu Thr Lys Ala

US 12,385,041 B2

183

184

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1010	1015	1020
Lys Val Lys Leu Glu Gln Gln	Val Asp Asp Leu Glu Gly Ser Leu	
1025	1030	1035
Asp Gln Asp Lys Lys Val Arg Met Asp Leu Glu Arg Ala Lys Arg		
1040	1045	1050
Lys Leu Glu Gly Asp Leu Lys Leu Thr Gln Glu Ser Ile Met Asp		
1055	1060	1065
Leu Glu Asn Asp Lys Gln Gln Leu Asp Glu Arg Leu Lys Lys Lys		
1070	1075	1080
Asp Phe Glu Leu Asn Ala Leu Asn Ala Arg Ile Glu Asp Glu Gln		
1085	1090	1095
Ala Leu Gly Ser Gln Leu Gln Lys Lys Leu Lys Glu Leu Gln Ala		
1100	1105	1110
Arg Ile Glu Glu Leu Glu Glu Glu Leu Glu Ala Glu Arg Thr Ala		
1115	1120	1125
Arg Ala Lys Val Glu Lys Leu Arg Ser Asp Leu Ser Arg Glu Leu		
1130	1135	1140
Glu Glu Ile Ser Glu Arg Leu Glu Glu Ala Gly Gly Ala Thr Ser		
1145	1150	1155
Val Gln Ile Glu Met Asn Lys Lys Arg Glu Ala Glu Phe Gln Lys		
1160	1165	1170
Met Arg Arg Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr		
1175	1180	1185
Ala Ala Ala Leu Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu		
1190	1195	1200
Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys Gln Lys Leu Glu		
1205	1210	1215
Lys Glu Lys Ser Glu Phe Lys Leu Glu Leu Asp Asp Val Thr Ser		
1220	1225	1230
Asn Met Glu Gln Ile Ile Lys Ala Lys Ala Asn Leu Glu Lys Met		
1235	1240	1245
Cys Arg Thr Leu Glu Asp Gln Met Asn Glu His Arg Ser Lys Ala		
1250	1255	1260
Glu Glu Thr Gln Arg Ser Val Asn Asp Leu Thr Arg Gln Arg Ala		
1265	1270	1275
Lys Leu Gln Thr Glu Asn Gly Glu Leu Ser Arg Gln Leu Asp Glu		
1280	1285	1290
Lys Glu Ala Leu Ile Ser Gln Leu Thr Arg Gly Lys Leu Thr Tyr		
1295	1300	1305
Thr Gln Gln Leu Glu Asp Leu Lys Arg Gln Leu Glu Glu Glu Val		
1310	1315	1320
Lys Ala Lys Asn Ala Leu Ala His Ala Leu Gln Ser Ala Arg His		
1325	1330	1335
Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu Glu Thr Glu Ala		
1340	1345	1350
Lys Ala Glu Leu Gln Arg Val Leu Ser Lys Ala Asn Ser Glu Val		
1355	1360	1365
Ala Gln Trp Arg Thr Lys Tyr Glu Thr Asp Ala Ile Gln Arg Thr		
1370	1375	1380
Glu Glu Leu Glu Glu Ala Lys Lys Lys Leu Ala Gln Arg Leu Gln		
1385	1390	1395
Asp Ala Glu Glu Ala Val Glu Ala Val Asn Ala Lys Cys Ser Ser		
1400	1405	1410

US 12,385,041 B2

185**186**

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Leu Glu Lys Thr Lys His Arg Leu Gln Asn Glu Ile Glu Asp Leu
 1415 1420 1425
 Met Val Asp Val Glu Arg Ser Asn Ala Ala Ala Ala Ala Leu Asp
 1430 1435 1440
 Lys Lys Gln Arg Asn Phe Asp Lys Ile Leu Val Glu Trp Lys Gln
 1445 1450 1455
 Lys Tyr Glu Glu Ser Gln Ser Glu Leu Glu Ser Ser Gln Lys Glu
 1460 1465 1470
 Ala Arg Ser Leu Ser Thr Glu Leu Phe Lys Leu Lys Asn Ala Tyr
 1475 1480 1485
 Glu Glu Ser Leu Glu His Leu Glu Thr Phe Lys Arg Glu Asn Lys
 1490 1495 1500
 Asn Leu Gln Glu Glu Ile Ser Asp Leu Thr Glu Gln Leu Gly Ser
 1505 1510 1515
 Thr Gly Lys Ser Ile His Glu Leu Glu Lys Ile Arg Lys Gln Leu
 1520 1525 1530
 Glu Ala Glu Lys Leu Glu Leu Gln Ser Ala Leu Glu Glu Ala Glu
 1535 1540 1545
 Ala Ser Leu Glu His Glu Glu Gly Lys Ile Leu Arg Ala Gln Leu
 1550 1555 1560
 Glu Phe Asn Gln Ile Lys Ala Glu Ile Glu Arg Lys Leu Ala Glu
 1565 1570 1575
 Lys Asp Glu Glu Met Glu Gln Ala Lys Arg Asn His Leu Arg Val
 1580 1585 1590
 Val Asp Ser Leu Gln Thr Ser Leu Asp Ala Glu Thr Arg Ser Arg
 1595 1600 1605
 Asn Glu Ala Leu Arg Val Lys Lys Met Glu Gly Asp Leu Asn
 1610 1615 1620
 Glu Met Glu Ile Gln Leu Ser His Ala Asn Arg Met Ala Ala Glu
 1625 1630 1635
 Ala Gln Lys Gln Val Lys Ser Leu Gln Ser Leu Leu Lys Asp Thr
 1640 1645 1650
 Gln Ile Gln Leu Asp Asp Ala Val Arg Ala Asn Asp Asp Leu Lys
 1655 1660 1665
 Glu Asn Ile Ala Ile Val Glu Arg Arg Asn Asn Leu Leu Gln Ala
 1670 1675 1680
 Glu Leu Glu Glu Leu Arg Ala Val Val Glu Gln Thr Glu Arg Ser
 1685 1690 1695
 Arg Lys Leu Ala Glu Gln Glu Leu Ile Glu Thr Ser Glu Arg Val
 1700 1705 1710
 Gln Leu Leu His Ser Gln Asn Thr Ser Leu Ile Asn Gln Lys Lys
 1715 1720 1725
 Lys Met Asp Ala Asp Leu Ser Gln Leu Gln Thr Glu Val Glu Glu
 1730 1735 1740
 Ala Val Gln Glu Cys Arg Asn Ala Glu Glu Lys Ala Lys Lys Ala
 1745 1750 1755
 Ile Thr Asp Ala Ala Met Met Ala Glu Glu Leu Lys Lys Glu Gln
 1760 1765 1770
 Asp Thr Ser Ala His Leu Glu Arg Met Lys Asn Asn Met Glu Gln
 1775 1780 1785
 Thr Ile Lys Asp Leu Gln His Arg Leu Asp Glu Ala Glu Gln Ile
 1790 1795 1800

US 12,385,041 B2

187**188**

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Ala	Leu	Lys	Gly	Gly	Lys	Lys	Gln	Leu	Gln	Lys	Leu	Glu	Ala	Arg
1805					1810					1815				
Val	Arg	Glu	Leu	Glu	Asn	Glu	Leu	Glu	Ala	Glu	Gln	Lys	Arg	Asn
1820					1825					1830				
Ala	Glu	Ser	Val	Lys	Gly	Met	Arg	Lys	Ser	Glu	Arg	Arg	Ile	Lys
1835					1840					1845				
Glu	Leu	Thr	Tyr	Gln	Thr	Glu	Glu	Asp	Arg	Lys	Asn	Leu	Leu	Arg
1850					1855					1860				
Leu	Gln	Asp	Leu	Val	Asp	Lys	Leu	Gln	Leu	Lys	Val	Lys	Ala	Tyr
1865					1870					1875				
Lys	Arg	Gln	Ala	Glu	Glu	Ala	Glu	Glu	Gln	Ala	Asn	Thr	Asn	Leu
1880					1885					1890				
Ser	Lys	Phe	Arg	Lys	Val	Gln	His	Glu	Leu	Asp	Glu	Ala	Glu	Glu
1895					1900					1905				
Arg	Ala	Asp	Ile	Ala	Glu	Ser	Gln	Val	Asn	Lys	Leu	Arg	Ala	Lys
1910					1915					1920				
Ser	Arg	Asp	Ile	Gly	Ala	Lys	Gly	Leu	Asn	Glu	Glu			
1925					1930					1935				

<210> SEQ ID NO 163

<211> LENGTH: 5923

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 163

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aatctgagaa	ggagcggctg	gaggcgcaga	ccaggccctt	tgacctcaag	aaagatgttt	120
tttgtgcgtga	tgacaaaagaa	gagtttgtca	aggccaagat	cgtgtctcg	gaggggtggca	180
aagtccaccgc	tgagacagag	aatggcaaga	cggtgactgt	gaaggaggac	caggtgtatgc	240
agcagaacccc	tcccaagttc	gacaagatcg	aggacatggc	catgctgacc	ttccctgcacg	300
agccggctgt	gctctacaat	ctcaaggaga	ggtacgcgttc	ctggatgtac	tacacctact	360
caggcctctt	ctgtgtcacc	gtcaacccct	ataagtggtt	gccagtgtac	aatgegcaag	420
tggtagctgc	ctaccggggc	aagaagagga	gcgaggctcc	accccacatc	ttctccatct	480
ctgacaacgc	ctatcgtac	atgtgtacag	atcggggaa	ccagtcacatc	ctcatcacccg	540
gagaatccgg	agctggtaag	accgtcaaca	ccaagagggt	catccaatat	tttgcgttta	600
ttgtgtccat	tgggggaccgc	agcagaagg	accagacccc	aggcaagggc	accttggaa	660
atcaaatcat	ccaagccaac	cccgctctgg	aggccttgg	caatgccaag	acagttcgga	720
atgataactc	ctccccattt	gggaaattca	ttcgaatcca	ttttggggca	acaggaaagt	780
tggcatctgc	agatatacgag	acctacacctc	tggaaaaatc	cagagtattt	ttccagctga	840
aagcagaaag	agattatcac	attttctacc	aaatcctgtc	taataaaaaag	cctgagcttc	900
tagacatgt	gctgtatcacc	aacaacccct	acgattatgc	gttcttctcc	cagggagaga	960
cgactgtggc	ctcaatagat	gactctgaag	agcacatggc	caccgatagc	gcctttgatg	1020
tgttgggtt	cactccagaa	gagaagaact	ccatttacaa	gtgacaggc	gccatcatgc	1080
actttggaaa	catgaagttc	aaacagaagc	agagggagga	gcagggcagag	ccagacggca	1140
cggagaaggc	tgacaagtca	gcctacactca	tgggactgaa	ctcggctgac	ctgctcaagg	1200
ggtttgtgcca	ccctcgagtc	aaagtgggc	acgagtatgt	caccaaaggg	cagaatgtcc	1260
agcaggtggc	atatgccatc	ggggcactgg	ccaagtcagt	gtacgagaag	atgttcaact	1320

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ggatggtgac acgcatcaac gcaaccctgg agaccaagca gccacgcag tacttcata	1380
gtgtcctgga catgcgcggc ttttagatct ttgatttcaa cagctttag cagctgtca	1440
tcaacttcac caatgagaag ctgcagcagt tcttcaacca ccacatgtc gtgctggagc	1500
aggaggagta caagaaggaa ggcatcgagt ggacgtttat tgacttcggc atggacctgc	1560
aggcctgcat cgacccatc gagaagccca tgggcatcat gtccatcctg gaggaggat	1620
gcatgttccc caaggcacag gacatgaccc tcaaggccaa gctgtacgac aaccacctgg	1680
gcaagtc当地 caacttccag aagcctcgca atatcaaggg aaagcaggaa gcccacttct	1740
ctctgatcca ctatgttgc accgtggact acaatatcctt gggctggcta cagaagaaca	1800
aggaccctct caatgagacg gtggggggc tgtaccagaa gtcctccctc aagtcctaa	1860
gtaatctgtt tgcccaactat gctggagctg atgcacccctg agacaaggc aaaggcaag	1920
caaagaaaagg ctcatccctt cagaccgtgt ccgcactgca cagggaaaat ctgaacaaac	1980
ttatgacaaa cctgcgcctcc acgcacccctc actttgtacg ctgcacatc cccaatgaga	2040
cgaagtctcc aggggtgatg gacaaccccc tggcatgca ccagctgcga tgcaacggag	2100
tgctggaggg tatccgcatac tggtaggaaagg gttttcccaa ccgcattttt tatggggact	2160
tccggcagag gtatcgaatc ctgaacccag cagccatccc tgagggccaa ttcatgtata	2220
gccggaaaagg ggctgagaag ctgctggctt ccctggacat tgaccacaaac cagtcataag	2280
ttggccacac caaggtgttc ttcaaggccgg ggctgctggg gctgctggag gagatgcgag	2340
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gaatggagtt taagaagctg ctggagcgca gagactccct gctgattatc cagtggaaaca	2460
tccgcgcctt catgggggtc aagaattggc cgtggatgaa gctctacttc aagatcaagc	2520
cgctgctgaa gagcgcagag acagagaagg agatggccaa catgaaggag gagttcgggc	2580
gagtcaaaga tgcactagag aagtctgagg ctcgcgc当地 ggagctggag gagaagatgg	2640
tgtccctgt gcaggagaag aatgacactgc agctccaagt gcagggggaa caagacaacc	2700
tggcagatgc cgaggagcgc tgccgaccagg tgcataagaa caagatccag ctggaggccaa	2760
aggtgaagga gatgaccggc aggctggagg acgaggaggaa gatgaacgcc gagctcacgg	2820
ccaagaagcg ccaaactggaa gacgagtgct cagagctaa gagagatatac gatgacccctgg	2880
agctgaccct ggcccaagggtg gagaaggaaa agcacgc当地 agagaacaag gtgaaaaacc	2940
tgacagagga gatggctggg ctggacgaga tcattgtcaa gctgaccaag gagaagaaag	3000
ctctacaaga ggcccaccag caagccctag atgaccctca ggctgaggag gacaaggctca	3060
acactctgac caaggccaaag gtcaagctgg agcagcaagt ggatgatctg gagggatccc	3120
tggatcagga caagaagggtg cgcacggacc tggagcgagc aaagcggaaag ctggagggtg	3180
acctgaagct gacccaggag agcatcatgg acctggagaa cgacaaggcag cagttggatg	3240
agcgactcaa aaagaaggac ttttagttaa atgcactcaa cgccaggatt gaggatgagc	3300
aggccctggg cagccagctg cagaagaago tcaaaggact tcaggcacgc atcgaggagc	3360
tggaggagga gctggaggct gagcgc当地 cccggggccaa ggtggagaag ctgcgc当地	3420
acctgtcccg ggagctggag gagaatcgtg agaggctaga ggaaggccggt gggggccacat	3480
ctgtgcagat agagatgaac aagaaggc当地 agggccgagtt ccagaaggatg cggcgggacc	3540
tagaggaggc cacgctgc当地 catggggccaa cagctgc当地 cctgc当地aaacacgc当地	3600
acagcgtggc cgagctgggc gagcagatag acaatctaca ggggtgaag cagaagctgg	3660
agaaagagaa gagcgc当地 aagctggagc tggatgacgt tacctccaaat atggagcaga	3720

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tcatcaaggc caaggctaac ctggagaaga tgtgccggac cctggaggac cagatgaatg	3780
aacaccggag caaggctgag gagacacago gttctgtcaa tgacctacc cgcgcggg	3840
ccaagctgca gacagagaat ggggagctgt ccagacagct ggatgagaag gaggcttta	3900
tctctcagct gaccggagc aagctcacgt ataccagca gctggaggac ctcaagaggc	3960
agctggagga ggaggtcaag gccaaatacg ccctggccca cgcaactgcag tcagcccgc	4020
atgattgcga cctgcgtgcgg gaacagtacg aggaggaaac agaageccaag gctgagctgc	4080
agcgtgtctt gtccaaggcc aactcagagg tggcccagtg gaggaccaag tatgagacgg	4140
acgcctatac gaggacggag gagctggagg aagccaagaa gaagctggct cagaggcttc	4200
aggatgctga ggaggcagtg gaggccgtca acgccaagtg ctccctcgctg gagaagacca	4260
agcacagggc gcagaacgag atcggaggacc tgatgggtgg tggtggagcgc tccaatgcgg	4320
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agaagtatga ggagtcggcag tcagagctgg agtcttccca gaaggaggcgc cgctccctga	4440
gcacagagct cttcaagctg aagaatgcct atgaggagtc totggagcac ctggagacct	4500
tcaagcggga gaacaagaac ctccaggagg agatctcaga cctgactgaa cagctgggct	4560
caactggaa gagcatccac gagctggaga agatccgaaa gcaactggag gctgagaagc	4620
tggagctgca gtcagccctg gaagaggctg aggccctccct ggagcatgag gagggcaaga	4680
tcctccgagc ccagctggag ttcaaccaga tcaaggcaga gatcgaaagg aagctggcag	4740
agaaggacga ggagatggag caggccaago gcaaccaccc gccccggggactggactccctgc	4800
agacccctt ggatgccgag acgegcagec gcaacgaggc cctgcgggtg aagaagaaga	4860
tggagggcga cctcaacgag atggagatcc agctcagtc tgccaaaccgc atggctgctg	4920
aggcccagaa acaagtgaag agcctccaga gtttgcgtaa ggacactcaa atccagctgg	4980
atgacgcagt ccgtgc当地 gacgacccatg aggagaacat cgccatcgat gacggccgca	5040
acaacccctgcgc cagggccggag ctggaggagc tgccggccgt ggtggagcag acggaggccgt	5100
ctcggaaatc ggcagagcag gagctgatec agaccagcga gccccggggactggactcc	5160
cccaaaaaac cagccctatc aaccagaaga agaagatgga tgccagaccc tcccaagctcc	5220
agacagaggt ggaggaggcgt gtgcaggagt gtaggaacgc agaggagaag gccaagaagg	5280
ccatcacaga tgccgc当地 atggccgagg agctgaagaa ggagcaggac accagcgccc	5340
acctggagcg catgaagaat aacatggacg agaccatcaa ggacccctgcag caccggctgg	5400
acgaggcaga gcagatcgcc ctcaagggtg gcaagaagca gctgcagaag ctggaggccc	5460
gggtccggga gctggagaat gagctggagg ctgagccatg gcgcaatgcg gagtcgggtga	5520
aggccatgag gaagagcgcg cggccatca aggacccatgc ctaccagacca gaggaaacca	5580
ggaagaacactc actgc当地 caggacccatgg tggacaagct gcagttaaag gtgaaggccct	5640
acaaggccca ggctggaggag gcccggaaac agggccacac caacccatgtcc aagttccgc	5700
agggtgc当地 cggactggat gaggcaggagg agagggccggaa cattggccag tcccaaggatca	5760
acaagctgcg gcccggaaac cgtgc当地 gcccggggccctt gatgtaaacatct	5820
tgtgcttccca accccatgtca atgcctgtca agccctgtca cctggaggccctt gaaacacgc	5880
acctttaggca gaaacacaat aaagcaattt tccttcaagc caa	5923

<210> SEQ ID NO 164

<211> LENGTH: 152

<212> TYPE: PRT

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<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 164

Met	Gly	Ser	Phe	Ser	Ile	Thr	Lys	Gly	Phe	Phe	Leu	Phe	Leu	Ala	Phe
1					5			10			15				
Trp	Leu	Pro	Gly	His	Ile	Gly	Ala	Asn	Pro	Val	Tyr	Ser	Ala	Val	Ser
	20					25					30				
Asn	Thr	Asp	Leu	Met	Asp	Phe	Lys	Asn	Leu	Leu	Asp	His	Leu	Glu	Glu
	35					40					45				
Lys	Met	Pro	Val	Glu	Asp	Glu	Val	Met	Pro	Pro	Gln	Ala	Leu	Ser	Glu
	50					55					60				
Gln	Thr	Asp	Glu	Ala	Gly	Ala	Ala	Leu	Ser	Ser	Leu	Ser	Glu	Val	Pro
	65					70			75					80	
Pro	Trp	Thr	Gly	Glu	Val	Asn	Pro	Ser	Gln	Arg	Asp	Gly	Gly	Ala	Leu
		85					90				95				
Gly	Arg	Gly	Pro	Trp	Asp	Pro	Ser	Asp	Arg	Ser	Ala	Leu	Leu	Lys	Ser
		100				105					110				
Lys	Leu	Arg	Ala	Leu	Leu	Ala	Gly	Pro	Arg	Ser	Leu	Arg	Arg	Ser	Ser
	115				120					125					
Cys	Phe	Gly	Gly	Arg	Ile	Asp	Arg	Ile	Gly	Ala	Gln	Ser	Gly	Leu	Gly
	130					135					140				
Cys	Asn	Ser	Phe	Arg	Tyr	Arg	Arg								
	145				150										

<210> SEQ ID NO 165

<211> LENGTH: 831

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 165

cggacaaaagg	ctgagagaga	aaccagagag	tgagccgaga	cagcaaacat	cagatcg	60
cccgaccac	gccagcatgg	gctccttctc	catcaccaag	ggcttcttcc	tcttcgttgc	120
cttttggctc	ccaggccata	ttggagcaaa	tcccgtatac	agtgcggtgt	ccaacacaga	180
tctgatggat	ttcaagaacc	tgcttagatca	cctggaggag	aagatgcggg	tagaagatga	240
ggtcatgcct	ccgcaggccc	tgagcgagca	gaccgatgaa	gcggggccgg	cacttagctc	300
cctctctgag	gtgcctccct	ggactgggga	agtcaacccg	tctcagagag	atgggggtgc	360
tctcggggcc	ggcccttggg	accctccga	tagatctgcc	ctcttgaaaa	gcaaaactgag	420
ggctctgtctc	gctggccctc	ggagctcg	aaggtcaagg	tgcttcgggg	gtaggattga	480
caggatttgg	ccccagagcg	gactaggctg	caacagcttc	cggttaccgaa	gataacagcc	540
aaatctgtctc	gagcagatcg	caaaaatcc	caagcccttgc	cggtgtgtca	cacagcttgg	600
tgcatttgc	actgagaggt	ggtgaatacc	ctcttggagc	tgcagtttcc	tgttttcatc	660
tatcacgtc	gatgttaagt	gtatgtatgt	ggtttagtgc	ggctttagtgc	ctccccactct	720
gcatatataag	gtatgtatctc	accctttca	gaaagcagt	ggaaaaaaat	aaatccgaaat	780
aaacttcagc	accacggaca	gacgctgagg	cctgaaaaaa	aaaaaaaaaa	a	831

<210> SEQ ID NO 166

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 166

Met Asp Leu Gln Lys Val Leu Pro Gln Met Ile Leu Leu Leu Phe

US 12,385,041 B2

195**196**

-continued

1	5	10	15
Leu Asn Leu Ser Pro Leu Gly Gly His Ser His Pro Leu Gly Ser Pro			
20	25	30	
Ser Gln Ser Pro Glu Gln Ser Thr Met Gln Lys Leu Leu Glu Leu Ile			
35	40	45	
Arg Glu Lys Ser Glu Glu Met Ala Gln Arg Gln Leu Ser Lys Asp Gln			
50	55	60	
Gly Pro Thr Lys Glu Leu Leu Lys Arg Val Leu Arg Ser Gln Asp Ser			
65	70	75	80
Ala Phe Arg Ile Gln Glu Arg Leu Arg Asn Ser Lys Met Ala His Ser			
85	90	95	
Ser Ser Cys Phe Gly Gln Lys Ile Asp Arg Ile Gly Ala Val Ser Arg			
100	105	110	
Leu Gly Cys Asp Gly Leu Arg Leu Phe			
115	120		

<210> SEQ ID NO 167

<211> LENGTH: 628

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 167

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gcgagacaag agagagcagg acaccatcg agctgcctgg cccatcaatt ctgcagcatg      60
gatctccaga aggtgctgcc ccagatgatt ctgctcctgc ttttccttaa tctgtcgccg      120
ctgggaggctc actccccatcc cctgggaagt ccttagccagt ctccagaaca atccacatg      180
cagaagctgc tggagctgat aagagaaaag tcagaggaaa tggctcagag acagctctca      240
aaggaccaag gccctacaaa agaacttcta aaaagagtcc ttaggtctca agacagcgcc      300
ttccggatcc aggagagact tcgaaattcc aagatggcac atagttcaag ctgctttgg      360
cagaagatag accggatcg cgcaagtca gcttgggct gtgacgggct gaggttgg      420
taggaagacc tcctggctgc agactccggc ttctgactct gcctgcggct cttctttccc      480
cagctctggg accacctctc aagtgtatct gtttatttat ttgtttatattt atttatttt      540
atgttgctga ttttctacaa gactgtttct tatcttccag cacaaacttg ccacagtgtta      600
ataaacatag cctatttctt gcttttgg                                628

```

<210> SEQ ID NO 168

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 168

```

gguccagca uggggcuuug cuggcaccuc c                                31

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<210> SEQ ID NO 169

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 169

```

ccagggcuga gcagaucaag auguggcaaa g                                31

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<210> SEQ ID NO 170

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

US 12,385,041 B2

197

-continued

<400> SEQUENCE: 170

cagggcugag cagaaucaaga uguggcaaag c

31

<210> SEQ ID NO 171

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 171

gcuggcaccu ccagggcuga gcagaucaag a

31

<210> SEQ ID NO 172

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 172

caggcuccag cauggggcuu ugcuggcacc u

31

<210> SEQ ID NO 173

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 173

aggcuccagc auggggcuuu gcuggcaccu c

31

<210> SEQ ID NO 174

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 174

gcuccagcau gggccuuugc uggcaccucc a

31

<210> SEQ ID NO 175

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 175

cuccagcaug gggccuuugc ggcaccucca g

31

<210> SEQ ID NO 176

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 176

uccagcaugg ggcuuugcug gcaccuccag g

31

<210> SEQ ID NO 177

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 177

auucugcuuc cuccaagga gcuguuacac a

31

<210> SEQ ID NO 178

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 178

uccaggcug agcagaucaa gauguggcaa a

31

<210> SEQ ID NO 179

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 179

uguuacacag gcuccagcau gggcuuugc u

31

<210> SEQ ID NO 180

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 180

cuccaggcu gagcagauc a g a u g g g c a

31

<210> SEQ ID NO 181

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 181

cucccaagga gcuguuacac aggcccac a

31

<210> SEQ ID NO 182

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 182

cccaaggc uguuacacag gcuccagcau g

31

<210> SEQ ID NO 183

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 183

caaggagcug uuacacaggc uccagcaugg g

31

<210> SEQ ID NO 184

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 184

aaggagcug uacacaggc ccagcauggg g

31

<210> SEQ ID NO 185

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 185

gcuguuacac aggcccac a u g g g c u u u g

31

<210> SEQ ID NO 186

<211> LENGTH: 31

<212> TYPE: RNA

-continued

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 186

cuguuuacaca ggcuccagca uggggcuuug c

31

<210> SEQ ID NO 187

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 187

guuacacagg cuccagcaug gggcuuugcu g

31

<210> SEQ ID NO 188

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 188

uuacacaggc uccagcaugg ggcuuyugcug g

31

<210> SEQ ID NO 189

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 189

cuggcaccuc caggcgugag cagaaucaaga u

31

<210> SEQ ID NO 190

<211> LENGTH: 31

<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 190

uggcaccucc agggcugagc agaucaagau g

31

<210> SEQ ID NO 191

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US 12,385,041 B2

225**226**

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31

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31

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31

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31

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gcagcagaga ccccaggggg caggagccuc u 31

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caucaaacc a cuuuaucuac aguuuagcaua a 31

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277

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31

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31

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31

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31

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31

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caaaccacuu uaucuacagu uagcauaa g

31

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uuuaucuaca guuagcauaa gaugugagaa g

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<400> SEQUENCE: 502

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caggagccuc uugcagucug ucccuaggcc c

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31

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31

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31

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<400> SEQUENCE: 513

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31

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<400> SEQUENCE: 514

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31

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31

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cagucugucc cuaggeccag cccugcuug u 31

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<400> SEQUENCE: 564

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<210> SEQ ID NO 566

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<210> SEQ ID NO 567

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<210> SEQ ID NO 568

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<400> SEQUENCE: 568

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31

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<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

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aggugagguu cuaccuuaaa auuuaaugca u

31

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31

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acaggugagg uucuacccu aaauuuuaaug c

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<210> SEQ ID NO 572

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<400> SEQUENCE: 576

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31

<210> SEQ ID NO 577

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<400> SEQUENCE: 577

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31

<210> SEQ ID NO 578

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aaauuuuaaug cauggggugg gagaggcgag g

31

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<212> TYPE: RNA

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<213> ORGANISM: Homo sapiens

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31

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<212> TYPE: RNA
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31

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<212> TYPE: RNA
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31

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<212> TYPE: RNA
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<400> SEQUENCE: 594

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<210> SEQ ID NO 595

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<212> TYPE: RNA
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<400> SEQUENCE: 595

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<210> SEQ ID NO 596

<211> LENGTH: 31

<212> TYPE: RNA
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<400> SEQUENCE: 596

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31

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<213> ORGANISM: Mus musculus

<400> SEQUENCE: 598
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31

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<400> SEQUENCE: 614

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31

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<400> SEQUENCE: 615

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31

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<400> SEQUENCE: 616

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31

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<400> SEQUENCE: 617

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31

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31

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31

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<213> ORGANISM: Mus musculus

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31

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<213> ORGANISM: Mus musculus

<400> SEQUENCE: 623

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31

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31

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31

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31

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31

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<400> SEQUENCE: 747

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31

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31

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31

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31

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31

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31

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31

<210> SEQ ID NO 884

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<213> ORGANISM: Homo sapiens

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31

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31

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31

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31

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31

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31

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31

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31

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caaagguaag aaaccaucuu auauaaaaca a

31

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31

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aagguaagaa accaucuuau auaaaacaau c

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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acaauaaauac auuuuuuuuu ugagucacuu c 31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

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31

<210> SEQ ID NO 1110
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31

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31

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31

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31

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<212> TYPE: RNA

<213> ORGANISM: Mus musculus

<400> SEQUENCE: 1122

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31

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31

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31

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31

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31

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31

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31

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<212> TYPE: RNA

<213> ORGANISM: Mus musculus

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31

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<212> TYPE: RNA

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<213> ORGANISM: *Mus musculus*

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31

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<213> ORGANISM: *Mus musculus*

<400> SEQUENCE: 1135

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31

<210> SEQ ID NO 1136

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<213> ORGANISM: *Mus musculus*

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31

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<212> TYPE: RNA

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<400> SEQUENCE: 1137

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31

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<212> TYPE: RNA

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31

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<211> LENGTH: 31

<212> TYPE: RNA

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<400> SEQUENCE: 1139

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31

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<400> SEQUENCE: 1140

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31

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<212> TYPE: RNA

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31

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<212> TYPE: RNA
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31

<210> SEQ ID NO 1143

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<213> ORGANISM: Mus musculus

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cuaccuuau augcagagug ggagagguaa g

31

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<212> TYPE: RNA

<213> ORGANISM: Mus musculus

<400> SEQUENCE: 1145

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31

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<212> TYPE: RNA

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<400> SEQUENCE: 1146

gucccguggug cugaaguuu uucggauuu u

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<213> ORGANISM: Mus musculus

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31

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31

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<210> SEQ ID NO 1157
<211> LENGTH: 31
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US 12,385,041 B2

447**448**

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31

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31

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31

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31

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31

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31

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<400> SEQUENCE: 1172

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31

<210> SEQ ID NO 1173
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31

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31

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31

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ggaucuuuug cgaucugcuc gagcagauuu g
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31

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US 12,385,041 B2

455

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US 12,385,041 B2

469

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470

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31

What is claimed is:

1. A conditional RNA-sensor complex comprising:
a sensor strand comprising at least one toehold segment,
wherein the toehold segment capable of binding a pathological biomarker present in or overexpressed in a target cell, wherein the pathological biomarker comprises a molecule that encodes ANP, BNP, MHC β , mir-23a-3p, mir-125-6p, or mir-199b-5p; and
a double stranded pro-RNA molecule comprising
a guide strand comprising an RNA molecule capable of binding a therapeutic target molecule in the target cell, wherein the therapeutic target molecule is an RNA molecule that encodes calcineurin or histone deacetylase 2 (HDAC2); and
a core strand comprising
a first portion comprising a passenger strand that is fully or partially complimentary to and binds the guide strand,
a second portion comprising a first protection segment that is fully or partially complimentary to and binds the sensor strand, and
a first linker that joins a first end of the passenger strand to the first protection segment.

2. The conditional RNA-sensor complex of claim 1, wherein the core strand further comprises a third portion comprising a second protection segment that is fully or partially complimentary to and binds the sensor strand, and a second linker that joins a second end of the passenger strand to the second protection segment.

3. The conditional RNA-sensor complex of claim 1, wherein the toehold segment is an aptamer.

4. The conditional RNA-sensor complex of claim 1, wherein the sensor strand is displaced from the double stranded pro-RNA molecule when the pathological biomarker binds the toehold segment and the resulting double stranded pro-RNA molecule is a substrate for Dicer.

5. The conditional RNA-sensor complex of claim 1, wherein the target cell is a cardiac myocyte.

6. The conditional RNA-sensor complex of claim 1, wherein the molecule that encodes ANP, BNP, or MHC β is an mRNA molecule and the molecule that encodes mir-23a-3p, mir-125-6p, or mir-199b-5p is a miRNA molecule.

7. The conditional RNA-sensor complex of claim 6, wherein the molecule that encodes ANP comprises a sequence selected from SEQ ID Nos: 8-10, the molecule that encodes BNP comprises a sequence selected from SEQ ID Nos: 4-6, the molecule that encodes MHC β comprises a sequence of SEQ ID NO: 7, and the molecule that encodes mir-23a-3p comprises a sequence selected from SEQ ID Nos: 1-3.

8. The conditional RNA-sensor complex of claim 7, wherein the sensor strand further comprises one or more chemical modifications to the RNA sequence, wherein the one or more chemical modifications are selected from a locked nucleic acid (LNA) modification, a peptide nucleic acid (PNA) modification, a 2'-O-methyl modification, morpholino modification, a phosphorothioate modification, a terminal modification, or a linker modification.

9. The conditional RNA-sensor complex of claim 5, wherein the double stranded pro-RNA molecule is an RNA interference (RNAi) molecule.

10. The conditional RNA-sensor complex of claim 9, wherein the guide strand comprises a sequence selected from SEQ ID NOS: 11-16.

11. The conditional RNA-sensor complex of claim 2, wherein the first linker, the second linker, or both the first and second linkers is a C3 spacer.

12. The conditional RNA-sensor complex of claim 9, wherein the guide strand further comprises one or more chemical modifications to the RNA sequence, wherein the one or more chemical modifications are selected from a locked nucleic acid (LNA) modification, a peptide nucleic acid (PNA) modification, a 2'-O-methyl modification, morpholino modification, a phosphorothioate modification, a terminal modification, or a linker modification.

13. The conditional RNA-sensor complex of claim 2, wherein the core strand comprises

a passenger strand;
a first linker that joins a 3' end of the passenger strand to the first protection segment; and
a second linker that joins a 5' end of the passenger strand to the second protection segment.

14. The conditional RNA-sensor complex of claim 13, wherein the core strand comprises a sequence selected from SEQ ID NOS: 17-26.

15. The conditional RNA-sensor complex of claim 13, wherein the core strand further comprises one or more chemical modifications to the RNA sequence, wherein the one or more chemical modifications are selected from a locked nucleic acid (LNA) modification, a peptide nucleic acid (PNA) modification, a 2'-O-methyl modification, morpholino modification, a phosphorothioate modification, a terminal modification, or a linker modification.

16. The conditional RNA-sensor complex of claim 1, wherein:

(a) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:4, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:21, SEQ ID NO: 49, and SEQ ID NO: 50, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:15;

(b) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:5, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:22, SEQ ID NO: 49, and SEQ ID NO: 51, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:15;

(c) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:6, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:23, SEQ ID NO: 49, and SEQ ID NO: 52, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:15;

(d) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:7, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:24, SEQ ID NO: 49, and SEQ ID NO: 53,

473

- and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:15;
- (e) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:8, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:25, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:16;
- (f) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:8, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:18, SEQ ID NO: 45, and SEQ ID NO: 47, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:11;
- (g) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:10, the core strand comprises a sequence having at least 95% homology to SEQ ID NO:19, SEQ ID NO: 45, and SEQ ID NO: 48, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:12;
- (h) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:1, the core strand comprises a sequence having at least 95% homology to SEQ ID NO: 41, SEQ ID NO: 45, and SEQ ID NO: 56, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:12;
- (i) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:2, the core strand comprises a sequence having at least 95% homology to SEQ ID NO: 41, SEQ ID NO: 45, and SEQ ID NO: 56, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO: 12; or

474

- (j) the sensor strand comprises a sequence having at least 95% homology to SEQ ID NO:39, the core strand comprises a sequence having at least 95% homology to SEQ ID NO: 41, SEQ ID NO: 45, and SEQ ID NO: 56, and the guide strand comprises a sequence having at least 95% homology to SEQ ID NO:12.

17. The conditional RNA-sensor complex of claim **16**, wherein the sensor strand, the guide strand and/or the core strand further comprises one or more chemical modifications to the RNA sequence, wherein the one or more chemical modifications are selected from a locked nucleic acid (LNA) modification, a peptide nucleic acid (PNA) modification, a 2'-O-methyl modification, morpholino modification, a phosphorothioate modification, a terminal modification, or a linker modification.

18. A pharmaceutical composition comprising:
a conditional RNA-sensor complex of claim **1**; and
a pharmaceutically acceptable carrier or excipient.

19. A method of treating a pathological condition comprising administering a therapeutically effective amount of a conditional RNA-sensor complex of claim **1** to a subject suffering from the pathological condition, wherein the pathological condition is myocardial infarction (MI), or cardiac hypertrophy.

20. The method of claim **19**, wherein administering a therapeutically effective amount comprises an intramyocardial injection of the conditional RNA-sensor complex or the pharmaceutical composition after detection of MI.

21. The conditional RNA-sensor complex of claim **1**, wherein the passenger strand bound to the guide strand forms a duplex between 15 and 30 base pairs in length.

* * * * *