

<110> TOOLGEN INCORPORATED

<120> Composition for cleaving a target DNA comprising a guide RNA specific for the target DNA and Cas protein-encoding nucleic acid or Cas protein, and use thereof

<130> OPA13141PCT

<150> US 61/717,324
<151> 2012-10-23

<150> US 61/803,599
<151> 2013-03-20

<150> US 61/837,481
<151> 2013-06-20

<160> 111

<170> KopatentIn 2.0

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<223> Cas9-coding sequence

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cacagcatca agaagaacct gatcggcgcc ctgctgttcg acagcggcga gaccgccgag 180
gccacccgcc tgaagcgcac cgcccgccgc cgctacaccc gccgcaagaa ccgcatctgc 240
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aacatcgtgg acgaggtggc ctaccacgag aagtacccca ccatctacca cctgcgcaag 420
aagctggtgg acagcaccga caaggccgac ctgcgcctga tctacctggc cctggcccac 480
atgatcaagt tccgcggcca cttcctgata gagggcgacc tgaaccccgga caacagcgac 540
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atcaacgcca gcggcgtgga cgccaaggcc atcctgagcg cccgcctgag caagagccgc 660

720	cgcctggaga acctgacgc ccagctggcc ggagagaga agaagggct gttcggaac
780	ctgacggcc tgaagctggg cctgacccc aactcaaga gcaacttga cctggccgag
840	gagcccaagc tgcagctgag caaggaacc tacgacgag acctggaca cctgctggcc
900	cagatcggcg accagtacgc cgacctgttc ctggccgcca agaactgag cgagcccatc
960	ctgttgagcg acatcctgcg cgtgaacacc gagatcaca agggccccc gaggccagcg
1020	atgataagc gtaagaca gcaaccag gacctgacc tgtgaagcg cctggtgcgc
1080	cagcagctgc ccgagaagta caaggagatc ttcttcgacc agagcaagaa cggctagcc
1140	ggctacatcg acggcgcgcg cagccaggag ggtttcata agttcataa gcccattcctg
1200	gagaagatgg accgaccca gtagctgctg gtagagctga accgagagga cctgctgcgc
1260	aagcagcgca ccttcgaca ccgagacat cccaacaga tcaacctggg cgagctgcac
1320	ggcatcctgc gccgcagga ggaatttac ccttcctga aggaacaacc cgagaagatc
1380	gagaagatcc tgaaccttcg catccctac tactgtggcc cctggcccg cggcaacagc
1440	cgttcgctt gtagaccgg caagagcgag gagaccata ccccttgaa cttcgaggag
1500	gtgttgaca agggcgccag cgcacgagc ttcatcgagc gcatgacca cttcgcaag
1560	aaactggcca acgagaaggt gctggccaa gacagcctgc tgtacgagta cttcacctg
1620	tacaacgagc tgaaccaaggt gaagtagtg accgagggca tgcgcaagcc cgccttcctg
1680	agcggcgagc agaaagagc catcgttgag cgtgtgtca agaccaaccg caaggtgacc
1740	gtgaagcagc tgaaggagga ctactcaag aagatcgagt gcttcgacag cgtggagatc
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1860	atcaaggaca aggaattcct ggaacaacgag gagaacgag gacatcctgga ggaatcctg
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2040	cgcctgagcc gcaagcttat caaggcatc cgggacaagc agagcggcaa gacctcctg
2100	gacttcctga agagcgagcg cttcgccaac cgcaactca tgcagctgat ccaagcagac
2160	agcctgacct tcaaggagga catccagag gcccaagtga gggccaggg cgacagcctg
2220	cacgagcaca tcgccaacct ggccggcagc ccgccaata agaagggcat cctgagacc

3780 cactacagaga agcttgaaaggc cagcccccag agacaacagagc agaaagcagct gttcgtggag
3720 cagaaaggcga acgagctggc cctggcccagc aagtaagta acttccgta cctggccagc
3660 tacagccgtt tcgagctggga gaacggccc agcgcagtc tggccagcgc cggcgagctg
3600 ttcttgagag ccaaggagta caaggaggtg aaagagagac tgaatcataa gctggccaaag
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2880 accaagtacg acgagaaag caagctgac cgcgaggtga aggtgatcac cctgaaagagc
2820 ctggtggaga cccgcagat caccagcac gtggccaga tccctggacg cccgatgaac
2760 accaaggccg agcgcgcgcg cctgagcgag ctggacaagg cggcttcac caagcgccag
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2640 gacaagaacc gcgcaagag gcacaacgtg ccagcgaggg aggtgtgaa gaaagatgaag
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2520 gacatgtacg tggaccagga gctgggacatc aaccgctga gcaactaga cgtgggacac
2460 gtggagaaca cccagctga gaacgagag ctgtacctgt actacctgca gaacggccgc
2400 atgaagcgca tcgagaggg catcaaggag ctggcgagc agatccctga gtagcacccc
2340 atcgagatgg ccgcgagaa ccagacaccc cagaagggcc agaagaacag ccgcgagcgc
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 gacctgagcc agctgggagg cgactaa 4107

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 1 5 10 15
 Val Pro Asp Tyr Ala
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<210> 3
 <211> 34
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> F primer for CCR5

<400> 3
 aattcatgac atcaattatt atacatcgga ggag 34

<210> 4
 <211> 34
 <212> DNA
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<220>
 <223> R primer for CCR5

<400> 4
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<210> 5
<211> 20
<212> DNA
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<220>
<223> F1 primer for CCR5

<400> 5
ctccatggtg ctatagagca 20

<210> 6
<211> 21
<212> DNA
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<220>
<223> F2 primer for CCR5

<400> 6
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<210> 7
<211> 20
<212> DNA
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<220>
<223> R primer for CCR5

<400> 7
gccctgtcaa gagttgacac 20

<210> 8
<211> 20
<212> DNA
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<220>
<223> F1 primer for C4BPB

<400>	8	
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<210>	9	
<211>	24	
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aaagtcatga	aataaacaca ccca	24
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<210>	11	
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<400> 13
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<210> 14
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<220>
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<400> 14
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<210> 15
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<400> 15
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<210> 16
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<220>
 <223> F primer for KCNJ6

<400> 16
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<210> 17
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<212> DNA
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<220>
<223> R1 primer for KCNJ6

<400> 17
tggagccatt ggtttgcata 20

<210> 18
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<220>
<223> R2 primer for KCNJ6

<400> 18
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<210> 19
<211> 20
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<220>
<223> F1 primer for CNTNAP2

<400> 19
atcaccgaca accagtttcc 20

<210> 20
<211> 20
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<220>
<223> F2 primer for CNTNAP2

<400> 20
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<210> 21
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<220>
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<210> 22
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<400> 22
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<210> 23
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<220>
 <223> R1 primer for N/A Chr. 5

<400> 23
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<210> 24
 <211> 22
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<220>
 <223> F2 primer for N/A Chr. 5

<400> 24
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<210> 25
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<220>
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<400> 25
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<210> 26
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<220>
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<400> 26
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<210> 27
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 <212> DNA
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<220>
 <223> R primer for deletion

<400> 27
 tcacaagccc acagatattt 20

<210> 28
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 <212> RNA
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<220>
 <223> sgRNA for CCR5

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uccguuauca acuugaaaaa guggcaccga gucggugcuu uuuuu 105

<210> 29
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<400> 29
ggugacauca auuauuauac auguuuuaga gcuavgcugu uuug 44

<210> 30
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<220>
<223> tracrRNA for CCR5

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aguggcaccg agucggugcu uuuuuu 86

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tagcaagtta aaataaggct agtccg 86

<210> 32
<211> 86

<212> DNA
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 <223> Foxn1 #2 sgRNA

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 <223> Foxn1 #3 sgRNA

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 tagcaagtta aaataaggct agtccg 86

 <210> 34
 <211> 86
 <212> DNA
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 <223> Foxn1 #4 sgRNA

 <400> 34
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 tagcaagtta aaataaggct agtccg 86

 <210> 35
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 <223> Foxn1 #5 sgRNA

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tagcaagtta aaataaggct agtccg 86

<210> 36
<211> 86
<212> DNA
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<220>
<223> Prkdc #1 sgRNA

<400> 36
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tagcaagtta aaataaggct agtccg 86

<210> 37
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<212> DNA
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<220>
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<400> 37
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<210> 38
<211> 86
<212> DNA
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 <223> Prkdc #4 sgRNA

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 <210> 40
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 <400> 40
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 <210> 41
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<210> 43
 <211> 32
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<400> 43
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<400> 44
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<210> 45
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<400> 45
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<210> 46
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<210> 47
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<210> 49
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<210> 50
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<210> 56
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<400> 64
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<210> 65
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<210> 66
<211> 17
<212> DNA
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<400> 66
gggaggcaga ggcaggt 17

<210> 67
<211> 23
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<220>
<223> F2 primer for Prkdc

<400> 67
ggatctctgt gagtttgagg cca 23

<210> 68
<211> 24
<212> DNA
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<400> 68
gctccagaac tcactcttag gctc 24

<210> 69
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<210> 70
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<223> Primer for Foxn1

<400> 70
ccaggcctag gttccaggta 20

<210> 71
 <211> 20
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<400> 71
 ccccagcatt gcagatttcc 20

<210> 72
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<400> 72
 agggcttctt ctctacaatc acg 23

<210> 73
 <211> 86
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tagcaagtta aaataaggct agtccg 86

<210> 74
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tagcaagtta aaataaggct agtccg 86

<210> 75

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<223> Universal

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ttgc 64

<210> 76

<211> 65

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<223> Templates for crRNA

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gaaattaata cgactcacta taggnnnnnn nnnnnnnnnn nnnngtttta gagctatgct 60

gtttt 65

<210> 77

<211> 67

<212> DNA

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<223> tracrRNA

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tagtccg 67

<210> 78

<211> 69

<212> DNA
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<220>
 <223> tracrRNA

<400> 78
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 cttgctatg 69

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<400> 80
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<400> 81
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<220>
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<400> 82
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<400> 83
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<210> 87
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<400> 87
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<210> 88
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<400> 89
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<210> 90
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<220>
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<400> 90
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<210> 91
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<220>
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<400> 91
actcactatc cacagttcag catttacc 28

<210> 92
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<220>
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<400> 92
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<210> 93
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<220>
<223> Primer

<400> 93
caacaaagca aaggtaaagt tggtaatag 29

<210> 94
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 94
ggtttcagga gatgtgttac aaggc

25

<210> 95
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 95
gattgtgcaa ttcctatgca atcggtc

27

<210> 96
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 96
cactgggtac ttaatctgta gcctc

25

<210> 97
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<212> DNA
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<220>
<223> Primer

<400> 97
ggttccaagt cattcccagt agc

23

<210> 98
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<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 98
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<210> 99
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<212> DNA
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<220>
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<400> 99
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<210> 100
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<220>
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<400> 100
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<400> 101
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<220>
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<400> 102
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<210> 103
 <211> 22
 <212> DNA
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<220>
 <223> Primer

<400> 103
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<210> 104
 <211> 23
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<220>
 <223> Target sequence of RGEN

<400> 104
 aatgaccact acatcctcaa ggg 23

<210> 105
 <211> 23
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Target sequence of RGEN

<400> 105
 agatgatgtc tcatcatcag agg 23

<210> 106
 <211> 4170
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Cas9-coding sequence in p3s-Cas9HC (humanized, C-term tagging,
 human cell experiments)

<400> 106
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 cacagcatca agaagaacct gatcggcgcc ctgctgttcg acagcggcga gaccgccgag 180
 gccacccgcc tgaagcgcac cgcccgccgc cgctacacc gccgcaagaa ccgcatctgc 240
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2760
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2820

2880 accaagtacg acgagaacga caagctgatac cggagaggtga aggtgatcac cctgaagagac
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3240 cccctgatic agaccaacgg cgagaccggc gagatcgtgt ggagacaagggg ccgcgacttc
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3720 cagaagggca acgagctggc cctggccagc aagtaagtgta acttcctgta cctgggccaagc
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3840 cagcaacaagc actacctgga cgaatcatc gagcagatca gcgagtctag caagcgcgtg
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4080 gaggtgctgg accccaact gatccaacag agcatcaccg gttctgtacga gacccgcatc
4140 gacctgagcc agctggggcg cgacggcggc tcgggacctc caaagaaaaa gagaaaaagta
4170 taccctacg acgtgcccga ctacgctaa

<210> 107
<211> 4194
<212> DNA
<213> Artificial Sequence

<220>

<223> Cas9 coding sequence in p3s-Cas9HN (humanized codon, N-term
tagging (underlined), human cell experiments)

<400> 107

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ggtaccaaca gcgtgggctg ggccgtgata accgacgagt acaagggtgcc cagcaagaag      180
ttcaagggtgc tgggcaacac cgaccgccac agcatcaaga agaacctgat cggcgccctg      240
ctgttcgaca gcggcgagac cgccgaggcc acccgctga agcgcaccgc ccgccgccgc      300
tacacccgcc gcaagaaccg catctgctac ctgcaggaga tcttcagcaa cgagatggcc      360
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2940

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<213> Artificial Sequence

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<223> Cas9-coding sequence in Streptococcus pyogenes

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 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
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 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110
 His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
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 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
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 Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
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 Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
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Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
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Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
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Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
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Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
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Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
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Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
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Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
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Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
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Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly

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590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
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Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
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His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
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Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
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Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
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Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
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Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
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Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
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Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
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Val Pro Ser Lys Lys Phe Lys Val Leu Gly Asn Thr Asp Arg His Ser
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Arg Lys Asn Arg Ile Cys Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met
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Ala Lys Val Asp Asp Ser Phe Phe His Arg Leu Glu Glu Ser Phe Leu
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Val Glu Glu Asp Lys Lys His Glu Arg His Pro Ile Phe Gly Asn Ile
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Val Asp Glu Val Ala Tyr His Glu Lys Tyr Pro Thr Ile Tyr His Leu
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Arg Lys Lys Leu Val Asp Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile
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Tyr Leu Ala Leu Ala His Met Ile Lys Phe Arg Gly His Phe Leu Ile
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Glu Gly Asp Leu Asn Pro Asp Asn Ser Asp Val Asp Lys Leu Phe Ile
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Gln Leu Val Gln Thr Tyr Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn
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Ala Ser Gly Val Asp Ala Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys
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Ser Arg Arg Leu Glu Asn Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys

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Ser Lys Asp Thr Tyr Asp Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile
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Gly Asp Gln Tyr Ala Asp Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp
 325 330 335

Ala Ile Leu Leu Ser Asp Ile Leu Arg Val Asn Thr Glu Ile Thr Lys
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Ala Pro Leu Ser Ala Ser Met Ile Lys Arg Tyr Asp Glu His His Gln
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Tyr Lys Glu Ile Phe Phe Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr
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Arg Glu Asp Leu Leu Arg Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile
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 515 520 525

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Arg	Leu	Lys	Thr	Tyr	Ala	His	Leu	Phe	Asp	Asp	Lys	Val	Met	Lys	Gln
		675					680					685			
Leu	Lys	Arg	Arg	Arg	Tyr	Thr	Gly	Trp	Gly	Arg	Leu	Ser	Arg	Lys	Leu
	690					695					700				
Ile	Asn	Gly	Ile	Arg	Asp	Lys	Gln	Ser	Gly	Lys	Thr	Ile	Leu	Asp	Phe
705					710					715					720
Leu	Lys	Ser	Asp	Gly	Phe	Ala	Asn	Arg	Asn	Phe	Met	Gln	Leu	Ile	His
				725					730					735	
Asp	Asp	Ser	Leu	Thr	Phe	Lys	Glu	Asp	Ile	Gln	Lys	Ala	Gln	Val	Ser
			740					745					750		
Gly	Gln	Gly	Asp	Ser	Leu	His	Glu	His	Ile	Ala	Asn	Leu	Ala	Gly	Ser
		755					760					765			
Pro	Ala	Ile	Lys	Lys	Gly	Ile	Leu	Gln	Thr	Val	Lys	Val	Val	Asp	Glu
	770					775					780				
Leu	Val	Lys	Val	Met	Gly	Arg	His	Lys	Pro	Glu	Asn	Ile	Val	Ile	Glu
785					790					795					800
Met	Ala	Arg	Glu	Asn	Gln	Thr	Thr	Gln	Lys	Gly	Gln	Lys	Asn	Ser	Arg
				805					810					815	

Glu Arg Met Lys Arg Ile Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln
 820 825 830
 Ile Leu Lys Glu His Pro Val Glu Asn Thr Gln Leu Gln Asn Glu Lys
 835 840 845
 Leu Tyr Leu Tyr Tyr Leu Gln Asn Gly Arg Asp Met Tyr Val Asp Gln
 850 855 860
 Glu Leu Asp Ile Asn Arg Leu Ser Asp Tyr Asp Val Asp His Ile Val
 865 870 875 880
 Pro Gln Ser Phe Leu Lys Asp Asp Ser Ile Asp Asn Lys Val Leu Thr
 885 890 895
 Arg Ser Asp Lys Asn Arg Gly Lys Ser Asp Asn Val Pro Ser Glu Glu
 900 905 910
 Val Val Lys Lys Met Lys Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys
 915 920 925
 Leu Ile Thr Gln Arg Lys Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly
 930 935 940
 Gly Leu Ser Glu Leu Asp Lys Ala Gly Phe Ile Lys Arg Gln Leu Val
 945 950 955 960
 Glu Thr Arg Gln Ile Thr Lys His Val Ala Gln Ile Leu Asp Ser Arg
 965 970 975
 Met Asn Thr Lys Tyr Asp Glu Asn Asp Lys Leu Ile Arg Glu Val Lys
 980 985 990
 Val Ile Thr Leu Lys Ser Lys Leu Val Ser Asp Phe Arg Lys Asp Phe
 995 1000 1005
 Gln Phe Tyr Lys Val Arg Glu Ile Asn Asn Tyr His His Ala His Asp
 1010 1015 1020
 Ala Tyr Leu Asn Ala Val Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro
 1025 1030 1035 1040
 Lys Leu Glu Ser Glu Phe Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val
 1045 1050 1055
 Arg Lys Met Ile Ala Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala
 1060 1065 1070
 Lys Tyr Phe Phe Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile
 1075 1080 1085
 Thr Leu Ala Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn

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1090          1095          1100
Gly Glu Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr
1105          1110          1115          1120
Val Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
          1125          1130          1135
Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg
          1140          1145          1150
Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys
          1155          1160          1165
Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val Leu Val Val
          1170          1175          1180
Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys Ser Val Lys Glu
1185          1190          1195          1200
Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser Phe Glu Lys Asn Pro
          1205          1210          1215
Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu
          1220          1225          1230
Ile Ile Lys Leu Pro Lys Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg
          1235          1240          1245
Lys Arg Met Leu Ala Ser Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu
          1250          1255          1260
Ala Leu Pro Ser Lys Tyr Val Asn Phe Leu Tyr Leu Ala Ser His Tyr
1265          1270          1275          1280
Glu Lys Leu Lys Gly Ser Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe
          1285          1290          1295
Val Glu Gln His Lys His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser
          1300          1305          1310
Glu Phe Ser Lys Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val
          1315          1320          1325
Leu Ser Ala Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala
          1330          1335          1340
Glu Asn Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala
1345          1350          1355          1360
Ala Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
          1365          1370          1375

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Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr Gly
1380 1385 1390

Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
1395 1400 1405