

SEQUENCE LISTING

<110> RetroSense Therapeutics

<120> IDENTIFICATION OF MUTATIONS IN CHANNELOPSIN VARIANTS HAVING IMPROVED LIGHT SENSITIVITY AND METHODS OF USE THEREOF

<130> RTR0-707/001W0

<150> US 62/380,871

<151> 2016-08-29

<160> 10

<170> PatentIn version 3.5

<210> 1

<211> 864

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic sequence

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ggcttcagca tcctgatcct gatgttctac gcctaccaga cttggagagc cacttgcggt	180
tgggaggagg tctacgtctg ttgcgtcgag ctgaccaagg tcatcatcga gttcttccac	240
gagttcgacg accccagcat gctgtacctg gctaacggac accgagtcca gtggctgaga	300
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ctgaaggacg actacagcaa gcggaccatg aggctgctgg tgtcagacgt gggaaccatc	420
gtgtggggag ctacaagcgc catgagcaca ggctacgtca aggtcatctt cttcgtgctg	480
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cacgtggtgc caaagggcag acctagaacc gtcgtgcgga tcatggcttg gctgttcttc	600
ctgtcttggg gcatgttccc cgtgctgttc gtcgtgggac cagaaggatt cgacgccatc	660
agcgtgtacg gctctaccat tggccacacc atcatcgacc tcatgagcaa gaattgttgg	720
ggcctgctgg gacactatct gagagtgtg atccaccagc acatcatcat ctacggcgac	780
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<400> 2

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Leu
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

<210> 3
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<212> PRT
<213> Artificial

<220>
<223> synthetic sequence

<400> 3

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Cys
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
 275 280 285

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Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
 1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
 20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
 35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
 50 55 60

Tyr Val Cys Ser Ile Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
 65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
 85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Leu
 100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
 115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
 130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
 145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

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<223> synthetic sequence

<400> 5

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Leu
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Cys Ile Val Trp Gly Ala
130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

<210> 6
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<400> 6

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Leu
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
130 135 140

Ala Ala Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

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<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic sequence

<400> 7

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Thr Leu Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Leu
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

<210> 8
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic sequence

<400> 8

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
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Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly His Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Cys
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Cys Ile Val Trp Gly Ala
130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

<210> 9
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic sequence

<400> 9

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly Glu Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Cys
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
130 135 140

Thr Ser Ala Met Ser Thr Gly Tyr Val Lys Val Ile Phe Phe Val Leu
145 150 155 160

Gly Cys Ile Tyr Gly Ala Asn Thr Phe Phe His Ala Ala Lys Val Tyr
165 170 175

Ile Glu Ser Tyr His Val Val Pro Lys Gly Arg Pro Arg Thr Val Val
180 185 190

Arg Ile Met Ala Trp Leu Phe Phe Leu Ser Trp Gly Met Phe Pro Val
195 200 205

Leu Phe Val Val Gly Pro Glu Gly Phe Asp Ala Ile Ser Val Tyr Gly
210 215 220

Ser Thr Ile Gly His Thr Ile Ile Asp Leu Met Ser Lys Asn Cys Trp
225 230 235 240

Gly Leu Leu Gly His Tyr Leu Arg Val Leu Ile His Gln His Ile Ile
245 250 255

Ile Tyr Gly Asp Ile Arg Lys Lys Thr Lys Ile Asn Val Ala Gly Glu
260 265 270

Glu Met Glu Val Glu Thr Met Val Asp Gln Glu Asp Glu Glu Thr Val
275 280 285

<210> 10
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic sequence

<400> 10

Met Leu Gly Asn Gly Ser Ala Ile Val Pro Ile Asp Gln Cys Phe Cys
1 5 10 15

Leu Ala Trp Thr Asp Ser Leu Gly Ser Asp Thr Glu Gln Leu Val Ala
20 25 30

Asn Ile Leu Gln Trp Phe Ala Phe Gly Phe Ser Ile Leu Ile Leu Met
35 40 45

Phe Tyr Ala Tyr Gln Thr Trp Arg Ala Thr Cys Gly Trp Glu Glu Val
50 55 60

Tyr Val Cys Cys Val Glu Leu Thr Lys Val Ile Ile Glu Phe Phe His
65 70 75 80

Glu Phe Asp Asp Pro Ser Met Leu Tyr Leu Ala Asn Gly Glu Arg Val
85 90 95

Gln Trp Leu Arg Tyr Ala Glu Trp Leu Leu Thr Cys Pro Val Ile Cys
100 105 110

Ile His Leu Ser Asn Leu Thr Gly Leu Lys Asp Asp Tyr Ser Lys Arg
115 120 125

Thr Met Arg Leu Leu Val Ser Asp Val Gly Thr Ile Val Trp Gly Ala
130 135 140

Thr	Ser	Ala	Met	Ser	Thr	Gly	Tyr	Val	Lys	Val	Ile	Phe	Phe	Val	Leu
145					150					155					160

Gly	Cys	Ile	Tyr	Gly	Ala	Asn	Thr	Phe	Phe	His	Ala	Ala	Lys	Val	Tyr
				165					170					175	

Ile	Glu	Ser	Tyr	His	Val	Val	Pro	Lys	Gly	Arg	Pro	Arg	Thr	Val	Val
			180					185					190		

Arg	Ile	Met	Ala	Trp	Leu	Phe	Phe	Leu	Ser	Trp	Gly	Met	Phe	Pro	Val
		195					200					205			

Leu	Phe	Val	Val	Gly	Pro	Glu	Gly	Phe	Asp	Ala	Ile	Ser	Val	Tyr	Gly
	210					215					220				

Ser	Thr	Ile	Gly	His	Thr	Ile	Ile	Asp	Leu	Met	Ser	Lys	Asn	Cys	Trp
225					230					235					240

Gly	Leu	Leu	Gly	His	Tyr	Leu	Arg	Val	Leu	Ile	His	Gln	His	Ile	Ile
				245					250					255	

Ile	Tyr	Gly	Asp	Ile	Arg	Lys	Thr	Thr	Lys	Ile	Asn	Val	Ala	Gly	Glu
			260					265					270		

Glu	Met	Glu	Val	Glu	Thr	Met	Val	Asp	Gln	Glu	Asp	Glu	Glu	Thr	Val
		275					280					285			