

LISTADO DE SECUENCIAS

<110> Solicitante: THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA

<120> Título de la invención: TERAPIA GÉNICA PARA TRATAR HIPERCOLESTEROLEMIA FAMILIAR

<130> Número de referencia: UPN-16-7717PCT

<150> Número de solicitud previa: US 62/269,440

<151> Fecha de presentación de la solicitud previa: 2015-12-18

<150> Número de solicitud previa: US 62/266,383

<151> Fecha de presentación de la solicitud previa: 2015-12-11

<160> Número de secuencias: 7

<170> Software: PatentIn version 3.5

<210> SEQ ID NO: 1

<211> Longitud: 5292

<212> Tipo: ADN

<213> Organismo: Homo sapiens

<220> Característica:

<221> Clave: exón

<222> Ubicación: (1)..(254)

<220> Característica:

<221> Clave: misc_característica

<222> Ubicación: (188)..(2770)

<223> Otra información: isoforma 1 del LDLR codificada por CDS de longitud completa, 188-2770; otras variantes codificadas por variantes de empalme alternativas que carecen de un exón; variante más común careciendo del cuarto exón o doceavo exón

<220> Característica:

<221> Clave: misc_señal

<222> Ubicación: (188)..(250)

<220> Característica:

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<222> Ubicación: (251)..(2767)

<223> Otra información: Proteína madura de la isoforma 1

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<222> Ubicación: (255)..(377)

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<222> Ubicación: (378)..(500)

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 <222> Ubicación: (1774)..(1892)

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 <222> Ubicación: (1893)..(2032)

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 <222> Ubicación: (2328)..(2498)

 <220> Característica:
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 <222> Ubicación: (5252)..(5257)

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 <222> Ubicación: (5284)..(5284)

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<210> SEQ ID NO: 2
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 <213> Organismo: Homo sapiens

<220> Característica:
 <221> Clave: CDS
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<400> Secuencia: 2

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Ser Val Thr Cys Lys Ser Gly Asp Phe Ser Cys Gly Gly Arg Val Asn	
65 70 75 80	
cgc tgc att cct cag ttc tgg agg tgc gat ggc caa gtg gac tgc gac	288
Arg Cys Ile Pro Gln Phe Trp Arg Cys Asp Gly Gln Val Asp Cys Asp	
85 90 95	

aac ggc tca gac gag caa ggc tgt ccc ccc aag acg tgc tcc cag gac	336
Asn Gly Ser Asp Glu Gln Gly Cys Pro Pro Lys Thr Cys Ser Gln Asp	
100 105 110	
gag ttt cgc tgc cac gat ggg aag tgc atc tct cgg cag ttc gtc tgt	384
Glu Phe Arg Cys His Asp Gly Lys Cys Ile Ser Arg Gln Phe Val Cys	
115 120 125	
gac tca gac cgg gac tgc ttg gac ggc tca gac gag gcc tcc tgc ccg	432
Asp Ser Asp Arg Asp Cys Leu Asp Gly Ser Asp Glu Ala Ser Cys Pro	
130 135 140	
gtg ctc acc tgt ggt ccc gcc agc ttc cag tgc aac agc tcc acc tgc	480
Val Leu Thr Cys Gly Pro Ala Ser Phe Gln Cys Asn Ser Ser Thr Cys	
145 150 155 160	
atc ccc cag ctg tgg gcc tgc gac aac gac ccc gac tgc gaa gat ggc	528
Ile Pro Gln Leu Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly	
165 170 175	
tcg gat gag tgg ccg cag cgc tgt agg ggt ctt tac gtg ttc caa ggg	576
Ser Asp Glu Trp Pro Gln Arg Cys Arg Gly Leu Tyr Val Phe Gln Gly	
180 185 190	
gac agt agc ccc tgc tcg gcc ttc gag ttc cac tgc cta agt ggc gag	624
Asp Ser Ser Pro Cys Ser Ala Phe Glu Phe His Cys Leu Ser Gly Glu	
195 200 205	
tgc atc cac tcc agc tgg cgc tgt gat ggt ggc ccc gac tgc aag gac	672
Cys Ile His Ser Ser Trp Arg Cys Asp Gly Gly Pro Asp Cys Lys Asp	
210 215 220	
aaa tct gac gag gaa aac tgc gct gtg gcc acc tgt cgc cct gac gaa	720
Lys Ser Asp Glu Glu Asn Cys Ala Val Ala Thr Cys Arg Pro Asp Glu	
225 230 235 240	
ttc cag tgc tct gat gga aac tgc atc cat ggc agc cgg cag tgt gac	768
Phe Gln Cys Ser Asp Gly Asn Cys Ile His Gly Ser Arg Gln Cys Asp	
245 250 255	
cgg gaa tat gac tgc aag gac atg agc gat gaa gtt ggc tgc gtt aat	816
Arg Glu Tyr Asp Cys Lys Asp Met Ser Asp Glu Val Gly Cys Val Asn	
260 265 270	
gtg aca ctc tgc gag gga ccc aac aag ttc aag tgt cac agc ggc gaa	864
Val Thr Leu Cys Glu Gly Pro Asn Lys Phe Lys Cys His Ser Gly Glu	
275 280 285	
tgc atc acc ctg gac aaa gtc tgc aac atg gct aga gac tgc cgg gac	912
Cys Ile Thr Leu Asp Lys Val Cys Asn Met Ala Arg Asp Cys Arg Asp	
290 295 300	
tgg tca gat gaa ccc atc aaa gag tgc ggg acc aac gaa tgc ttg gac	960
Trp Ser Asp Glu Pro Ile Lys Glu Cys Gly Thr Asn Glu Cys Leu Asp	
305 310 315 320	

aac aac ggc ggc tgt tcc cac gtc tgc aat gac ctt aag atc ggc tac Asn Asn Gly Gly Cys Ser His Val Cys Asn Asp Leu Lys Ile Gly Tyr 325 330 335	1008
gag tgc ctg tgc ccc gac ggc ttc cag ctg gtg gcc cag cga aga tgc Glu Cys Leu Cys Pro Asp Gly Phe Gln Leu Val Ala Gln Arg Arg Cys 340 345 350	1056
gaa gat atc gat gag tgt cag gat ccc gac acc tgc agc cag ctc tgc Glu Asp Ile Asp Glu Cys Gln Asp Pro Asp Thr Cys Ser Gln Leu Cys 355 360 365	1104
gtg aac ctg gag ggt ggc tac aag tgc cag tgt gag gaa ggc ttc cag Val Asn Leu Glu Gly Gly Tyr Lys Cys Gln Cys Glu Glu Gly Phe Gln 370 375 380	1152
ctg gac ccc cac acg aag gcc tgc aag gct gtg ggc tcc atc gcc tac Leu Asp Pro His Thr Lys Ala Cys Lys Ala Val Gly Ser Ile Ala Tyr 385 390 395 400	1200
ctc ttc ttc acc aac cgg cac gag gtc agg aag atg acg ctg gac cgg Leu Phe Phe Thr Asn Arg His Glu Val Arg Lys Met Thr Leu Asp Arg 405 410 415	1248
agc gag tac acc agc ctc atc ccc aac ctg agg aac gtg gtc gct ctg Ser Glu Tyr Thr Ser Leu Ile Pro Asn Leu Arg Asn Val Val Ala Leu 420 425 430	1296
gac acg gag gtg gcc agc aat aga atc tac tgg tct gac ctg tcc cag Asp Thr Glu Val Ala Ser Asn Arg Ile Tyr Trp Ser Asp Leu Ser Gln 435 440 445	1344
aga atg atc tgc agc acc cag ctt gac aga gcc cac ggc gtc tct tcc Arg Met Ile Cys Ser Thr Gln Leu Asp Arg Ala His Gly Val Ser Ser 450 455 460	1392
tat gac acc gtc atc agc agg gac atc cag gcc ccc gac ggg ctg gct Tyr Asp Thr Val Ile Ser Arg Asp Ile Gln Ala Pro Asp Gly Leu Ala 465 470 475 480	1440
gtg gac tgg atc cac agc aac atc tac tgg acc gac tct gtc ctg ggc Val Asp Trp Ile His Ser Asn Ile Tyr Trp Thr Asp Ser Val Leu Gly 485 490 495	1488
act gtc tct gtt gcg gat acc aag ggc gtg aag agg aaa acg tta ttc Thr Val Ser Val Ala Asp Thr Lys Gly Val Lys Arg Lys Thr Leu Phe 500 505 510	1536
agg gag aac ggc tcc aag cca agg gcc atc gtg gtg gat cct gtt cat Arg Glu Asn Gly Ser Lys Pro Arg Ala Ile Val Val Asp Pro Val His 515 520 525	1584
ggc ttc atg tac tgg act gac tgg gga act ccc gcc aag atc aag aaa Gly Phe Met Tyr Trp Thr Asp Trp Gly Thr Pro Ala Lys Ile Lys Lys 530 535 540	1632

ggg ggc ctg aat ggt gtg gac atc tac tcg ctg gtg act gaa aac att Gly Gly Leu Asn Gly Val Asp Ile Tyr Ser Leu Val Thr Glu Asn Ile 545 550 555 560	1680
cag tgg ccc aat ggc atc acc cta gat ctc ctc agt ggc cgc ctc tac Gln Trp Pro Asn Gly Ile Thr Leu Asp Leu Leu Ser Gly Arg Leu Tyr 565 570 575	1728
tgg gtt gac tcc aaa ctt cac tcc atc tca agc atc gat gtc aat ggg Trp Val Asp Ser Lys Leu His Ser Ile Ser Ser Ile Asp Val Asn Gly 580 585 590	1776
ggc aac cgg aag acc atc ttg gag gat gaa aag agg ctg gcc cac ccc Gly Asn Arg Lys Thr Ile Leu Glu Asp Glu Lys Arg Leu Ala His Pro 595 600 605	1824
ttc tcc ttg gcc gtc ttt gag gac aaa gta ttt tgg aca gat atc atc Phe Ser Leu Ala Val Phe Glu Asp Lys Val Phe Trp Thr Asp Ile Ile 610 615 620	1872
aac gaa gcc att ttc agt gcc aac cgc ctc aca ggt tcc gat gtc aac Asn Glu Ala Ile Phe Ser Ala Asn Arg Leu Thr Gly Ser Asp Val Asn 625 630 635 640	1920
ttg ttg gct gaa aac cta ctg tcc cca gag gat atg gtc ctc ttc cac Leu Leu Ala Glu Asn Leu Leu Ser Pro Glu Asp Met Val Leu Phe His 645 650 655	1968
aac ctc acc cag cca aga gga gtg aac tgg tgt gag agg acc acc ctg Asn Leu Thr Gln Pro Arg Gly Val Asn Trp Cys Glu Arg Thr Thr Leu 660 665 670	2016
agc aat ggc ggc tgc cag tat ctg tgc ctc cct gcc ccg cag atc aac Ser Asn Gly Gly Cys Gln Tyr Leu Cys Leu Pro Ala Pro Gln Ile Asn 675 680 685	2064
ccc cac tcg ccc aag ttt acc tgc gcc tgc ccg gac ggc atg ctg ctg Pro His Ser Pro Lys Phe Thr Cys Ala Cys Pro Asp Gly Met Leu Leu 690 695 700	2112
gcc agg gac atg agg agc tgc ctc aca gag gct gag gct gca gtg gcc Ala Arg Asp Met Arg Ser Cys Leu Thr Glu Ala Glu Ala Ala Val Ala 705 710 715 720	2160
acc cag gag aca tcc acc gtc agg cta aag gtc agc tcc aca gcc gta Thr Gln Glu Thr Ser Thr Val Arg Leu Lys Val Ser Ser Thr Ala Val 725 730 735	2208
agg aca cag cac aca acc acc cgg cct gtt ccc gac acc tcc cgg ctg Arg Thr Gln His Thr Thr Thr Arg Pro Val Pro Asp Thr Ser Arg Leu 740 745 750	2256
cct ggg gcc acc cct ggg ctc acc acg gtg gag ata gtg aca atg tct Pro Gly Ala Thr Pro Gly Leu Thr Thr Val Glu Ile Val Thr Met Ser 755 760 765	2304

cac	caa	gct	ctg	ggc	gac	gtt	gct	ggc	aga	gga	aat	gag	aag	aag	ccc	2352
His	Gln	Ala	Leu	Gly	Asp	Val	Ala	Gly	Arg	Gly	Asn	Glu	Lys	Lys	Pro	
	770					775					780					

agt	agc	gtg	agg	gct	ctg	tcc	att	gtc	ctc	ccc	atc	gtg	ctc	ctc	gtc	2400
Ser	Ser	Val	Arg	Ala	Leu	Ser	Ile	Val	Leu	Pro	Ile	Val	Leu	Leu	Val	
	785				790					795					800	

ttc	ctt	tgc	ctg	ggg	gtc	ttc	ctt	cta	tgg	aag	aac	tgg	cgg	ctt	aag	2448
Phe	Leu	Cys	Leu	Gly	Val	Phe	Leu	Leu	Trp	Lys	Asn	Trp	Arg	Leu	Lys	
				805					810					815		

aac	atc	aac	agc	atc	aac	ttt	gac	aac	ccc	gtc	tat	cag	aag	acc	aca	2496
Asn	Ile	Asn	Ser	Ile	Asn	Phe	Asp	Asn	Pro	Val	Tyr	Gln	Lys	Thr	Thr	
			820					825					830			

gag	gat	gag	gtc	cac	att	tgc	cac	aac	cag	gac	ggc	tac	agc	tac	ccc	2544
Glu	Asp	Glu	Val	His	Ile	Cys	His	Asn	Gln	Asp	Gly	Tyr	Ser	Tyr	Pro	
		835					840					845				

tcg	aga	cag	atg	gtc	agt	ctg	gag	gat	gac	gtg	gcg	tag				2583
Ser	Arg	Gln	Met	Val	Ser	Leu	Glu	Asp	Asp	Val	Ala					
	850					855					860					

<210> SEQ ID NO: 3
 <211> Longitud: 860
 <212> Tipo: PRT
 <213> Organismo: Homo sapiens

<400> Secuencia: 3

Met	Gly	Pro	Trp	Gly	Trp	Lys	Leu	Arg	Trp	Thr	Val	Ala	Leu	Leu	Leu
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Ala	Ala	Ala	Gly	Thr	Ala	Val	Gly	Asp	Arg	Cys	Glu	Arg	Asn	Glu	Phe
			20					25					30		

Gln	Cys	Gln	Asp	Gly	Lys	Cys	Ile	Ser	Tyr	Lys	Trp	Val	Cys	Asp	Gly
		35					40					45			

Ser	Ala	Glu	Cys	Gln	Asp	Gly	Ser	Asp	Glu	Ser	Gln	Glu	Thr	Cys	Leu
	50					55					60				

Ser	Val	Thr	Cys	Lys	Ser	Gly	Asp	Phe	Ser	Cys	Gly	Gly	Arg	Val	Asn
65					70					75					80

Arg	Cys	Ile	Pro	Gln	Phe	Trp	Arg	Cys	Asp	Gly	Gln	Val	Asp	Cys	Asp
				85					90					95	

Asn Gly Ser Asp Glu Gln Gly Cys Pro Pro Lys Thr Cys Ser Gln Asp
100 105 110

Glu Phe Arg Cys His Asp Gly Lys Cys Ile Ser Arg Gln Phe Val Cys
115 120 125

Asp Ser Asp Arg Asp Cys Leu Asp Gly Ser Asp Glu Ala Ser Cys Pro
130 135 140

Val Leu Thr Cys Gly Pro Ala Ser Phe Gln Cys Asn Ser Ser Thr Cys
145 150 155 160

Ile Pro Gln Leu Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly
165 170 175

Ser Asp Glu Trp Pro Gln Arg Cys Arg Gly Leu Tyr Val Phe Gln Gly
180 185 190

Asp Ser Ser Pro Cys Ser Ala Phe Glu Phe His Cys Leu Ser Gly Glu
195 200 205

Cys Ile His Ser Ser Trp Arg Cys Asp Gly Gly Pro Asp Cys Lys Asp
210 215 220

Lys Ser Asp Glu Glu Asn Cys Ala Val Ala Thr Cys Arg Pro Asp Glu
225 230 235 240

Phe Gln Cys Ser Asp Gly Asn Cys Ile His Gly Ser Arg Gln Cys Asp
245 250 255

Arg Glu Tyr Asp Cys Lys Asp Met Ser Asp Glu Val Gly Cys Val Asn
260 265 270

Val Thr Leu Cys Glu Gly Pro Asn Lys Phe Lys Cys His Ser Gly Glu
275 280 285

Cys Ile Thr Leu Asp Lys Val Cys Asn Met Ala Arg Asp Cys Arg Asp
290 295 300

Trp Ser Asp Glu Pro Ile Lys Glu Cys Gly Thr Asn Glu Cys Leu Asp
305 310 315 320

Asn Asn Gly Gly Cys Ser His Val Cys Asn Asp Leu Lys Ile Gly Tyr
325 330 335

Glu Cys Leu Cys Pro Asp Gly Phe Gln Leu Val Ala Gln Arg Arg Cys
340 345 350

Glu Asp Ile Asp Glu Cys Gln Asp Pro Asp Thr Cys Ser Gln Leu Cys
355 360 365

Val Asn Leu Glu Gly Gly Tyr Lys Cys Gln Cys Glu Glu Gly Phe Gln
370 375 380

Leu Asp Pro His Thr Lys Ala Cys Lys Ala Val Gly Ser Ile Ala Tyr
385 390 395 400

Leu Phe Phe Thr Asn Arg His Glu Val Arg Lys Met Thr Leu Asp Arg
405 410 415

Ser Glu Tyr Thr Ser Leu Ile Pro Asn Leu Arg Asn Val Val Ala Leu
420 425 430

Asp Thr Glu Val Ala Ser Asn Arg Ile Tyr Trp Ser Asp Leu Ser Gln
435 440 445

Arg Met Ile Cys Ser Thr Gln Leu Asp Arg Ala His Gly Val Ser Ser
450 455 460

Tyr Asp Thr Val Ile Ser Arg Asp Ile Gln Ala Pro Asp Gly Leu Ala
465 470 475 480

Val Asp Trp Ile His Ser Asn Ile Tyr Trp Thr Asp Ser Val Leu Gly
485 490 495

Thr Val Ser Val Ala Asp Thr Lys Gly Val Lys Arg Lys Thr Leu Phe
500 505 510

Arg Glu Asn Gly Ser Lys Pro Arg Ala Ile Val Val Asp Pro Val His
515 520 525

Gly Phe Met Tyr Trp Thr Asp Trp Gly Thr Pro Ala Lys Ile Lys Lys
530 535 540

Gly Gly Leu Asn Gly Val Asp Ile Tyr Ser Leu Val Thr Glu Asn Ile
545 550 555 560

Gln Trp Pro Asn Gly Ile Thr Leu Asp Leu Leu Ser Gly Arg Leu Tyr
565 570 575

Trp Val Asp Ser Lys Leu His Ser Ile Ser Ser Ile Asp Val Asn Gly
580 585 590

Gly Asn Arg Lys Thr Ile Leu Glu Asp Glu Lys Arg Leu Ala His Pro
595 600 605

Phe Ser Leu Ala Val Phe Glu Asp Lys Val Phe Trp Thr Asp Ile Ile
610 615 620

Asn Glu Ala Ile Phe Ser Ala Asn Arg Leu Thr Gly Ser Asp Val Asn
625 630 635 640

Leu Leu Ala Glu Asn Leu Leu Ser Pro Glu Asp Met Val Leu Phe His
645 650 655

Asn Leu Thr Gln Pro Arg Gly Val Asn Trp Cys Glu Arg Thr Thr Leu
660 665 670

Ser Asn Gly Gly Cys Gln Tyr Leu Cys Leu Pro Ala Pro Gln Ile Asn
675 680 685

Pro His Ser Pro Lys Phe Thr Cys Ala Cys Pro Asp Gly Met Leu Leu
690 695 700

Ala Arg Asp Met Arg Ser Cys Leu Thr Glu Ala Glu Ala Ala Val Ala
705 710 715 720

Thr Gln Glu Thr Ser Thr Val Arg Leu Lys Val Ser Ser Thr Ala Val
725 730 735

Arg Thr Gln His Thr Thr Thr Arg Pro Val Pro Asp Thr Ser Arg Leu
740 745 750

Pro Gly Ala Thr Pro Gly Leu Thr Thr Val Glu Ile Val Thr Met Ser
755 760 765

His Gln Ala Leu Gly Asp Val Ala Gly Arg Gly Asn Glu Lys Lys Pro
770 775 780

Ser Ser Val Arg Ala Leu Ser Ile Val Leu Pro Ile Val Leu Leu Val
785 790 795 800

Phe Leu Cys Leu Gly Val Phe Leu Leu Trp Lys Asn Trp Arg Leu Lys
805 810 815

Asn Ile Asn Ser Ile Asn Phe Asp Asn Pro Val Tyr Gln Lys Thr Thr
820 825 830

Glu Asp Glu Val His Ile Cys His Asn Gln Asp Gly Tyr Ser Tyr Pro
835 840 845

Ser Arg Gln Met Val Ser Leu Glu Asp Asp Val Ala
850 855 860

<210> SEQ ID NO: 4
<211> Longitud: 2583
<212> Tipo: ADN
<213> Organismo: Secuencia artificial

<220> Característica:
<223> Otra información: hLDLR artificial

<220> Característica:
<221> Clave: misc_característica
<222> Ubicación: (1)..(2583)
<223> Otra información: secuencia de codificación del hLDLR artificial

<400> Secuencia: 4
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gagcaggggtt gccctcctaa gacttgcagc caggacgaat tccgctgtca cgacggcaag 360
tgcatcagca ggcagttcgt ctgcgacagc gacagggatt gtctggacgg aagcgacgag 420
gcctcttgct ctgtgctgac ttgtggccca gccagcttcc agtgcaactc cagcacttgc 480

atccacagc	tctgggcttg	cgacaacgac	ccagattgcg	aggacggatc	agacgagtgg	540
ccacagcgct	gcagaggcct	gtacgtgttt	cagggcgatt	ccagcccttg	cagcgctttt	600
gagttccact	gcctgagcgg	cgagtgcatt	cactcttctt	ggaggtgcga	cggtggccca	660
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accgacatca	tcaacgaggc	catcttcagc	gccaacaggc	tgacaggaag	cgacgtgaac	1920
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tgcttgccag	cccctcagat	taaccctcac	agccccaagt	tcacttgcg	ttgccagac	2100
ggcatgctgc	tggccagaga	tatgcggtct	tgtctgacag	aagccgaagc	cgctgtggct	2160

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gagaagaagc ctagcagcgt gagagccctg tctatcgtgc tgcccatcgt gctgctggtg      2400
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atcaacttcg acaacccctg gtaccagaag accaccgagg acgaggtgca catttgccac      2520
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<210> SEQ ID NO: 5

<211> Longitud: 738

<212> Tipo: PRT

<213> Organismo: Secuencia artificial

<220> Característica:

<223> Otra información: proteína de la cápside vp1 de virus adeno-asociado 8

<400> Secuencia: 5

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```

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Glu Gly Ile Arg Glu Trp Trp Ala Leu Lys Pro Gly Ala Pro Lys Pro
          20           25           30

```

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Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro
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```

```

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro
50           55           60

```

```

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp
65           70           75           80

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Gln Gln Leu Gln Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala
          85           90           95

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Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly
          100          105          110

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Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro

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115					120					125					
Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg
	130					135					140				
Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile
145					150					155					160
Gly	Lys	Lys	Gly	Gln	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln
				165					170					175	
Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro
			180					185						190	
Pro	Ala	Ala	Pro	Ser	Gly	Val	Gly	Pro	Asn	Thr	Met	Ala	Ala	Gly	Gly
		195					200					205			
Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser
	210					215					220				
Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val
225					230					235					240
Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His
				245					250					255	
Leu	Tyr	Lys	Gln	Ile	Ser	Asn	Gly	Thr	Ser	Gly	Gly	Ala	Thr	Asn	Asp
			260					265						270	
Asn	Thr	Tyr	Phe	Gly	Tyr	Ser	Thr	Pro	Trp	Gly	Tyr	Phe	Asp	Phe	Asn
		275					280					285			
Arg	Phe	His	Cys	His	Phe	Ser	Pro	Arg	Asp	Trp	Gln	Arg	Leu	Ile	Asn
	290					295					300				
Asn	Asn	Trp	Gly	Phe	Arg	Pro	Lys	Arg	Leu	Ser	Phe	Lys	Leu	Phe	Asn
305					310					315					320
Ile	Gln	Val	Lys	Glu	Val	Thr	Gln	Asn	Glu	Gly	Thr	Lys	Thr	Ile	Ala
				325					330					335	
Asn	Asn	Leu	Thr	Ser	Thr	Ile	Gln	Val	Phe	Thr	Asp	Ser	Glu	Tyr	Gln

340				345				350							
Leu	Pro	Tyr 355	Val	Leu	Gly	Ser	Ala 360	His	Gln	Gly	Cys	Leu 365	Pro	Pro	Phe
Pro	Ala 370	Asp	Val	Phe	Met	Ile 375	Pro	Gln	Tyr	Gly	Tyr 380	Leu	Thr	Leu	Asn
Asn 385	Gly	Ser	Gln	Ala	Val 390	Gly	Arg	Ser	Ser	Phe 395	Tyr	Cys	Leu	Glu	Tyr 400
Phe	Pro	Ser	Gln	Met 405	Leu	Arg	Thr	Gly	Asn 410	Asn	Phe	Gln	Phe	Thr 415	Tyr
Thr	Phe	Glu	Asp 420	Val	Pro	Phe	His	Ser 425	Ser	Tyr	Ala	His	Ser 430	Gln	Ser
Leu	Asp	Arg 435	Leu	Met	Asn	Pro	Leu 440	Ile	Asp	Gln	Tyr	Leu 445	Tyr	Tyr	Leu
Ser	Arg 450	Thr	Gln	Thr	Thr	Gly 455	Gly	Thr	Ala	Asn	Thr 460	Gln	Thr	Leu	Gly
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Leu	Pro	Gly	Pro	Cys 485	Tyr	Arg	Gln	Gln	Arg 490	Val	Ser	Thr	Thr	Thr 495	Gly
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Asn Leu

<210> SEQ ID NO: 6
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 <213> Organismo: Secuencia artificial

<220> Característica:
 <223> Otra información: pAAV.TBG.PI.hLDLRco.RGB

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<223> Otra información: 5' ITR

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<222> Ubicación: (221)..(320)
<223> Otra información: Alpha mic/bik

<220> Característica:
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<222> Ubicación: (327)..(426)
<223> Otra información: Alpha mic/bik

<220> Característica:
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<223> Otra información: TBG

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<223> Otra información: hLDLR optimizado con codón

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<223> Otra información: Globina poli A de conejo

<220> Característica:
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<222> Ubicación: (3818)..(3947)
<223> Otra información: 3' ITR

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<223> Otra información: f1 ori

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<223> Otra información: AP(R)

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<400> Secuencia: 6

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<210> SEQ ID NO: 7
<211> Longitud: 860
<212> Tipo: PRT
<213> Organismo: Secuencia artificial

<220> Característica:
<223> Otra información: Constructo sintético

<400> Secuencia: 7

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```

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```

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```

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Val	Leu	Thr	Cys	Gly	Pro	Ala	Ser	Phe	Gln	Cys	Asn	Ser	Ser	Thr	Cys	
		145			150					155					160	
Ile	Pro	Gln	Leu	Trp	Ala	Cys	Asp	Asn	Asp	Pro	Asp	Cys	Glu	Asp	Gly	
				165					170					175		
Ser	Asp	Glu	Trp	Pro	Gln	Arg	Cys	Arg	Gly	Leu	Tyr	Val	Phe	Gln	Gly	
			180					185					190			
Asp	Ser	Ser	Pro	Cys	Ser	Ala	Phe	Glu	Phe	His	Cys	Leu	Ser	Gly	Glu	
		195				200						205				
Cys	Ile	His	Ser	Ser	Trp	Arg	Cys	Asp	Gly	Gly	Pro	Asp	Cys	Lys	Asp	
		210				215					220					
Lys	Ser	Asp	Glu	Glu	Asn	Cys	Ala	Val	Ala	Thr	Cys	Arg	Pro	Asp	Glu	
		225			230					235					240	
Phe	Gln	Cys	Ser	Asp	Gly	Asn	Cys	Ile	His	Gly	Ser	Arg	Gln	Cys	Asp	
				245					250					255		
Arg	Glu	Tyr	Asp	Cys	Lys	Asp	Met	Ser	Asp	Glu	Val	Gly	Cys	Val	Asn	
			260					265					270			
Val	Thr	Leu	Cys	Glu	Gly	Pro	Asn	Lys	Phe	Lys	Cys	His	Ser	Gly	Glu	
		275					280					285				
Cys	Ile	Thr	Leu	Asp	Lys	Val	Cys	Asn	Met	Ala	Arg	Asp	Cys	Arg	Asp	
		290				295					300					
Trp	Ser	Asp	Glu	Pro	Ile	Lys	Glu	Cys	Gly	Thr	Asn	Glu	Cys	Leu	Asp	
		305			310					315					320	
Asn	Asn	Gly	Gly	Cys	Ser	His	Val	Cys	Asn	Asp	Leu	Lys	Ile	Gly	Tyr	

				325						330						335			
Glu	Cys	Leu	Cys	Pro	Asp	Gly	Phe	Gln	Leu	Val	Ala	Gln	Arg	Arg	Cys				
			340					345					350						
Glu	Asp	Ile	Asp	Glu	Cys	Gln	Asp	Pro	Asp	Thr	Cys	Ser	Gln	Leu	Cys				
		355					360					365							
Val	Asn	Leu	Glu	Gly	Gly	Tyr	Lys	Cys	Gln	Cys	Glu	Glu	Gly	Phe	Gln				
	370					375					380								
Leu	Asp	Pro	His	Thr	Lys	Ala	Cys	Lys	Ala	Val	Gly	Ser	Ile	Ala	Tyr				
385					390					395					400				
Leu	Phe	Phe	Thr	Asn	Arg	His	Glu	Val	Arg	Lys	Met	Thr	Leu	Asp	Arg				
				405					410					415					
Ser	Glu	Tyr	Thr	Ser	Leu	Ile	Pro	Asn	Leu	Arg	Asn	Val	Val	Ala	Leu				
			420					425					430						
Asp	Thr	Glu	Val	Ala	Ser	Asn	Arg	Ile	Tyr	Trp	Ser	Asp	Leu	Ser	Gln				
		435					440					445							
Arg	Met	Ile	Cys	Ser	Thr	Gln	Leu	Asp	Arg	Ala	His	Gly	Val	Ser	Ser				
	450					455						460							
Tyr	Asp	Thr	Val	Ile	Ser	Arg	Asp	Ile	Gln	Ala	Pro	Asp	Gly	Leu	Ala				
465					470					475					480				
Val	Asp	Trp	Ile	His	Ser	Asn	Ile	Tyr	Trp	Thr	Asp	Ser	Val	Leu	Gly				
				485					490					495					
Thr	Val	Ser	Val	Ala	Asp	Thr	Lys	Gly	Val	Lys	Arg	Lys	Thr	Leu	Phe				
			500					505					510						
Arg	Glu	Asn	Gly	Ser	Lys	Pro	Arg	Ala	Ile	Val	Val	Asp	Pro	Val	His				
		515					520					525							
Gly	Phe	Met	Tyr	Trp	Thr	Asp	Trp	Gly	Thr	Pro	Ala	Lys	Ile	Lys	Lys				
	530					535					540								
Gly	Gly	Leu	Asn	Gly	Val	Asp	Ile	Tyr	Ser	Leu	Val	Thr	Glu	Asn	Ile				

545					550					555					560
Gln	Trp	Pro	Asn	Gly	Ile	Thr	Leu	Asp	Leu	Leu	Ser	Gly	Arg	Leu	Tyr
				565					570					575	
Trp	Val	Asp	Ser	Lys	Leu	His	Ser	Ile	Ser	Ser	Ile	Asp	Val	Asn	Gly
			580					585					590		
Gly	Asn	Arg	Lys	Thr	Ile	Leu	Glu	Asp	Glu	Lys	Arg	Leu	Ala	His	Pro
		595					600					605			
Phe	Ser	Leu	Ala	Val	Phe	Glu	Asp	Lys	Val	Phe	Trp	Thr	Asp	Ile	Ile
	610					615					620				
Asn	Glu	Ala	Ile	Phe	Ser	Ala	Asn	Arg	Leu	Thr	Gly	Ser	Asp	Val	Asn
625					630					635					640
Leu	Leu	Ala	Glu	Asn	Leu	Leu	Ser	Pro	Glu	Asp	Met	Val	Leu	Phe	His
				645					650					655	
Asn	Leu	Thr	Gln	Pro	Arg	Gly	Val	Asn	Trp	Cys	Glu	Arg	Thr	Thr	Leu
			660					665					670		
Ser	Asn	Gly	Gly	Cys	Gln	Tyr	Leu	Cys	Leu	Pro	Ala	Pro	Gln	Ile	Asn
		675					680					685			
Pro	His	Ser	Pro	Lys	Phe	Thr	Cys	Ala	Cys	Pro	Asp	Gly	Met	Leu	Leu
	690					695					700				
Ala	Arg	Asp	Met	Arg	Ser	Cys	Leu	Thr	Glu	Ala	Glu	Ala	Ala	Val	Ala
705					710				715						720
Thr	Gln	Glu	Thr	Ser	Thr	Val	Arg	Leu	Lys	Val	Ser	Ser	Thr	Ala	Val
				725					730					735	
Arg	Thr	Gln	His	Thr	Thr	Thr	Arg	Pro	Val	Pro	Asp	Thr	Ser	Arg	Leu
			740					745					750		
Pro	Gly	Ala	Thr	Pro	Gly	Leu	Thr	Thr	Val	Glu	Ile	Val	Thr	Met	Ser
		755					760					765			
His	Gln	Ala	Leu	Gly	Asp	Val	Ala	Gly	Arg	Gly	Asn	Glu	Lys	Lys	Pro

770					775					780					
Ser	Ser	Val	Arg	Ala	Leu	Ser	Ile	Val	Leu	Pro	Ile	Val	Leu	Leu	Val
785					790					795				800	
Phe	Leu	Cys	Leu	Gly	Val	Phe	Leu	Leu	Trp	Lys	Asn	Trp	Arg	Leu	Lys
				805					810					815	
Asn	Ile	Asn	Ser	Ile	Asn	Phe	Asp	Asn	Pro	Val	Tyr	Gln	Lys	Thr	Thr
			820					825					830		
Glu	Asp	Glu	Val	His	Ile	Cys	His	Asn	Gln	Asp	Gly	Tyr	Ser	Tyr	Pro
		835					840					845			
Ser	Arg	Gln	Met	Val	Ser	Leu	Glu	Asp	Asp	Val	Ala				
	850					855					860				