

Figura 1A-2

```
AAV4capPro 180 DGP---PEGSTSGAMS--DDSEMRAAAGGAAVEGGGADGVGNASGDWHCDSTWSEGHVT 234
AAV2capPro 181 SVPDPQPLGPPAAPSGLTNTMATGSGAPMADNNEGADGVGNSSGNWHCSTWMGDRVI 240
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

AAV4capPro 235 TTSTRTWLPTYNHLYKRLG---ESLQSNNTYNGFSTPWGYDFNRFHCHFSPRDWQRLI 291
AAV2capPro 241 TTSTRTWALPTYNHLYKQISSQSGASNDNHYFGYSTPWGYDFNRFHCHFSPRDWQRLI 300
          *****
          . . * * * * * * * * * * * * * * * * * * * * * * * * * * *
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

AAV4capPro 292 NNNWGMRPKAMRVKIFNIQVKEVTTSNGETTVANNLTSTVQIFADSSYELPYVMDAGQEG 351
AAV2capPro 301 NNNWGFPRKRLNFKLFNIQVKEVTQNDGTTIANNLTSTVQVFTDSEYQPLPYVLGSAHQG 360
          *****
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

AAV4capPro 352 SLPPFPNDVFMVPQYGYCGLVTGNTSQQQTDNRNAYCYCLEYFPSQMLRTGNNFETYSFEK 411
AAV2capPro 361 CLPPFPADVFMVPQYGYLTLNNG--SQAVGRSSFYCYLFPSQMLRTGNNFTFSYTFED 417
          *****
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

AAV4capPro 412 VPFHSMYAHSQSLDRLMNPLIDQYLWGLQSTTTGTTLNAGTATTNFTKLRPTNFSNFKKN 471
AAV2capPro 418 VPFHSSYAHSQSLDRLMNPLIDQYLYLRSRTNTPSGTTT-QSRLQFSQAGASDIRDQSRN 476
          *****
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

AAV4capPro 472 WLPGPSIKQQGFSKTANQNYKIPATGSDSLIKYETHSTLDGRWSALTGPPPMATAGPADS 531
AAV2capPro 477 WLPGPCYRQQRVSKTSADNNNSEYSWTG-----ATKYHLNGRDSLVPNPGPAMASHKDDEE 531
          *****
          * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
```


Figura 1B-1

ClustalW (vl. 83) alineamiento de secuencia múltiple

2 secuencias alineadas Puntaje de alineamiento = nan
Espacios insertados = 10 Identidades conservadas = 1440

Modo de alineamiento de pares: Lento
Parámetros de alineamiento de pares:
 Penalización de apertura Penalización por
 de espacio = 10.0 espacio extendido= 5.0
Parámetros de alineamiento múltiple:
 Penalización de Penalización por
 apertura de espacio = 30.0 espacio extendido= 5.0
 Divergente de retraso= 40% Transiciones: pesado
Tiempo de procesamiento: 1.8 segundos

1. AAV2capNuc vs. AAV4capNuc1

Longitud alineada= 2235 Espacios= 10
Identidades= 1440 (65%)

AAV2capNuc	1	ATGGCTGCCGATGGTTATCTTCCAGATTGGCTCGAGGACACTCTCTCTGAAGGAATAAGA	60
AAV4capNuc1	1	---ATGACTGACGGTTACCTTCCAGATTGGCTAGAGGACAACCTCTCTGAAGGCGTTCGA	57
		* ** ***** ***** ***** ***** * **	
AAV2capNuc	61	CAGTGGTGGGAAGCTCAAACTGGCCACCAACCACCAAGCCCGCAGAGCGGCATAAGGAC	120
AAV4capNuc1	58	GAGTGGTGGGCGCTGCAACTGGAGCCCCCTAAACCCCAAGGCAATCAACAACATCAGGAC	117
		***** *** ***** * ** *** ** * * * * *	

Figura 1B-2

AAV2capNuc	121	GACAGCAGGGGTCCTTGTCCTTCTGGGTACAAGTACCTCGGACCCCTTCAACGGACTCGAC	180
AAV4capNuc1	118	AACGCTCGGGGTCCTTGTCCTTCCGGGTTACAAATACCTCGGACCCGGCAACGGACTCGAC	177
		** ***** ** ***** ** ***** *****	
AAV2capNuc	181	AAGGGAGAGCCGGTCAACGAGGCAGACGCCGGGCCCTCGAGCAGACAAAGCCTACGAC	240
AAV4capNuc1	178	AAGGGGAACCCGTTCAACGAGCGGACGGCGAGCCCTCGAGCAGACAAAGCCTACGAC	237
		***** ** ** ***** ** ***** ***** *****	
AAV2capNuc	241	CGGCAGCTCGACAGCGGAGACAAACCCGTACCTCAAGTACAACCAACGCGCGGAGTTT	300
AAV4capNuc1	238	CAGCAGCTCAAGGCCGGTGACAAACCCCTACCTCAAGTACAACCAACGCGCGGAGTTT	297
		* ***** * ** ***** ***** ***** *****	
AAV2capNuc	301	CAGGAGCGCCTTAAAGAAGATACGTCTTTTGGGGCAACCTCGGACGAGCAGTCTTCCAG	360
AAV4capNuc1	298	CAGCAGCGGCTTCAGGGCGGACACATCGTTTGGGGCAACCTCGGACGAGCAGTCTTCCAG	357
		*** ***** * * * * * ***** ***** *****	
AAV2capNuc	361	GCGAATAAAGAGGGTTCTTGAACTCTTGGGCTGGTTGAGGAACCTGTTAAGACGGCTCCG	420
AAV4capNuc1	358	GCCATAAAGAGGGTTCTTGAACTCTTGGTCTGGTTGAGCAAGCGGGTGAGACGGCTCCT	417
		** ***** ***** ** * * *****	
AAV2capNuc	421	GGATAAAGAGGCGCGGTAGAGCACTCTCTGTGGAGCCAGACTCCTCTCGGGAACCGGA	480
AAV4capNuc1	418	GGAAAGAGAGACCGTTGATTGAATCCCCCAGCAGCCCGACTCCTCACGGGTATCGGC	477
		***** ***** * * * * * ***** ***** * * *	
AAV2capNuc	481	AAGGCGGGCCAGCAGCCCTGCAAGAAAAAGATTGAATTTTGGTCAGACTGGAGACGCAGAC	540
AAV4capNuc1	478	AAAAAGGCAAGCAGCCGCTAAAAAGAGCTCGTTTTCGA-----AGACGAAACT	528
		** *** ***** ** * * * * * * * * ***** *	

Figura 1B-3

AAV2capNuc	541	TCAGTACCTGACCCCGAGCCTCTCGGACAGCCACCAGCAGCCCCCTCTGTGGTCTGGGAACT	600
AAV4capNuc1	529	GGAGCAGGCGACGGACCCCTGAGGGATCAACTTCCGGAGCCATGCTCTGAT-----GAC	582
		** * ** * ** * ** * ** * ** * ** * ** *	
AAV2capNuc	601	AATACGATGGCTACAGGCAGTGGCGCACCAATGGCAGACAAATAACGAGGGCGCCGACGGA	660
AAV4capNuc1	583	AGTGAGATGCGTGACAGCAGCTGGCGGAGCTGCAGTCCGAGGGCGGACAAGGTGCCGATGGA	642
		* * ** * ** * ** * ** * ** * ** * ** *	
AAV2capNuc	661	GTGGGTAAATTCTCGGGAAATTGGCATTTGCGATTCCACATGGATGGGCGACAGAGTCAATC	720
AAV4capNuc1	643	GTGGGTAAATGCCCTCGGGTGATTGGCATTTGCGATTCCACCTGGTCTGAGGGCCACGTCACG	702
		***** ***** ***** ***** ***** *	
AAV2capNuc	721	ACCACAGCACCCGAACTCTGGGCCCTGCCACCTACAACAACCACTCTACAAACAAATT	780
AAV4capNuc1	703	ACCACAGCACCAAGAACCTTGGGTCTTGCCCACTACAACAACCACTCTACAAAGCGACTC	762
		***** ***** ***** ***** ***** * * *	
AAV2capNuc	781	TCCAGCCAATCAGGAGCCTCGAACGACAAATCACTACTTTGGCTACAGCACCCCTTGGGGG	840
AAV4capNuc1	763	GG-----AGAGAGCCTGCAGTCCCAACACCTACAACGGATTCTCCACCCCTTGGGGA	813
		** * * * * ** * ** * ** * ** * ** * ** *	
AAV2capNuc	841	TATTTTGACTTCAACAGATTCCACTGCCACTTTTCAACACGTGACTGGCAAGACTCATC	900
AAV4capNuc1	814	TACTTTGACTTCAACCGCTTCCACTGCCACTTCTCAACACGTGACTGGCAGCGACTCATC	873
		** ***** ** ***** ***** ***** *****	
AAV2capNuc	901	AACAACAACCTGGGGATTCCGACCCCAAGAGACTCAACTTCAAGCTCTTTAACAATTCAAAGTC	960
AAV4capNuc1	874	AACAACAACCTGGGGCATGCGACCCCAAGCCATGCGGGTCAAAATCTTCAACATCCAGGTC	933
		***** ***** * ***** * ***** * ** * ** *	

Figure 1B-4

```
AAV2capNuc 961 AAAGAGGTACGCAGAAATGACGGTACGACGACGATTGCCAATAACCTTACCAGCACGGTT 1020
AAV4capNuc1 934 AAGGAGGTCACGACGTCGAACGGCGAGACAACGGTGGCTAATAACCTTACCAGCACGGTT 993
** ***** * **** ** ** * ** *****
** *****

AAV2capNuc 1021 CAGGTGTTTACTGACTCGGAGTACCAGCTCCCGTACGTCTCGGCTCGGCGCATCAAGGA 1080
AAV4capNuc1 994 CAGATCTTTGCGGACTCGTCTGTAACGAACTGCCGTACGTGATGGATGCGGGTCAAGAGGGC 1053
*** * *** * ***** **** * ** ***** * * ** * **

AAV2capNuc 1081 TGCCTCCCGCCGTTCCAGCAGACGTCTTTCATGGTGCCACAGTATGGATACCTCACCTTG 1140
AAV4capNuc1 1054 AGCTGCTCTCTTTTCCCAACGACGTCTTTATGGTGCCCCCAGTACGGCTACTGTGGA CTG 1113
**** ** ** ** * **** * **** * **** * ** * **

AAV2capNuc 1141 AACAAACGGGAGT--CAGGCAGTAGGACGCTC-----TTCATTTTACTGCTTGAGTAC 1191
AAV4capNuc1 1114 GTGACCGGCAACACTTCGCAGCAACAGACTGACAGAAATGCCCTTCTACTGCTTGAGTAC 1173
* *** * **** * * ** * * **** * **** * ****

AAV2capNuc 1192 TTTCTTCTCAGATGCTGCGTACCGGAAACAACCTTTACCTTCAGCTACACTTTTGAGGAC 1251
AAV4capNuc1 1174 TTTCTTTCGCAGATGCTGCGGACTGGCAACAACCTTTGAAATTACGTACAGTTTGTGAGAAG 1233
***** ***** ** ** ***** * * **** * **** *

AAV2capNuc 1252 GTTCTTTCCACAGCAGCTACGCTCACAGCCAGAGTCTGGACCGTCTCATGAATCTCTC 1311
AAV4capNuc1 1234 GTGCTTTTCCACTCGATGTACGCGCACAGCCAGAGCCCTGGACCGGCTGATGAACCTCTC 1293
** ***** * ***** ***** ** *****

AAV2capNuc 1312 ATCGACCAGTACCTGTATTACTTGTAGCAGAAACAACACTCCAAGTGGAACCAACACGCGAG 1371
AAV4capNuc1 1294 ATCGACCAGTACCTGTGCGGACTGCAATCGACCAACCGGAACCACTTGAATGCCGGG 1353
***** ***** ** ** * **** * * * *
```


Figura 1B-7

AAV2capNuc 2194 ACTCGTAATCTGTAA 2208
AAV4capNuc1 2191 ACCACCACTGTAA 2205
** * * *****

Figura 2

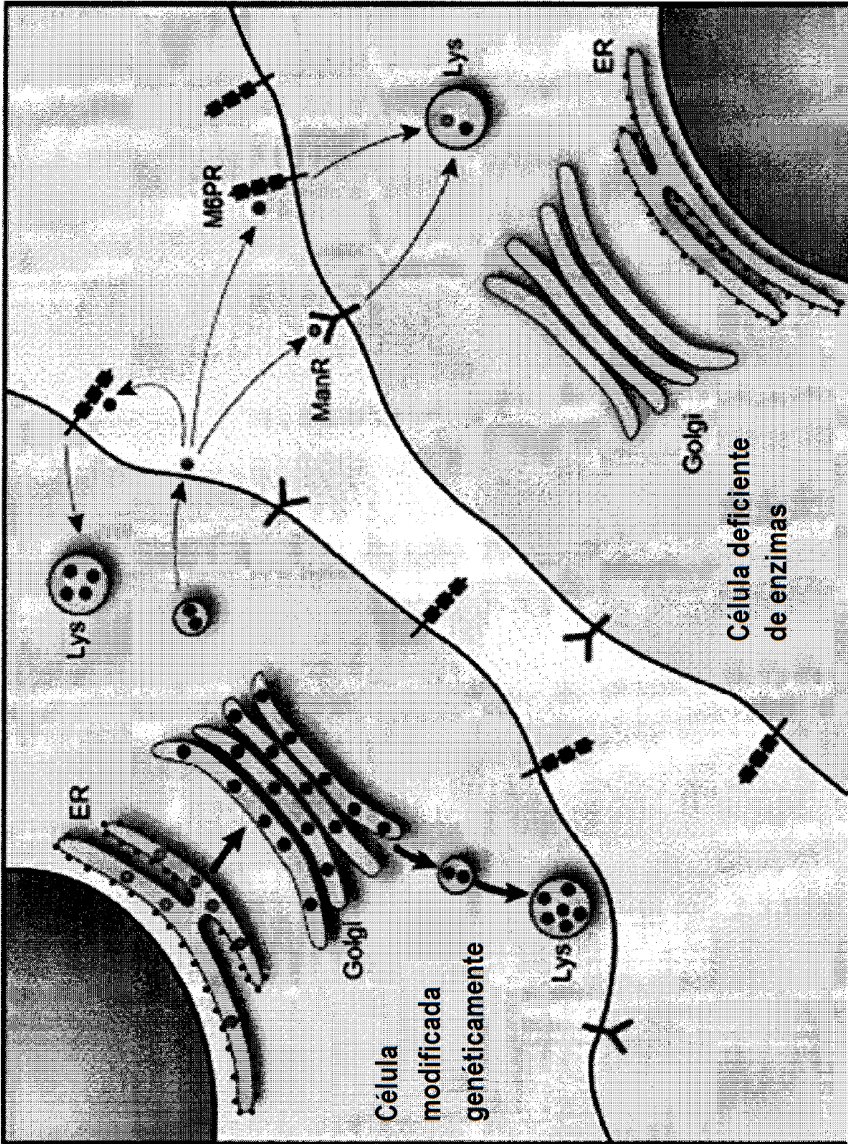


Fig. 3
Expresiones de TPP1 en perro *Cln2^{-/-}* después de suministro de AAV

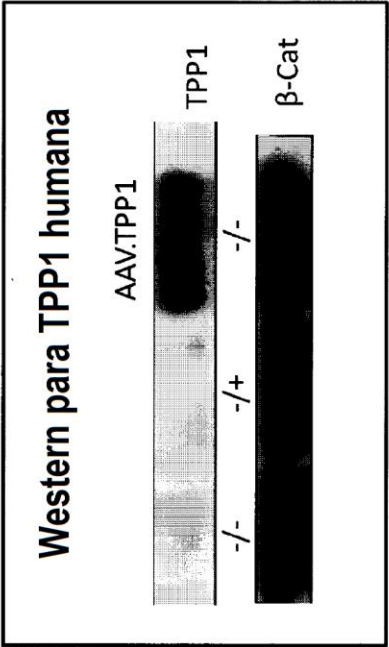
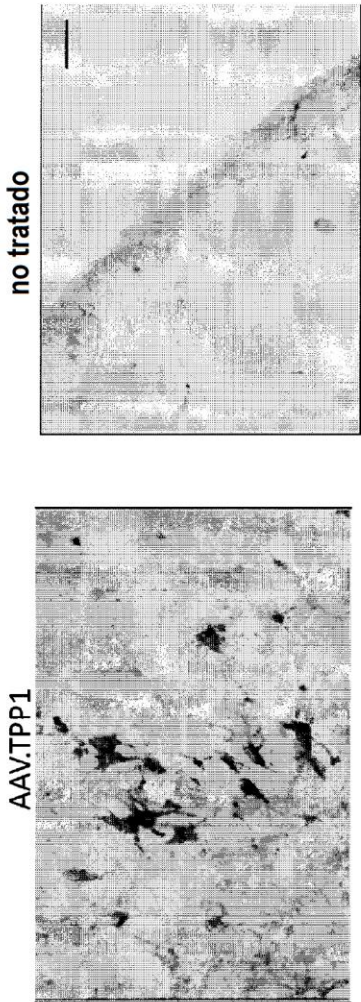


Figura 4A
Efecto de AAV-TPP1 sobre autofluorescencia

AAV2/2.TPP1



Control

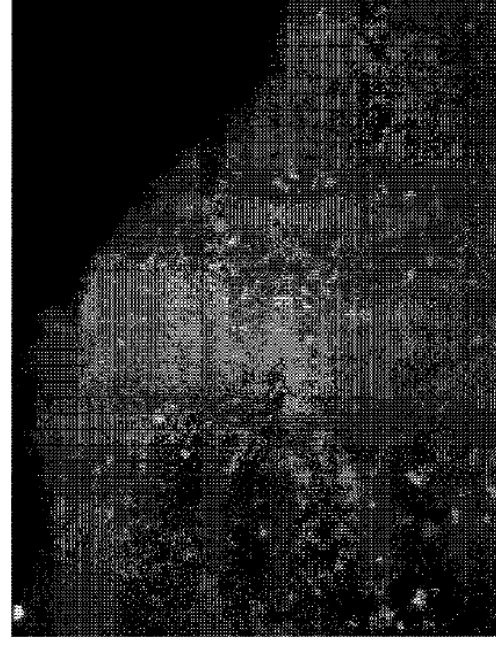
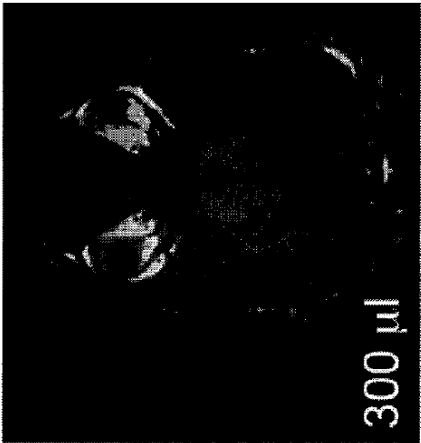


Figura 4B

No tratado -/-



Tratado -/-



No tratado +/-



Tratado +/-

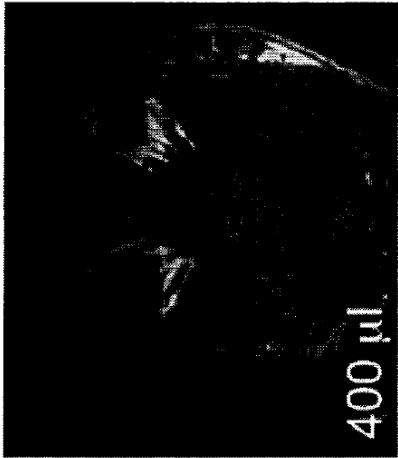


Figura 4C

No tratado -/- No tratado +/-



Tratado -/-

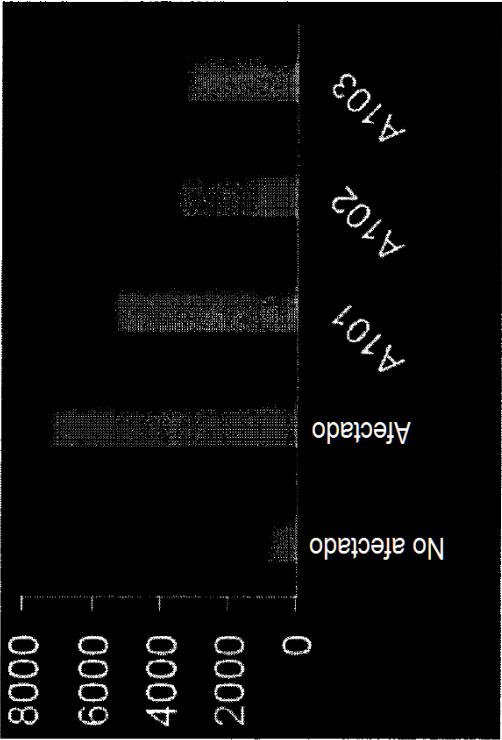
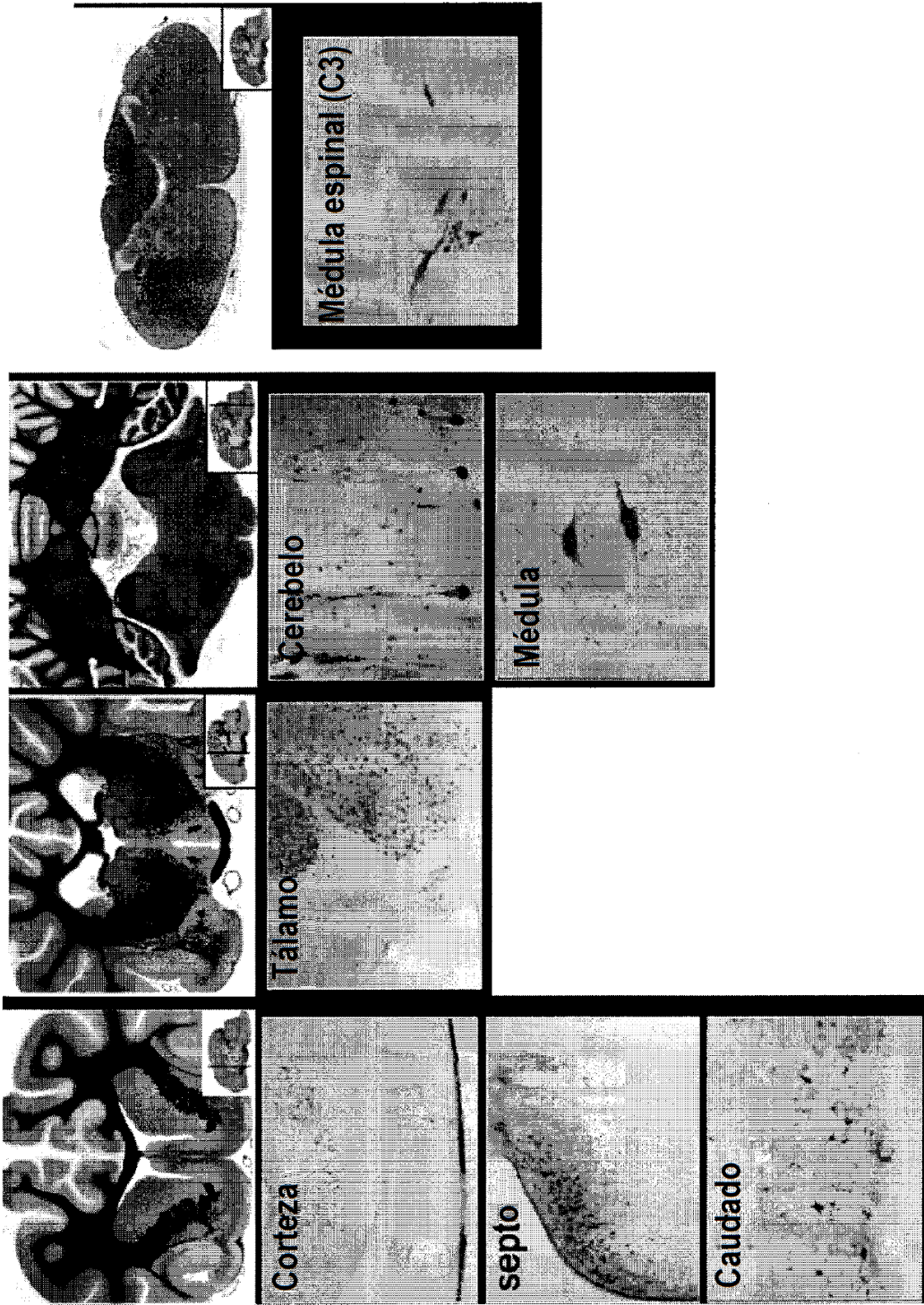


Figura 4D



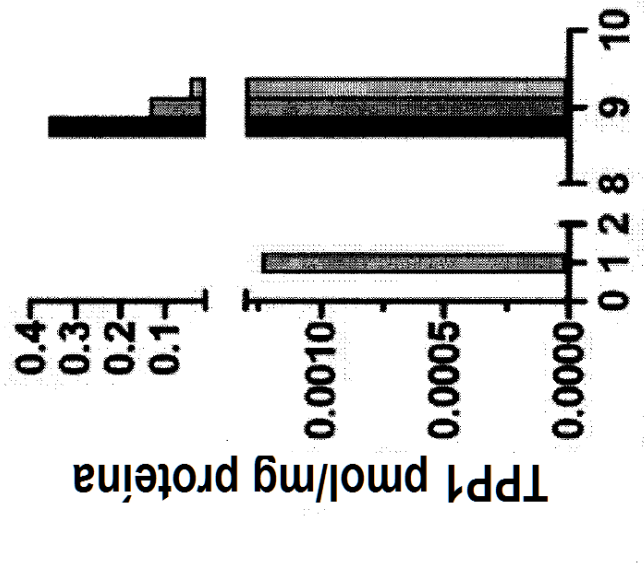


Figura 5

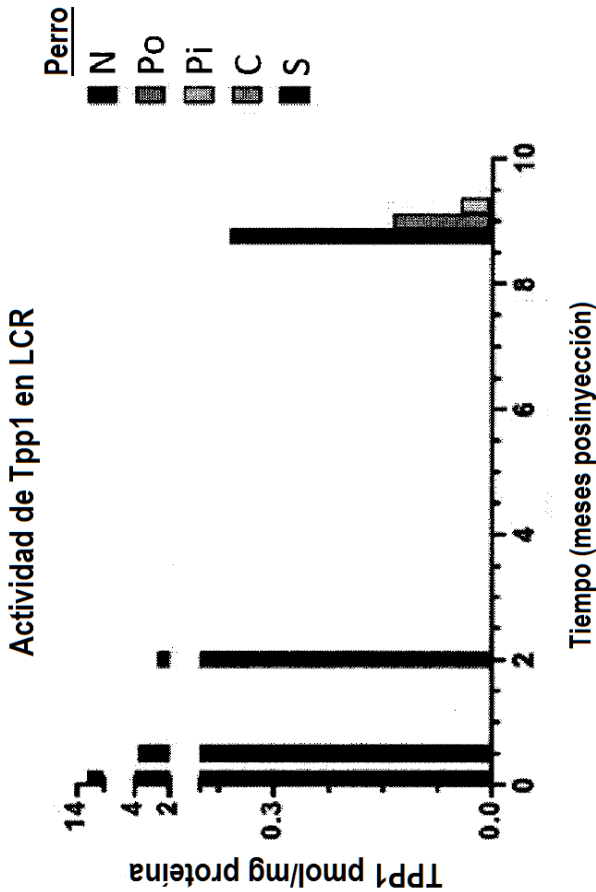


Figura 6

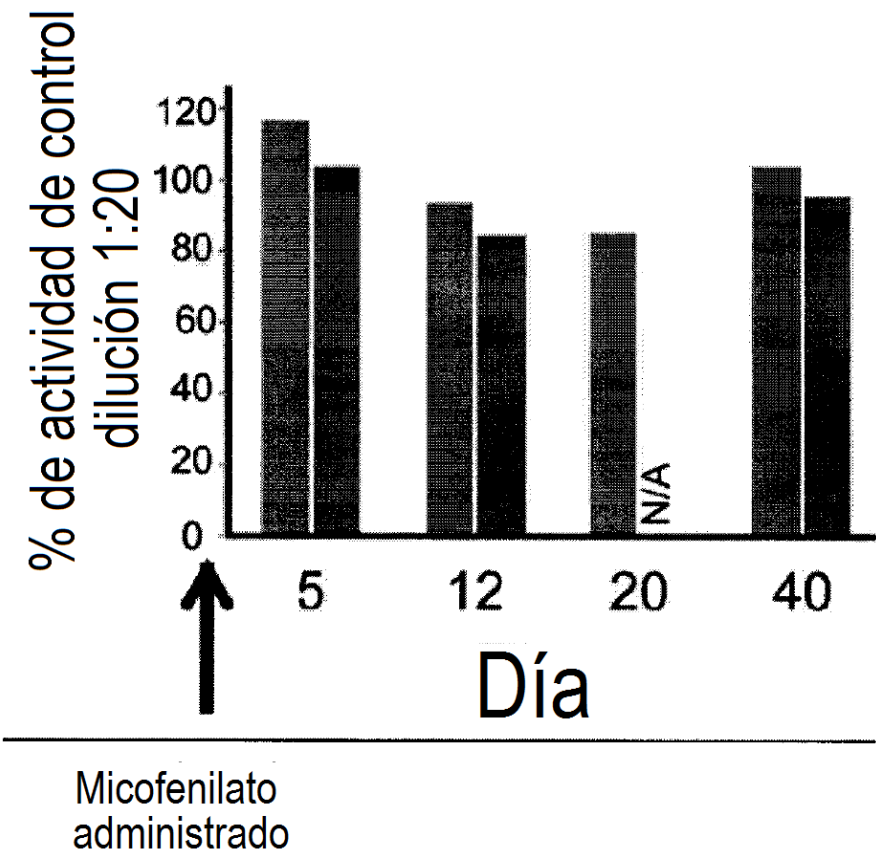


Figura 7

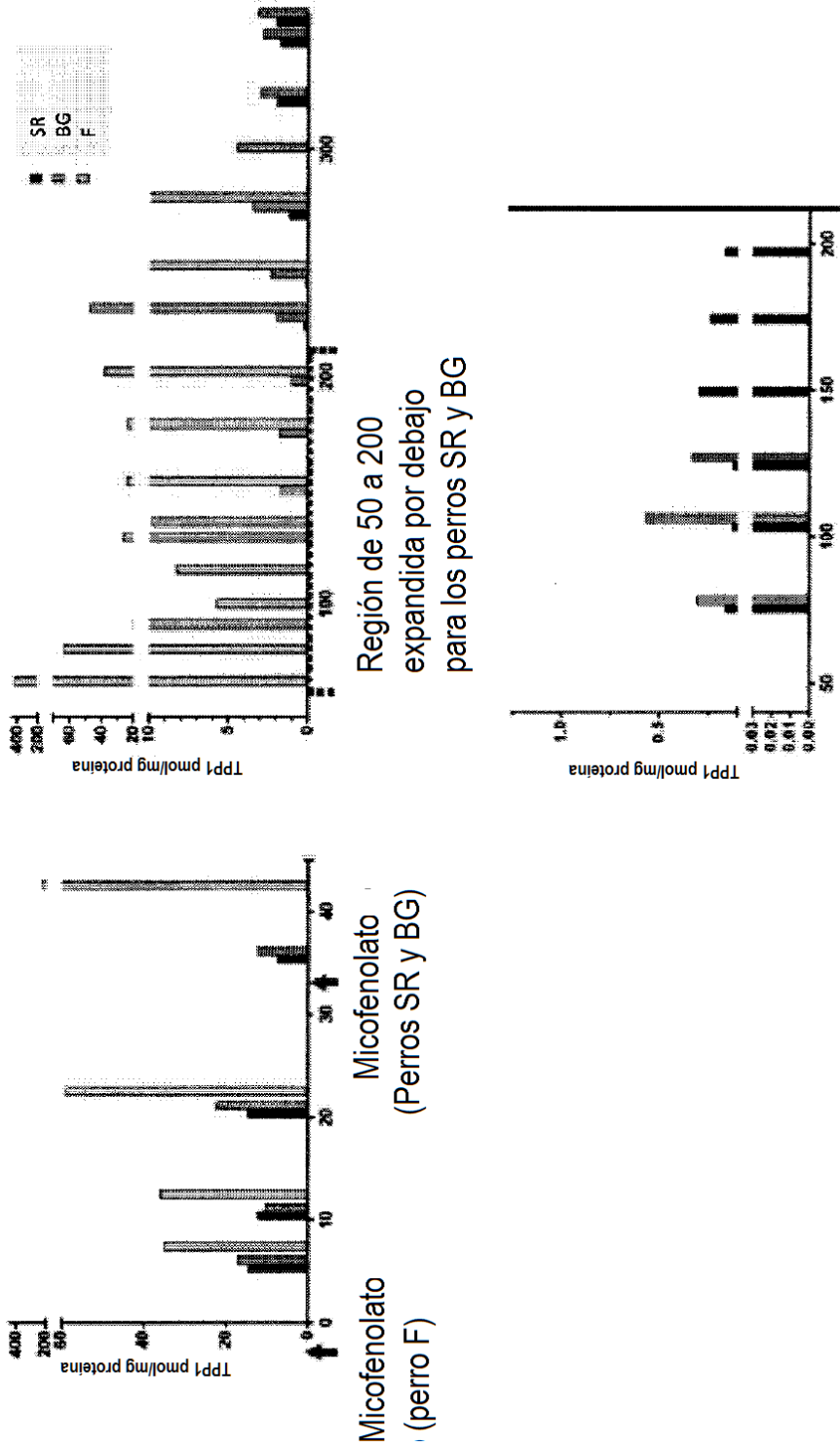


Figura 8

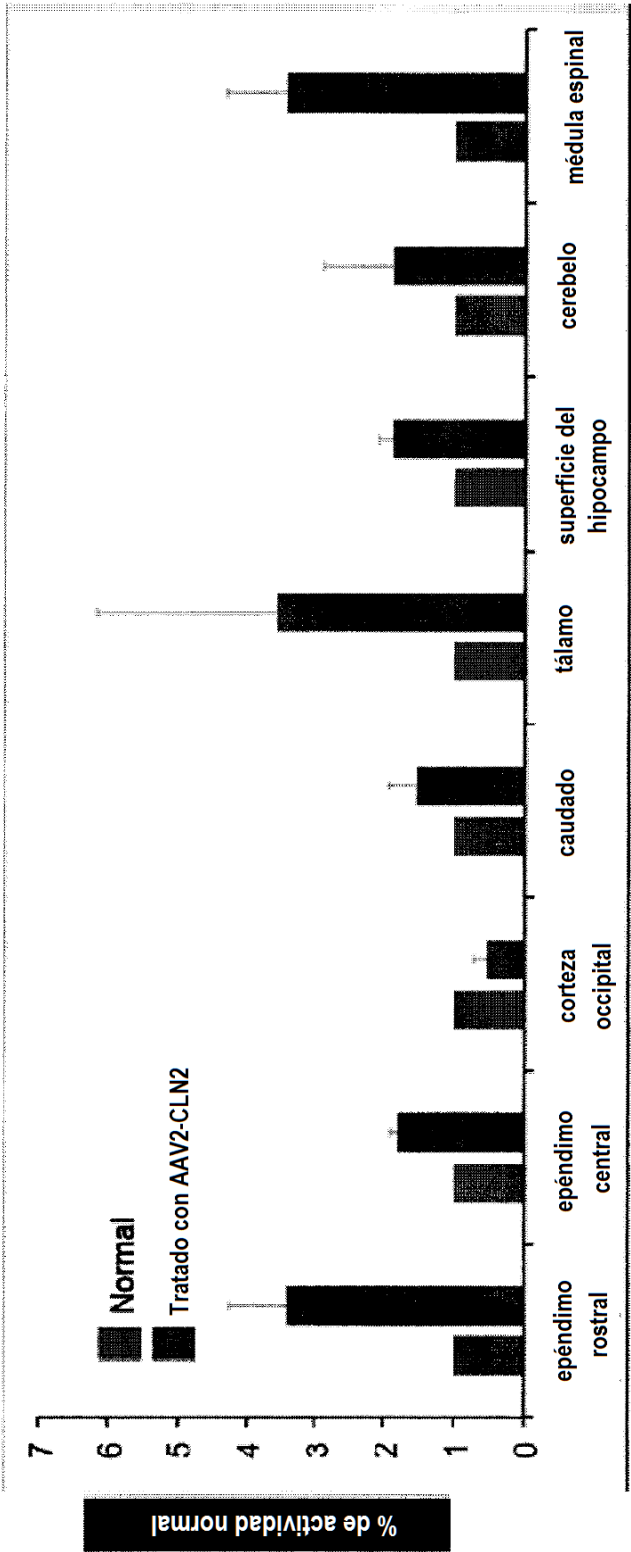


Figura 9A

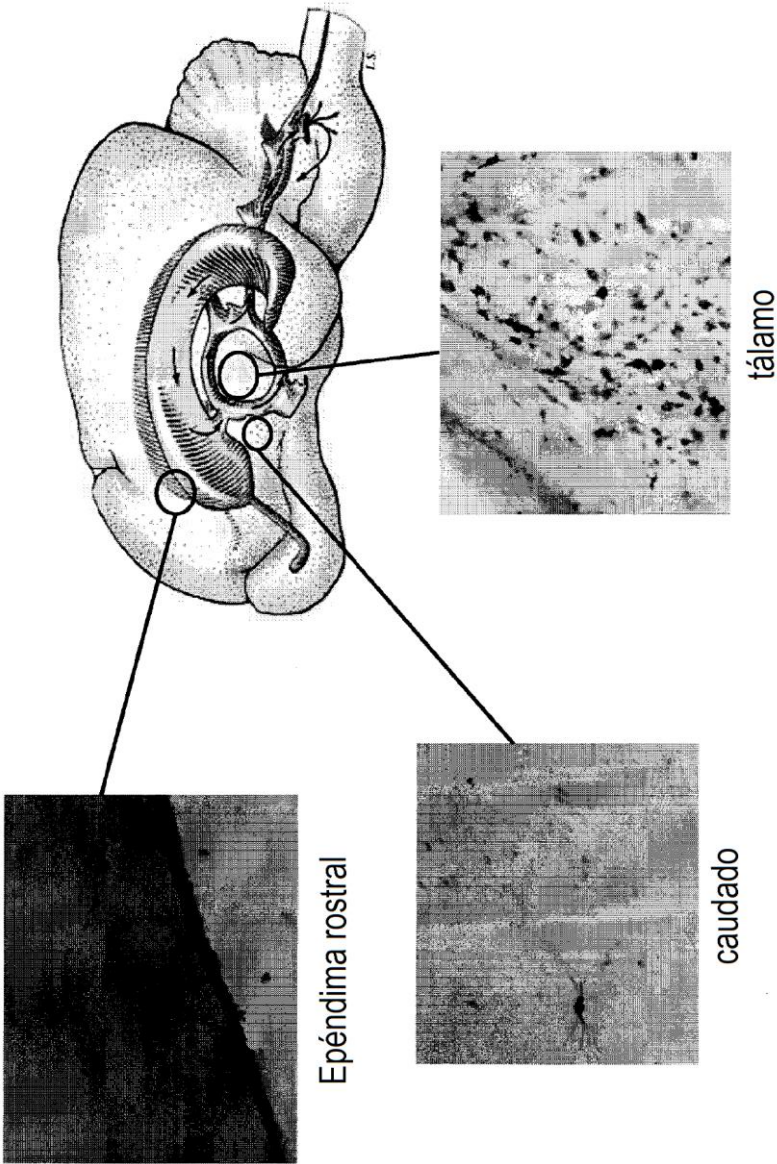


Figura 9B

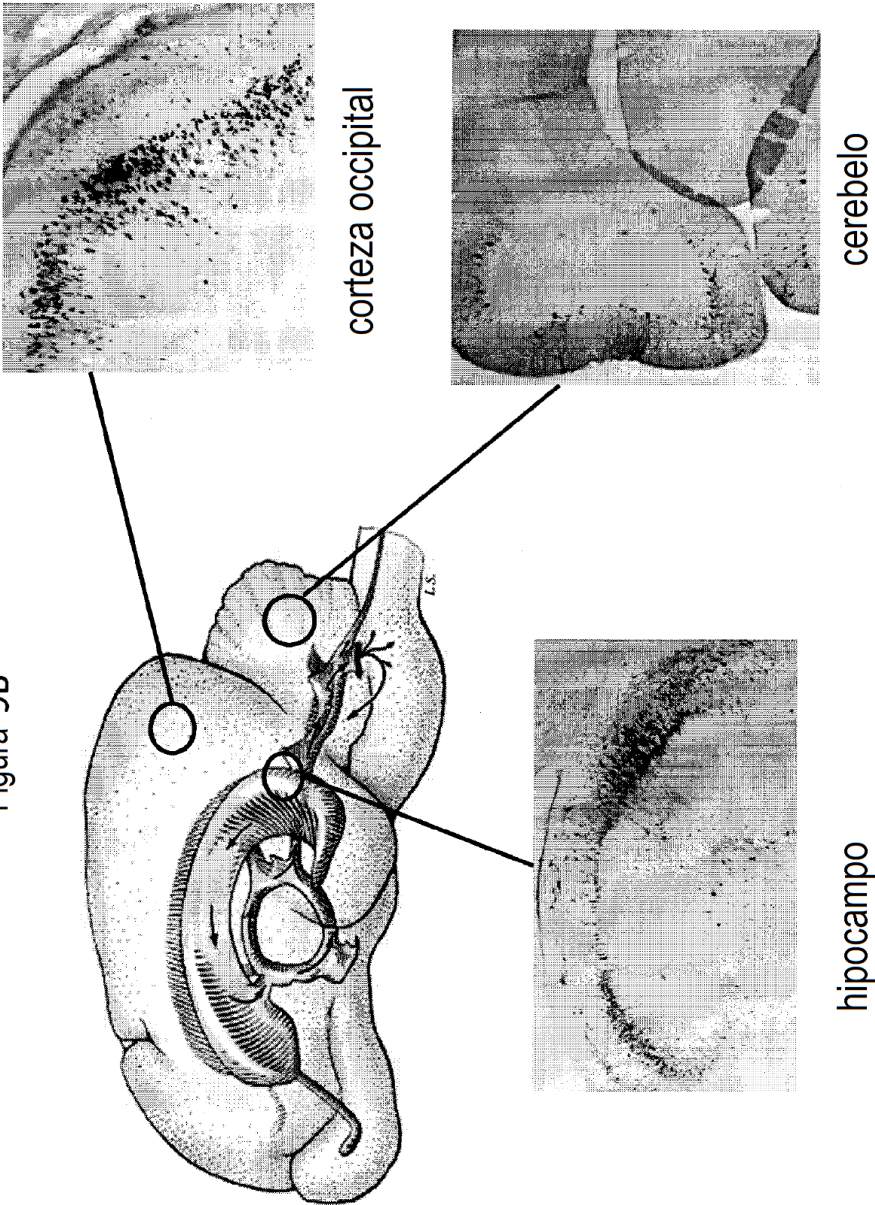


Figura 10

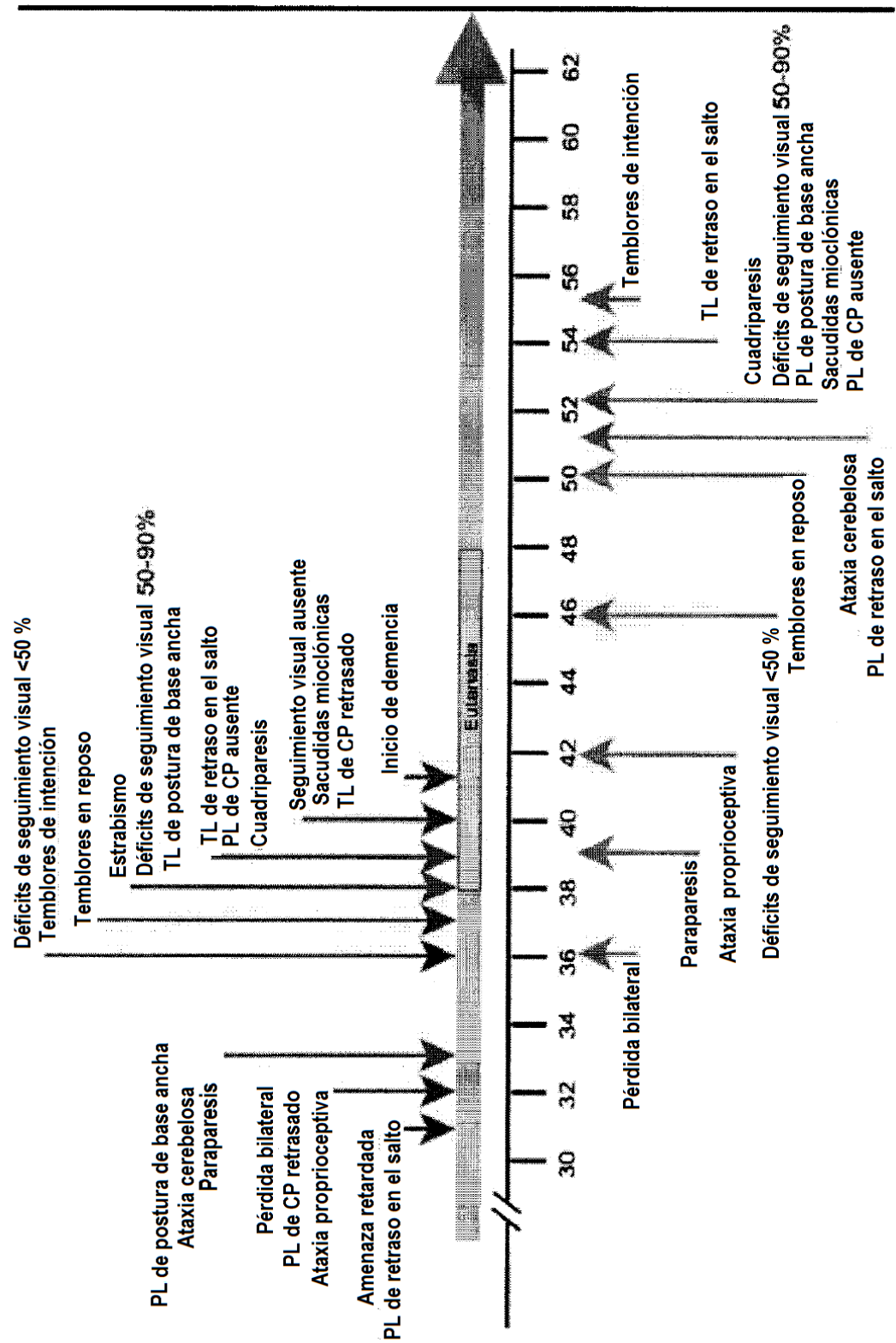


Figura 11

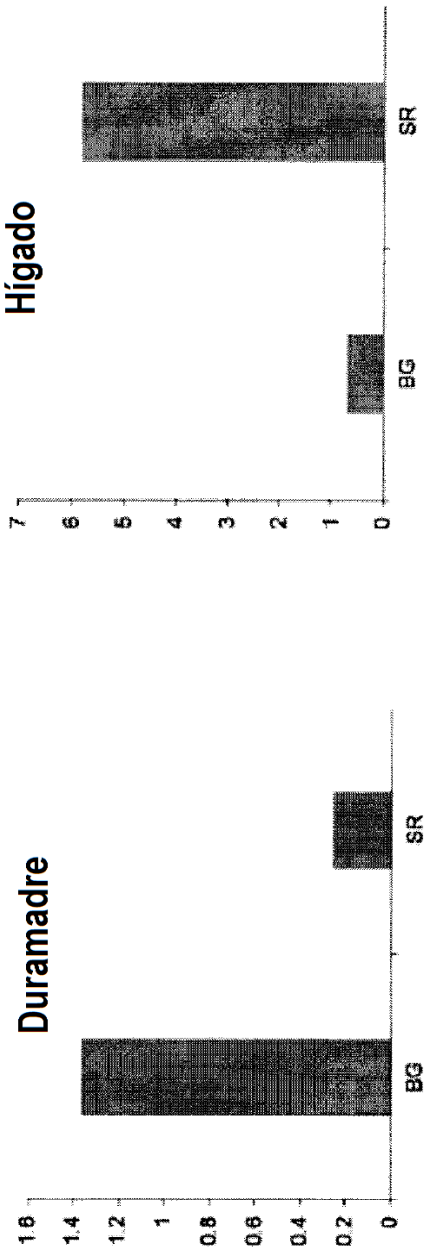


Figura 12

Evaluación *in vivo* de AAV2/2

Suministro de TPP1 en cerebro de rhesus

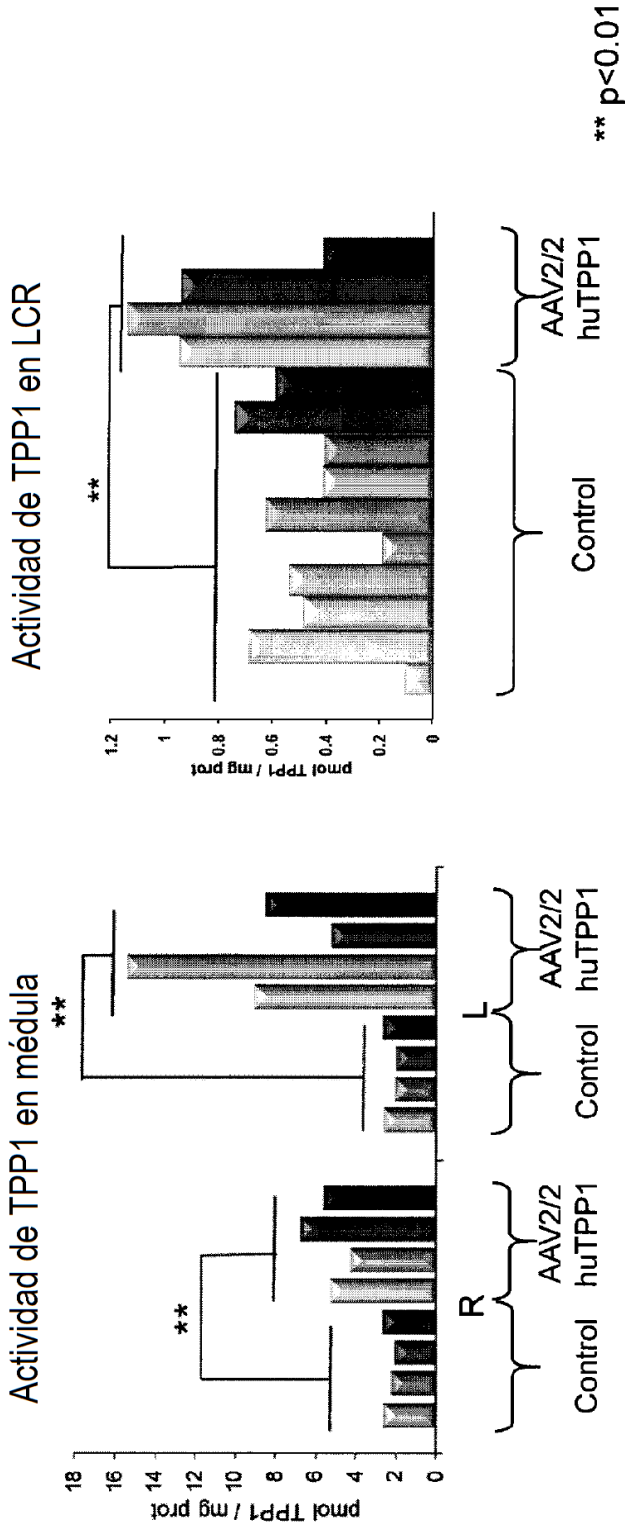
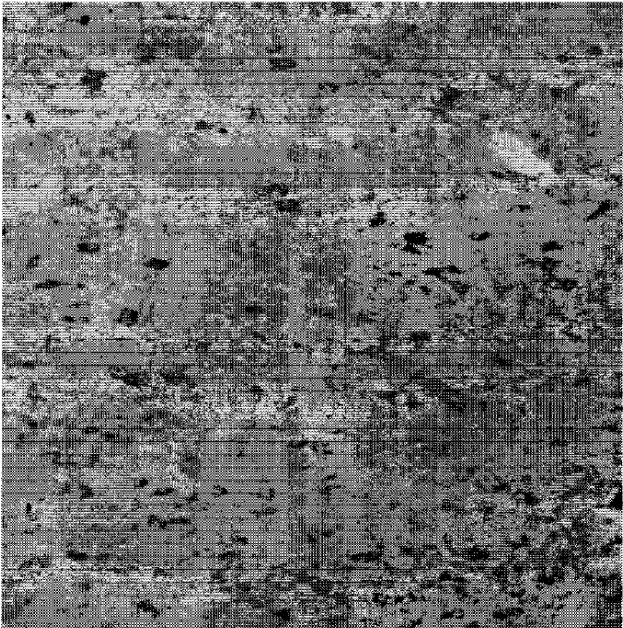


Figura 13

AAV2/2 huCLN2



Control

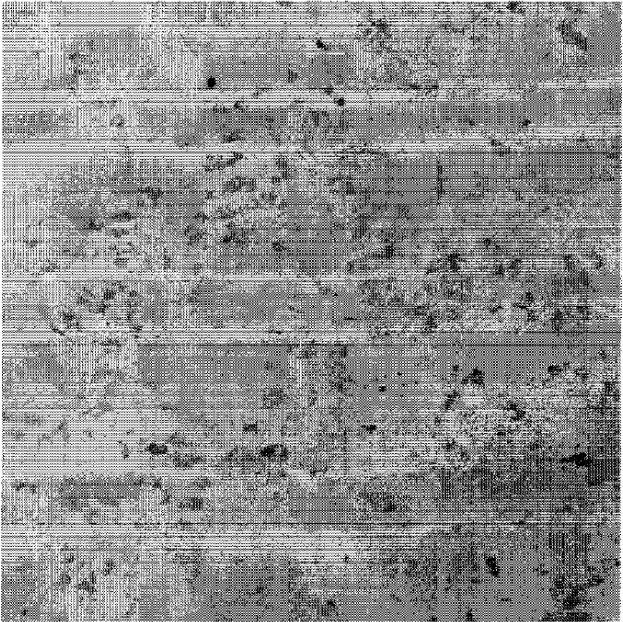


Figura 14**Secuencia de aminoácidos de TPP1 humana:**

MGLQACLLGLFALILSGKCSYSPEPDQRRTLPPGWVSLGRADPEEELSITFALRQONVERLSEL
 VQAVSDPSSPOYGKYLLENVADLVRPSPLTLHTVQKWLLAAGAOKCHSVITQDFLTCWLSIRQ
 AELLPLGAEFHHYVGGPTETHVVRSPHPYQLPQALAPHVDFVGGLLHHFPPTSSLRQRPEPQVTG
 TVGLHLGVTPSVIRKRYNLTSQDVSGTSNNSQACAQFLEQYFHDSDLAQFMRLFNGNFAHQAS
 VARVVGQQGRGRAGIEASLDVQYLSMAGANIISTWVYSSPGRHEGQEPFLQWLMLLSNESALPHV
 HTVSYGDDDESLSSAYIQRVNTELMKAAARGLTLLFASGDSGAGCWSVSGRHQFRPTFPASSPY
 VTTVGGTSFQEPFLITNEIVDYISGGGFSNVFPRPSYQEEAVTKFLSSSPHLPSSYFNASGRA
 YPDVAALSDGYWVVSNRVPIPVWSGTSASTPVFGGILSLINEHRILSGRPPLGFLNPRLYQQHG
 AGLFDVTRGCHESCLDEEVEGQGFCSGPGWDPVTGWGTPNFPALLKTLNLP

Figura 15 -- Secuencia de ácidos nucleicos de TPP1 humana:

1	cgcggaagg	cagaatgga	ctccaagcct	gcctcctagg	gctctttgcc	ctcctcctct
61	ctggcaaatg	cagttacagc	ccggagcccg	accagcggag	gacgetgccc	ccaggetggg
121	tgtccctggg	ccgtgcccac	cctgaggaag	agctgagtct	cacctttgcc	ctgagacagc
181	agaatgtgga	aagactctcg	gagctggtgc	aggctgtgtc	ggatcccagc	tctcctcaat
241	acggaaaata	cctgacccta	gagaatgtgg	ctgatctggt	gaggccatcc	ccactgaccc
301	tccacacggt	gcaaaaatgg	ctcttgccag	ccggagccca	gaagtgccat	tctgtgatca
361	cacaggactt	tctgacttgc	tggctgagca	tccgacaagc	agagctgctg	ctccctgggg
421	ctgagtttca	tactatgtg	ggaggaccta	cggaaaccca	tgttgtaagg	tccccacatc
481	cctaccagct	tccacaggcc	ttggccccc	atgtggactt	tgtgggggga	ctgcaccatt
541	ttcccccaac	atcatccctg	aggcaacgtc	ctgagccgca	ggtgacaggg	actgtaggcc
601	tgcactctgg	ggtaaccccc	tctgtgatcc	gtaagcgata	caacttgacc	tcacaagacg
661	tgggctctgg	caccagcaat	aacagccaag	cctgtgccc	gttccctggg	cagtatttcc
721	atgactcaga	cctggctcag	ttcatgcgcc	tcttcgggtg	caactttgca	catcaggcat
781	cagtagcccg	tgtggttgg	caacagggcc	ggggccgggc	cgggattgag	gccagtctag
841	atgtgcagta	cctgatgagt	gctggtgcc	acatctccac	ctgggtctac	agtagccctg
901	gccggcatga	gggacaggag	cccttcctgc	agtggtcat	gctgctcagt	aatgagtcag
961	ccctgccaca	tgtgcatact	gtgagctatg	gagatgatga	ggactccctc	agcagcgcct
1021	acatccagcg	ggtcaacact	gagctcatga	aggctgctgc	tccgggtctc	accctctctc
1081	tgcctcagg	tgacagtggg	gccgggtgtt	ggtctgtctc	tgggaagacac	cagttccgcc
1141	ctaccttccc	tgctccagc	ccctatgtca	ccacagtggg	aggcacatcc	ttccaggaac
1201	ctttcctcat	cacaaatgaa	attgttgact	atatcagtgg	tgggtgcttc	agcaatgtgt
1261	tcccacggcc	ttcataccag	gaggaagctg	taacgaagtt	cctgagctct	agccccacc
1321	tgccaccatc	cagttacttc	aatgccagtg	gccgtgctta	cccagatgtg	gctgcacttt
1381	ctgatggcta	ctgggtgggc	agcaacagag	tgccatttcc	atgggtgtcc	ggaacctcgg
1441	cctctactcc	agtgtttggg	gggatccctat	ccttgatcaa	tgagcacagg	atccttagtg
1501	gccgcccccc	tcttggtttt	ctcaacccaa	ggctctacca	gcagcatggg	gcaggactct
1561	ttgatgtaac	ccgtggctgc	catgagctct	gtctggatga	agaggttagag	ggccagggtt
1621	tctgctctgg	tcctggctgg	gatcctgtaa	caggctgggg	aacacccaac	ttcccagctt
1681	tgtgaagac	tctactcaac	ccctgaccct	ttcctatcag	gagagatggc	ttgtccctcg
1741	ccctgaagct	ggcagttcag	tcccttatcc	tgccctgttg	gaagccctgc	tgaaccttca
1801	actattgact	gctgcagaca	gcttatctcc	ctaaccctga	aatgctgtga	gcttgacttg
1861	actcccaacc	ctaccatgct	ccatcatact	caggtctccc	tactcctgcc	ttagattcct
1921	caataagatg	ctgtaactag	cattttttga	atgcctctcc	ctcgcctctc	catctttctc
1981	ttttcaatca	ggcttttcca	aagggttgta	tacagactct	gtgcactatt	tcacttgata
2041	ttcattcccc	aattcaactgc	aaggagacct	ctactgtcac	cgtttactct	ttcctacctc
2101	gacatccaga	aacaatggcc	tocagtgcac	acttctcaat	ctttgcttta	tggcctttcc
2161	atcatagttg	cccactccct	ctccttactt	agcttccagg	tcttaacttc	tctgactact
2221	cttgtcttcc	tctctcatca	atttctgctt	cttcatggaa	tgtgtacctt	cattgtctca
2281	ttttagattt	tttgccttcc	tcagtttact	cattgtcccc	tggaaacaaat	cactgacatc

```

2341 tacaaccatt accatctcac taaataagac tttctatcca ataatgattg atacctcaaa
2401 tgtaagatgc gtgatactca acatttcacg gtccaccttc ccaaccccaa acaattccat
2461 ctcgtttctt cttggtaaat gatgctatgc tttttccaac caagccagaa acctgtgtca
2521 tcttttcacc ccaccttcaa tcaacaagtc ctcaatcaac aagtcctact gactgcacat
2581 cttaaatata tctttatcag tccacaagtc cttccaatta tatttcccaa gtatatctag
2641 aacttatcca cttatatccc cactgctact accttagttt agggctatat tctottgaaa
2701 aaaagtgtcc ttacttcctg ccaatcccca agtcatcttc cagagtaaaa tgcaaatccc
2761 atcaggccac ttggatgaaa acccttcaag gattactgga tagaattcag gctttccctt
2821 ccagccccc aatcatagctc acaaaccttc cttgctatct gttcttaagt aaaaaatcat
2881 ttttctctct cctccccc aacccaagga actctcactc ttgctcaagc tgttcctgct
2941 ccttaccacc cctgatacaa ctgccagggtt aatttccaga attcttgcaa gactcagttc
3001 agaagtcacc ttctttcgtg aatgttttga ttccctgagg ctactttatt ttggtatggc
3061 tgaaaaatcc tagattttct aaacaaaacc tgtttgaatc ttggttctga tatggactag
3121 gagagagact gggtaagta agcttatctc cctgaggctg tttctcctgc tgtaagtgt
3181 gaatatcaat acctgccttt cataatcac agggataaaa gtggaataat gttgataaca
3241 gtgcttggca cctggaagta ggtggcagat gttaacgcc ttctccctt gcactgcgcc
3301 cctgtgcct acctctagca ttgtaacgac cacatagtat tgaaatggcc agtttacttg
3361 tctgccttcc tttccaagac cgttggtgcc tagaggacta gaatcgtgtc ctatttaact
3421 ttgtgttccc aggtcctagc tcaggagttg gcaaataaga attaatgtc tgctacaccg
3481 aaacaaa

```

Figura 23 – Secuencia de TTP1 de Macaca mulatta (macaco rhesus)

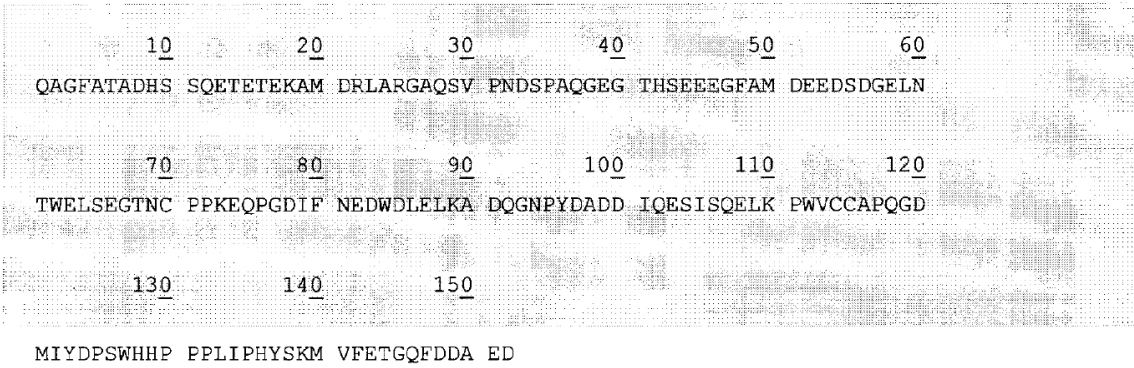


Figura 24 -- Secuencia de TTP1 de Macaca fascicularis (macaco cangrejero) (mono Cynomolgus)

