AVV2capPro (SEQ ID NO:1) - AVV4capPro (SEQ ID NO:2) Alignment

```
CLUSTALW (v1.83) multiple sequence alignment

2 Sequences Aligned          Alignment Score = nan
Gaps Inserted = 7            Conserved Identities = 446

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
    Open Gap Penalty = 10.0   Extend Gap Penalty = 0.1
    Similarity Matrix: gonnet

Multiple Alignment Parameters:
    Open Gap Penalty = 10.0   Extend Gap Penalty = 0.1
    Delay Divergent = 40%     Gap Distance = 8
    Similarity Matrix: gonnet

Processing time: 0.2 seconds

AAV4capPro     1 -MTDGVLPDWLEDNLSEGVREWWALQPGAPKPKANQQHQDNARGLVLPGYKYLGPGNGLD  59
AAV2capPro     1 MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD  60
                 .*************.*****.*.** *.** * **  ..*.* .****************** ****

AAV4capPro    60 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQQRLQGDTSFGGNLGRAVFQ 119
AAV2capPro    61 KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
                 ****** ***************.** .*********************.**. ********************

AAV4capPro   120 AKKRVLEPLGLVEQAGETAPGKKRPLIESPQQPDSSTGIGKKGKQPAKKKLVFEDETGAG 179
AAV2capPro   121 AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPVEPDSSSGTGKAGQQPARKRLNFGQTGDAD 180
                 ****************.   ********** ** .****.* ** *.***.*.* *     *
```

FIG.1A


AAV4capPro 180 DGP---PEGSTSGAMS--DDSEMRAAAGGAAVEGGQGADGVGNASGDWHCDSTWSEGHVT 234
AAV2capPro 181 SVPDPQPLGQPPAAPSGLGTNTMATGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDRVI 240
AAV4capPro 235 TTSTRTWVLPTYNNHLYKRLG---ESLQSNTYNGFSTPWGYFDFNRFHCHFSPRDWQRLI 291
AAV2capPro 241 TTSTRTWALPTYNNHLYKQISSQSGASNDNHYFGYSTPWGYFDFNRFHCHFSPRDWQRLI 300
AAV4capPro 292 NNNWGMRPKAMRVKIFNIQVKEVTTSNGETTVANNLTSTVQIFADSSYELPYVMDAGQEG 351
AAV2capPro 301 NNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGSAHQG 360
AAV4capPro 352 SLPPFPNDVFMVPQYGYCGLVTGNTSQQQTDRNAFYCLEYFPSQMLRTGNNFEITYSFEK 411
AAV2capPro 361 CLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSYTFED 417
AAV4capPro 412 VPFHSMYAHSQSLDRLMNPLIDQYLWGLQSTTTGTTLNAGTATTNFTKLRPTNFSNFKKN 471
AAV2capPro 418 VPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTNTPSGTTT-QSRLQFSQAGASDIRDQSRN 476
AAV4capPro 472 WLPGPSIKQQGFSKTANQNYKIPATGSDSLIKYETHSTLDGRWSALTPGPPMATAGPADS 531
AAV2capPro 477 WLPGPCYRQQRVSKTSADNNNSEYSWTG-----ATKYHLNGRDSLVNPGPAMASHKDDEE 531

FIG.1B

```
AAV4capPro   532 KFS-NSQLIFAGPKQNGNTATVPGTLIFTSEEELAATNATDTDMWGNLPGGDQSNSNLPT 590
AAV2capPro   532 KFFPQSGVLIFGKQGSEKTNVDIEKVMITDEEEIRTTNPVATEQYGSVSTNLQRGNRQAA 591
                 *  .* ..  * .   *     .. * ***. .**   *.  * .  . * .   .

AAV4capPro   591 VDRLTALGAVPGMVWQNRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKHPPPQIFIKNT 650
AAV2capPro   592 TADVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPPQILIKNT 651
                    ... * .******* **.* ********************.**********  ****

AAV4capPro   651 PVPANPATTFSSTPVNSFITQYSTGQVSVQIDWEIQKERSKRWNPEVQFTSNYGQQNSLL 710
AAV2capPro   652 PVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYNKSVNVD 711
                 *******.*****..    ********************.*.**.**** ********.*.*****..   .

AAV4capPro   711 WAPDAAGKYTEPRAIGTRYLTHHL 734
AAV2capPro   712 FTVDTNGVYSEPRPIGTRYLTRNL 735
                    . *. * *.**** *********..*
```

FIG.1C

AVV2capNuc (SEQ ID NO:3) - AVV4capNuc1 (SEQ ID NO:4) Alignment

```
ClustalW (v1.83) multiple sequence alignment

2 Sequences Aligned          Alignment Score = nan
Gaps Inserted = 10           Conserved Identities = 1440

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
    Open Gap Penalty = 10.0   Extend Gap Penalty = 5.0

Multiple Alignment Parameters:
    Open Gap Penalty = 30.0   Extend Gap Penalty = 5.0
    Delay Divergent = 40%     Transitions: Weighted

Processing time: 1.8 seconds


1. AAV2capNuc vs. AAV4capNuc1

   Aligned Length = 2235   Gaps = 10
   Identities = 1440 (65%)

AAV2capNuc      1 ATGGCTGCCGATGGTTATCTTCCAGATTGGCTCGAGGACACTCTCTCTGAAGGAATAAGA   60
AAV4capNuc1     1 ---ATGACTGACGGTTACCTTCCAGATTGGCTAGAGGACAACCTCTCTGAAGGCGTTCGA   57
                      * ** ***** ************** *******  ***********  *  **

AAV2capNuc     61 CAGTGGTGGAAGCTCAAACCTGGCCCACCACCACCAAAGCCCGCAGAGCGGCATAAGGAC  120
AAV4capNuc1    58 GAGTGGTGGGCGCTGCAACCTGGAGCCCCTAAACCCAAGGCAAATCAACAACATCAGGAC  117
                   ********  ***  *******  * **   *** *** *     * *  *** *****
```

FIG.2A

```
AAV2capNuc   121 GACAGCAGGGGTCTTGTGCTTCCTGGGTACAAGTACCTCGGACCCTTCAACGGACTCGAC 180
AAV4capNuc1  118 AACGCTCGGGGTCTTGTGCTTCCGGGTTACAAATACCTCGGACCCGGCAACGGACTCGAC 177
                   **    ********************** ****** ********************** 

AAV2capNuc   181 AAGGGAGAGCCCGGTCAACGAGGCAGACGCCGCGGCCCTCGAGCACGACAAAGCCTACGAC 240
AAV4capNuc1  178 AAGGGGGAACCCGTCAACGCAGCGGACGCGGCAGCCCTCGAGCACGACAAGGCCTACGAC 237
                 ***** ** ** ********  ** ***** ** ********************** **********

AAV2capNuc   241 CGGCAGCTCGACAGCGGAGACAACCCGTACCTCAAGTACAACCACGCCGACGCGGAGTTT 300
AAV4capNuc1  238 CAGCAGCTCAAGGCCGGTGACAACCCCTACCTCAAGTACAACCACGCCGACGCGGAGTTC 297
                 * ********  ***  ********** ********************************** 

AAV2capNuc   301 CAGGAGCGCCTTAAAGAAGATACGTCTTTTGGGGGCAACCTCGGACGAGCAGTCTTCCAG 360
AAV4capNuc1  298 CAGCAGCGGCTTCAGGGCGACACATCGTTTGGGGGCAACCTCGGCAGAGCAGTCTTCCAG 357
                 *** ***** *** * *  ** ** ** ********************  ********** 

AAV2capNuc   361 GCGAAAAAGAGGGTTCTTGAACCTCTGGGCCTGGTTGAGGAACCTGTTAAGACGGCTCCG 420
AAV4capNuc1  358 GCCAAAAAGAGGGTTCTTGAACCTCTTGGTCTGGTTGAGCAAGCGGGTGAGACGGCTCCT 417
                 ** ********************** ** ********** ** * * * * ********** 

AAV2capNuc   421 GGAAAAAAGAGGCCGGTAGAGCACTCTCCTGTGGAGCCAGACTCCTCCTCGGGAACCGGA 480
AAV4capNuc1  418 GGAAAGAAGACCGTTGATTGAATCCCCCCAGCAGCCCGACTCCTCCACGGGTATCGGC 477
                   ***** ***** *** *     * ** **   * **** ********** **** * *** 

AAV2capNuc   481 AAGGCGGGCCAGCAGCCTGCAAGAAAAAGATTGAATTTTGGTCAGACTGGAGACGCAGAC 540
AAV4capNuc1  478 AAAAAAGGCAAGCAGCCGGCTAAAAAGAAGCTCGTTTTCGA----------AGACGAAACT 528
                   **    *** ******** ** * *** *   *   *** *                *****  *
```

FIG.2B

```
AAV2capNuc   541 TCAGTACCTGACCCCCAGCCTCTCGGACAGCCACCAGCAGCCCCCTCTGGTCTGGGAACT 600
AAV4capNucl  529 GGAGCCAGGCGACGGGACCCCCCTGAGGGATCAACTTCCGGAGCCCATGTCTGAT------GAC 582
                    ** *   ***   *  ***    ***     *  * * * ****   **** *

AAV2capNuc   601 AATACGATGGCTACAGGCAGTGGCGCACCAATGGCAGACAATAACGAGGGCGCCCGACGGA 660
AAV4capNucl  583 AGTGAGATGCGTGCAGCAGCTGGCGAGGCTGCAGTCGAGGGCGGACAAGGTGCCGATGGA 642
                  * *  ****  * ***    *****  * *    *   **     * ** ***** ***

AAV2capNuc   661 GTGGGTAATTCCTCGGGAAATTGGCATTGCGATTCCACATGGATGGGCGACAGAGTCATC 720
AAV4capNucl  643 GTGGGTAATGCCTCGGGTGATTGGCATTGCGATTCCACCTGGTCTGAGGGCCACGTCACG 702
                  ********* ********  ********************** ***   *  * *   ****

AAV2capNuc   721 ACCACCAGCACCCGAACCTGGGCCCTGCCCACCTACAACAACCACCTCTACAAACAAATT 780
AAV4capNucl  703 ACCACCAGCACCAGAACCTGGGTCTTGCCCACCTACAACAACCACCTCTACAAGCGACTC 762
                  ********** ********** * ********************************* * * *

AAV2capNuc   781 TCCAGCCAATCAGGAGCCTCGAACGACAATCACTACTTTGGCTACAGCACCCCTTGGGGG 840
AAV4capNucl  763 GG---------AGAGAGCCTGCAGTCCAACACCTACAACGGATTCTCCACCCCCTGGGGA 813
                           **   * * *  ***   ****   ** * *  ****** *****

AAV2capNuc   841 TATTTTGACTTCAACAGATTCCACTGCCACTTTTCACCACGTGACTGGCAAAGACTCATC 900
AAV4capNucl  814 TACTTTGACTTCAACCGCTTCCACTGCCACTTCTCACCACGTGACTGGCAGCGGACTCATC 873
                  ** ********** * ********** ********** ********** *********

AAV2capNuc   901 AACAACAACTGGGGATTCCGACCCAAGAGACTCAACTTCAAGCTCTTTAACATTCAAGTC 960
AAV4capNucl  874 AACAACAACTGGGGCATGCGACCCAAAGCCATGCGGGTCAAAATCTTCAACATCCAGGTC 933
                  ********** * *********     *     ****  **** ***** ** ***
```

FIG.2C

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

AAV2capNuc  1021 CAGGTGTTTACTGACTCGGAGTACCAGCTCCCGTACGTCCTCGGCTCGGCGCATCAAGGA 1080
AAV4capNuc1  994 CAGATCTTTGCGGACTCGTCGTACGAACTGCCGTACGTGATGGATGCGGGTCAAGAGGGC 1053
                 *** * *** * ******  **** * ** *********  * *   ***  **  * **

AAV2capNuc  1081 TGCCTCCCGCCCGTTCCCAGCAGACGTCTTCATGGTGCCACAGTATGGATACCTCACCCTG 1140
AAV4capNuc1 1054 AGCCTGCCTCCTTTTCCCAACGACGTCTTTATGGTGCCCCAGTACGGCTACTGTGGACTG 1113
                 ****  ** ** ** **    *********  ********* ***** ** ***     ***

AAV2capNuc  1141 AACAACGGGAGT--CAGGCAGTAGGACGCTC-------TTCATTTTACTGCCTGGAGTAC 1191
AAV4capNuc1 1114 GTGACCGGCAACACTTCGCAGCAACAGACTGACAGAAATGCCTTCTACTGCCTGGAGTAC 1173
                       * *** *      **** *  *  **        * * ** **********

AAV2capNuc  1192 TTTCCTTCTCAGATGCTGCGTACCGGAAACAACTTTACCTTCAGCTACACTTTTGAGGAC 1251
AAV4capNuc1 1174 TTTCCTTCGCAGATGCTGCGGACTGGCAACAACTTTGAAATTACGTACAGTTTTGAGAAG 1233
                 ********* ********** ** ** **********    * *   **** ******* *

AAV2capNuc  1252 GTTCCTTTTCCACAGCAGCTACGCTCACAGCCAGAGTCTGGACCGTCTCATGAATCCTCTC 1311
AAV4capNuc1 1234 GTGCCTTTTCCACTCGATGTACGCGCACAGCCAGAGCCCTGGACCGGCTGATGAACCCTCTC 1293
                 ** **********   *  ****** ********** ********** ** ****** *******

AAV2capNuc  1312 ATCGACCAGTACCTGTATTACTTGAGCAGAACAAACACTCCAAGTGGAACCACCACGCAG 1371
AAV4capNuc1 1294 ATCGACCAGTACCTGTGGGGACTGCAATCGACCACCACCGGAACCACCCTGAATGCCGGG 1353
                 **********  **     ** * ***  **      *   *  *
```

FIG.2D

```
AAV2capNuc  1372 TCAA--GGCTTCAGTTTCTCAGGCCGGAGCG-AGTGACATTCGGGACCAGTCTAGGAAC 1428
AAV4capNuc1 1354 ACTGCCACCACCAACTTTACCAAGCTGCGGCCTACCAACTTTTCCAACTTTAAAAAGAAC 1413
                   *   **  ***  ** ** *  **  *   ** **    **      * ****

AAV2capNuc  1429 TGGCTTCCTGGACCCTGTTACCGCCAGCAGCGAGTATCAAAGACATCTGCGGATAACAAC 1488
AAV4capNuc1 1414 TGGCTGCCCGGGCCTTCAATCAAGCAGCAGGGCTTCTCAAAGACTGCCAATCAAAACTAC 1473
                 ***** ** ** ** *    *   ****** *  * ********* *    * *** **

AAV2capNuc  1489 AACAG---TGAATACTCGTGGACTGGAGCTACCAAGTACCA----------------CCTCAAT 1533
AAV4capNuc1 1474 AAGATCCCTGCCACCGGGTCAGACAGTCTCATCAAATACGAGACGGCACAGCACTCTGGAC 1533
                 ** *   **    *  **      *   * *** *** *                ** *

AAV2capNuc  1534 GGCAGAGACTCTCTGGTGAATCCGGGCCCGGCCATGGCAAGCCACAAGGACGATGAAGAA 1593
AAV4capNuc1 1534 GGAAGATGGAGTGCCCTGACCCCCGGACCTCCAATGGCCACGGCTGGACCTGCGGACAGC 1593
                   ** ***    *   ***  ** ** **  * ***** *          *  **

AAV2capNuc  1594 AAGTTTTTTCCTCAGAGCGGGGGTTCTCATCTTTGGGAAGCAAGGCTCAGAGAAAACAAAT 1653
AAV4capNuc1 1594 AAGTTCAG--CAACAGCCAGCTCATCTTTGCGGGGCCTAAACAGAACGGCAACACGGCC 1650
                   *****      * ***  * *  ** *     ***     **      *  ** **

AAV2capNuc  1654 GTGGACATTGAAAAGGTCATGATTACAGACGAAGAGGAAATCAGGACAACCAATCCCGTG 1713
AAV4capNuc1 1651 ACCGTACCCGGGACTCTGATCTTCACCTCTGAGGAGGAGCTGGCAGCCACCAACGCCACC 1710
                       *   *  *  ** *  **     ** *****  *    * ***** **

AAV2capNuc  1714 GCTACGGAGCAGTATGGTTCTGTATCTACCAACCTCCAGAGAGGCAACAGACAAGCAGCT 1773
AAV4capNuc1 1711 GATACGGACATGTGGGGCAACCTACCTGGCGGTGACCAGAGGCAACAGCCTGCCGACC 1770
                   * *******  **  **  ** **  *     ******  ** **  *  *  * *
```

FIG.2E

```
AAV2capNuc  1774 ACCGCAGATGTCAACACACAAGGCGTTCTTCCAGGCATGGTCTGGCAGGACAGAGATGTG 1833
AAV4capNuc1 1771 GTGGACAGACTGACAGCCTTGGGAGCCGTGCCTGGAATGGTCTGGCAAAACAGAGACATT 1830
                       *   *  *    *  * *  **  ** ********** ********  *

AAV2capNuc  1834 TACCTTCAGGGGCCCATCTGGGCAAAGATTCCACACACGGACGGACATTTTCACCCCTCT 1893
AAV4capNuc1 1831 TACTACCAGGGTCCCATTTGGGCCAAGATTCCTCATACCGATGGACACTTTCACCCCTCA 1890
                    ***   ***** ***** ***** ********** ** ** ** ****** **********

AAV2capNuc  1894 CCCCTCATGGGTGGATTCGGACTTAAACACCCTCCTCCACAGATTCTCATCAAGAACACC 1953
AAV4capNuc1 1891 CCGCTGATTGGTGGGTTTGGGCTGAAACACCCGCCTCCTCAAATTTTTATCAAGAACACC 1950
                    ** ** ** ***** ** ** ** ********** ***** ** *** * ***********

AAV2capNuc  1954 CCGGTACCTGCGAATCCTTCGACCACCTTCAGTGCGGCAAAGTTTGCTTCCTTCATCACA 2013
AAV4capNuc1 1951 CCGGTACCTGCGAATCCTGCAACGACCTTCAGCTCTACTCCGGTAAACTCCTTCATTACT 2010
                    ********************* * ** ********* *  *  * *    ********* **

AAV2capNuc  2014 CAGTACTCCACGGGACAGGTCAGCGTGGAGATCGAGTGGGAGCTGCAGAAGGAAAACAGC 2073
AAV4capNuc1 2011 CAGTACAGCACTGGCCAGGTGTCGGTGCAGATTGACTGGGAGATCCAGAAGGAGCGGTCC 2070
                    *******  *** ** *****    *** **** ** ******* * ********* *

AAV2capNuc  2074 AAACGCTGGAATCCCGAAATTCAGTACACTTCCAACTACAACAAGTCTGTTAATGTGGAC 2133
AAV4capNuc1 2071 AAACGCTGGAACCCCGAGGTCCAGTTTACCTCCAACTACGGACAGCAAAACTCTCTGTTG 2130
                    ********** *****  * **** ** ********** **      * **

AAV2capNuc  2134 TTTACTGTGGACACTAATGGCGTGTATTCAGAGCCTCGCCCCATTGGCACCAGATACCTG 2193
AAV4capNuc1 2131 TGGGCTCCCGATGCGGCTGGGAAATACACTGAGCCTAGGGCTATCGGTACCCGCTACCTC 2190
                    *   **  **  *  ***    **  * ******* *  * ** ** *** * * *****
```

FIG.2F

```
AAV2capNuc  2194 ACTCGTAATCTGTAA 2208
AAV4capNuc1 2191 ACCCACCACCTGTAA 2205
                  ** *   * ******
```

FIG.2G

Human TPP1 amino acid sequence (SEQ ID NO:5).

MGLQACLLGLFALILSGKCSYSPEPDQRRTLPPGWVSLGRADPEEELSLTFALRQQNVER
LSELVQAVSDPSSPQYGKYLTLENVADLVRPSPLTLHTVQKWLLAAGAQKCHSVITQDF
LTCWLSIRQAELLLPGAEFHHYVGGPTETHVVRSPHPYQLPQALAPHVDFVGGLHHFPPT
SSLRQRPEPQVTGTVGLHLGVTPSVIRKRYNLTSQDVGSGTSNNSQACAQFLEQYFHDSD
LAQFMRLFGGNFAHQASVARVVGQQGRGRAGIEASLDVQYLMSAGANISTWVYSSPGR
HEGQEPFLQWLMLLSNESALPHVHTVSYGDDEDSLSSAYIQRVNTELMKAAARGLTLLF
ASGDSGAGCWSVSGRHQFRPTFPASSPYVTTVGGTSFQEPFLITNEIVDYISGGGFSNVFP
RPSYQEEAVTKFLSSSPHLPPSSYFNASGRAYPDVAALSDGYWVVSNRVPIPWVSGTSAS
TPVFGGILSLINEHRILSGRPPLGFLNPRLYQQHGAGLFDVTRGCHESCLDEEVEGQGFCS
GPGWDPVTGWGTPNFPALLKTLLNP
(SEQ ID NO:5)

FIG.3

Human TPP1 nucleic acid sequence (SEQ ID NO:6)

1	cgcggaaggg	cagaatggga	ctccaagcct	gcctcctagg	gctctttgcc	ctcatcctct
61	ctggcaaatg	cagttacagc	ccggagcccg	accagcggag	gacgctgccc	ccaggctggg
121	tgtccctggg	ccgtgcggac	cctgaggaag	agctgagtct	caccttigcc	ctgagacagc
181	agaatgtgga	aagactctcg	gagctggtgc	aggctgtgtc	ggatcccagc	tctcctcaat
241	acggaaaata	cctgacccta	gagaatgtgg	ctgatctggt	gaggccatcc	ccactgaccc
301	tccacacggt	gcaaaaatgg	ctcttggcag	ccggagccca	gaagtgccat	tctgtgatca
361	cacaggactt	tctgacttgc	tggctgagca	tccgacaagc	agagctgctg	ctccctgggg
421	ctgagtttca	tcactatgtg	ggaggaccta	cggaaaccca	tgttgtaagg	tccccacatc
481	cctaccagct	tccacaggcc	ttggcccccc	atgtggactt	tgtgggggga	ctgcaccatt
541	ttcccccaac	atcatccctg	aggcaacgtc	ctgagccgca	ggtgacaggg	actgtaggcc
601	tgcatctggg	ggtaaccccc	tctgtgatcc	gtaagcgata	caacttgacc	tcacaagacg
661	tgggctctgg	caccagcaat	aacagccaag	cctgtgccca	gttcctggag	cagtatttcc
721	atgactcaga	cctggctcag	ttcatgcgcc	tcttcggtgg	caactttgca	catcaggcat
781	cagtagcccg	tgtggttgga	caacagggcc	ggggccgggc	cgggattgag	gccagtctag
841	atgtgcagta	cctgatgagt	gctggtgcca	acatctccac	ctgggtctac	agtagccctg
901	gccggcatga	gggacaggag	cccttcctgc	agtggctcat	gctgctcagt	aatgagtcag
961	ccctgccaca	tgtgcatact	gtgagctatg	gagatgatga	ggactccctc	agcagcgcct
1021	acatccagcg	ggtcaacact	gagctcatga	aggctgctgc	tcggggtctc	accctgctct
1081	tcgcctcagg	tgacagtggg	gccgggtgtt	ggtctgtctc	tggaagacac	cagttccgcc
1141	ctaccttccc	tgcctccagc	ccctatgtca	ccacagtggg	aggcacatcc	ttccaggaac
1201	ctttcctcat	cacaaatgaa	attgttgact	atatcagtgg	tggtggcttc	agcaatgtgt
1261	tcccacggcc	ttcataccag	gaggaagctg	taacgaagtt	cctgagctct	agcccccacc
1321	tgccaccatc	cagttacttc	aatgccagtg	gccgtgccta	cccagatgtg	gctgcacttt
1381	ctgatggcta	ctgggtggtc	agcaacagag	tgcccattcc	atgggtgtcc	ggaacctcgg
1441	cctctactcc	agtgtttggg	gggatcctat	ccttgatcaa	tgagcacagg	atccttagtg
1501	gccgcccccc	tcttggcttt	ctcaacccaa	ggctctacca	gcagcatggg	gcaggactct
1561	ttgatgtaac	ccgtggctgc	catgagtcct	gtctggatga	agaggtagag	ggccagggtt

FIG.4A

1621	tctgctctgg	tcctggctgg	gatcctgtaa	caggctgggg	aacacccaac	ttcccagctt
1681	tgctgaagac	tctactcaac	ccctgaccct	ttcctatcag	gagagatggc	ttgtcccctg
1741	ccctgaagct	ggcagttcag	tcccttattc	tgccctgttg	gaagccctgc	tgaaccctca
1801	actattgact	gctgcagaca	gcttatctcc	ctaaccctga	aatgctgtga	gcttgacttg
1861	actcccaacc	ctaccatgct	ccatcatact	caggtctccc	tactcctgcc	ttagattcct
1921	caataagatg	ctgtaactag	catttttga	atgcctctcc	ctccgcatct	catctttctc
1981	ttttcaatca	ggcttttcca	aagggttgta	tacagactct	gtgcactatt	tcacttgata
2041	ttcattcccc	aattcactgc	aaggagacct	ctactgtcac	cgtttactct	ttcctaccct
2101	gacatccaga	aacaatggcc	tccagtgcat	acttctcaat	ctttgcttta	tggcctttcc
2161	atcatagttg	cccactccct	ctccttactt	agcttccagg	tcttaacttc	tctgactact
2221	cttgtcttcc	tctctcatca	atttctgctt	cttcatggaa	tgctgacctt	cattgctcca
2281	tttgtagatt	tttgctcttc	tcagtttact	cattgtcccc	tggaacaaat	cactgacatc
2341	tacaaccatt	accatctcac	taaataagac	tttctatcca	ataatgattg	atacctcaaa
2401	tgtaagatgc	gtgatactca	acatttcatc	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	tctcttgaaa
2701	aaaagtgtcc	ttacttcctg	ccaatcccca	agtcatcttc	cagagtaaaa	tgcaaatccc
2761	atcaggccac	ttggatgaaa	acccttcaag	gattactgga	tagaattcag	gcttttcccct
2821	ccagccccca	atcatagctc	acaaaccttc	cttgctattt	gttcttaagt	aaaaaatcat
2881	ttttcctcct	ccctccccaa	accccaagga	actctcactc	ttgctcaagc	tgttccgtcc
2941	ccttaccacc	cctgatacaa	ctgccaggtt	aatttccaga	attcttgcaa	gactcagttc
3001	agaagtcacc	ttcttttcgtg	aatgttttga	ttccctgagg	ctactttatt	ttggtatggc
3061	tgaaaaatcc	tagatttttct	aaacaaaacc	tgtttgaatc	ttggttctga	tatggactag
3121	gagagagact	gggtcaagta	agcttatctc	cctgaggctg	tttcctcgtc	tgttaagtgt

FIG.4B

3181 gaatatcaat acctgccttt cataatcacc agggaataaa gtggaataat gttgataaca

3241 gtgcttggca cctggaagta ggtggcagat gttaacgccc ttcctccctt gcactgcgcc

3301 ccctgtgcct acctctagca ttgtaacgac cacatagtat tgaaatggcc agtttacttg

3361 tctgccttcc tttccaagac cgttggtgcc tagaggacta gaatcgtgtc ctatttaact

3421 ttgtgttccc aggtcctagc tcaggagttg gcaaataaga attaaatgtc tgctacaccg

3481 aaacaaa

(SEQ ID NO:6)

FIG.4C

Macaca mulatta (Rhesus macaque) TPP1 amino acid sequence (SEQ ID NO:7)

```
                10                  20                  30                  40                  50                  60
QAGFATADHS SQETETEKAM DRLARGAQSV PNDSPAQGEG THSEEEGFAM DEEDSDGELN

                70                  80                  90                 100                 110                 120
TWELSEGTNC PPKEQPGDIF NEDWDLELKA DQGNPYDADD IQESISQELK PWVCCAPQGD

               130                 140                 150
MIYDESWHHP PPLIPHYSFM VFETGQFDDA ED
```

FIG.5

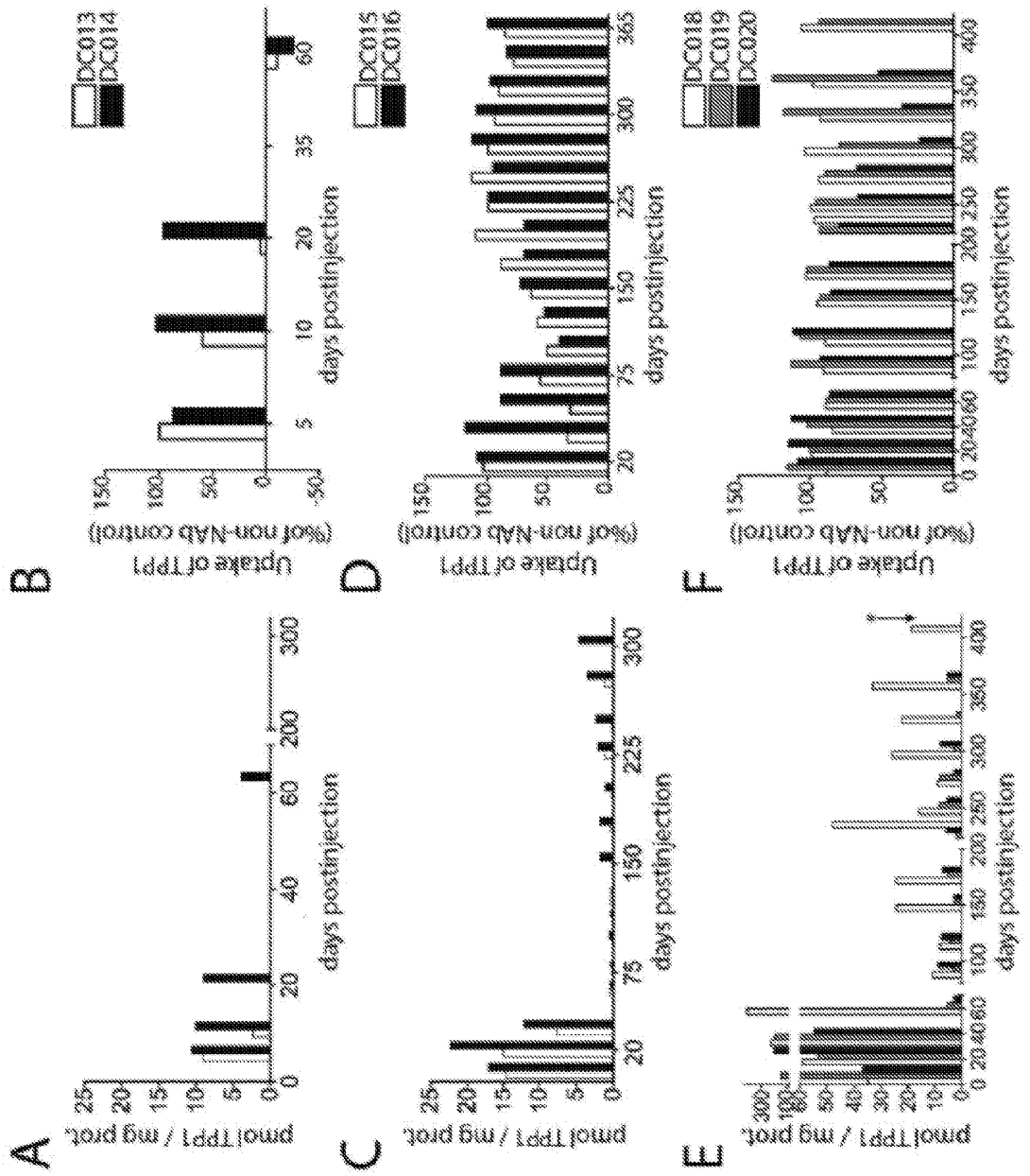
Macaca fascicularis (Crab-eating macaque) (Cynomolgus monkey) TPP1 amino acid sequence (SEQ ID NO:8)

```
                10                  20                  30                  40                  50                  60
QAGFATADHS SQERETEKAM DRLARGAQSV PNDSPARGBG THSEEBGFAM DEEDSDGELN

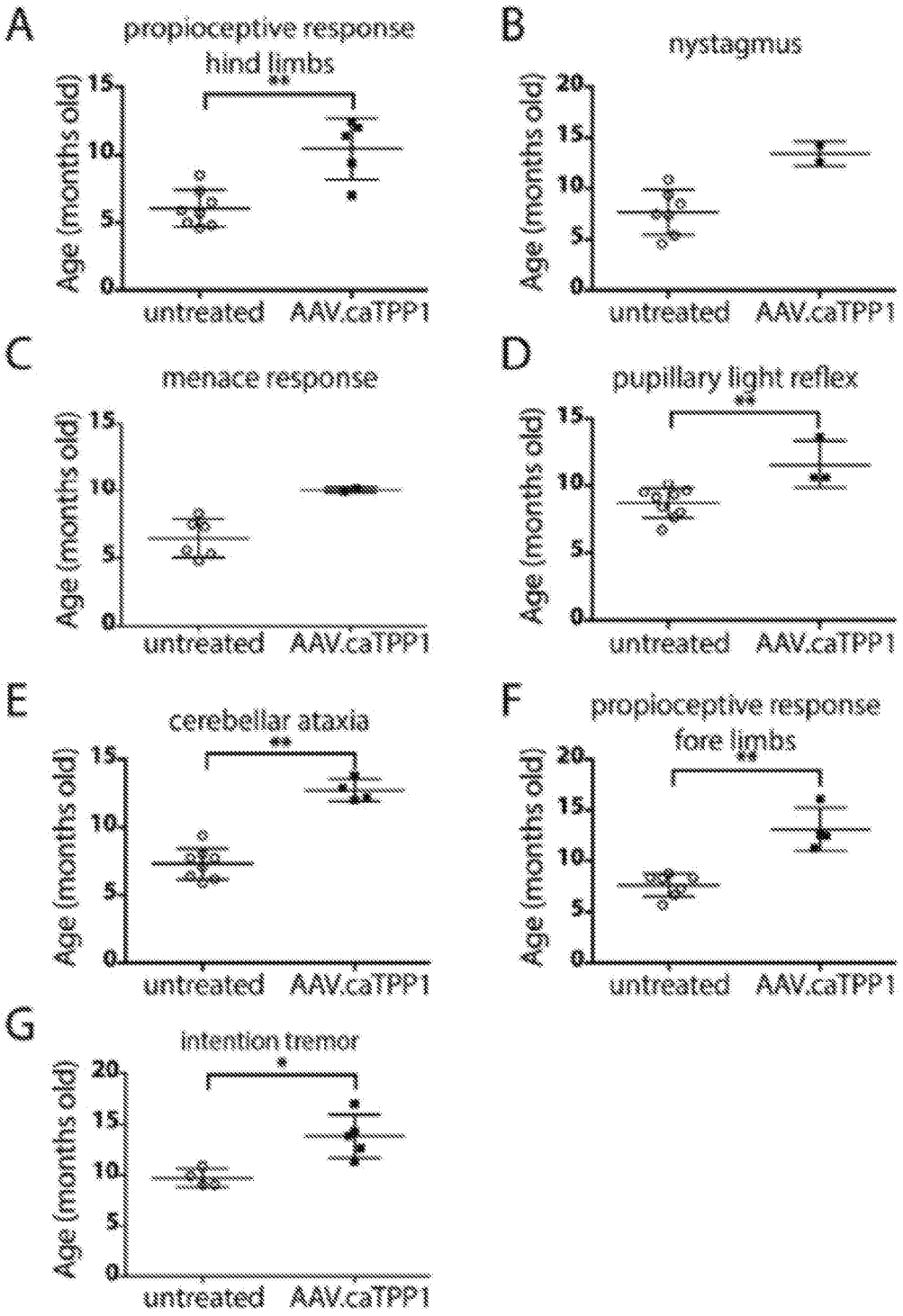
                70                  80                  90                 100                 110                 120
TWELSEGTMC PPKEQPGDIF MEIWDLELKA DQGNPYDADD IQESISQELK FWVCCAPQGD

               130                 140                 150
MIYDFSWHHP PPLIPHYSKM VFETGQFDDA ED
```

FIG.6


A
pmol TPP1 / mg prot.
days postinjection
B
Uptake of TPP1 (%of non-NAb control)
DC013
DC014
days postinjection
C
pmol TPP1 / mg prot.
days postinjection
D
Uptake of TPP1 (%of non-NAb control)
DC015
DC016
days postinjection
E
pmol TPP1 / mg prot.
days postinjection
F
Uptake of TPP1 (%of non-NAb control)
DC018
DC019
DC020
days postinjection

FIGS. 7A-7F


A
propioceptive response
hind limbs
**
Age (months old)
15
10
5
0
untreated
AAV.caTPP1
B
nystagmus
Age (months old)
20
15
10
5
0
untreated
AAV.caTPP1
C
menace response
Age (months old)
15
10
5
0
untreated
AAV.caTPP1
D
pupillary light reflex
**
Age (months old)
15
10
5
0
untreated
AAV.caTPP1
E
cerebellar ataxia
**
Age (months old)
15
10
5
0
untreated
AAV.caTPP1
F
propioceptive response
fore limbs
**
Age (months old)
20
15
10
5
0
untreated
AAV.caTPP1
G
intention tremor
*
Age (months old)
20
15
10
5
0
untreated
AAV.caTPP1

FIGS. 8A-8G

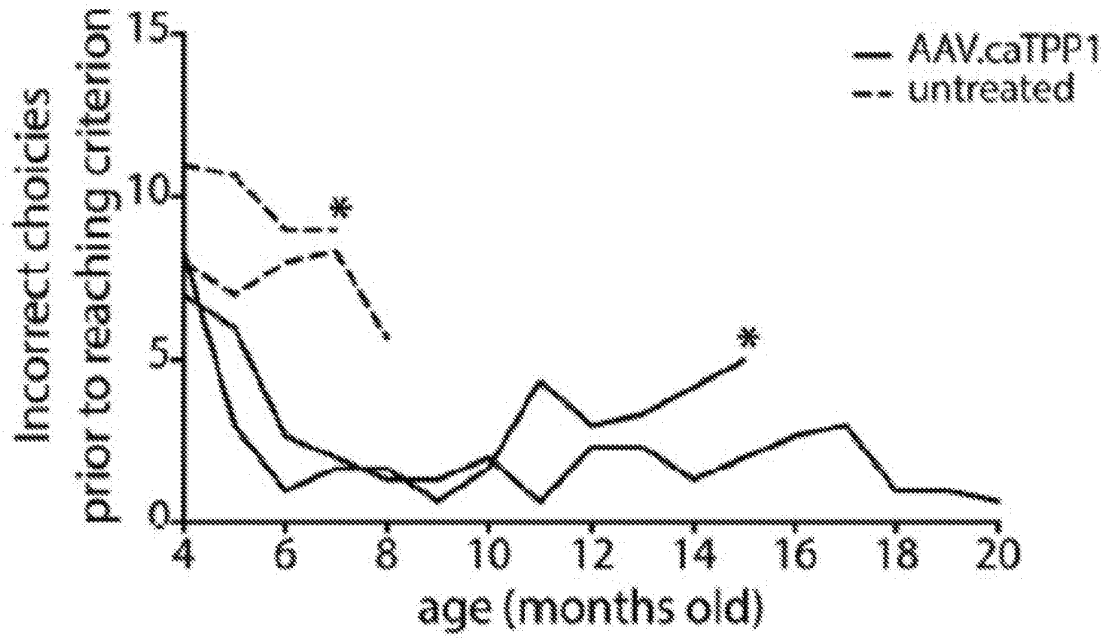

Incorrect choices
prior to reaching criterion
15
10
5
0
4
6
8
10
12
14
16
18
20
age (months old)
AAV.caTPP1
untreated
*
*

FIG.9

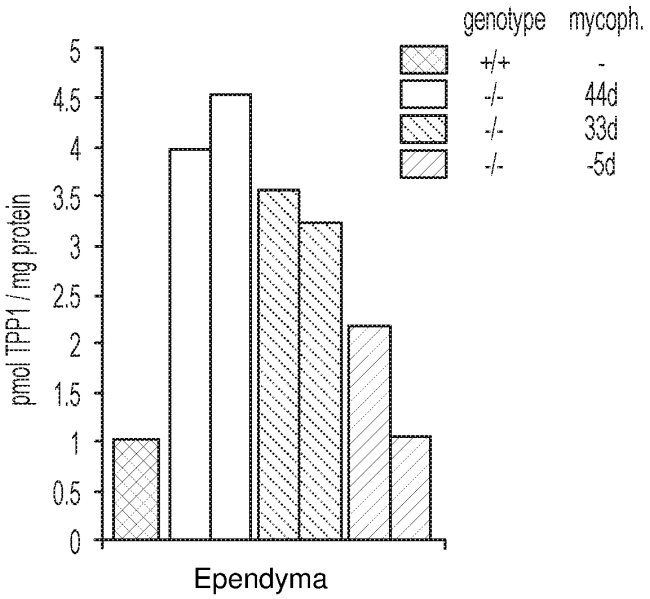

genotype
mycoph.
+/+
-
-/-
44d
-/-
33d
-/-
-5d
pmol TPP1 / mg protein
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Ependyma

FIG. 10A

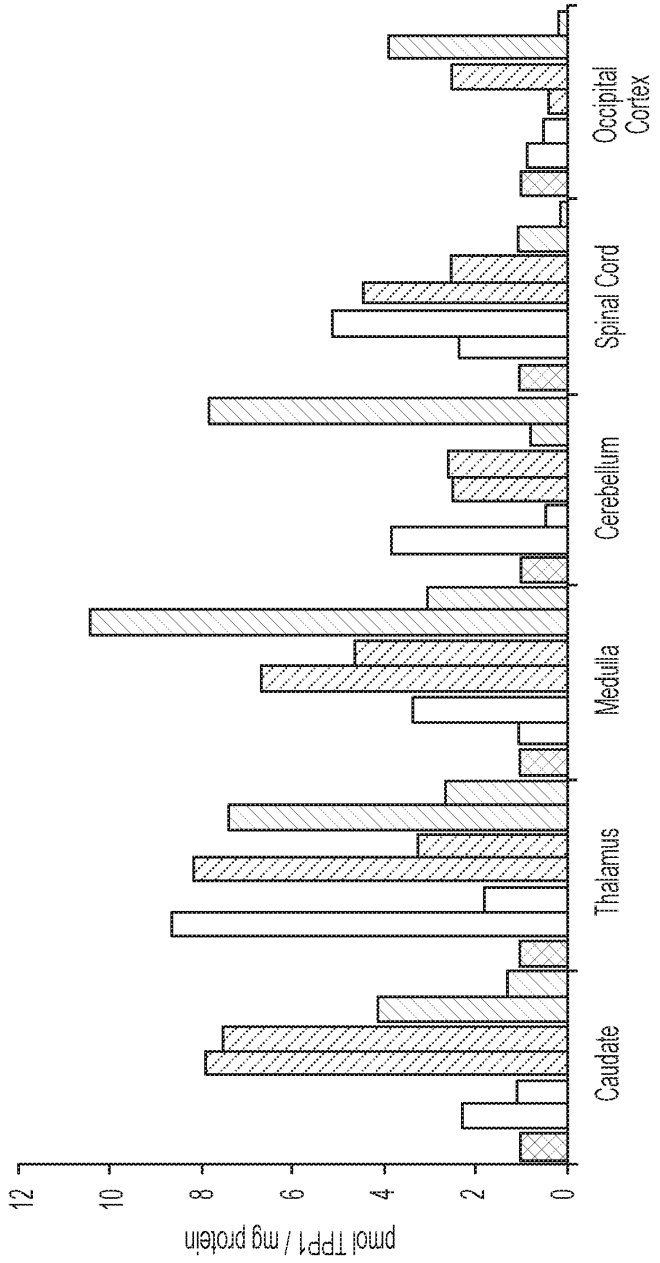

pmol TPP1 / mg protein
0
2
4
6
8
10
12
Caudate
Thalamus
Medulla
Cerebellum
Spinal Cord
Occipital Cortex

FIG. 10B

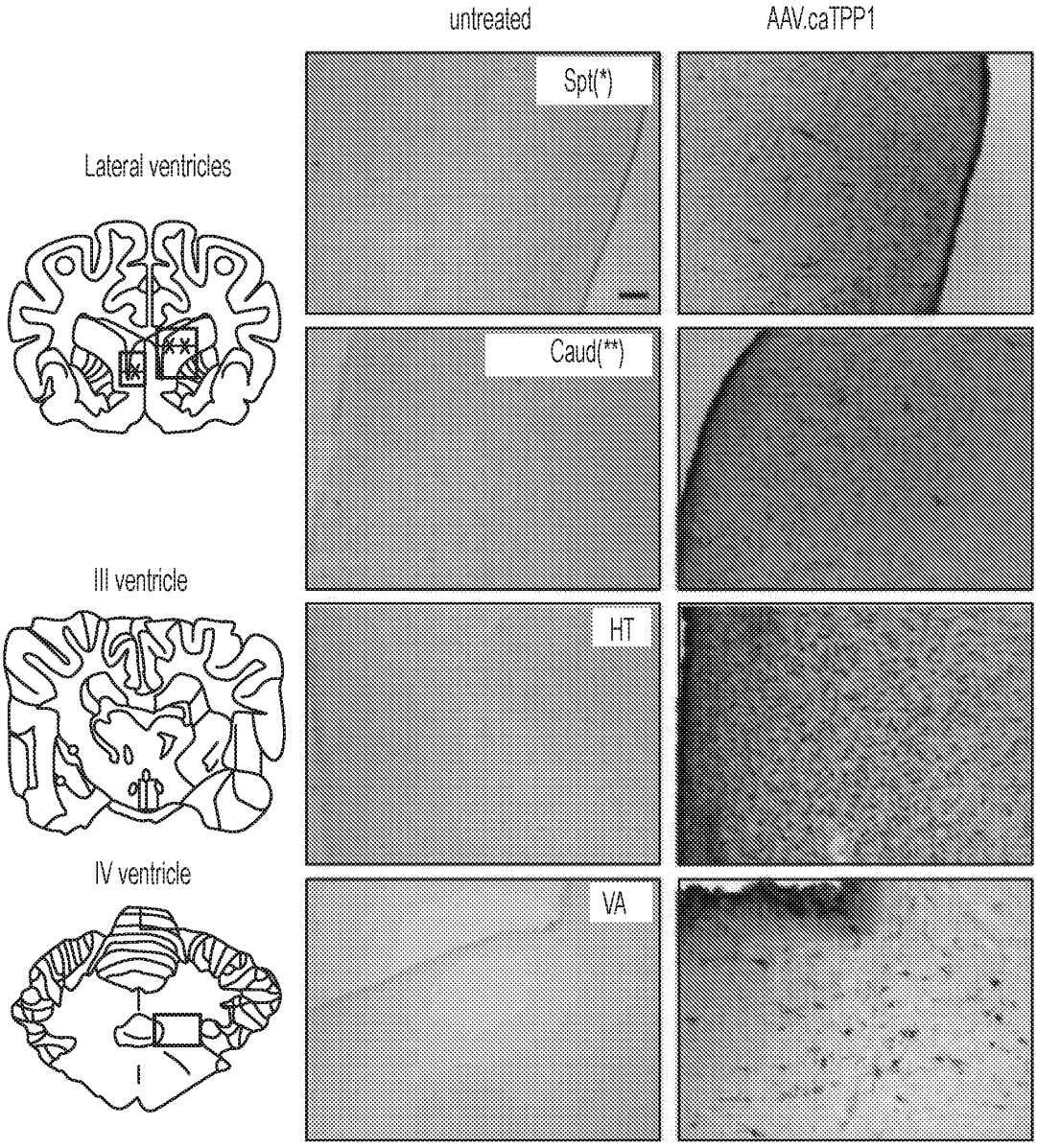

untreated
AAV.caTPP1
Lateral ventricles
III ventricle
IV ventricle
Spt(*)
Caud(**)
HT
VA

FIG. 11A

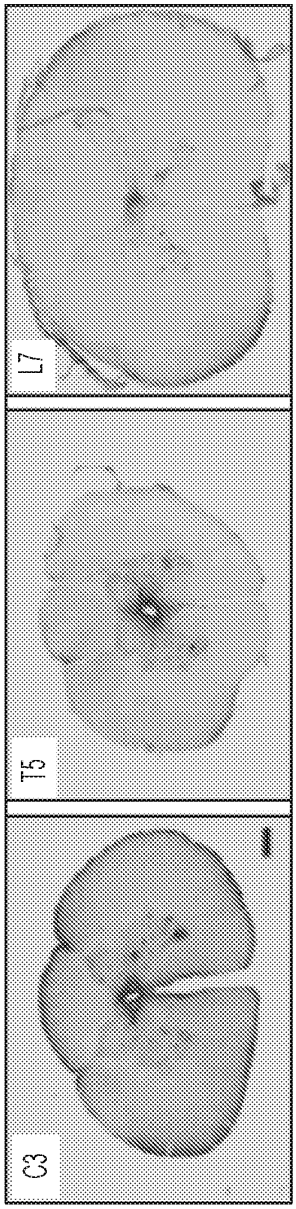


FIG. 11B

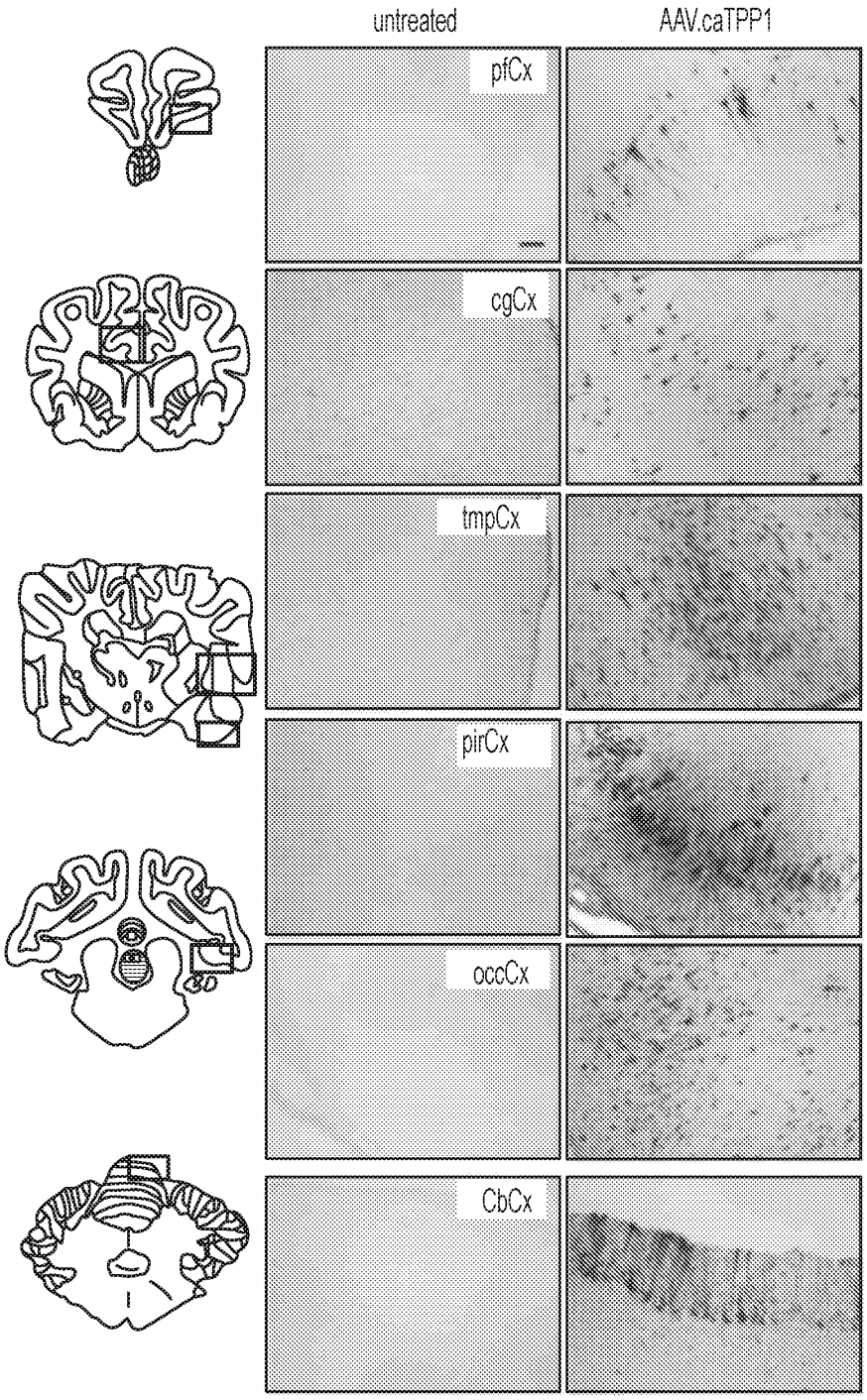


FIG. 11C

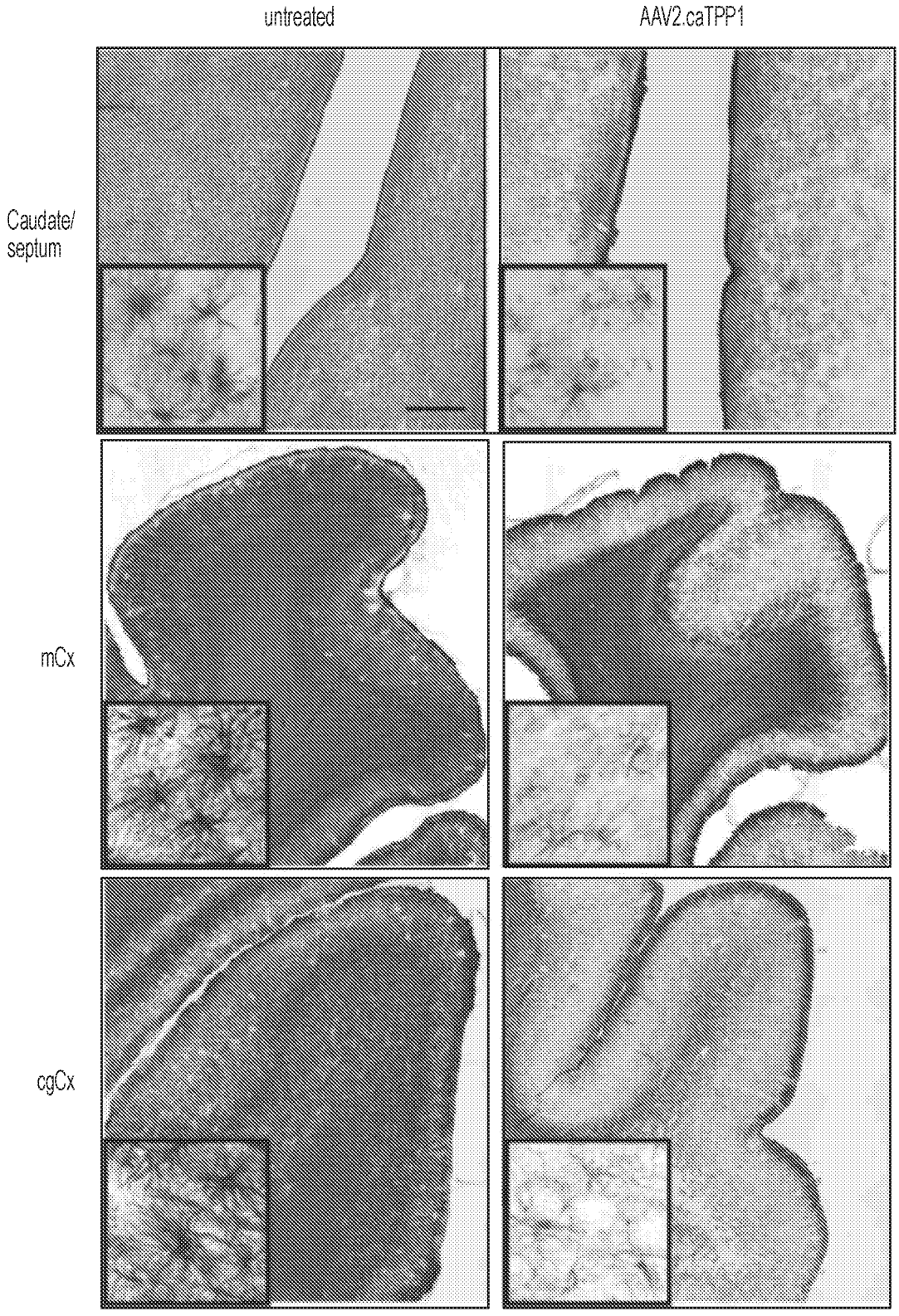


FIG. 12

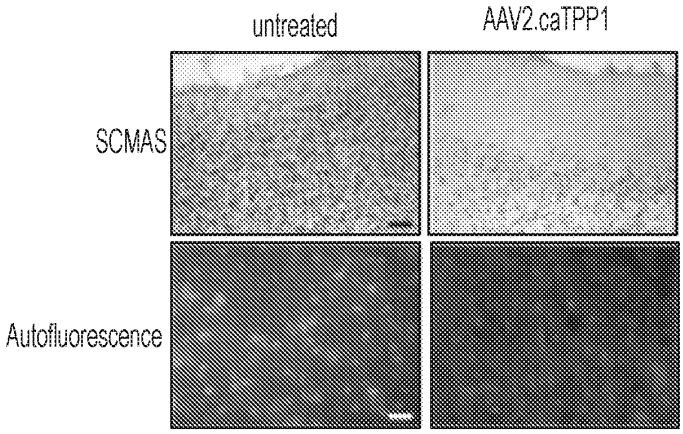


FIG. 13A

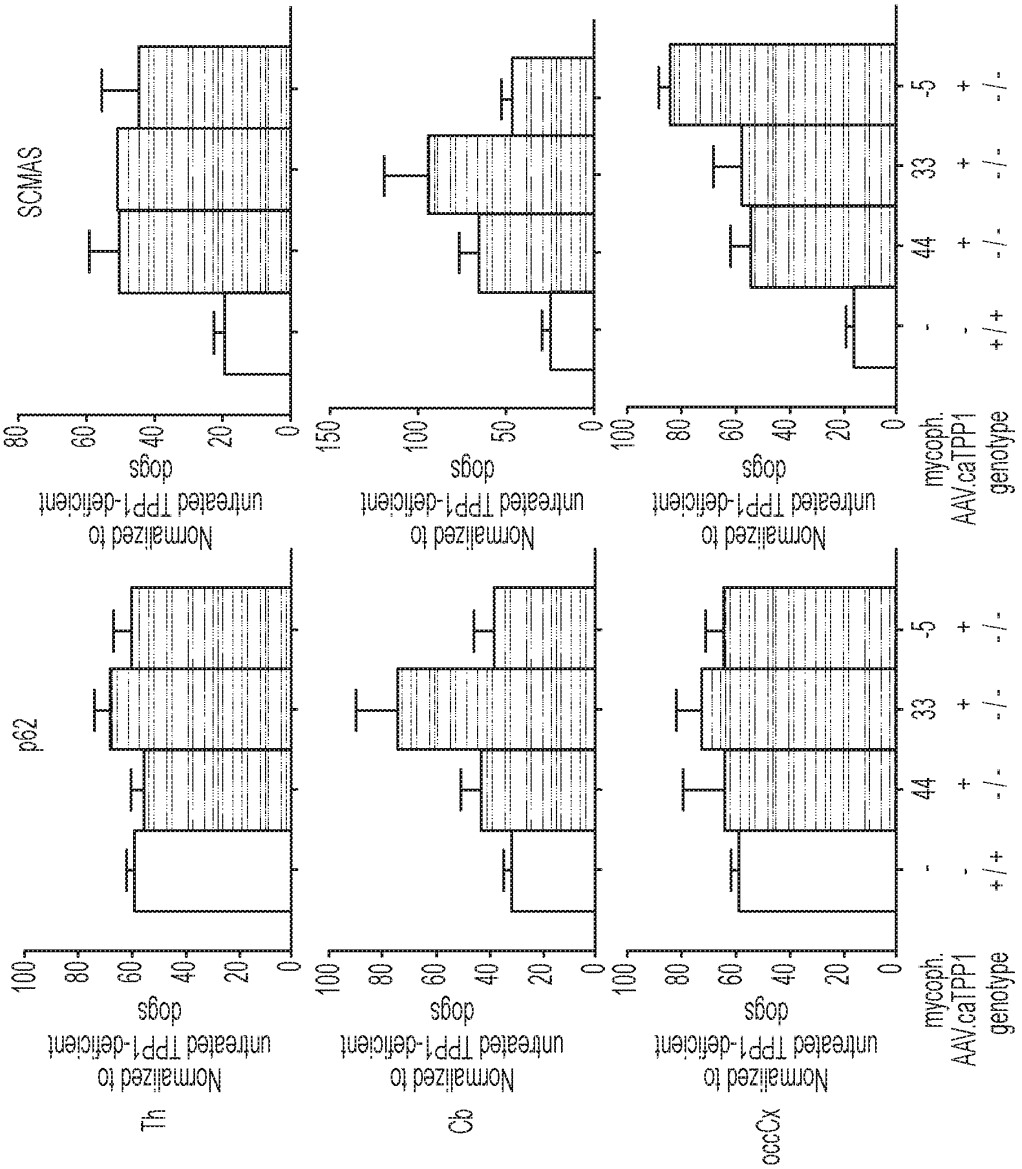

SCMAS
p62
Th
Cb
occCx
Normalized to untreated TPP1-deficient dogs
mycoph. AAV.caTPP1 genotype
- 44 33 -5
+/+ -/- +/+ -/-

FIG. 13B

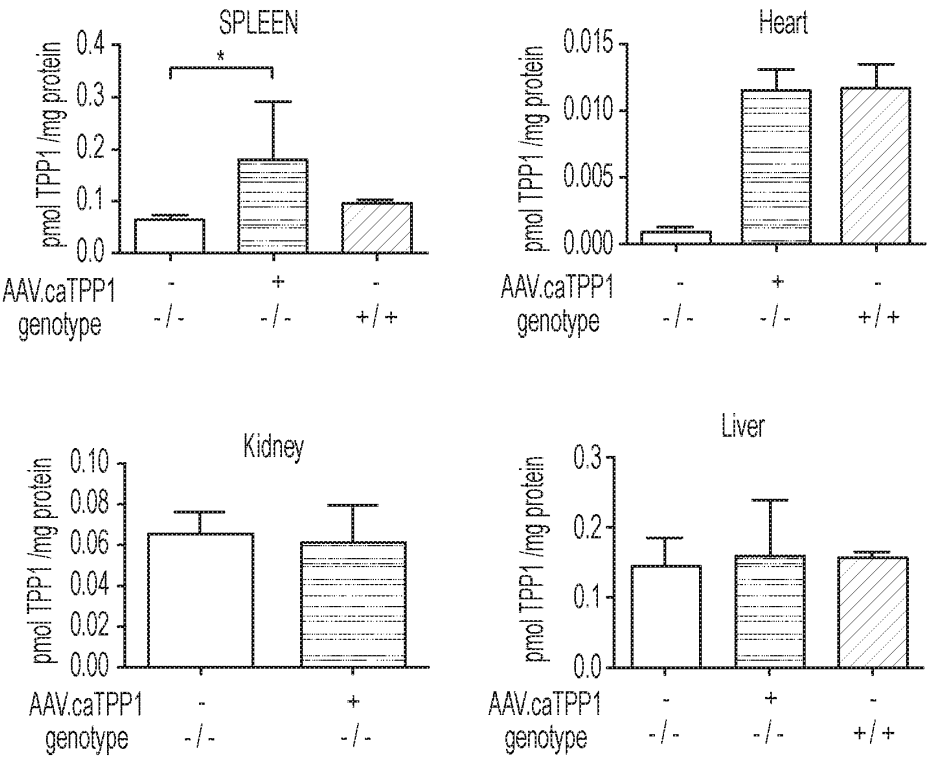

SPLEEN
pmol TPP1 /mg protein
0.4
0.3
0.2
0.1
0.0
*
AAV.caTPP1 - + -
genotype -/- -/- +/+
Heart
pmol TPP1 /mg protein
0.015
0.010
0.005
0.000
AAV.caTPP1 - + -
genotype -/- -/- +/+
Kidney
pmol TPP1 /mg protein
0.10
0.08
0.06
0.04
0.02
0.00
AAV.caTPP1 - +
genotype -/- -/-
Liver
pmol TPP1 /mg protein
0.3
0.2
0.1
0.0
AAV.caTPP1 - + -
genotype -/- -/- +/+

FIG. 14

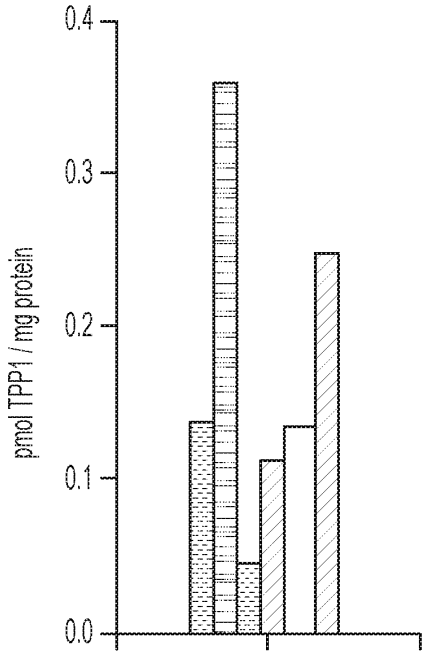

pmol TPP1 / mg protein
0.4
0.3
0.2
0.1
0.0

FIG. 15

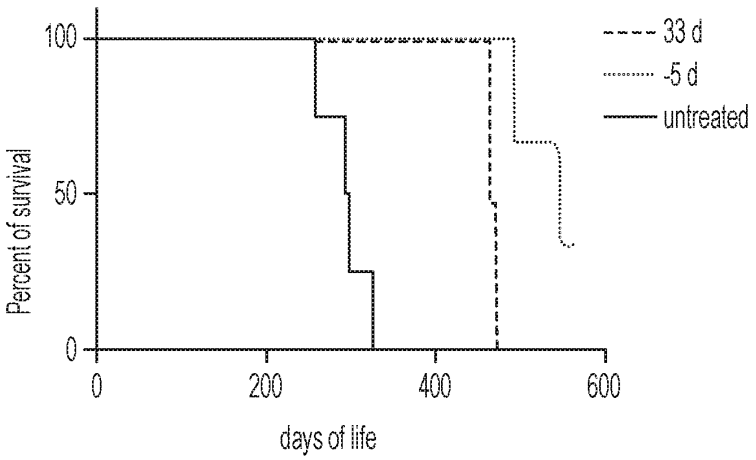

100
50
0
Percent of survival
0
200
400
600
days of life
33 d
-5 d
untreated

FIG. 16