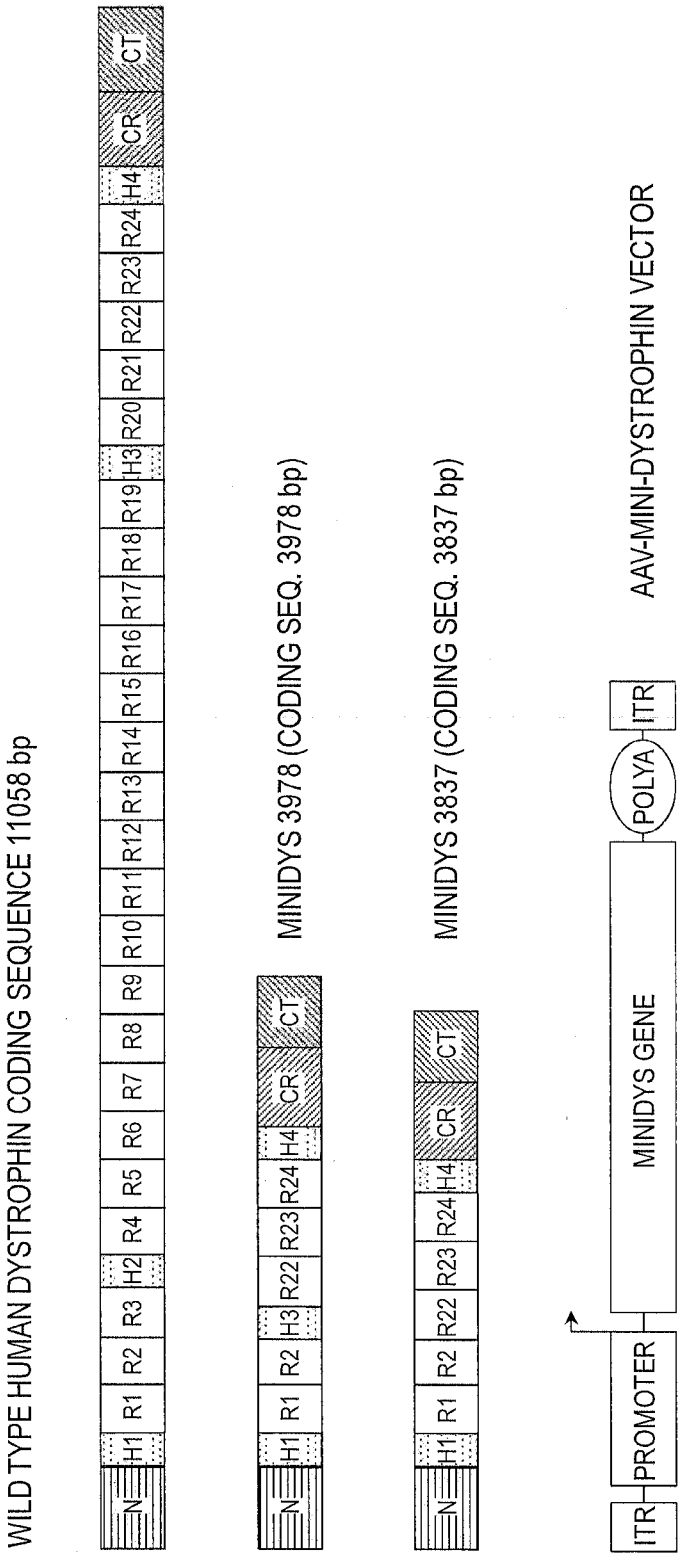

WILD TYPE HUMAN DYSTROPHIN CODING SEQUENCE 11058 bp
N
H1
R1
R2
R3
H2
R4
R5
R6
R7
R8
R9
R10
R11
R12
R13
R14
R15
R16
R17
R18
R19
H3
R20
R21
R22
R23
R24
H4
CR
CT
MINIDYS 3978 (CODING SEQ. 3978 bp)
MINIDYS 3837 (CODING SEQ. 3837 bp)
ITR
PROMOTER
MINIDYS GENE
POLYA
ITR
AAV-MINI-DYSTROPHIN VECTOR

FIG. 1

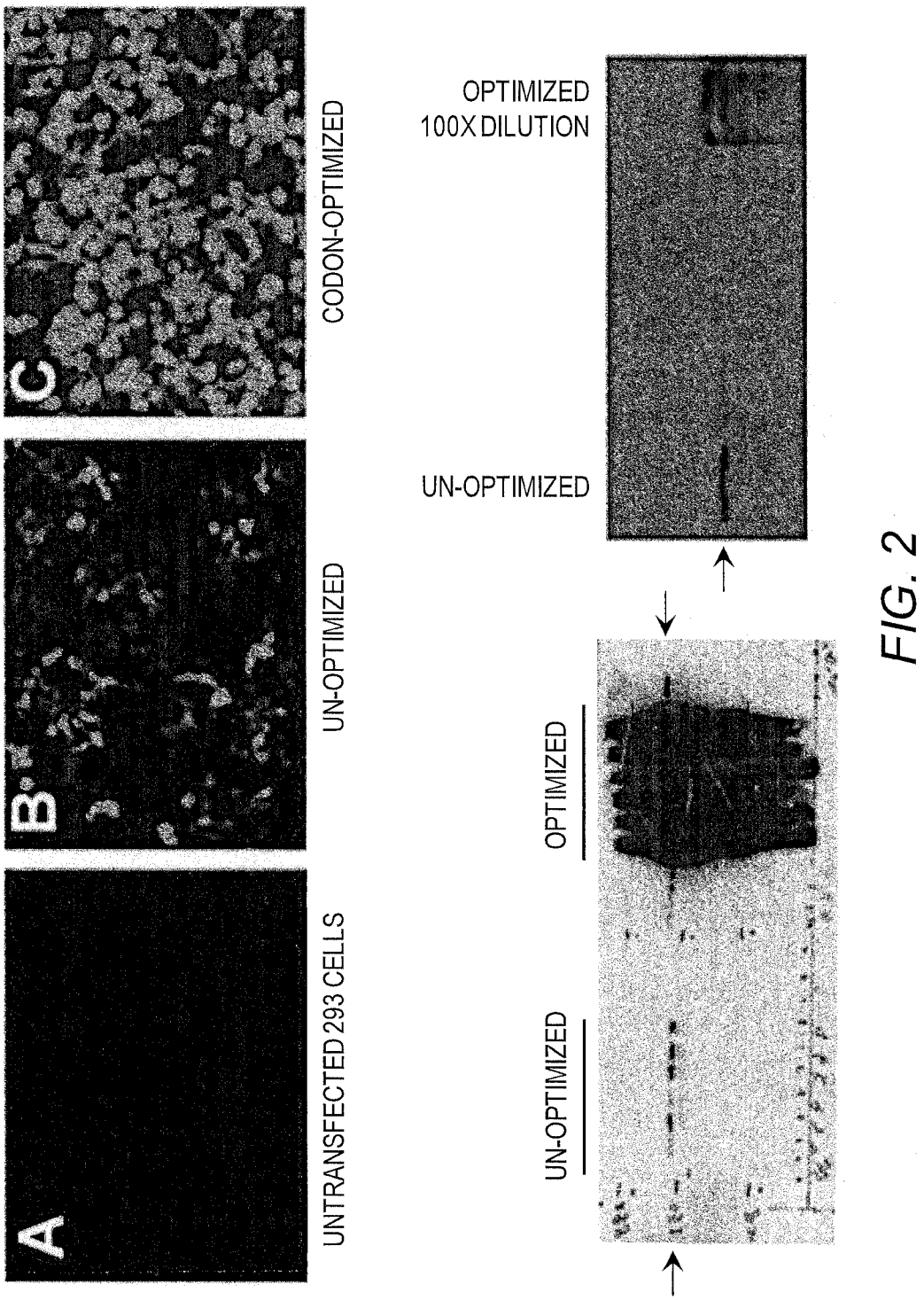

A
UNTRANSFECTED 293 CELLS
B
UN-OPTIMIZED
C
CODON-OPTIMIZED
OPTIMIZED
100X DILUTION
UN-OPTIMIZED
OPTIMIZED
UN-OPTIMIZED

FIG. 2

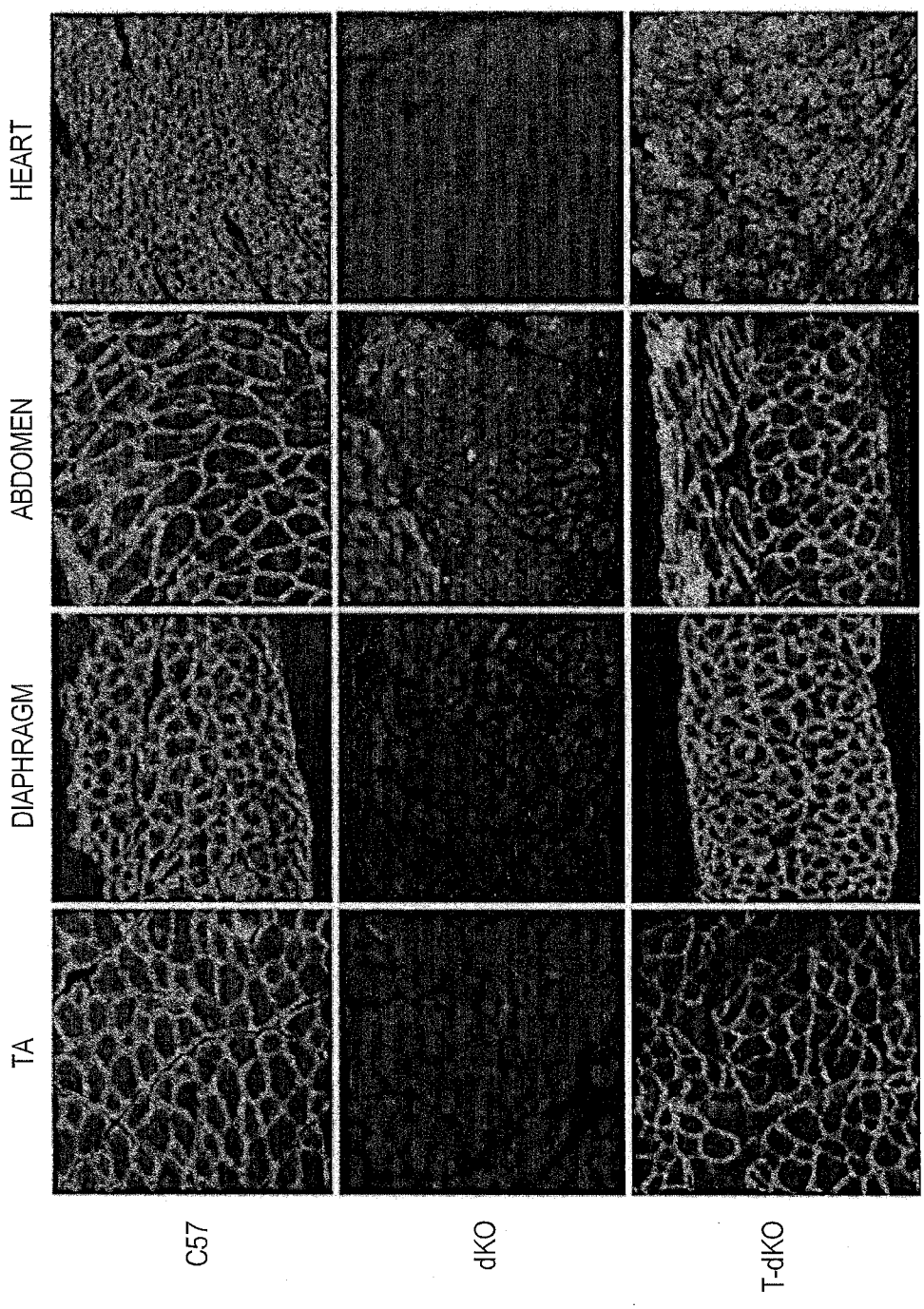


FIG. 3

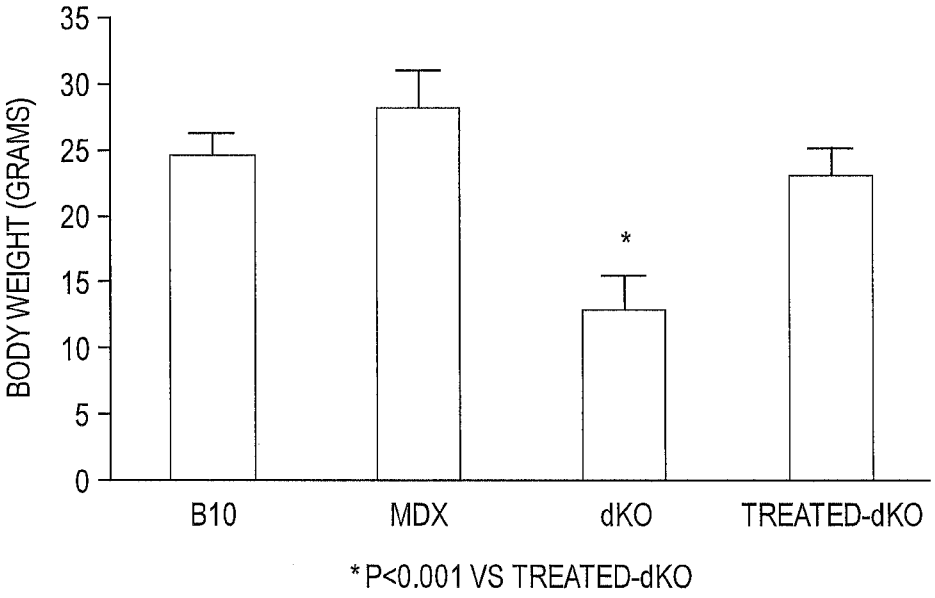
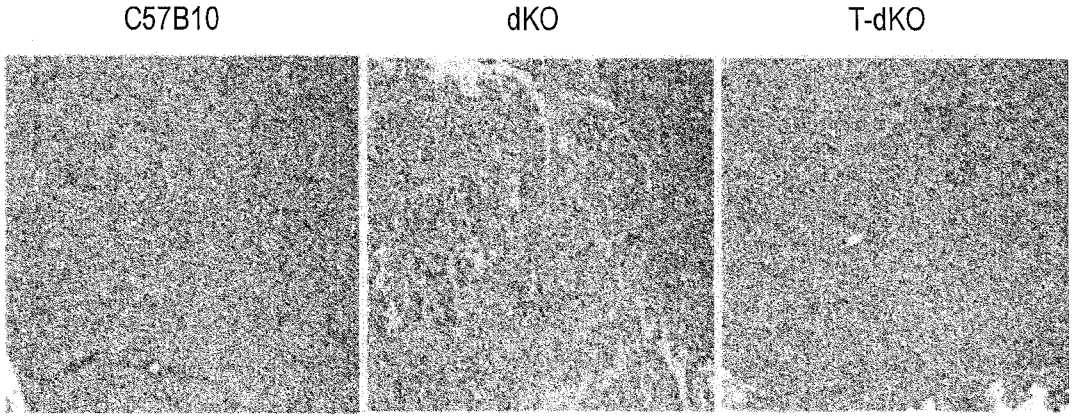


FIG. 4



H&E STAINING OF CRYOSECTIONS (8µm) OF TIBIALIS ANTERIOR MUSCLES, 10X MAGNIFICATION.

FIG. 6A

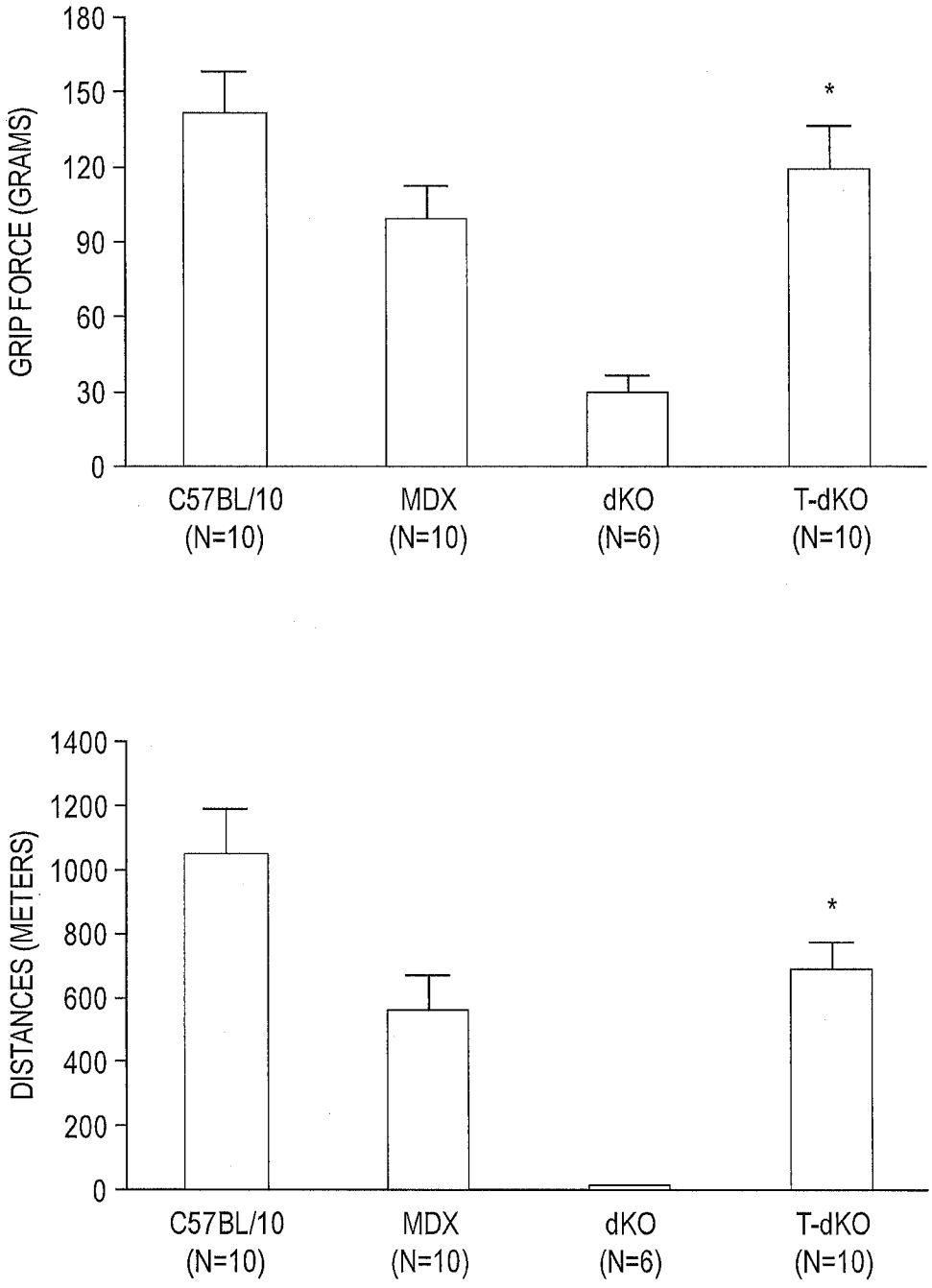

GRIP FORCE (GRAMS)
180
150
120
90
60
30
0
*
C57BL/10 (N=10)
MDX (N=10)
dKO (N=6)
T-dKO (N=10)
DISTANCES (METERS)
1400
1200
1000
800
600
400
200
0
*
C57BL/10 (N=10)
MDX (N=10)
dKO (N=6)
T-dKO (N=10)
* P<0.05 VS MDX

FIG. 5

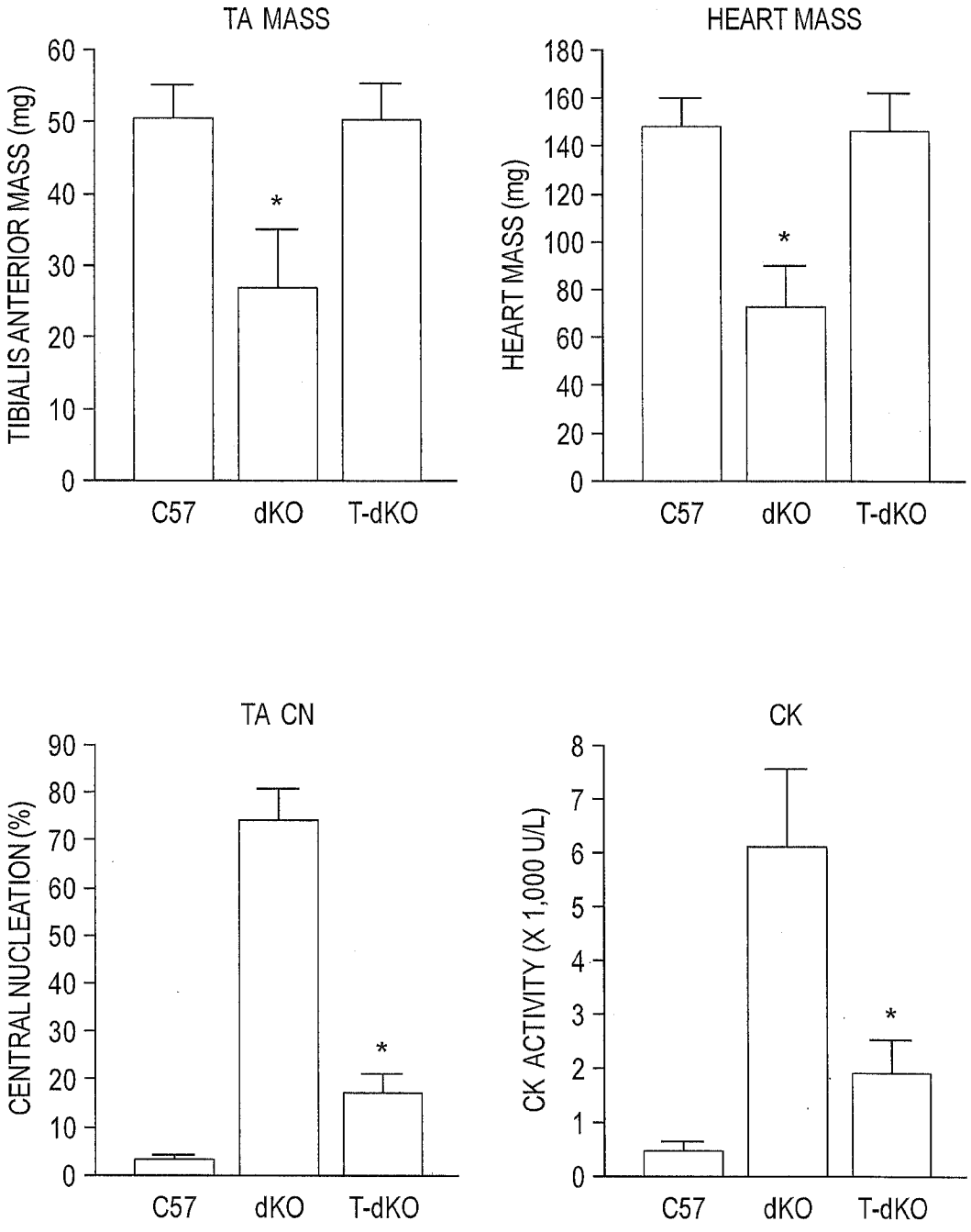

TA MASS
TIBIALIS ANTERIOR MASS (mg)
60
50
40
30
20
10
0
*
C57
dKO
T-dKO
HEART MASS
HEART MASS (mg)
180
160
140
120
100
80
60
40
20
0
*
C57
dKO
T-dKO
TA CN
CENTRAL NUCLEATION (%)
90
80
70
60
50
40
30
20
10
0
*
C57
dKO
T-dKO
CK
CK ACTIVITY (X 1,000 U/L)
8
7
6
5
4
3
2
1
0
*
C57
dKO
T-dKO

FIG. 6B

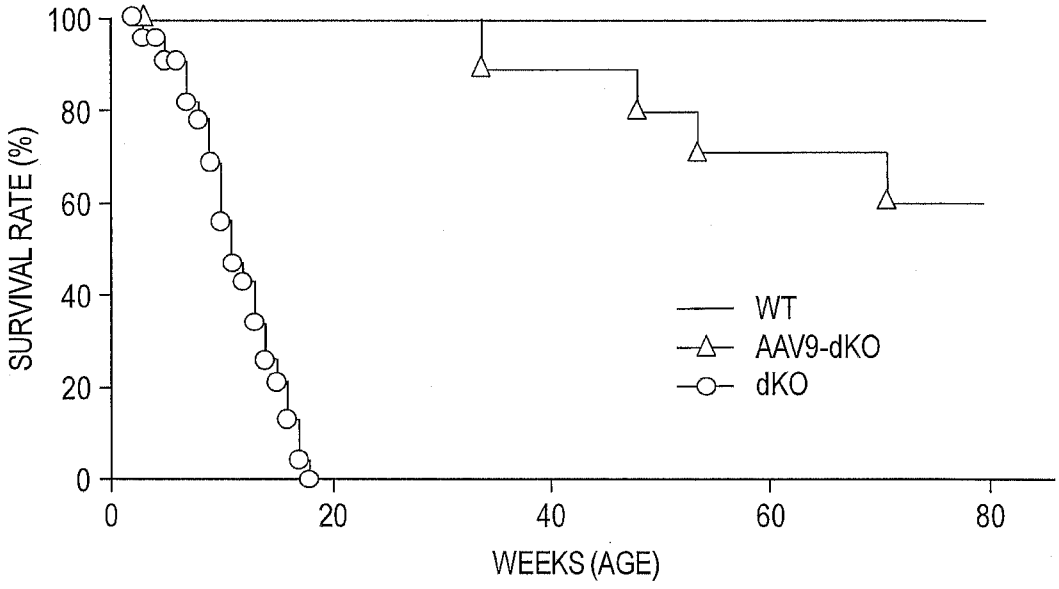

100
80
60
40
20
0
SURVIVAL RATE (%)
0
20
40
60
80
WEEKS (AGE)
WT
AAV9-dKO
dKO

FIG. 7

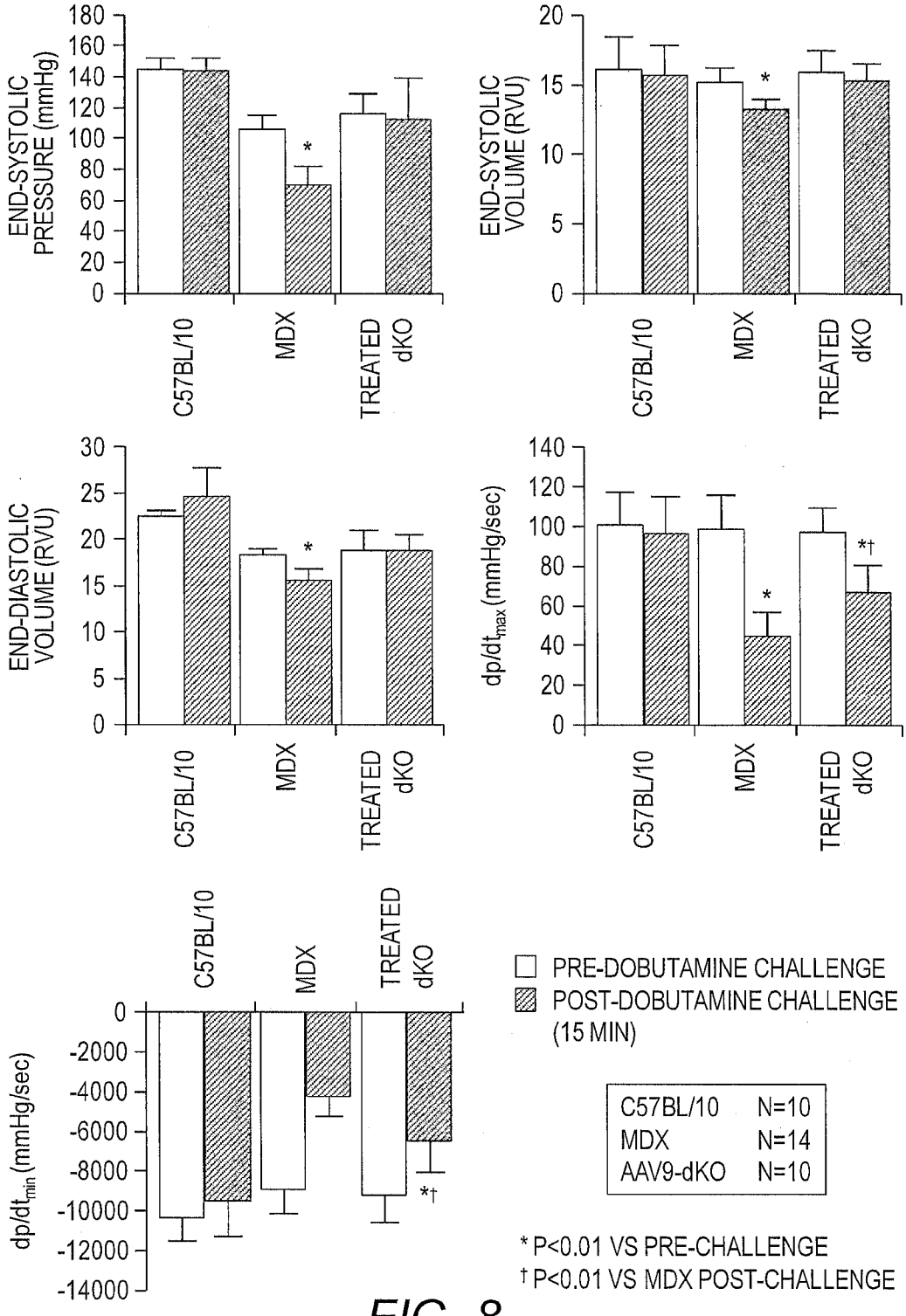

END-SYSTOLIC PRESSURE (mmHg)
180
160
140
120
100
80
60
40
20
0
*
C57BL/10
MDX
TREATED dKO
END-SYSTOLIC VOLUME (RVU)
20
15
10
5
0
*
C57BL/10
MDX
TREATED dKO
END-DIASTOLIC VOLUME (RVU)
30
25
20
15
10
5
0
*
C57BL/10
MDX
TREATED dKO
dp/dtmax (mmHg/sec)
140
120
100
80
60
40
20
0
*
*†
C57BL/10
MDX
TREATED dKO
dp/dtmin (mmHg/sec)
0
-2000
-4000
-6000
-8000
-10000
-12000
-14000
*†
C57BL/10
MDX
TREATED dKO
PRE-DOBUTAMINE CHALLENGE
POST-DOBUTAMINE CHALLENGE (15 MIN)
C57BL/10 N=10
MDX N=14
AAV9-dKO N=10
* P<0.01 VS PRE-CHALLENGE
† P<0.01 VS MDX POST-CHALLENGE

FIG. 8

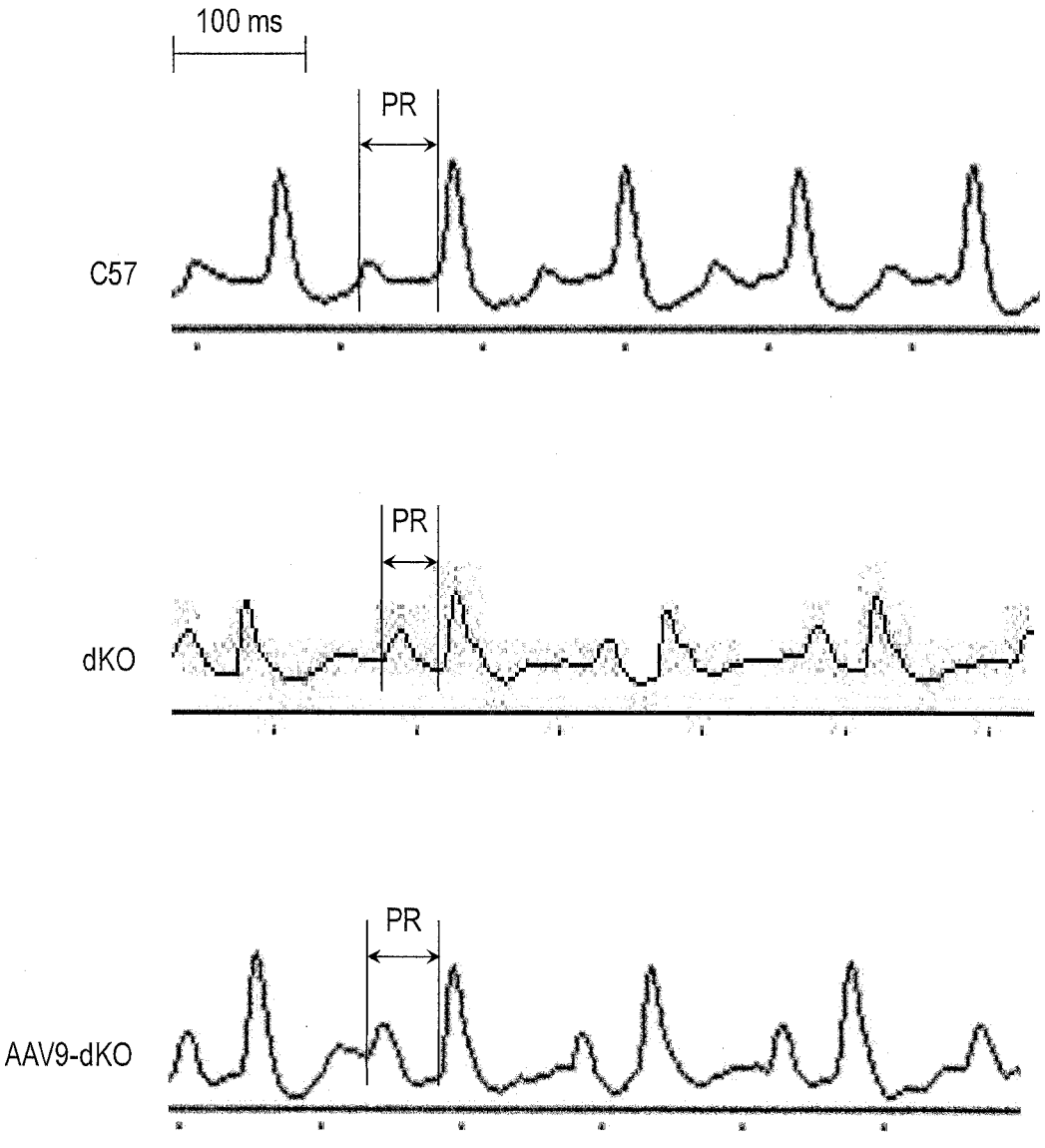
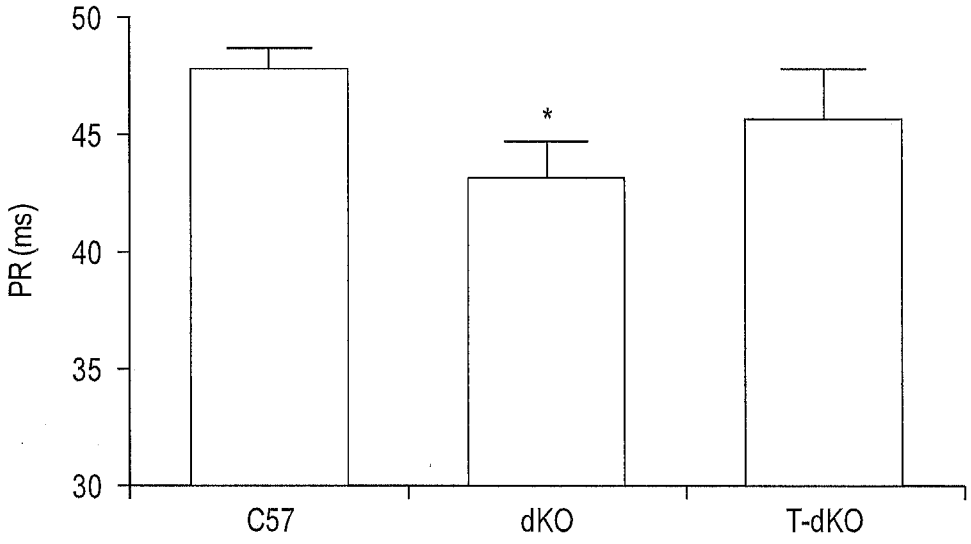


FIG. 9A


50
45
40
35
30
PR (ms)
*
C57
dKO
T-dKO

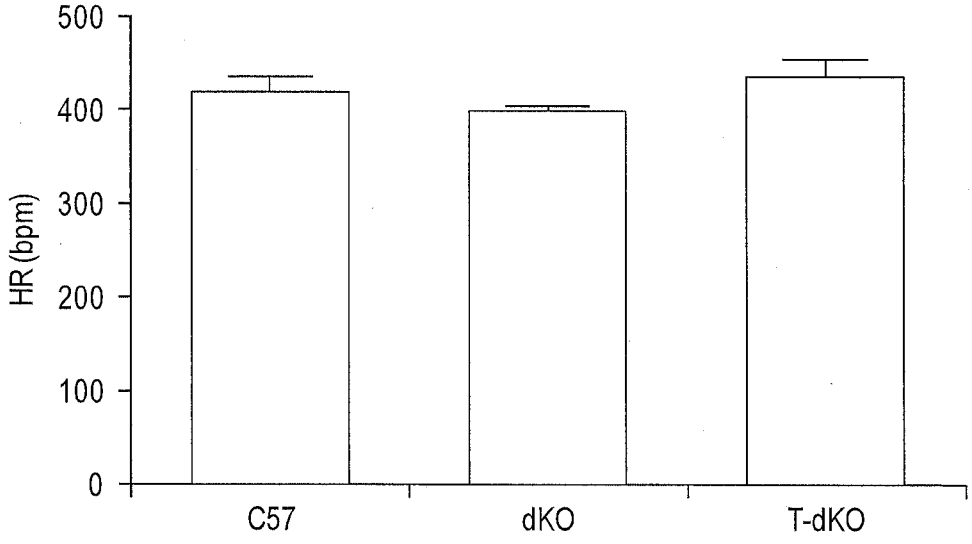

500
400
300
200
100
0
HR (bpm)
C57
dKO
T-dKO

FIG. 9B

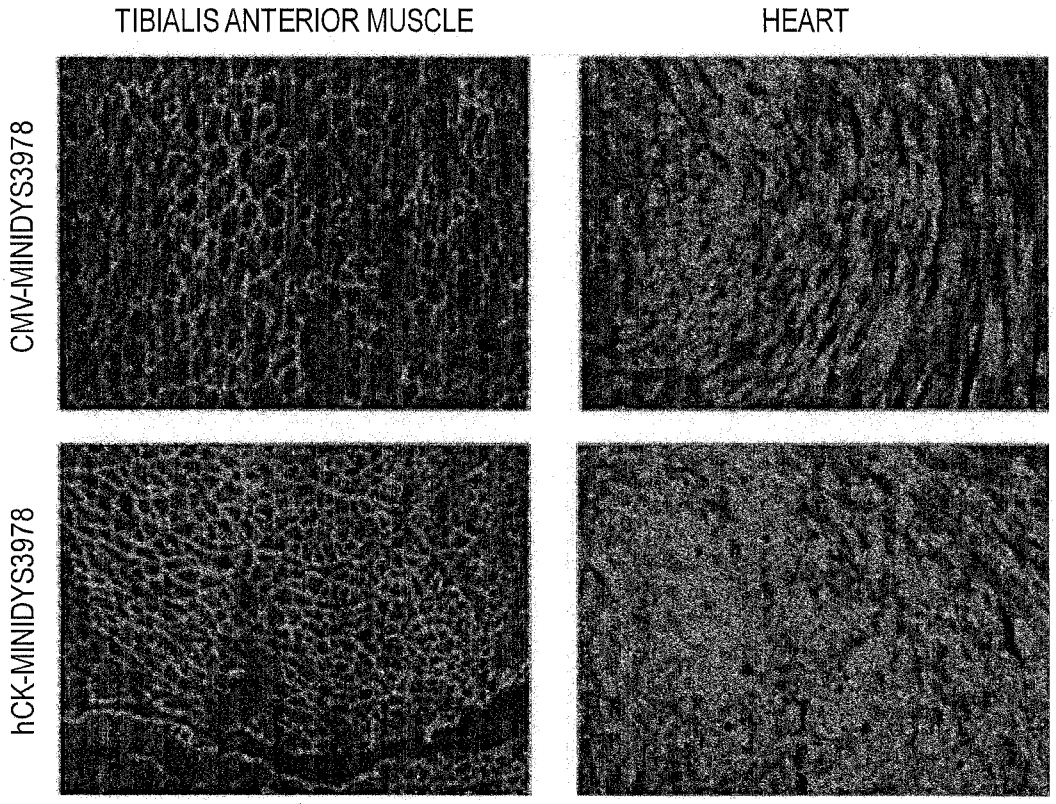

TIBIALIS ANTERIOR MUSCLE
HEART
CMV-MINIDYS3978
hCK-MINIDYS3978

FIG. 10


A
B
C
T2
T2 – FAT SATURATION
SEGMENTATION

FIG. 11

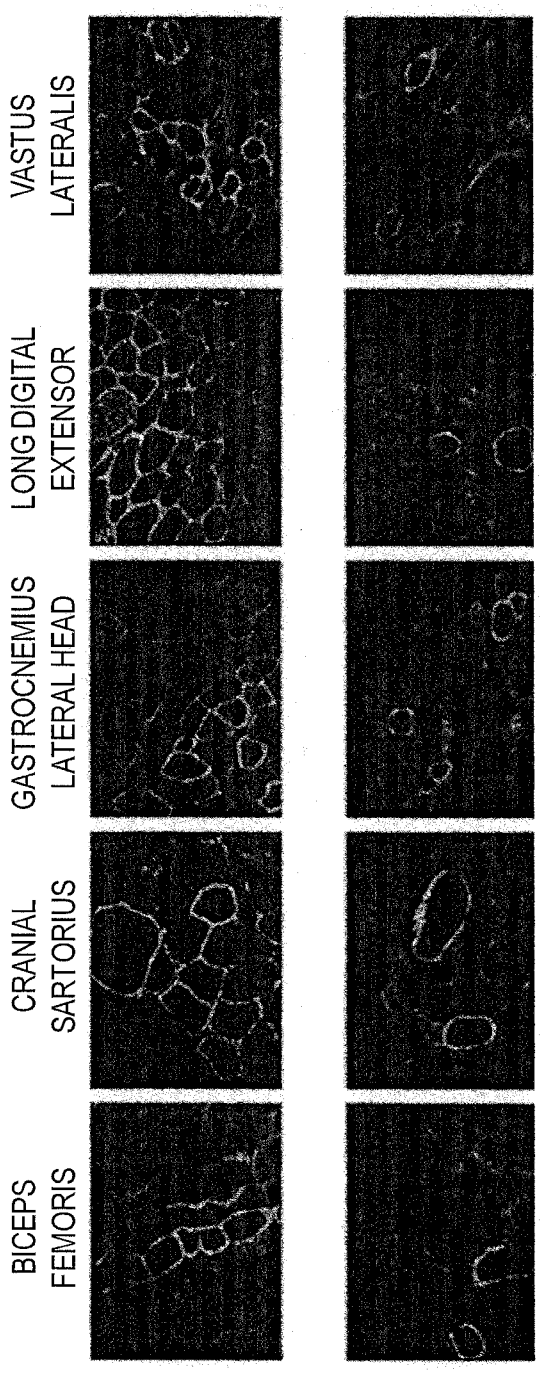

BICEPS FEMORIS
CRANIAL SARTORIUS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
VASTUS LATERALIS
LEFT LEG NON-INJECTED
RIGHT LEG INJECTED

FIG. 12

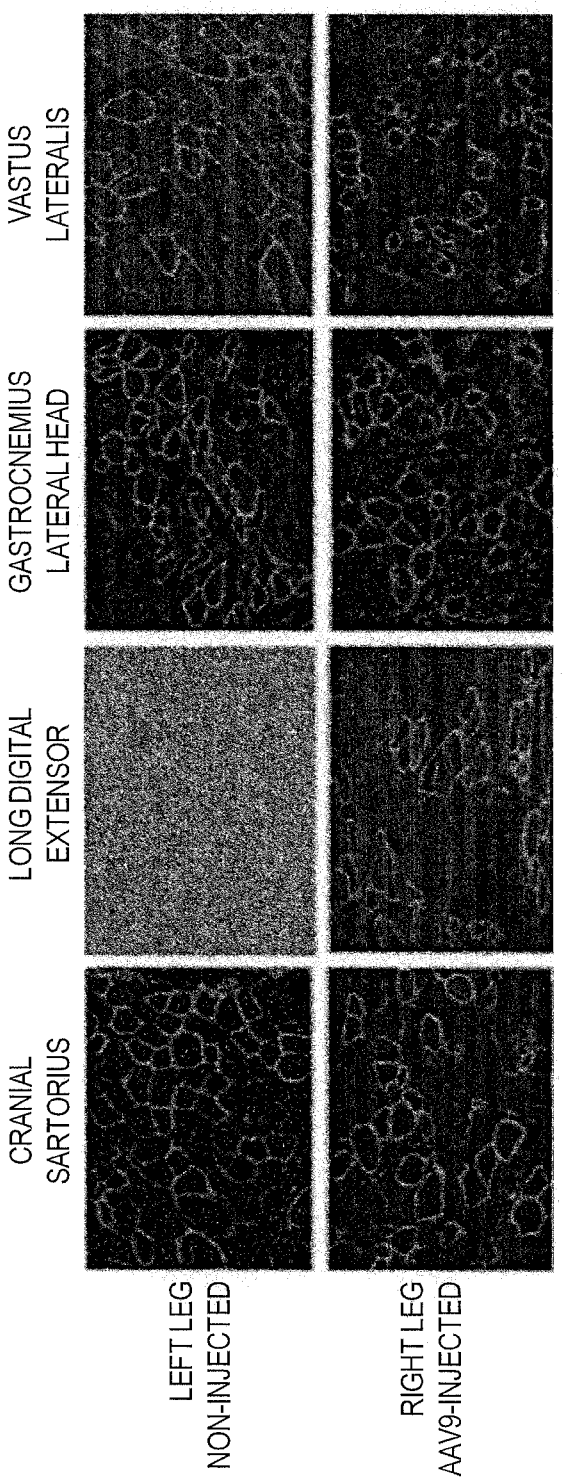

VASTUS LATERALIS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
CRANIAL SARTORIUS
LEFT LEG NON-INJECTED
RIGHT LEG AAV9-INJECTED
VASTUS LATERALIS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
CRANIAL SARTORIUS
AAV9-INJECTED LEG
VASTUS LATERALIS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
CRANIAL SARTORIUS
NON-INJECTED LEG

FIG. 13

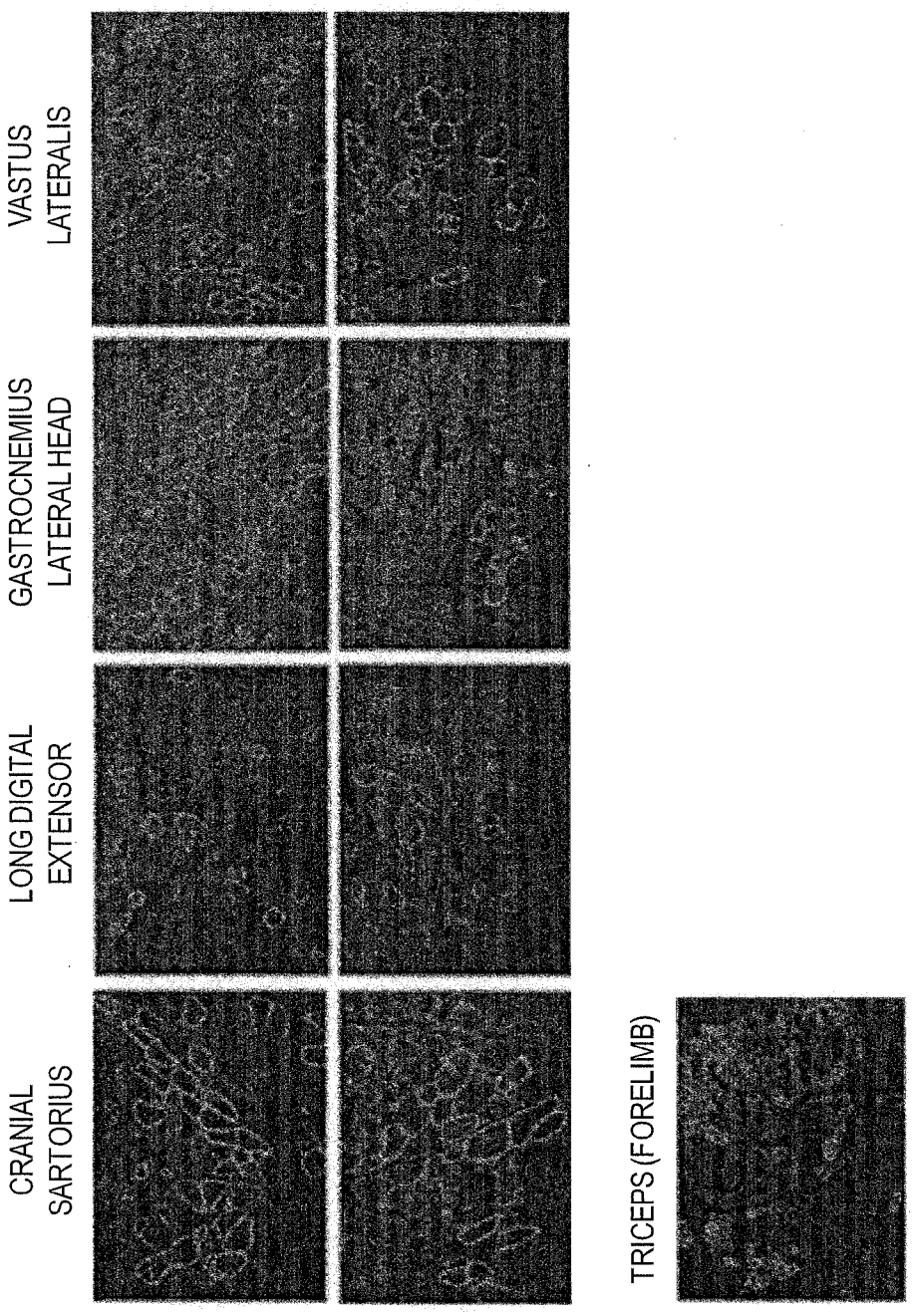

CRANIAL SARTORIUS
LONG DIGITAL EXTENSOR
GASTROCNEMIUS LATERAL HEAD
VASTUS LATERALIS
LEFT LEG NON-INJECTED
RIGHT LEG AAV9-INJECTED
TRICEPS (FORELIMB)

FIG. 14

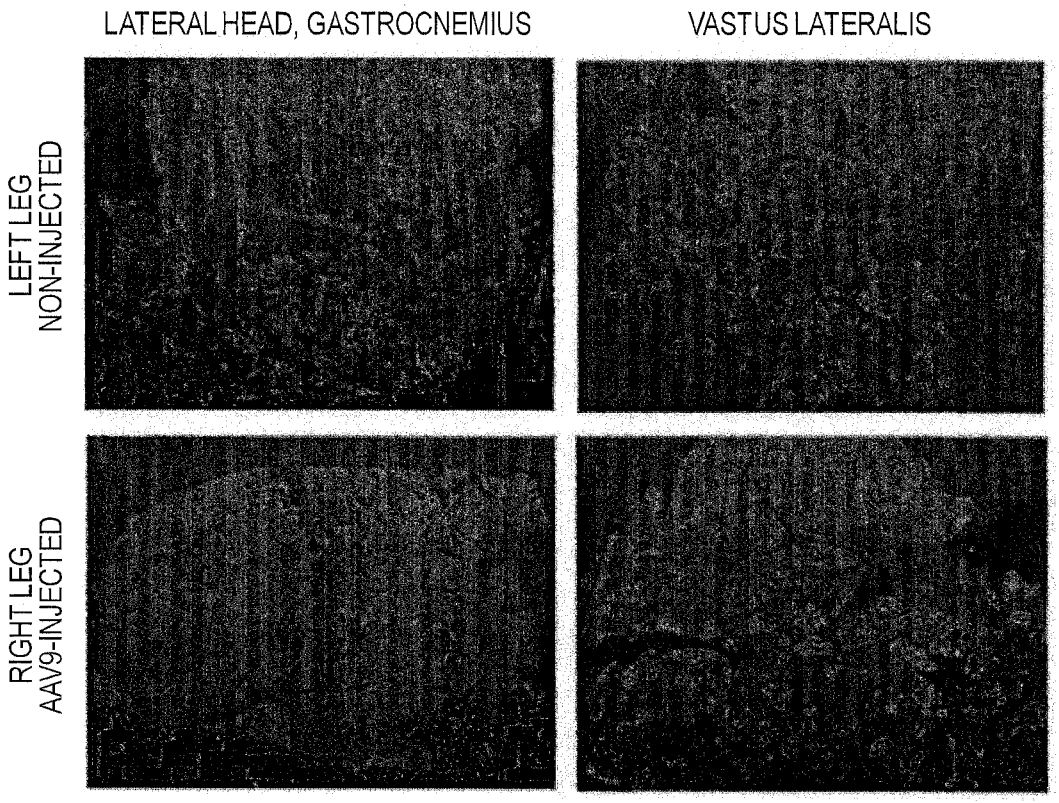

LATERAL HEAD, GASTROCNEMIUS
VASTUS LATERALIS
LEFT LEG
NON-INJECTED
RIGHT LEG
AAV9-INJECTED

FIG. 15

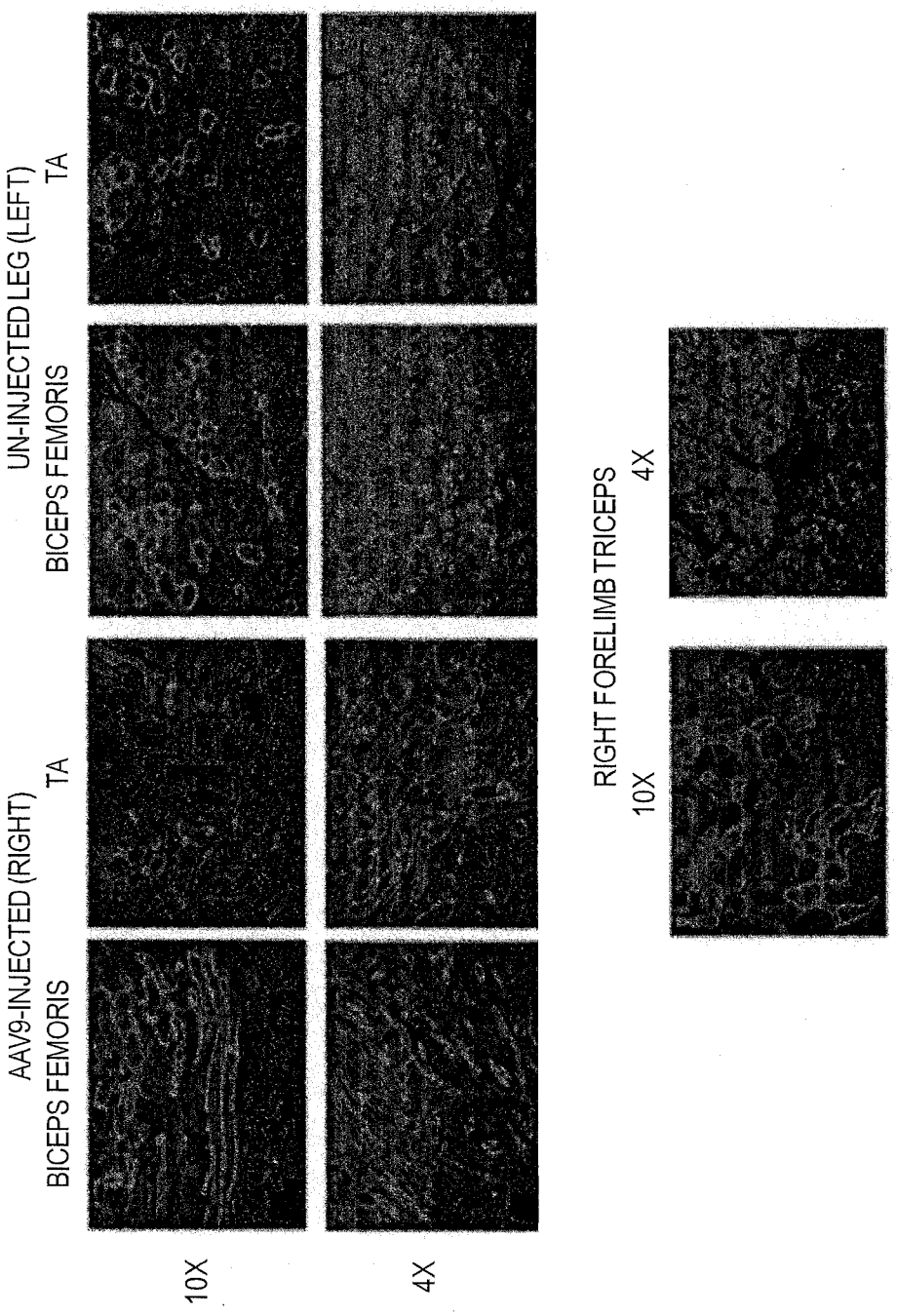

AAV9-INJECTED (RIGHT)
BICEPS FEMORIS
TA
UN-INJECTED LEG (LEFT)
BICEPS FEMORIS
TA
10X
4X
RIGHT FORELIMB TRICEPS
10X
4X

FIG. 16

LEFT HINDLIMB (NON-INJECTED SIDE) CRANIAL SARTORIUS MUSCLE

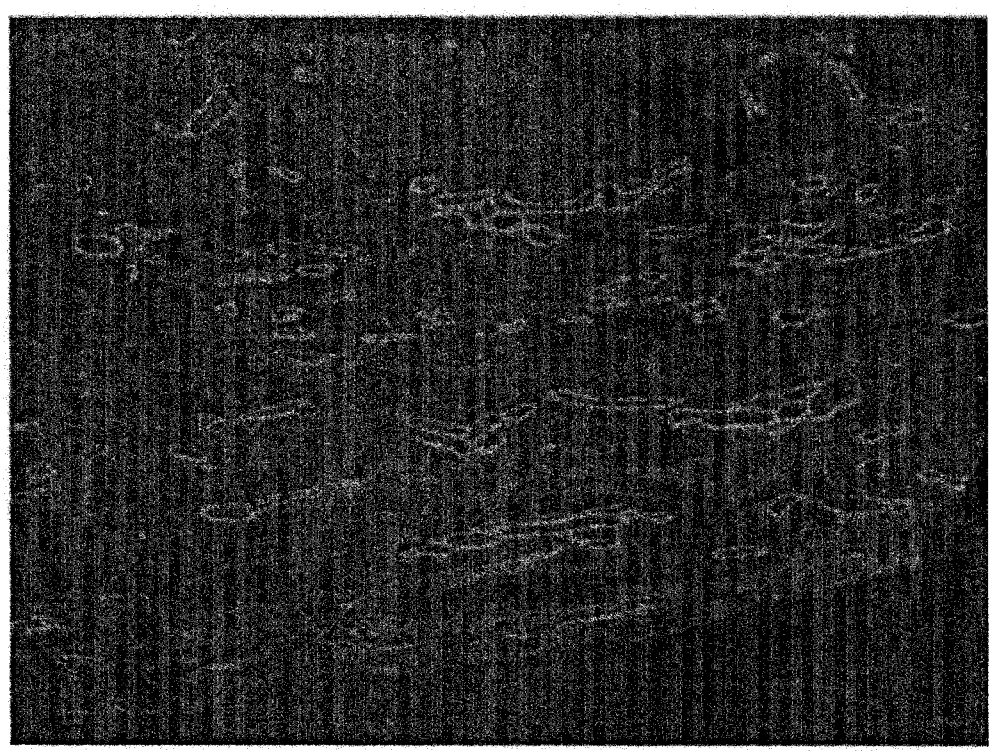


FIG. 17

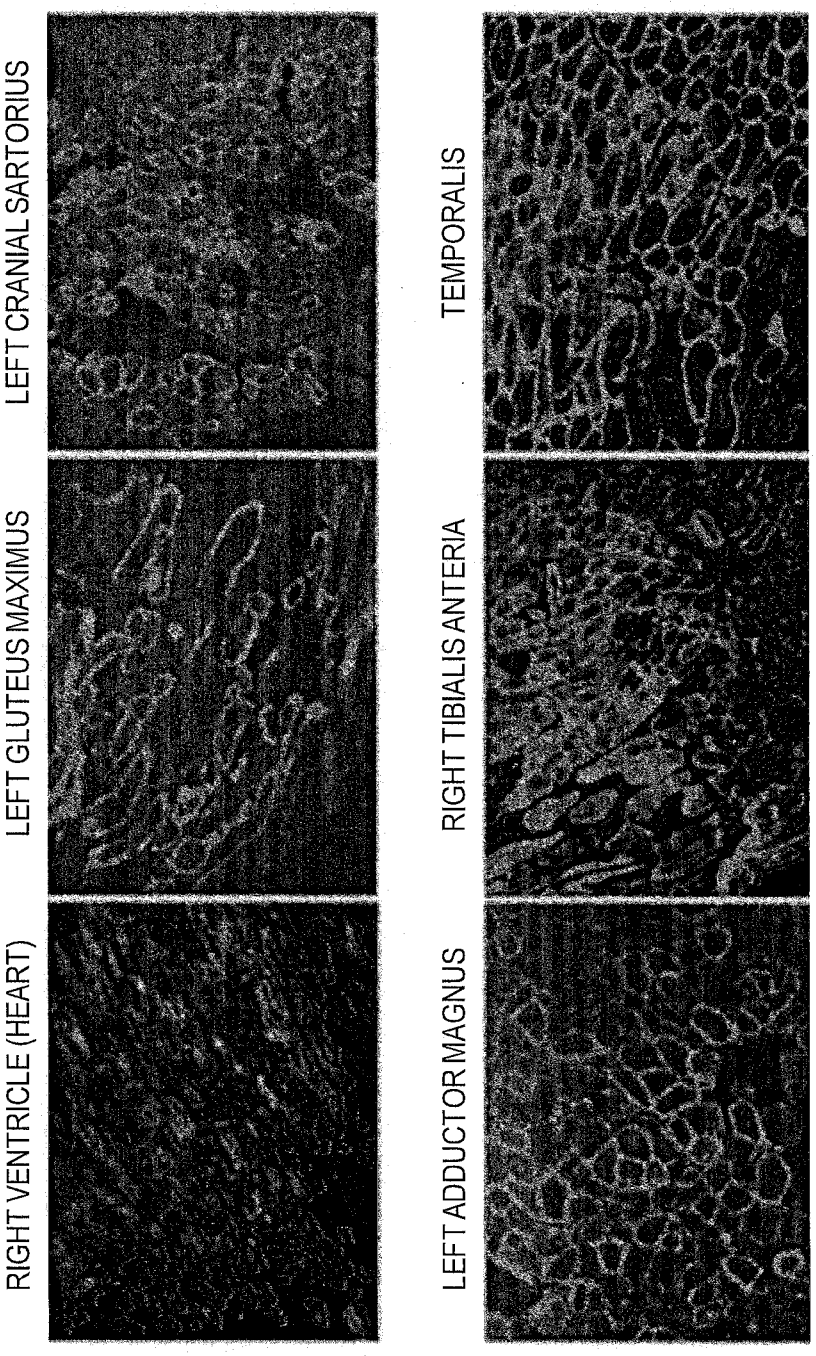

RIGHT VENTRICLE (HEART)
LEFT GLUTEUS MAXIMUS
LEFT CRANIAL SARTORIUS
LEFT ADDUCTOR MAGNUS
RIGHT TIBIALIS ANTERIA
TEMPORALIS

FIG. 18

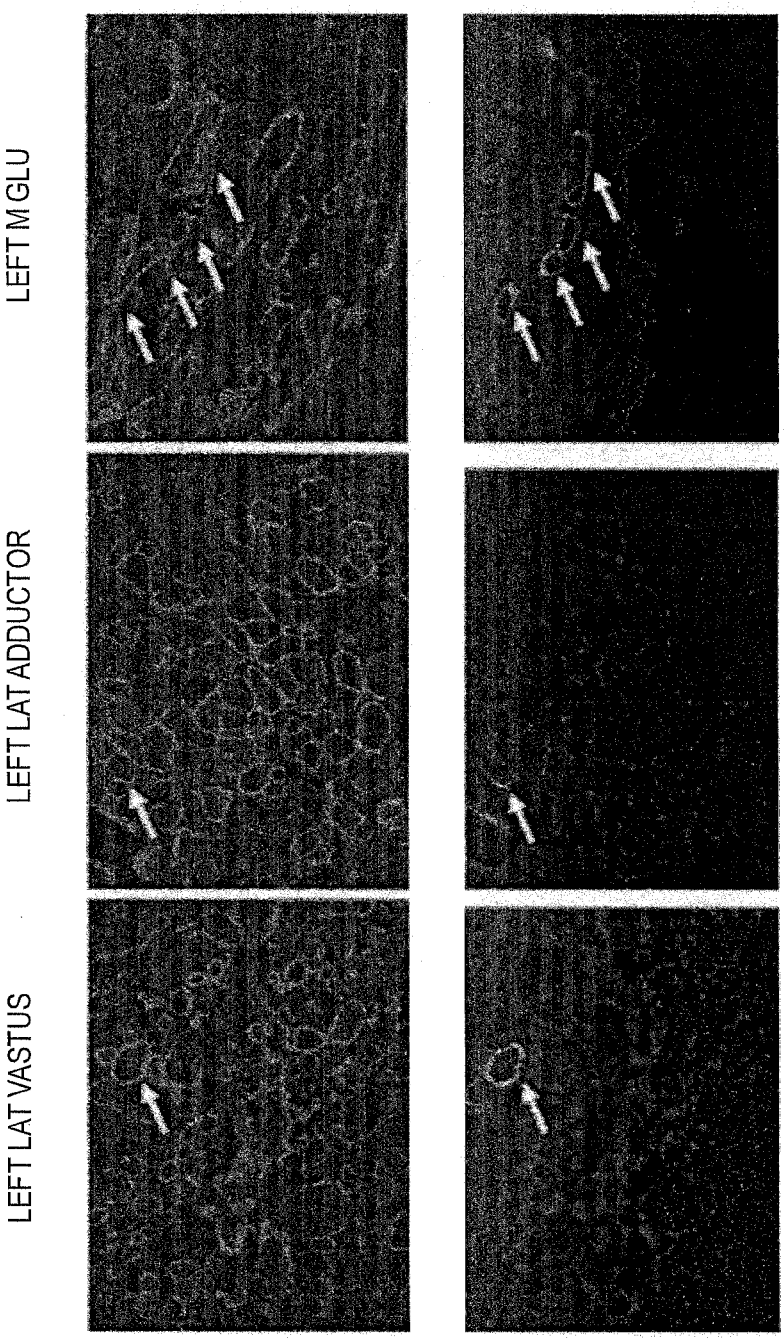


FIG. 19

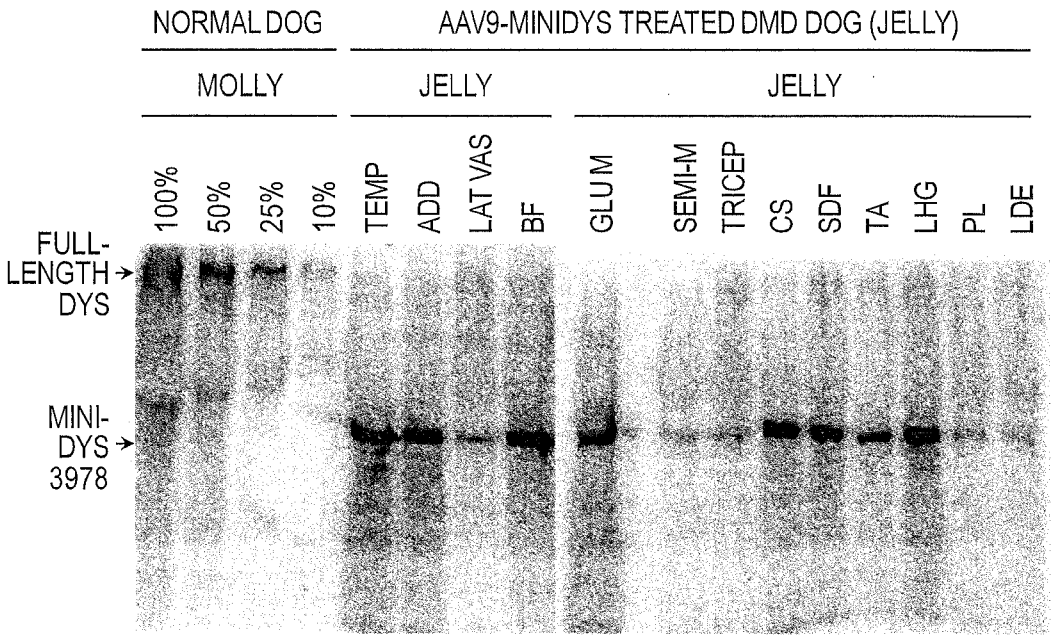

NORMAL DOG
AAV9-MINIDYS TREATED DMD DOG (JELLY)
MOLLY
JELLY
JELLY
100%
50%
25%
10%
TEMP
ADD
LAT VAS
BF
GLU M
SEMI-M
TRICEP
CS
SDF
TA
LHG
PL
LDE
FULL-LENGTH DYS
MINI-DYS 3978

FIG. 20

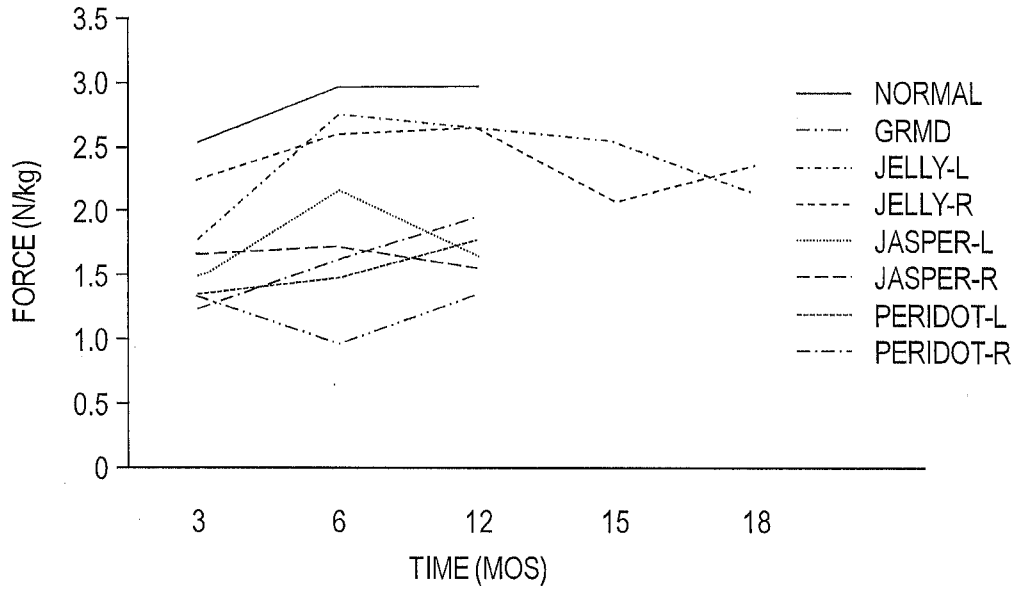

FORCE (N/kg)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
3
6
12
15
18
TIME (MOS)
NORMAL
GRMD
JELLY-L
JELLY-R
JASPER-L
JASPER-R
PERIDOT-L
PERIDOT-R

FIG. 21

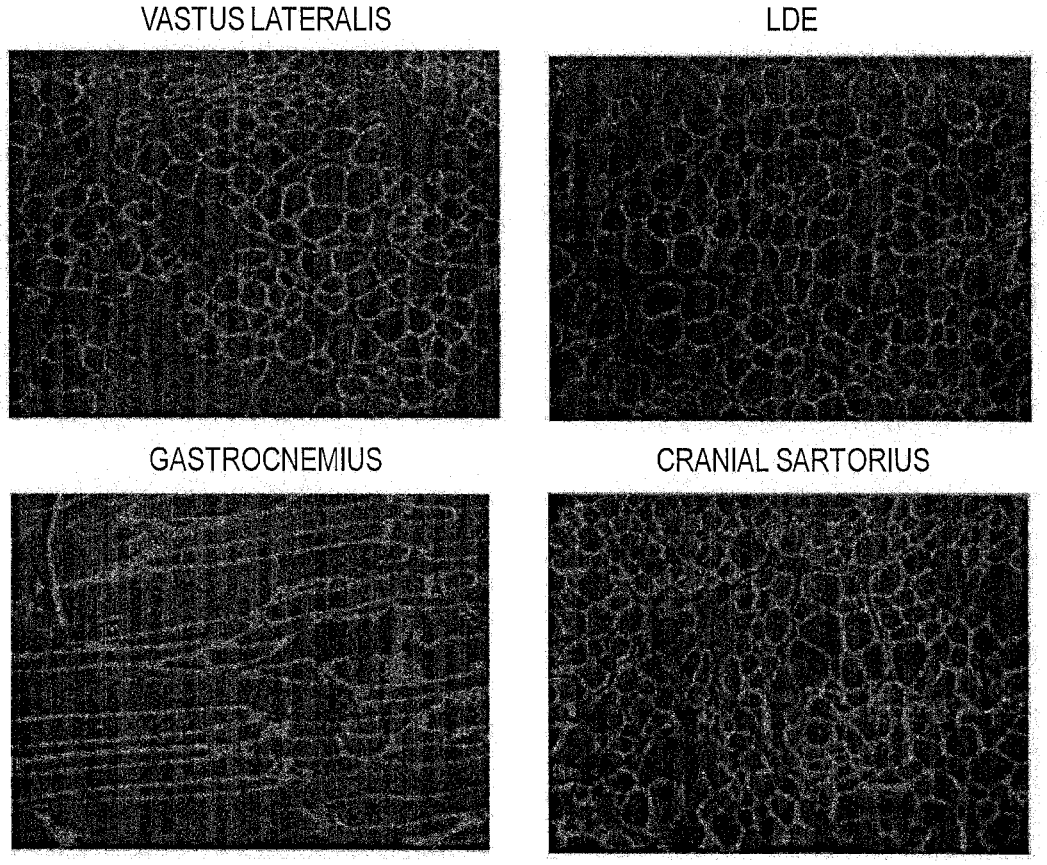


FIG. 22

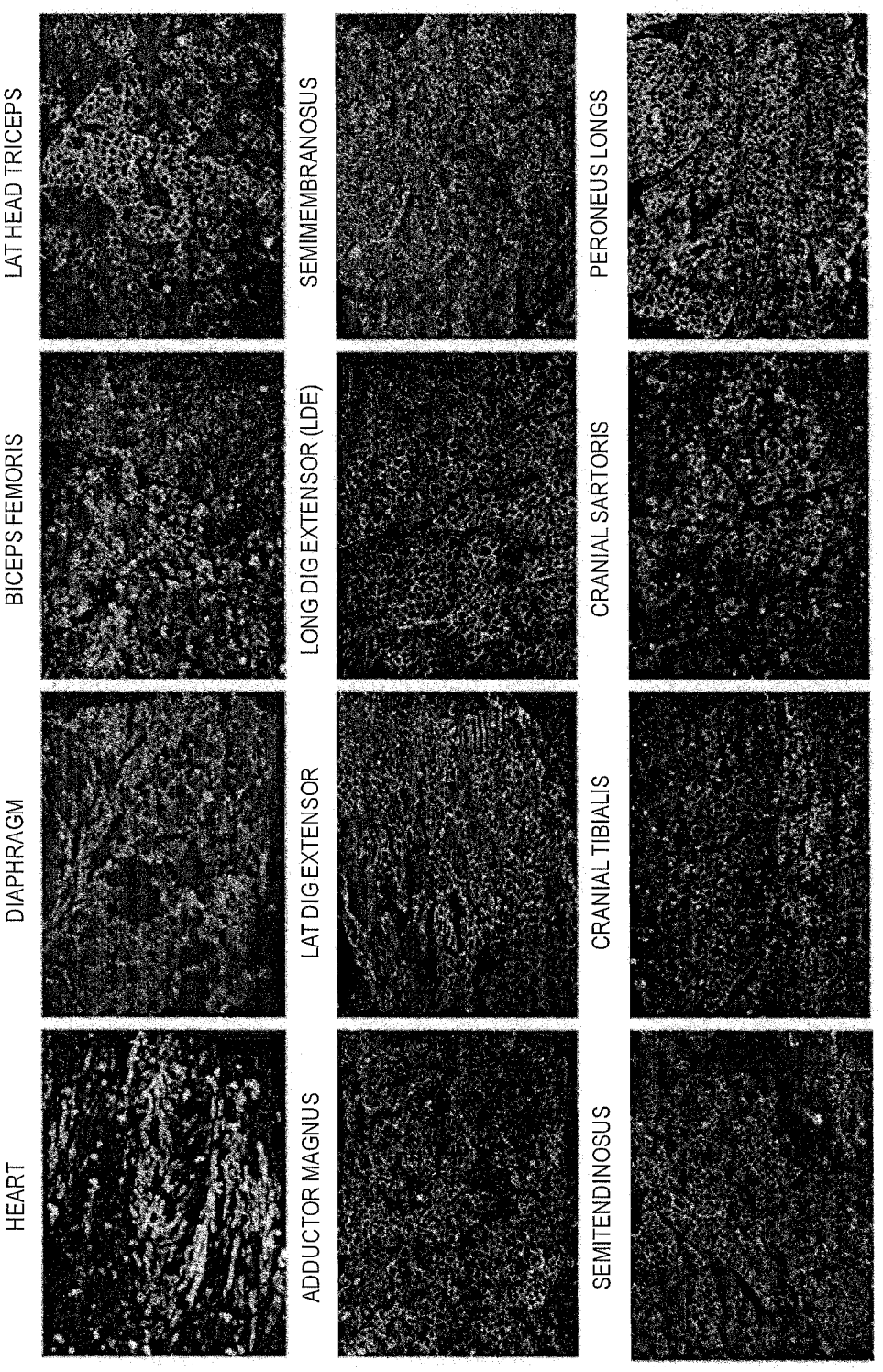

HEART
DIAPHRAGM
BICEPS FEMORIS
LAT HEAD TRICEPS
ADDUCTOR MAGNUS
LAT DIG EXTENSOR
LONG DIG EXTENSOR (LDE)
SEMIMEMBRANOSUS
SEMITENDINOSUS
CRANIAL TIBIALIS
CRANIAL SARTORIS
PERONEUS LONGS

FIG. 23

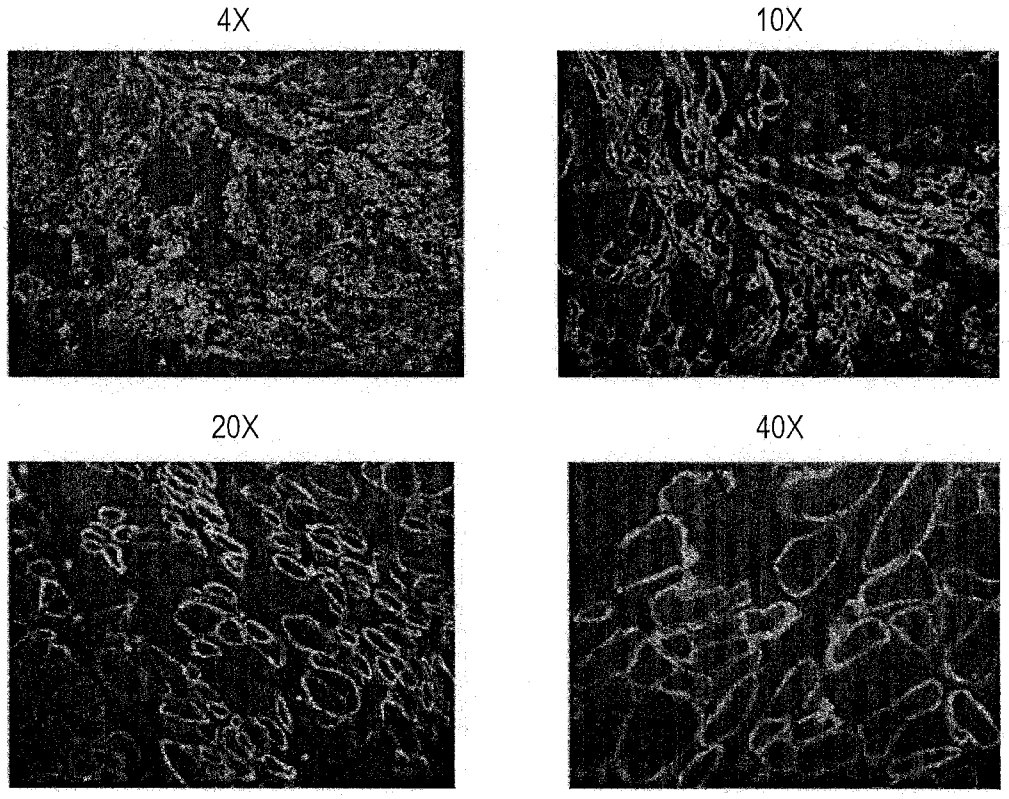


FIG. 24

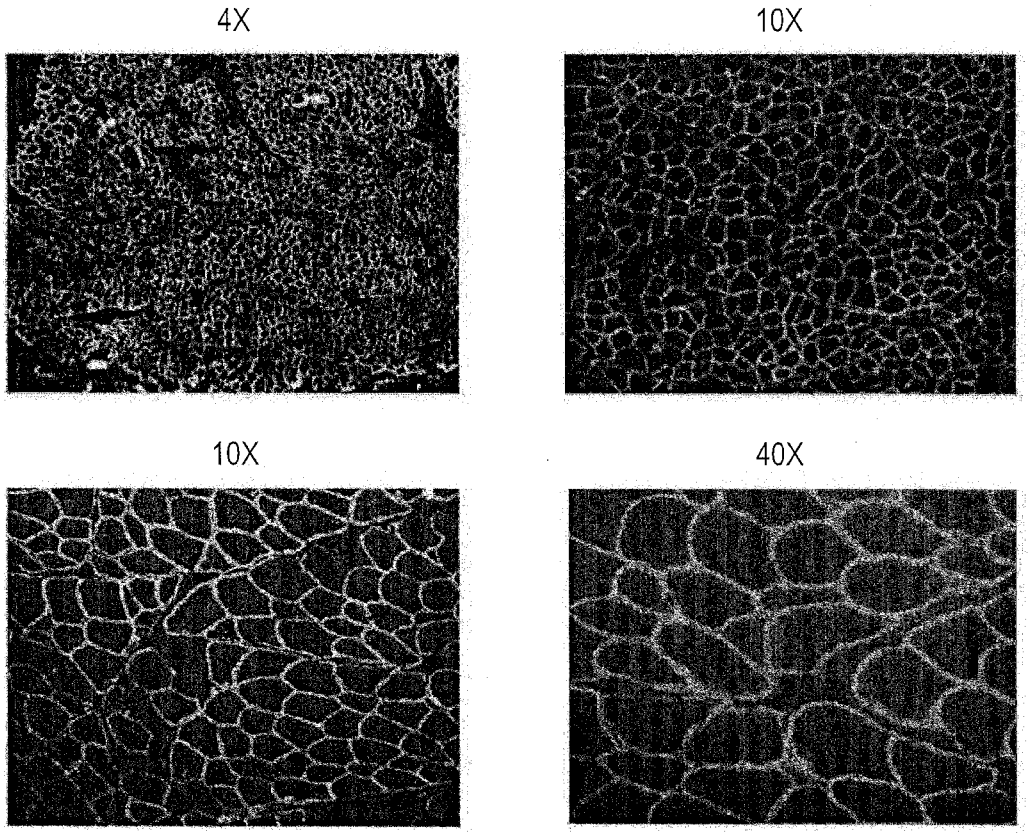


FIG. 25

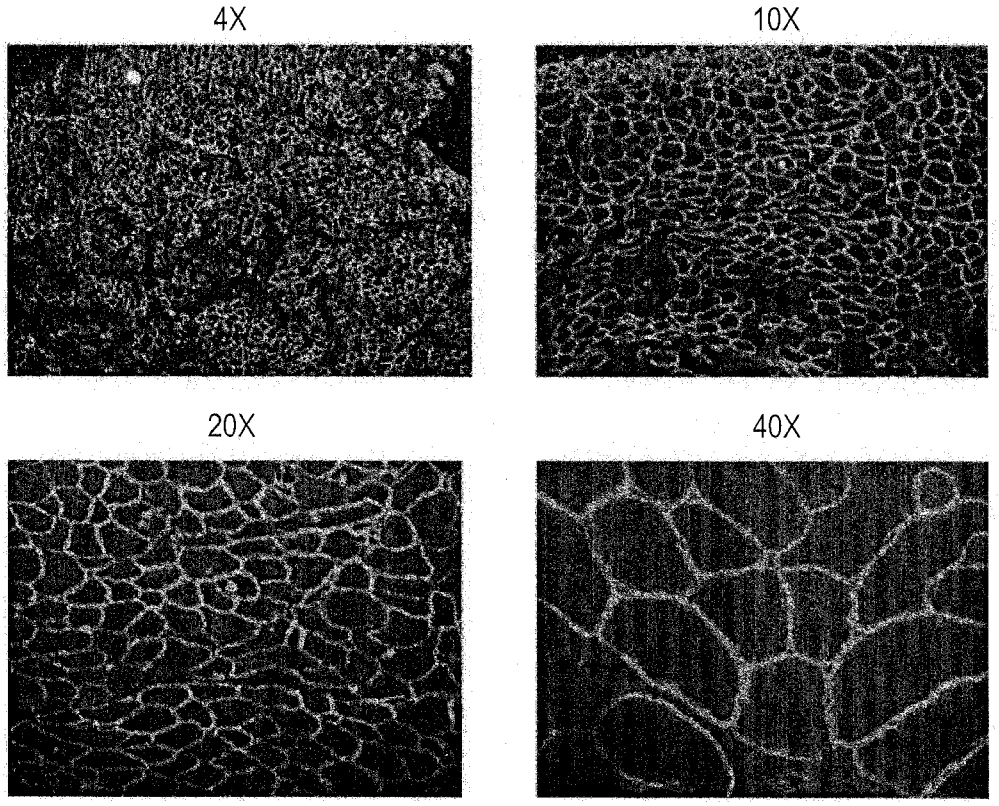


FIG. 26

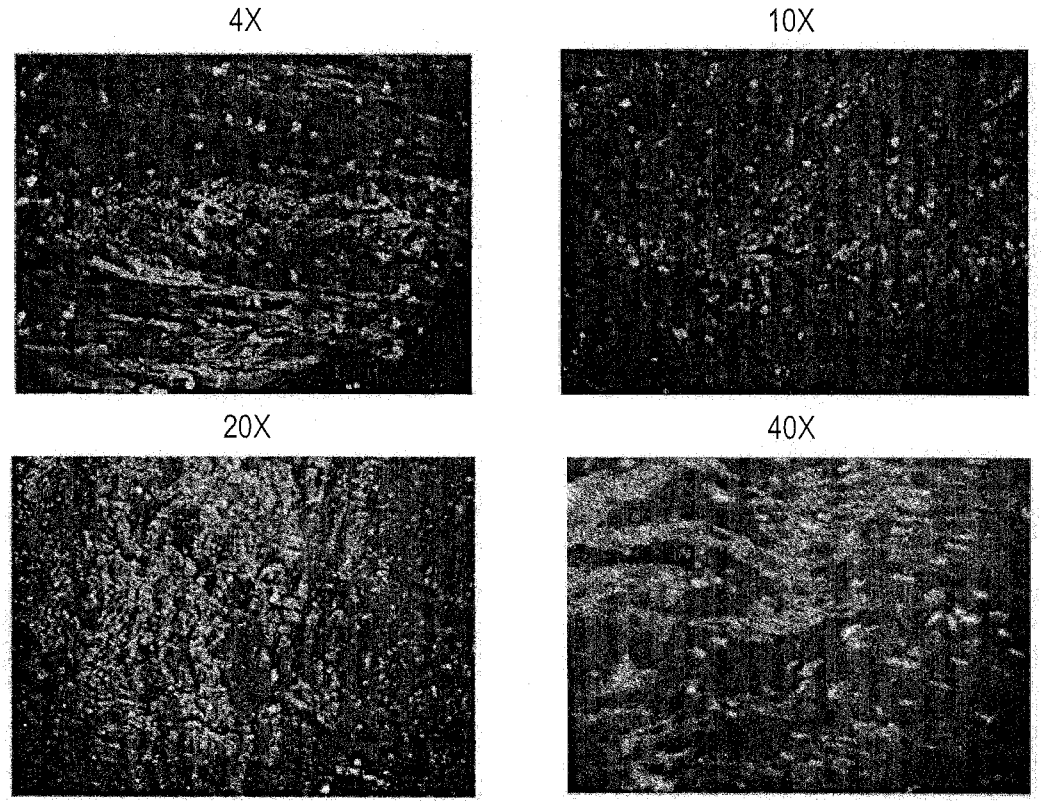


FIG. 27

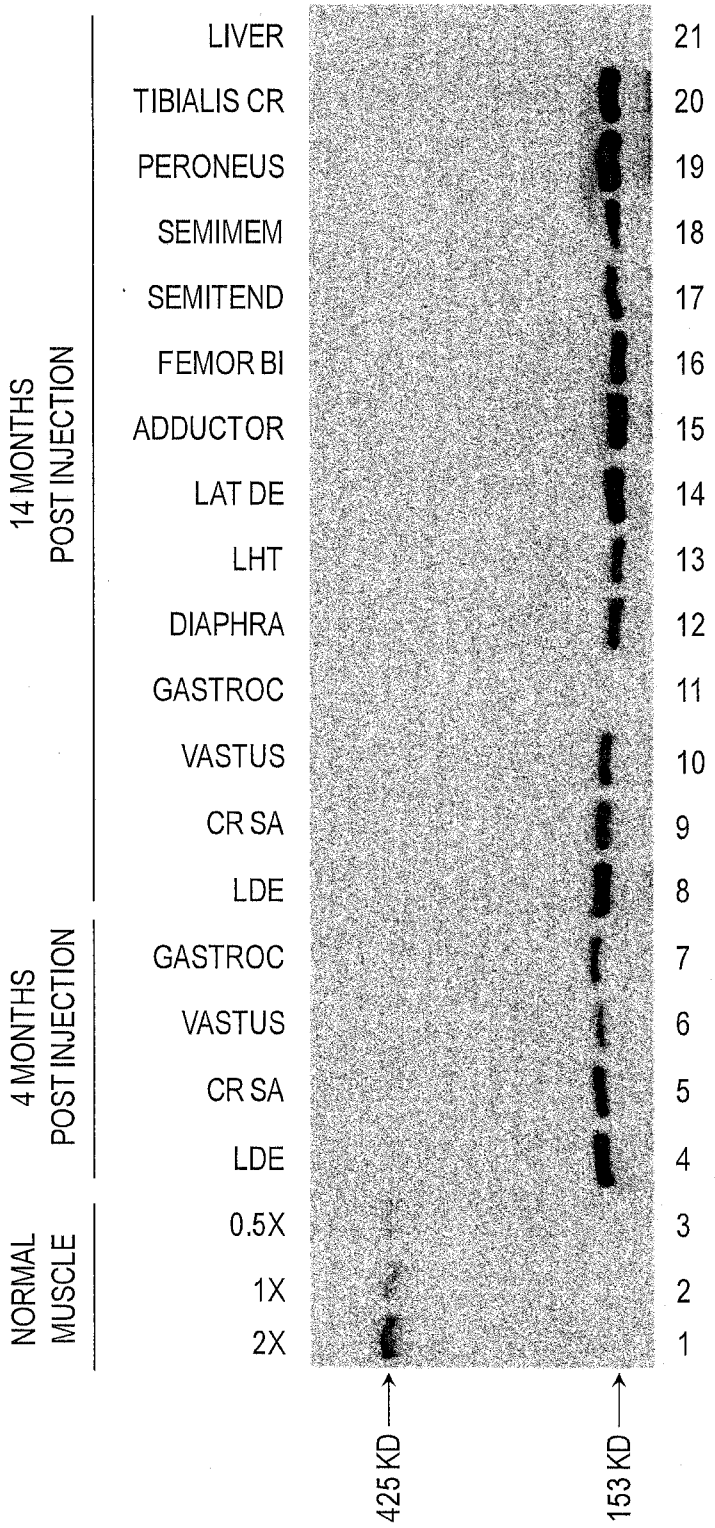

14 MONTHS POST INJECTION
4 MONTHS POST INJECTION
NORMAL MUSCLE
LIVER
TIBIALIS CR
PERONEUS
SEMIMEM
SEMITEND
FEMOR BI
ADDUCTOR
LAT DE
LHT
DIAPHRA
GASTROC
VASTUS
CR SA
LDE
GASTROC
VASTUS
CR SA
LDE
0.5X
1X
2X
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
425 KD
153 KD

FIG. 28

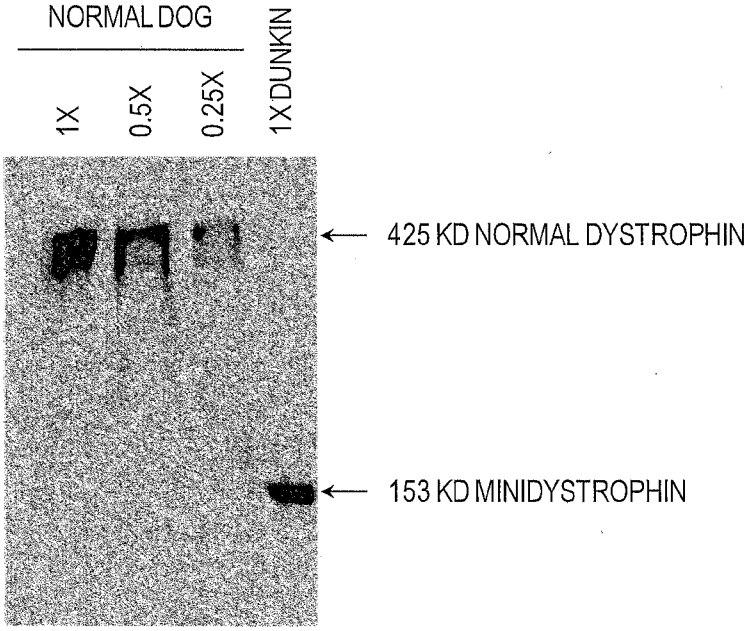

NORMAL DOG
1X
0.5X
0.25X
1X DUNKIN
425 KD NORMAL DYSTROPHIN
153 KD MINIDYSTROPHIN

FIG. 29

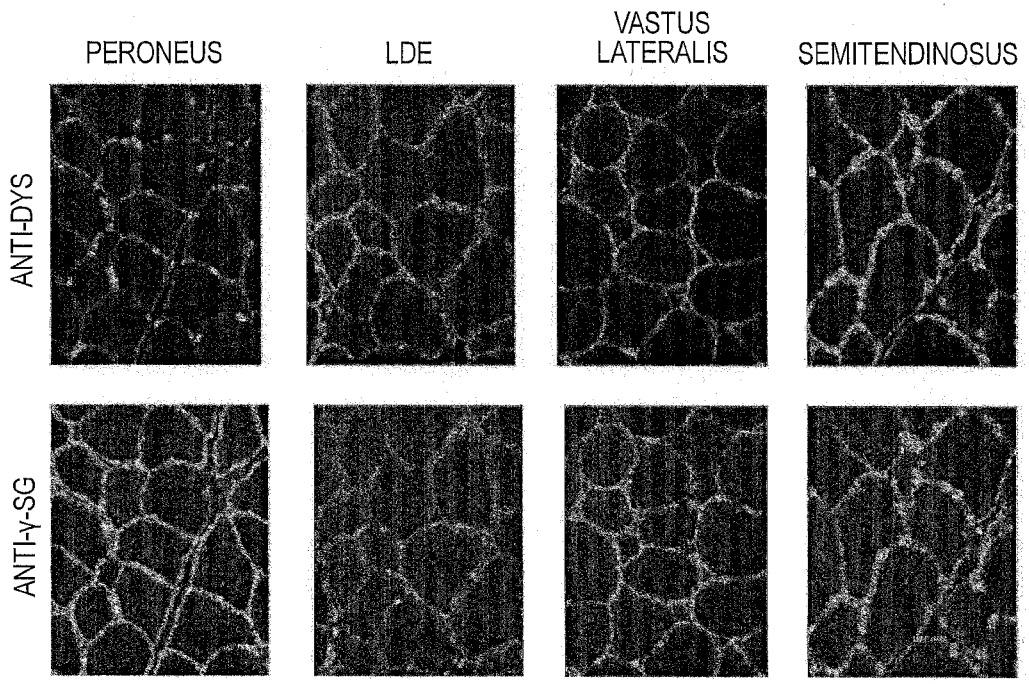

PERONEUS
LDE
VASTUS LATERALIS
SEMITENDINOSUS
ANTI-DYS
ANTI-γ-SG

FIG. 30

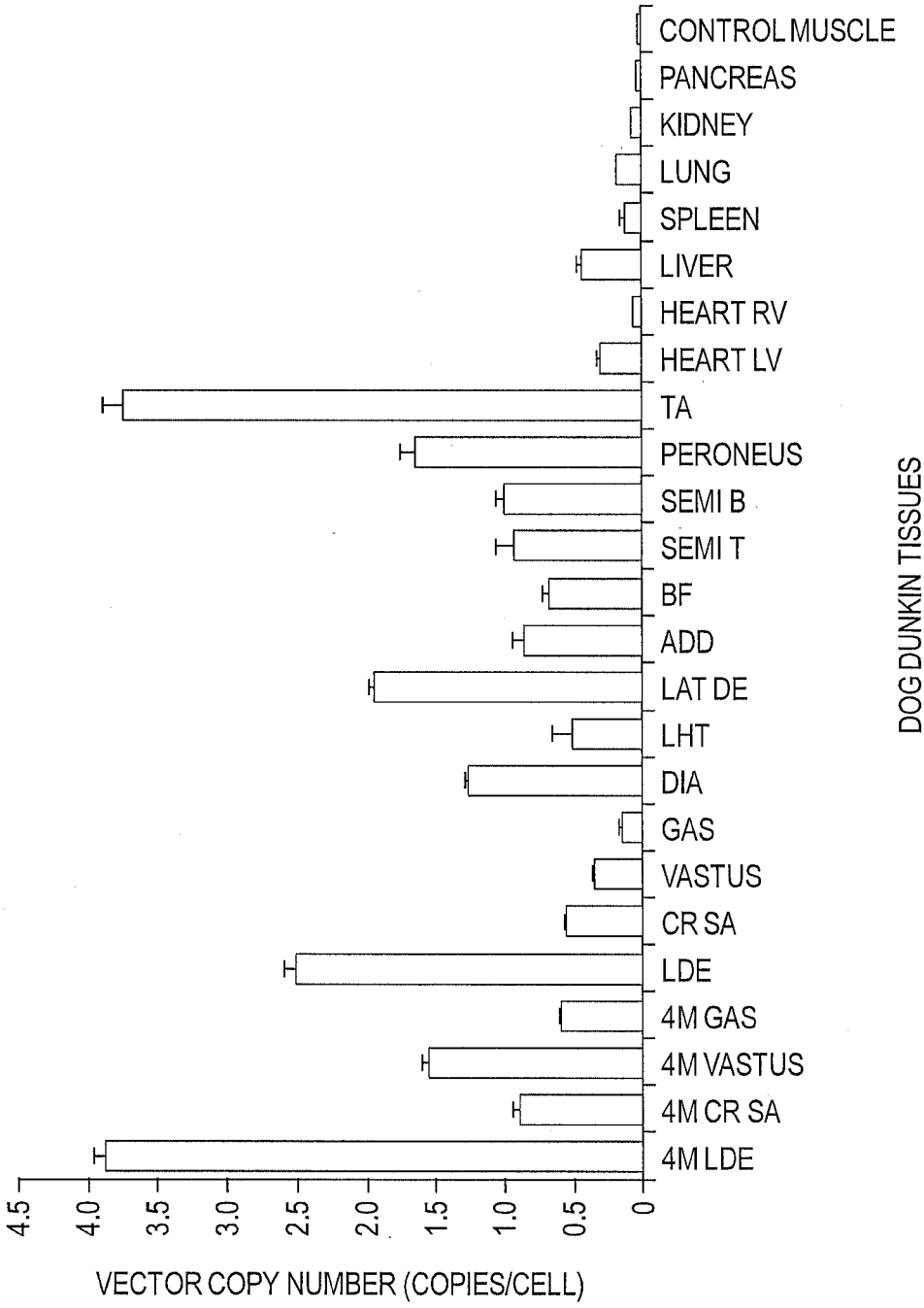

CONTROL MUSCLE
PANCREAS
KIDNEY
LUNG
SPLEEN
LIVER
HEART RV
HEART LV
TA
PERONEUS
SEMI B
SEMI T
BF
ADD
LAT DE
LHT
DIA
GAS
VASTUS
CR SA
LDE
4M GAS
4M VASTUS
4M CR SA
4M LDE
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
VECTOR COPY NUMBER (COPIES/CELL)
DOG DUNKIN TISSUES

FIG. 31

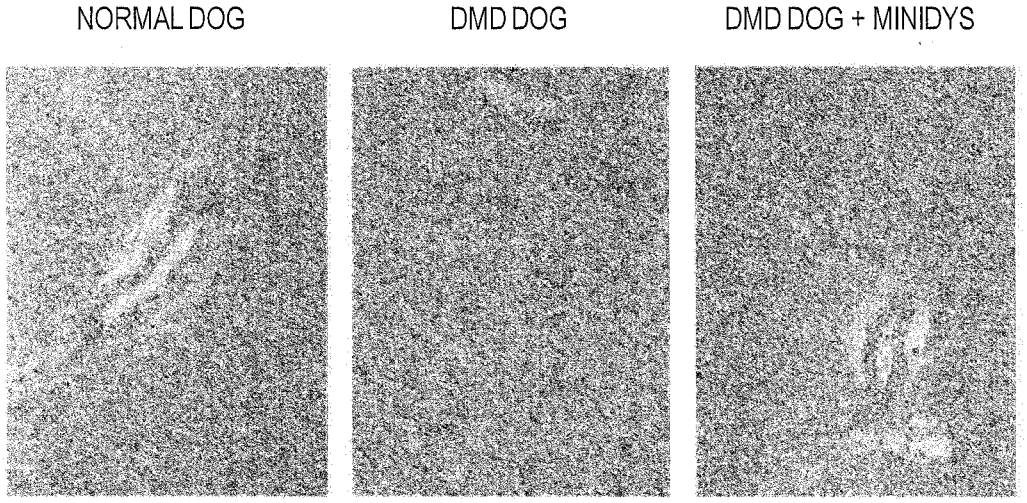

NORMAL DOG
DMD DOG
DMD DOG + MINIDYS

FIG. 32

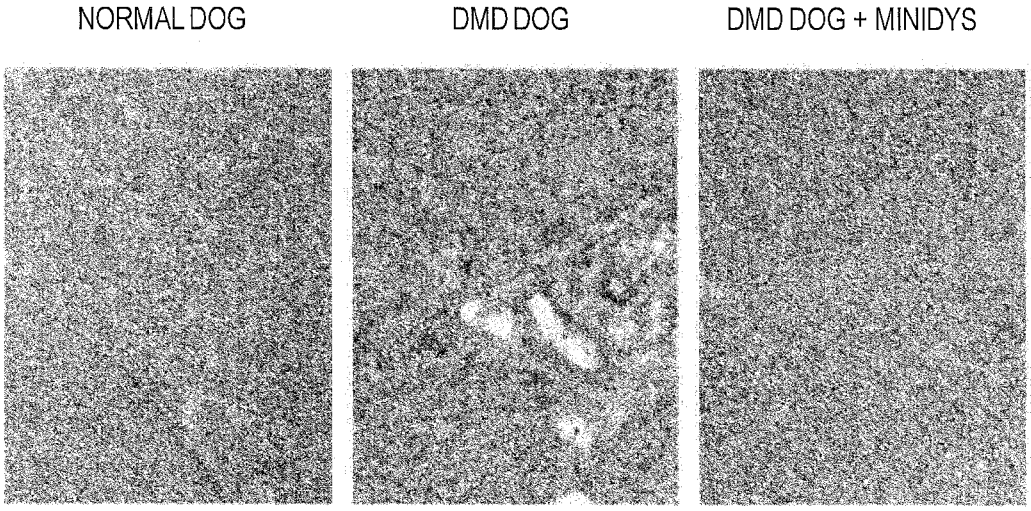

NORMAL DOG
DMD DOG
DMD DOG + MINIDYS

FIG. 33

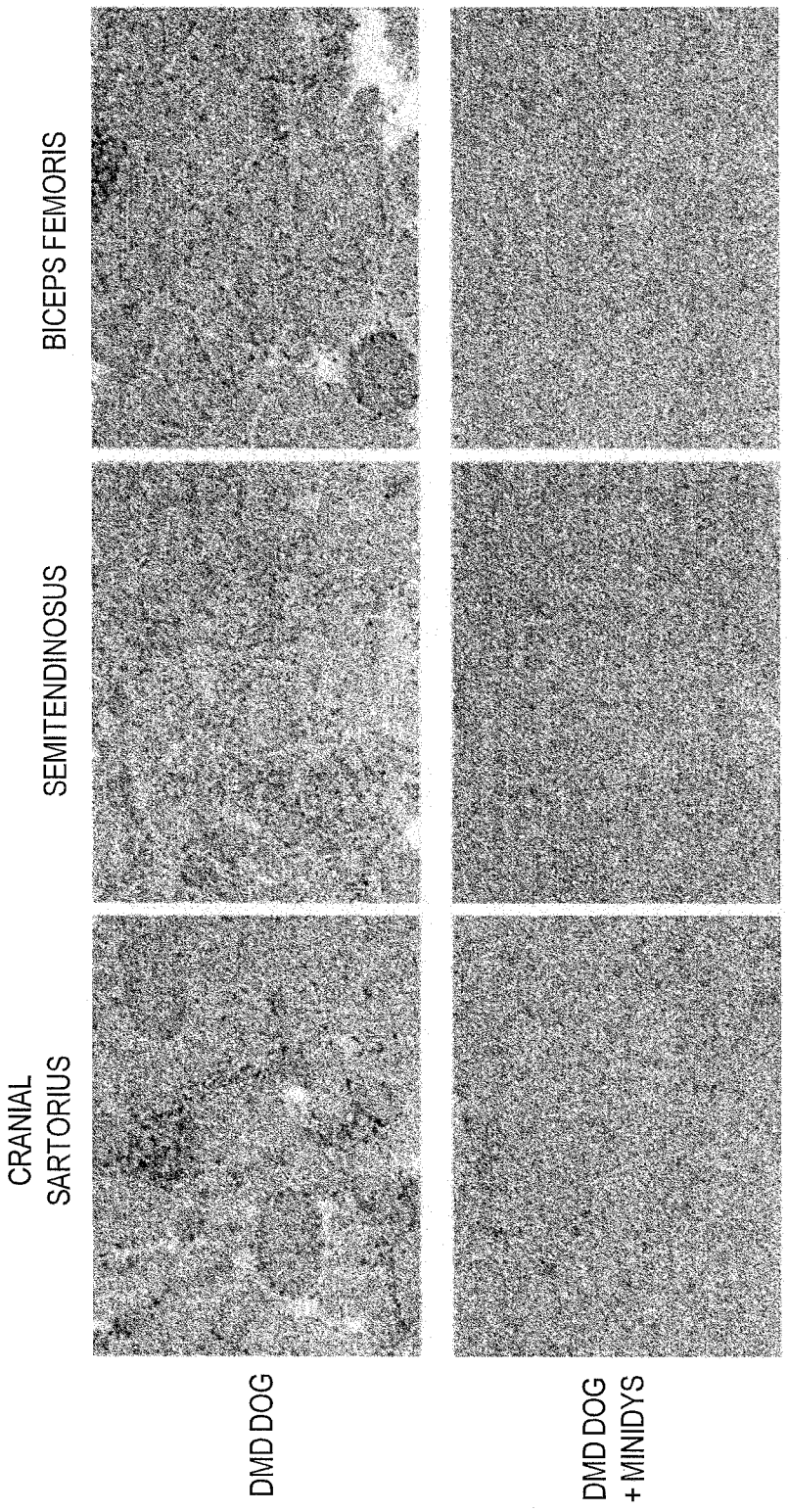

CRANIAL SARTORIUS
SEMITENDINOSUS
BICEPS FEMORIS
DMD DOG
DMD DOG + MINIDYS

FIG. 34

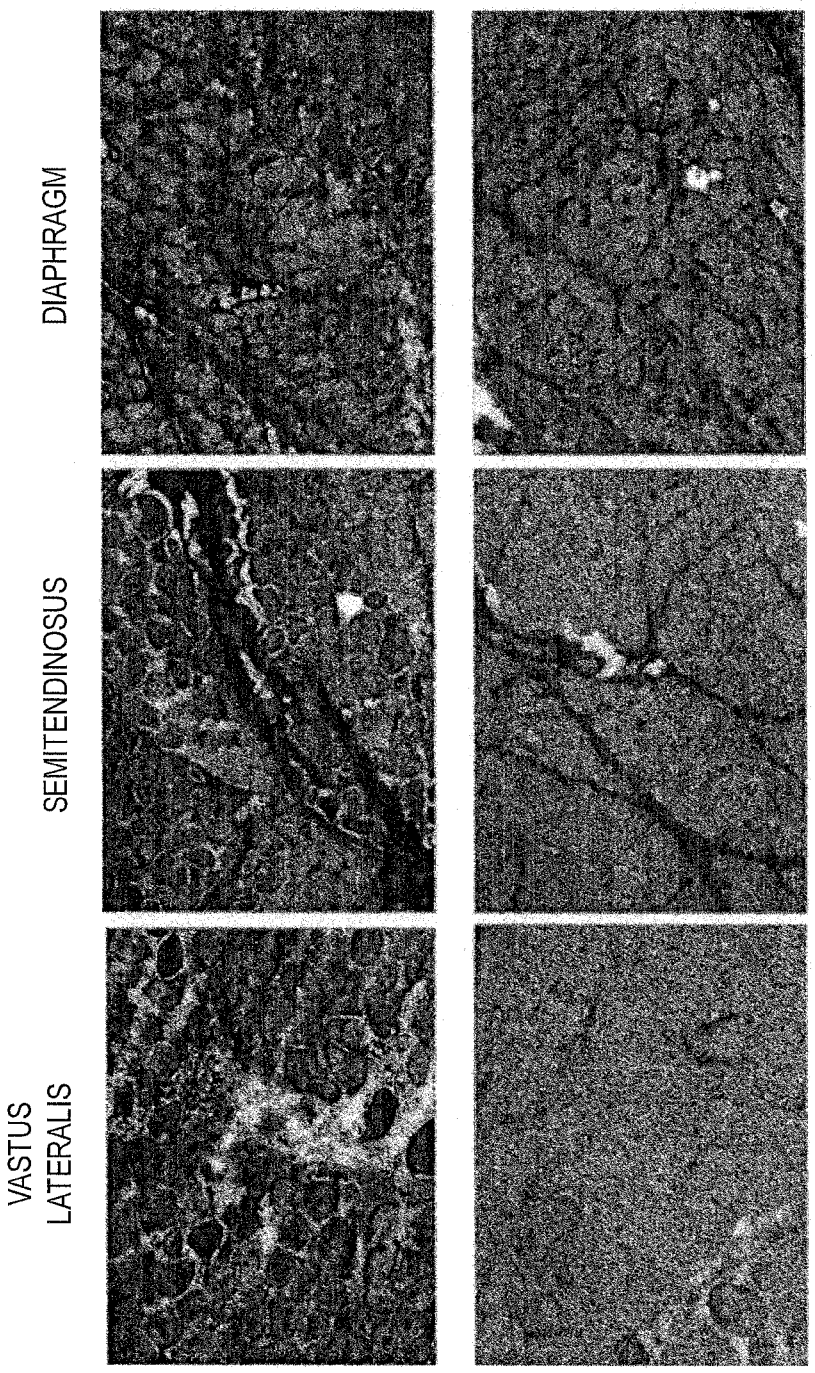

VASTUS LATERALIS
SEMITENDINOSUS
DIAPHRAGM
DMD DOG
DMD DOG + MINIDYS

FIG. 35

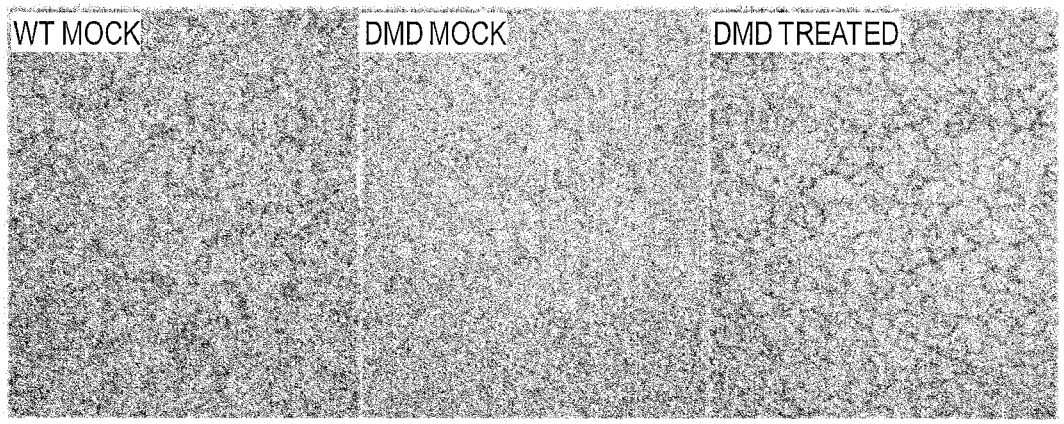


FIG. 36A

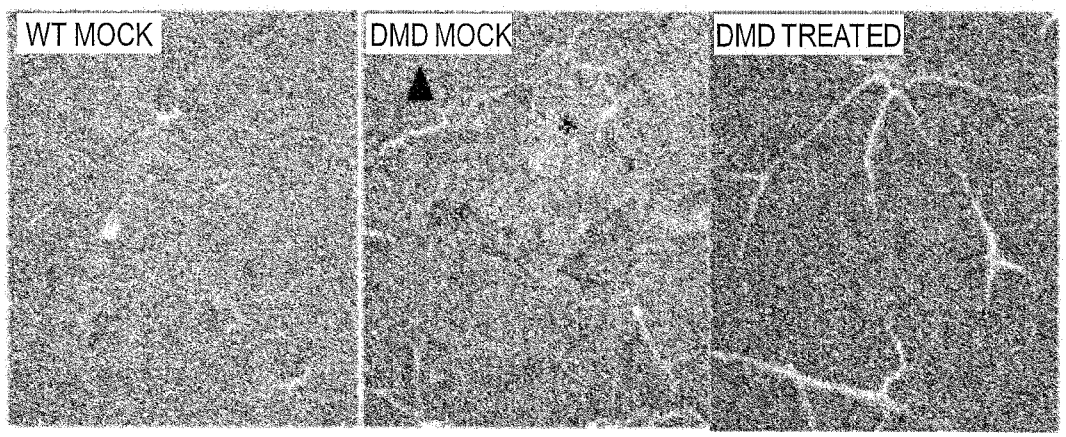


FIG. 36B

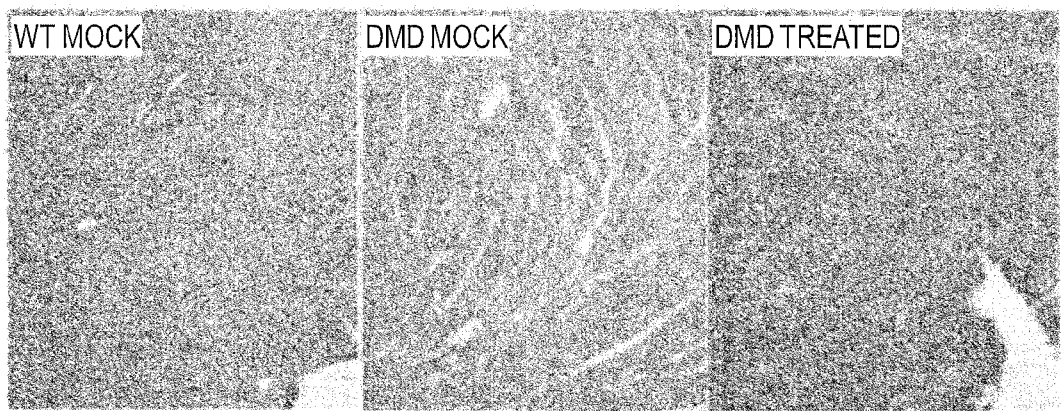


FIG. 36C

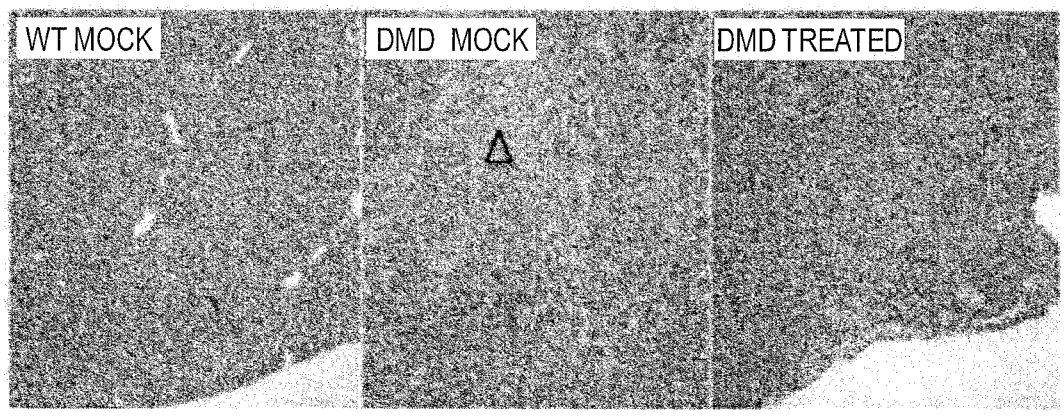


FIG. 36D

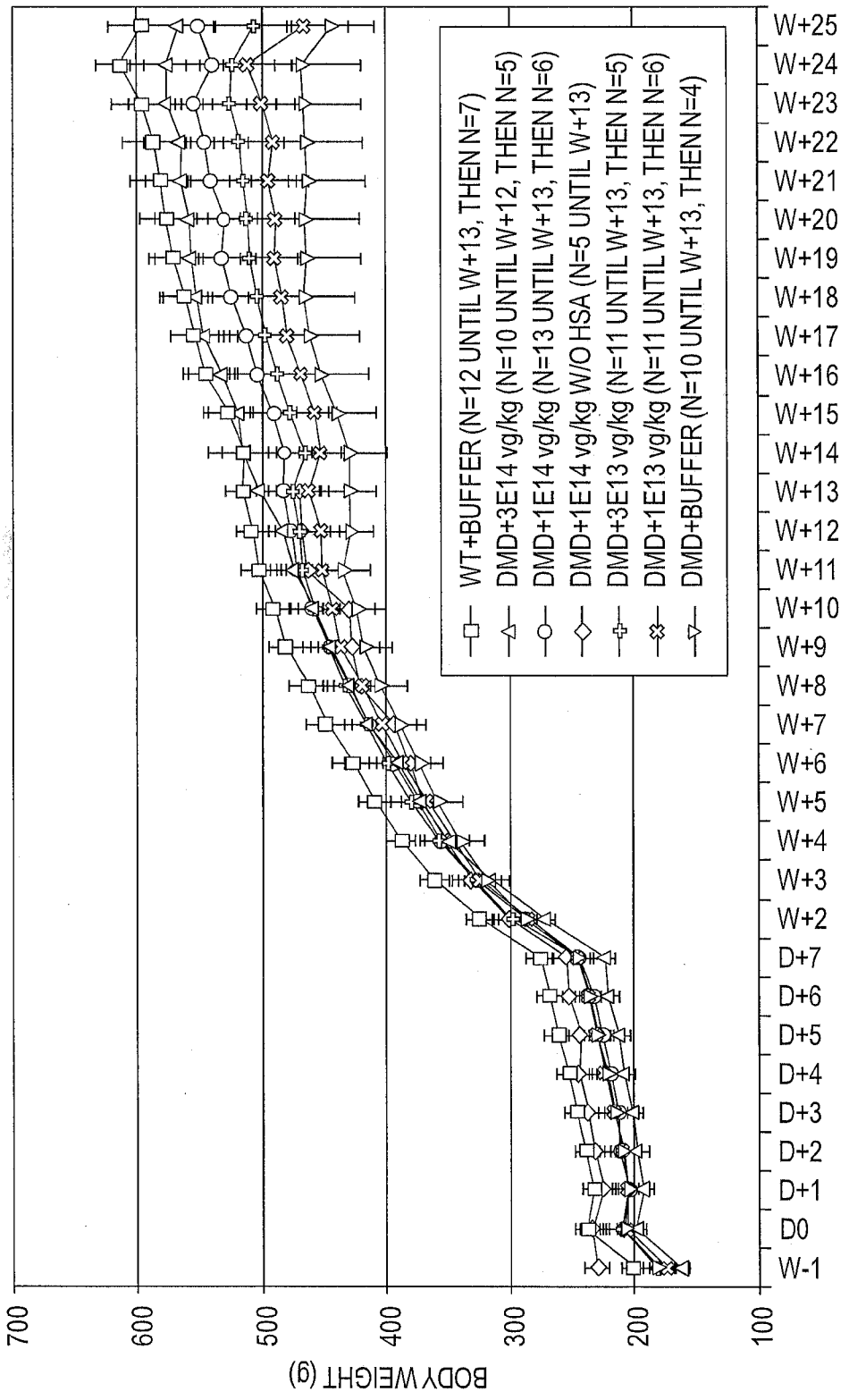

WT+BUFFER (N=12 UNTIL W+13, THEN N=7)
DMD+3E14 vg/kg (N=10 UNTIL W+12, THEN N=5)
DMD+1E14 vg/kg (N=13 UNTIL W+13, THEN N=6)
DMD+1E14 vg/kg W/O HSA (N=5 UNTIL W+13)
DMD+3E13 vg/kg (N=11 UNTIL W+13, THEN N=5)
DMD+1E13 vg/kg (N=11 UNTIL W+13, THEN N=6)
DMD+BUFFER (N=10 UNTIL W+13, THEN N=4)
BODY WEIGHT (g)
700
600
500
400
300
200
100
W+25
W+24
W+23
W+22
W+21
W+20
W+19
W+18
W+17
W+16
W+15
W+14
W+13
W+12
W+11
W+10
W+9
W+8
W+7
W+6
W+5
W+4
W+3
W+2
D+7
D+6
D+5
D+4
D+3
D+2
D+1
D0
W-1

FIG. 37

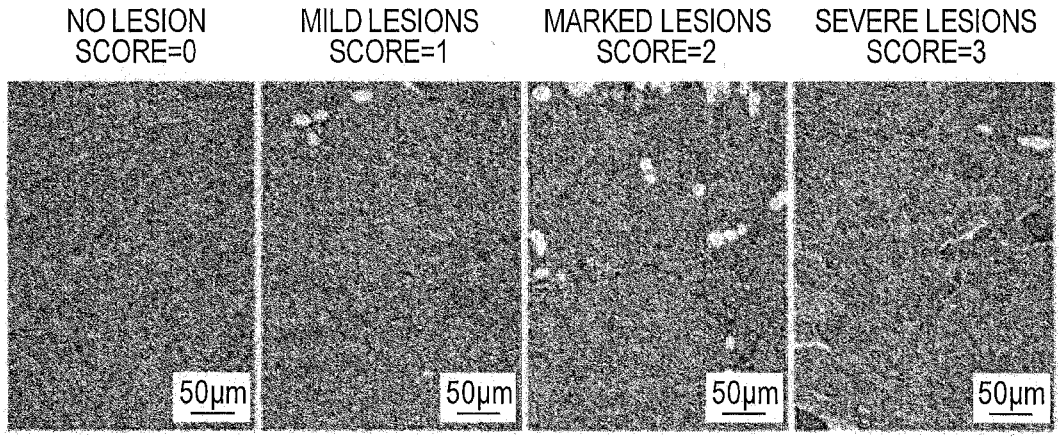


FIG. 38A

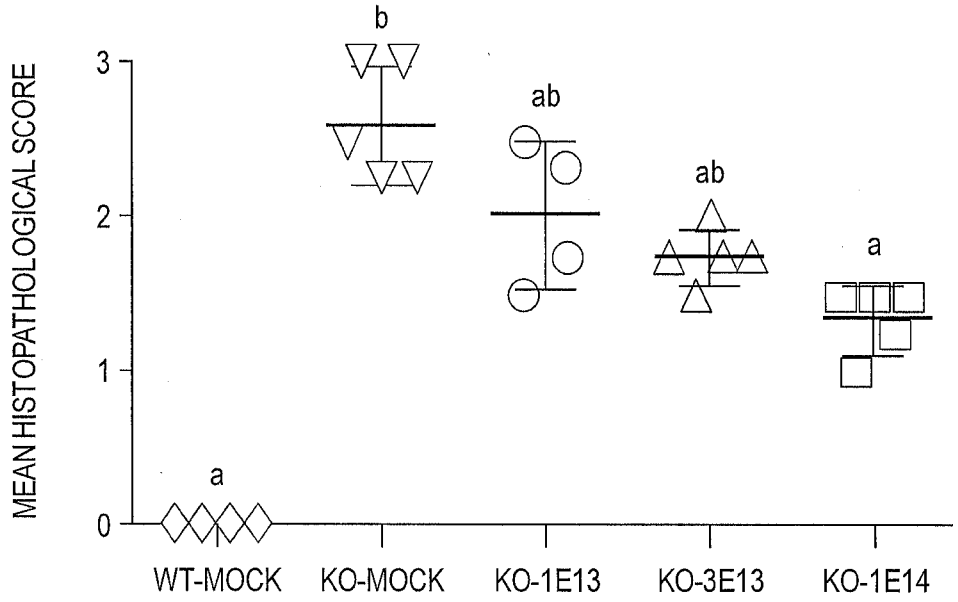


FIG. 38B

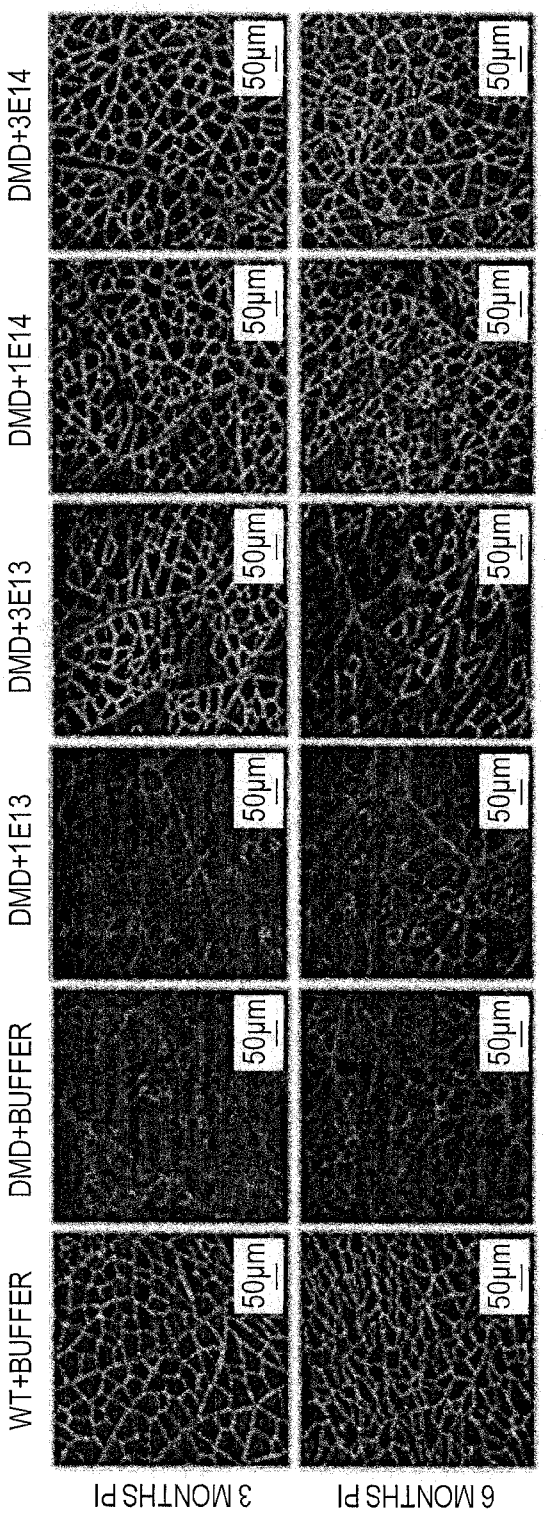


FIG. 39A

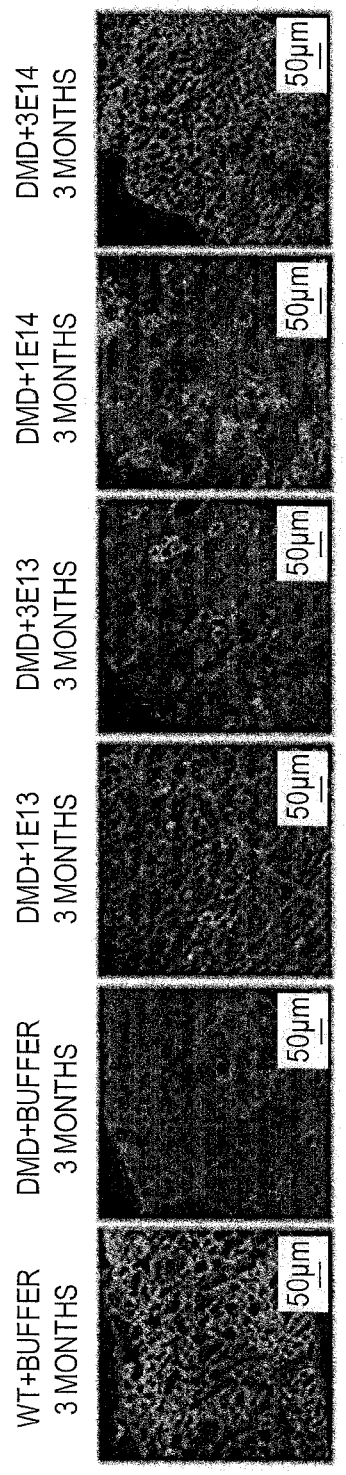


FIG. 40A

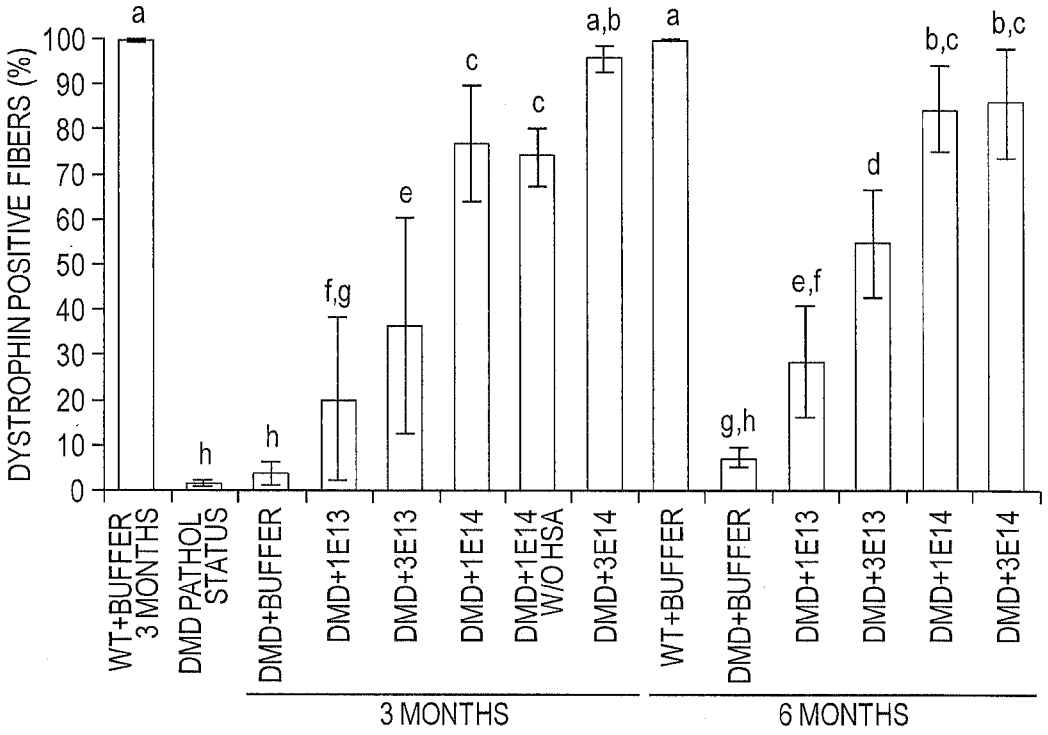


FIG. 39B

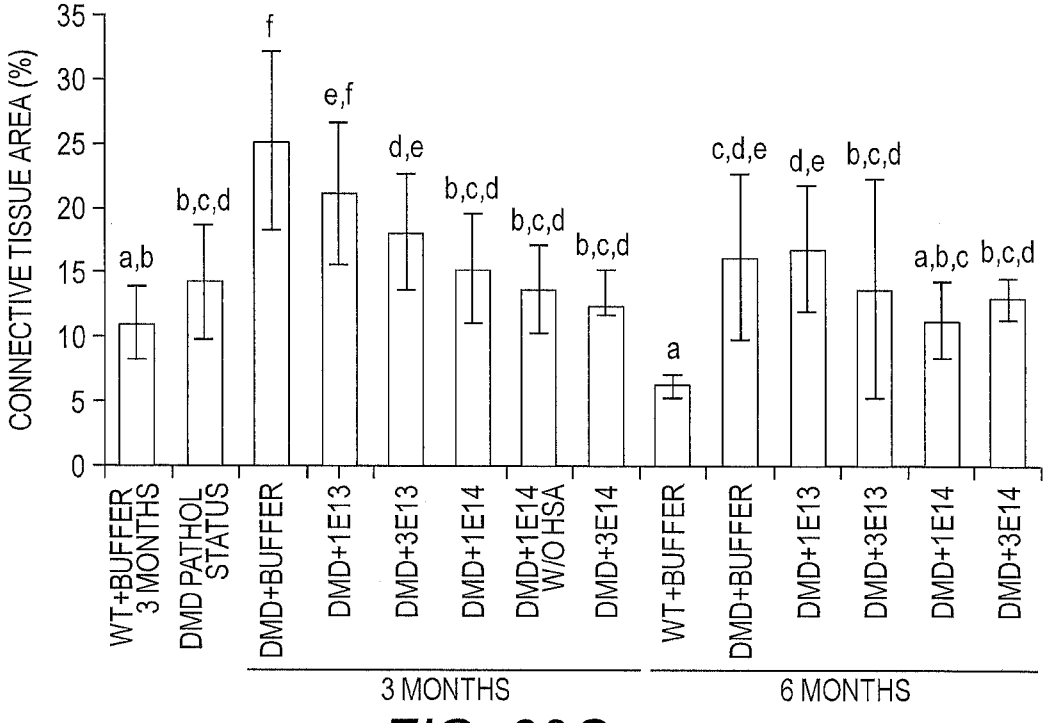


FIG. 39C

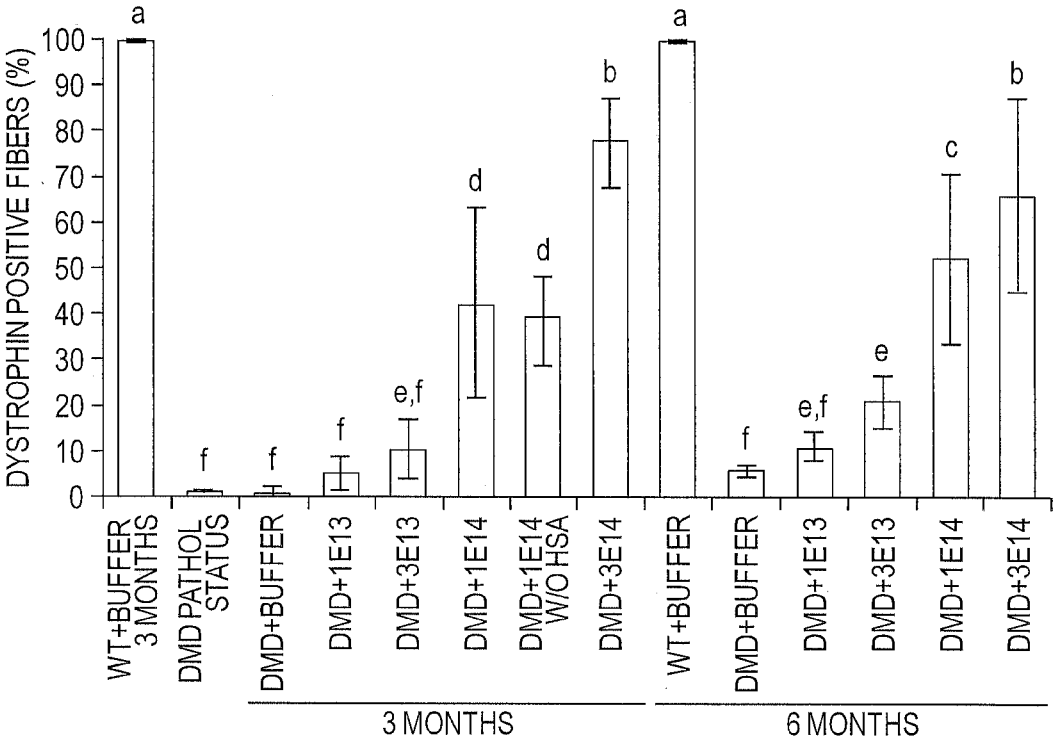


FIG. 40B

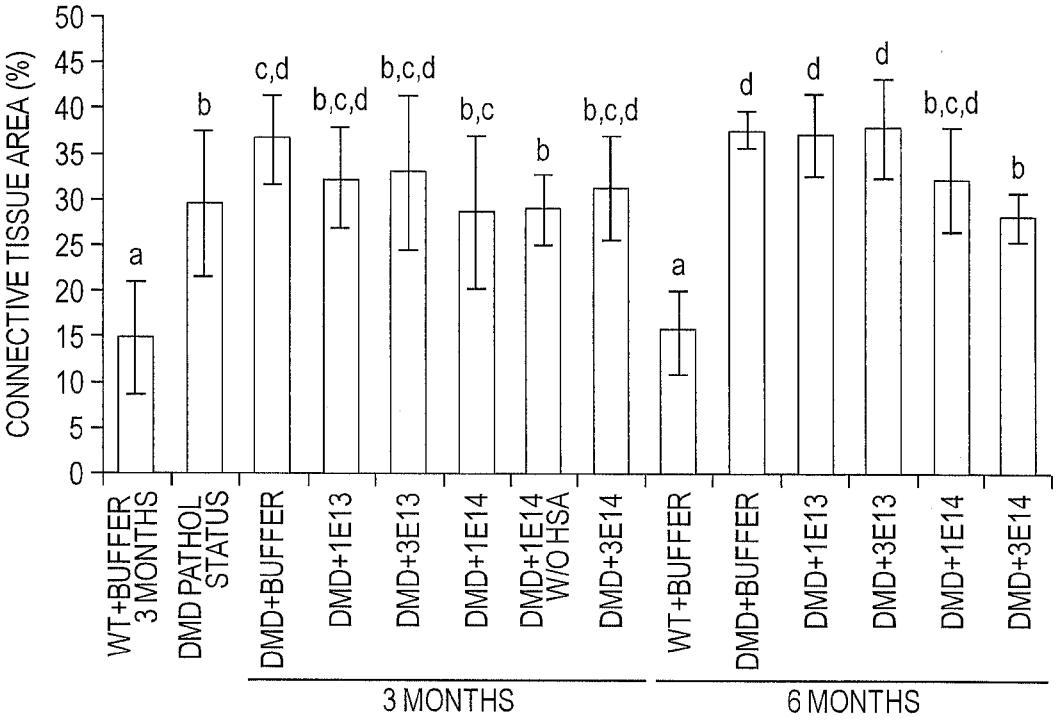


FIG. 40C

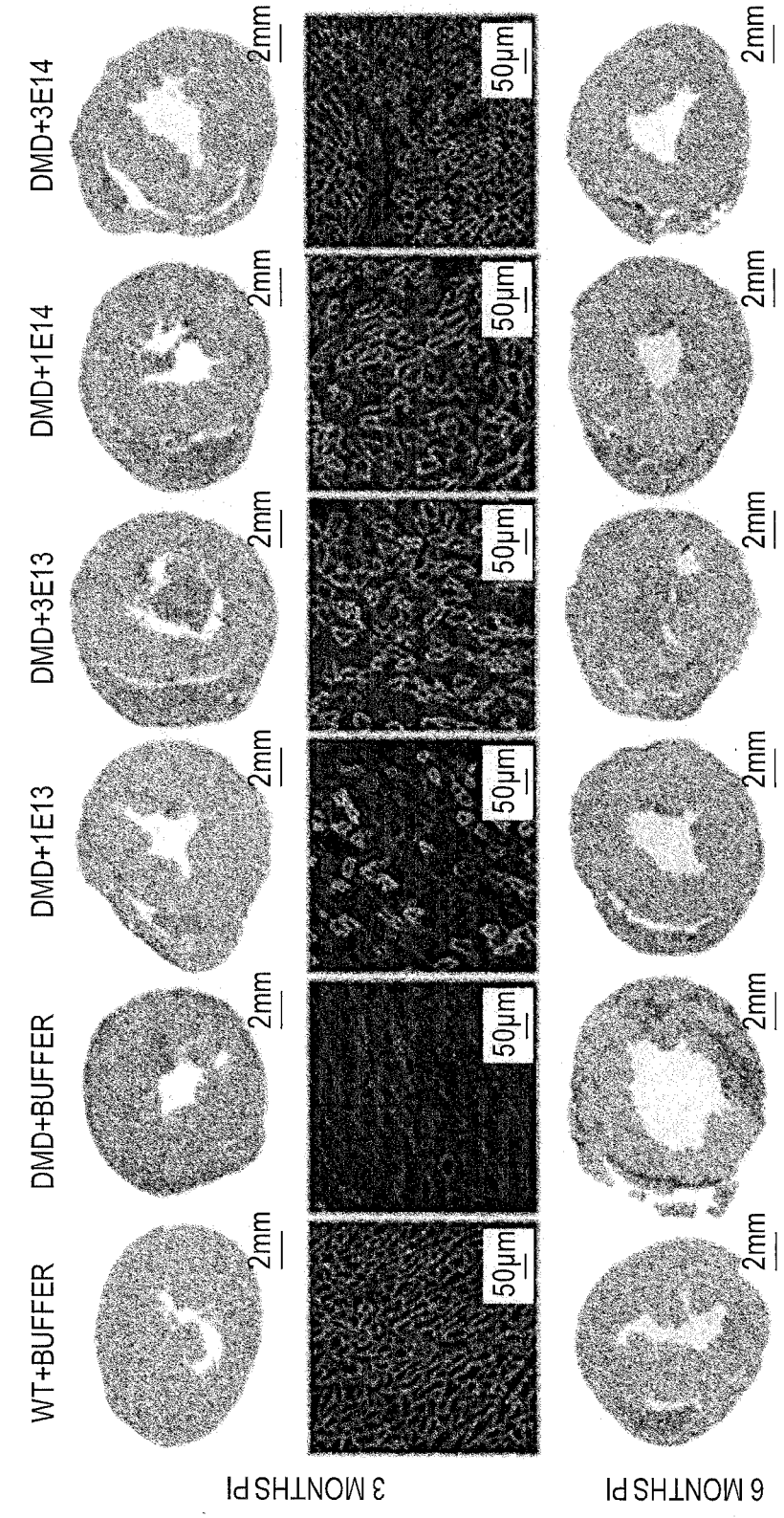

WT+BUFFER
DMD+BUFFER
DMD+1E13
DMD+3E13
DMD+1E14
DMD+3E14
3 MONTHS PI
6 MONTHS PI
2mm
50µm

FIG. 41A

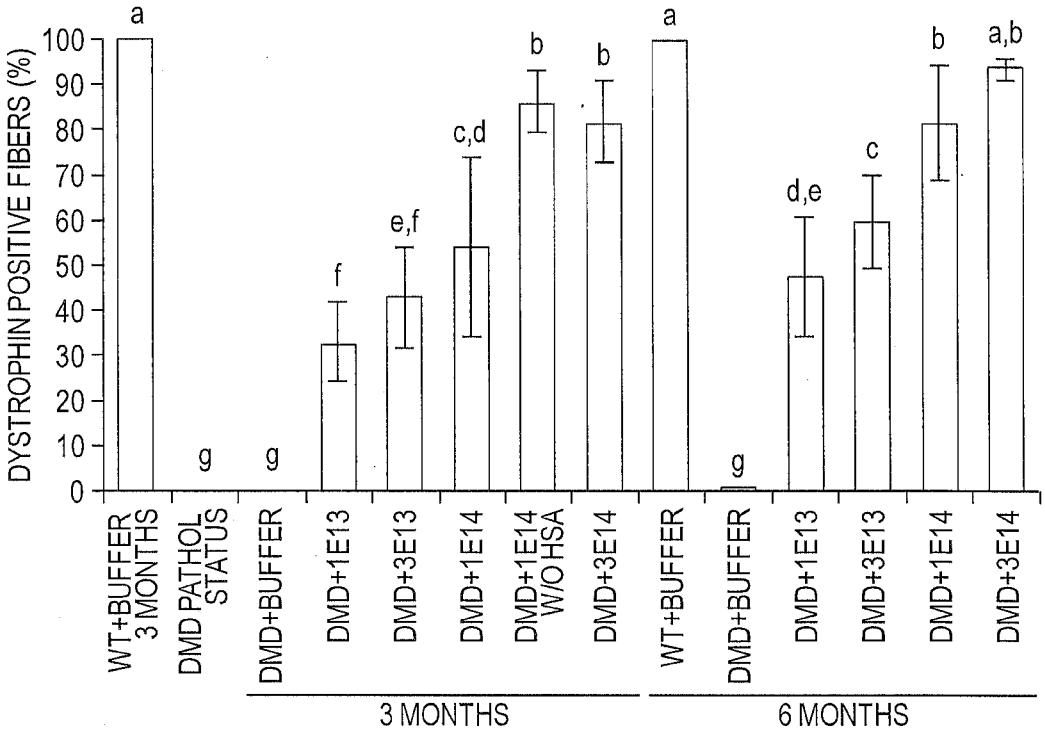


FIG. 41B

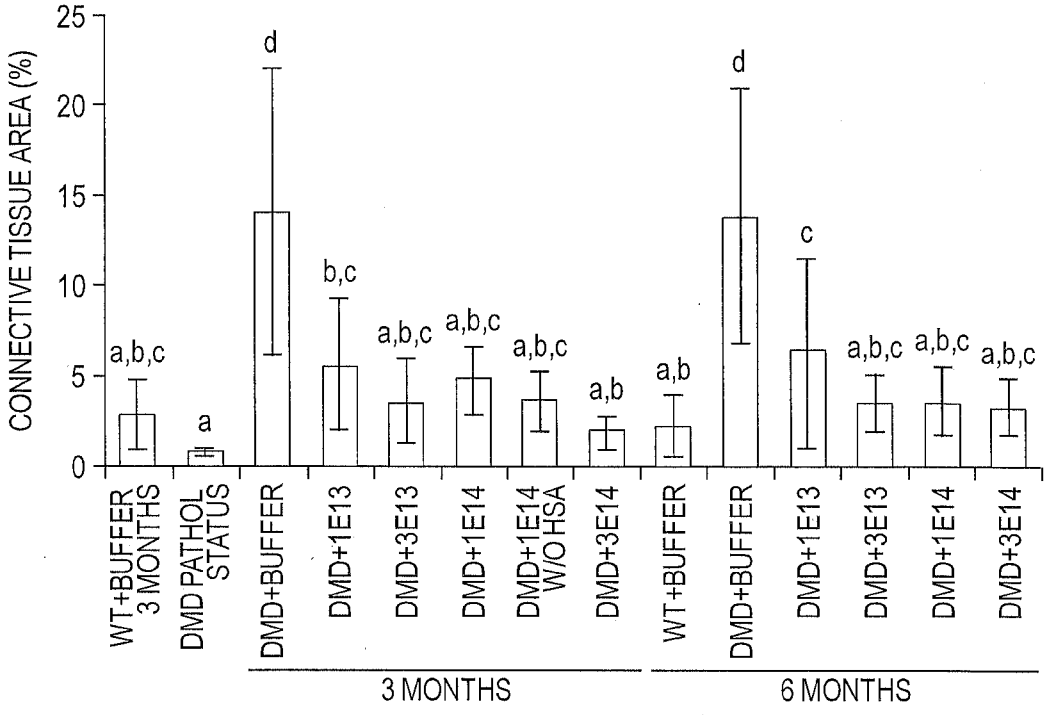


FIG. 41C

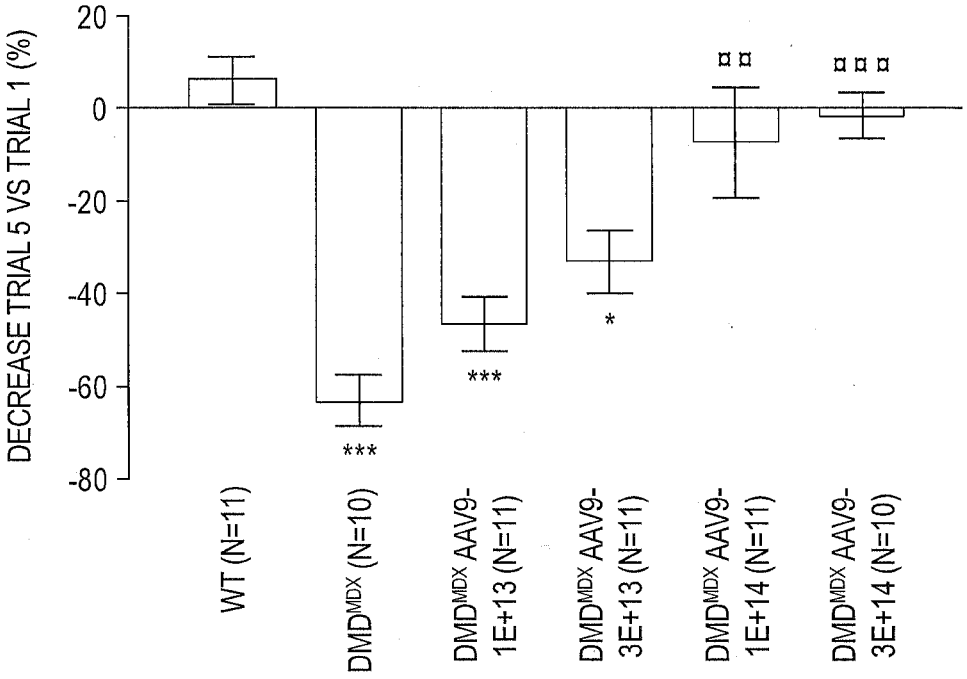


FIG. 42A

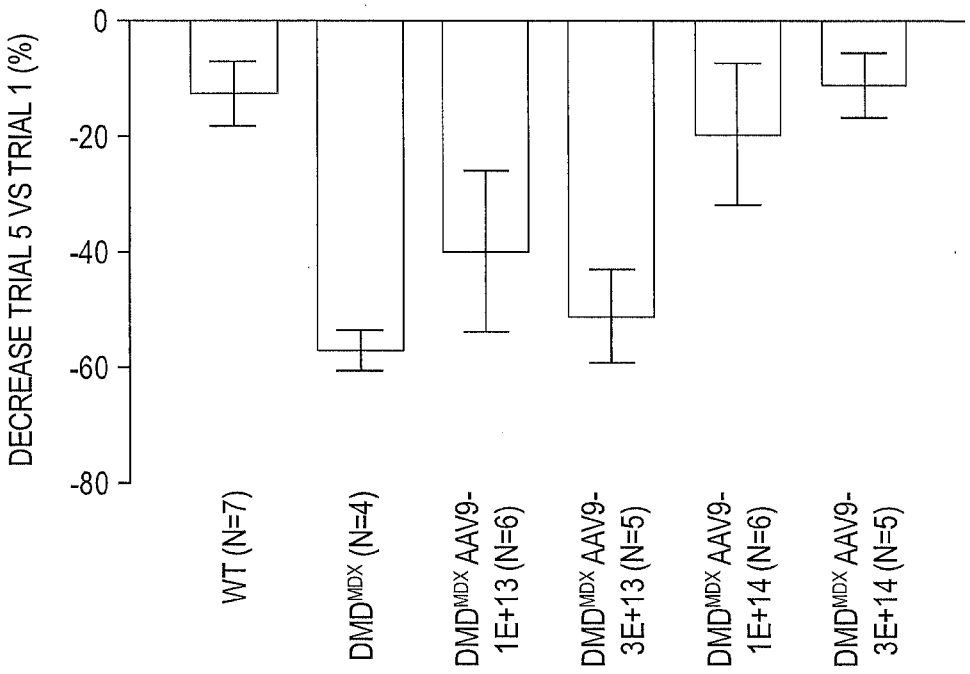


FIG. 42B

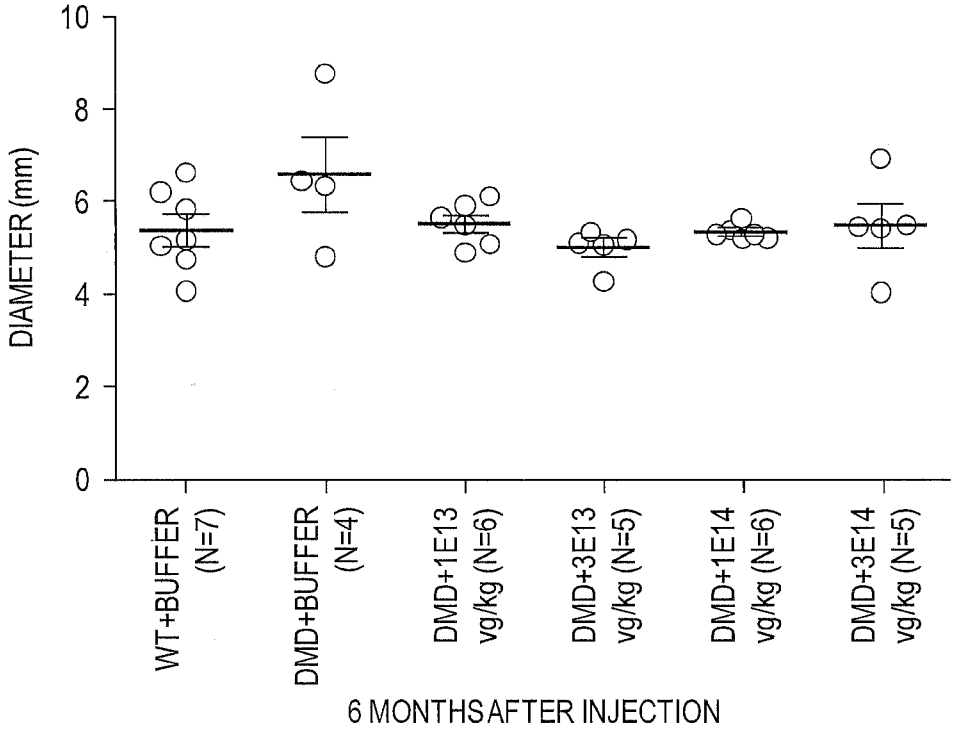

10
8
6
4
2
0
DIAMETER (mm)
WT+BUFFER (N=7)
DMD+BUFFER (N=4)
DMD+1E13 vg/kg (N=6)
DMD+3E13 vg/kg (N=5)
DMD+1E14 vg/kg (N=6)
DMD+3E14 vg/kg (N=5)
6 MONTHS AFTER INJECTION

FIG. 43

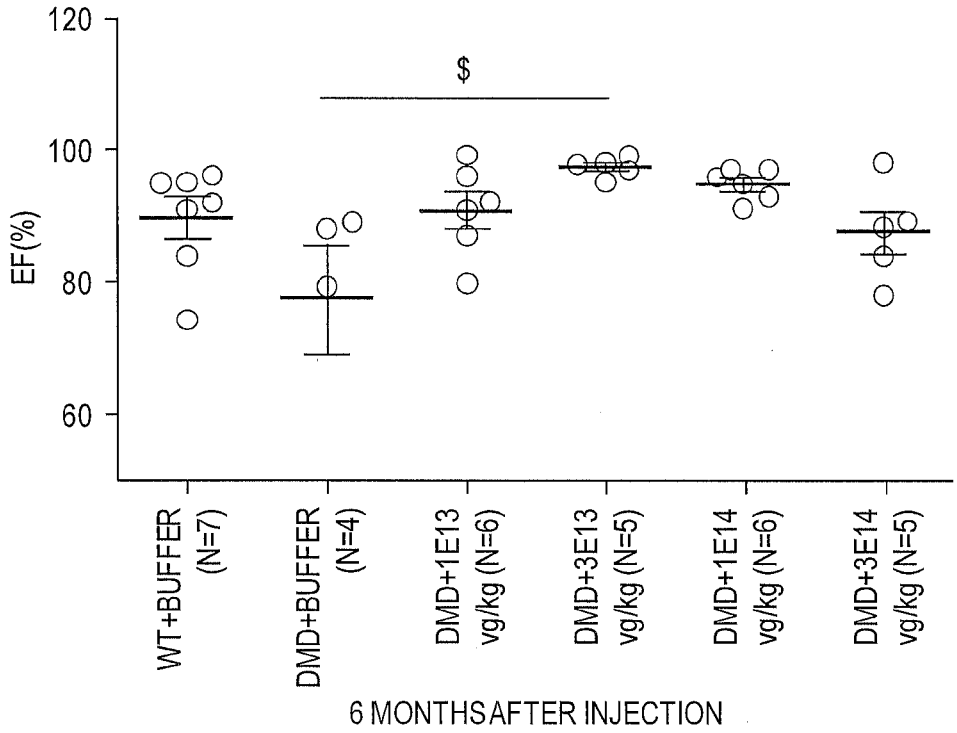

120
100
80
60
EF(%)
$
WT+BUFFER (N=7)
DMD+BUFFER (N=4)
DMD+1E13 vg/kg (N=6)
DMD+3E13 vg/kg (N=5)
DMD+1E14 vg/kg (N=6)
DMD+3E14 vg/kg (N=5)
6 MONTHS AFTER INJECTION

FIG. 44

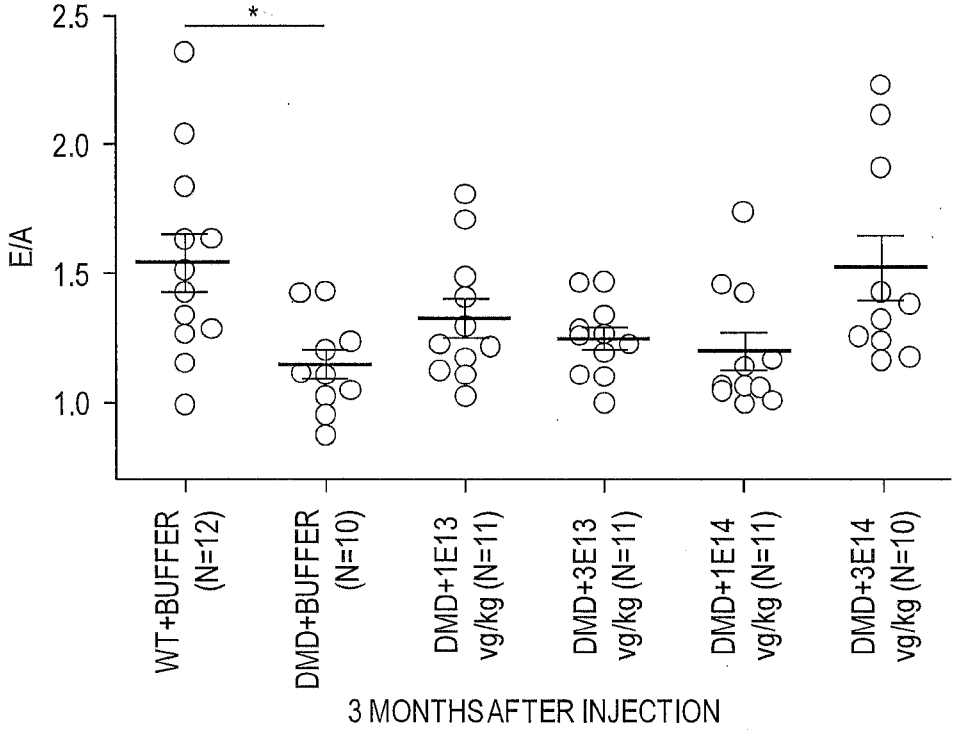


FIG. 45A

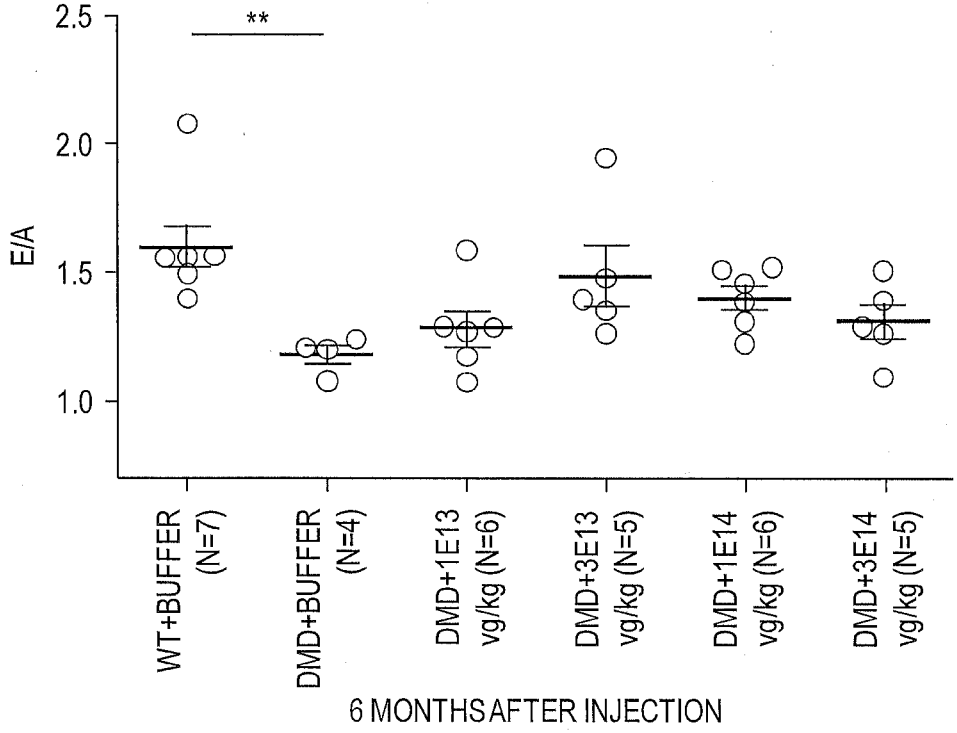


FIG. 45B

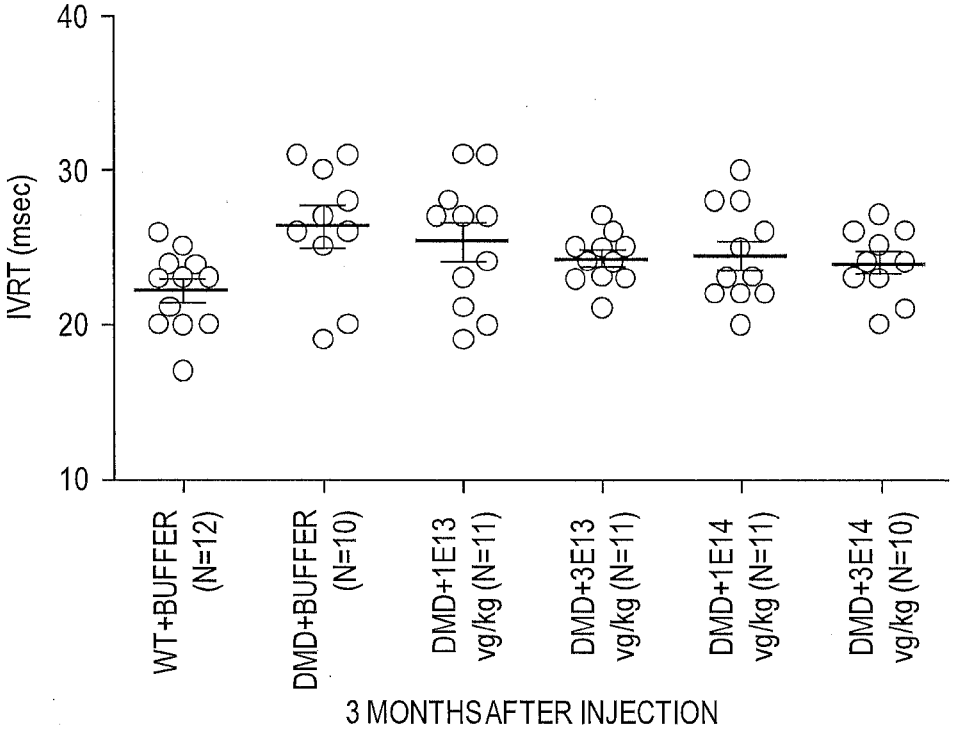


FIG. 46A

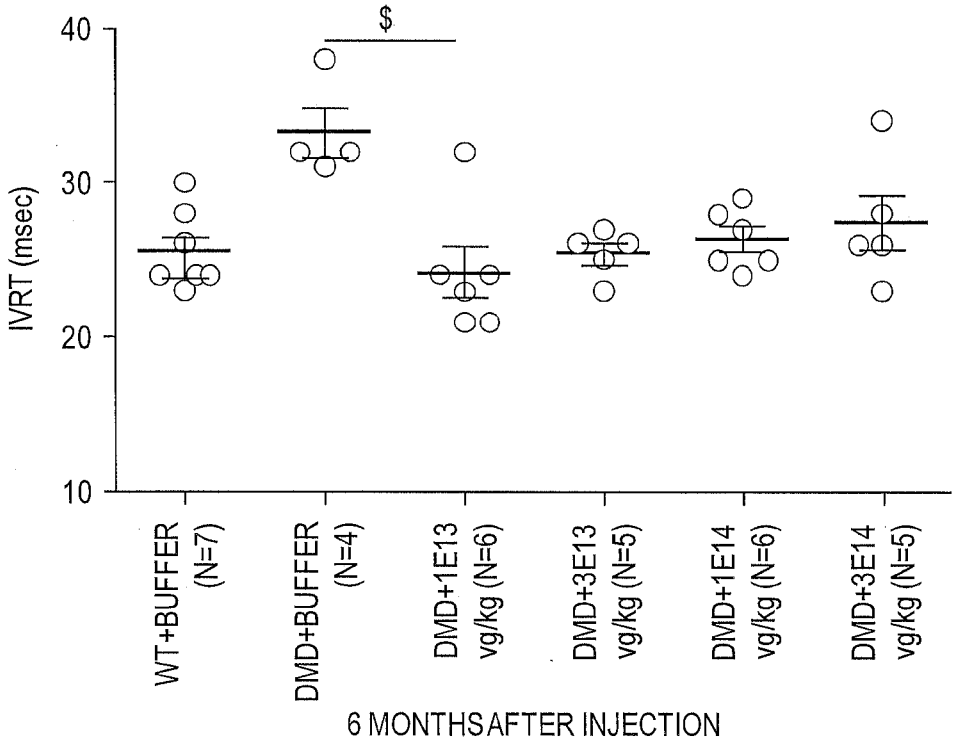


FIG. 46B

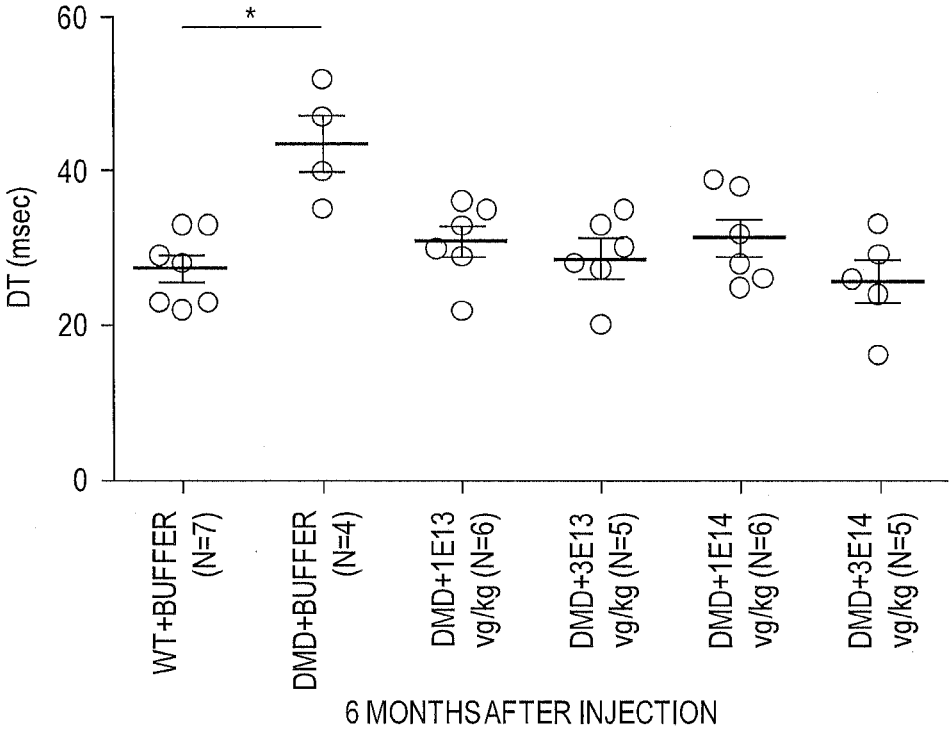


FIG. 47

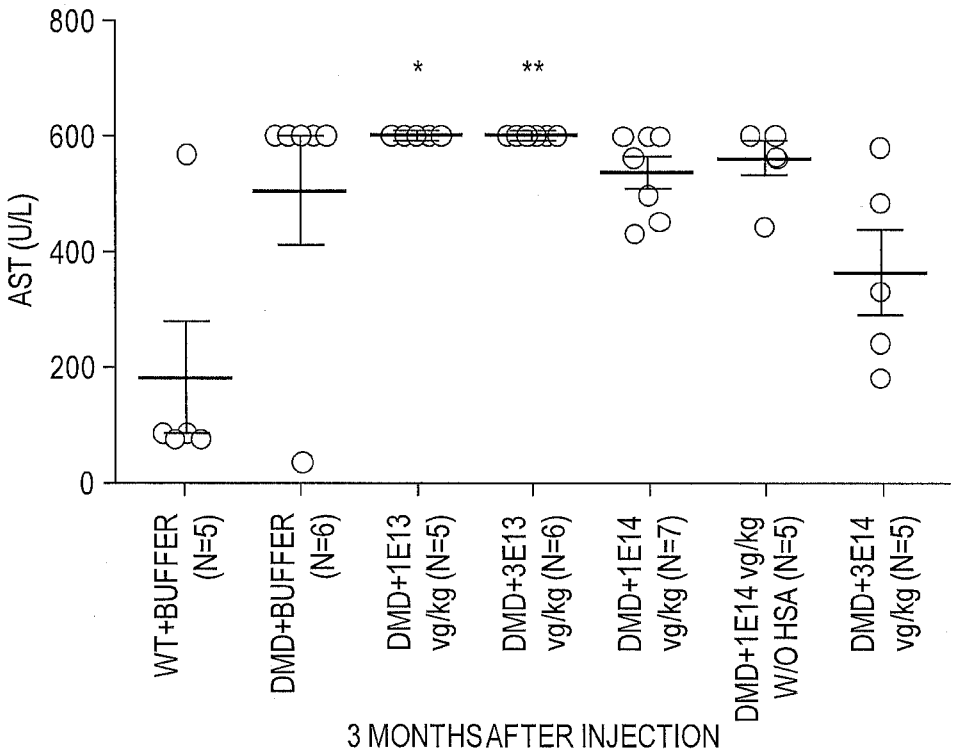


FIG. 48A

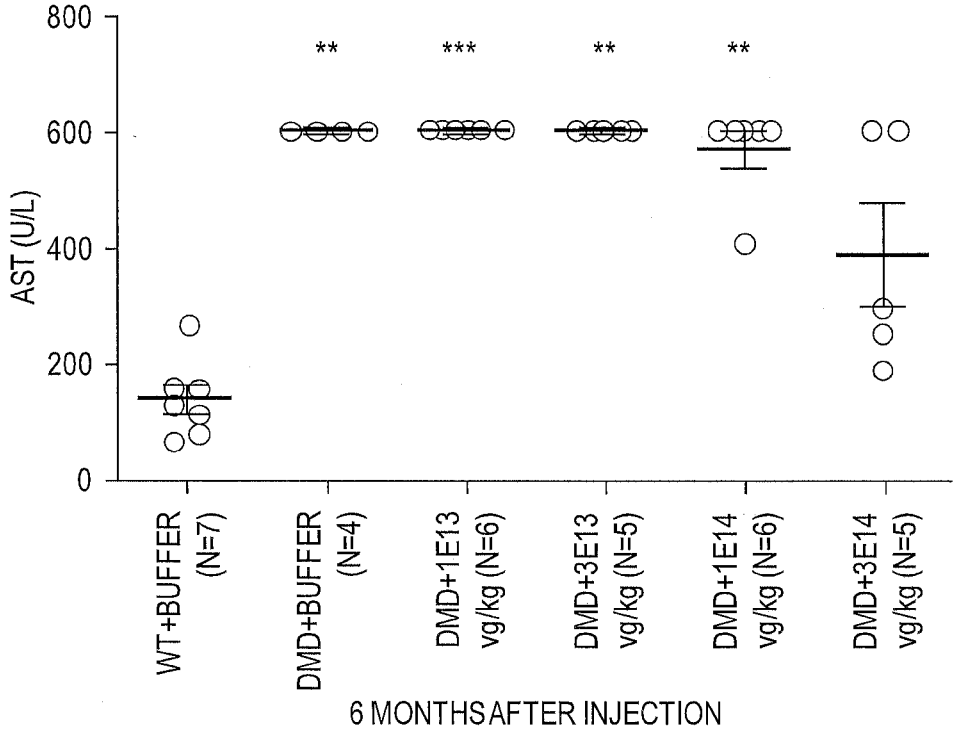


FIG. 48B

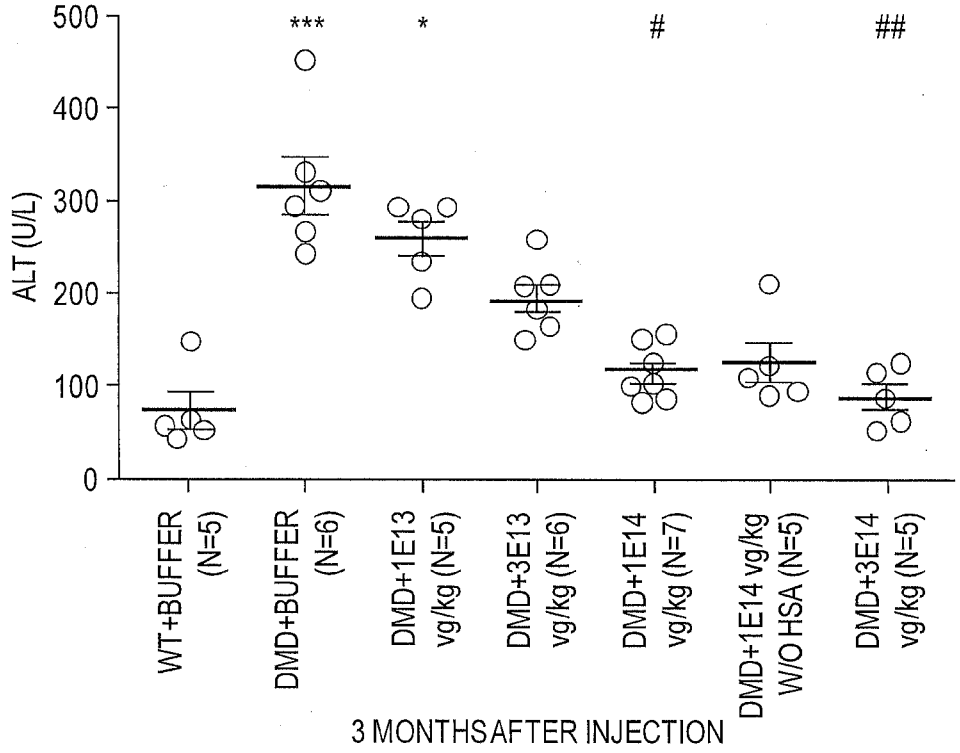


FIG. 49A

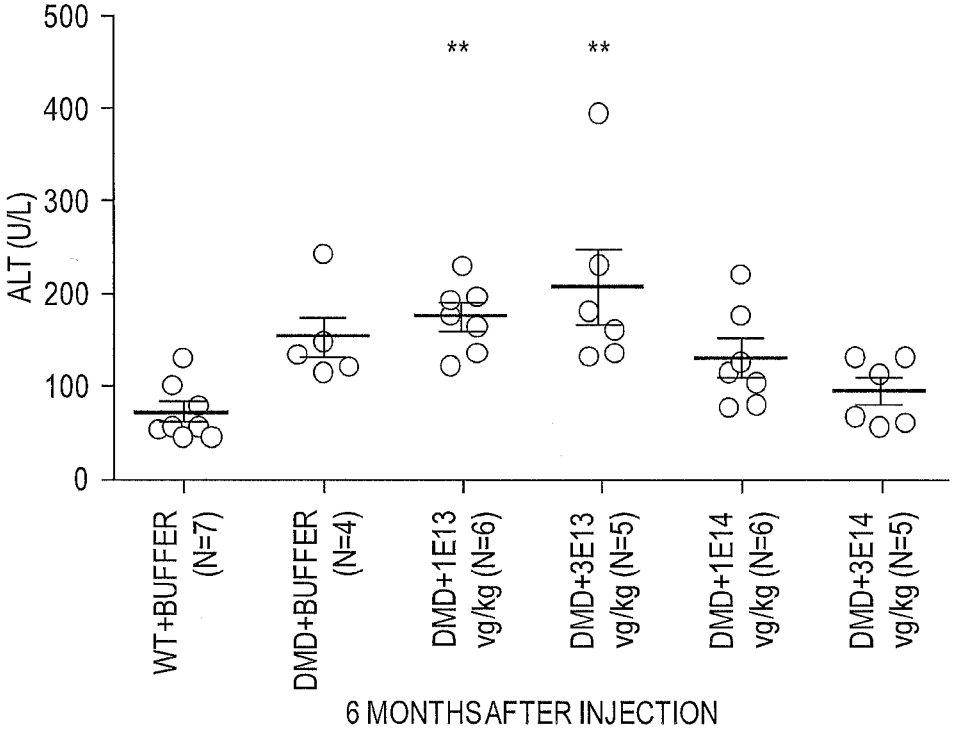


FIG. 49B

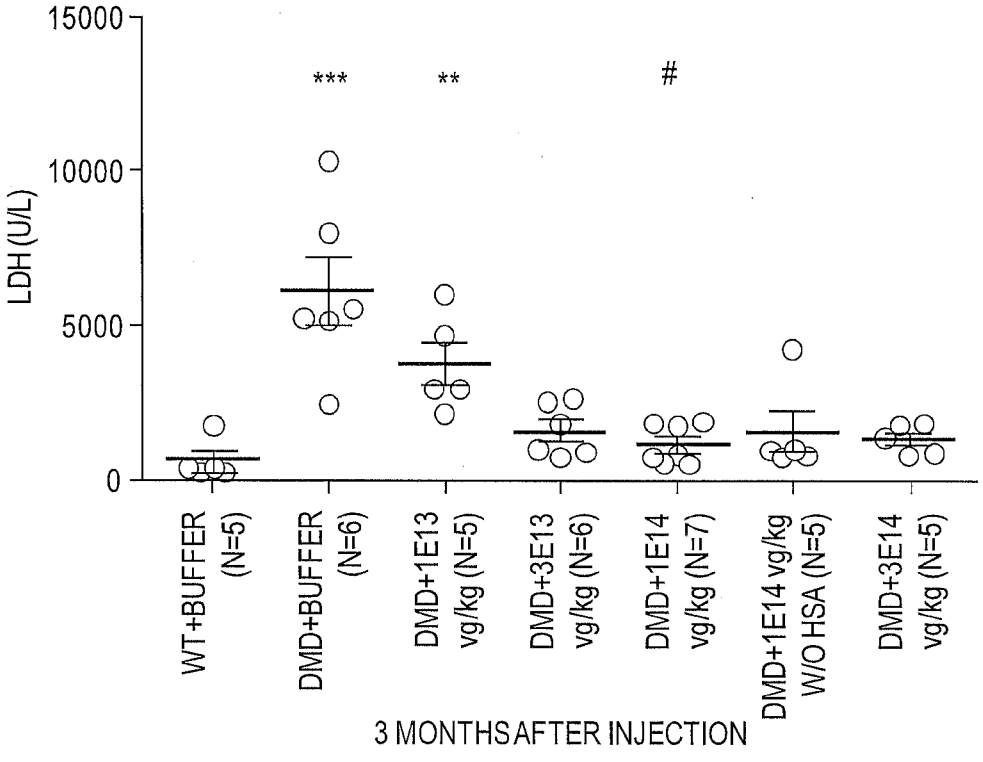


FIG. 50A

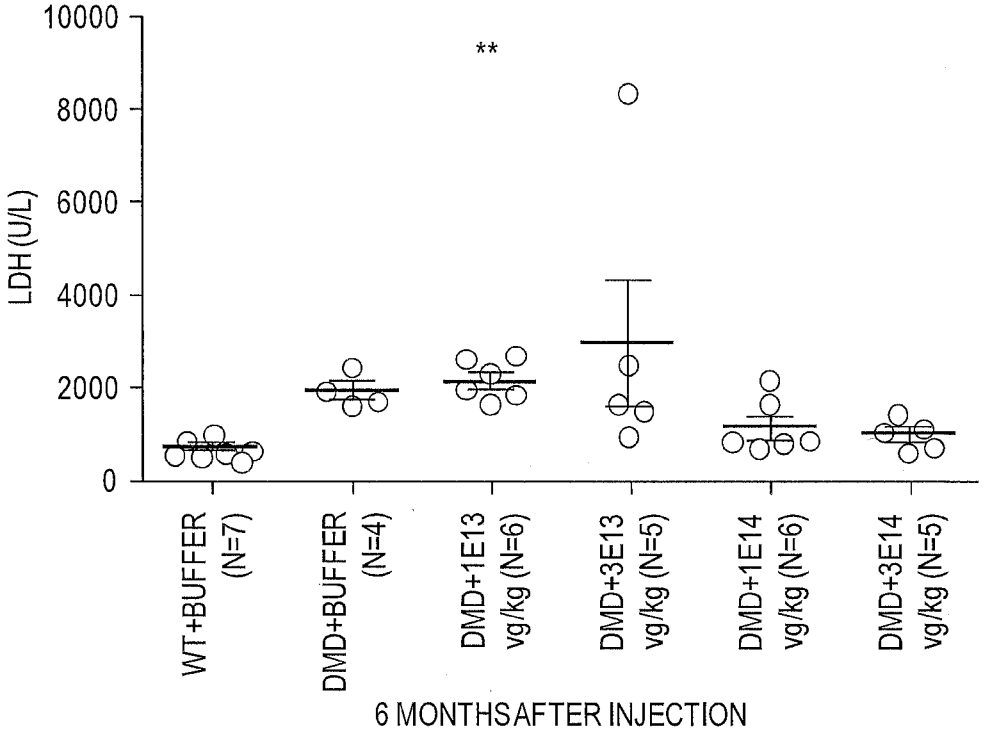


FIG. 50B

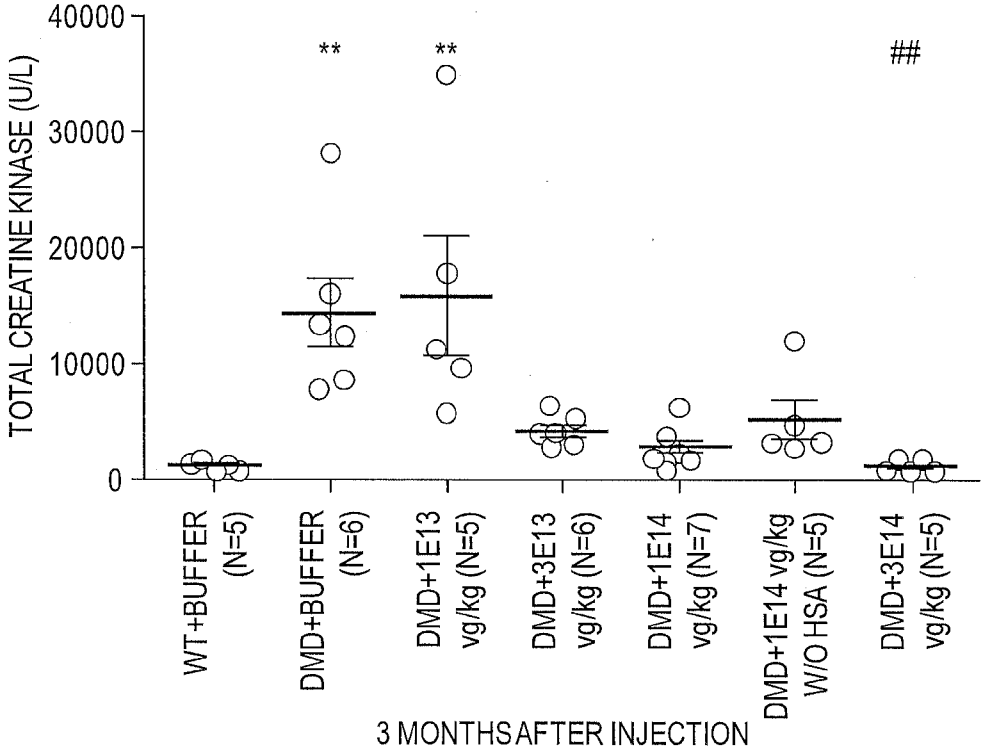


FIG. 51A

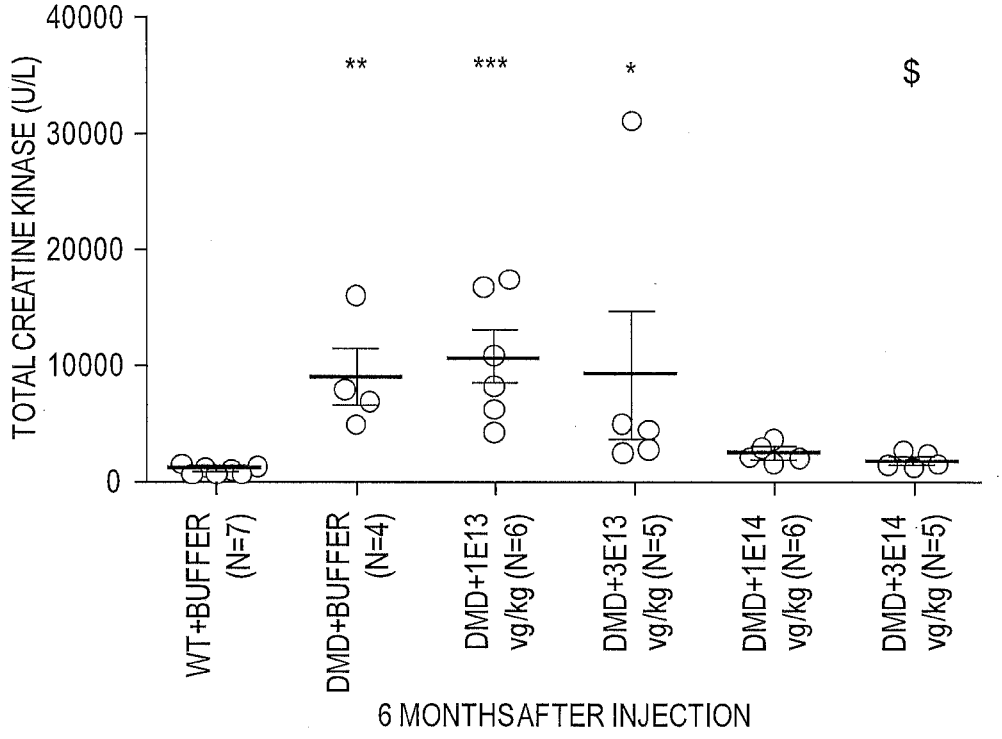


FIG. 51B

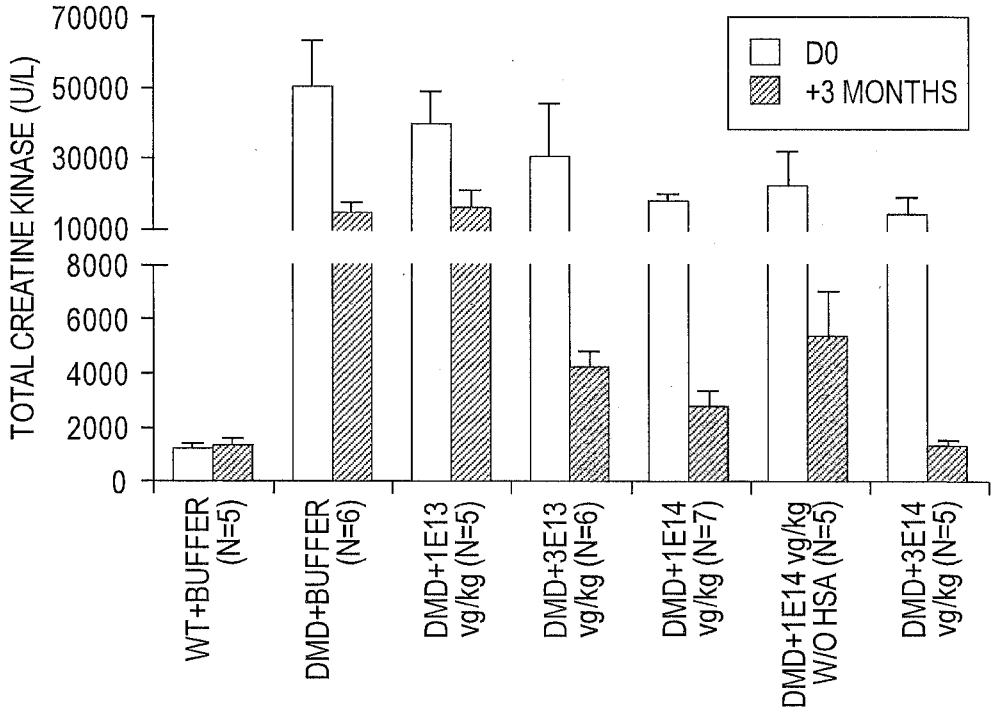


FIG. 52A

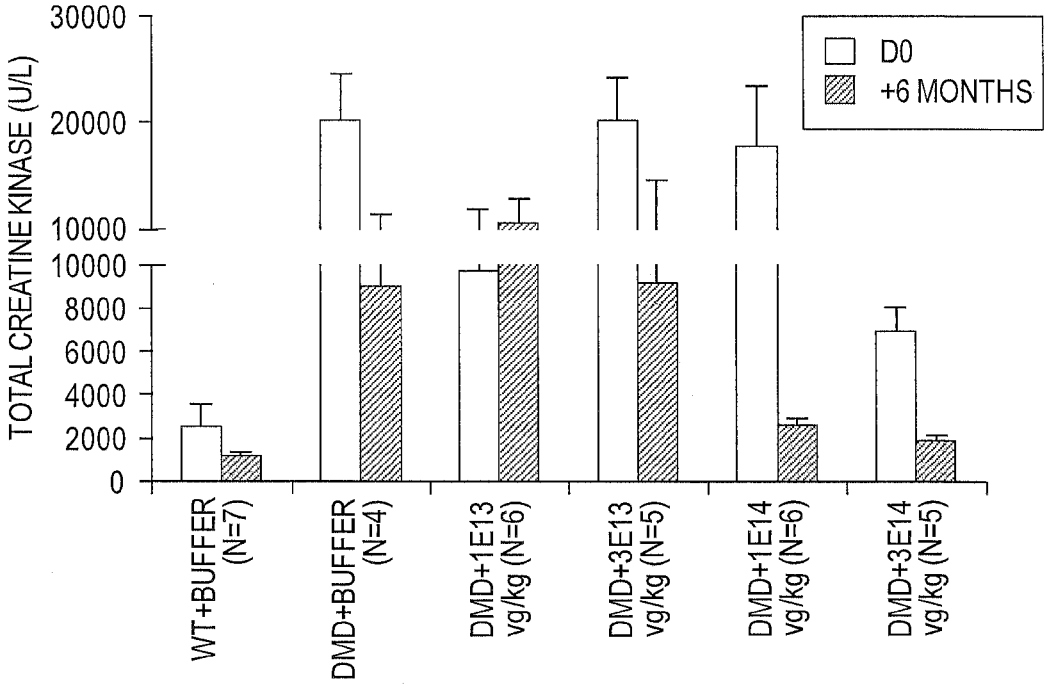


FIG. 52B

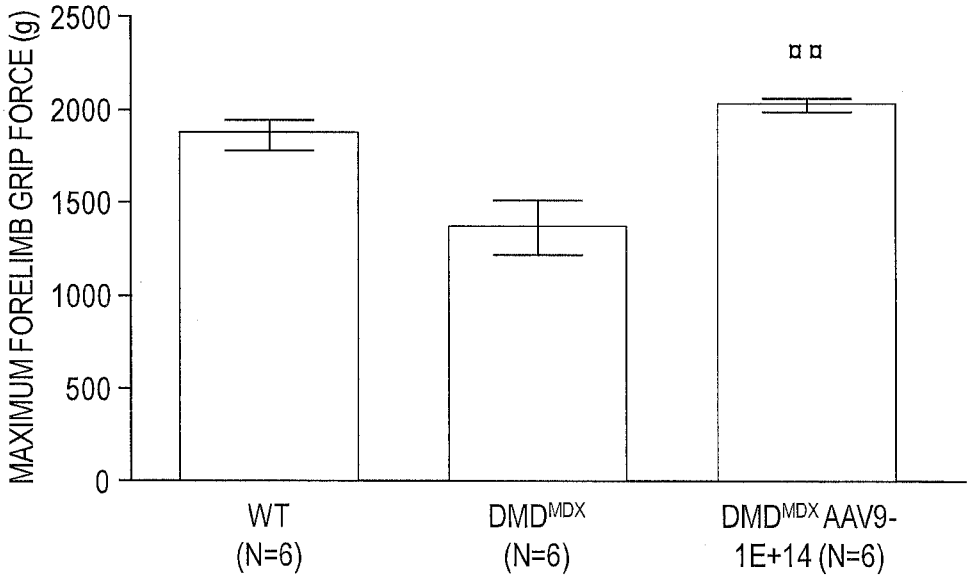


FIG. 53A

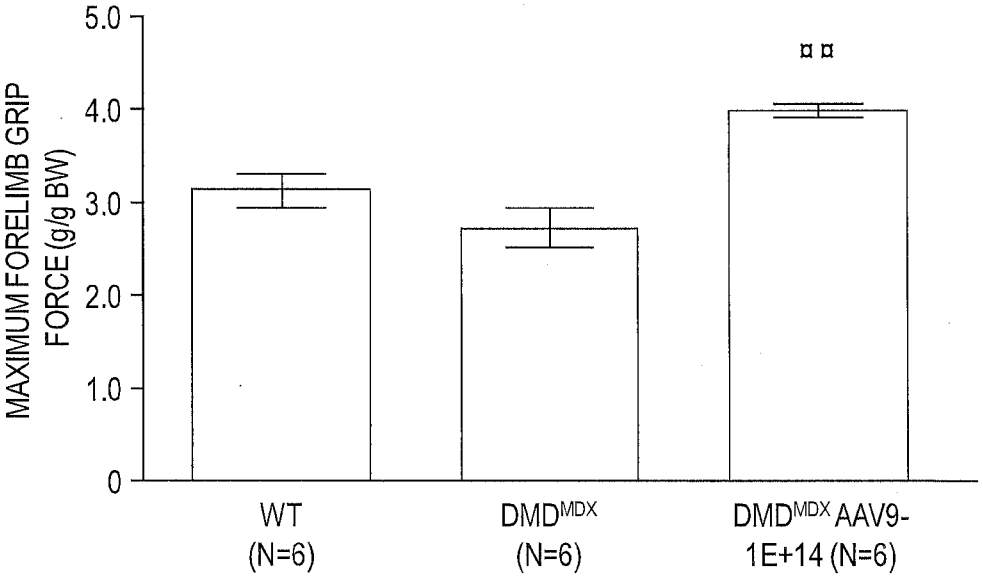


FIG. 53B

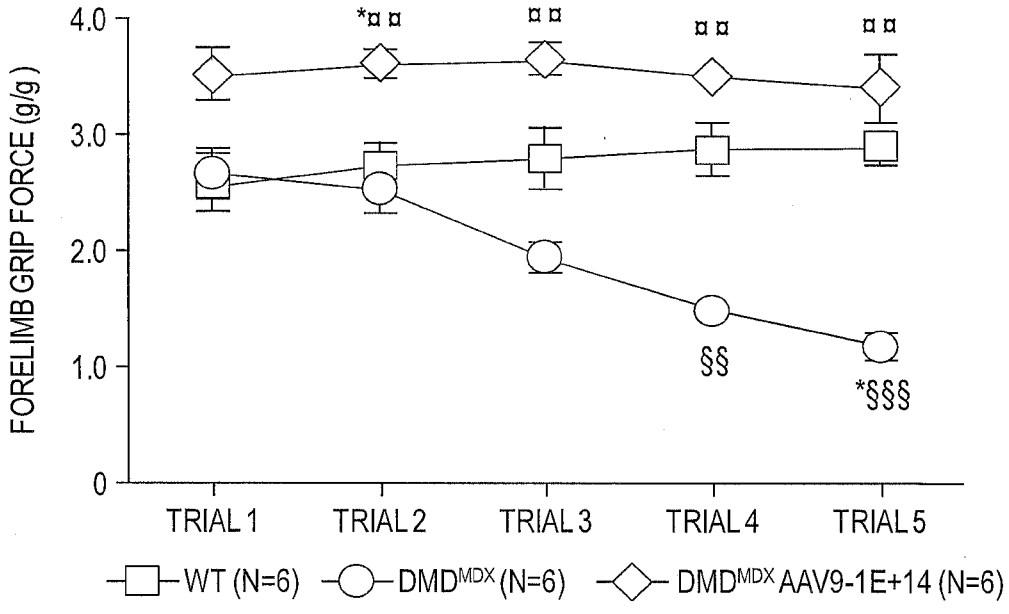


FIG. 53C

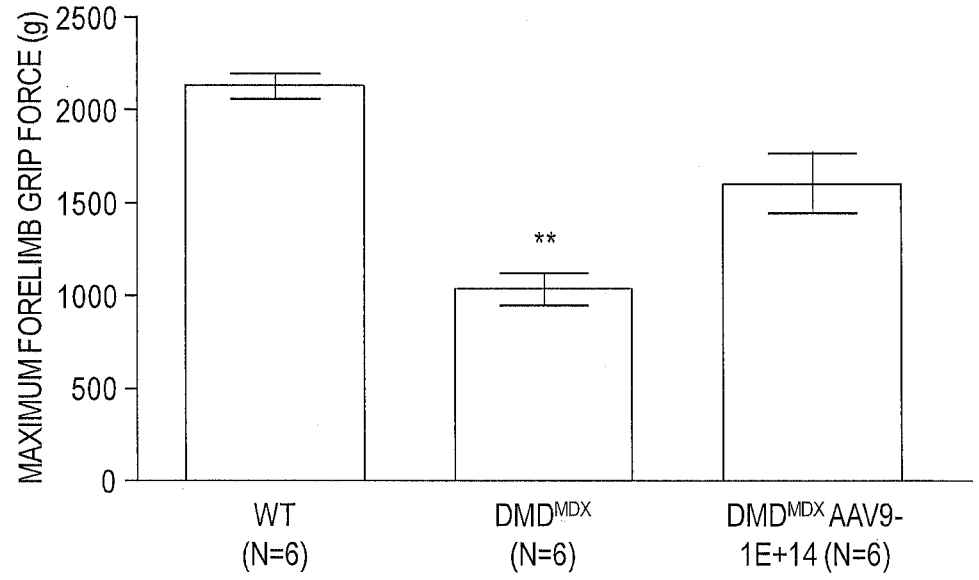


FIG. 54A

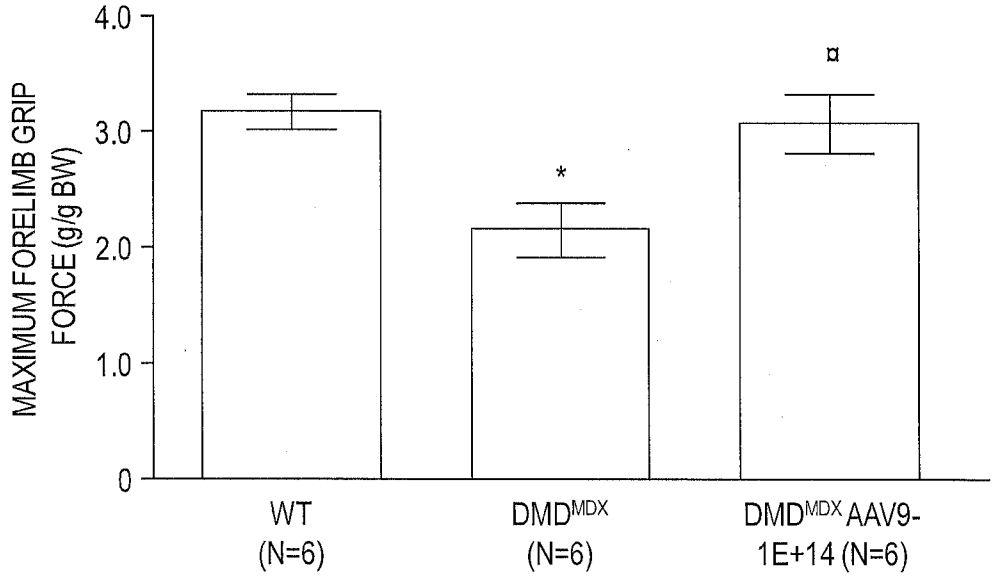


FIG. 54B

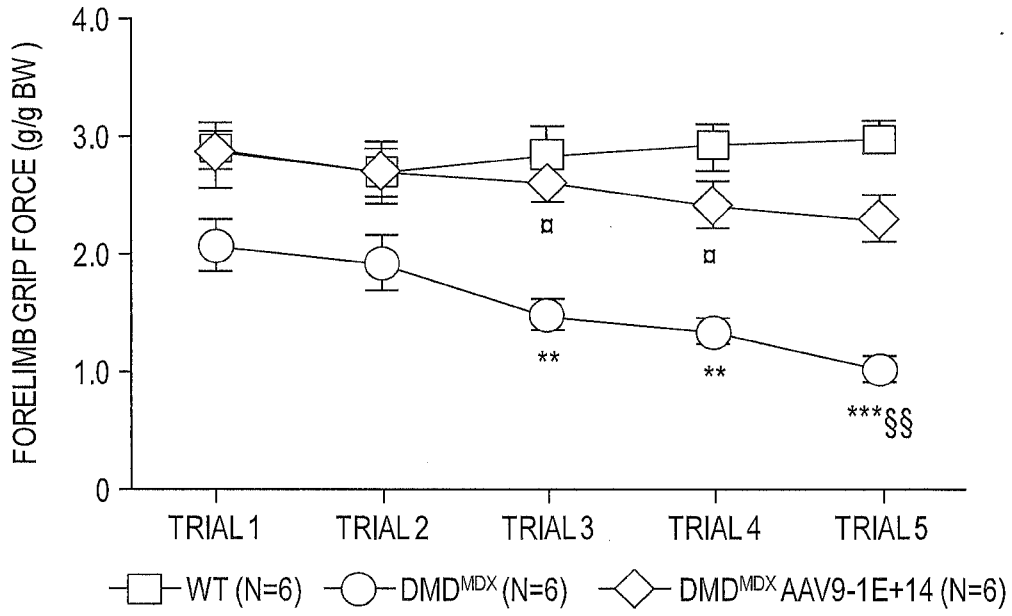

FORELIMB GRIP FORCE (g/g BW)
4.0
3.0
2.0
1.0
0
TRIAL 1
TRIAL 2
TRIAL 3
TRIAL 4
TRIAL 5
¤
¤
**
**
***§§
WT (N=6)
DMDMDX (N=6)
DMDMDX AAV9-1E+14 (N=6)

FIG. 54C

```
                    1                                                  60
Δ3990         (1)   MVWWEEVEDCYEREDVQKKTFTKWVNAQFSKFGKQHIENLFSDLQDGRRLLDLLEGLTGQ
Dys3978       (1)   MLWWEEVEDCYEREDVQKKTFTKWVNAQFSKFGKQHIENLFSDLQDGRRLLDLLEGLTGQ

                    61                                                 120
Δ3990        (61)   KLPKEKGSTRVHALNNVNKALRVLQNNNVDLVNIGSTDIVDGNHKLTLGLIWNIILHWQV
Dys3978      (61)   KLPKEKGSTRVHALNNVNKALRVLQNNNVDLVNIGSTDIVDGNHKLTLGLIWNIILHWQV

                   121                                                 180
Δ3990       (121)   KNVMKNIMAGLQQTNSEKILLSWVRQSTRNYPQVNVINFTTSWSDGLALNALIHSHRPDL
Dys3978     (121)   KNVMKNIMAGLQQTNSEKILLSWVRQSTRNYPQVNVINFTTSWSDGLALNALIHSHRPDL

                   181                                                 240
Δ3990       (181)   FDWNSVVCQQSATQRLEHAFNIARYQLGIEKLLDPEDVDTTYPDKKSILMYITSLFQVLP
Dys3978     (181)   FDWNSVVCQQSATQRLEHAFNIARYQLGIEKLLDPEDVDTTYPDKKSILMYITSLFQVLP

                   241                                                 300
Δ3990       (241)   QQVSIEAIQEVEMLPRPPKVTKEEHFQLHHQMHYSQQITVSLAQGYERTSSPKPRFKSYA
Dys3978     (241)   QQVSIEAIQEVEMLPRPPKVTKEEHFQLHHQMHYSQQITVSLAQGYERTSSPKPRFKSYA

                   301                                                 360
Δ3990       (301)   YTQAAYVTTSDPTRSPFPSQHLEAPEDKSFGSSLMESEVNLDRYQTALEEVLSWLLSAED
Dys3978     (301)   YTQAAYVTTSDPTRSPFPSQHLEAPEDKSFGSSLMESEVNLDRYQTALEEVLSWLLSAED

                   361                                                 420
Δ3990       (361)   TLQAQGEISNDVEVVKDQFHTHEGYMMDLTAHQGRVGNILQLGSKLIGTGKLSEDEETEV
Dys3978     (361)   TLQAQGEISNDVEVVKDQFHTHEGYMMDLTAHQGRVGNILQLGSKLIGTGKLSEDEETEV

                   421                                                 480
Δ3990       (421)   QEQMNLLNSRWECLRVASMEKQSNLHRVLMDLQNQKLKELNDWLTKTEERTRKMEEEPLG
Dys3978     (421)   QEQMNLLNSRWECLRVASMEKQSNLHRVLMDLQNQKLKELNDWLTKTEERTRKMEEEPLG
```

FIG. 55A

```
                481                                                   540
Δ3990      (481) PDLEDLKRQVQQHKVLQEDLEQEQVRVNSLTHMVVVVDESSGDHATAALEEQLKVLGDRW
Dys3978    (481) PDLEDLKRQVQQHKVLQEDLEQEQVRVNSLTHMVVVVDESSGDHATAALEEQLKVLGDRW

                541                                                   600
Δ3990      (541) ANICRWTEDRWVLLQDQPDLAPGLTTIGASPTQTVTLVTQPVVTKETAISKLEMPSSLML
Dys3978    (541) ANICRWTEDRWVLLQDQPDLAPGLTTIGASPTQTVTLVTQPVVTKETAISKLEMPSSLML

                601                                                   660
Δ3990      (601) EVPTHRLLQQFPLDLEKFLAWLTEAETTANVLQDATRKERLLEDSKGVKELMKQWQDLQG
Dys3978    (601) EVPTHRLLQQFPLDLEKFLAWLTEAETTANVLQDATRKERLLEDSKGVKELMKQWQDLQG

                661                                                   720
Δ3990      (661) EIEAHTDVYHNLDENSQKILRSLEGSDDAVLLQRRLDNMNFKWSELRKKSLNIRSHLEAS
Dys3978    (661) EIEAHTDVYHNLDENSQKILRSLEGSDDAVLLQRRLDNMNFKWSELRKKSLNIRSHLEAS

                721                                                   780
Δ3990      (721) SDQWKRLHLSLQELLVWLQLKDDELSRQAPIGGDFPAVQKQNDVHRAFKRELKTKEPVIM
Dys3978    (721) SDQWKRLHLSLQELLVWLQLKDDELSRQAPIGGDFPAVQKQNDVHRAFKRELKTKEPVIM

                781                                                   840
Δ3990      (781) STLETVRIFLTEQPLEGLEKLYQEPRELPPEERAQNVTRLLRKQAEEVNTEWEKLNLHSA
Dys3978    (781) STLETVRIFLTEQPLEGLEKLYQEPRELPPEERAQNVTRLLRKQAEEVNTEWEKLNLHSA

                841                                                   900
Δ3990      (841) DWQRKIDETLERLQELQEATDELDLKLRQAEVIKGSWQPVGDLLIDSLQDHLEKVKALRG
Dys3978    (841) DWQRKIDETLERLQELQEATDELDLKLRQAEVIKGSWQPVGDLLIDSLQDHLEKVKALRG

                901                                                   960
Δ3990      (901) EIAPLKENVSHVNDLARQLTTLGIQLSPYNLSTLEDLNTRWKLLQVAVEDRVRQLHEAHR
Dys3978    (901) EIAPLKENVSHVNDLARQLTTLGIQLSPYNLSTLEDLNTRWKLLQVAVEDRVRQLHEAHR
```

FIG. 55B

```
                961                                                1020
  Δ3990     (961) DFGPASQHFLSTSVQGPWERAISPNKVPYYINHETQTTCWDHPKMTELYQSLADLNNVRF
Dys3978     (961) DFGPASQHFLSTSVQGPWERAISPNKVPYYINHETQTTCWDHPKMTELYQSLADLNNVRF

               1021                                               1080
  Δ3990    (1021) SAYRTAMKLRRLQKALCLDLLSLSAACDALDQHNLKQNDQPMDILQIINCLTTIYDRLEQ
Dys3978    (1021) SAYRTAMKLRRLQKALCLDLLSLSAACDALDQHNLKQNDQPMDILQIINCLTTIYDRLEQ

               1081                                               1140
  Δ3990    (1081) EHNNLVNVPLCVDMCLNWLLNVYDTGRTGRIRVLSFKTGIISLCKAHLEDKYRYLFKQVA
Dys3978    (1081) EHNNLVNVPLCVDMCLNWLLNVYDTGRTGRIRVLSFKTGIISLCKAHLEDKYRYLFKQVA

               1141                                               1200
  Δ3990    (1141) SSTGFCDQRRLGLLLHDSIQIPRQLGEVASFGGSNIEPSVRSCFQFANNKPEIEAALFLD
Dys3978    (1141) SSTGFCDQRRLGLLLHDSIQIPRQLGEVASFGGSNIEPSVRSCFQFANNKPEIEAALFLD

               1201                                               1260
  Δ3990    (1201) WMRLEPQSMVWLPVLHRVAAAETAKHQAKCNICKECPIIGFRYRSLKHFNYDICQSCFFS
Dys3978    (1201) WMRLEPQSMVWLPVLHRVAAAETAKHQAKCNICKECPIIGFRYRSLKHFNYDICQSCFFS

               1261                                               1320
  Δ3990    (1261) GRVAKGHKMHYPMVEYCTPTTSGEDVRDFAKVLKNKFRTKRYFAKHPRMGYLPVQTVLEG
Dys3978    (1261) GRVAKGHKMHYPMVEYCTPTTSGEDVRDFAKVLKNKFRTKRYFAKHPRMGYLPVQTVLEG

               1321
  Δ3990    (1321) DNMETPDTM    SEQ ID NO:27
Dys3978    (1321) DNMET····    SEQ ID NO:7
```

FIG. 55C

```
                          1                                                  60
Wildtype Δ3990      (1)   ATGGTTTGGTGGGAAGAAGTAGAGGACTGTTATGAAAGAGAAGATGTTCAAAAGAAAACA
Hopti-Dys3978       (1)   ATGCTTTGGTGGGAGGAAGTGGAGGACTGCTACGAGAGAGAGGACGTGCAGAAGAAAACC

                          61                                                 120
Wildtype Δ3990     (61)   TTCACAAAATGGGTAAATGCACAATTTTCTAAGTTTGGGAAGCAGCATATTGAGAACCTC
Hopti-Dys3978      (61)   TTCACCAAGTGGGTGAACGCCCAGTTCAGCAAGTTCGGCAAGCAGCACATCGAGAACCTG

                         121                                                 180
Wildtype Δ3990    (121)   TTCAGTGACCTACAGGATGGGAGGCGCCTCCTAGACCTCCTCGAAGGCCTGACAGGGCAA
Hopti-Dys3978     (121)   TTCAGCGACCTGCAGGATGGCAGGAGACTGCTGGACCTGCTGGAGGGCCTGACCGGCCAG

                         181                                                 240
Wildtype Δ3990    (181)   AAACTGCCAAAAGAAAAAGGATCCACAAGAGTTCATGCCCTGAACAATGTCAACAAGGCA
Hopti-Dys3978     (181)   AAGCTGCCCAAGGAGAAGGGCAGCACCAGAGTGCACGCCCTGAACAACGTGAACAAGGCC

                         241                                                 300
Wildtype Δ3990    (241)   CTGCGGGTTTTGCAGAACAATAATGTTGATTTAGTGAATATTGGAAGTACTGACATCGTA
Hopti-Dys3978     (241)   CTGAGAGTGCTGCAGAACAACAACGTGGACCTGGTGAACATCGGCAGCACCGACATCGTG

                         301                                                 360
Wildtype Δ3990    (301)   GATGGAAATCATAAACTGACTCTTGGTTTGATTTGGAATATAATCCTCCACTGGCAGGTC
Hopti-Dys3978     (301)   GACGGCAACCACAAGCTGACCCTGGGCCTGATCTGGAACATCATCCTGCACTGGCAGGTG

                         361                                                 420
Wildtype Δ3990    (361)   AAAAATGTAATGAAAAATATCATGGCTGGATTGCAACAAACCAACAGTGAAAAGATTCTC
Hopti-Dys3978     (361)   AAGAACGTGATGAAGAACATCATGGCCGGCCTGCAGCAGACCAACAGCGAGAAGATCCTG

                         421                                                 480
Wildtype Δ3990    (421)   CTGAGCTGGGTCCGACAATCAACTCGTAATTATCCACAGGTTAATGTAATCAACTTCACC
Hopti-Dys3978     (421)   CTGAGCTGGGTGAGGCAGAGCACCAGAAACTACCCCCAGGTGAACGTGATCAACTTCACC
```

FIG. 56A

```
                          481                                                 540
Wildtype Δ3990      (481) ACCAGCTGGTCTGATGGCCTGGCTTTGAATGCTCTCATCCATAGTCATAGGCCAGACCTA
Hopti-Dys3978       (481) ACCTCCTGGAGCGACGGCCTGGCCCTGAACGCCCTGATCCACAGCCACAGACCCGACCTG

                          541                                                 600
Wildtype Δ3990      (541) TTTGACTGGAATAGTGTGGTTTGCCAGCAGTCAGCCACACAACGACTGGAACATGCATTC
Hopti-Dys3978       (541) TTCGACTGGAACAGCGTGGTGTGTCAGCAGAGCGCCACCCAGAGACTGGAGCACGCCTTC

                          601                                                 660
Wildtype Δ3990      (601) AACATCGCCAGATATCAATTAGGCATAGAGAAACTACTCGATCCTGAAGATGTTGATACC
Hopti-Dys3978       (601) AACATCGCCAGATACCAGCTGGGCATCGAGAAGCTGCTGGACCCCGAGGACGTGGACACC

                          661                                                 720
Wildtype Δ3990      (661) ACCTATCCAGATAAGAAGTCCATCTTAATGTACATCACATCACTCTTCCAAGTTTTGCCT
Hopti-Dys3978       (661) ACCTACCCCGACAAGAAAAGCATCCTCATGTACATTACCAGCCTGTTCCAGGTGCTGCCC

                          721                                                 780
Wildtype Δ3990      (721) CAACAAGTGAGCATTGAAGCCATCCAGGAAGTGGAAATGTTGCCAAGGCCACCTAAAGTG
Hopti-Dys3978       (721) CAGCAGGTGTCCATCGAGGCCATCCAGGAAGTGGAAATGCTGCCCAGGCCCCCCAAAGTG

                          781                                                 840
Wildtype Δ3990      (781) ACTAAAGAAGAACATTTTCAGTTACATCATCAAATGCACTATTCTCAACAGATCACGGTC
Hopti-Dys3978       (781) ACCAAGGAGGAGCACTTCCAGCTGCACCACCAGATGCACTACAGCCAGCAGATCACAGTG

                          841                                                 900
Wildtype Δ3990      (841) AGTCTAGCACAGGGATATGAGAGAACTTCTTCCCCTAAGCCTCGATTCAAGAGCTATGCC
Hopti-Dys3978       (841) AGCCTGGCCCAGGGCTATGAGAGAACCAGCAGCCCCAAGCCCAGATTCAAGAGCTACGCC

                          901                                                 960
Wildtype Δ3990      (901) TACACACAGGCTGCTTATGTCACCACCTCTGACCCTACACGGAGCCCATTTCCTTCACAG
Hopti-Dys3978       (901) TACACCCAGGCCGCCTACGTGACCACCTCCGACCCCACCAGAAGCCCCTTCCCCAGCCAG
```

FIG. 56B

		961	1020
Wildtype Δ3990	(961)	CATTTGGAAGCTCCTGAAGACAAGTCATTTGGCAGTTCATTGATGGAGAGTGAAGTAAAC	
Hopti-Dys3978	(961)	CACCTGGAGGCCCCCGAGGACAAGAGCTTCGGCAGCAGCCTGATGGAGAGCGAAGTGAAC	
		1021	**1080**
Wildtype Δ3990	(1021)	CTGGACCGTTATCAAACAGCTTTAGAAGAAGTATTATCGTGGCTTCTTTCTGCTGAGGAC	
Hopti-Dys3978	(1021)	CTGGACAGATACCAGACCGCCCTGGAGGAAGTGCTGTCCTGGCTGCTGAGCGCCGAGGAC	
		1081	**1140**
Wildtype Δ3990	(1081)	ACATTGCAAGCACAAGGAGAGATTTCTAATGATGTGGAAGTGGTGAAAGACCAGTTTCAT	
Hopti-Dys3978	(1081)	ACCCTGCAGGCCCAGGGCGAGATCAGCAACGACGTGGAAGTGGTGAAGGACCAGTTCCAC	
		1141	**1200**
Wildtype Δ3990	(1141)	ACTCATGAGGGGTACATGATGGATTTGACAGCCCATCAGGGCCGGGTTGGTAATATTCTA	
Hopti-Dys3978	(1141)	ACCCACGAGGGCTACATGATGGATCTGACCGCCCACCAGGGCAGAGTGGGCAATATCCTG	
		1201	**1260**
Wildtype Δ3990	(1201)	CAATTGGGAAGTAAGCTGATTGGAACAGGAAAATTATCAGAAGATGAAGAAACTGAAGTA	
Hopti-Dys3978	(1201)	CAGCTGGGCAGCAAGCTGATCGGCACCGGCAAGCTGAGCGAGGACGAGGAGACCGAAGTG	
		1261	**1320**
Wildtype Δ3990	(1261)	CAAGAGCAGATGAATCTCCTAAATTCAAGATGGGAATGCCTCAGGGTAGCTAGCATGGAA	
Hopti-Dys3978	(1261)	CAGGAGCAGATGAACCTGCTGAACAGCAGATGGGAGTGCCTGAGAGTGGCCAGCATGGAG	
		1321	**1380**
Wildtype Δ3990	(1321)	AAACAAAGCAATTTACATAGAGTTTTAATGGATCTCCAGAATCAGAAACTGAAAGAGTTG	
Hopti-Dys3978	(1321)	AAGCAGAGCAACCTGCACAGAGTGCTGATGGACCTGCAGAACCAGAAGCTGAAGGAGCTG	
		1381	**1440**
Wildtype Δ3990	(1381)	AATGACTGGCTAACAAAAACAGAAGAAAGAACAAGGAAAATGGAGGAAGAGCCTCTTGGA	
Hopti-Dys3978	(1381)	AACGACTGGCTGACCAAGACCGAGGAGCGGACCAGAAAGATGGAGGAGGAGCCCCTGGGC	

FIG. 56C

```
                          1441                                                1500
Wildtype Δ3990    (1441)  CCTGATCTTGAAGACCTAAAACGCCAAGTACAACAACATAAGGTGCTTCAAGAAGATCTA
Hopti-Dys3978     (1441)  CCCGACCTGGAGGACCTGAAGAGACAGGTGCAGCAGCACAAAGTGCTGCAGGAGGACCTG

                          1501                                                1560
Wildtype Δ3990    (1501)  GAACAAGAACAAGTCAGGGTCAATTCTCTCACTCACATGGTGGTGGTAGTTGATGAATCT
Hopti-Dys3978     (1501)  GAGCAGGAGCAGGTGCGCGTGAACAGCCTGACCCACATGGTGGTGGTCGTGGACGAGAGC

                          1561                                                1620
Wildtype Δ3990    (1561)  AGTGGAGATCACGCAACTGCTGCTTTGGAAGAACAACTTAAGGTATTGGGAGATCGATGG
Hopti-Dys3978     (1561)  AGCGGCGACCACGCCACAGCCGCCCTGGAAGAGCAGCTGAAAGTGCTGGGCGACAGATGG

                          1621                                                1680
Wildtype Δ3990    (1621)  GCAAACATCTGTAGATGGACAGAAGACCGCTGGGTTCTTTTACAAGACCAGCCTGACCTA
Hopti-Dys3978     (1621)  GCCAATATTTGTAGGTGGACCGAGGACAGATGGGTGCTGCTGCAGGACCAGCCCGACCTG

                          1681                                                1740
Wildtype Δ3990    (1681)  GCTCCTGGACTGACCACTATTGGAGCCTCTCCTACTCAGACTGTTACTCTGGTGACACAA
Hopti-Dys3978     (1681)  GCCCCTGGCCTGACCACCATCGGCGCCAGCCCCACCCAGACCGTGACCCTGGTGACCCAG

                          1741                                                1800
Wildtype Δ3990    (1741)  CCTGTGGTTACTAAGGAAACTGCCATCTCCAAACTAGAAATGCCATCTTCCTTGATGTTG
Hopti-Dys3978     (1741)  CCCGTGGTGACAAAGGAGACCGCCATCAGCAAGCTGGAGATGCCCAGCTCCCTGATGCTG

                          1801                                                1860
Wildtype Δ3990    (1801)  GAGGTACCTACTCATAGATTACTGCAACAGTTCCCCCTGGACCTGGAAAAGTTTCTTGCC
Hopti-Dys3978     (1801)  GAAGTGCCCACCCACCGCCTGCTCCAGCAGTTCCCCCTGGACCTGGAGAAGTTCCTGGCC

                          1861                                                1920
Wildtype Δ3990    (1861)  TGGCTTACAGAAGCTGAAACAACTGCCAATGTCCTACAGGATGCTACCCGTAAGGAAAGG
Hopti-Dys3978     (1861)  TGGCTGACCGAGGCCGAAACCACCGCCAATGTGCTCCAGGACGCCACTAGAAAGGAGAGG
```

FIG. 56D

```
                          1921                                                1980
Wildtype Δ3990    (1921) CTCCTAGAAGACTCCAAGGGAGTAAAAGAGCTGATGAAACAATGGCAAGACCTCCAAGGT
Hopti-Dys3978     (1921) CTGCTGGAGGACAGCAAGGGCGTGAAAGAGCTGATGAAGCAGTGGCAGGATCTGCAGGGC

                          1981                                                2040
Wildtype Δ3990    (1981) GAAATTGAAGCTCACACAGATGTTTATCACAACCTGGATGAAAACAGCCAAAAAATCCTG
Hopti-Dys3978     (1981) GAAATCGAGGCCCACACCGACGTGTACCACAACCTGGACGAGAACAGCCAGAAGATTCTG

                          2041                                                2100
Wildtype Δ3990    (2041) AGATCCCTGGAAGGTTCCGATGATGCAGTCCTGTTACAAAGACGTTTGGATAACATGAAC
Hopti-Dys3978     (2041) AGGAGCCTGGAGGGCAGCGACGACGCCGTCCTGCTCCAGAGGAGGCTGGACAACATGAAC

                          2101                                                2160
Wildtype Δ3990    (2101) TTCAAGTGGAGTGAACTTCGGAAAAAGTCTCTCAACATTAGGTCCCATTTGGAAGCCAGT
Hopti-Dys3978     (2101) TTCAAGTGGAGCGAGCTGCGGAAGAAGAGCCTGAACATCCGGAGCCACCTGGAAGCCAGC

                          2161                                                2220
Wildtype Δ3990    (2161) TCTGACCAGTGGAAGCGTCTGCACCTTTCTCTGCAGGAACTTCTGGTGTGGCTACAGCTG
Hopti-Dys3978     (2161) AGCGACCAGTGGAAGAGACTGCACCTGAGCCTGCAGGAGCTGCTGGTGTGGCTGCAGCTG

                          2221                                                2280
Wildtype Δ3990    (2221) AAAGATGATGAATTAAGCCGGCAGGCACCTATTGGAGGCGACTTTCCAGCAGTTCAGAAG
Hopti-Dys3978     (2221) AAGGACGACGAGCTGAGCAGACAGGCCCCCATCGGCGGCGACTTCCCCGCCGTGCAGAAG

                          2281                                                2340
Wildtype Δ3990    (2281) CAGAACGATGTACATAGGGCCTTCAAGAGGGAATTGAAAACTAAAGAACCTGTAATCATG
Hopti-Dys3978     (2281) CAGAACGACGTGCACCGGGCCTTCAAGAGGGAGCTGAAAACCAAGGAACCCGTGATCATG

                          2341                                                2400
Wildtype Δ3990    (2341) AGTACTCTTGAGACTGTACGAATATTTCTGACAGAGCAGCCTTTGGAAGGACTAGAGAAA
Hopti-Dys3978     (2341) AGCACCCTGGAGACAGTGCGGATCTTCCTGACCGAGCAGCCCCTGGAGGGACTGGAGAAG
```

FIG. 56E

		2401	2460
Wildtype Δ3990	(2401)	CTCTACCAGGAGCCCAGAGAGCTGCCTCCTGAGGAGAGAGCCCAGAATGTCACTCGGCTT	
Hopti-Dys3978	(2401)	CTGTACCAGGAGCCCAGAGAGCTGCCCCCCGAGGAGAGAGCCCAGAACGTGACCAGGCTG	

		2461	2520
Wildtype Δ3990	(2461)	CTACGAAAGCAGGCTGAGGAGGTCAATACTGAGTGGGAAAAATTGAACCTGCACTCCGCT	
Hopti-Dys3978	(2461)	CTGAGAAAGCAGGCCGAGGAAGTGAATACCGAGTGGGAGAAGCTGAATCTGCACAGCGCC	

		2521	2580
Wildtype Δ3990	(2521)	GACTGGCAGAGAAAAATAGATGAGACCCTTGAAAGACTCCAGGAACTTCAAGAGGCCACG	
Hopti-Dys3978	(2521)	GACTGGCAGAGAAAGATCGACGAGACCCTGGAGAGACTCCAGGAACTGCAGGAAGCCACC	

		2581	2640
Wildtype Δ3990	(2581)	GATGAGCTGGACCTCAAGCTGCGCCAAGCTGAGGTGATCAAGGGATCCTGGCAGCCCGTG	
Hopti-Dys3978	(2581)	GACGAGCTGGACCTGAAGCTGAGACAGGCCGAAGTGATCAAGGGCAGCTGGCAGCCTGTG	

		2641	2700
Wildtype Δ3990	(2641)	GGCGATCTCCTCATTGACTCTCTCCAAGATCACCTCGAGAAAGTCAAGGCACTTCGAGGA	
Hopti-Dys3978	(2641)	GGCGATCTGCTGATCGACTCCCTGCAGGATCACCTGGAGAAAGTGAAGGCCCTGCGGGGC	

		2701	2760
Wildtype Δ3990	(2701)	GAAATTGCGCCTCTGAAAGAGAACGTGAGCCACGTCAATGACCTTGCTCGCCAGCTTACC	
Hopti-Dys3978	(2701)	GAGATCGCCCCCCTGAAGGAGAATGTGAGCCACGTGAACGACCTGGCCAGACAGCTGACC	

		2761	2820
Wildtype Δ3990	(2761)	ACTTTGGGCATTCAGCTCTCACCGTATAACCTCAGCACTCTGGAAGACCTGAACACCAGA	
Hopti-Dys3978	(2761)	ACCCTGGGCATCCAGCTGAGCCCCTACAACCTGAGCACACTGGAGGATCTGAACACCCGG	

		2821	2880
Wildtype Δ3990	(2821)	TGGAAGCTTCTGCAGGTGGCCGTCGAGGACCGAGTCAGGCAGCTGCATGAAGCCCACAGG	
Hopti-Dys3978	(2821)	TGGAAACTGCTGCAGGTGGCCGTGGAGGATAGAGTGAGGCAGCTGCACGAAGCCCACAGA	

FIG. 56F

```
                          2881                                                2940
Wildtype Δ3990    (2881) GACTTTGGTCCAGCATCTCAGCACTTTCTTTCCACGTCTGTCCAGGGTCCCTGGGAGAGA
Hopti-Dys3978     (2881) GACTTCGGCCCTGCCTCCCAGCACTTCCTGAGCACCAGCGTGCAGGGCCCCTGGGAGAGA

                          2941                                                3000
Wildtype Δ3990    (2941) GCCATCTCGCCAAACAAAGTGCCCTACTATATCAACCACGAGACTCAAACAACTTGCTGG
Hopti-Dys3978     (2941) GCCATCTCCCCCAACAAAGTGCCCTACTACATCAACCACGAGACCCAGACCACCTGCTGG

                          3001                                                3060
Wildtype Δ3990    (3001) GACCATCCCAAAATGACAGAGCTCTACCAGTCTTTAGCTGACCTGAATAATGTCAGATTC
Hopti-Dys3978     (3001) GACCACCCTAAGATGACCGAGCTGTATCAGAGCCTGGCCGACCTGAACAATGTGCGGTTC

                          3061                                                3120
Wildtype Δ3990    (3061) TCAGCTTATAGGACTGCCATGAAACTCCGAAGACTGCAGAAGGCCCTTTGCTTGGATCTC
Hopti-Dys3978     (3061) AGCGCCTACAGAACCGCCATGAAGCTGCGGAGACTGCAGAAGGCCCTGTGCCTGGATCTG

                          3121                                                3180
Wildtype Δ3990    (3121) TTGAGCCTGTCAGCTGCATGTGATGCCTTGGACCAGCACAACCTCAAGCAAAATGACCAG
Hopti-Dys3978     (3121) CTGAGCCTGAGCGCCGCCTGCGACGCCCTGGACCAGCACAACCTGAAGCAGAATGACCAG

                          3181                                                3240
Wildtype Δ3990    (3181) CCCATGGATATCCTGCAGATTATTAATTGTTTGACCACTATTTATGACCGCCTGGAGCAA
Hopti-Dys3978     (3181) CCCATGGACATCCTGCAGATCATCAACTGCCTGACCACAATCTACGACCGGCTGGAACAG

                          3241                                                3300
Wildtype Δ3990    (3241) GAGCACAACAATTTGGTCAACGTCCCTCTCTGCGTGGATATGTGTCTGAACTGGCTGCTG
Hopti-Dys3978     (3241) GAGCACAACAACCTGGTGAATGTGCCCCTGTGCGTGGACATGTGCCTGAATTGGCTGCTG

                          3301                                                3360
Wildtype Δ3990    (3301) AATGTTTATGATACGGGACGAACAGGGAGGATCCGTGTCCTGTCTTTTAAAACTGGCATC
Hopti-Dys3978     (3301) AACGTGTACGACACCGGCAGGACCGGCAGAATCCGCGTGCTGAGCTTCAAGACCGGCATC
```

FIG. 56G

		3361	3420
Wildtype Δ3990	(3361)	ATTTCCCTGTGTAAAGCACATTTGGAAGACAAGTACAGATACCTTTTCAAGCAAGTGGCA	
Hopti-Dys3978	(3361)	ATCAGCCTGTGCAAGGCCCACCTGGAGGATAAGTACCGCTACCTGTTCAAGCAGGTGGCC	
		3421	**3480**
Wildtype Δ3990	(3421)	AGTTCAACAGGATTTTGTGACCAGCGCAGGCTGGGCCTCCTTCTGCATGATTCTATCCAA	
Hopti-Dys3978	(3421)	AGCAGCACCGGCTTCTGCGATCAGAGGAGACTGGGCCTGCTGCTGCACGATAGCATCCAG	
		3481	**3540**
Wildtype Δ3990	(3481)	ATTCCAAGACAGTTGGGTGAAGTTGCATCCTTTGGGGGCAGTAACATTGAGCCAAGTGTC	
Hopti-Dys3978	(3481)	ATCCCTAGGCAGCTGGGCGAAGTGGCCAGCTTTGGCGGCAGCAACATCGAGCCCTCTGTG	
		3541	**3600**
Wildtype Δ3990	(3541)	CGGAGCTGCTTCCAATTTGCTAATAATAAGCCAGAGATCGAAGCGGCCCTCTTCCTAGAC	
Hopti-Dys3978	(3541)	AGGAGCTGCTTCCAGTTCGCCAACAACAAGCCCGAGATCGAGGCCGCCCTGTTCCTGGAC	
		3601	**3660**
Wildtype Δ3990	(3601)	TGGATGAGACTGGAACCCCAGTCCATGGTGTGGCTGCCCGTCCTGCACAGAGTGGCTGCT	
Hopti-Dys3978	(3601)	TGGATGAGGCTGGAGCCTCAGAGCATGGTGTGGCTGCCTGTGCTGCACAGAGTGGCCGCC	
		3661	**3720**
Wildtype Δ3990	(3661)	GCAGAAACTGCCAAGCATCAGGCCAAATGTAACATCTGCAAAGAGTGTCCAATCATTGGA	
Hopti-Dys3978	(3661)	GCCGAGACCGCCAAGCACCAGGCCAAGTGCAATATCTGCAAGGAGTGCCCCATCATCGGC	
		3721	**3780**
Wildtype Δ3990	(3721)	TTCAGGTACAGGAGTCTAAAGCACTTTAATTATGACATCTGCCAAAGCTGCTTTTTTTCT	
Hopti-Dys3978	(3721)	TTCCGGTACAGGAGCCTGAAGCACTTCAACTACGACATCTGCCAGAGCTGCTTTTTCAGC	
		3781	**3840**
Wildtype Δ3990	(3781)	GGTCGAGTTGCAAAAGGCCATAAAATGCACTATCCCATGGTGGAATATTGCACTCCGACT	
Hopti-Dys3978	(3781)	GGCAGAGTGGCCAAGGGCCACAAAATGCACTACCCCATGGTGGAGTACTGCACCCCCACC	

FIG. 56H

```
                    3841                                                3900
Wildtype Δ3990 (3841) ACATCAGGAGAAGATGTTCGAGACTTTGCCAAGGTACTAAAAAACAAATTTCGAACCAAA
Hopti-Dys3978  (3841) ACCTCCGGCGAGGATGTGAGAGACTTCGCCAAAGTGCTGAAGAATAAGTTCCGGACCAAG

                    3901                                                3960
Wildtype Δ3990 (3901) AGGTATTTTGCGAAGCATCCCCGAATGGGCTACCTGCCAGTGCAGACTGTCTTAGAGGGG
Hopti-Dys3978  (3901) CGGTACTTTGCCAAGCACCCCAGGATGGGCTACCTGCCCGTGCAGACCGTGCTGGAAGGC

                    3961
Wildtype Δ3990 (3961) GACAACATGGAAACTCCCGACACAATGTAG   SEQ ID NO:28
Hopti-Dys3978  (3961) GACAACATGGAGACC··············TGA   SEQ ID NO:1
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FIG. 56I