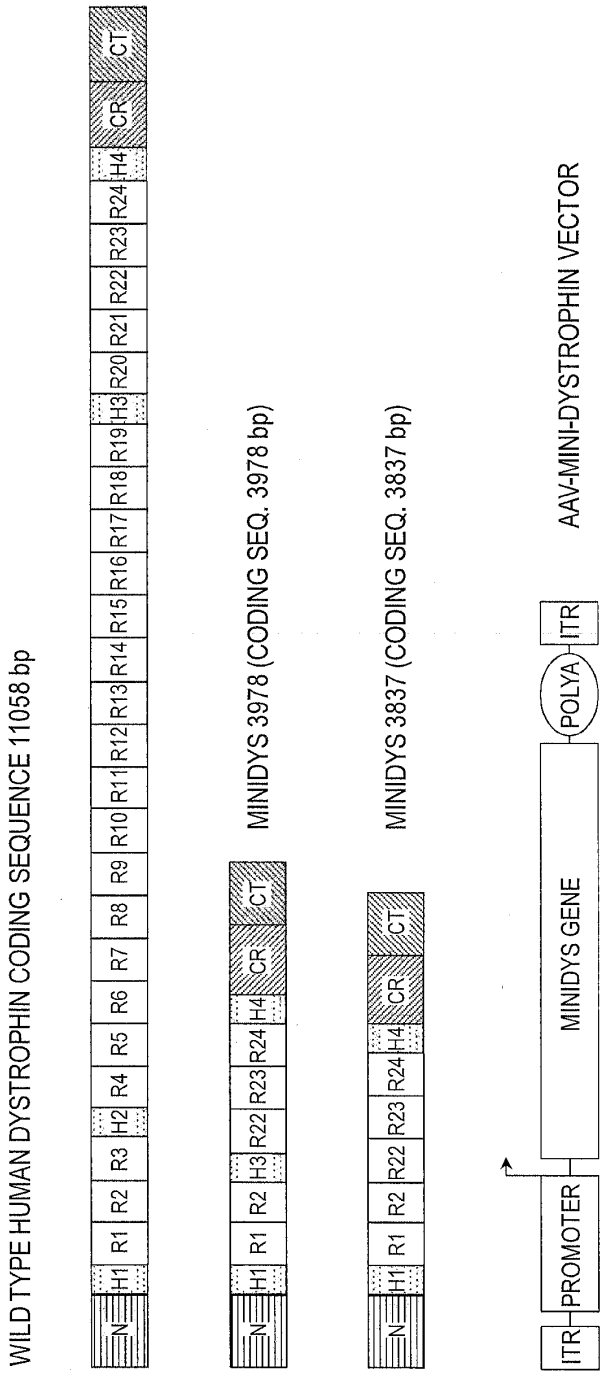

WILD TYPE HUMAN DYSTROPHIN CODING SEQUENCE 11058 bp
N
H1
R1
R2
R3
H2
R4
R5
R6
R7
R8
R9
R10
R11
R12
R13
R14
R15
R16
R17
R18
R19
H3
R20
R21
R22
R23
R24
H4
CR
CT
MINIDYS 3978 (CODING SEQ. 3978 bp)
MINIDYS 3837 (CODING SEQ. 3837 bp)
ITR
PROMOTER
MINIDYS GENE
POLYA
ITR
AAV-MINI-DYSTROPHIN VECTOR

FIG. 1

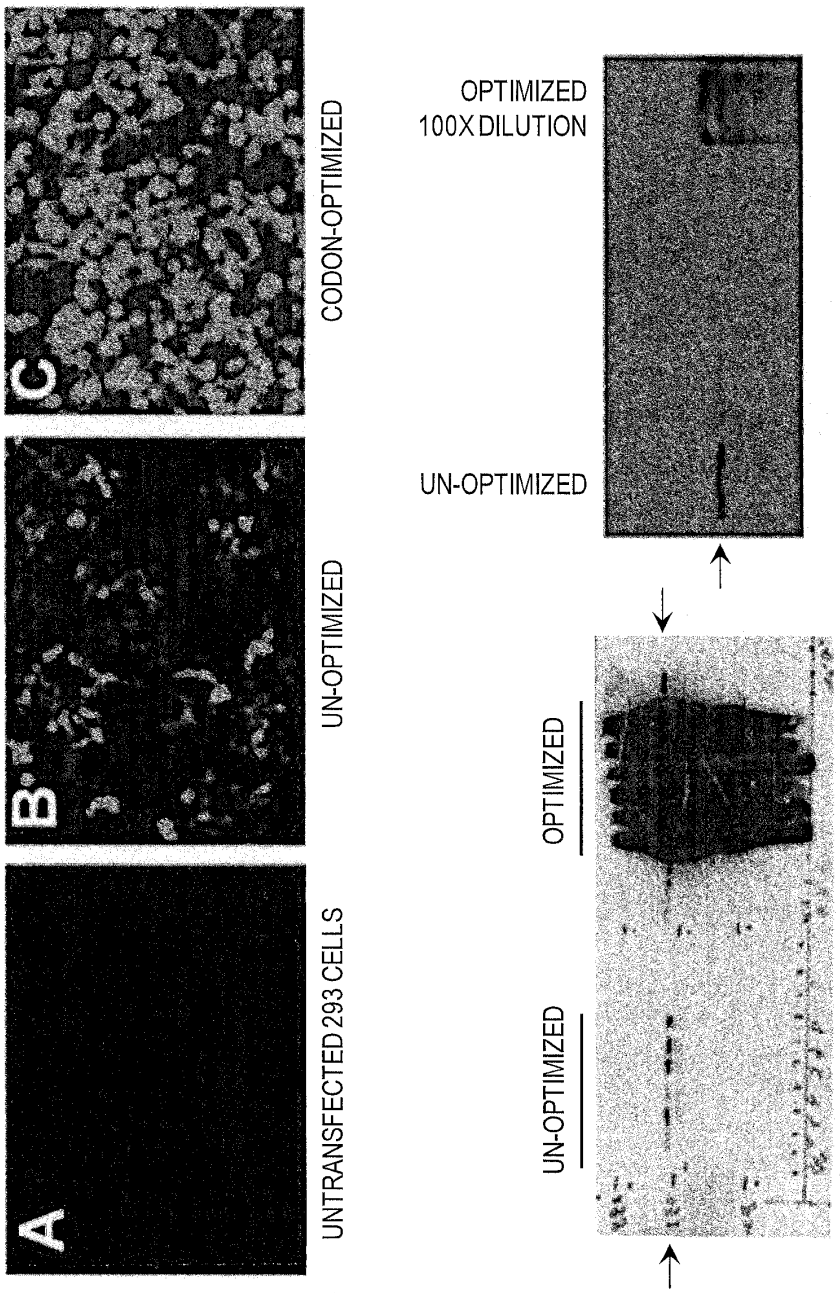

A
UNTRANSFECTED 293 CELLS
B
UN-OPTIMIZED
C
CODON-OPTIMIZED
OPTIMIZED
100X DILUTION
UN-OPTIMIZED
OPTIMIZED
UN-OPTIMIZED

FIG. 2

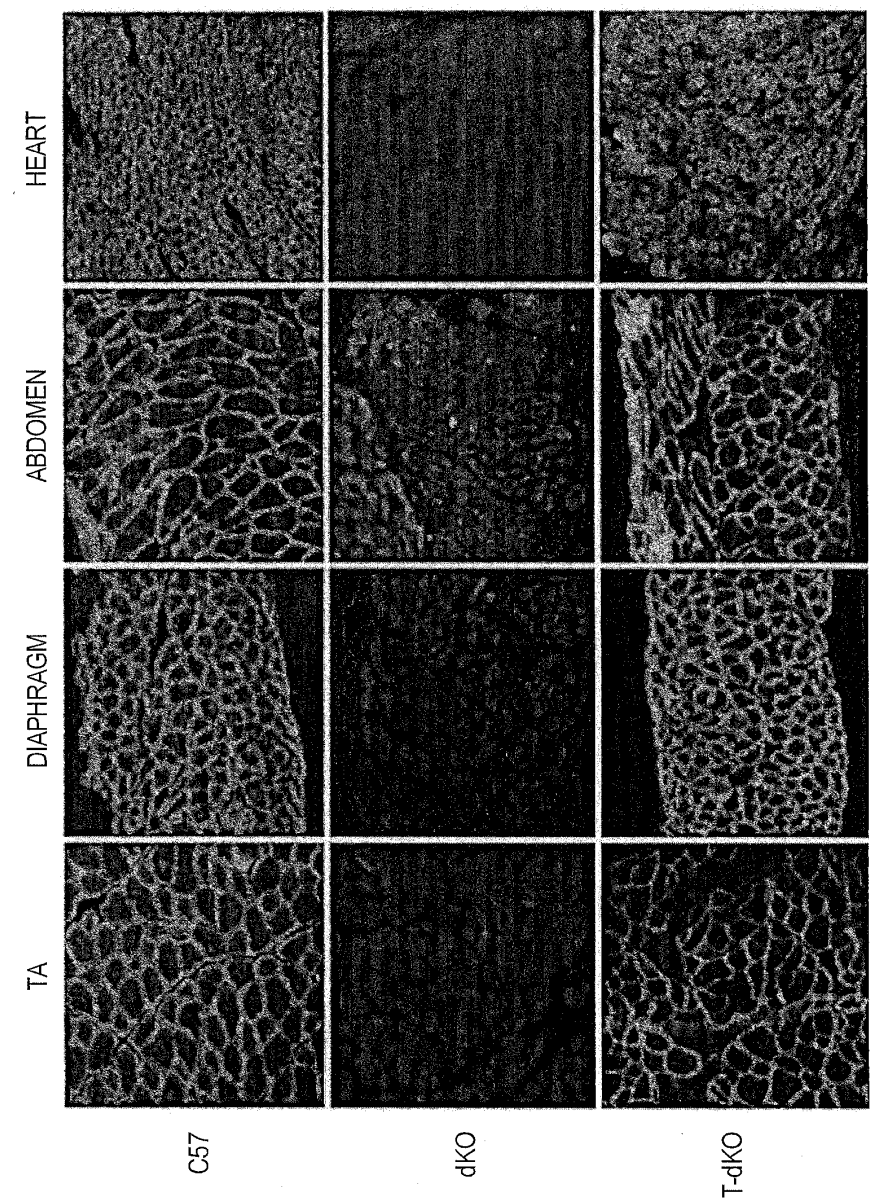


FIG. 3

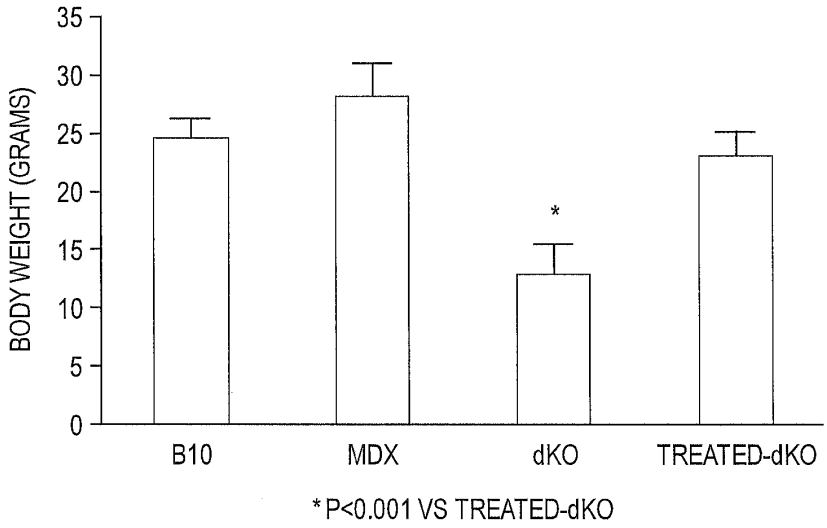
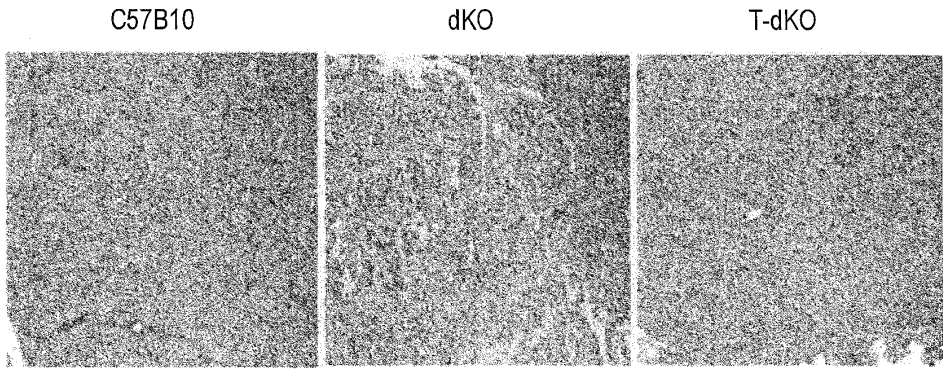
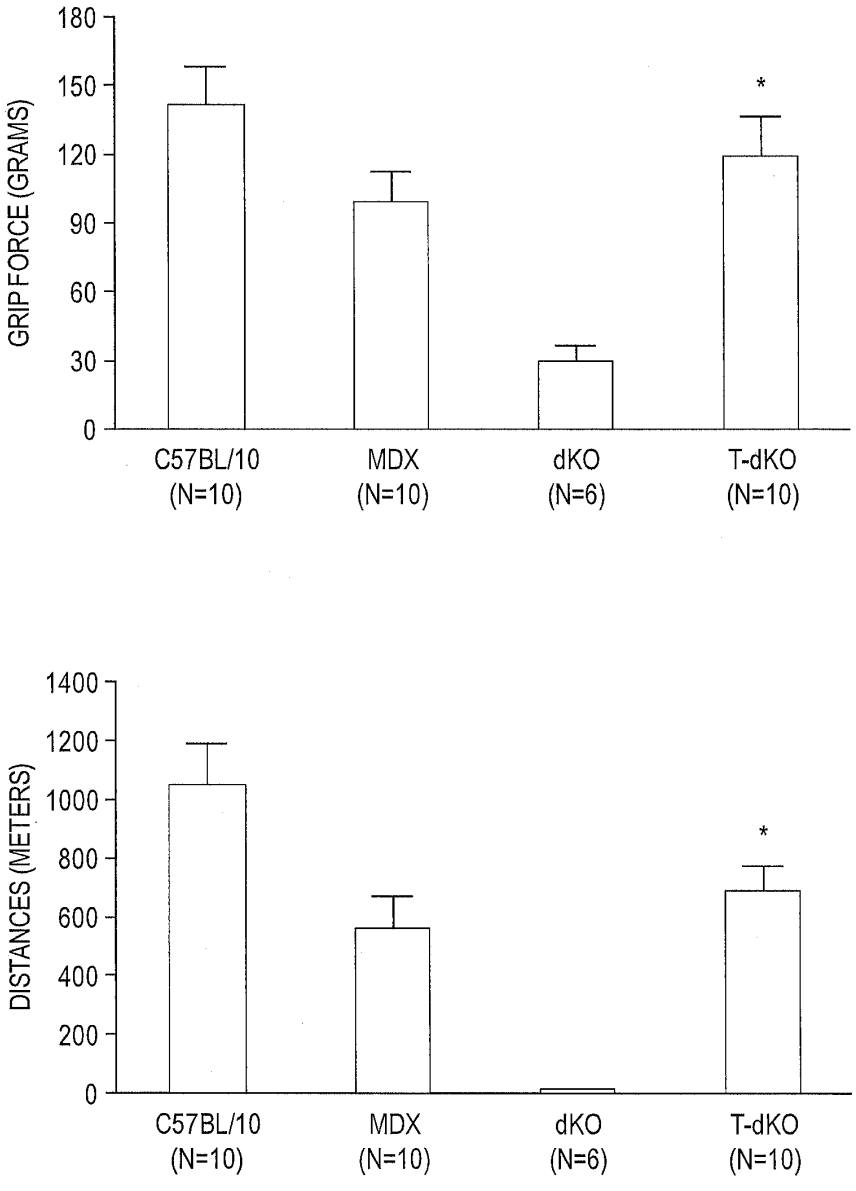


FIG. 4



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

FIG. 6A



* P<0.05 VS MDX

FIG. 5

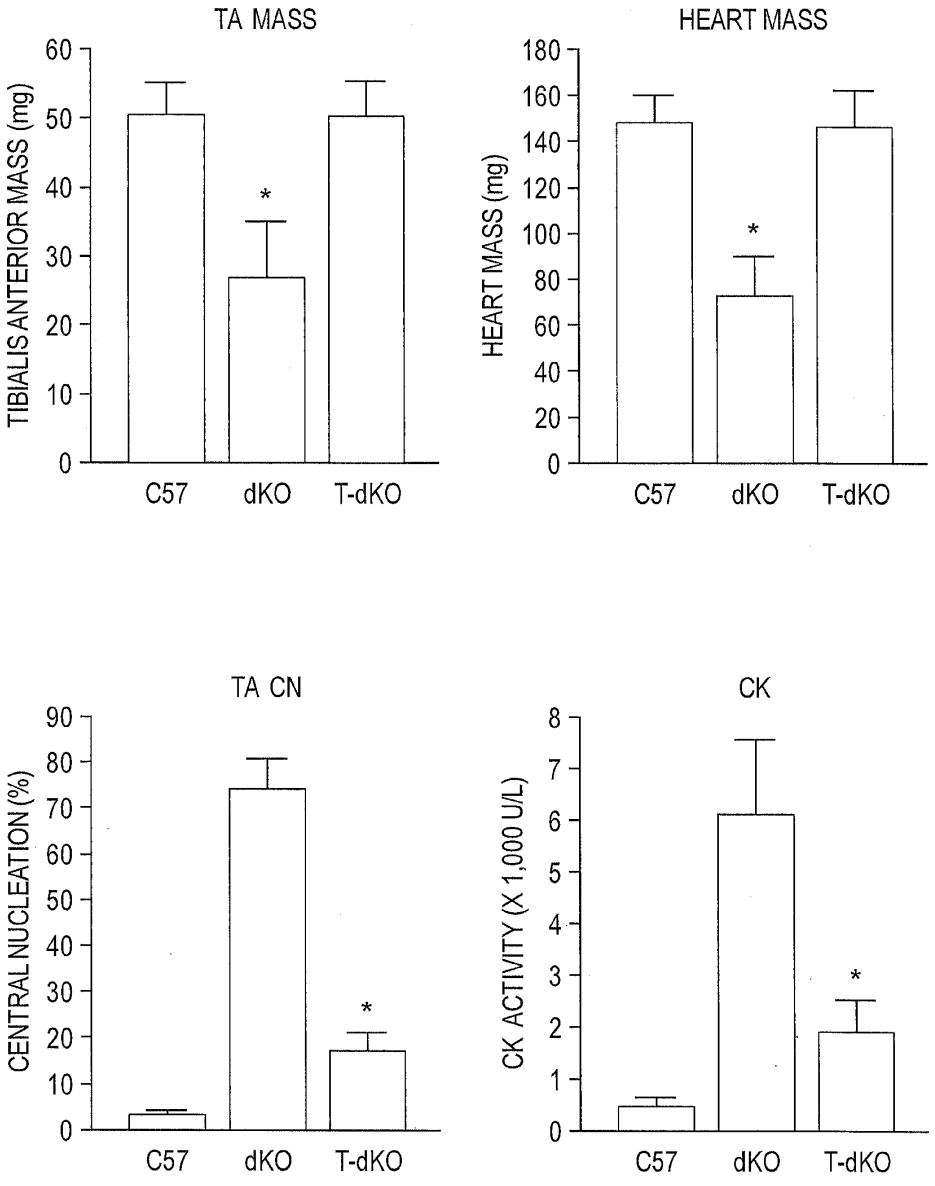

TA MASS
TIBIALIS ANTERIOR MASS (mg)
60
50
40
30
20
10
0
*
C57
dKO
T-dKO
HEART MASS
HEART MASS (mg)
180
160
140
120
100
80
60
40
20
0
*
C57
dKO
T-dKO
TA CN
CENTRAL NUCLEATION (%)
90
80
70
60
50
40
30
20
10
0
*
C57
dKO
T-dKO
CK
CK ACTIVITY (X 1,000 U/L)
8
7
6
5
4
3
2
1
0
*
C57
dKO
T-dKO

FIG. 6B

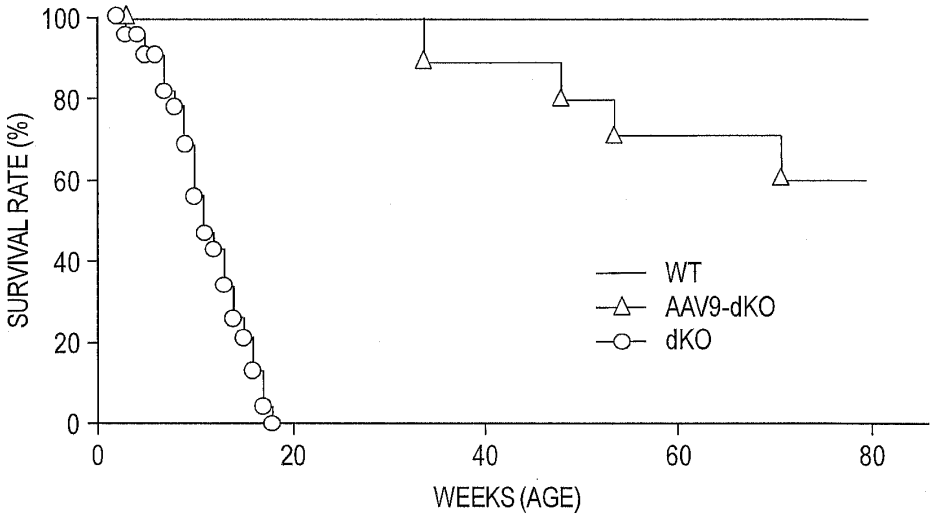

100
80
60
40
20
0
SURVIVAL RATE (%)
0
20
40
60
80
WEEKS (AGE)
WT
AAV9-dKO
dKO

FIG. 7

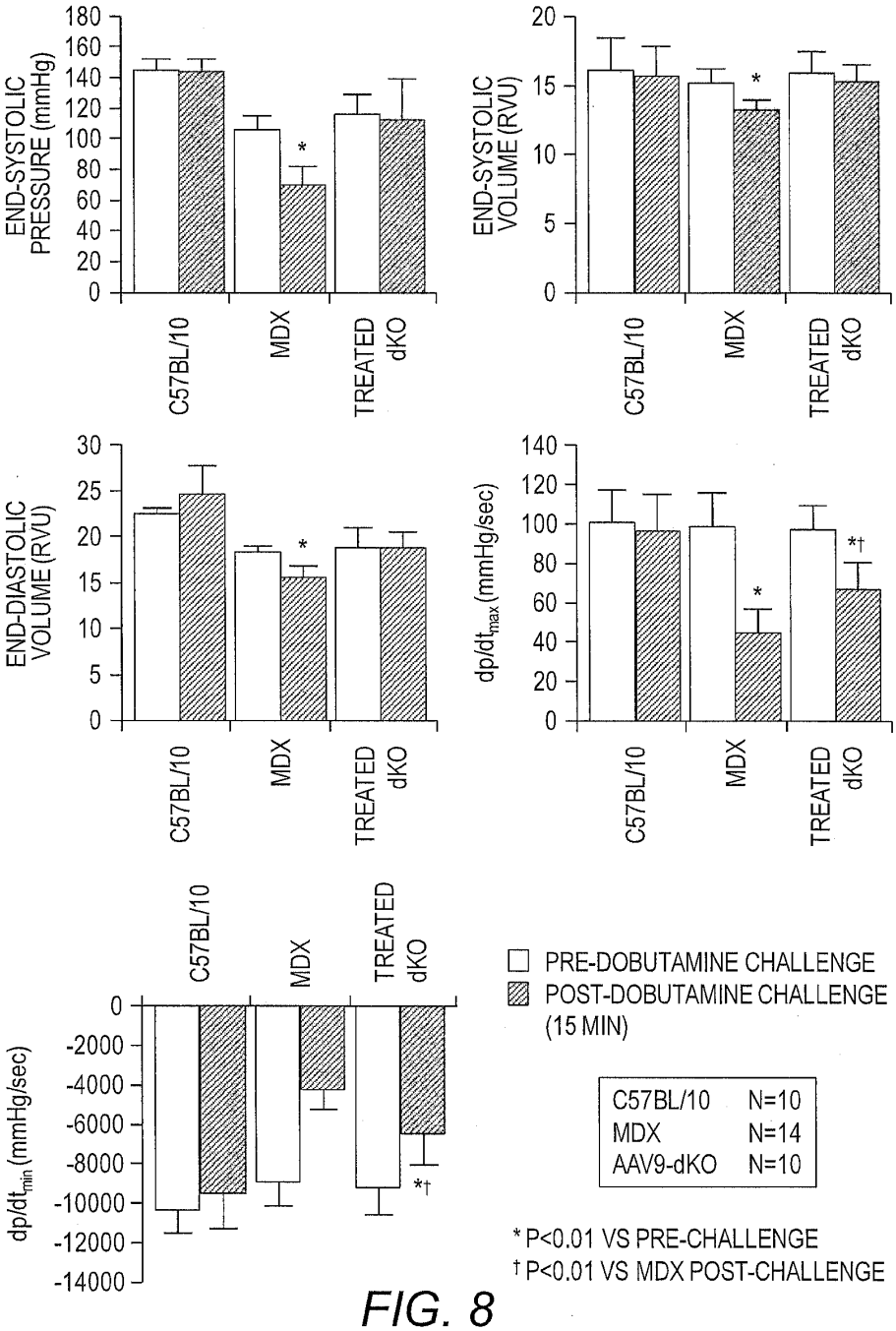

END-SYSTOLIC PRESSURE (mmHg)
180
160
140
120
100
80
60
40
20
0
*
C57BL/10
MDX
TREATED dKO
END-SYSTOLIC VOLUME (RVU)
20
15
10
5
0
*
C57BL/10
MDX
TREATED dKO
END-DIASTOLIC VOLUME (RVU)
30
25
20
15
10
5
0
*
C57BL/10
MDX
TREATED dKO
dp/dtmax (mmHg/sec)
140
120
100
80
60
40
20
0
*
*†
C57BL/10
MDX
TREATED 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

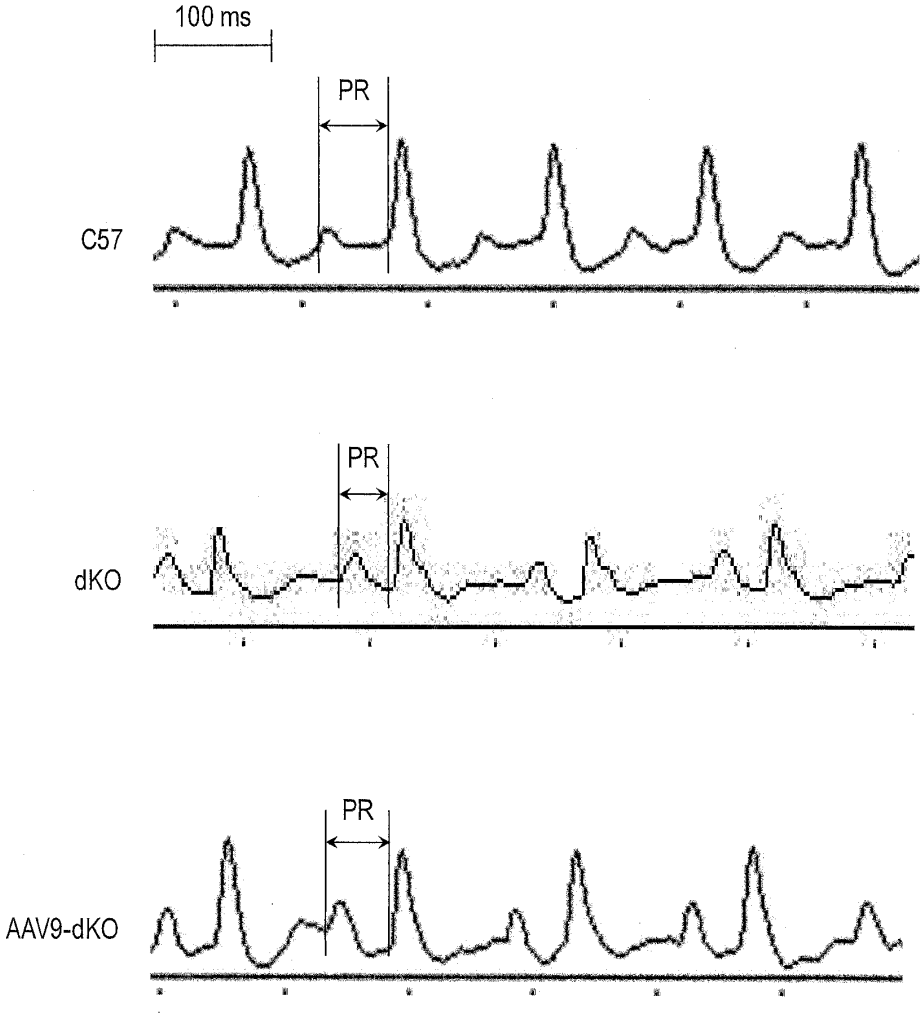


FIG. 9A

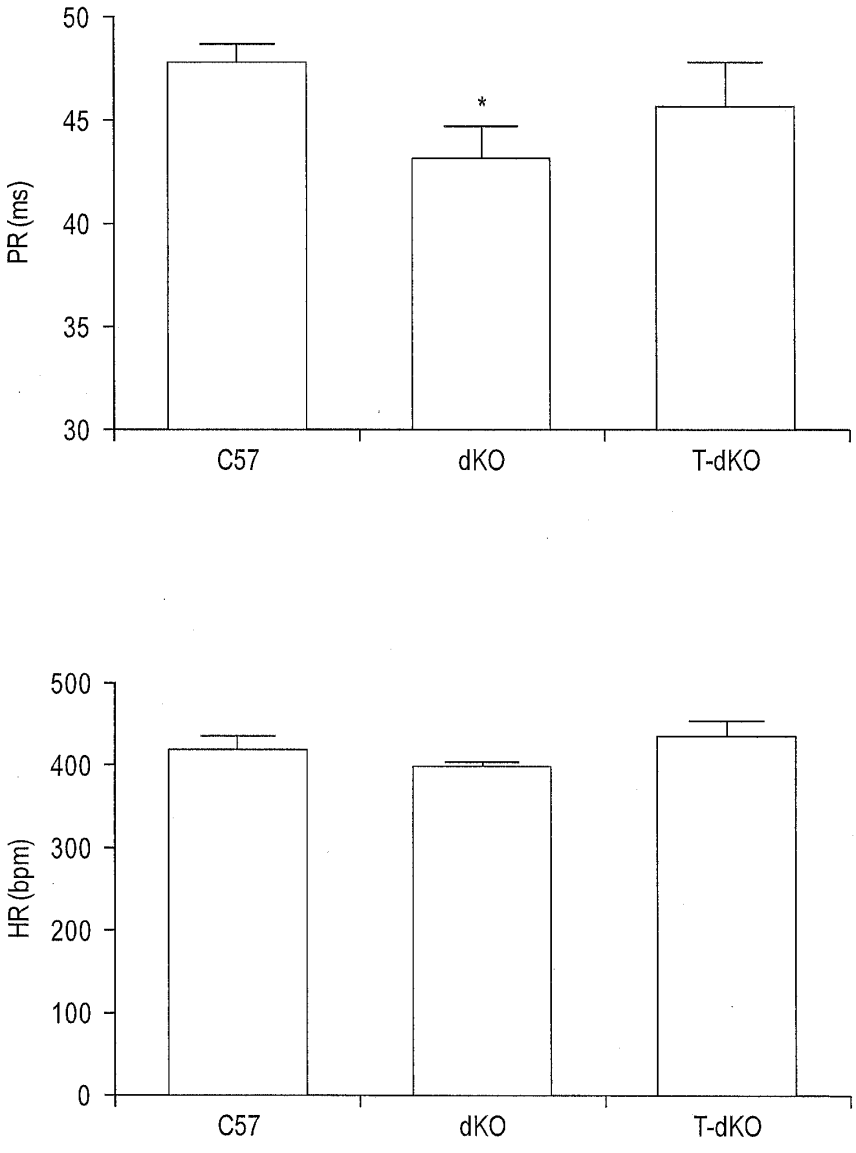

50
45
40
35
30
PR (ms)
*
C57
dKO
T-dKO
500
400
300
200
100
0
HR (bpm)
C57
dKO
T-dKO

FIG. 9B

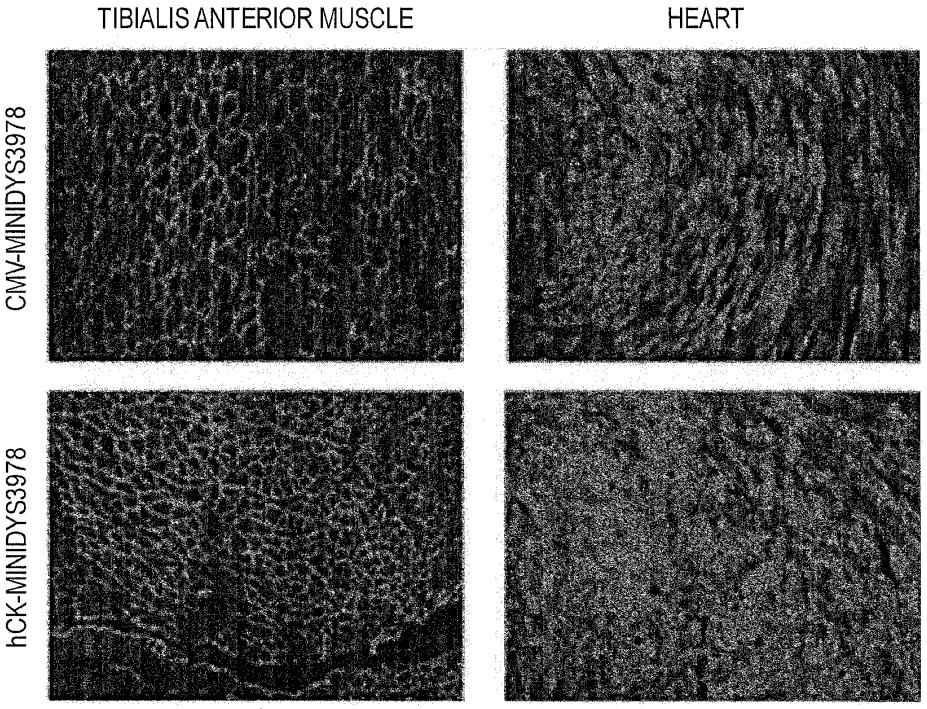

TIBIALIS ANTERIOR MUSCLE
HEART
CMV-MINIDYS3978
hCK-MINIDYS3978

FIG. 10

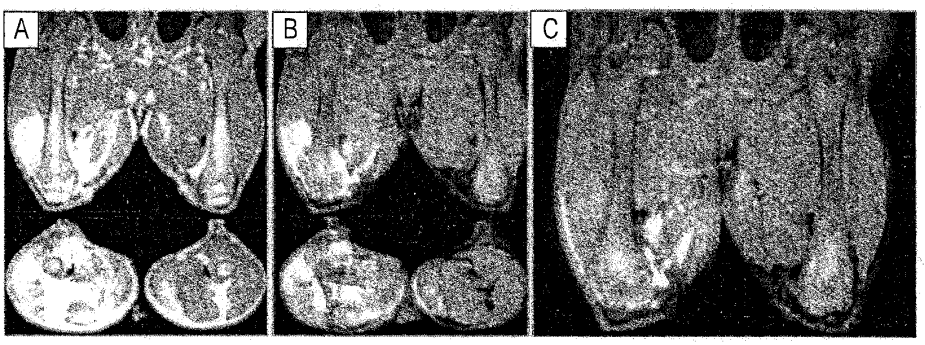

A
B
C
T2
T2 – FAT SATURATION
SEGMENTATION

FIG. 11

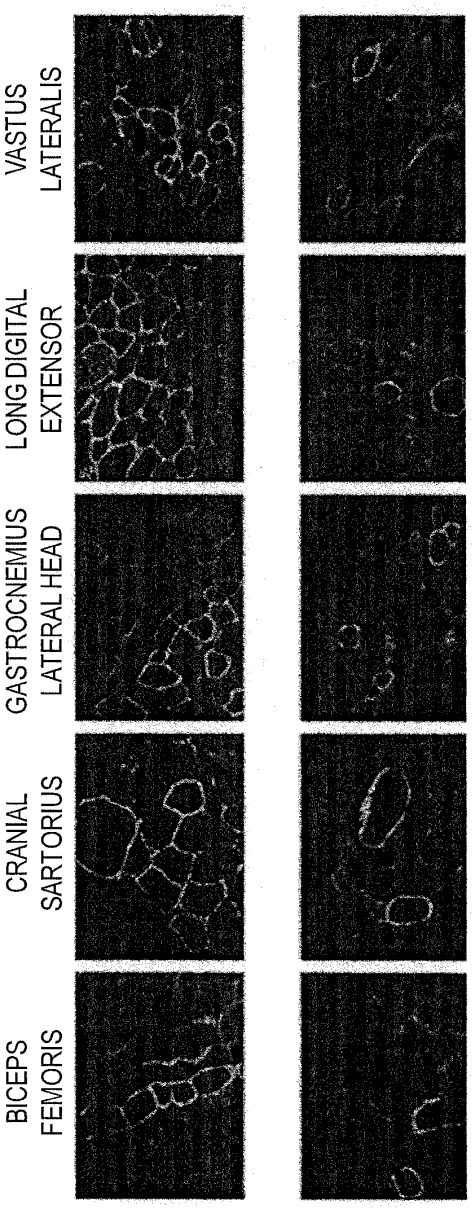

BICEPS FEMORIS
CRANIAL SARTORIUS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
VASTUS LATERALIS
LEFT LEG NON-INJECTED
RIGHT LEG INJECTED

FIG. 12

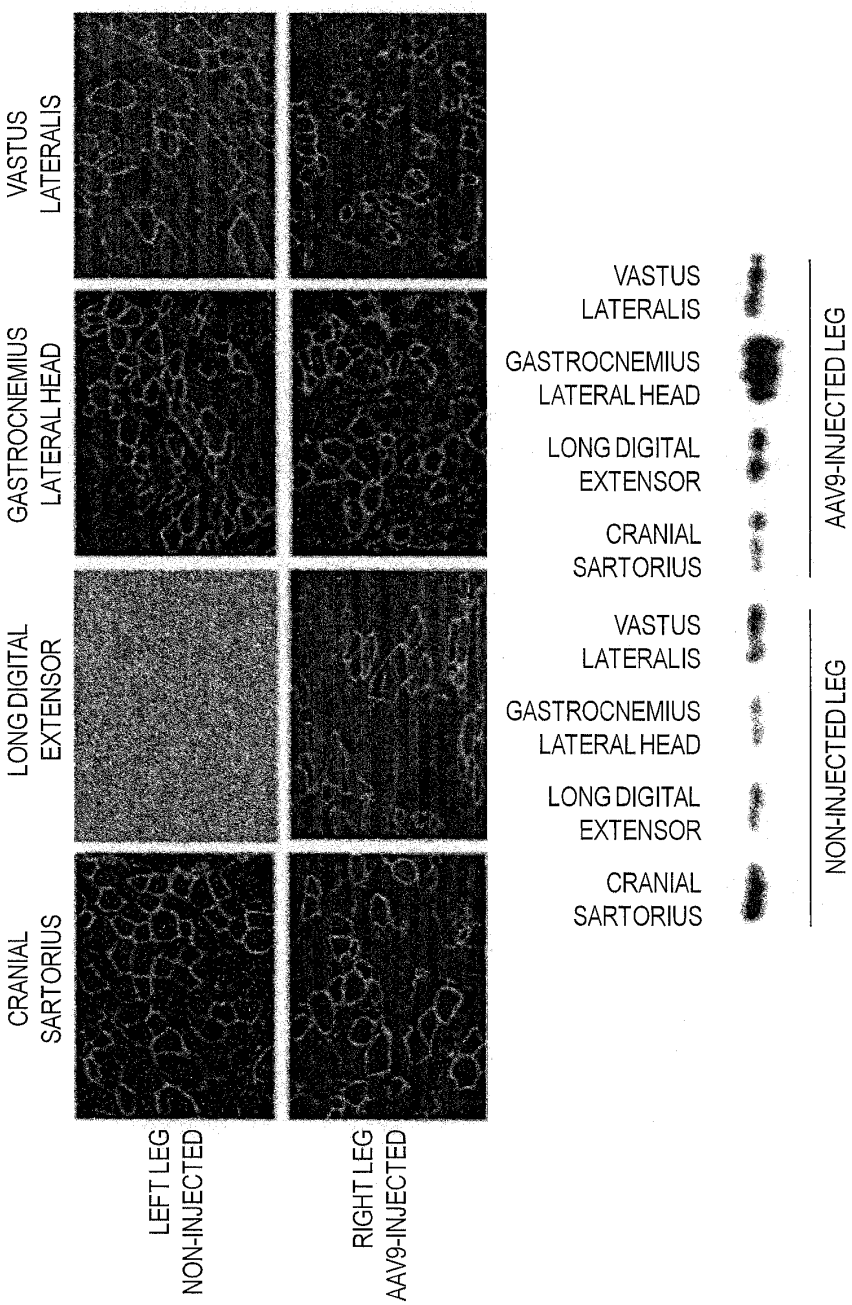

VASTUS LATERALIS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
CRANIAL SARTORIUS
LEFT LEG NON-INJECTED
RIGHT LEG AAV9-INJECTED
VASTUS LATERALIS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
CRANIAL SARTORIUS
AAV9-INJECTED LEG
VASTUS LATERALIS
GASTROCNEMIUS LATERAL HEAD
LONG DIGITAL EXTENSOR
CRANIAL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

FIG. 13

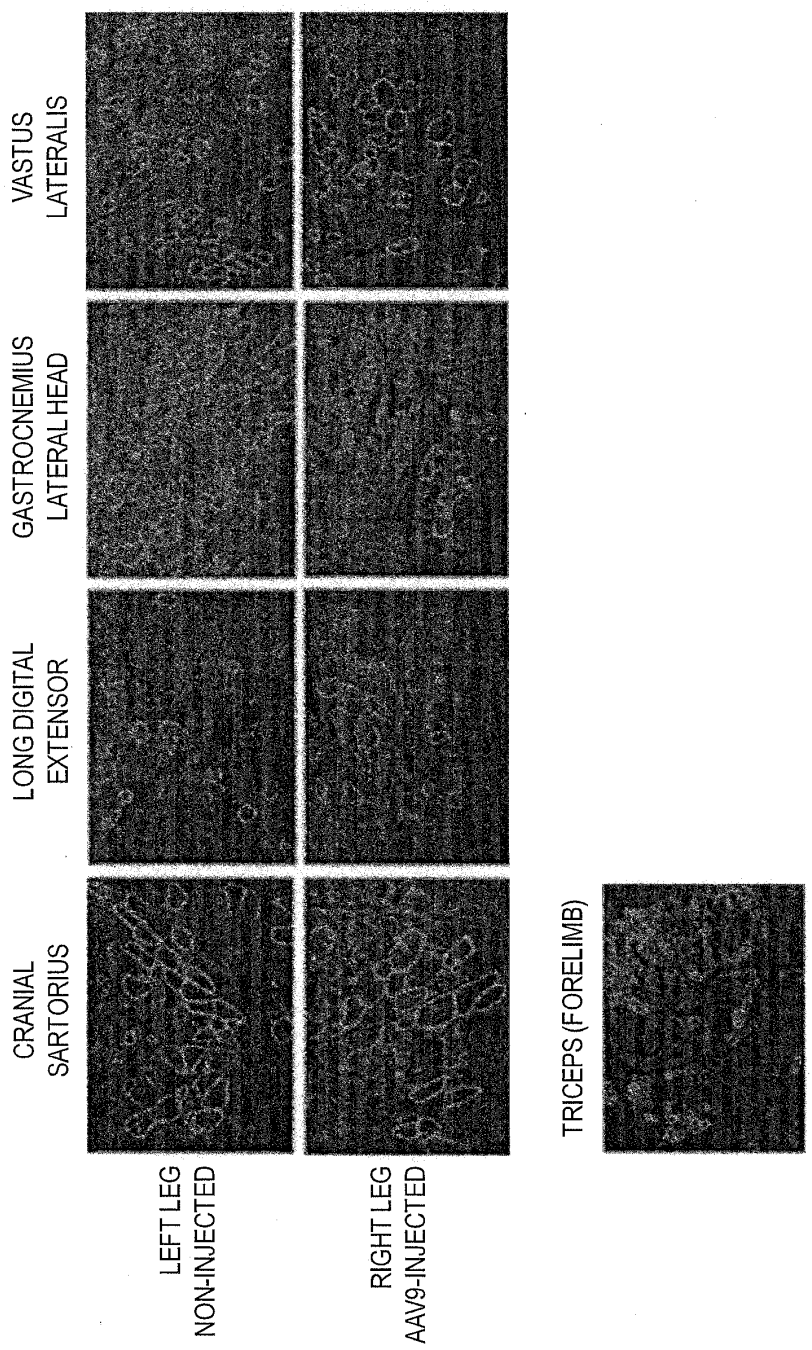

CRANIAL SARTORIUS
LONG DIGITAL EXTENSOR
GASTROCNEMIUS LATERAL HEAD
VASTUS LATERALIS
LEFT LEG NON-INJECTED
RIGHT LEG AAV9-INJECTED
TRICEPS (FORELIMB)

FIG. 14

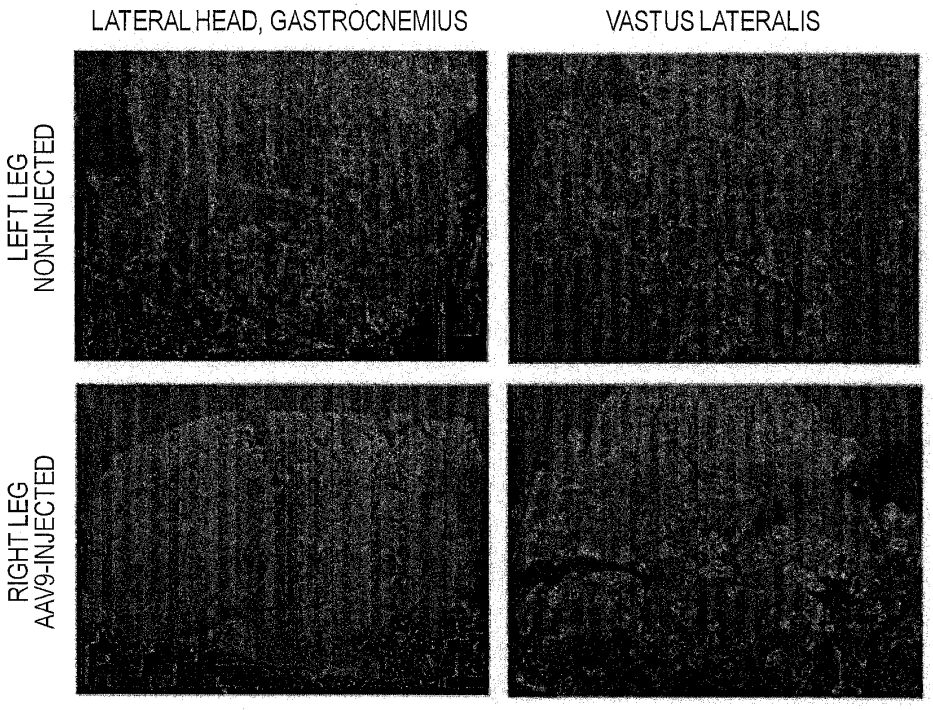

LATERAL HEAD, GASTROCNEMIUS
VASTUS LATERALIS
LEFT LEG
NON-INJECTED
RIGHT LEG
AAV9-INJECTED

FIG. 15

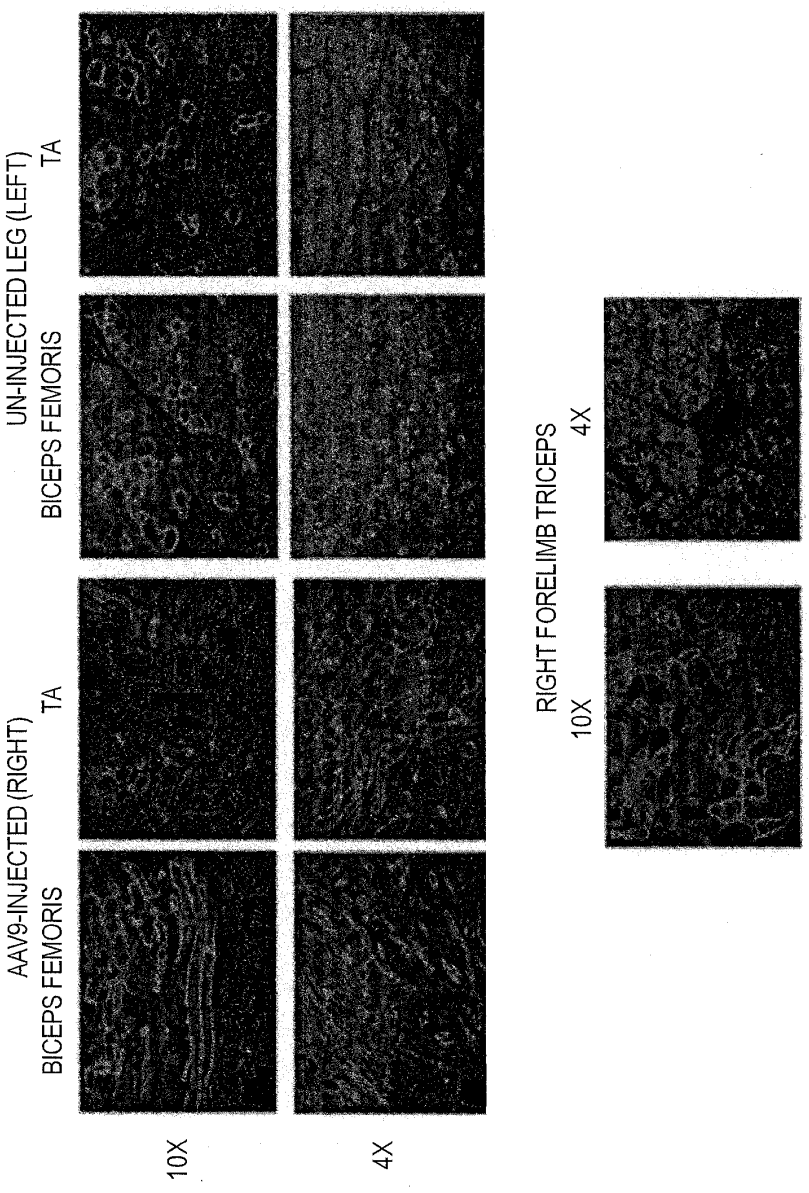

AAV9-INJECTED (RIGHT)
BICEPS FEMORIS
TA
UN-INJECTED LEG (LEFT)
BICEPS FEMORIS
TA
10X
4X
RIGHT FORELIMB TRICEPS
10X
4X

FIG. 16

LEFT HINDLIMB (NON-INJECTED SIDE) CRANIAL SARTORIUS MUSCLE

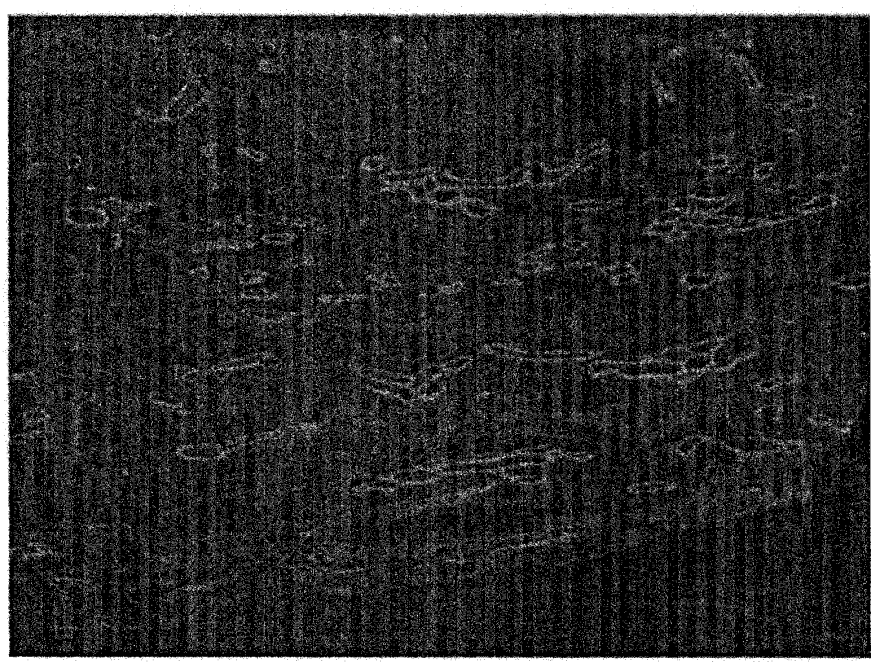


FIG. 17

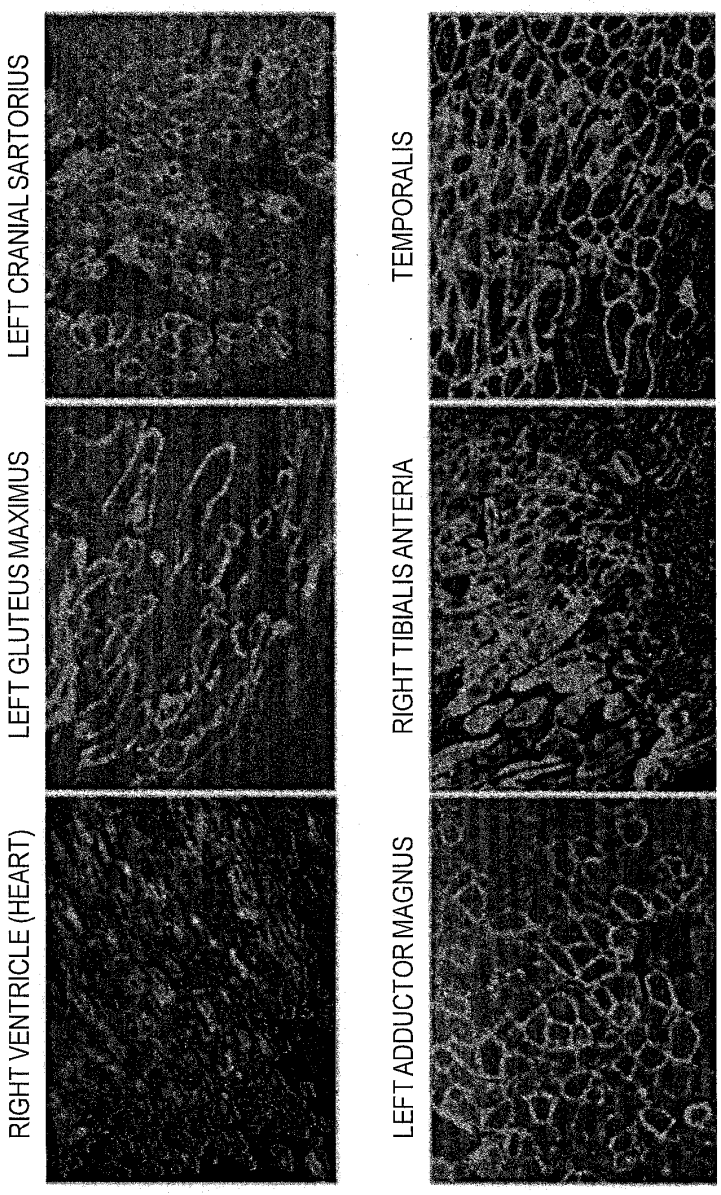

RIGHT VENTRICLE (HEART)
LEFT GLUTEUS MAXIMUS
LEFT CRANIAL SARTORIUS
LEFT ADDUCTOR MAGNUS
RIGHT TIBIALIS ANTERIA
TEMPORALIS

FIG. 18

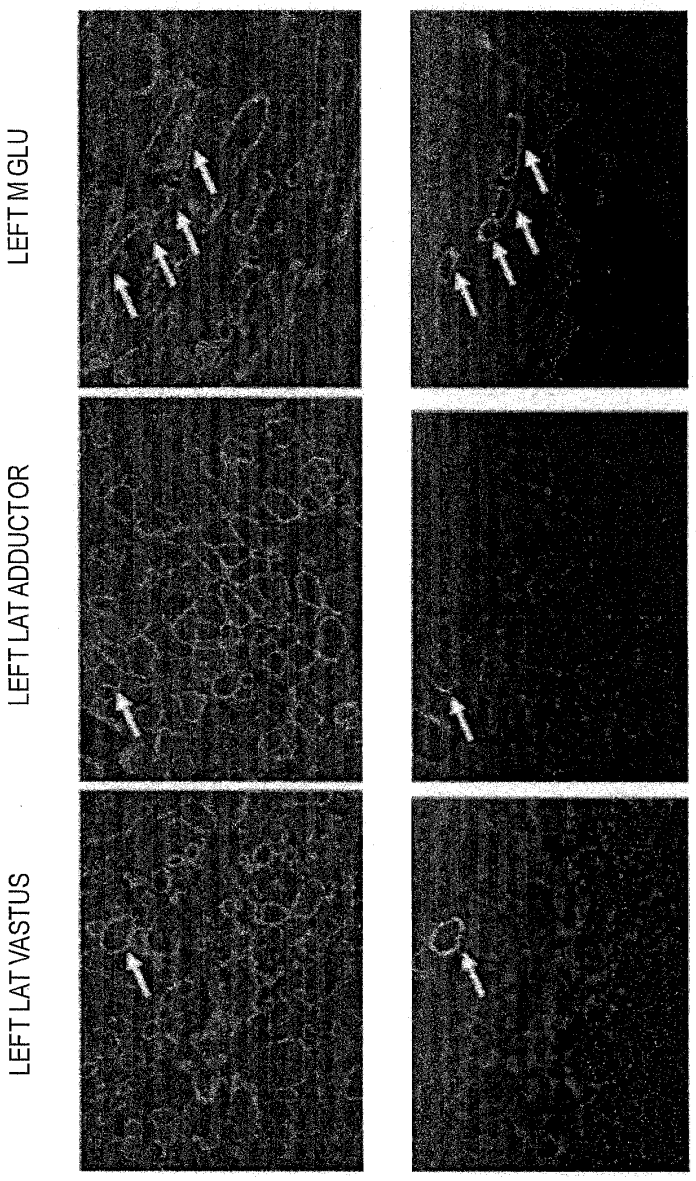


FIG. 19

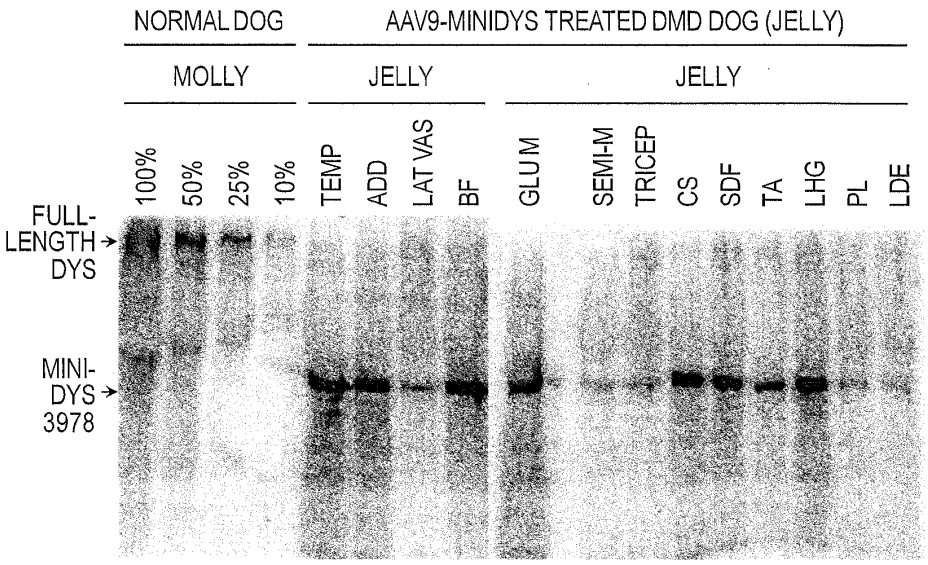

NORMAL DOG
AAV9-MINIDYS TREATED DMD DOG (JELLY)
MOLLY
JELLY
JELLY
100%
50%
25%
10%
TEMP
ADD
LAT VAS
BF
GLU M
SEMI-M
TRICEP
CS
SDF
TA
LHG
PL
LDE
FULL-LENGTH DYS
MINI-DYS 3978

FIG. 20

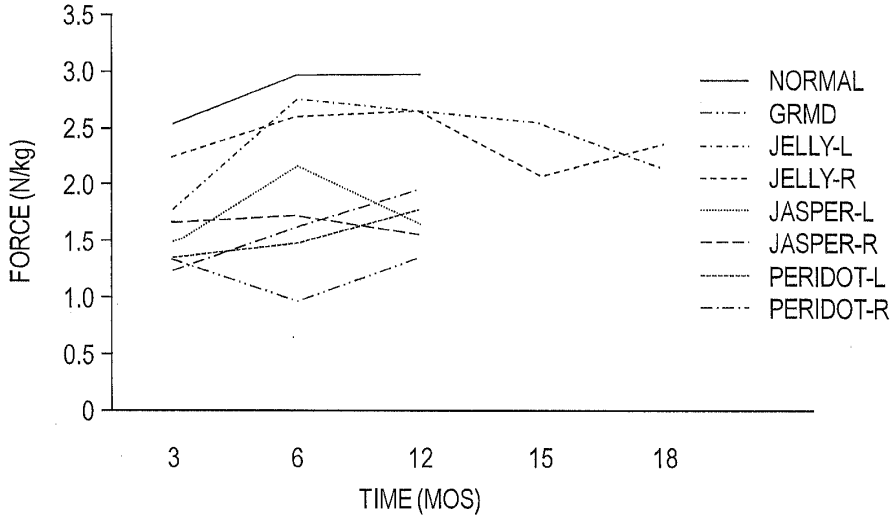

FORCE (N/kg)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
3
6
12
15
18
TIME (MOS)
NORMAL
GRMD
JELLY-L
JELLY-R
JASPER-L
JASPER-R
PERIDOT-L
PERIDOT-R

FIG. 21

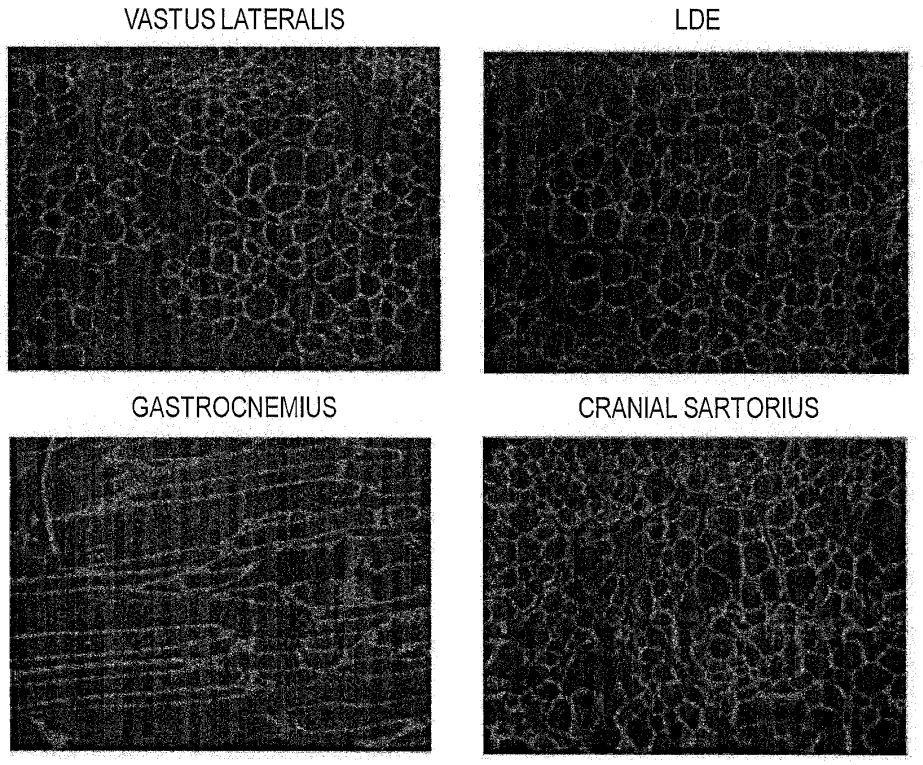


FIG. 22

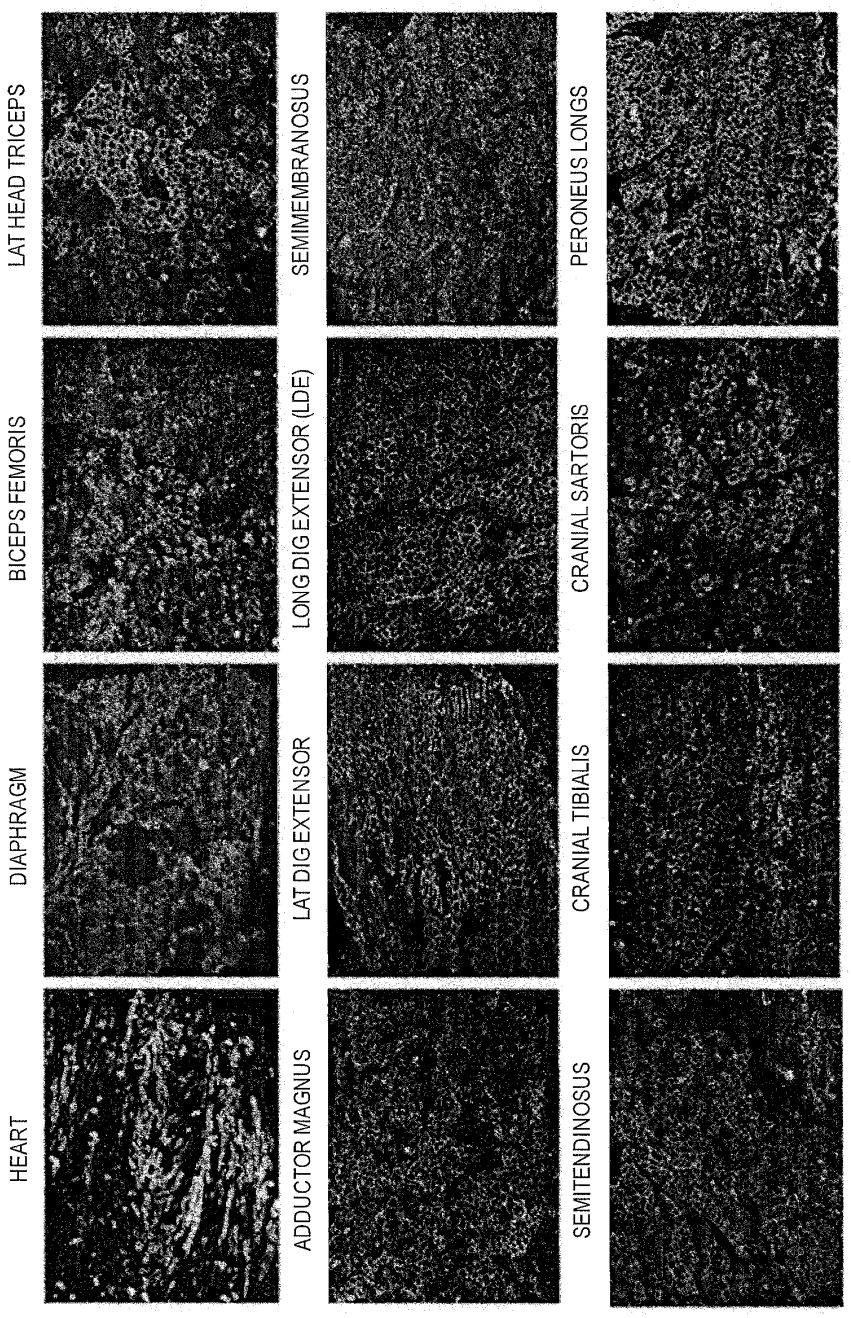

HEART
DIAPHRAGM
BICEPS FEMORIS
LAT HEAD TRICEPS
ADDUCTOR MAGNUS
LAT DIG EXTENSOR
LONG DIG EXTENSOR (LDE)
SEMIMEMBRANOSUS
SEMITENDINOSUS
CRANIAL TIBIALIS
CRANIAL SARTORIS
PERONEUS LONGS

FIG. 23

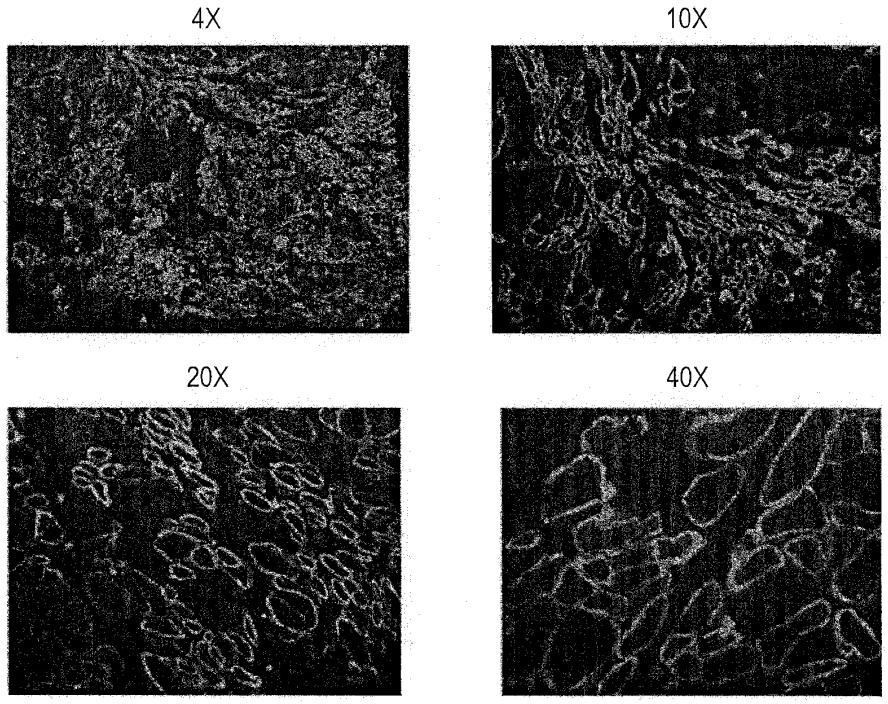


FIG. 24

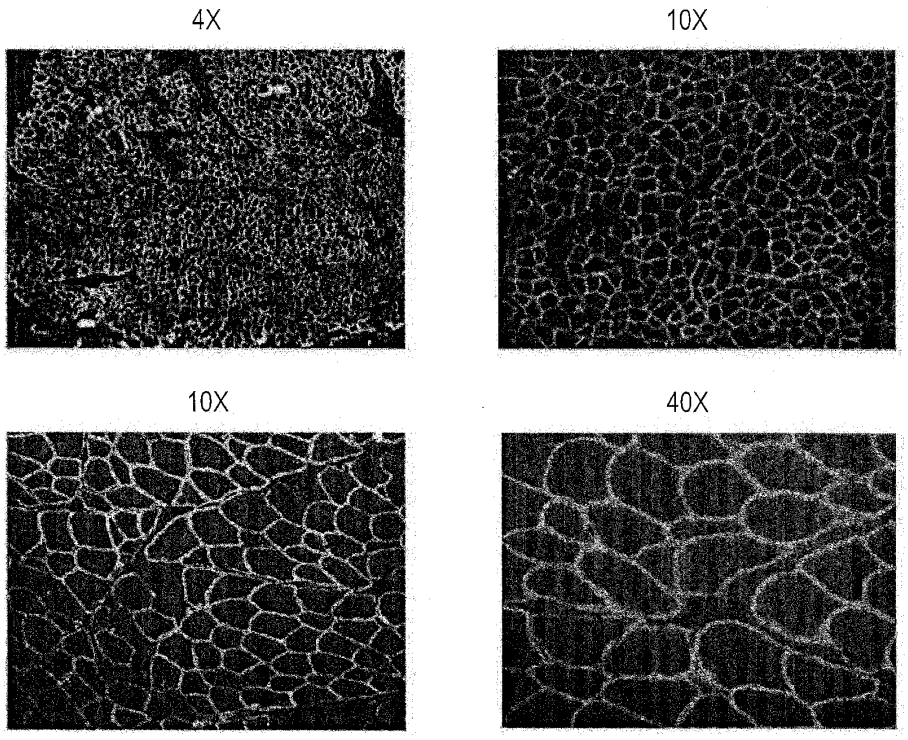


FIG. 25

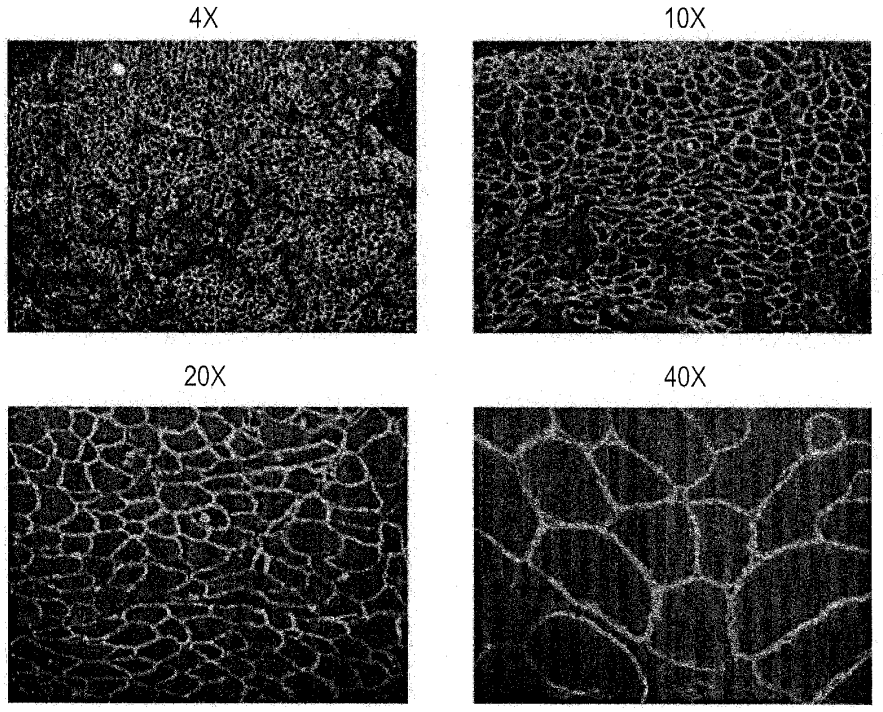


FIG. 26

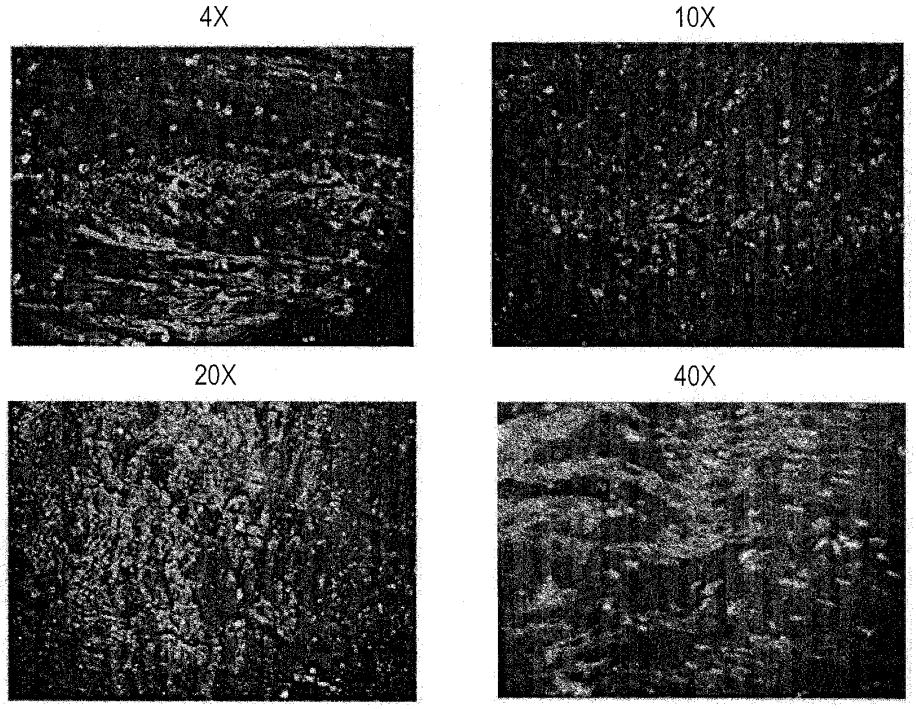


FIG. 27

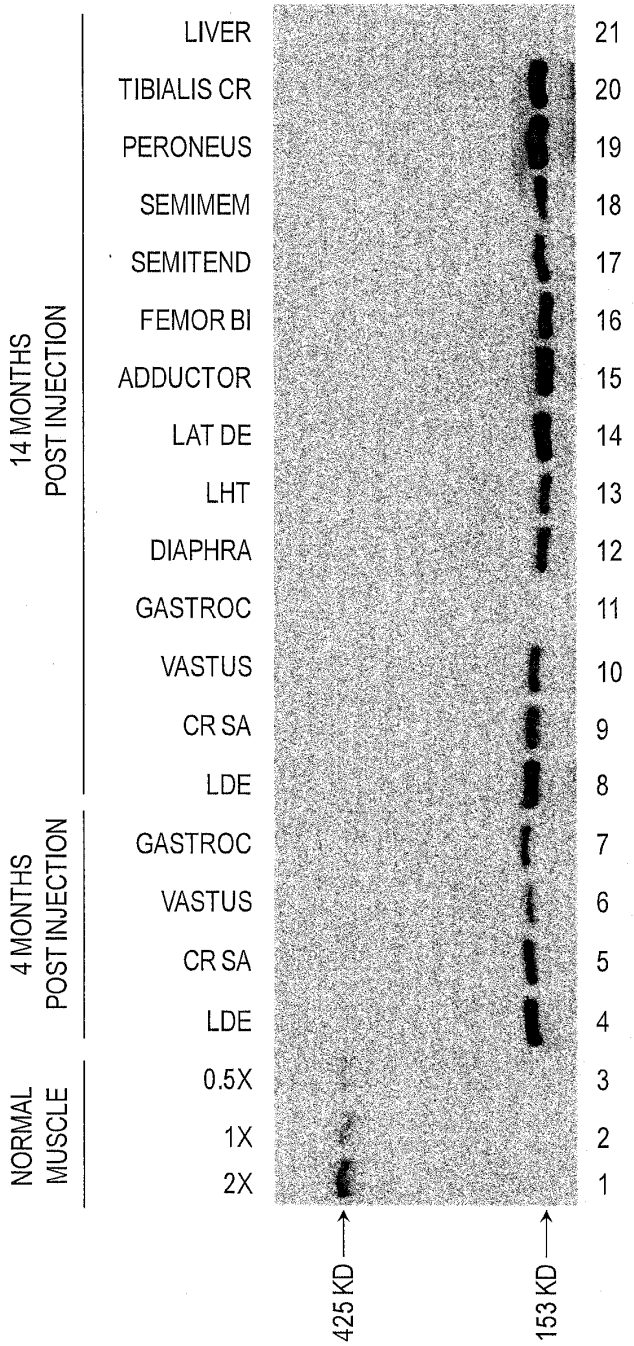

14 MONTHS POST INJECTION
4 MONTHS POST INJECTION
NORMAL MUSCLE
LIVER
TIBIALIS CR
PERONEUS
SEMIMEM
SEMITEND
FEMOR BI
ADDUCTOR
LAT DE
LHT
DIAPHRA
GASTROC
VASTUS
CR SA
LDE
GASTROC
VASTUS
CR SA
LDE
0.5X
1X
2X
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
425 KD
153 KD

FIG. 28

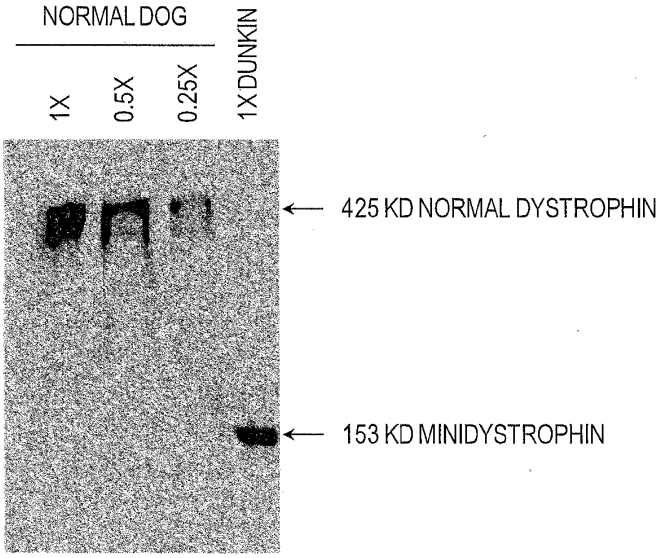

NORMAL DOG
1X
0.5X
0.25X
1X DUNKIN
425 KD NORMAL DYSTROPHIN
153 KD MINIDYSTROPHIN

FIG. 29

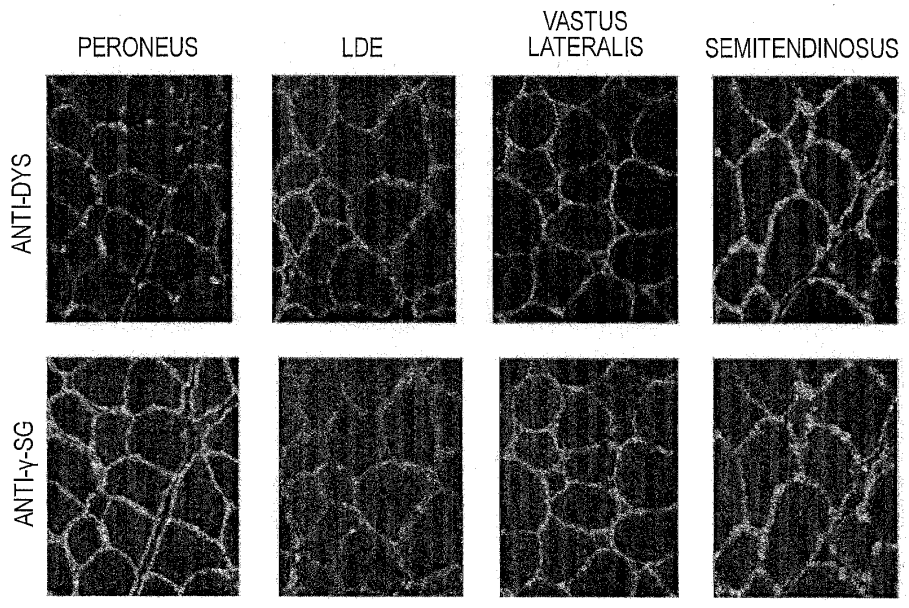

PERONEUS
LDE
VASTUS LATERALIS
SEMITENDINOSUS
ANTI-DYS
ANTI-γ-SG

FIG. 30

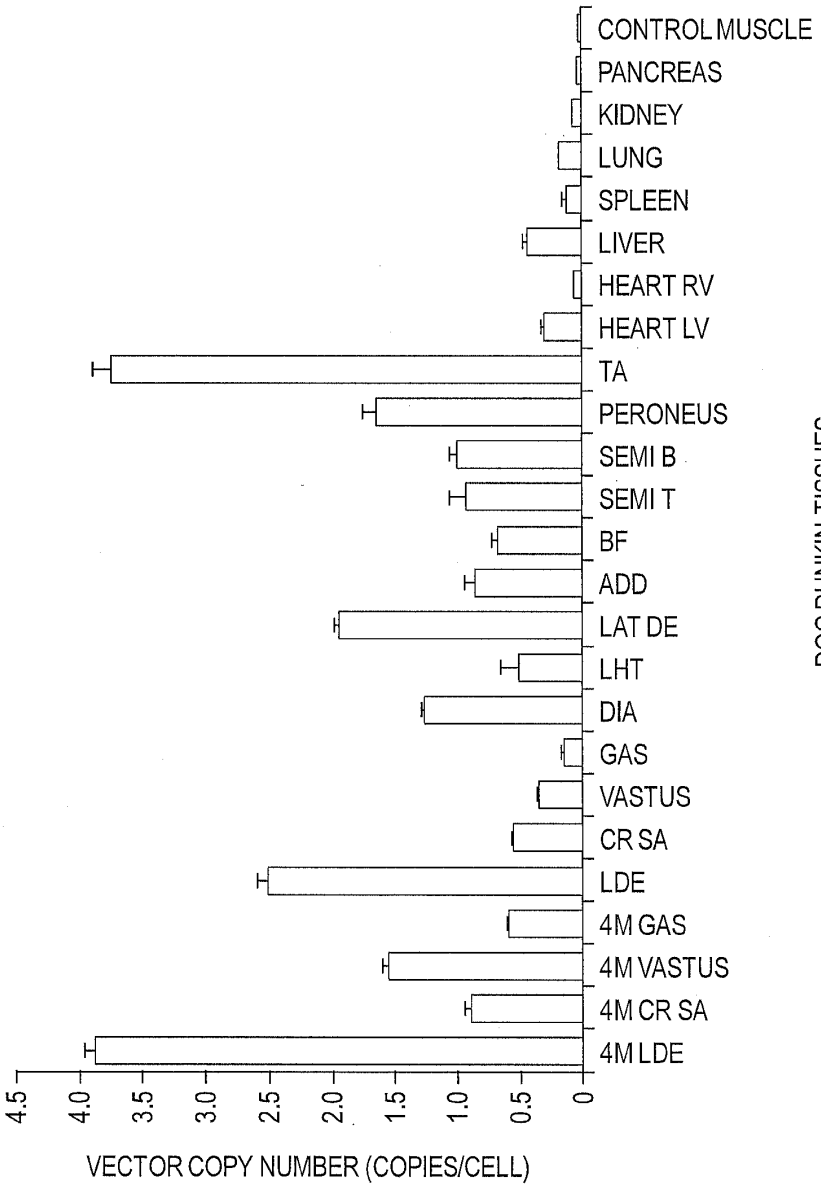

CONTROL MUSCLE
PANCREAS
KIDNEY
LUNG
SPLEEN
LIVER
HEART RV
HEART LV
TA
PERONEUS
SEMI B
SEMI T
BF
ADD
LAT DE
LHT
DIA
GAS
VASTUS
CR SA
LDE
4M GAS
4M VASTUS
4M CR SA
4M LDE
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
VECTOR COPY NUMBER (COPIES/CELL)
DOG DUNKIN TISSUES

FIG. 31

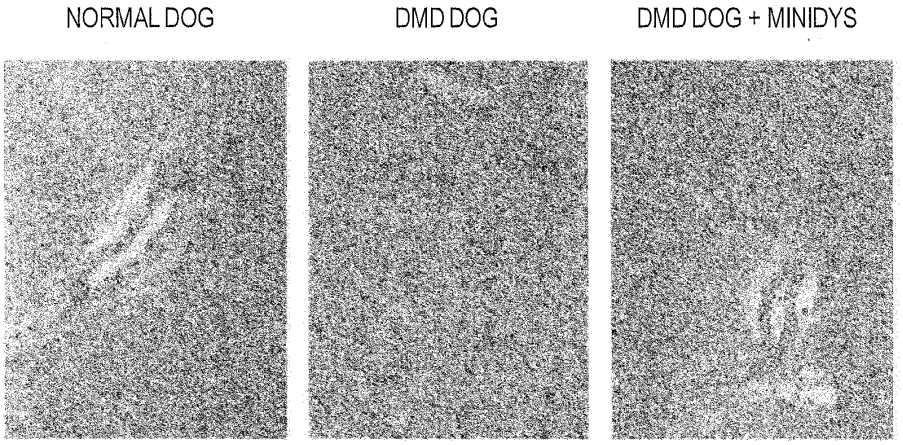

NORMAL DOG
DMD DOG
DMD DOG + MINIDYS

FIG. 32

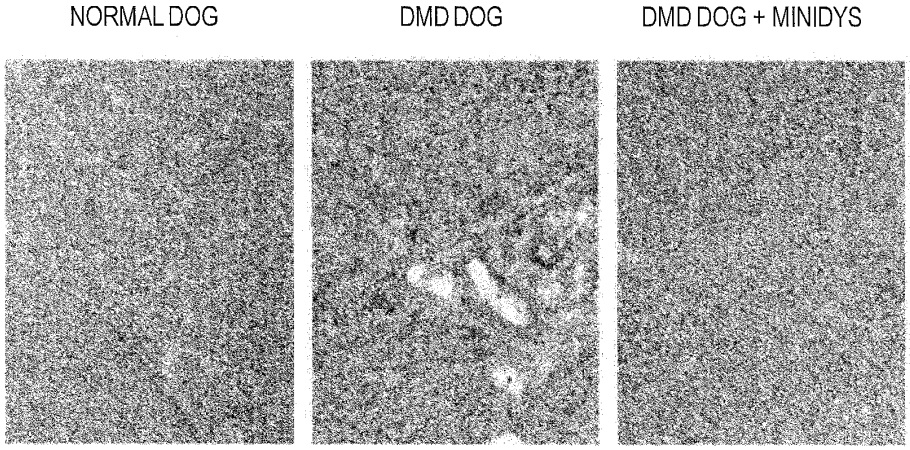

NORMAL DOG
DMD DOG
DMD DOG + MINIDYS

FIG. 33

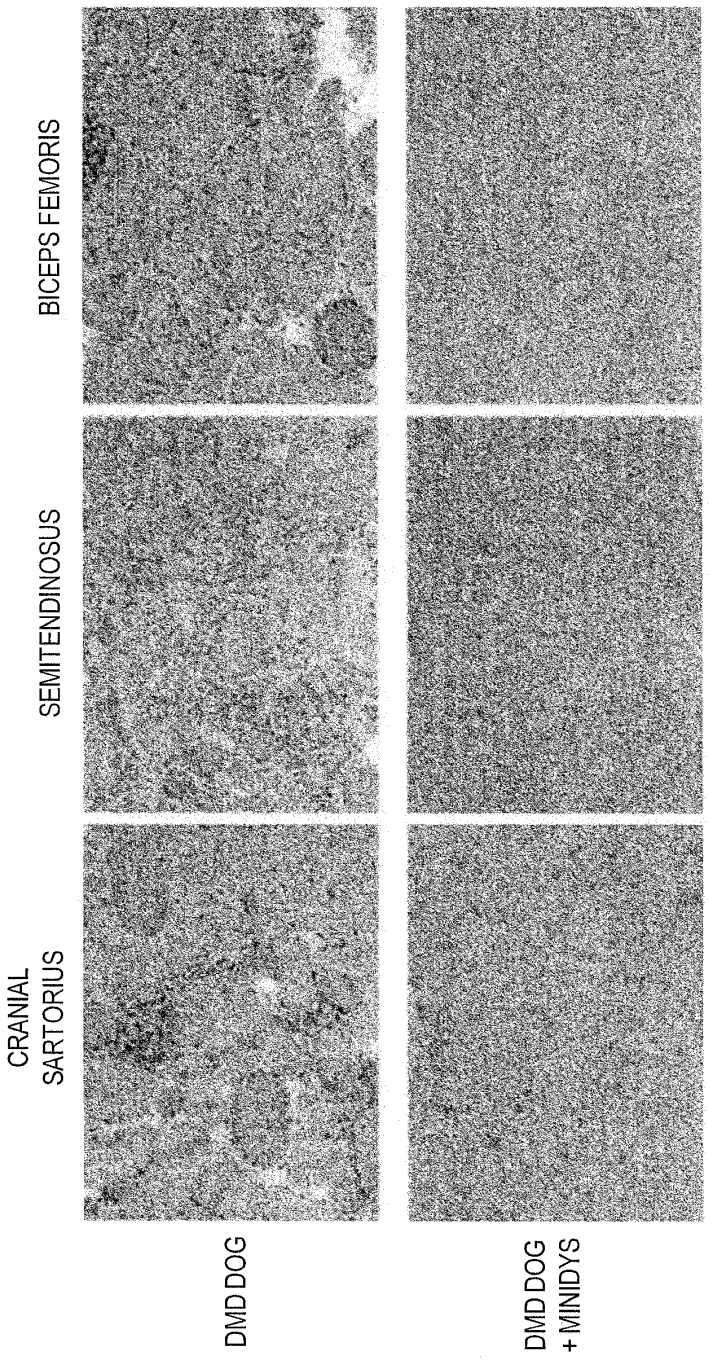

CRANIAL SARTORIUS
SEMITENDINOSUS
BICEPS FEMORIS
DMD DOG
DMD DOG + MINIDYS

FIG. 34

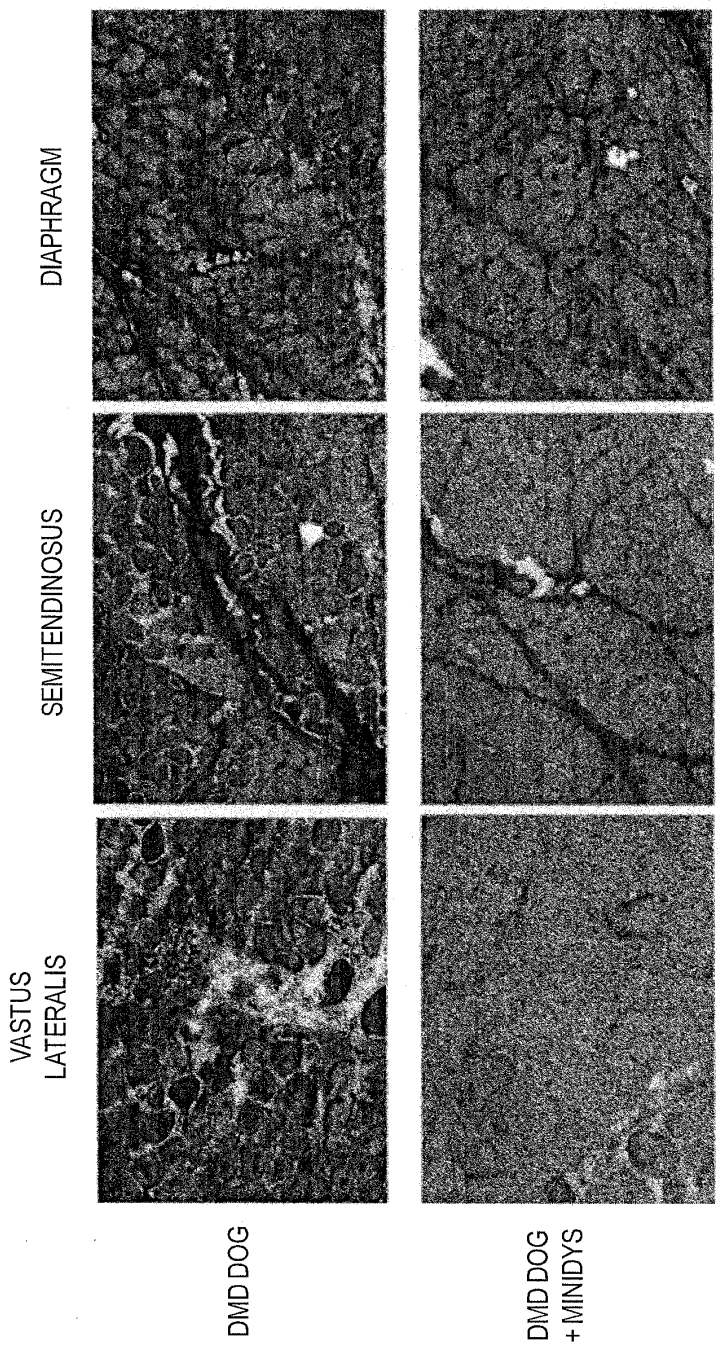

VASTUS LATERALIS
SEMITENDINOSUS
DIAPHRAGM
DMD DOG
DMD DOG + MINIDYS

FIG. 35

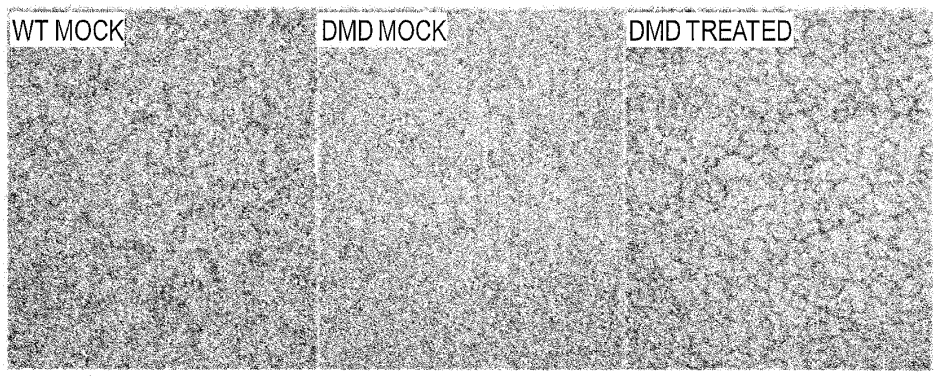


FIG. 36A

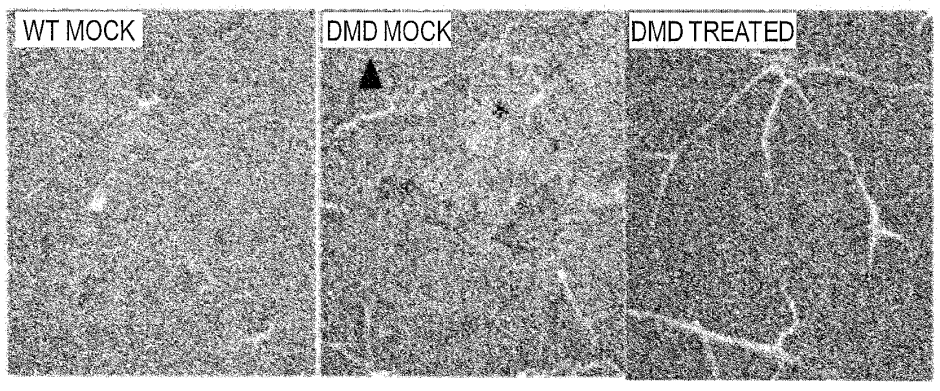


FIG. 36B

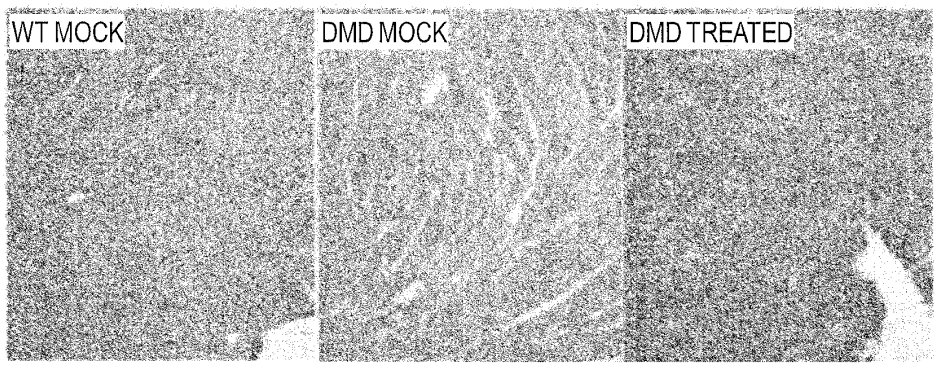


FIG. 36C

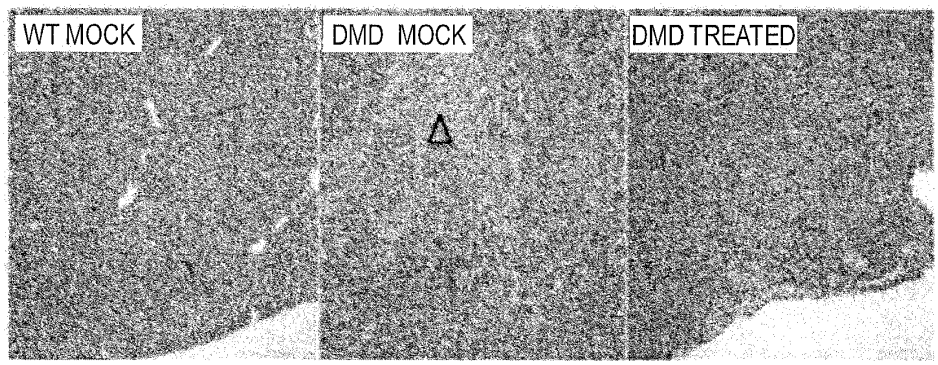


FIG. 36D

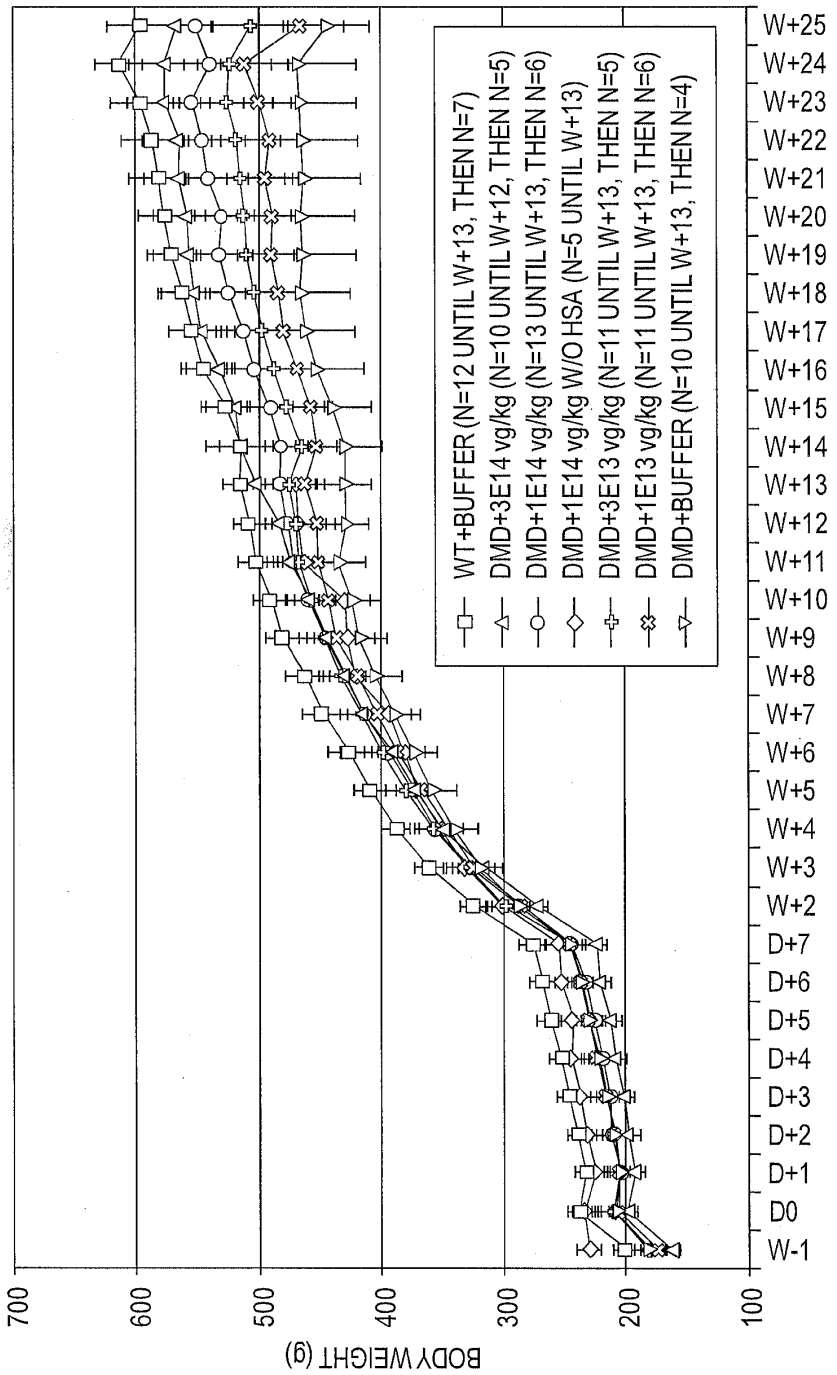

BODY WEIGHT (g)
700
600
500
400
300
200
100
W-1
D0
D+1
D+2
D+3
D+4
D+5
D+6
D+7
W+2
W+3
W+4
W+5
W+6
W+7
W+8
W+9
W+10
W+11
W+12
W+13
W+14
W+15
W+16
W+17
W+18
W+19
W+20
W+21
W+22
W+23
W+24
W+25
WT+BUFFER (N=12 UNTIL W+13, THEN N=7)
DMD+3E14 vg/kg (N=10 UNTIL W+12, THEN N=5)
DMD+1E14 vg/kg (N=13 UNTIL W+13,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

FIG. 37

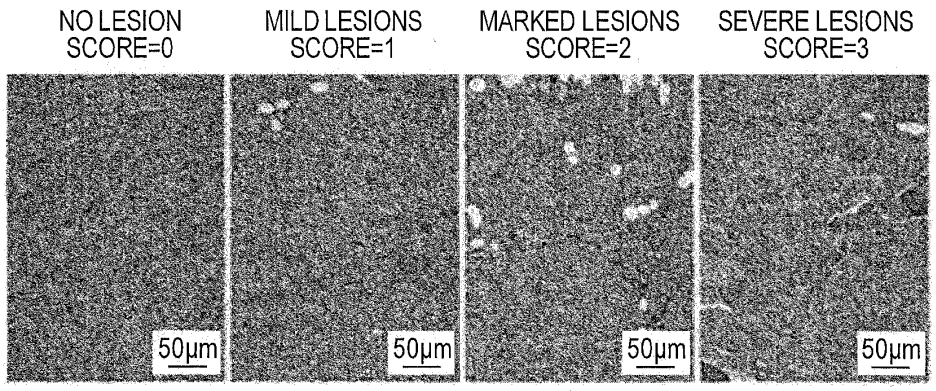


FIG. 38A

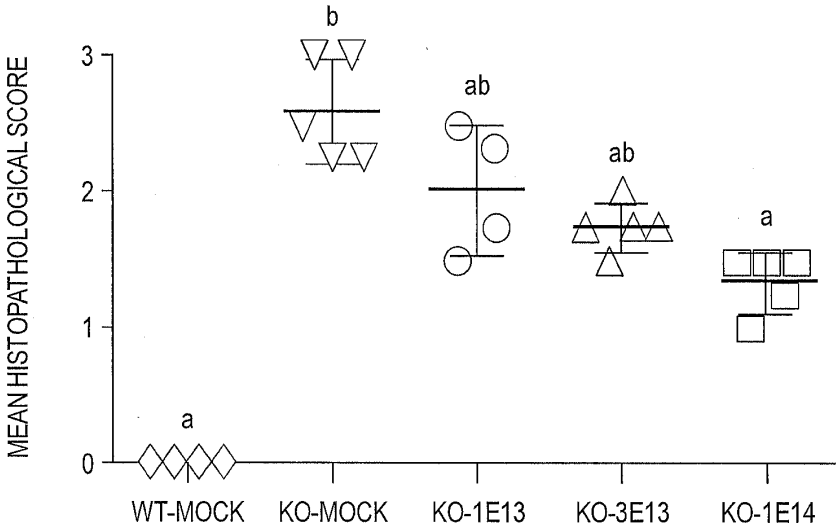


FIG. 38B

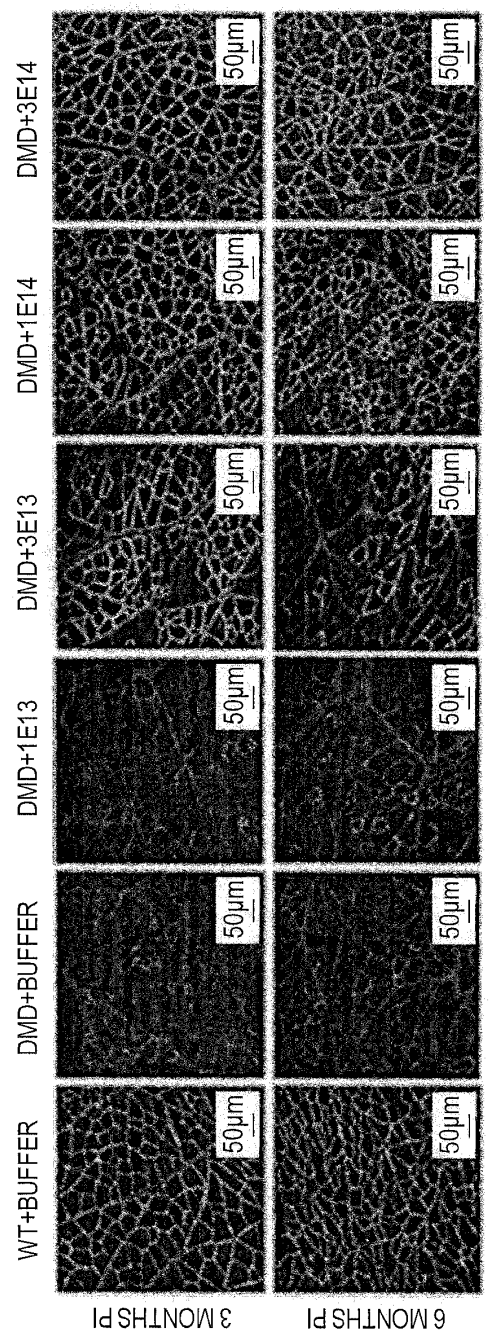


FIG. 39A

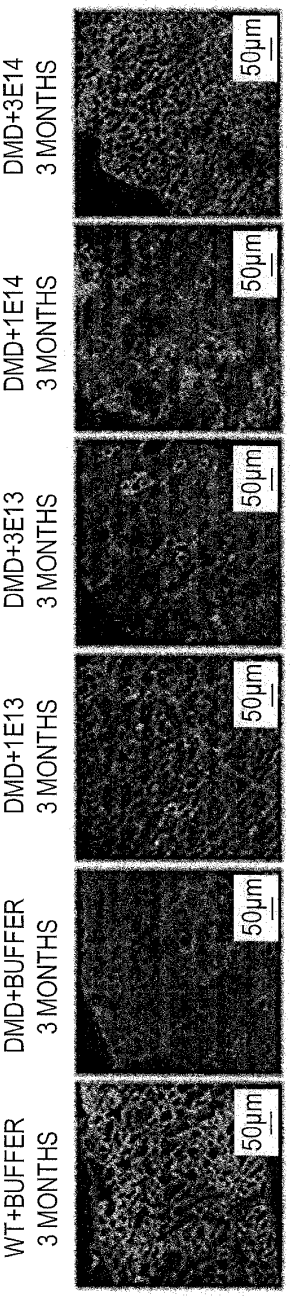


FIG. 40A

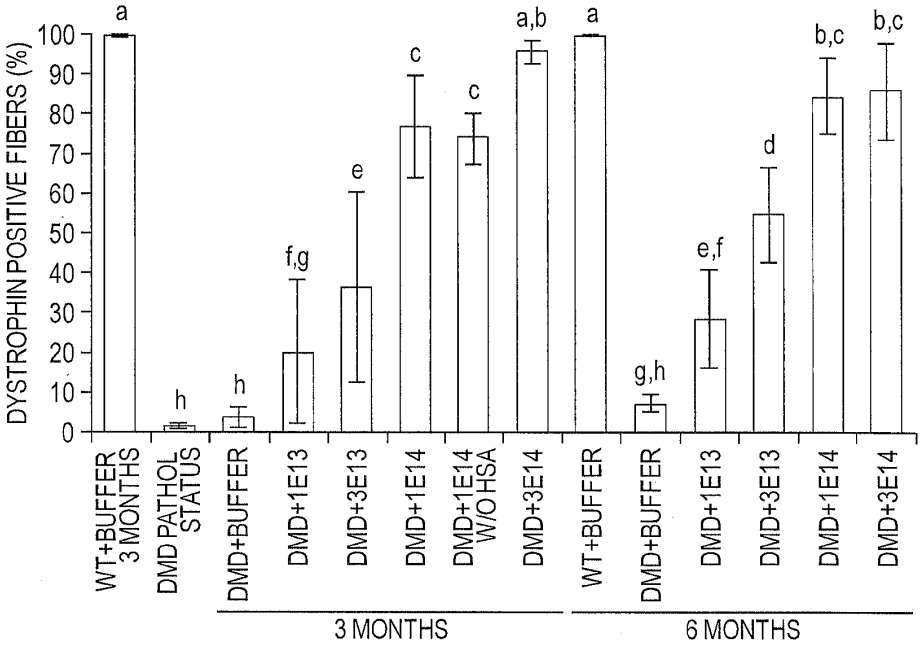


FIG. 39B

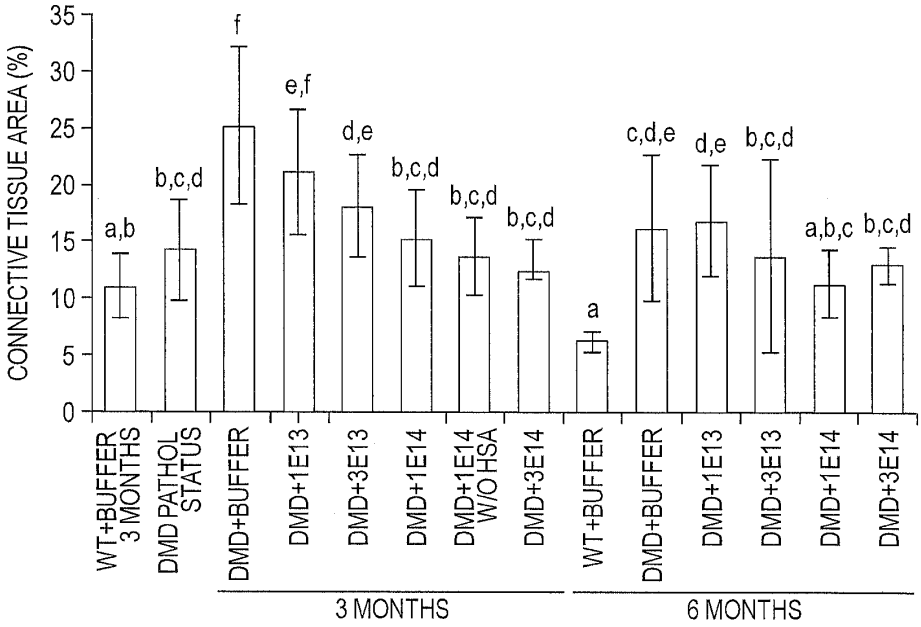


FIG. 39C

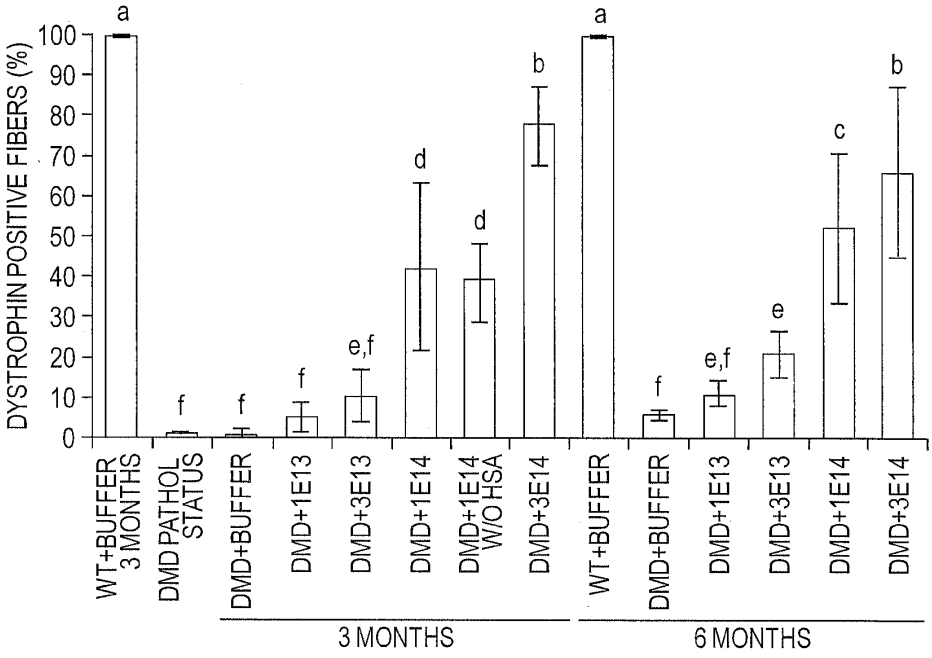


FIG. 40B

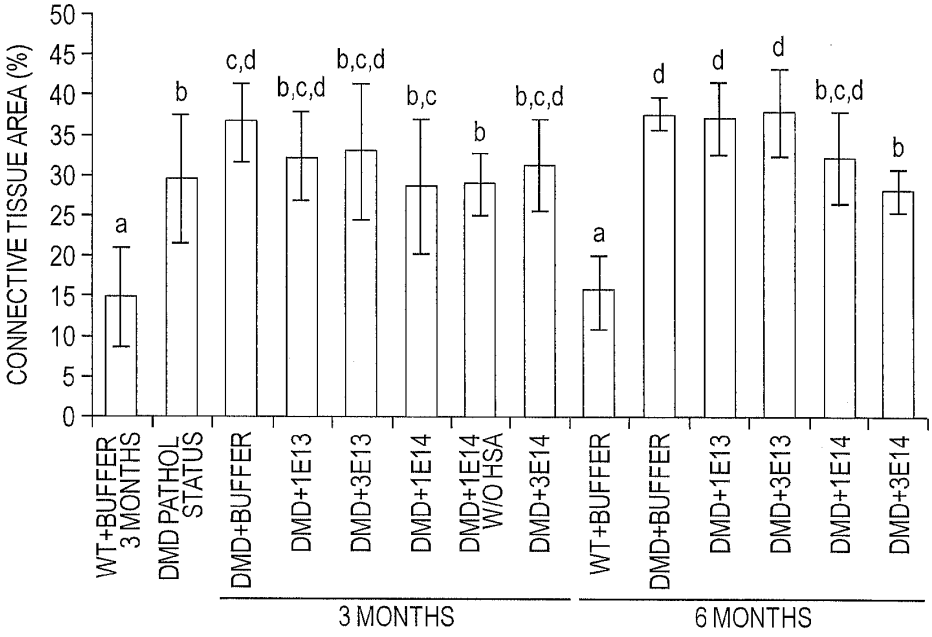


FIG. 40C

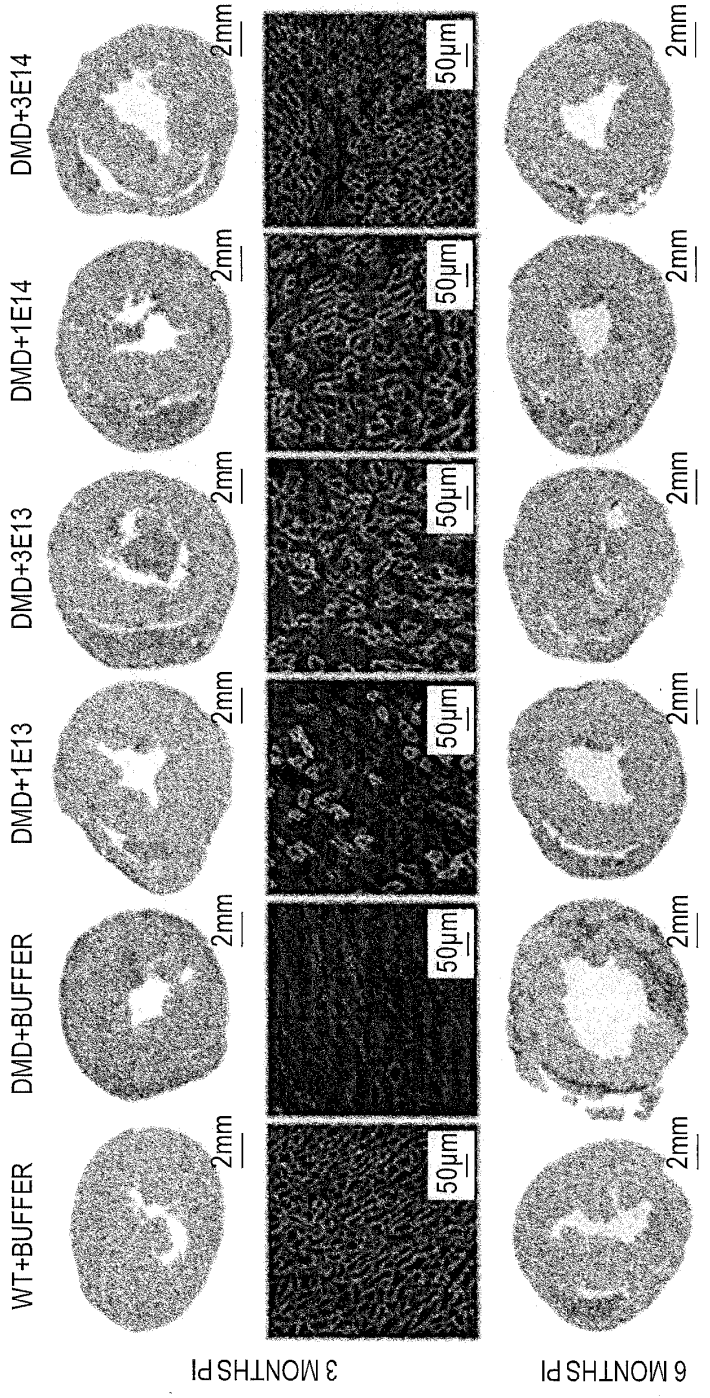

WT+BUFFER
DMD+BUFFER
DMD+1E13
DMD+3E13
DMD+1E14
DMD+3E14
2mm
50µm
3 MONTHS PI
6 MONTHS PI

FIG. 41A

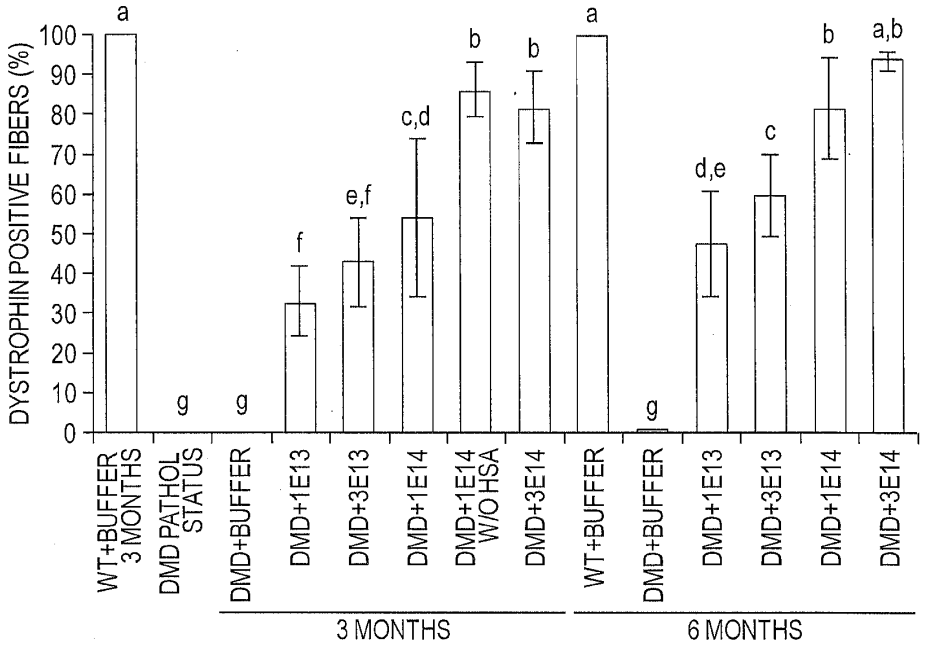


FIG. 41B

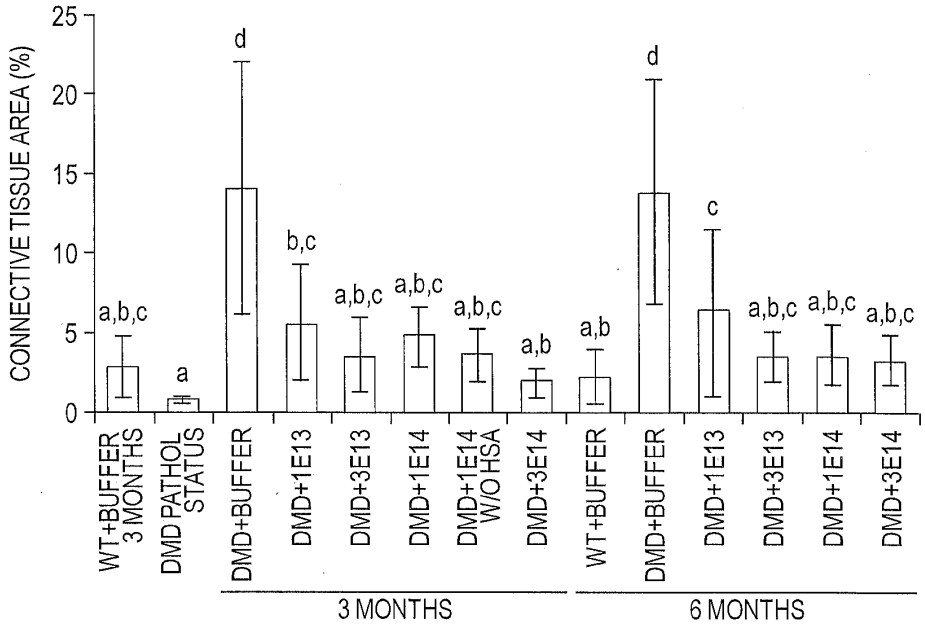


FIG. 41C

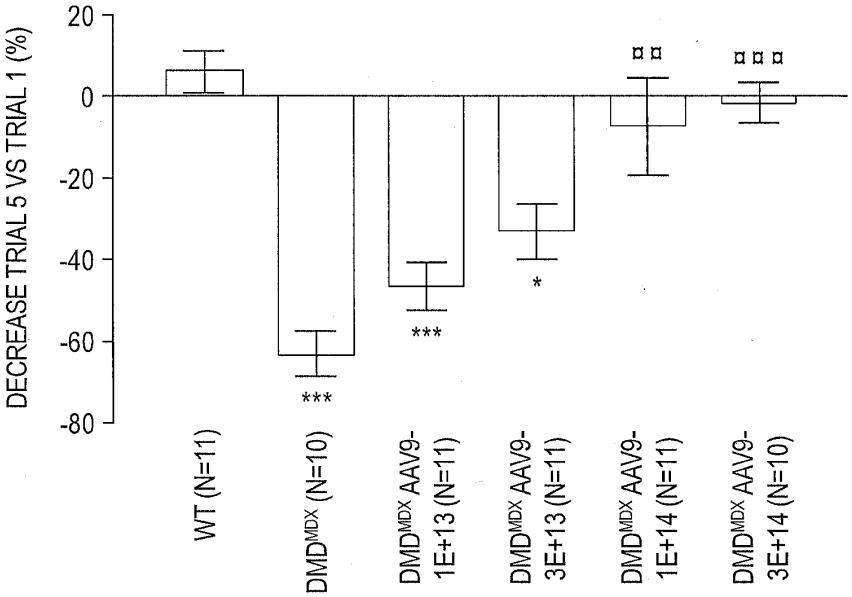


FIG. 42A

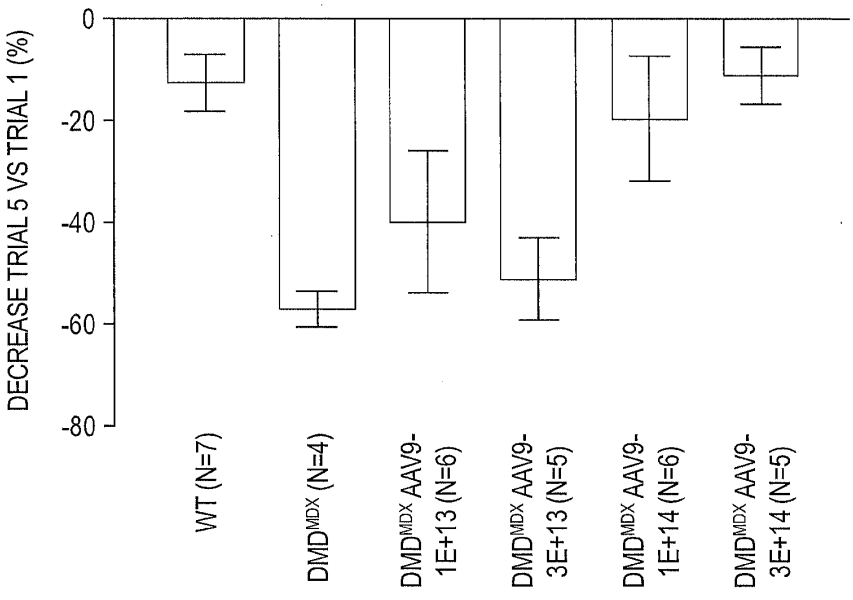


FIG. 42B

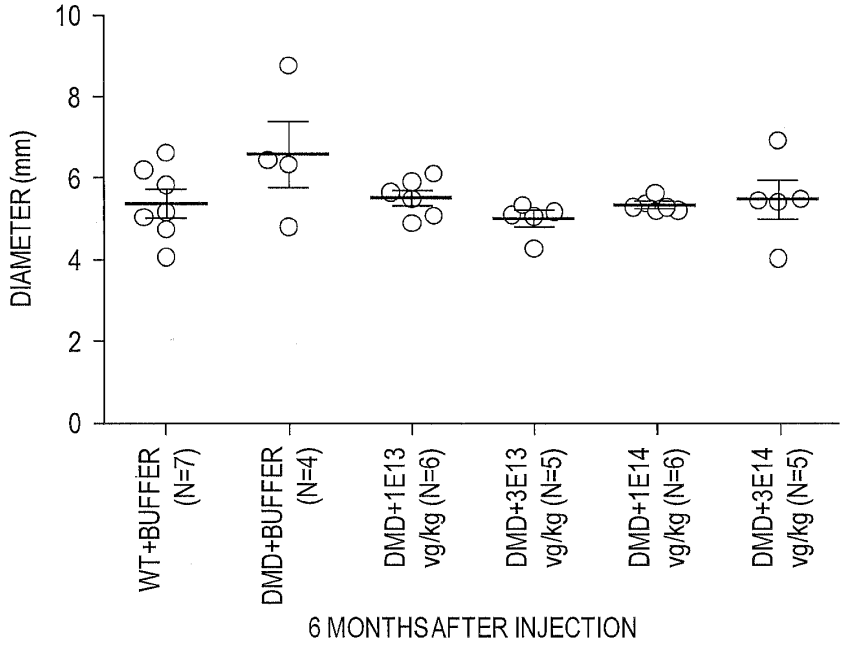

10
8
6
4
2
0
DIAMETER (mm)
WT+BUFFER (N=7)
DMD+BUFFER (N=4)
DMD+1E13 vg/kg (N=6)
DMD+3E13 vg/kg (N=5)
DMD+1E14 vg/kg (N=6)
DMD+3E14 vg/kg (N=5)
6 MONTHS AFTER INJECTION

FIG. 43

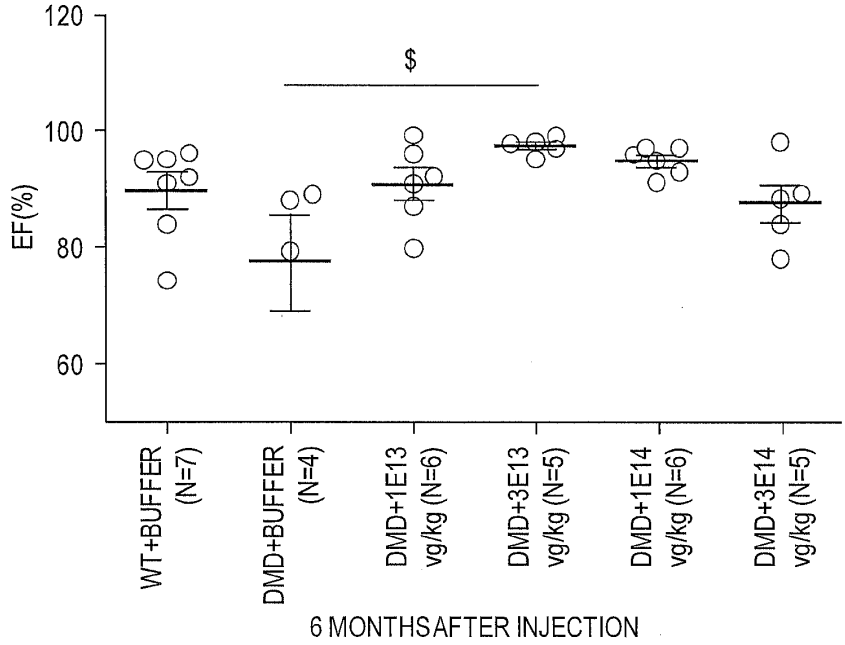

120
100
80
60
EF(%)
$
WT+BUFFER (N=7)
DMD+BUFFER (N=4)
DMD+1E13 vg/kg (N=6)
DMD+3E13 vg/kg (N=5)
DMD+1E14 vg/kg (N=6)
DMD+3E14 vg/kg (N=5)
6 MONTHS AFTER INJECTION

FIG. 44

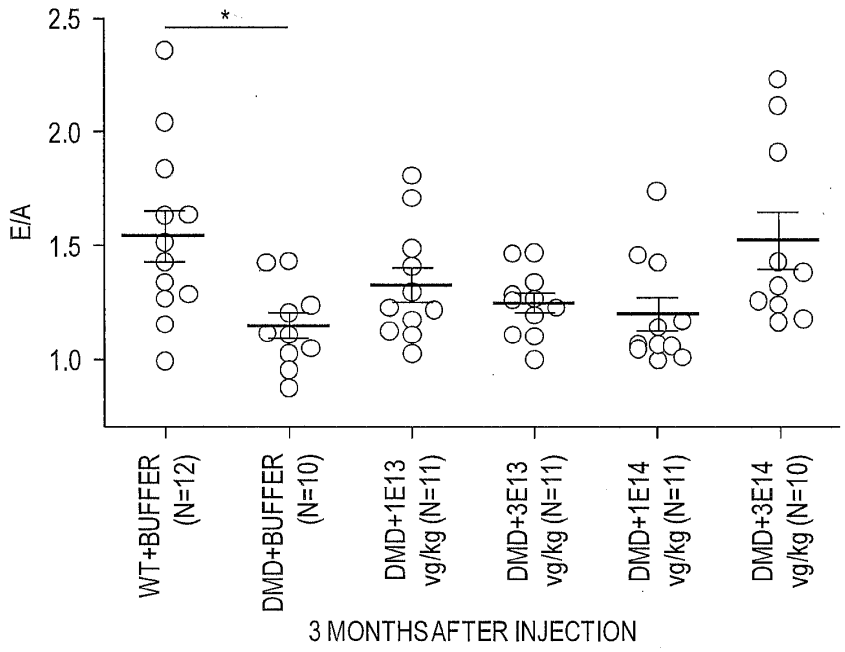


FIG. 45A

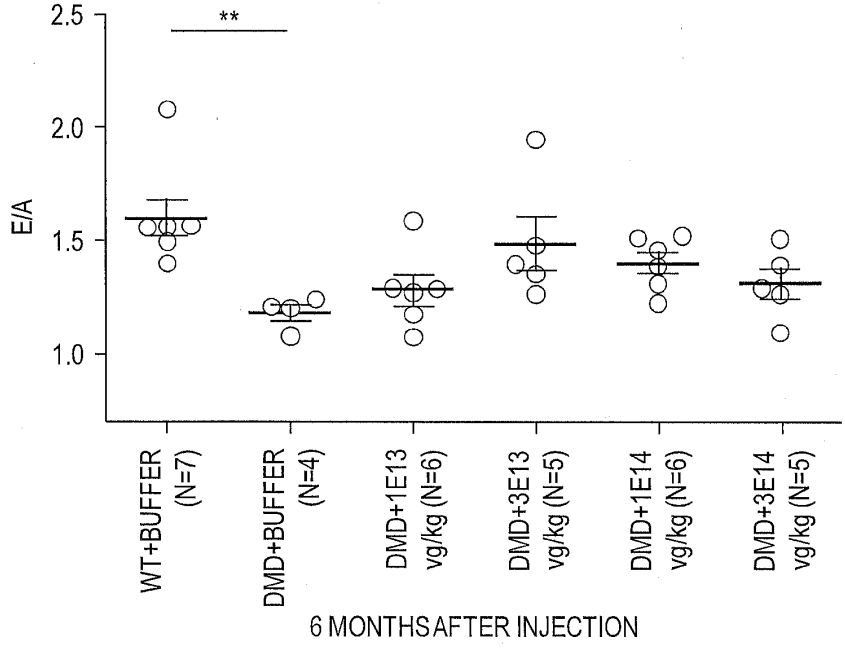


FIG. 45B

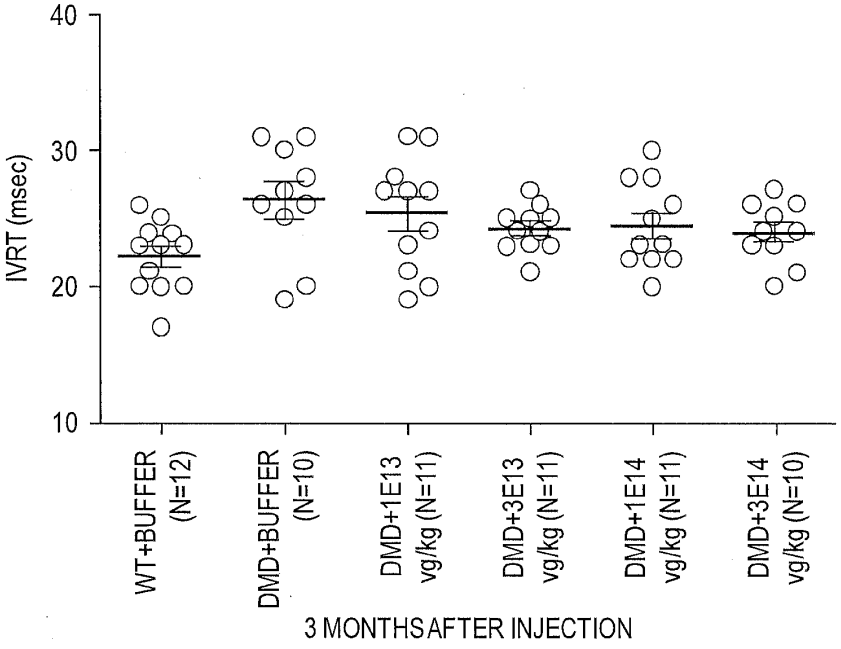


FIG. 46A

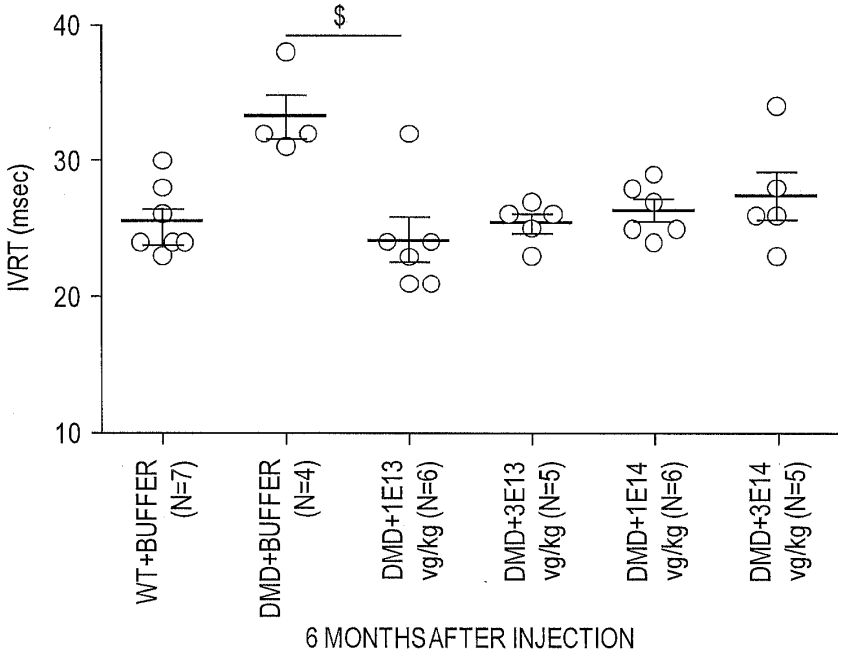


FIG. 46B

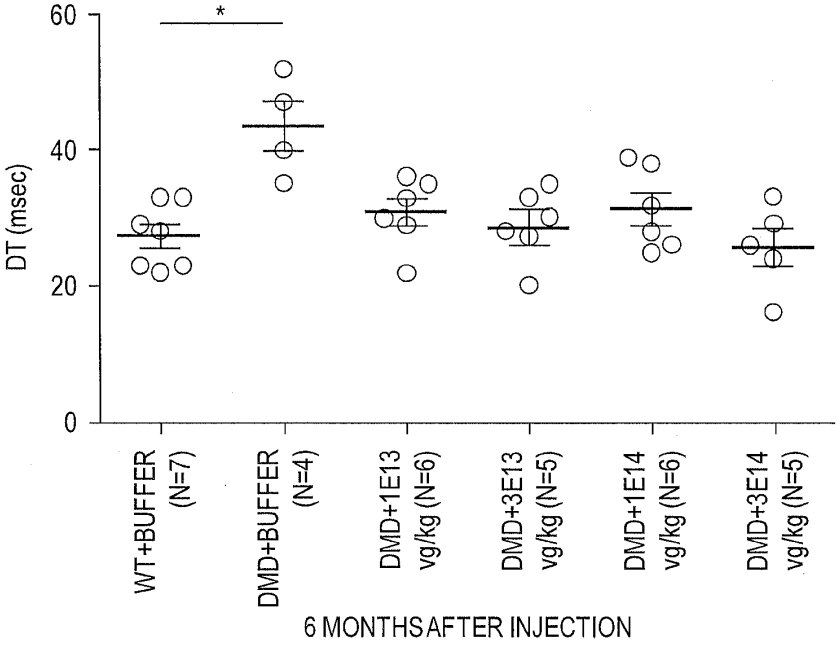


FIG. 47

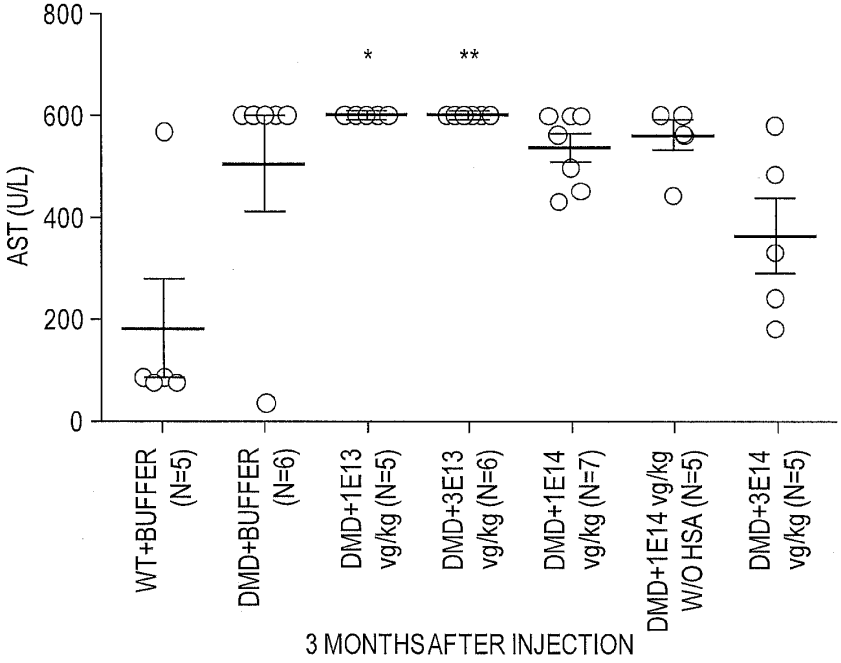


FIG. 48A

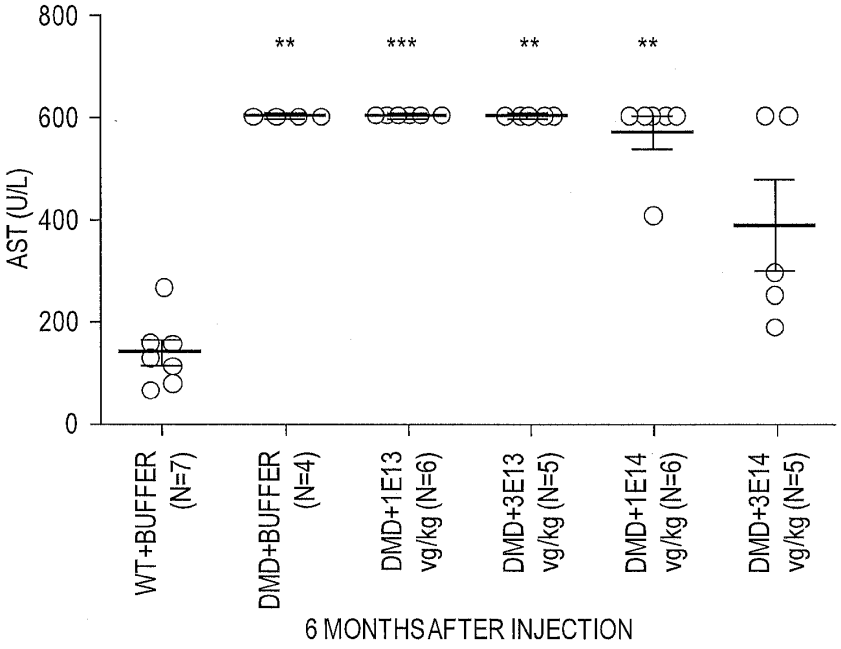


FIG. 48B

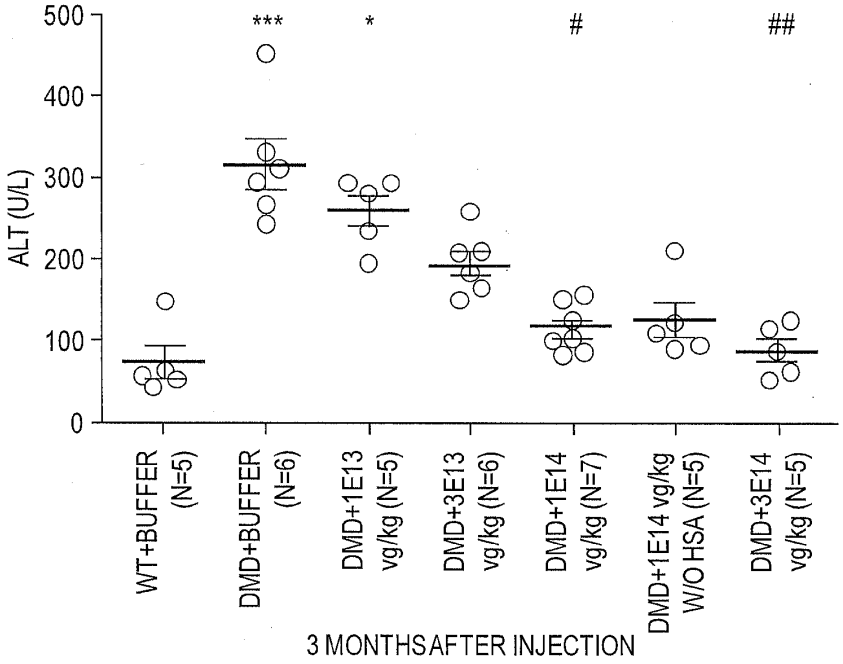


FIG. 49A

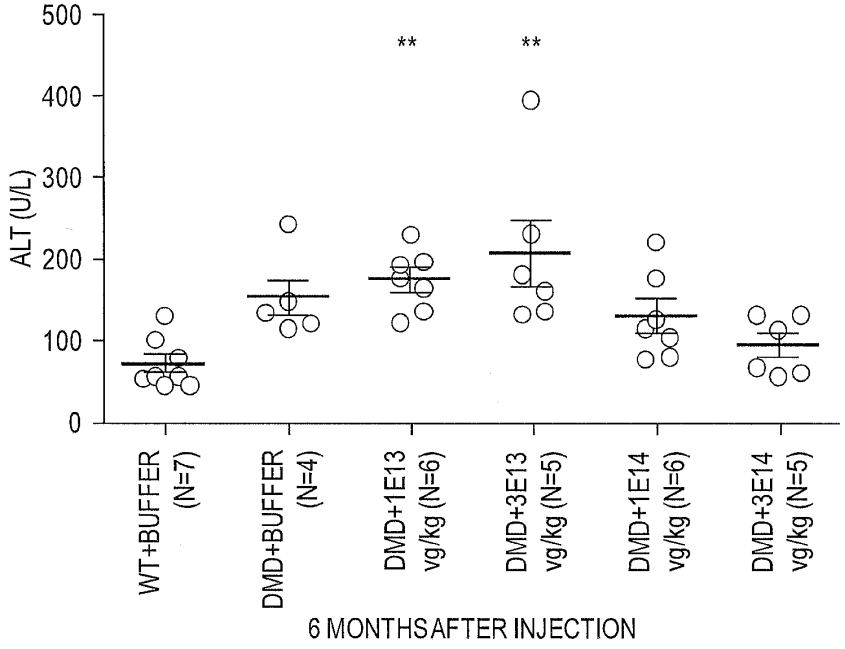


FIG. 49B

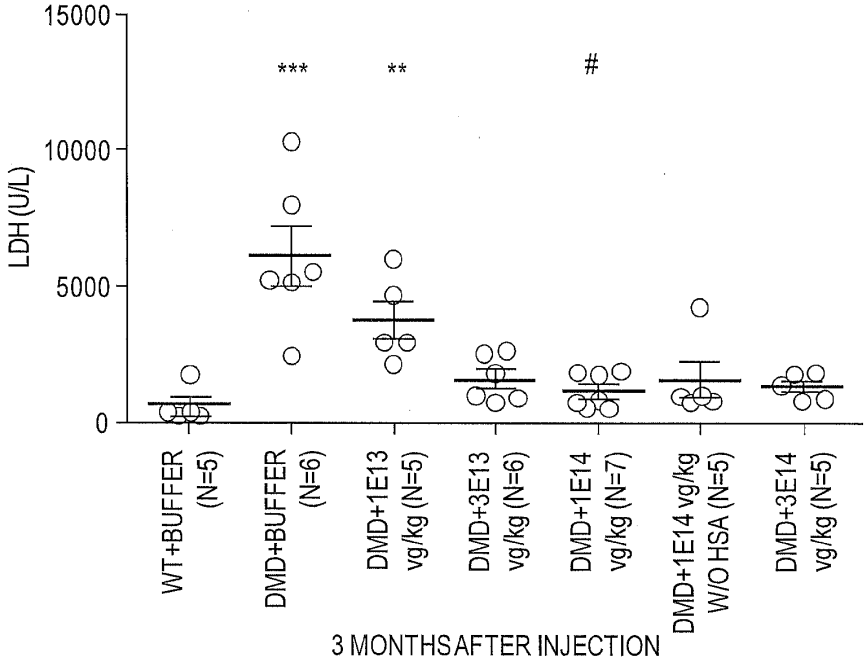


FIG. 50A

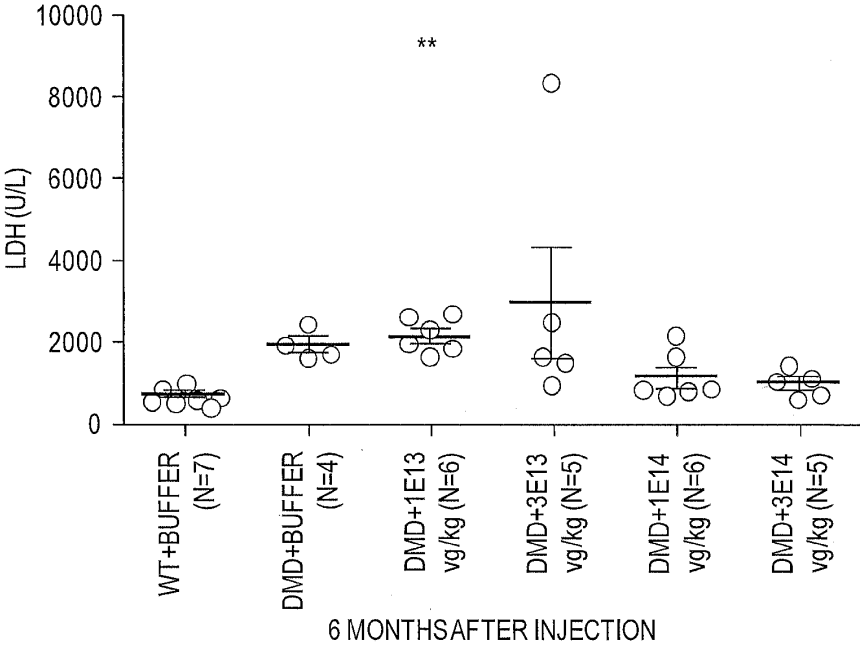


FIG. 50B

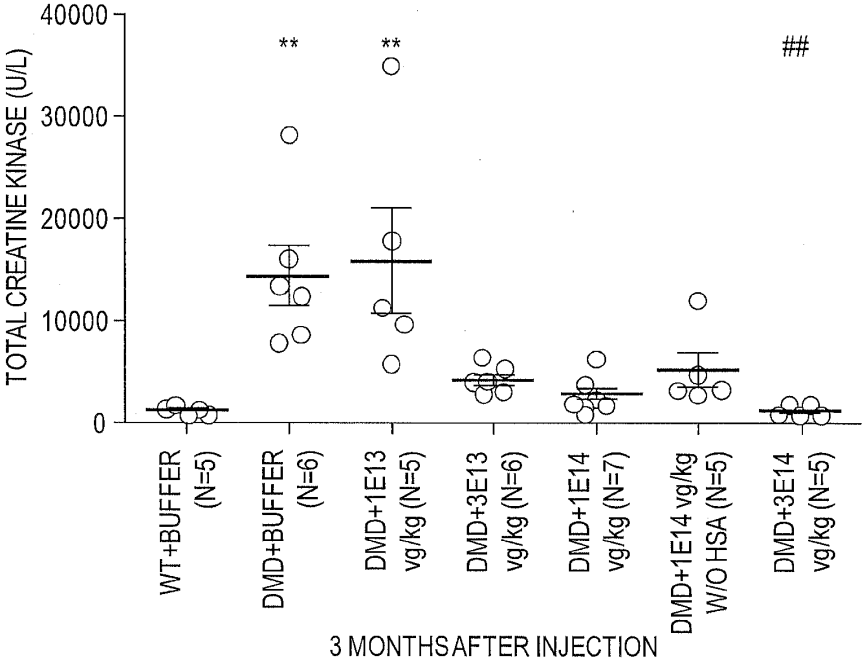


FIG. 51A

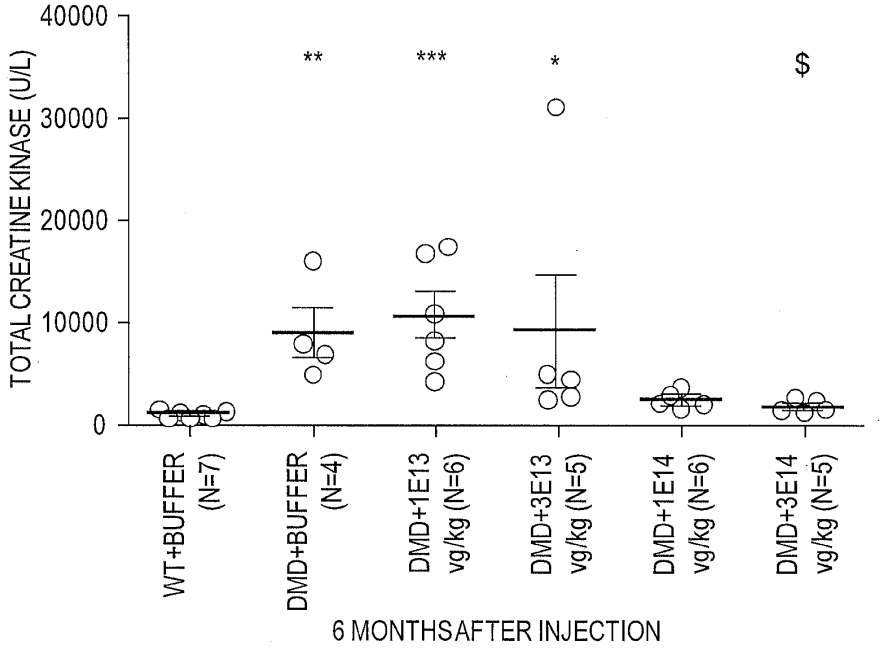


FIG. 51B

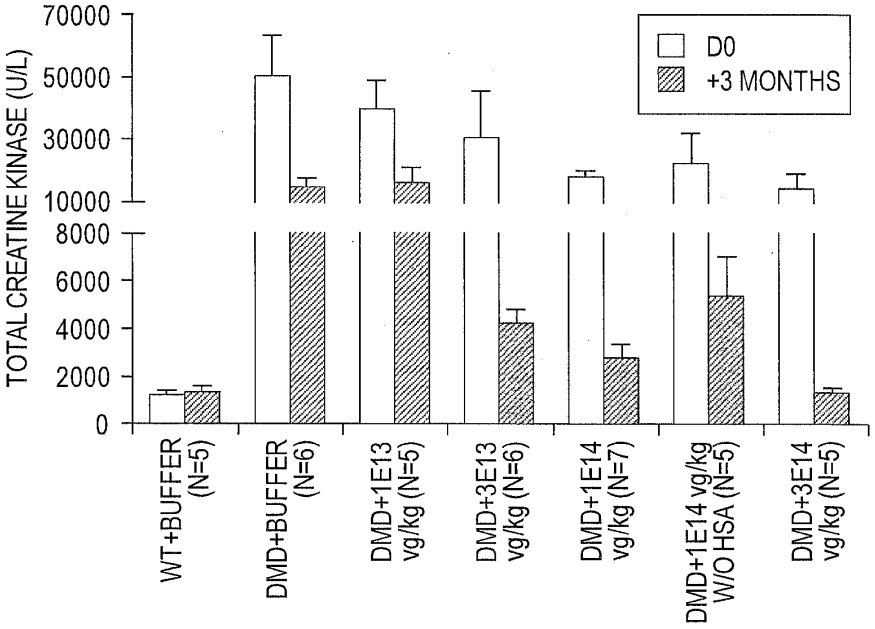


FIG. 52A

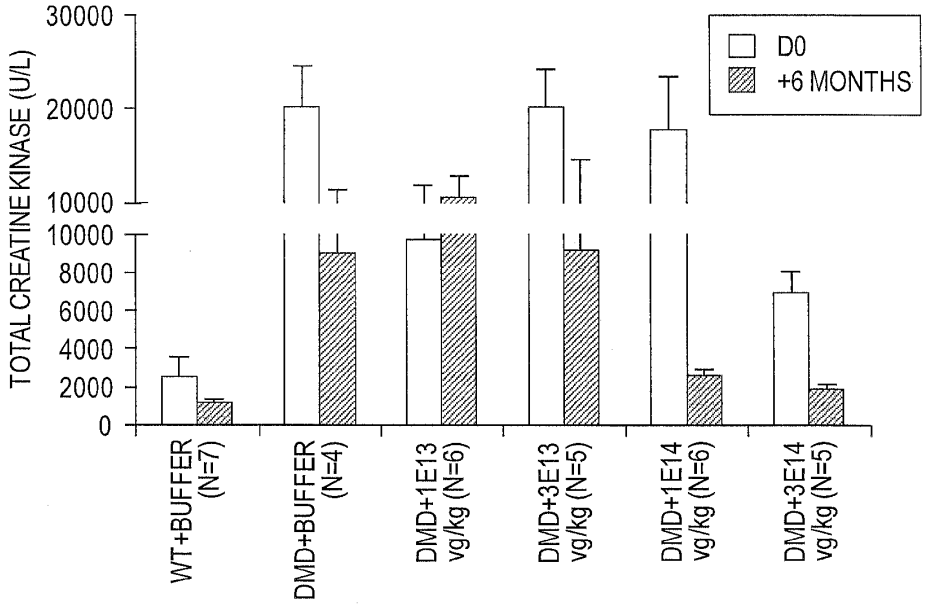


FIG. 52B

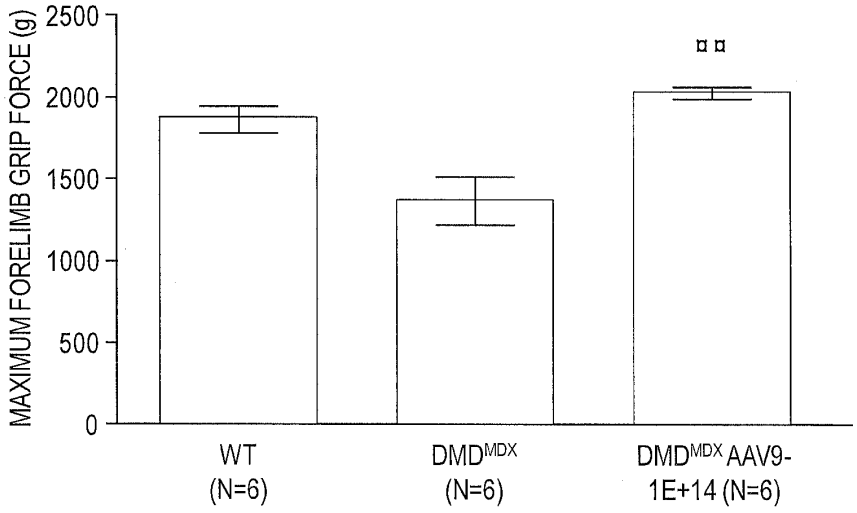


FIG. 53A

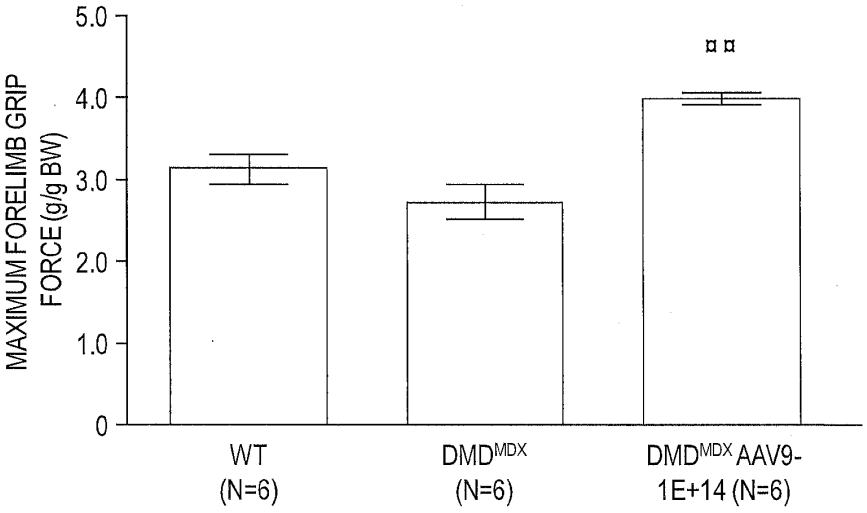


FIG. 53B

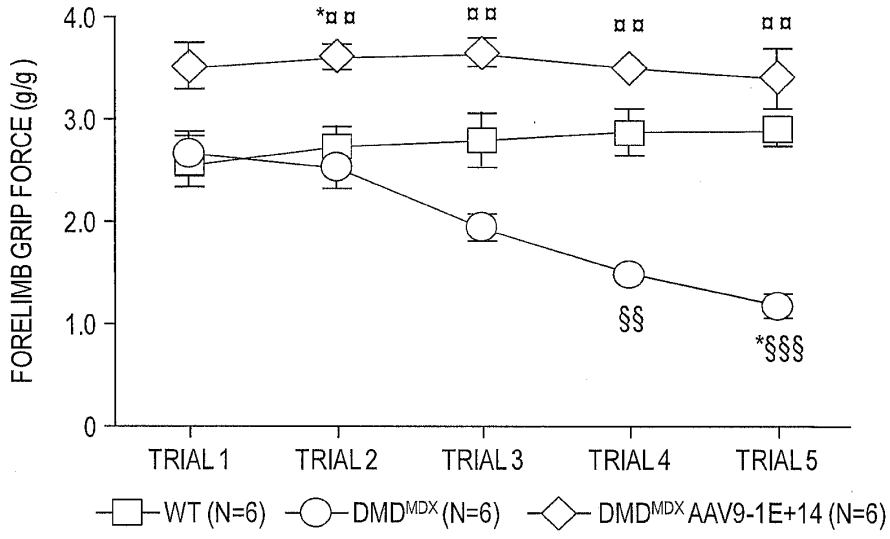


FIG. 53C

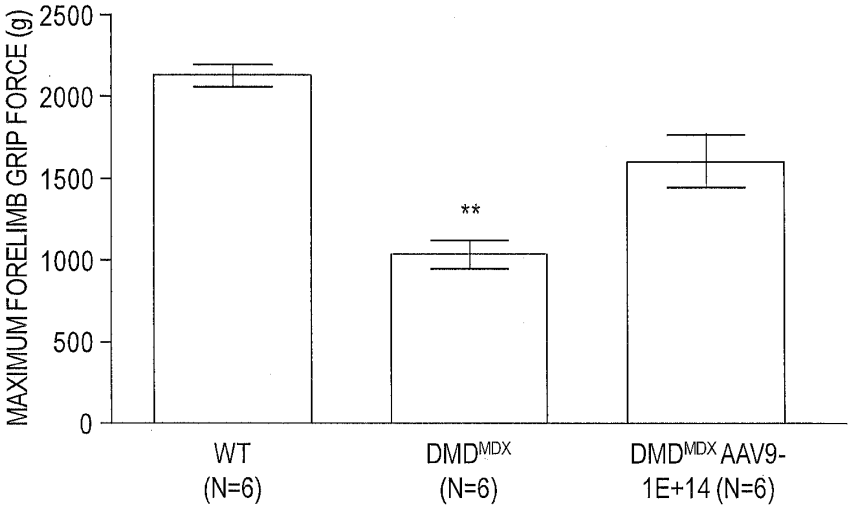


FIG. 54A

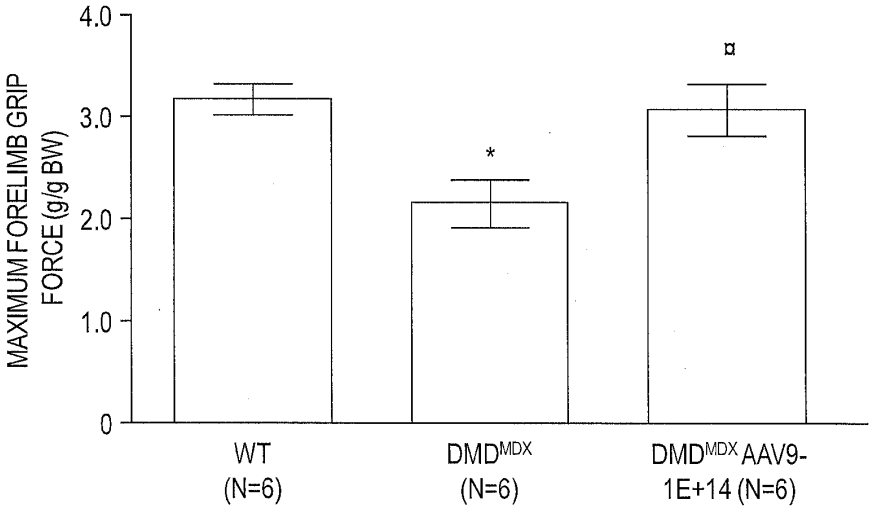


FIG. 54B

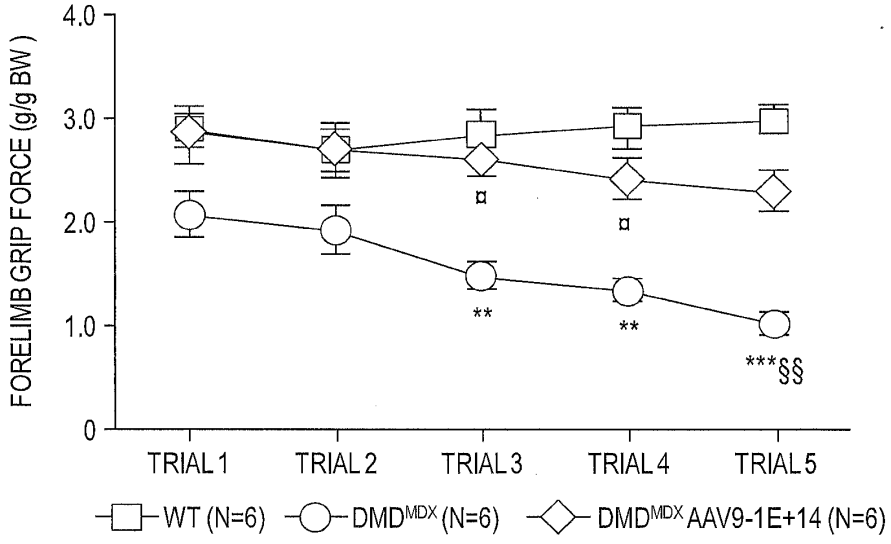

FORELIMB GRIP FORCE (g/g BW)
4.0
3.0
2.0
1.0
0
TRIAL 1
TRIAL 2
TRIAL 3
TRIAL 4
TRIAL 5
¤
¤
**
**
***§§
WT (N=6)
DMDMDX (N=6)
DMDMDX AAV9-1E+14 (N=6)

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)	CTGTACCAGGAGCCCAGAGAGCTGCCCCCCCGAGGAGAGAGCCCAGAACGTGACCAGGCTG	

		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
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FIG. 56H

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                    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