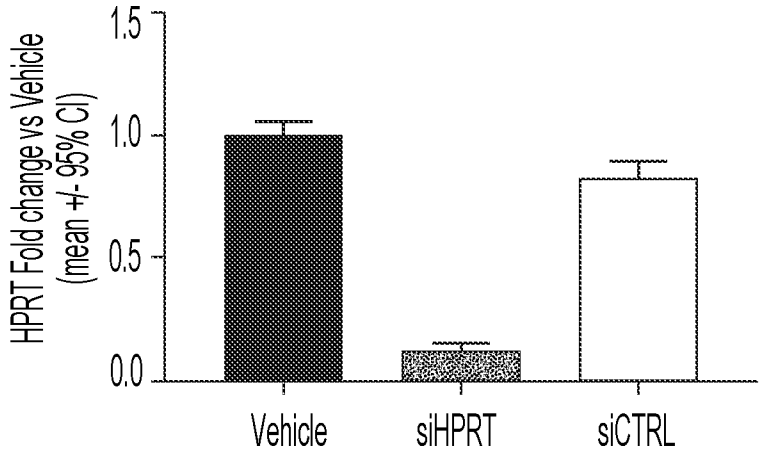
HPRT Fold change vs Vehicle
(mean +/- 95% CI)
1.5
1.0
0.5
0.0
Vehicle
siHPRT
siCTRL

FIG. 1

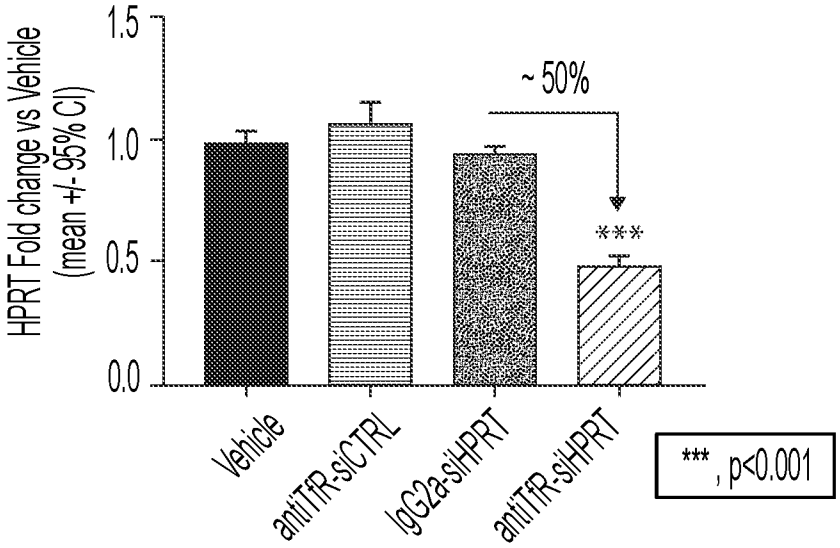
HPRT Fold change vs Vehicle
(mean +/- 95% CI)
1.5
1.0
0.5
0.0
~ 50%
***
Vehicle
antiTfR-siCTRL
IgG2a-siHPRT
antiTfR-siHPRT
***, p<0.001

FIG. 2

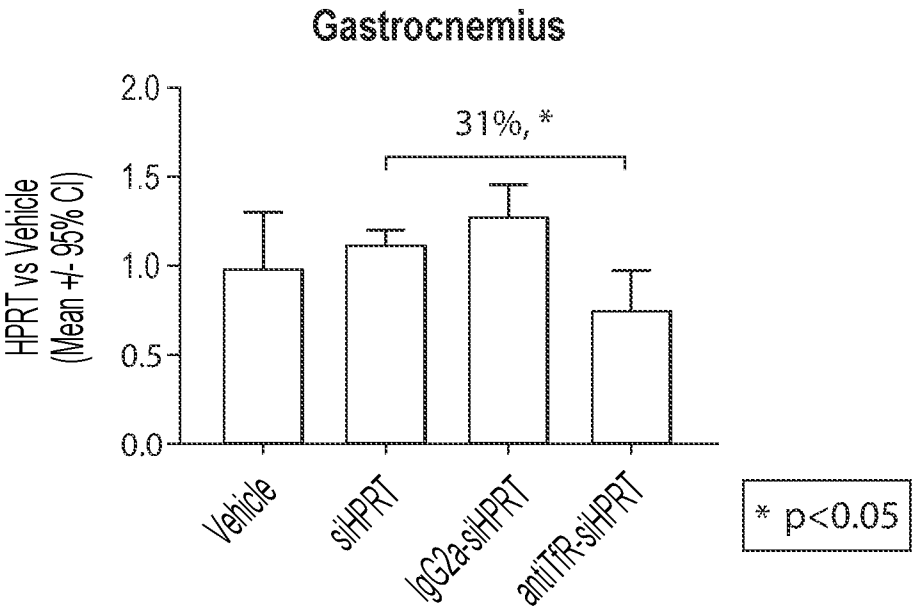
Gastrocnemius
HPRT vs Vehicle
(Mean +/- 95% CI)
2.0
1.5
1.0
0.5
0.0
31%, *
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT
* p<0.05

FIG. 3A

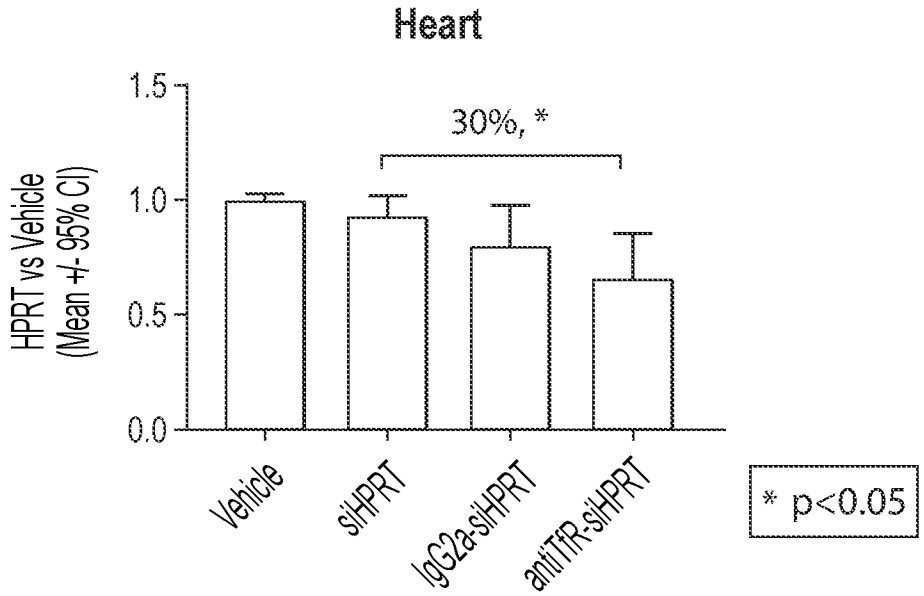
Heart
HPRT vs Vehicle
(Mean +/- 95% CI)
1.5
1.0
0.5
0.0
30%, *
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT
* p<0.05

FIG. 3B

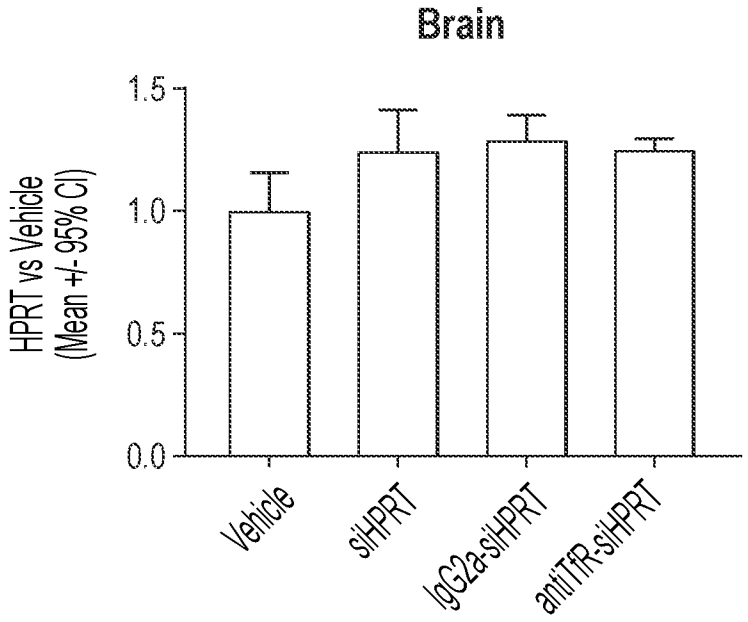
Brain
HPRT vs Vehicle
(Mean +/- 95% CI)
1.5
1.0
0.5
0.0
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT

FIG. 4A

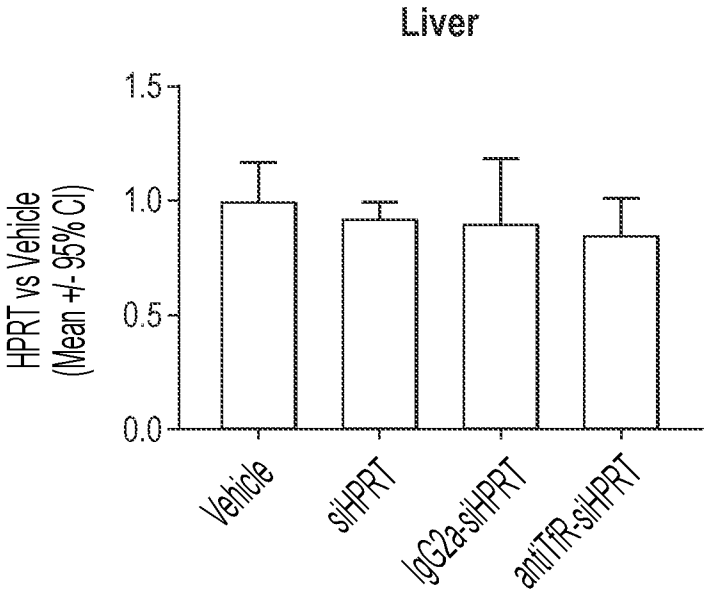
Liver
HPRT vs Vehicle
(Mean +/- 95% CI)
1.5
1.0
0.5
0.0
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT

FIG. 4B

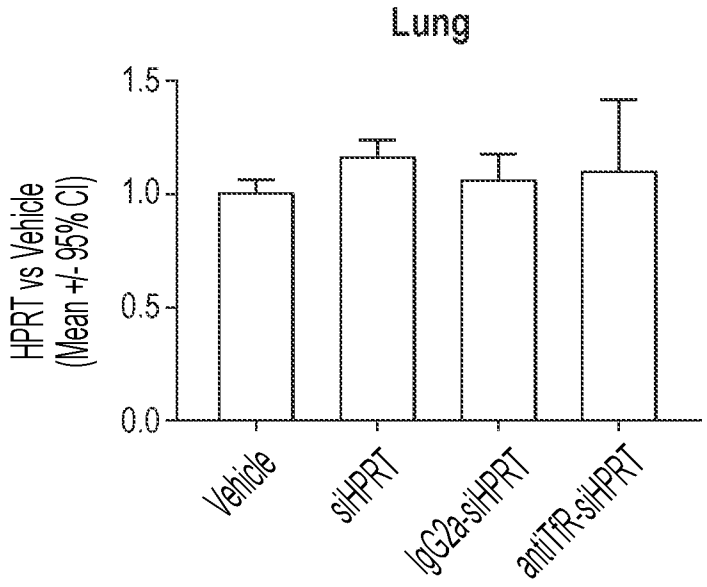
Lung
HPRT vs Vehicle
(Mean +/- 95% CI)
1.5
1.0
0.5
0.0
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT

FIG. 4C

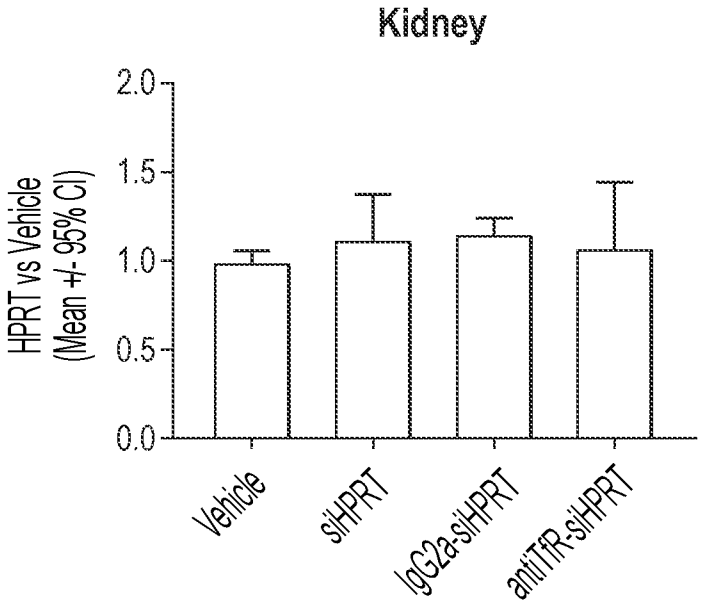
Kidney
HPRT vs Vehicle
(Mean +/- 95% CI)
2.0
1.5
1.0
0.5
0.0
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT

FIG. 4D

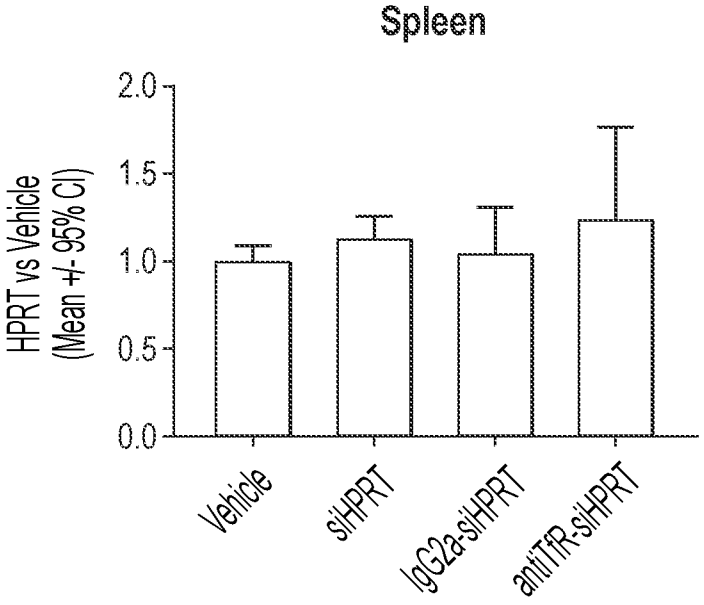
Spleen
HPRT vs Vehicle
(Mean +/- 95% CI)
2.0
1.5
1.0
0.5
0.0
Vehicle
siHPRT
IgG2a-siHPRT
antiTfR-siHPRT

FIG. 4E

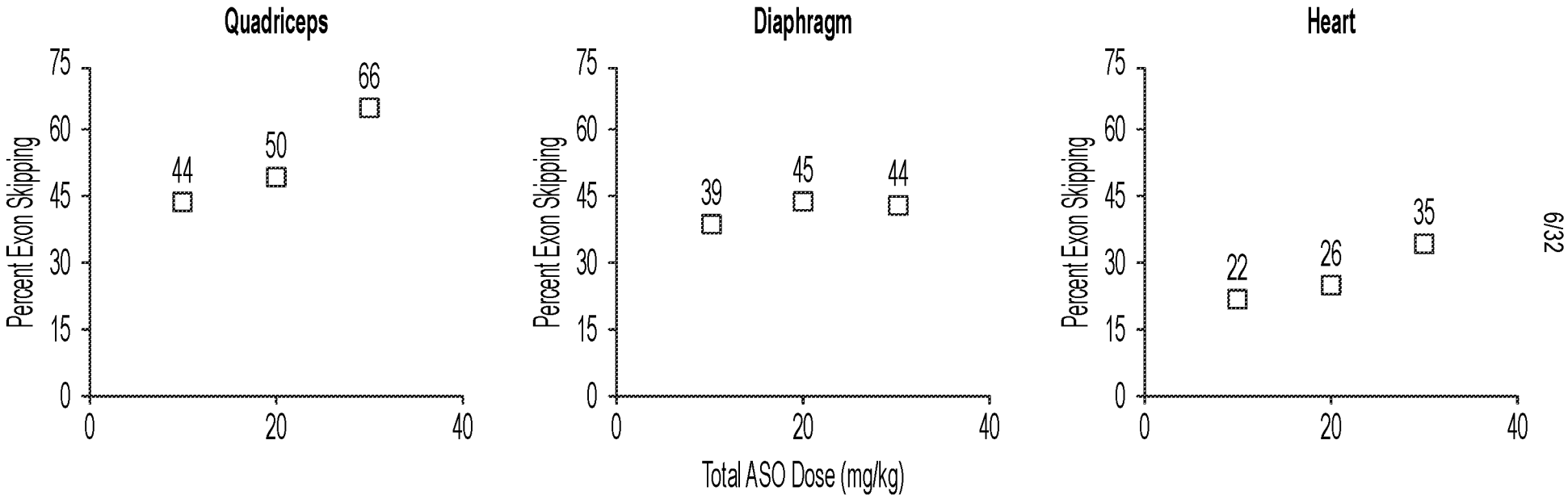
Quadriceps
Diaphragm
Heart
Percent Exon Skipping
Total ASO Dose (mg/kg)
0
15
30
45
60
75
0
20
40
44
50
66
39
45
44
22
26
35
6/32

FIG. 5

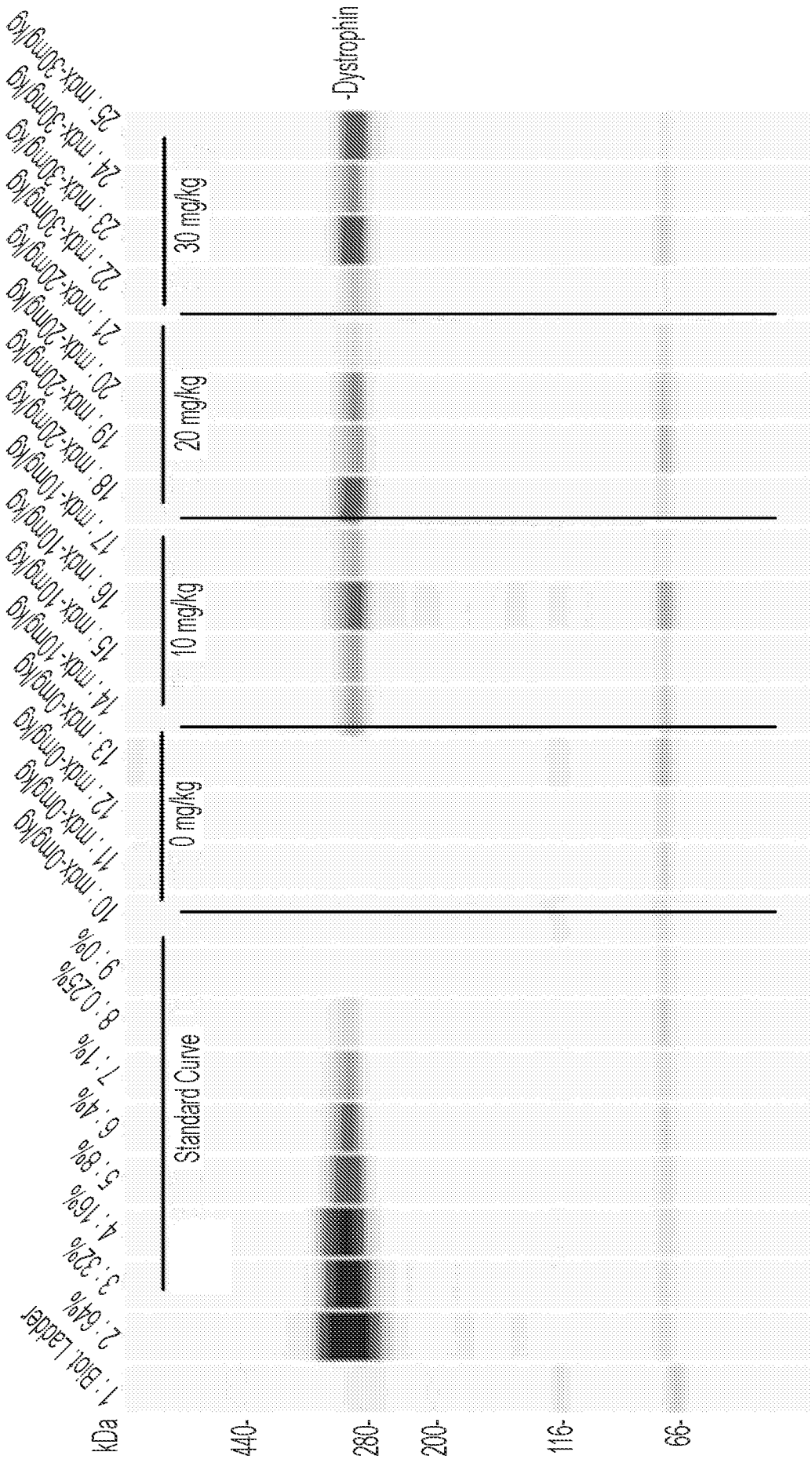
kDa
440-
280-
200-
116-
66-
-Dystrophin
0 mg/kg
10 mg/kg
20 mg/kg
30 mg/kg
Standard Curve
1. Biot Ladder
2. 64%
3. 32%
4. 16%
5. 8%
6. 4%
7. 1%
8. 0.25%
9. 0%
10. mdx-0mg/kg
11. mdx-0mg/kg
12. mdx-0mg/kg
13. mdx-0mg/kg
14. mdx-0mg/kg
15. mdx-10mg/kg
16. mdx-10mg/kg
17. mdx-10mg/kg
18. mdx-10mg/kg
19. mdx-20mg/kg
20. mdx-20mg/kg
21. mdx-20mg/kg
22. mdx-20mg/kg
23. mdx-30mg/kg
24. mdx-30mg/kg
25. mdx-30mg/kg

FIG. 6A

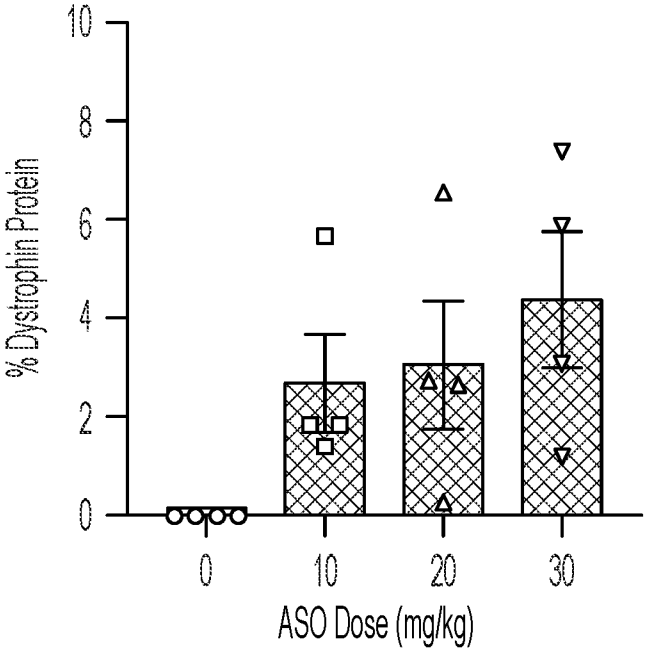

FIG. 6B

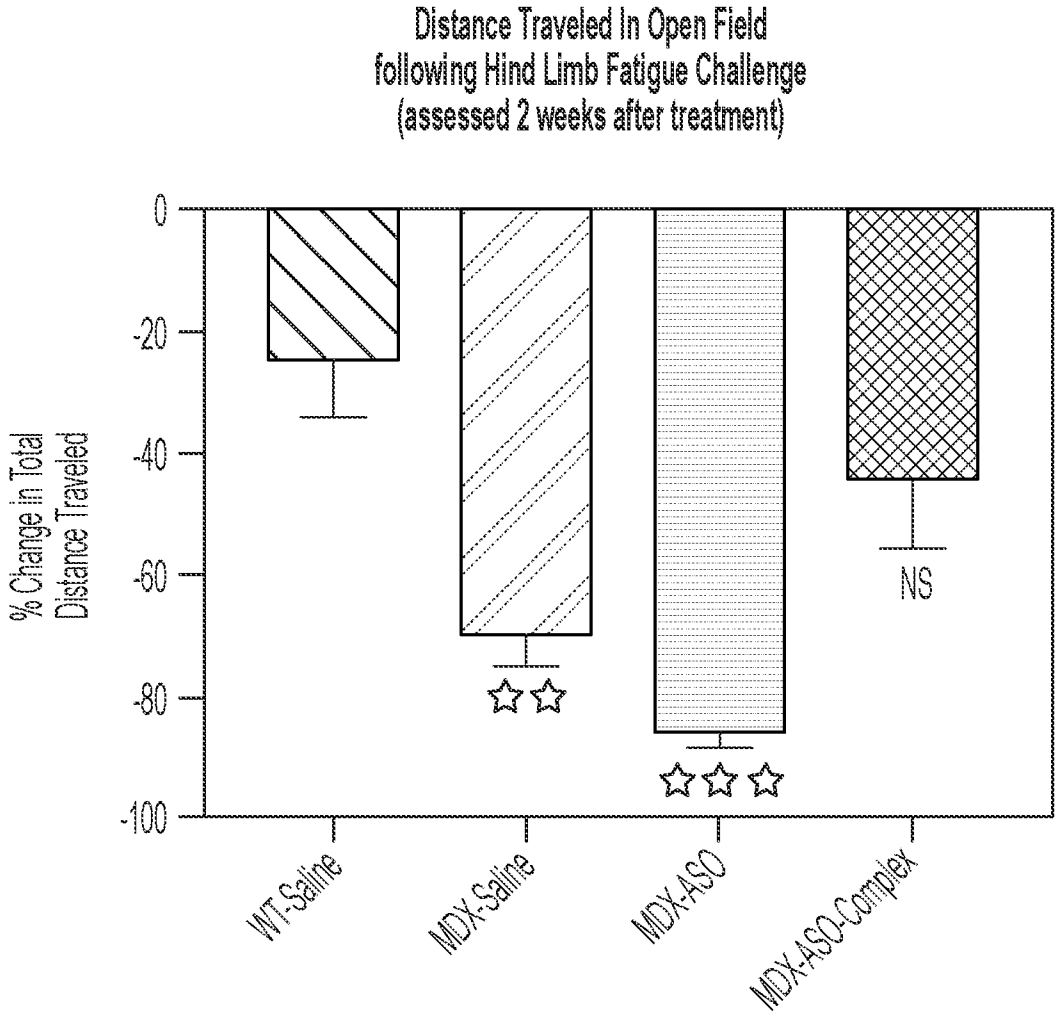
Distance Traveled In Open Field
following Hind Limb Fatigue Challenge
(assessed 2 weeks after treatment)
% Change in Total Distance Traveled
0
-20
-40
-60
-80
-100
NS
WT-Saline
MDX-Saline
MDX-ASO
MDX-ASO-Complex

FIG. 7A

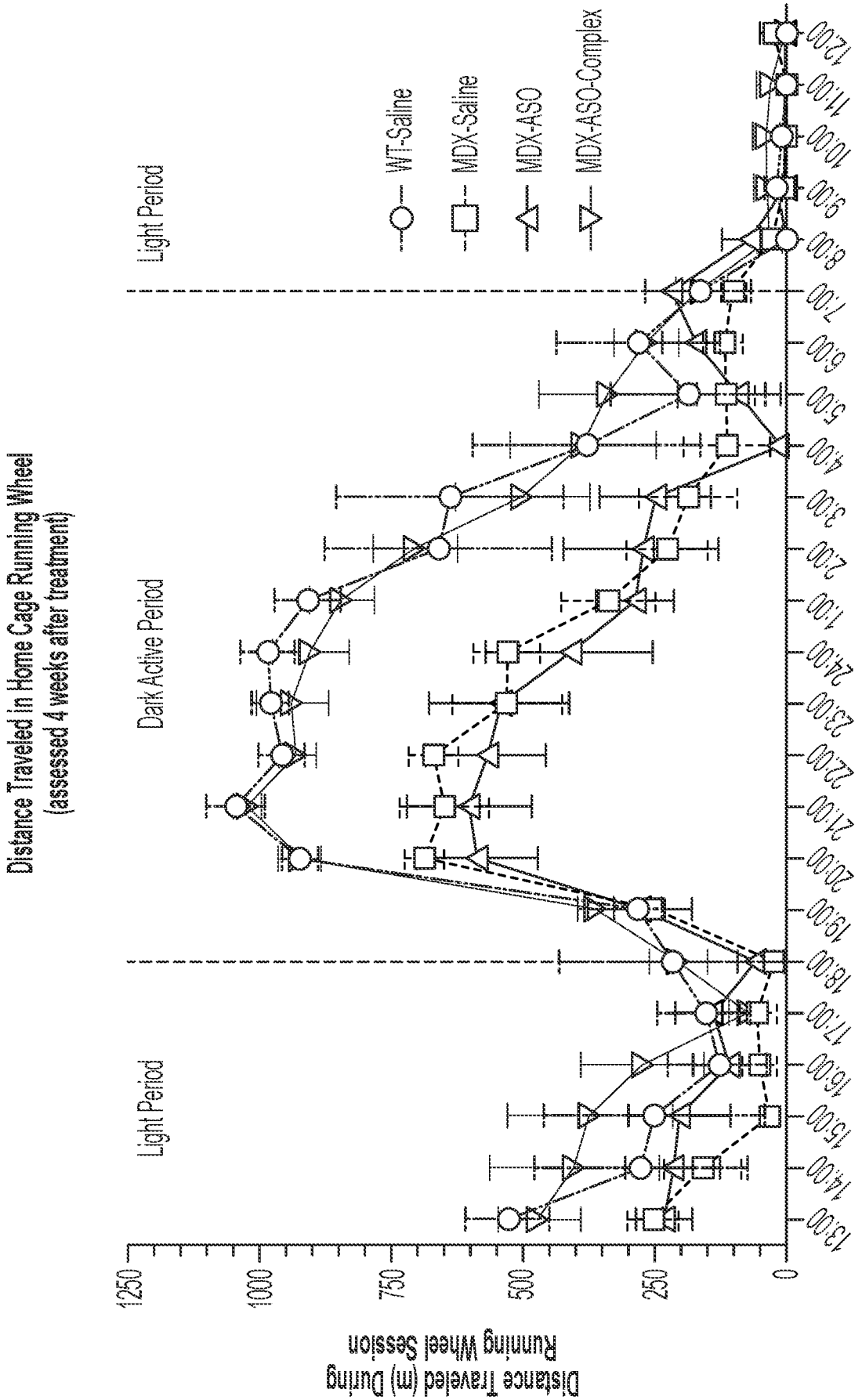
Distance Traveled in Home Cage Running Wheel
(assessed 4 weeks after treatment)
Distance Traveled (m) During Running Wheel Session
1250
1000
750
500
250
0
Light Period
Dark Active Period
Light Period
WT-Saline
MDX-Saline
MDX-ASO
MDX-ASO-Complex
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
24:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
Time of Day

FIG. 7B

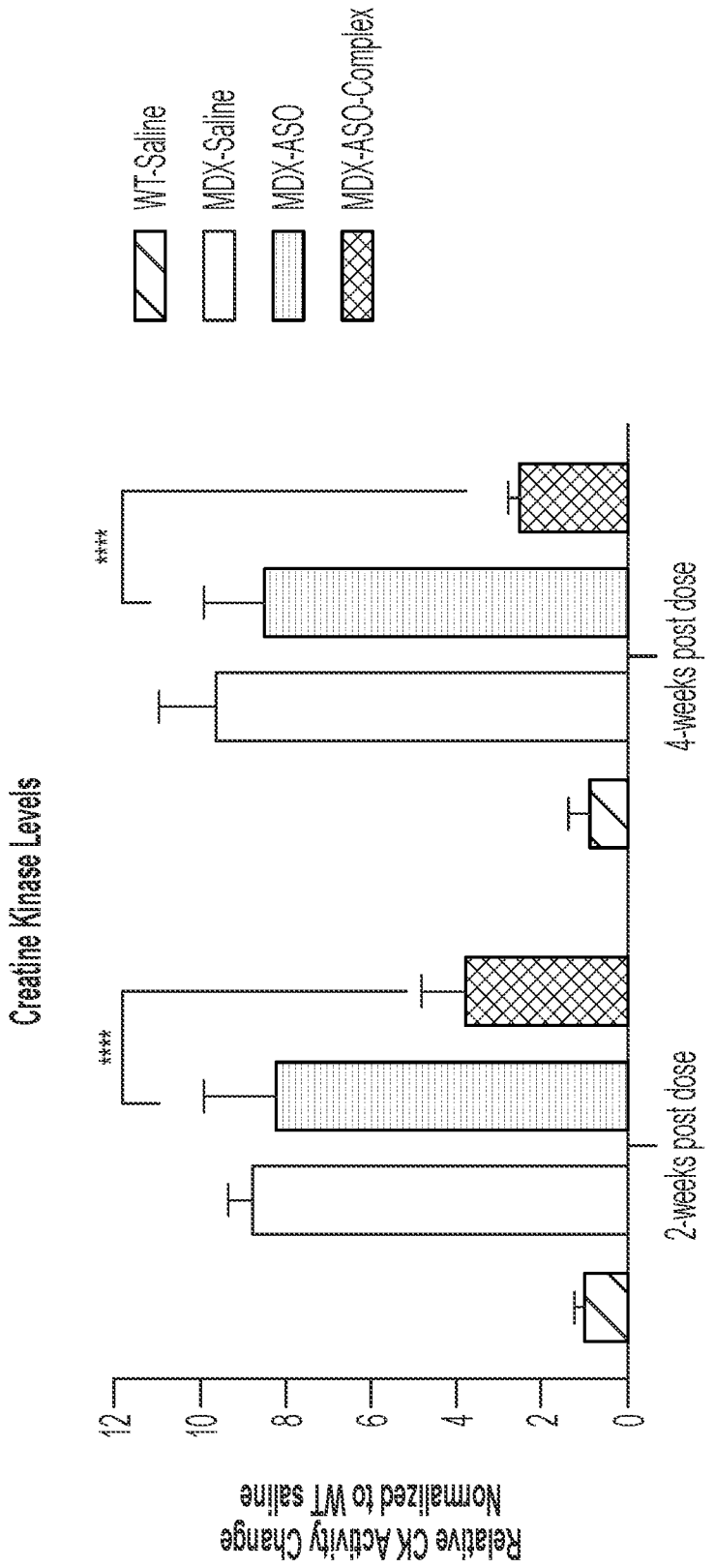
Creatine Kinase Levels
Relative CK Activity Change
Normalized to WT saline
12
10
8
6
4
2
0
2-weeks post dose
4-weeks post dose
****
****
WT-Saline
MDX-Saline
MDX-ASO
MDX-ASO-Complex

FIG. 7C

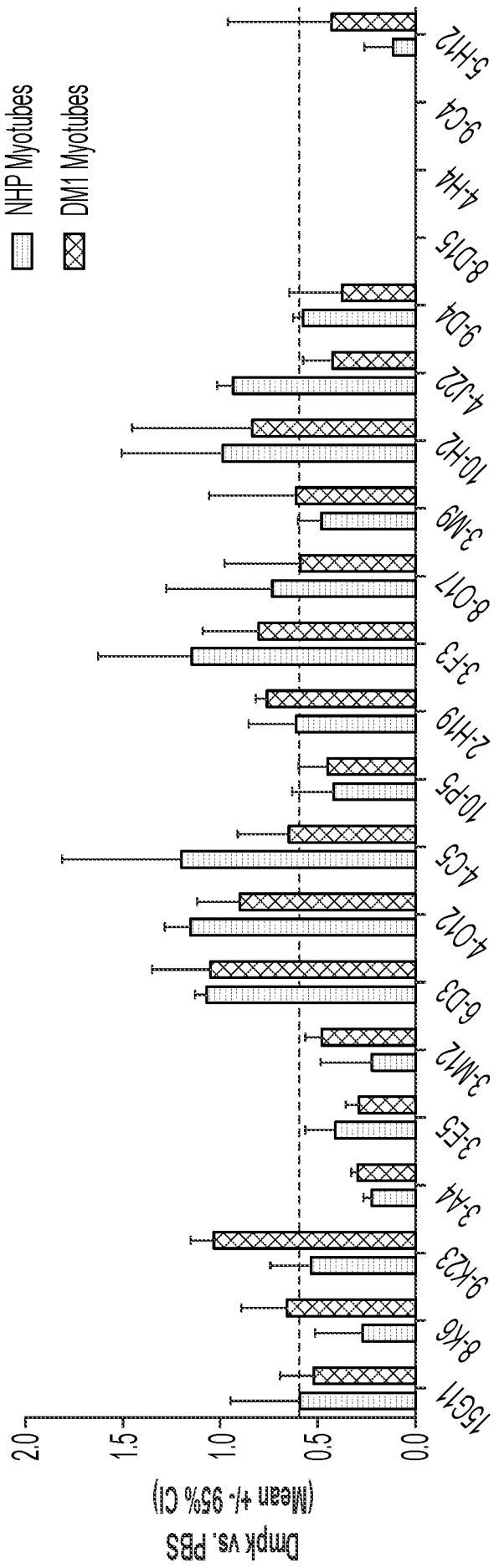
NHP Myotubes
DM1 Myotubes
Dmpk vs. PBS
(Mean +/- 95% CI)
2.0
1.5
1.0
0.5
0.0
15C11
8-K6
9-K23
3-A4
3-E5
3-M12
6-D3
4-O12
4-C5
10-P5
2-H19
3-F3
8-O17
3-M9
10-H2
4-J22
9-D4
8-D15
4-H4
9-C4
5-H12

FIG. 8

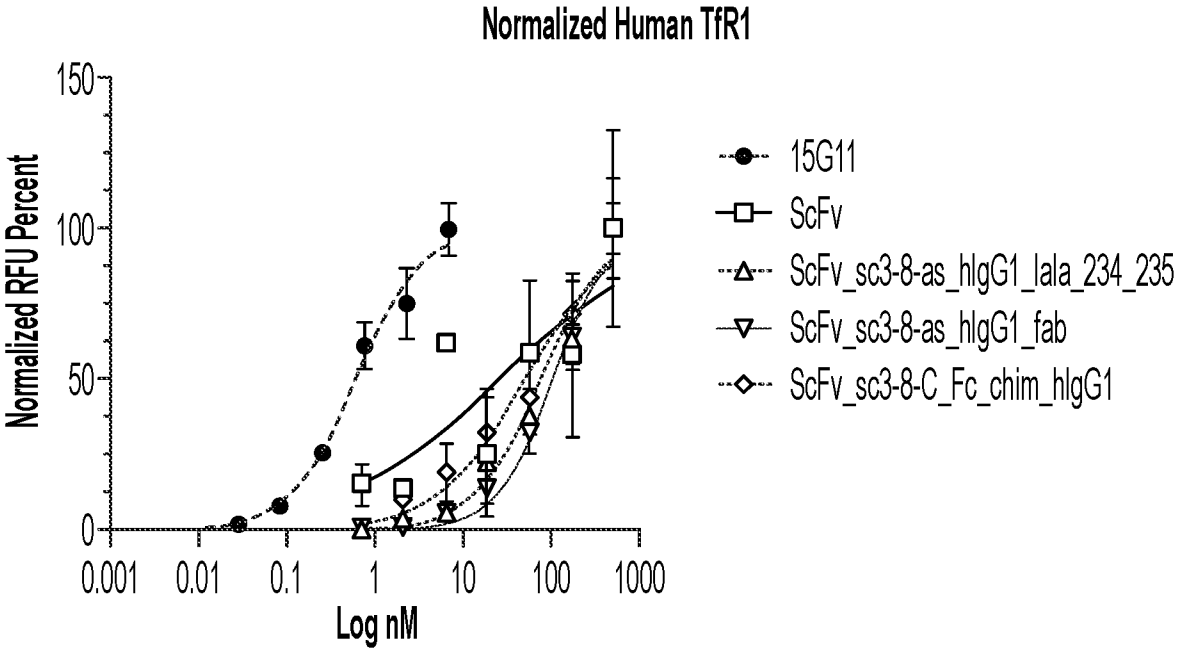
Normalized Human TfR1
Normalized RFU Percent
150
100
50
0
0.001
0.01
0.1
1
10
100
1000
Log nM
15G11
ScFv
ScFv_sc3-8-as_hIgG1_lala_234_235
ScFv_sc3-8-as_hIgG1_fab
ScFv_sc3-8-C_Fc_chim_hIgG1

FIG. 9A

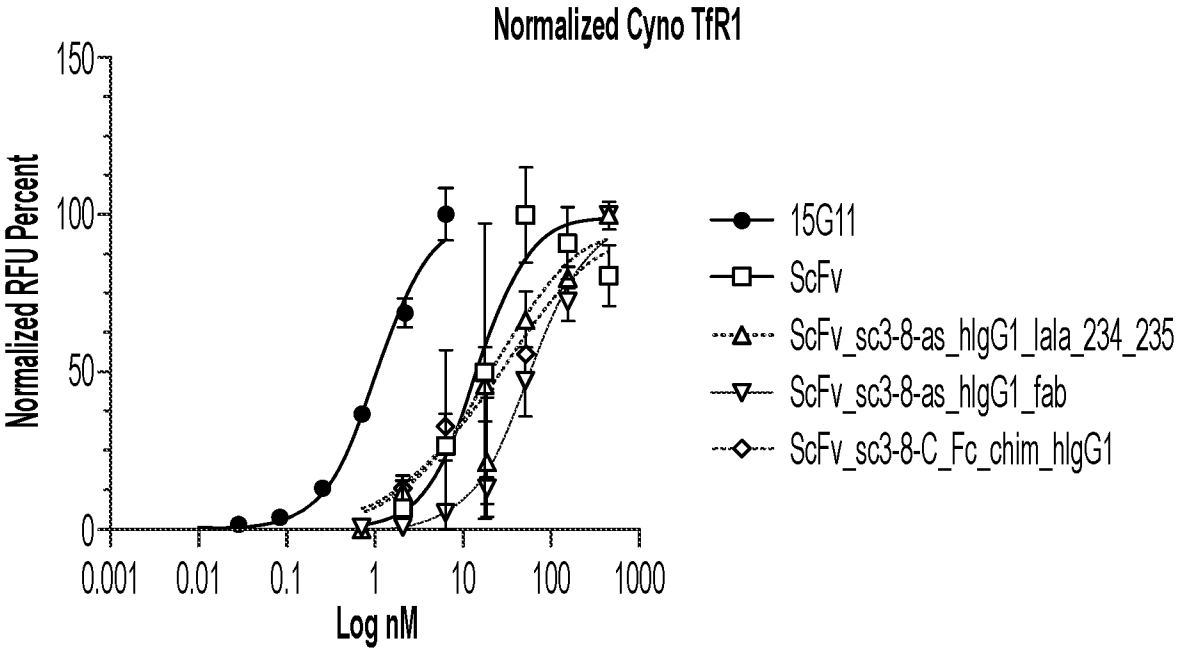
Normalized Cyno TfR1
Normalized RFU Percent
150
100
50
0
0.001
0.01
0.1
1
10
100
1000
Log nM
15G11
ScFv
ScFv_sc3-8-as_hIgG1_lala_234_235
ScFv_sc3-8-as_hIgG1_fab
ScFv_sc3-8-C_Fc_chim_hIgG1

FIG. 9B

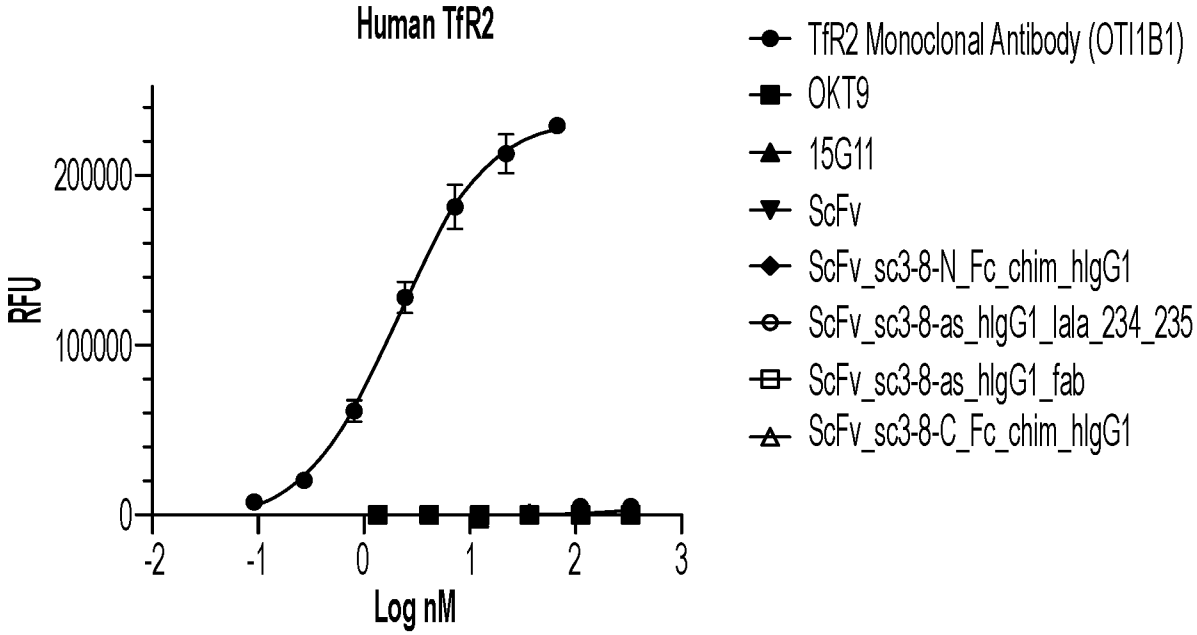
Human TfR2
RFU
200000
100000
0
-2
-1
0
1
2
3
Log nM
TfR2 Monoclonal Antibody (OTI1B1)
OKT9
15G11
ScFv
ScFv_sc3-8-N_Fc_chim_hIgG1
ScFv_sc3-8-as_hIgG1_lala_234_235
ScFv_sc3-8-as_hIgG1_fab
ScFv_sc3-8-C_Fc_chim_hIgG1

FIG. 10

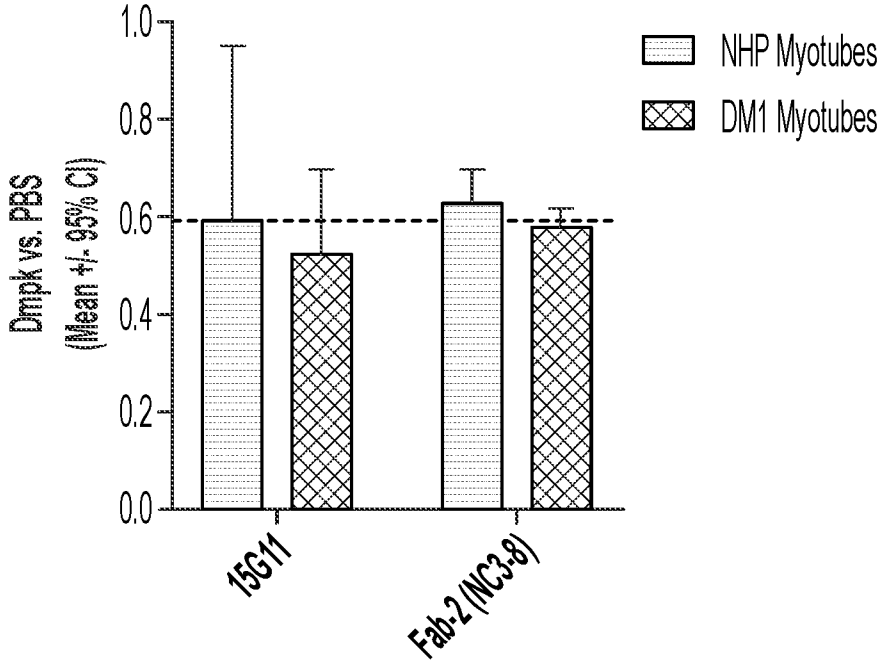
Dmpk vs. PBS
(Mean +/- 95% CI)
1.0
0.8
0.6
0.4
0.2
0.0
15G11
Fab-2(NC3-8)
NHP Myotubes
DM1 Myotubes

FIG. 11

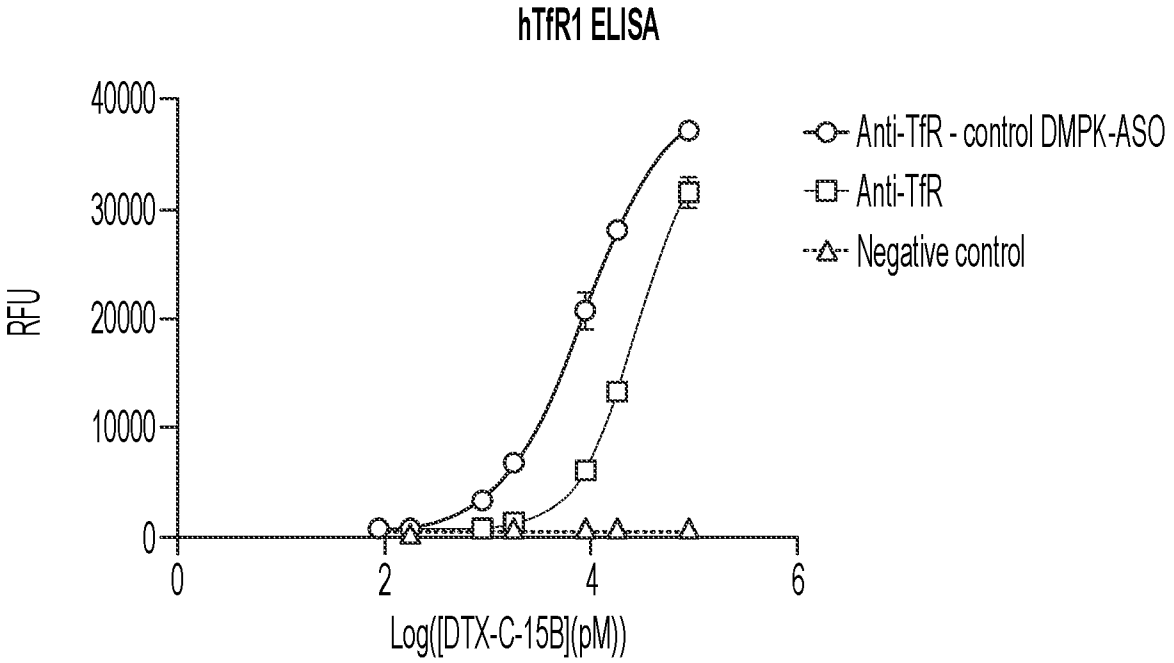

FIG. 12A

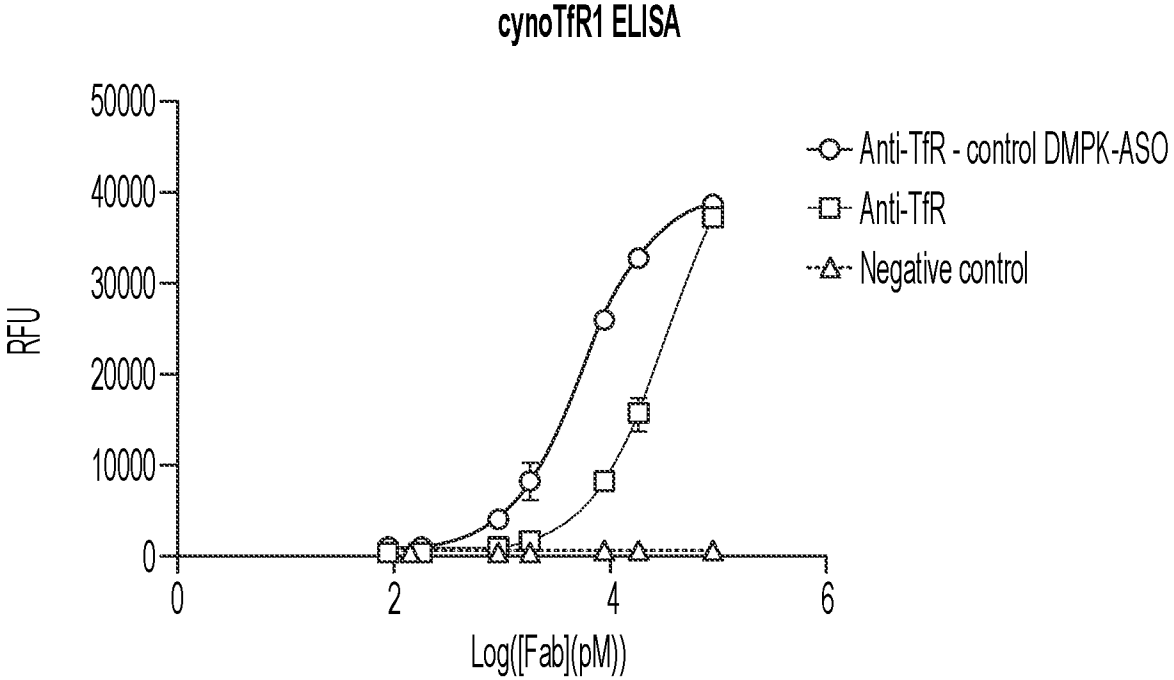

FIG. 12B

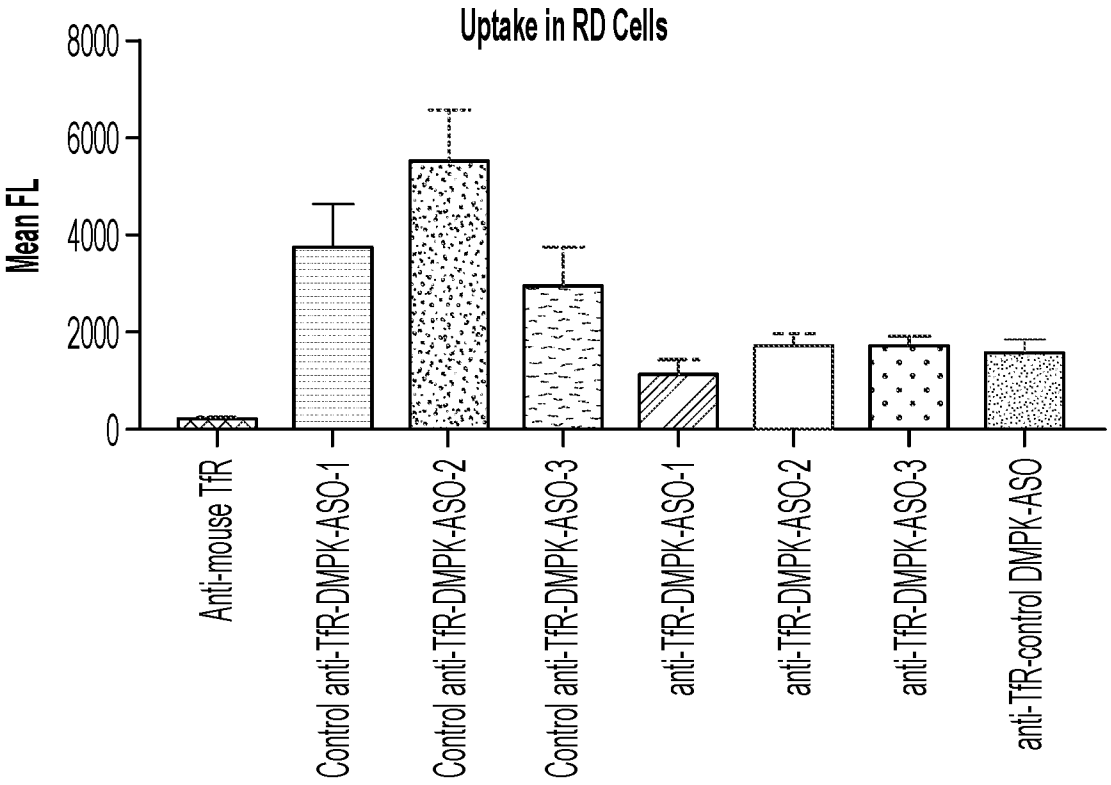
Uptake in RD Cells
Mean FL
8000
6000
4000
2000
0
Anti-mouse TfR
Control anti-TfR-DMPK-ASO-1
Control anti-TfR-DMPK-ASO-2
Control anti-TfR-DMPK-ASO-3
anti-TfR-DMPK-ASO-1
anti-TfR-DMPK-ASO-2
anti-TfR-DMPK-ASO-3
anti-TfR-control DMPK-ASO

FIG. 13

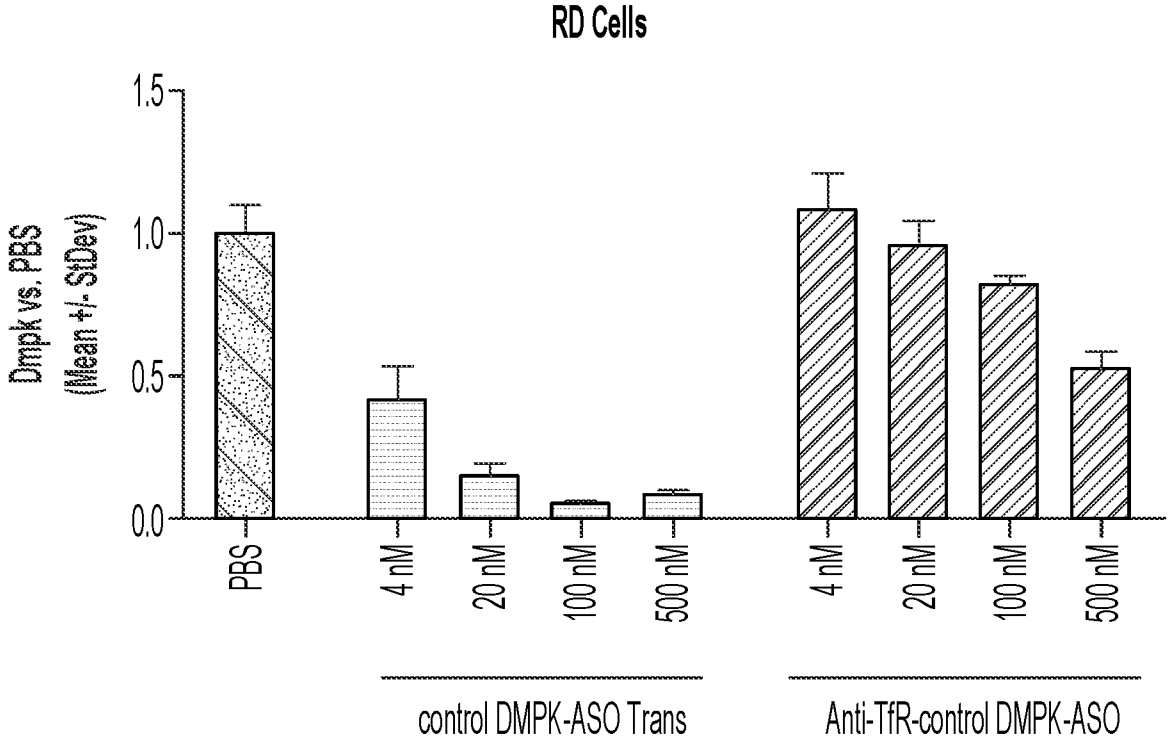
RD Cells
Dmpk vs. PBS
(Mean +/- StDev)
1.5
1.0
0.5
0.0
PBS
4 nM
20 nM
100 nM
500 nM
4 nM
20 nM
100 nM
500 nM
control DMPK-ASO Trans
Anti-TfR-control DMPK-ASO

FIG. 14

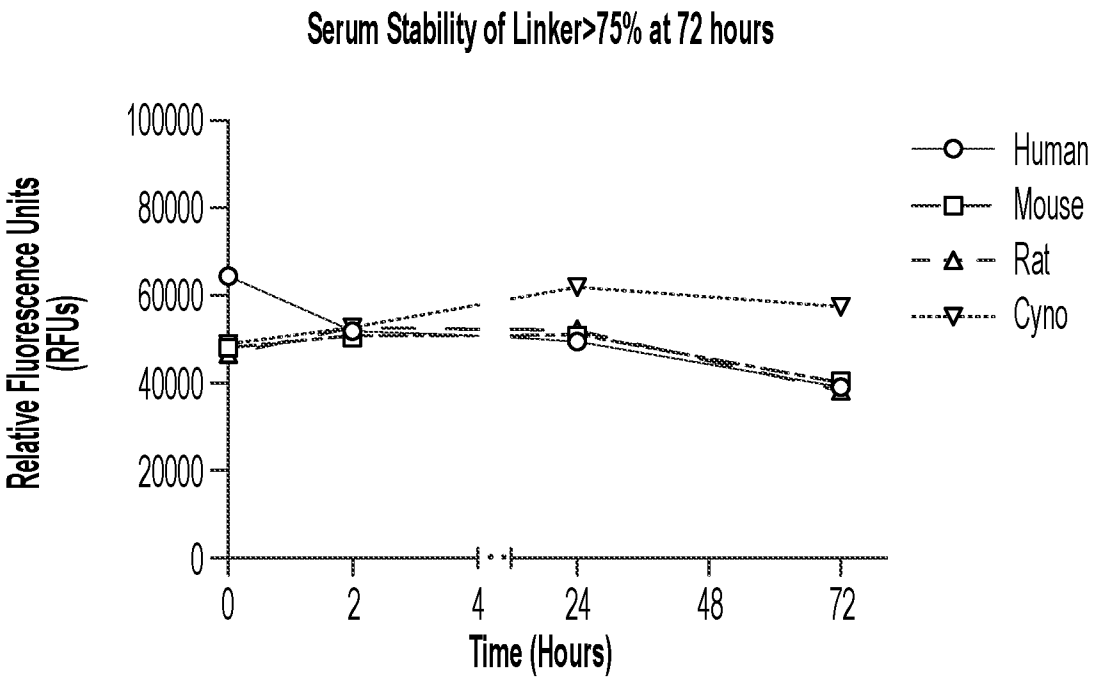
Serum Stability of Linker>75% at 72 hours
Relative Fluorescence Units (RFUs)
100000
80000
60000
40000
20000
0
0
2
4
24
48
72
Time (Hours)
Human
Mouse
Rat
Cyno

FIG. 15

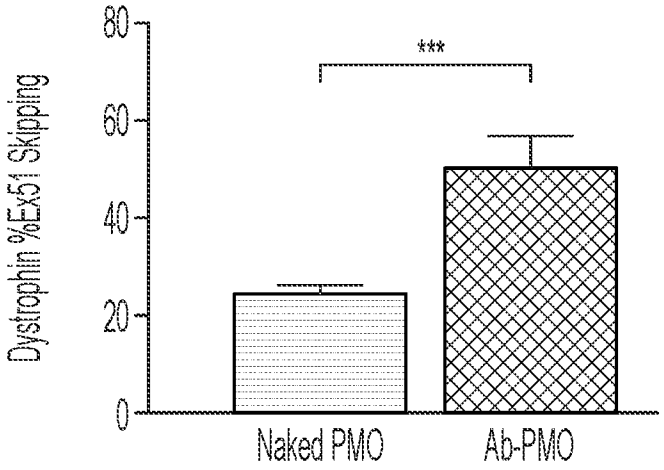

FIG. 16

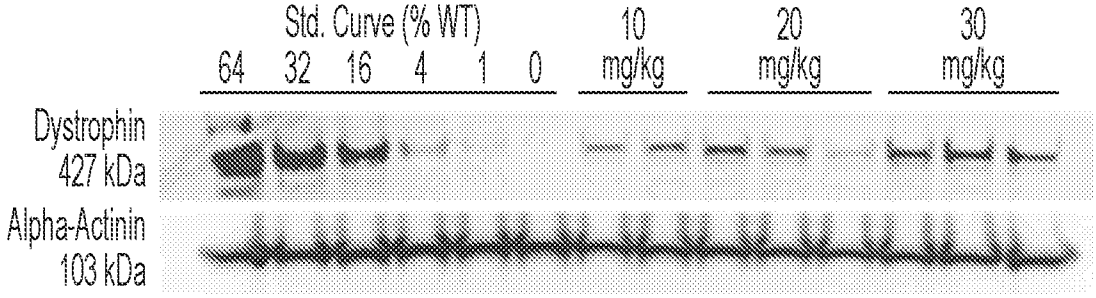

FIG. 17

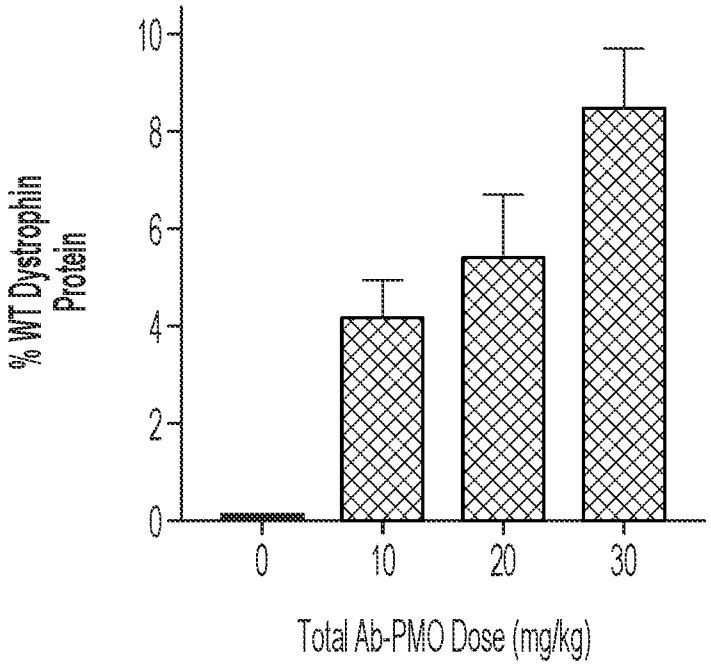

FIG. 18

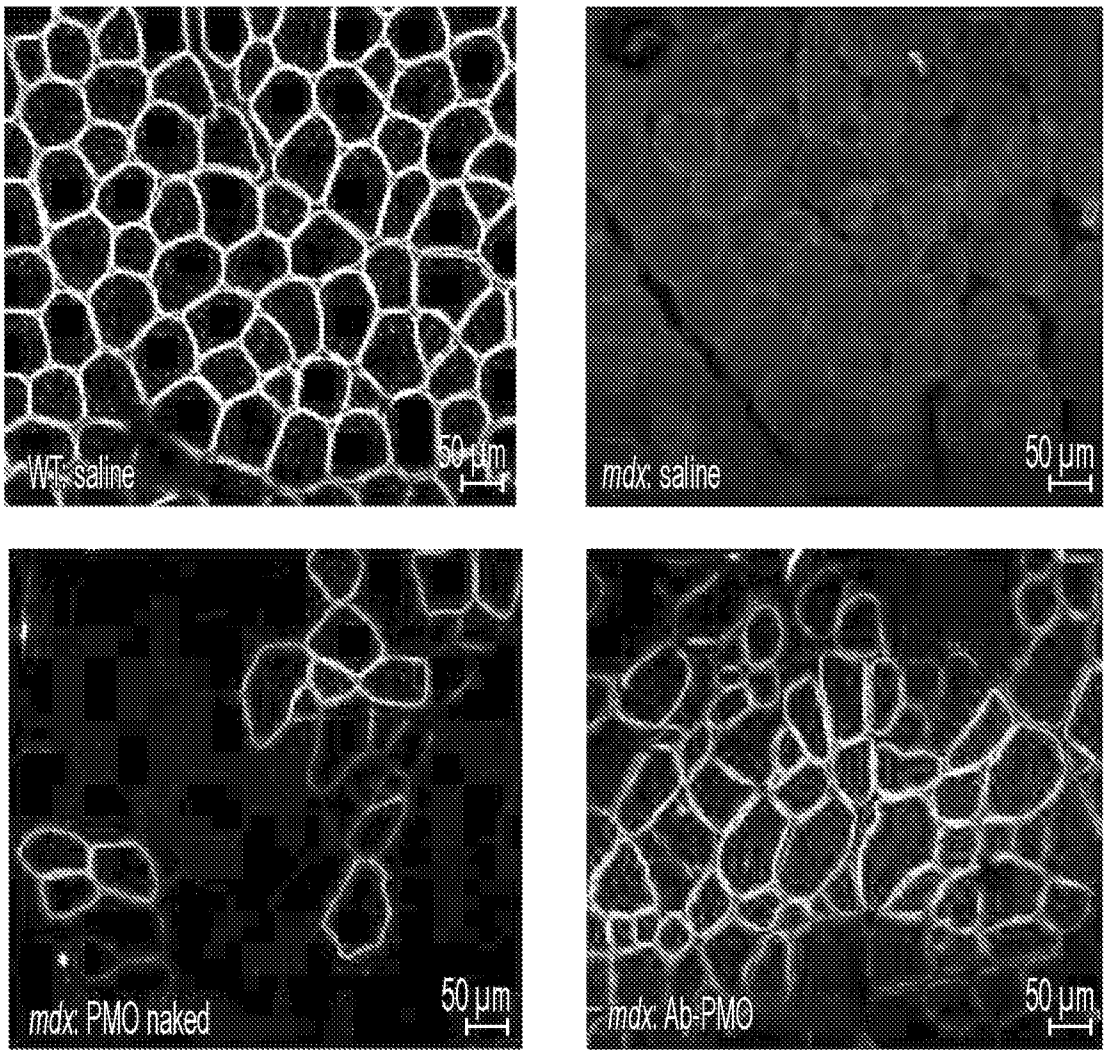
WT. saline
50 μm
mdx. saline
50 μm
mdx. PMO naked
50 μm
mdx. Ab-PMO
50 μm

FIG. 19

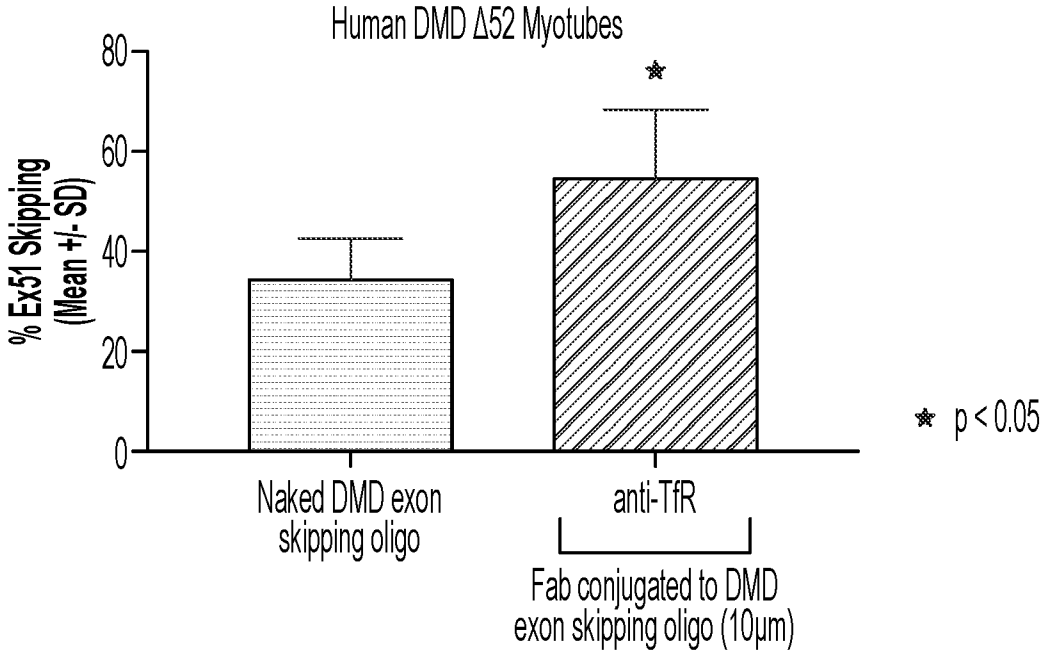
Human DMD Δ52 Myotubes
% Ex51 Skipping (Mean +/- SD)
80
60
40
20
0
Naked DMD exon skipping oligo
anti-TfR
Fab conjugated to DMD exon skipping oligo (10μm)
p < 0.05

FIG. 20

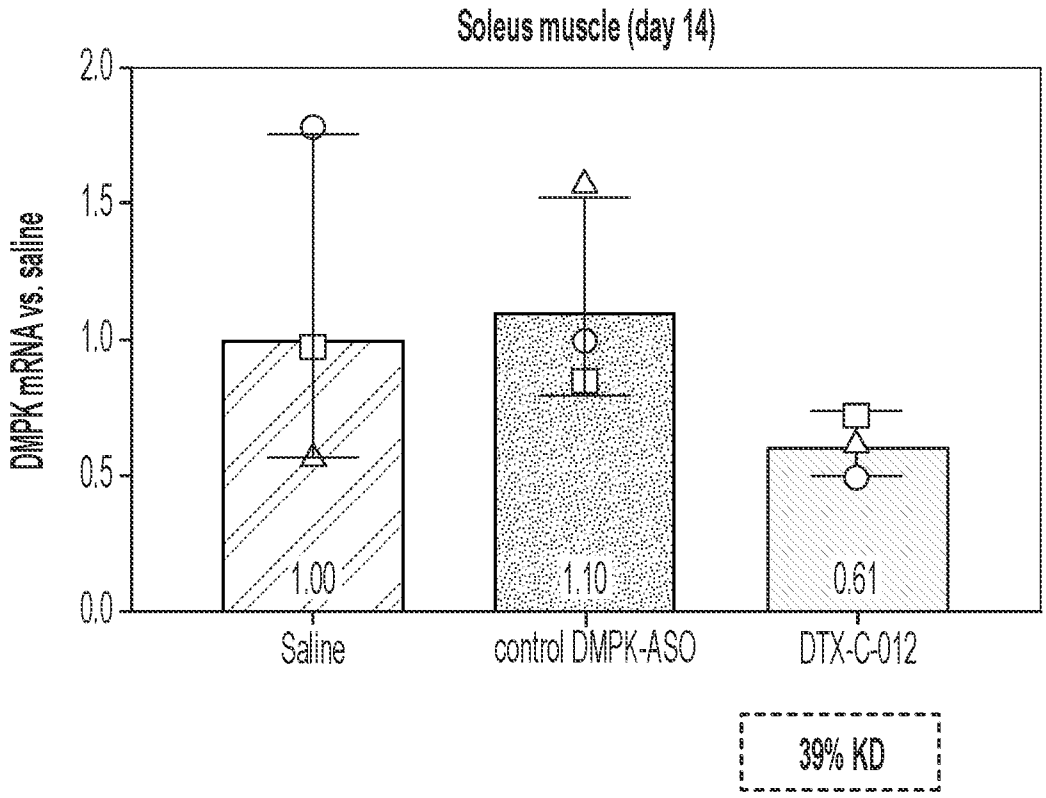
Soleus muscle (day 14)
DMPK mRNA vs. saline
2.0
1.5
1.0
0.5
0.0
1.00
1.10
0.61
Saline
control DMPK-ASO
DTX-C-012
39% KD

FIG. 21A

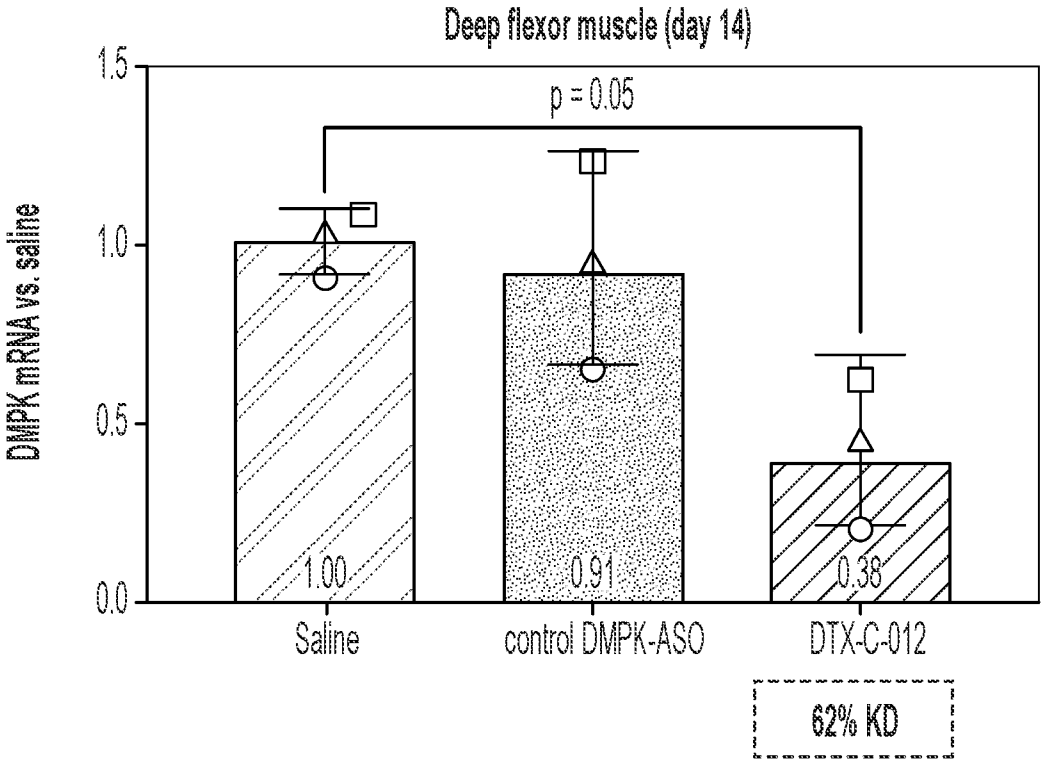

FIG. 21B

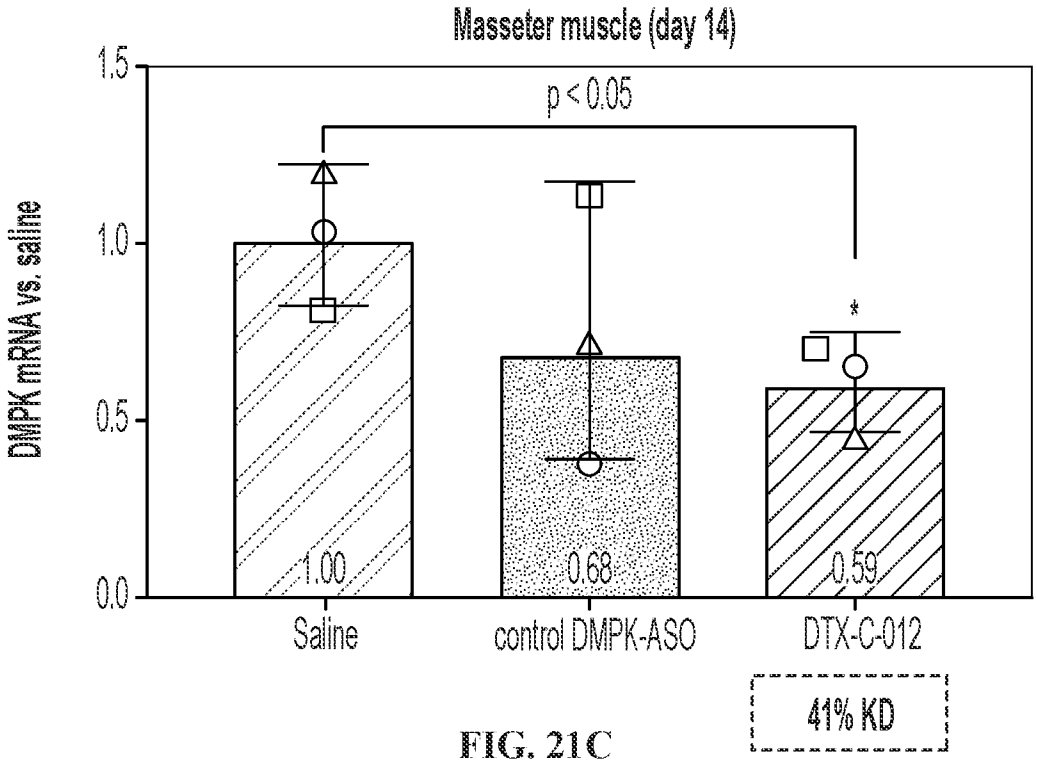

FIG. 21C

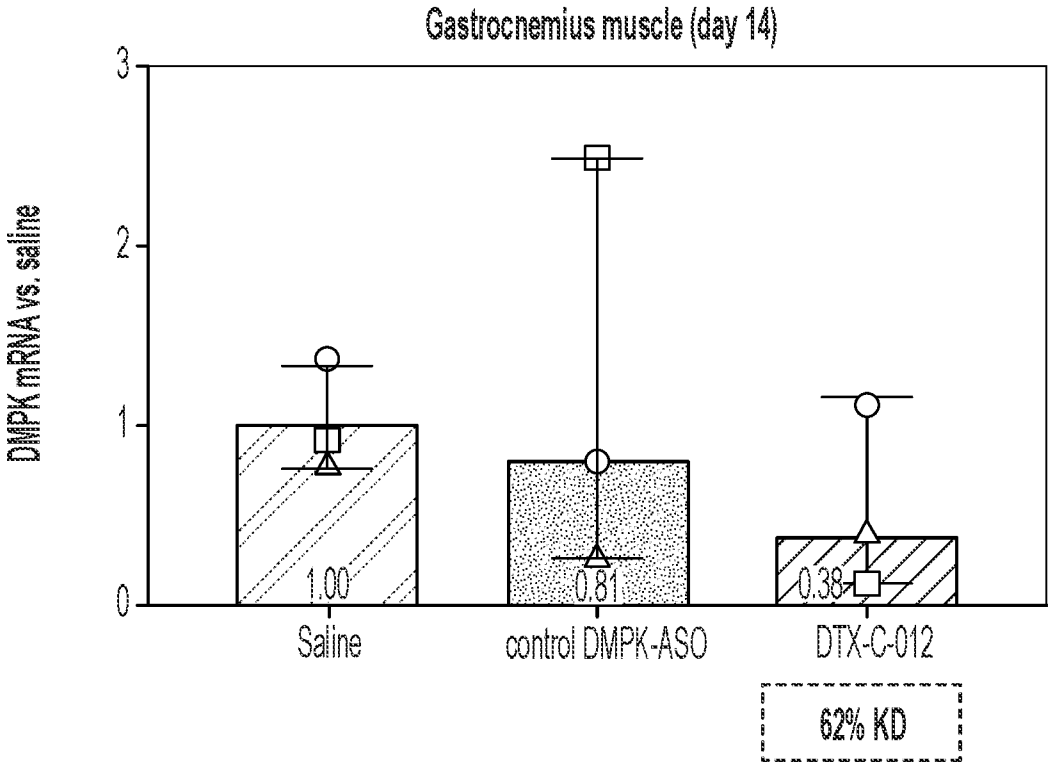

FIG. 21D

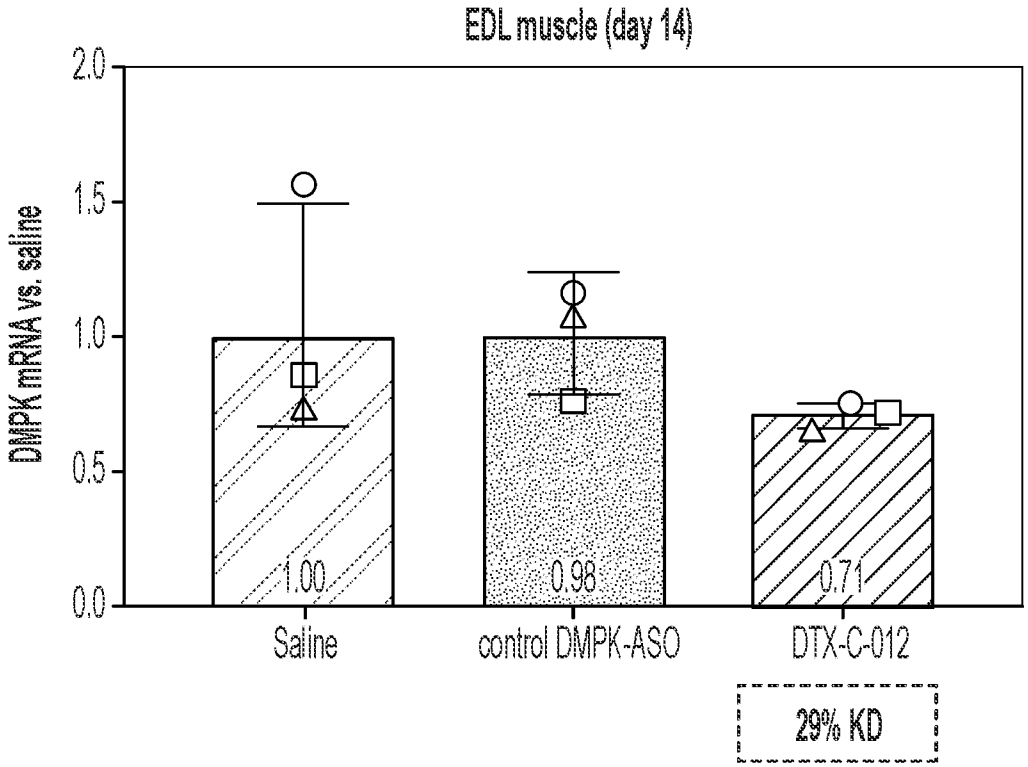

FIG. 21E

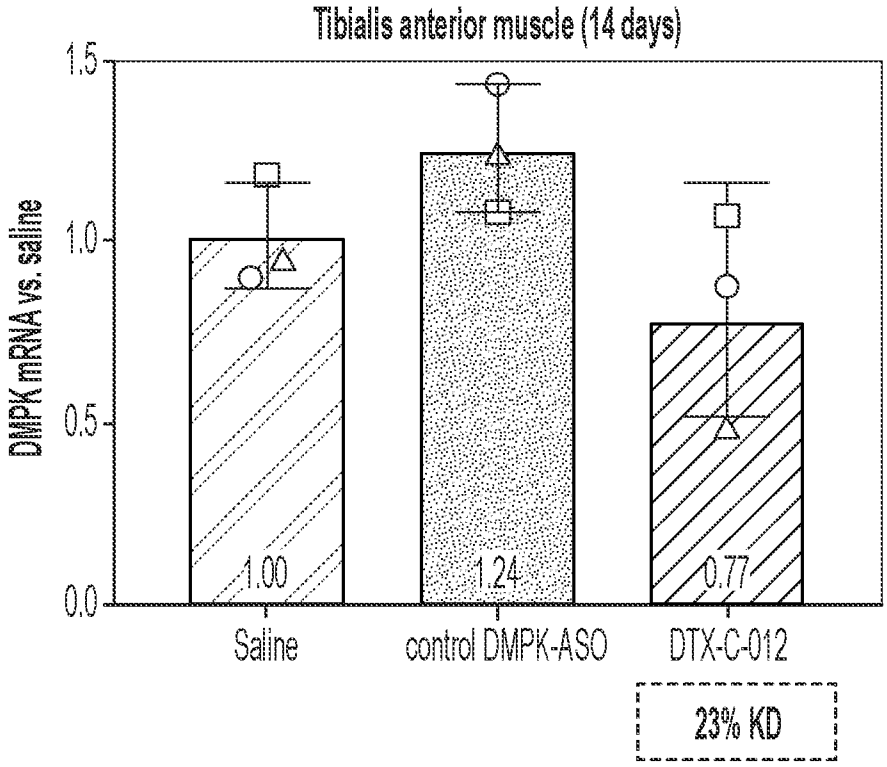

FIG. 21F

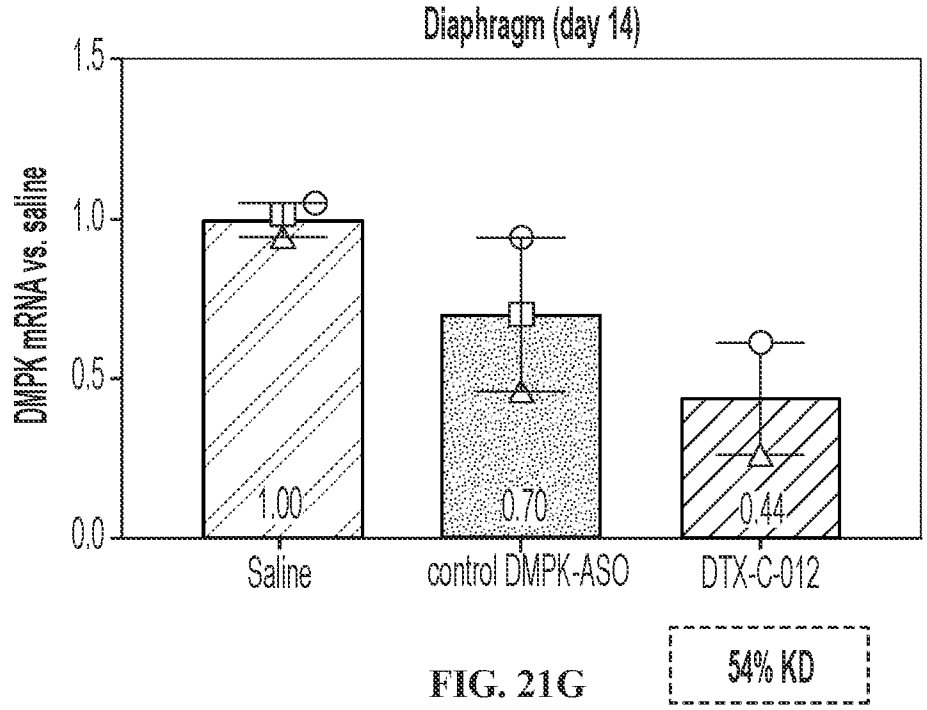

FIG. 21G

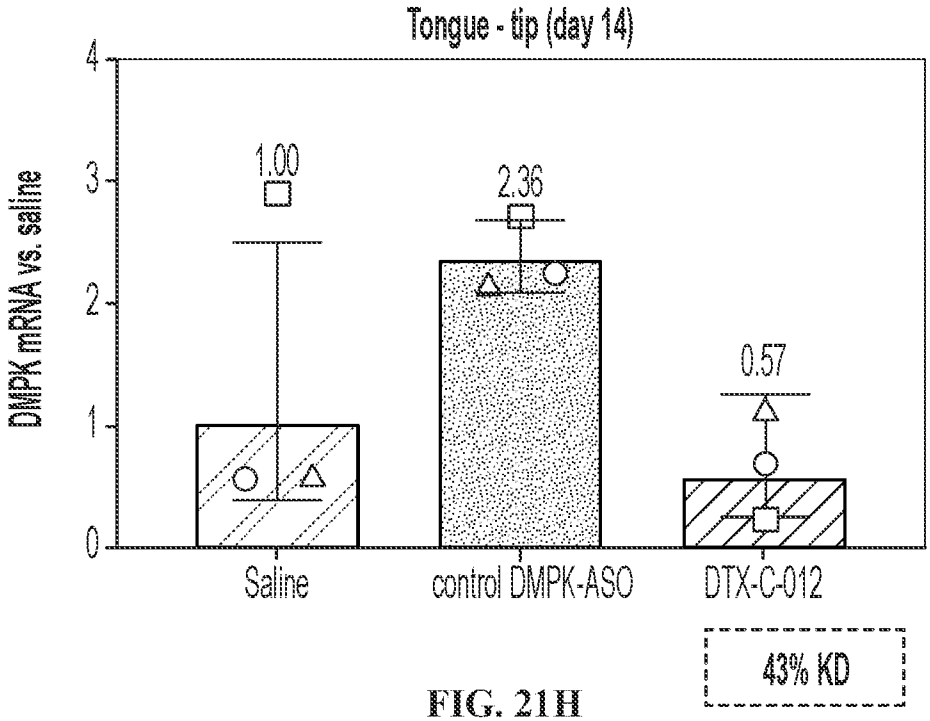

FIG. 21H

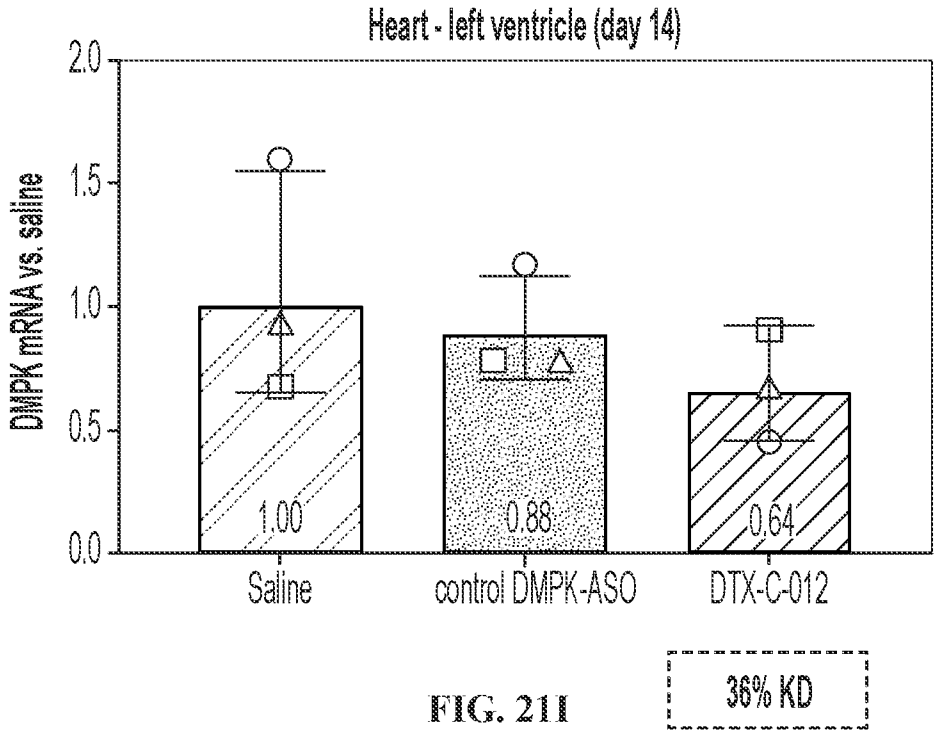

FIG. 21I

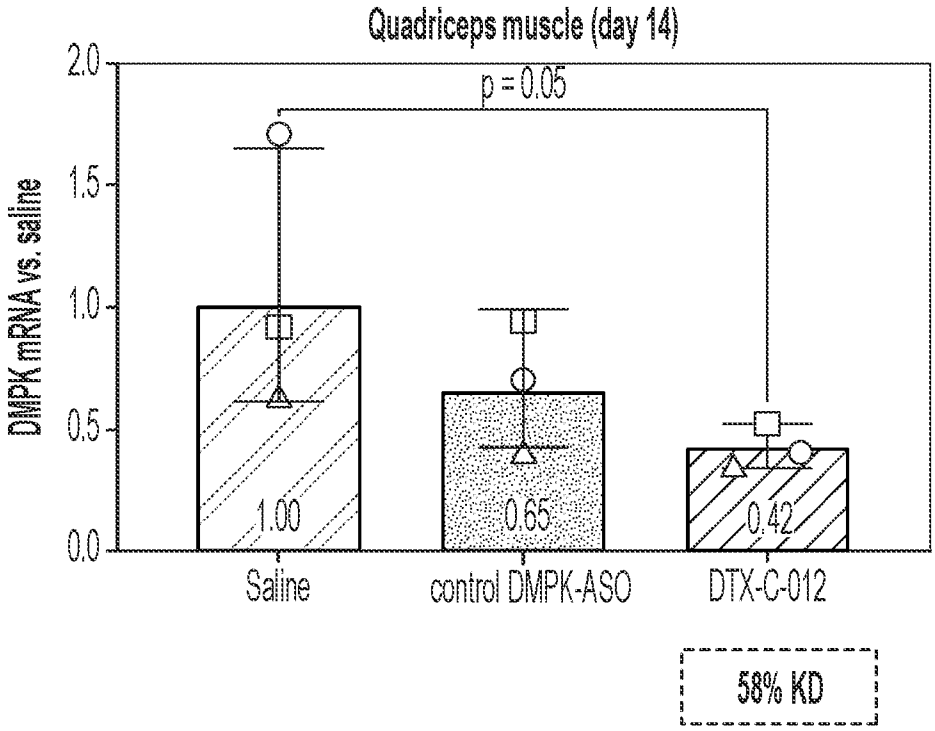

FIG. 21J

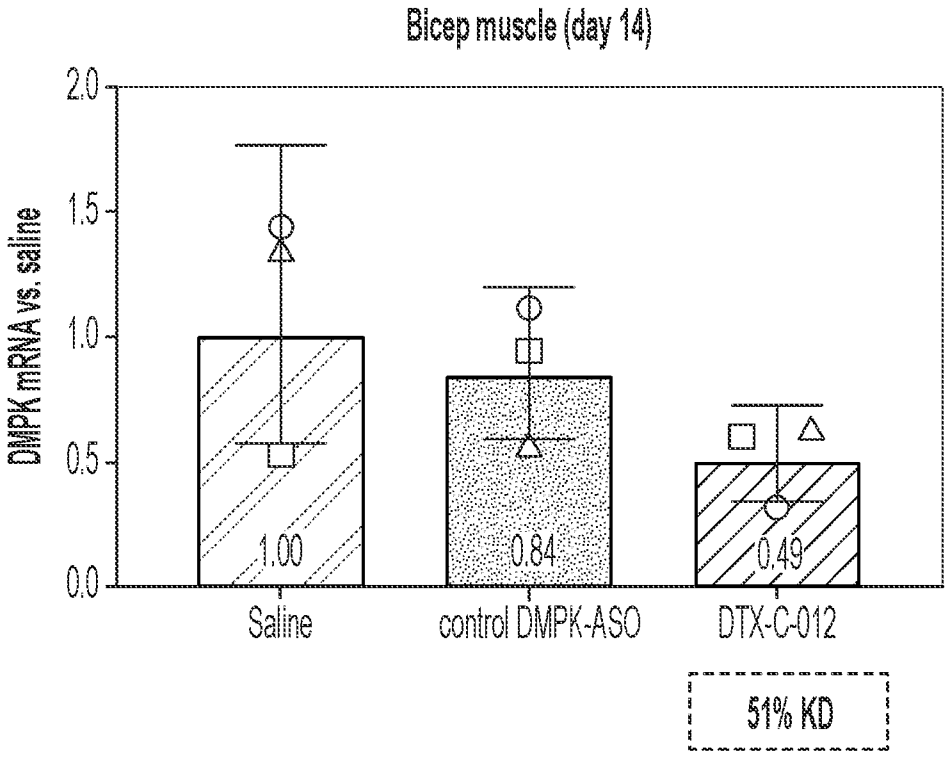

FIG. 21K

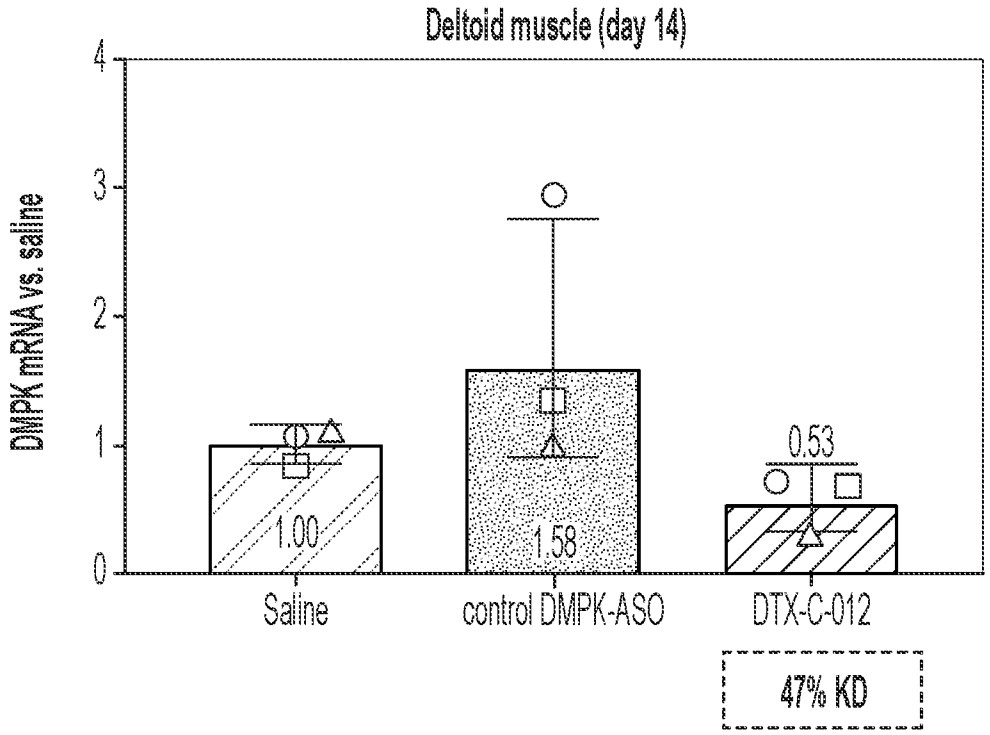

FIG. 21L

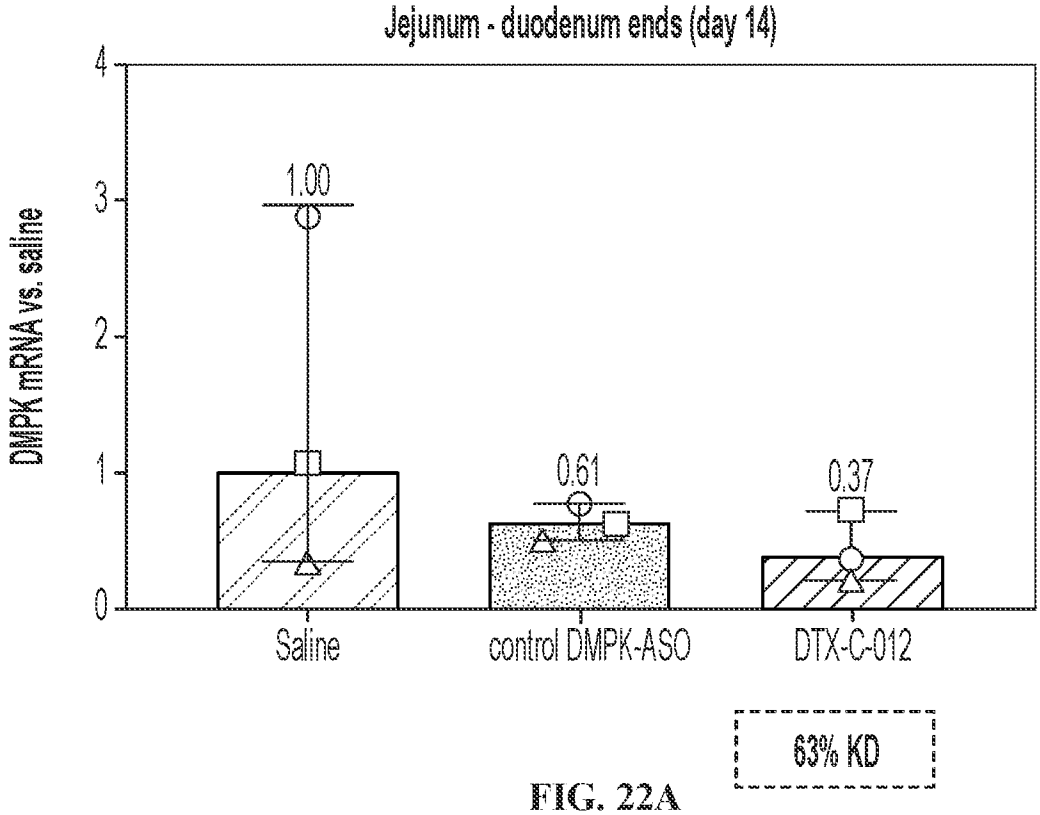

FIG. 22A

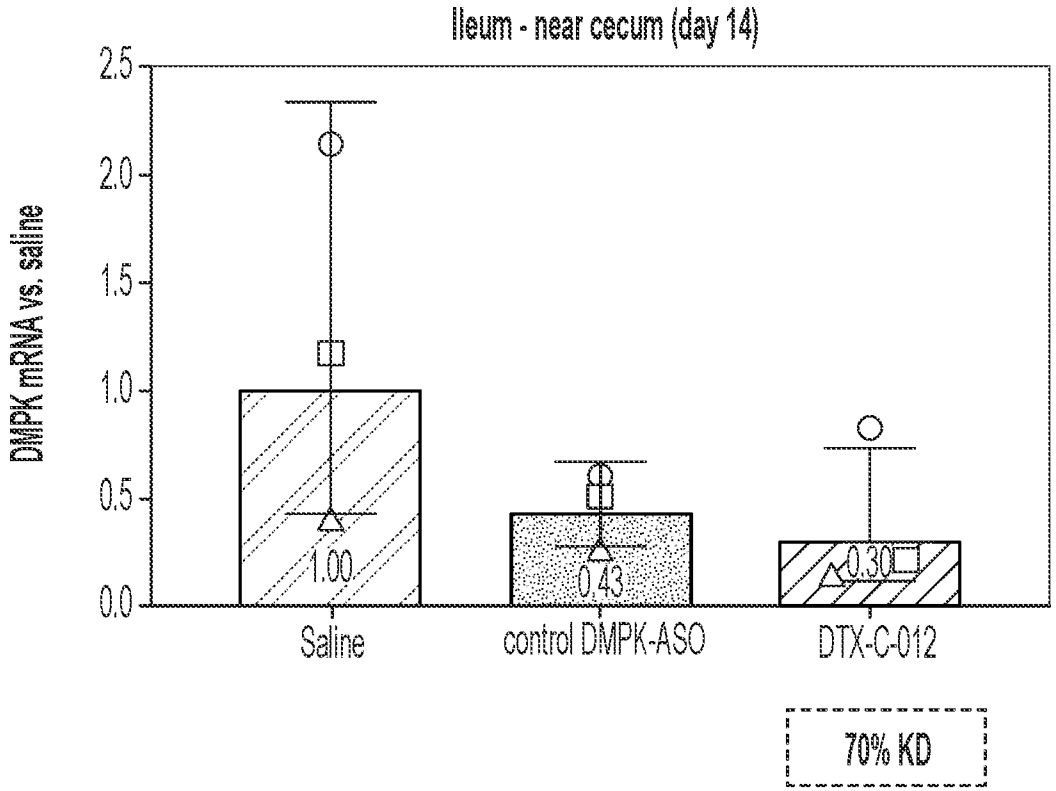

FIG. 22B

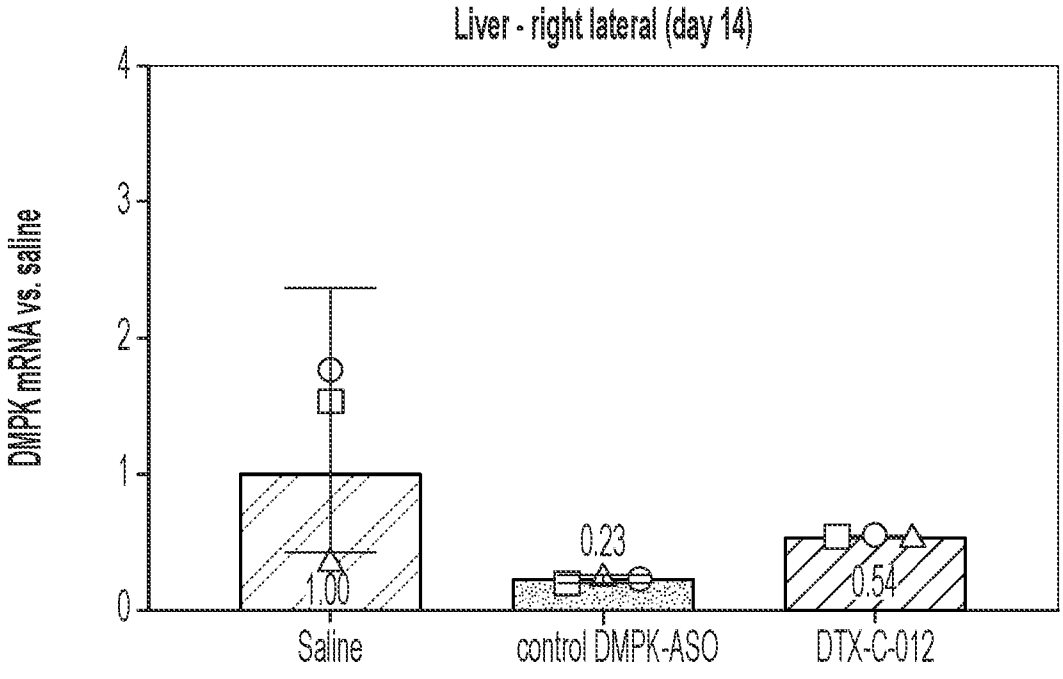

FIG. 23A

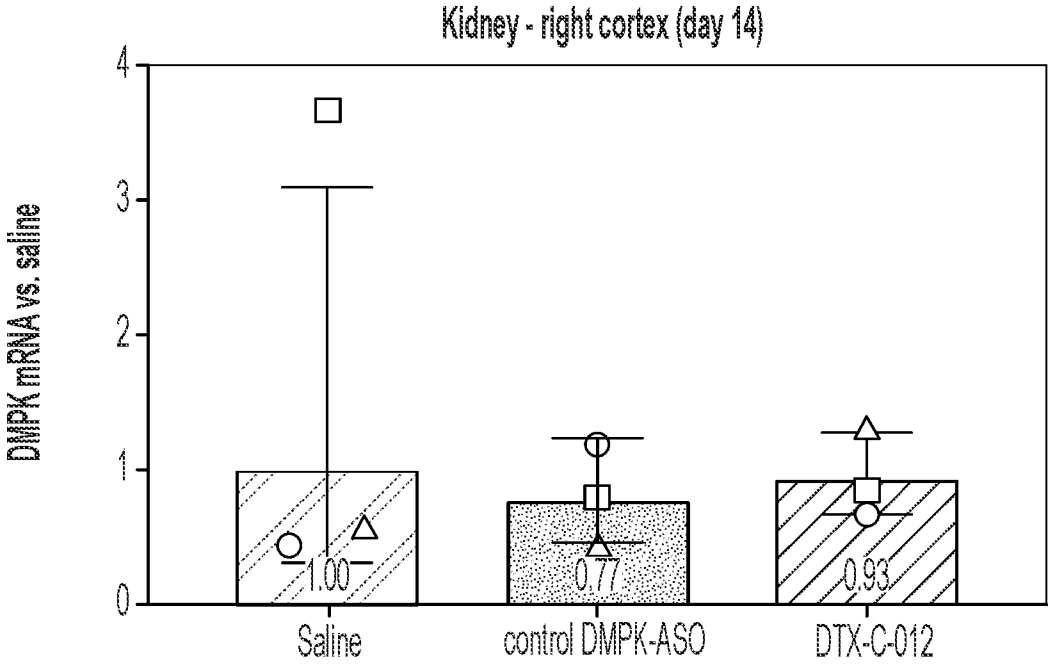

FIG. 23B

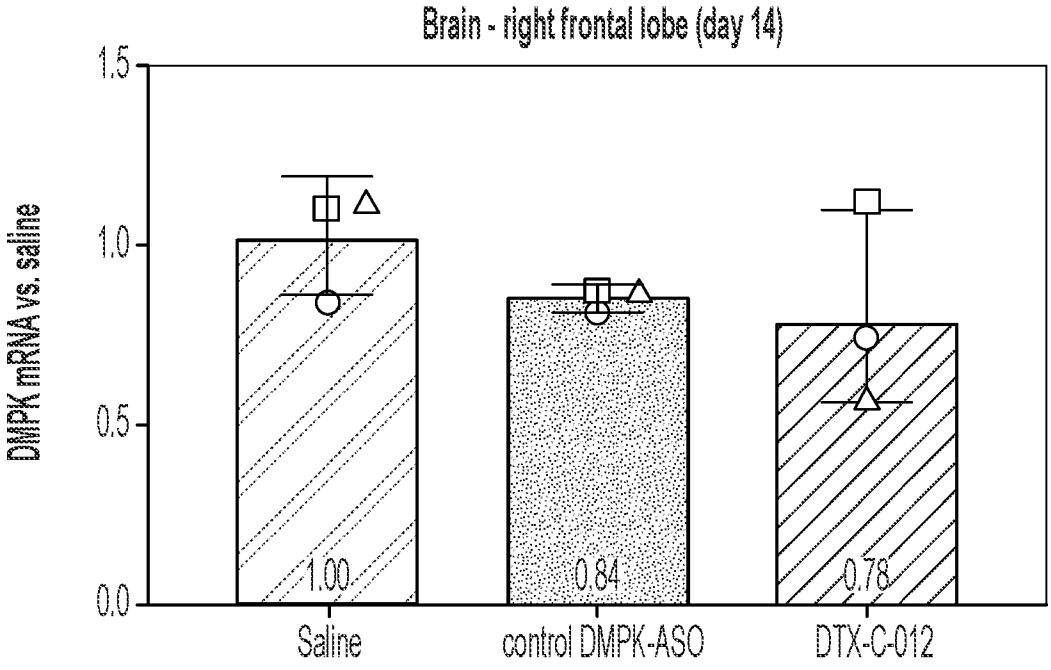

FIG. 23C

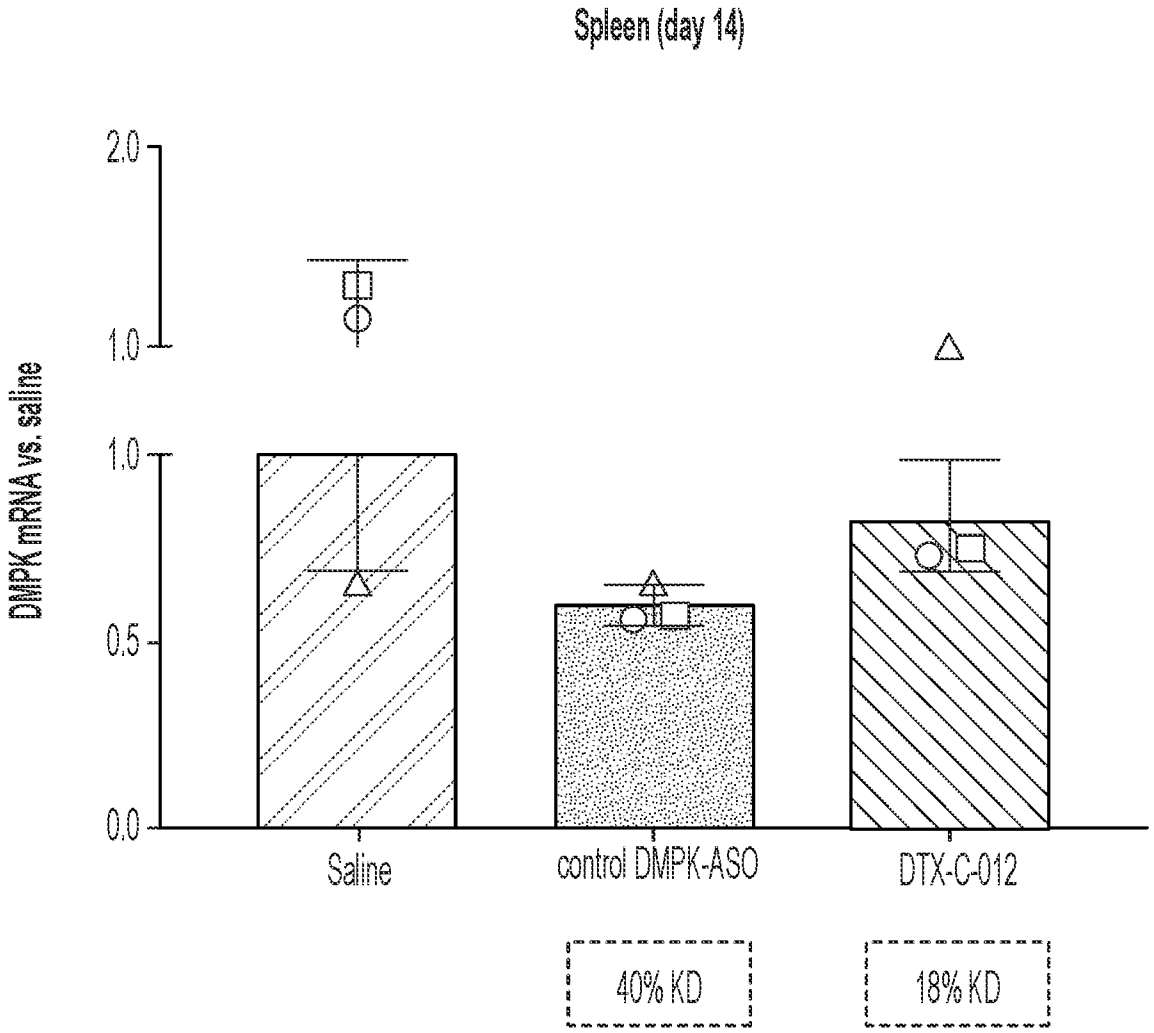
Spleen (day 14)
DMPK mRNA vs. saline
2.0
1.0
1.0
0.5
0.0
Saline
control DMPK-ASO
DTX-C-012
40% KD
18% KD

FIG. 23D

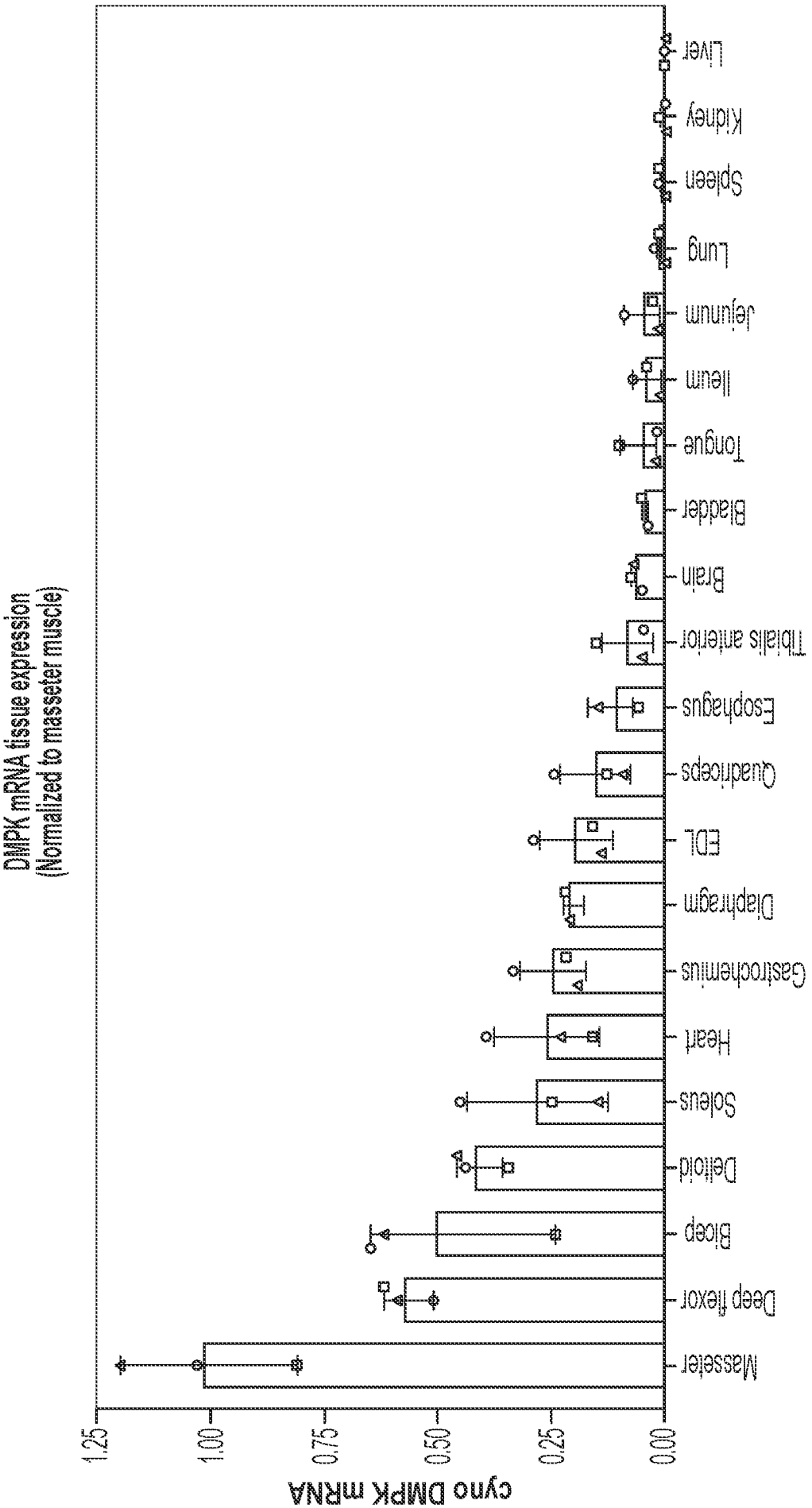
DMPK mRNA tissue expression
(Normalized to masseter muscle)
cyno DMPK mRNA
1.25
1.00
0.75
0.50
0.25
0.00
Masseter
Deep flexor
Bicep
Deltoid
Soleus
Heart
Gastrocnemius
Diaphragm
EDL
Quadriceps
Esophagus
Tibialis anterior
Brain
Bladder
Tongue
Ileum
Jejunum
Lung
Spleen
Kidney
Liver

FIG. 24

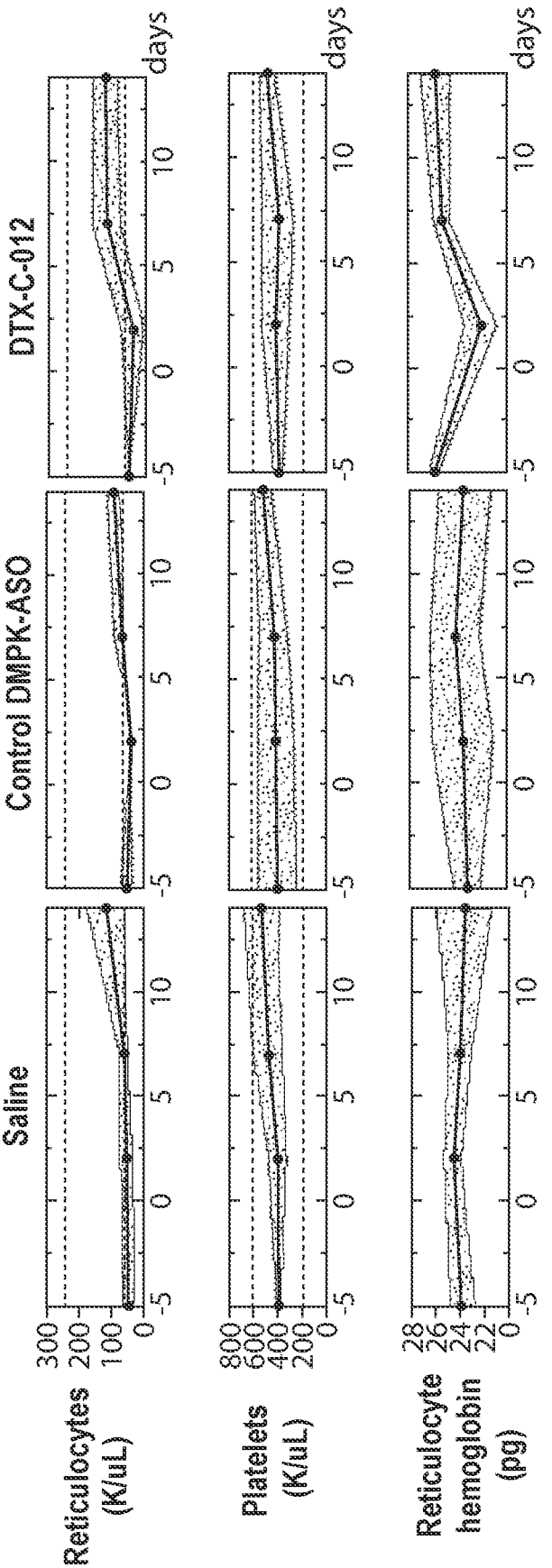
Saline
Control DMPK-ASO
DTX-C-012
Reticulocytes (K/uL)
Platelets (K/uL)
Reticulocyte hemoglobin (pg)
days

FIG. 25