Figure 1

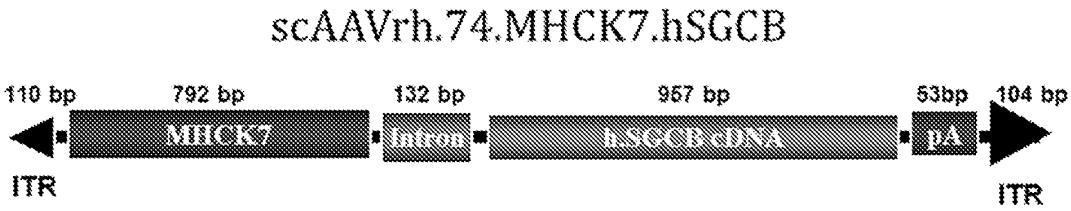
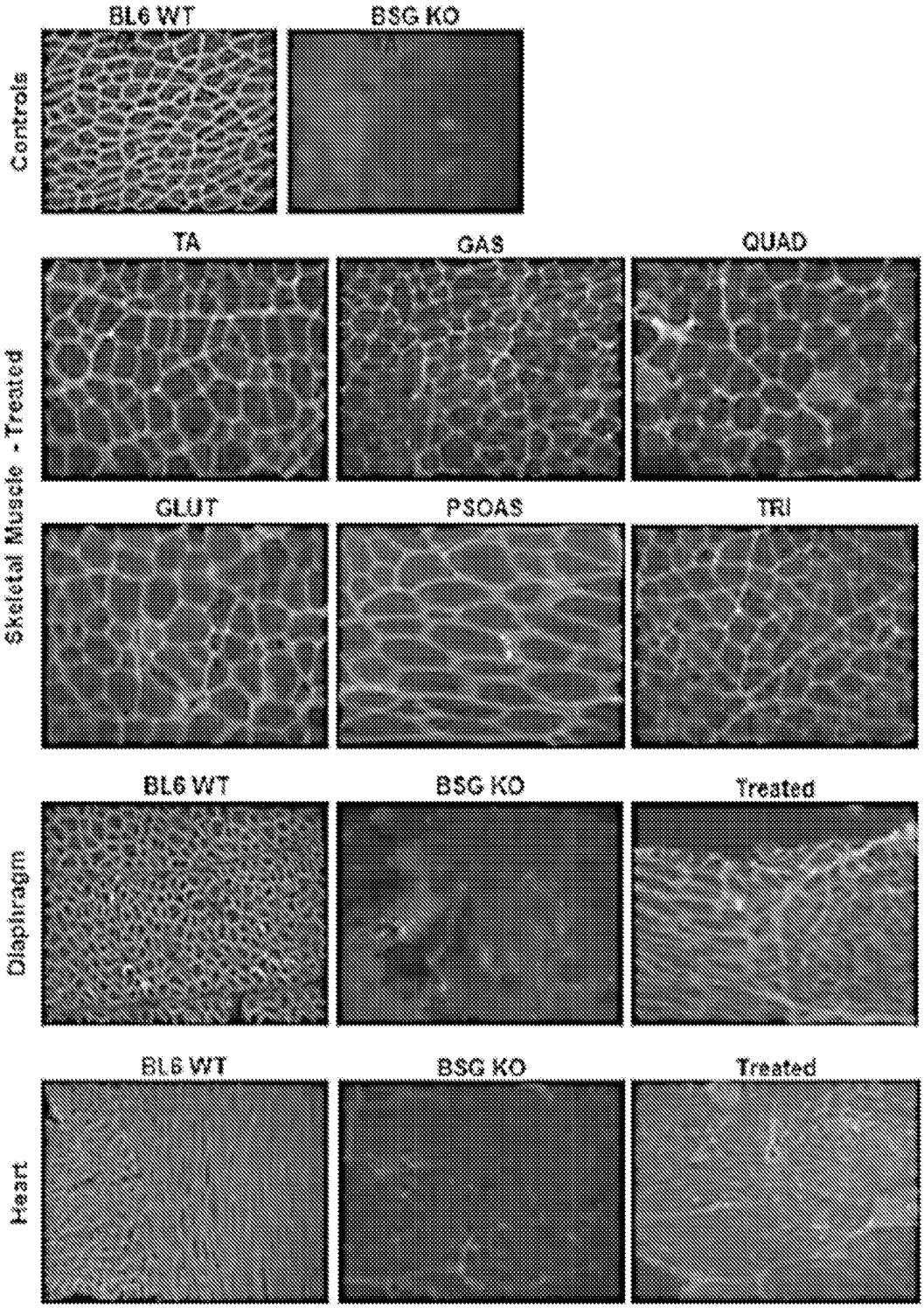

scAAVrh.74.MHCK7.hSGCB
110 bp
792 bp
132 bp
957 bp
53bp
104 bp
MHCK7
Intron
hSGCB cDNA
pA
ITR
ITR

Figure 2A


BL6 WT
BSG KO
Controls
TA
GAS
QUAD
Skeletal Muscle - Treated
GLUT
PSOAS
TRI
BL6 WT
BSG KO
Treated
Diaphragm
BL6 WT
BSG KO
Treated
Heart

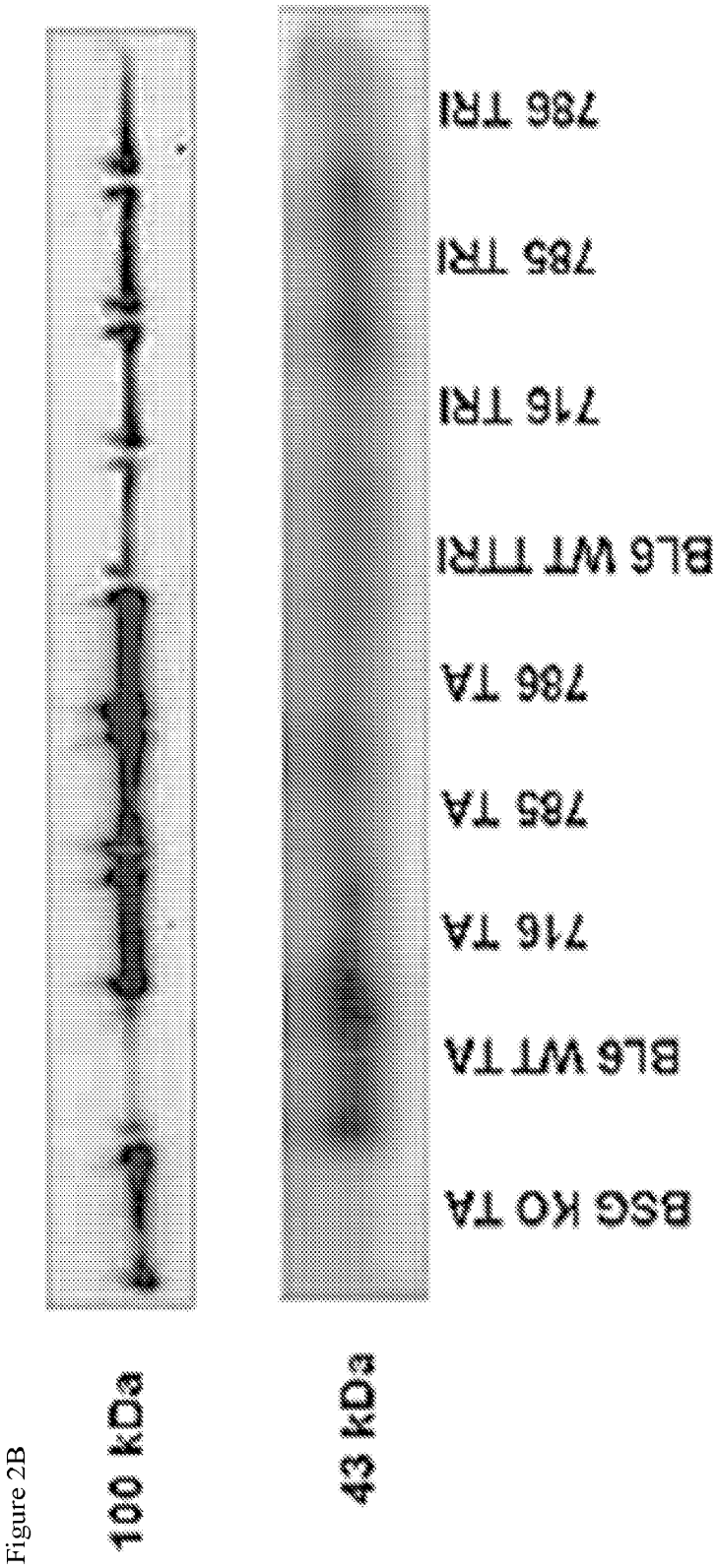
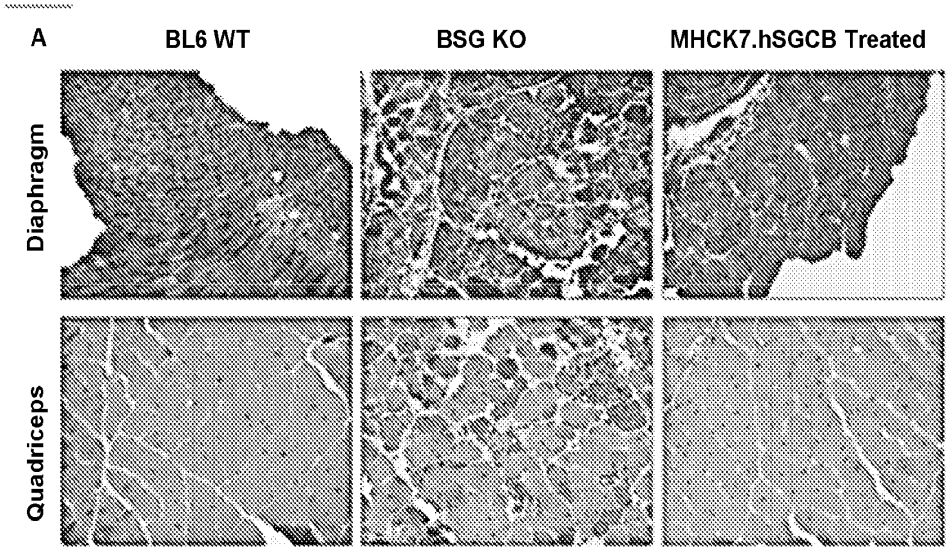

786 TRI
785 TRI
716 TRI
BL6 WT TTRI
786 TA
785 TA
716 TA
BL6 WT TA
BSG KO TA
100 kDa
43 kDa

Figure 2B

Figure 3


A
BL6 WT
BSG KO
MHCK7.hSGCB Treated
Diaphragm
Quadriceps

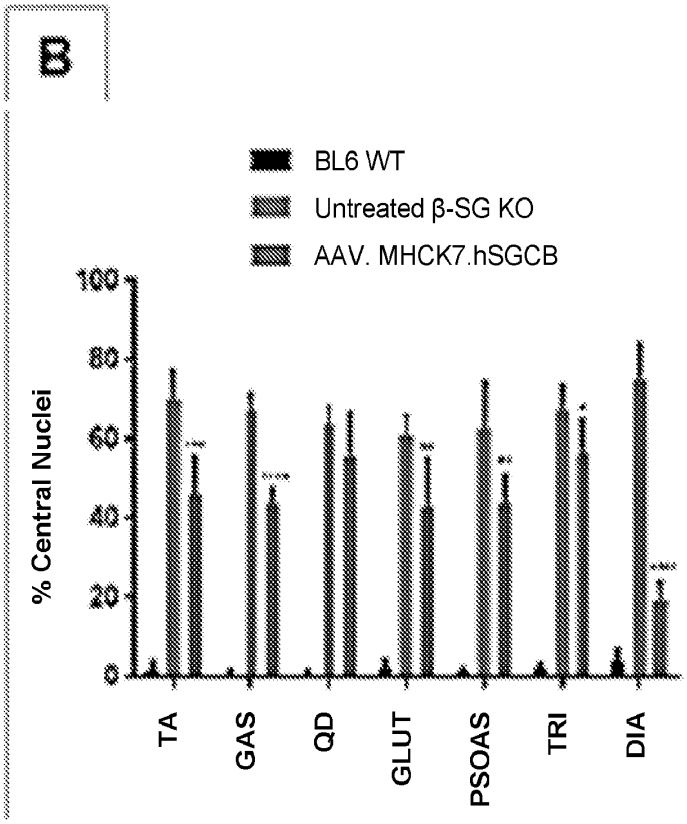
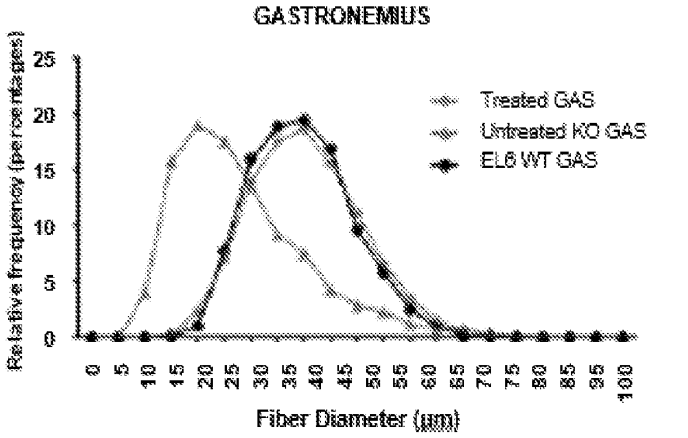
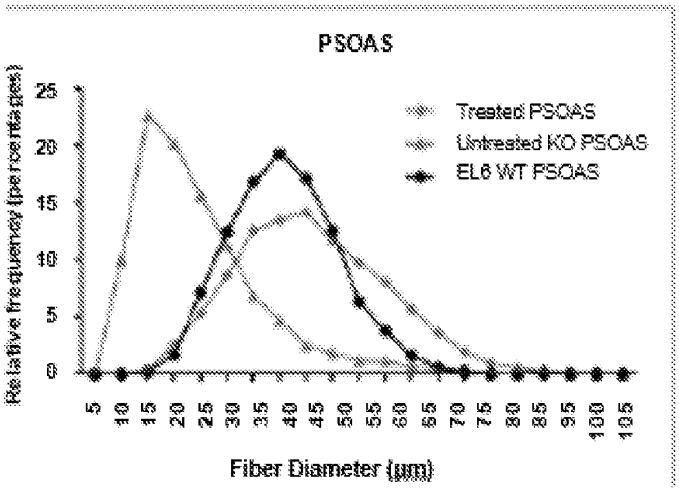
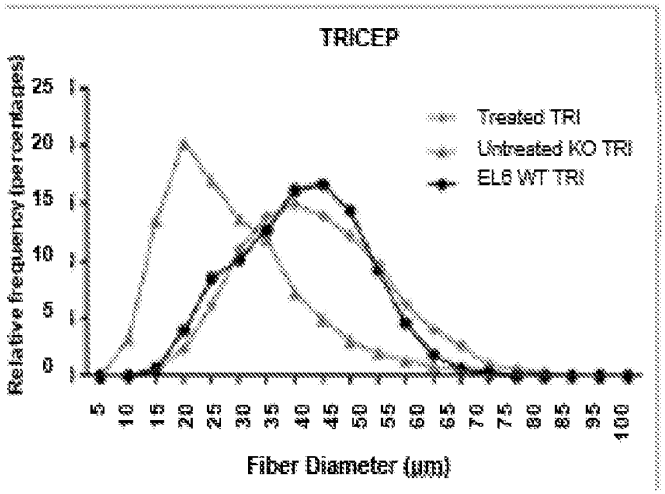

B
BL6 WT
Untreated β-SG KO
AAV. MHCK7.hSGCB
% Central Nuclei
100
80
60
40
20
0
TA
GAS
QD
GLUT
PSOAS
TRI
DIA

Figure 3

C


GASTRONEMIUS
Relative frequency (percentages)
Fiber Diameter (µm)
Treated GAS
Untreated KO GAS
EL6 WT GAS


PSOAS
Relative frequency (percentages)
Fiber Diameter (µm)
Treated PSOAS
Untreated KO PSOAS
EL6 WT PSOAS


TRICEP
Relative frequency (percentages)
Fiber Diameter (µm)
Treated TRI
Untreated KO TRI
EL6 WT TRI

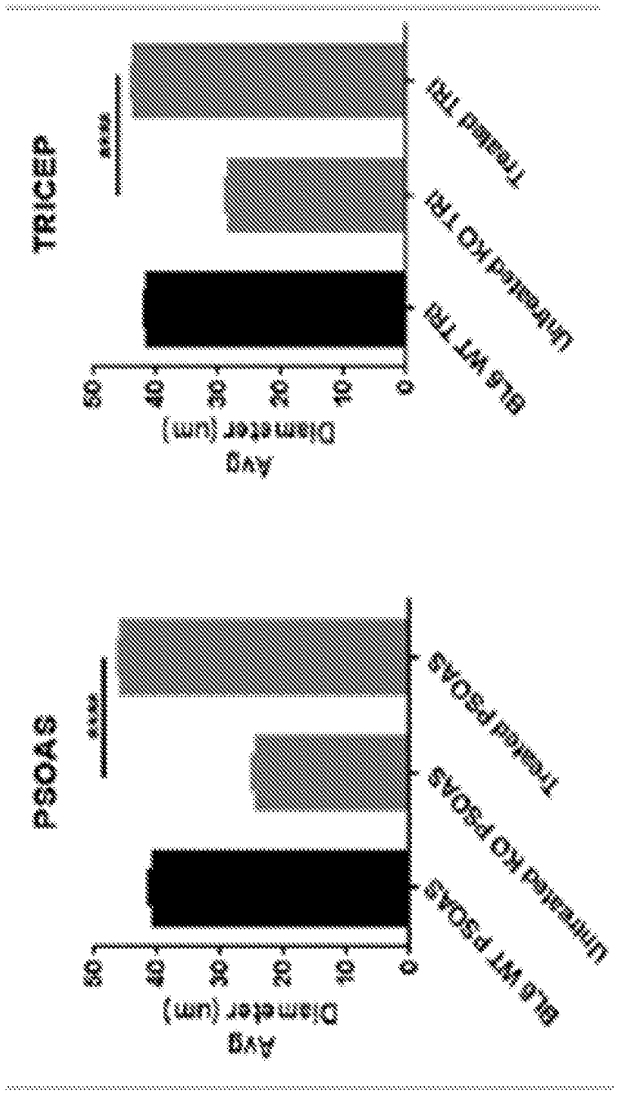

TRICEP
PSOAS
Castrocnemius
Avg Diameter (um)
BLS WT TRI
Untreated KO TRI
Treated TRI
BLS WT PSOAS
Untreated KO PSOAS
Treated PSOAS
BLS WT GAS
Untreated KO GAS
Treated GAS
****

Figure 3

D

Figure 4

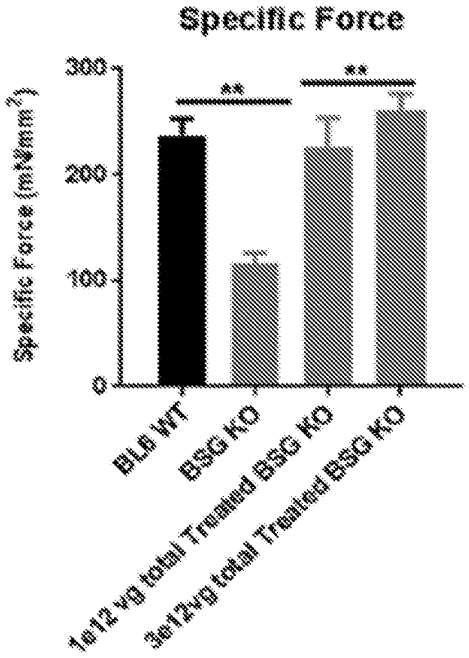
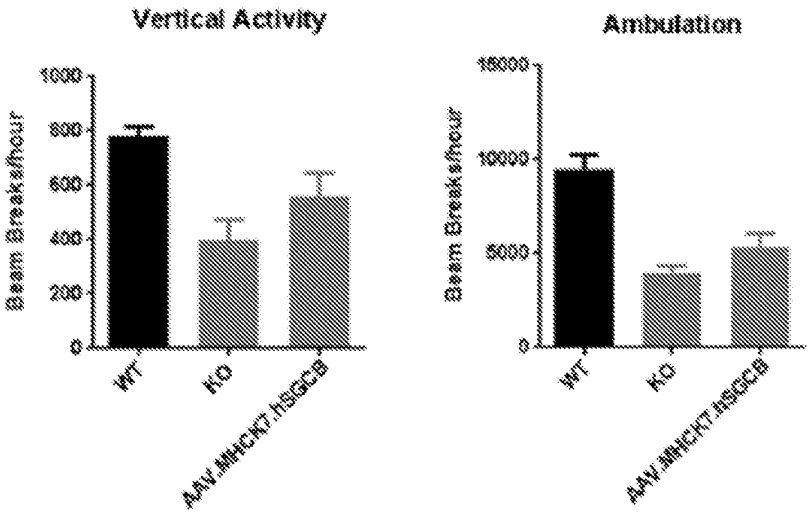

Specific Force
Specific Force (mN/mm²)
300
200
100
0
**
**
BL6 WT
BSG KO
1e12 vg total Treated BSG KO
3e12vg total Treated BSG KO

Figure 5


Vertical Activity
Beam Breaks/hour
1000
800
600
400
200
0
WT
KO
AAV.MHCK7.hSGCB
Ambulation
Beam Breaks/hour
15000
10000
5000
0
WT
KO
AAV.MHCK7.hSGCB

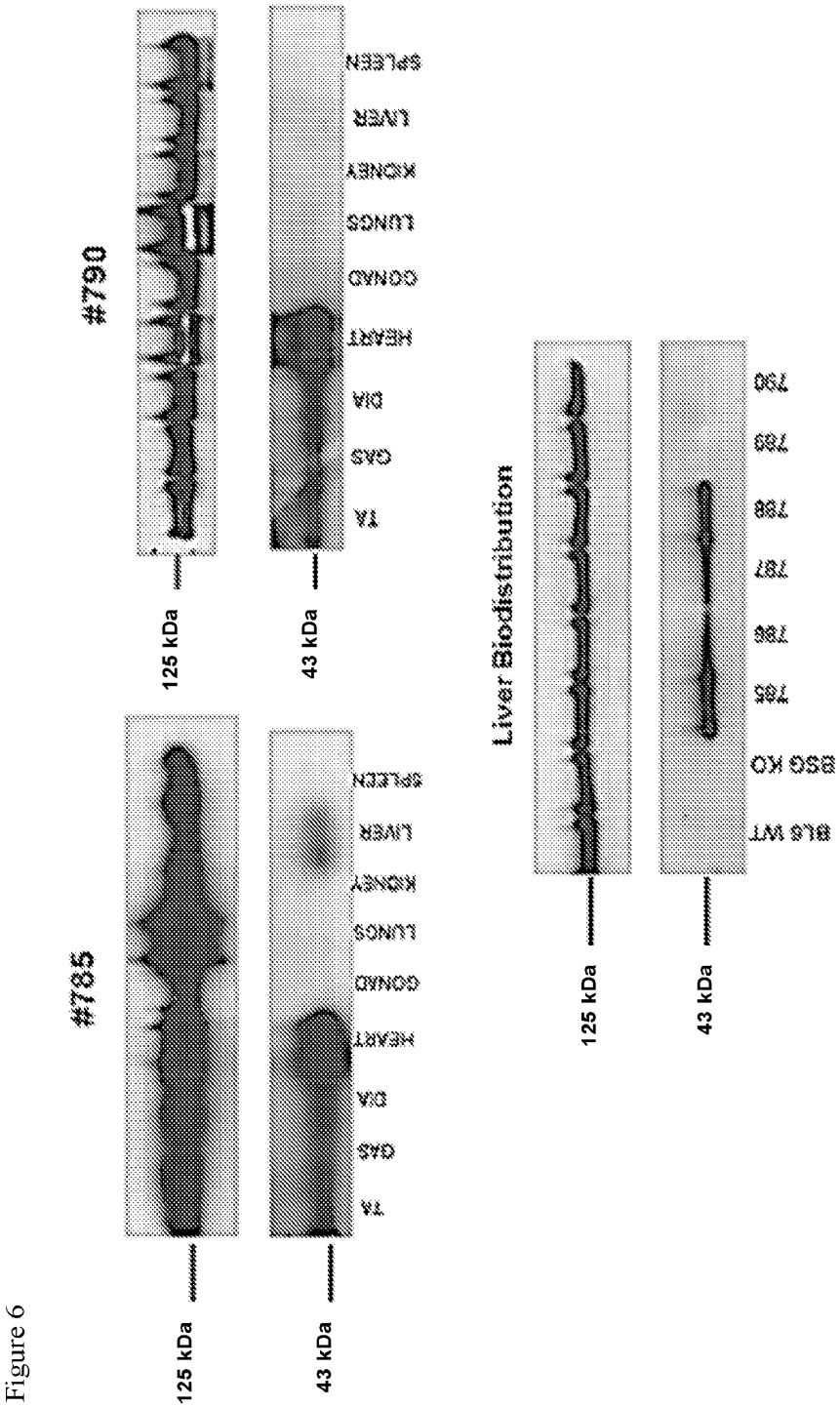

#790
125 kDa
43 kDa
TA
GAS
DIA
HEART
GONAD
LUNGS
KIDNEY
LIVER
SPLEEN
#785
125 kDa
43 kDa
TA
GAS
DIA
HEART
GONAD
LUNGS
KIDNEY
LIVER
SPLEEN
Liver Biodistribution
125 kDa
43 kDa
BLG WT
BSG KO
785
786
787
788
789
790

Figure 6

Figure 7

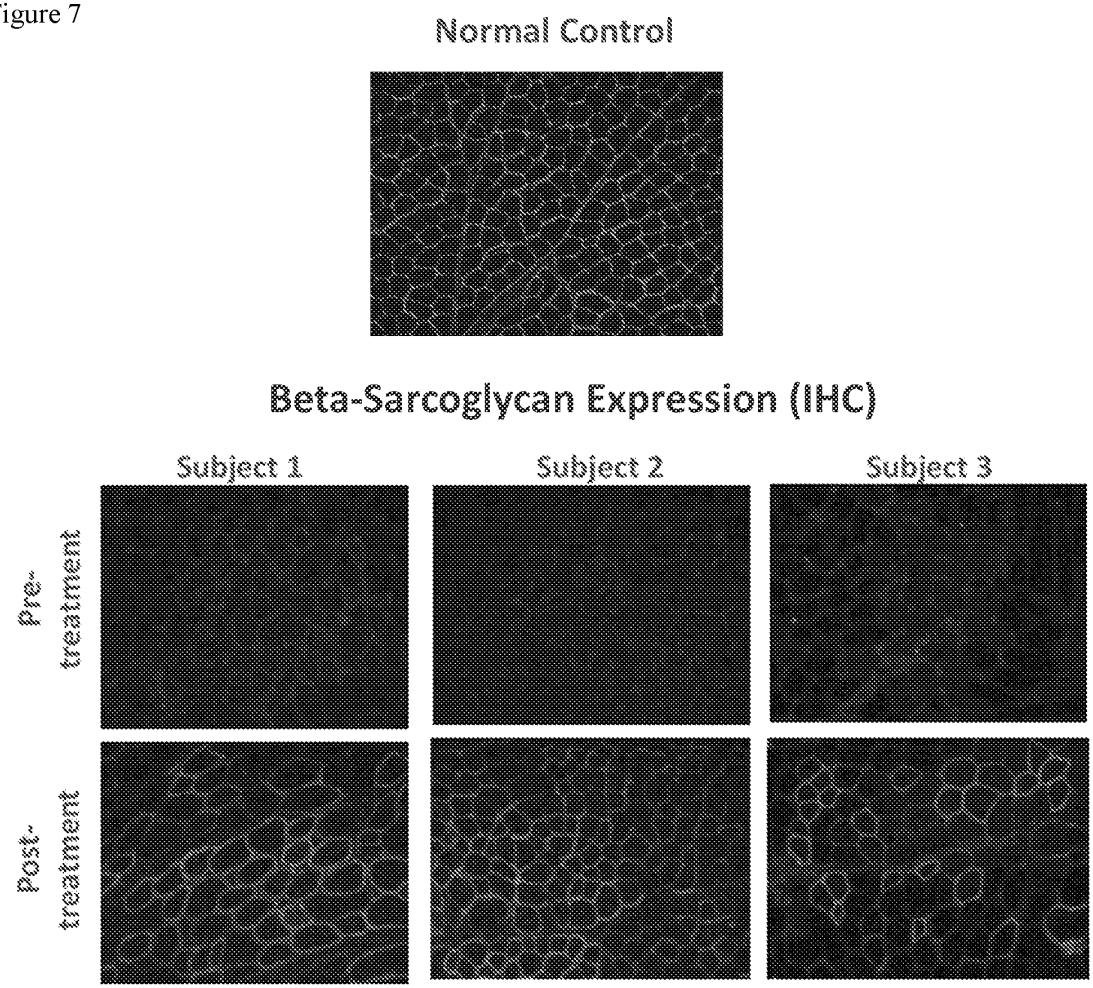
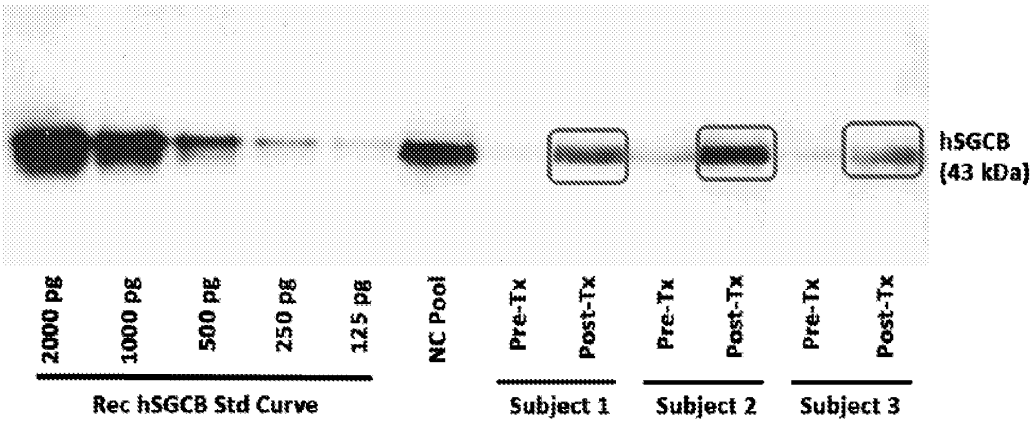

Normal Control
Beta-Sarcoglycan Expression (IHC)
Subject 1
Subject 2
Subject 3
Pre-treatment
Post-treatment

Figure 8


hSGCB
(43 kDa)
2000 pg
1000 pg
500 pg
250 pg
125 pg
NC Pool
Pre-Tx
Post-Tx
Pre-Tx
Post-Tx
Pre-Tx
Post-Tx
Rec hSGCB Std Curve
Subject 1
Subject 2
Subject 3

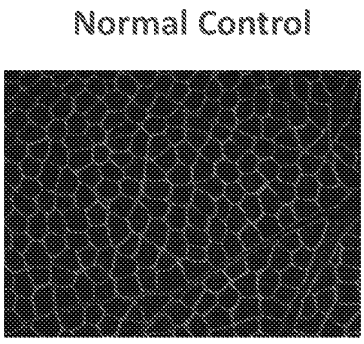

Normal Control

Figure 9

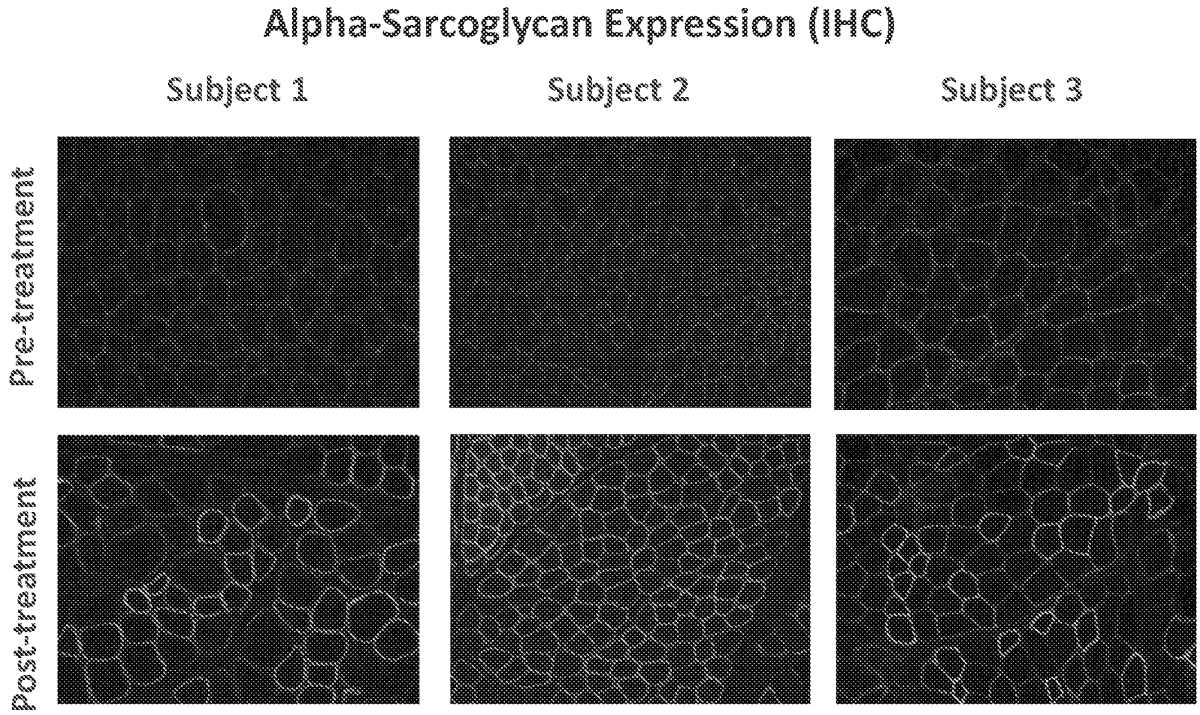
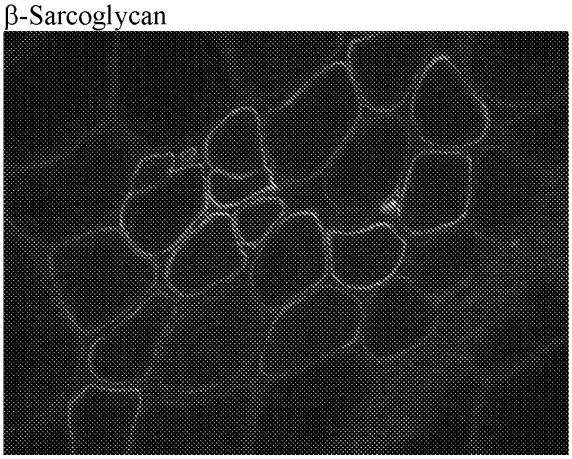
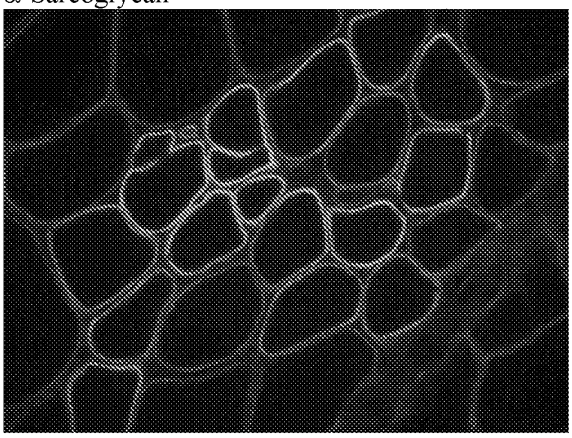

Alpha-Sarcoglycan Expression (IHC)
Subject 1
Subject 2
Subject 3
Pre-treatment
Post-treatment

Figure 10

β-Sarcoglycan



α-Sarcoglycan



Colocalization (Merge)

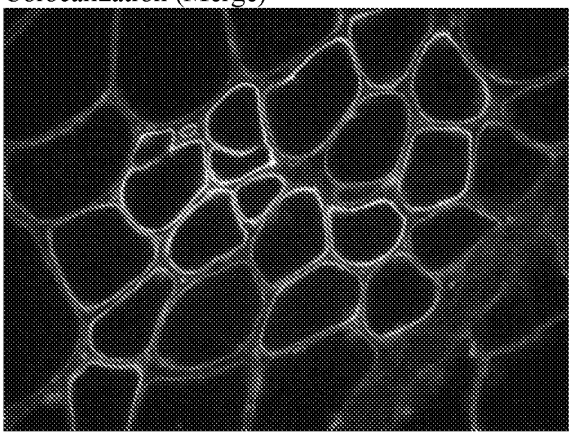
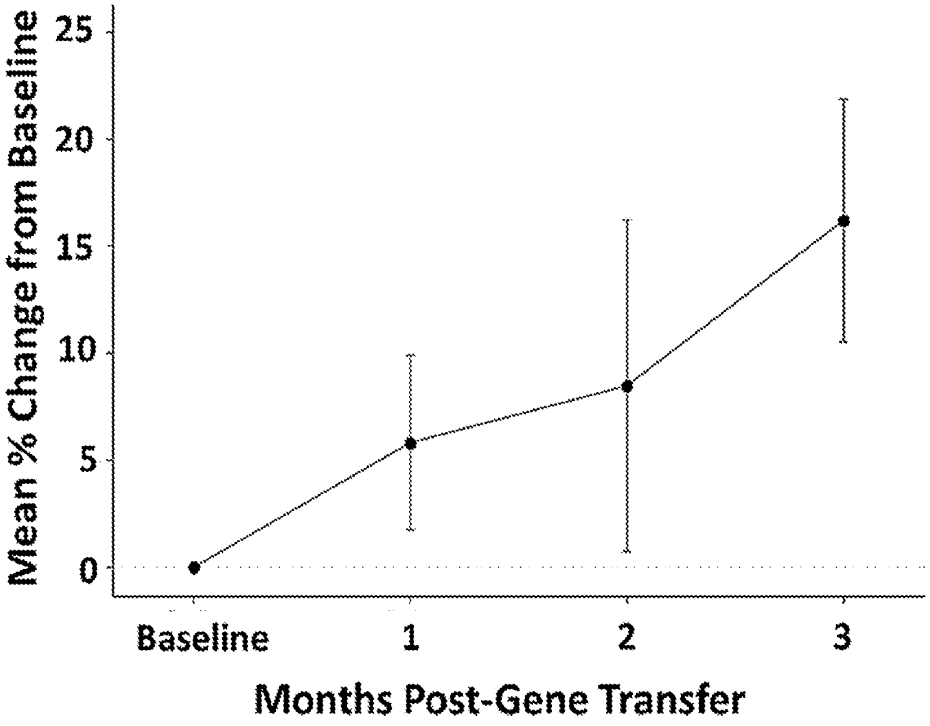


Figure 11


Mean % Change from Baseline
25
20
15
10
5
0
Baseline
1
2
3
Months Post-Gene Transfer

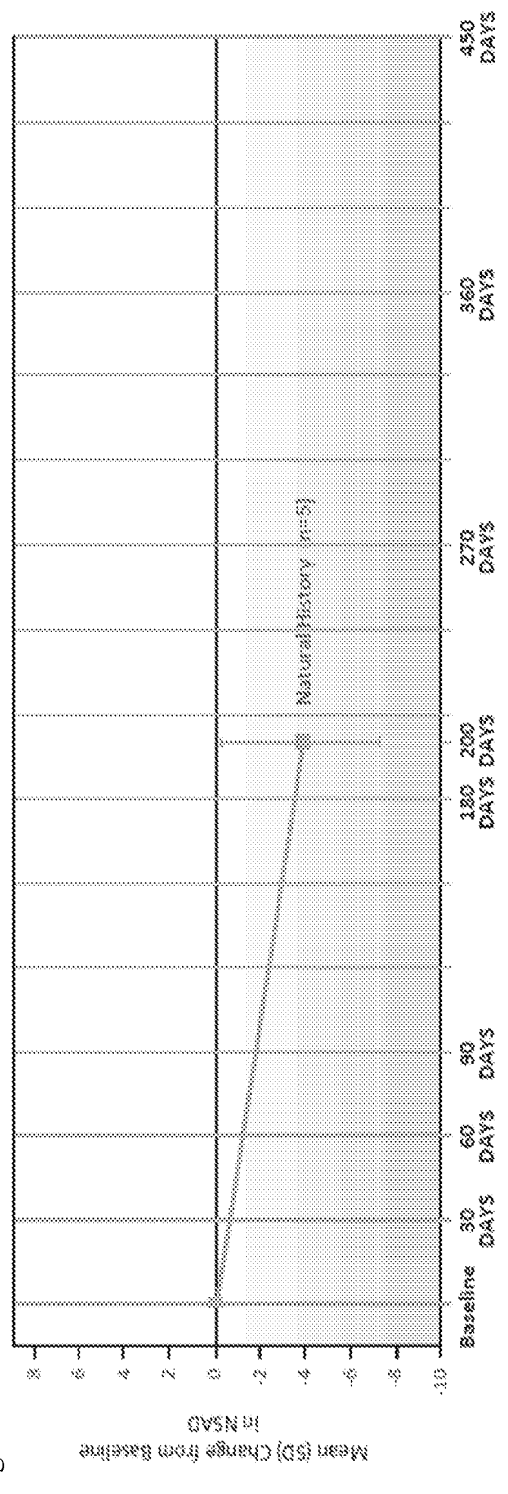



Figure 12A

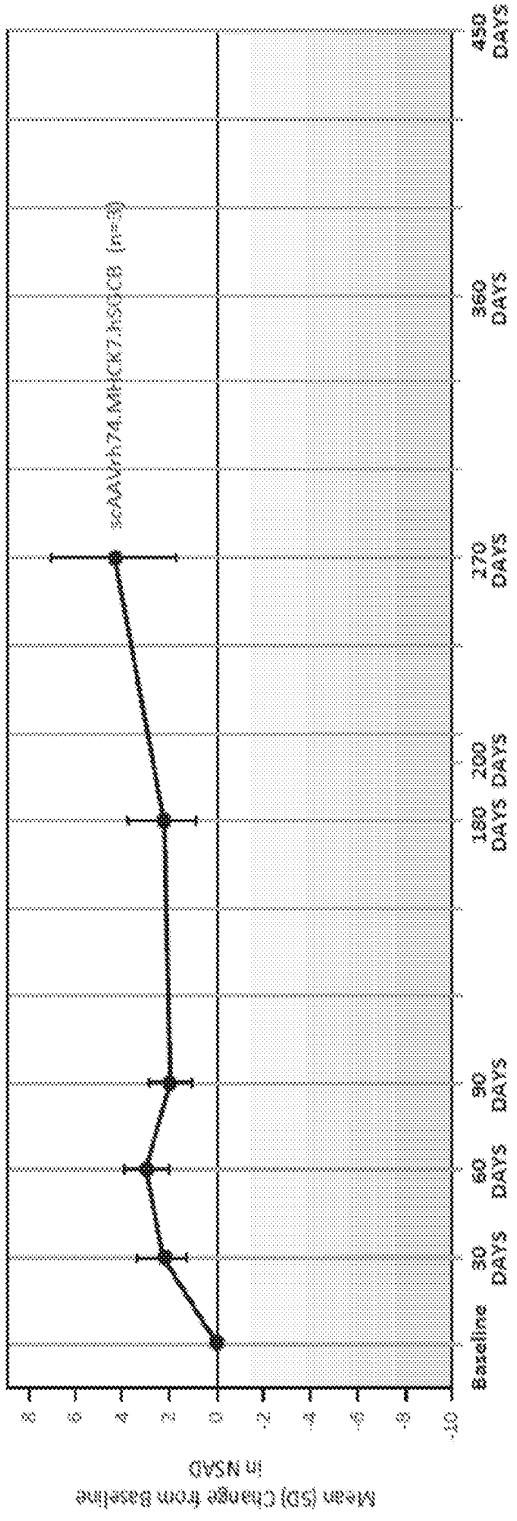



Figure 12B

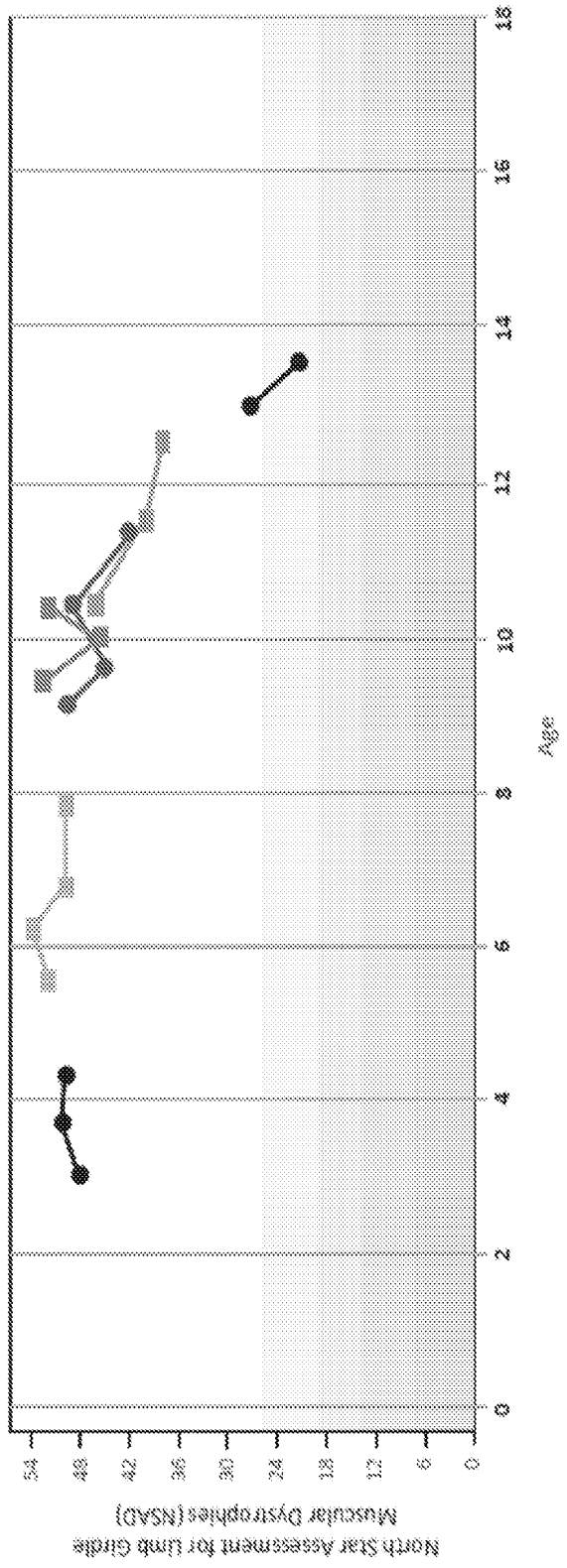
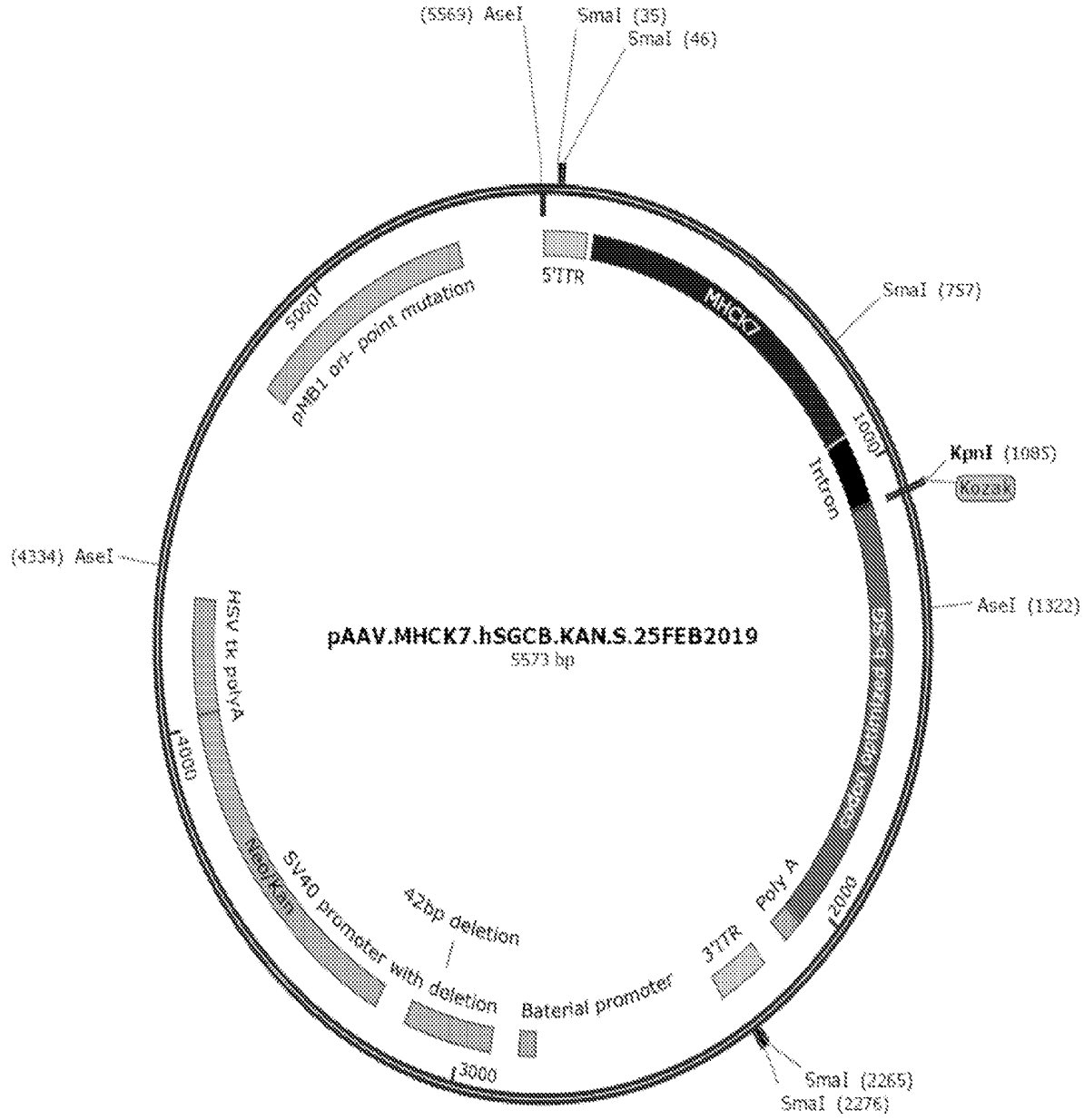

North Star Assessment for Limb Girdle
Muscular Dystrophies (NSAD)
54
48
42
36
30
24
18
12
6
0
0
2
4
6
8
10
12
14
16
18
Age

Figure 12C

Figure 13


(5569) AseI
SmaI (35)
SmaI (46)
5'ITR
MHCK7
SmaI (757)
1000
KpnI (1085)
Kozak
Intron
AseI (1322)
(4334) AseI
pAAV.MHCK7.hSGCB.KAN.S.25FEB2019
5573 bp
pMB1 ori- point mutation
5000
HSV TK polyA
4000
Kan/Neo
SV40 promoter with deletion
42bp deletion
3000
Baterial promoter
3'ITR
Poly A
2000
SmaI (2265)
SmaI (2276)