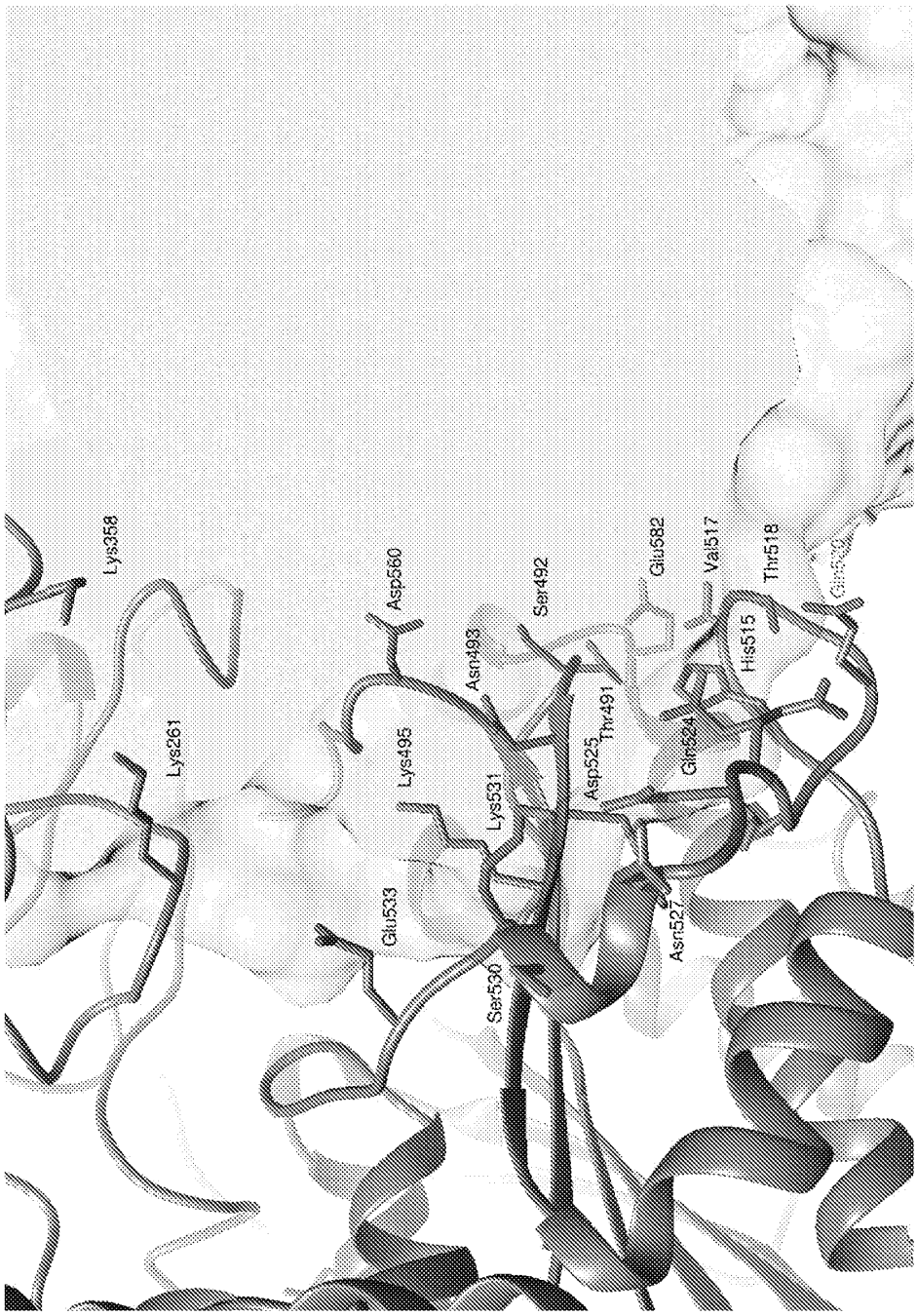
Lys358
Lys261
Asp560
Lys495
Asn493
Ser492
Glu582
Val517
Thr518
His515
Thr491
Asp525
Gln524
Lys531
Glu533
Asn527
Ser530

FIG. 1A

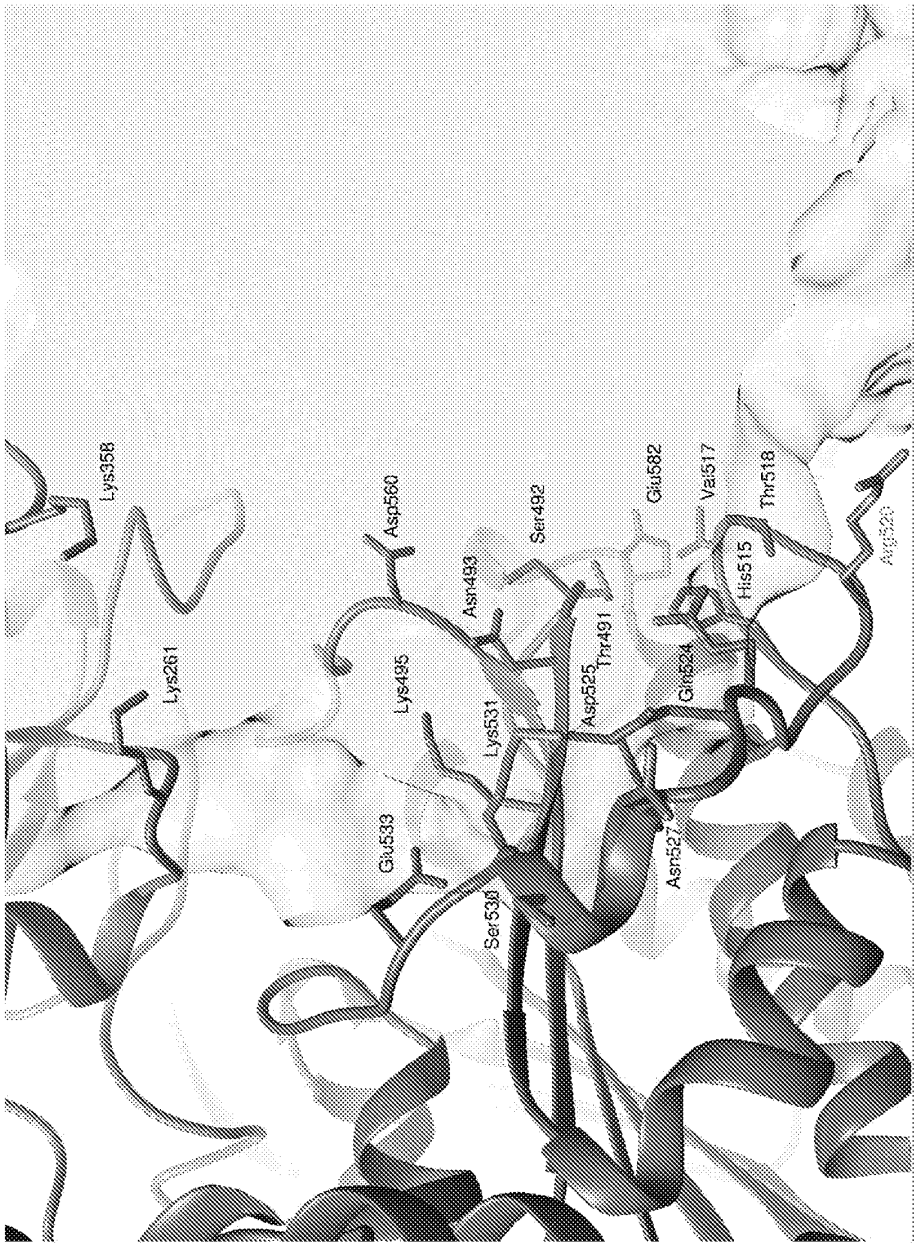
Lys358
Lys261
Asp560
Lys495
Asn493
Ser492
Glu582
Val517
Thr518
His515
Lys531
Asp525
Thr491
Glu524
Glu533
Asn527
Ser530

FIG. 1B

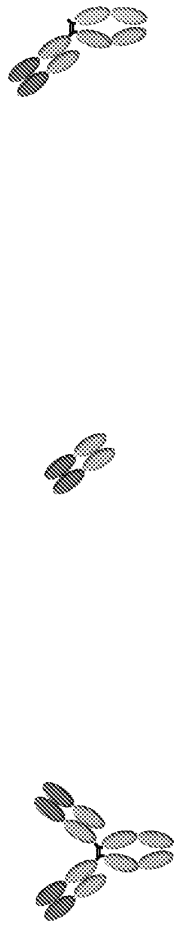
Anti-TfR mAb
Anti-TfR Fab
Anti-TfR Fab-FcOL

FIG. 2A


GAA
GAA
GAA
Fab-LC-GAA
Fab-FcOL-LC-GAA
Fab-FcOL-GAA
mAb-GAA

FIG. 2B

```
IGHV3_23_05                 EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEW
IGHJ6_01                    ----------------------------------------------
531 v1 VH                   EVQLLESGGGLVQPGGSLRLSCAASGYTFTRYWLNWVRQAPGKGLEW
531 v2 VH                   EVQLLESGGGLVQPGGSLRLSCAASGYTFTRYYLNWVRQAPGKGLEW

IGHV3_23_05 (cont'd)        VSAIYSSGSSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYY
IGHJ6_01 (cont'd)           ----------------------------------------------
531 v1 VH (cont'd)          IGMIDPSVSETHYADSVKGRATLSVDKSKNTAYLQMNSLRAEDTAVYY
531 v2 VH (cont'd)          IGMIDPSVSETHYADSVKGRATLSVDKSKNTAYLQMNSLRAEDTAVYY

IGHV3_23_05 (cont'd)        CAK---------------------- (SEQ ID NO:12)
IGHJ6_01 (cont'd)           -----YYYYYGMDVWGQGTTVTVSS (SEQ ID NO:14)
531 v1 VH (cont'd)          CSQIRLPYYYAMDSWGQGTTVTVSS (SEQ ID NO:17)
531 v2 VH (cont'd)          CSQIRLPYYYAMDSWGQGTTVTVSS (SEQ ID NO:18)
```

FIG. 3A

```
IGHV1_46_01                 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEW
IGHJ6_01                    ----------------------------------------------
531 v3 VH                   QVQLVQSGAEVKKPGASVKVSCKASDYTFTRYWLNWVRQAPGQGLEW
531 v4 VH                   QVQLVQSGAEVKKPGASVKVSCKASDYTFTRYWLNWVRQAPGQGLEW
531 v5 VH                   QVQLVQSGAEVKKPGASVKVSCKASGYTFTRYYLNWVRQAPGQGLEW

IGHV1_46_01 (cont'd)        MGIINPSGGSTSYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYY
IGHJ6_01 (cont'd)           ----------------------------------------------
531 v3 VH (cont'd)          IGMIDPSVSETHYAQKFQGRATLTVDKSTSTAYMELSSLRSEDTAVYY
531 v4 VH (cont'd)          MGMIDPSVSETHYAQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYY
531 v5 VH (cont'd)          IGMIDPSVSETHYAQKFQGRATLTVDKSTSTAYMELSSLRSEDTAVYY

IGHV1_46_01 (cont'd)        CAR---------------------- (SEQ ID NO:13)
IGHJ6_01 (cont'd)           -----YYYYYGMDVWGQGTTVTVSS (SEQ ID NO:14)
531 v3 VH (cont'd)          CSQIRLPYYYAMDSWGQGTTVTVSS (SEQ ID NO:19)
531 v4 VH (cont'd)          CSQIRLPYYYAMDSWGQGTTVTVSS (SEQ ID NO:20)
531 v5 VH (cont'd)          CSQIRLPYYYAMDSWGQGTTVTVSS (SEQ ID NO:21)
```

FIG. 3B

```
IGKV1_39_01_germline           DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQ
IGKJ4_01_germline              ---------------------------------------
531 v1 VL                      DIQMTQSPSSLSASVGDRVTITCRASQDINSFLNWYQQ
531 v2 VL                      DIQMTQSPSSLSASVGDRVTITCRASQDISSFLNWYQQ
531 v3 VL                      DIQMTQSPSSLSASVGDRVTITCRASQDISSFLNWYQQ
531 v4 VL                      DIQMTQSPSSLSASVGDRVTITCRASQDISSFLNWYQQ

IGKV1_39_01_germline (cont'd)  KPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISS
IGKJ4_01_germline (cont'd)     ---------------------------------------
531 v1 VL (cont'd)             KPGKAVKLLIYYTSRLQSGVPSRFSGSGSGTDYTLTISS
531 v2 VL (cont'd)             KPGKAVKLLIYYTSRLQSGVPSRFSGSGSGTDYTLTISS
531 v3 VL (cont'd)             KPGKAVKLLIYYTSRLQSGVPSRFSGSGSGTDFTLTISS
531 v4 VL (cont'd)             KPGKAPKLLIYYTSRLQSGVPSRFSGSGSGTDYTLTISS

IGKV1_39_01_germline (cont'd)  LQPEDFATYYCQQSYSTP---------- (SEQ ID NO:15)
IGKJ4_01_germline (cont'd)     ------------------LTFGGGTKVEIK (SEQ ID NO:16)
531 v1 VL (cont'd)             LQPEDFATYFCQQGNTLPRTFGGGTKVEIK (SEQ ID NO:22)
531 v2 VL (cont'd)             LQPEDFATYFCQQGNTLPRTFGGGTKVEIK (SEQ ID NO:23)
531 v3 VL (cont'd)             LQPEDFATYFCQQGNTLPRTFGGGTKVEIK (SEQ ID NO:24)
531 v4 VL (cont'd)             LQPEDFATYYCQQGNTLPRTFGGGTKVEIK (SEQ ID NO:25)
```

FIG. 3C

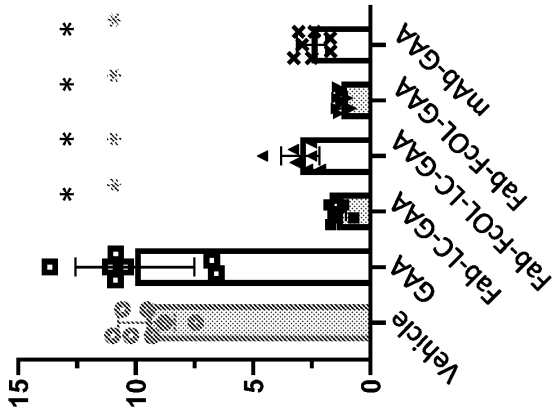
15
10
5
0
Vehicle
GAA
Fab-LC-GAA
Fab-FCOL-LC-GAA
Fab-FCOL-GAA
mAb-GAA

FIG. 4B

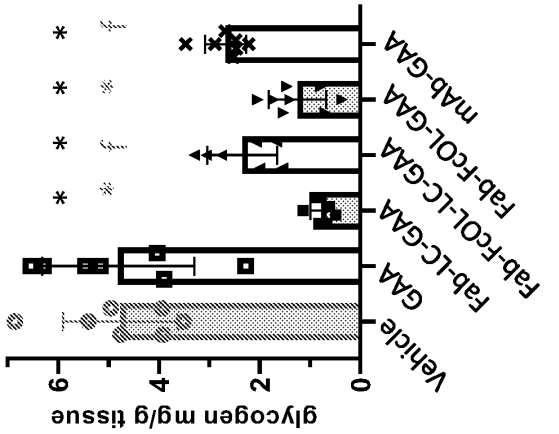
glycogen mg/g tissue
6
4
2
0
Vehicle
GAA
Fab-LC-GAA
Fab-FCOL-LC-GAA
Fab-FCOL-GAA
mAb-GAA

FIG. 4A

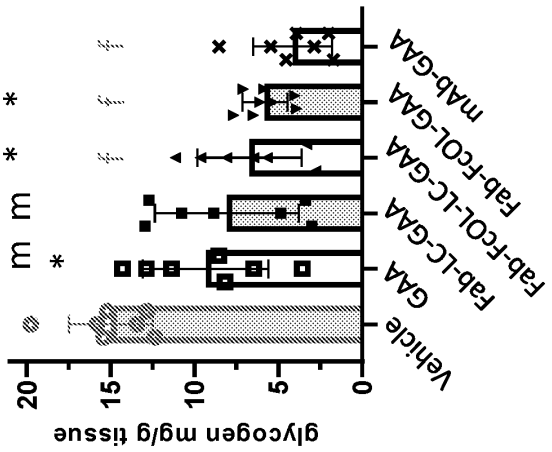
glycogen mg/g tissue
0
5
10
15
20
Vehicle
GAA
Fab-LC-GAA
Fab-FCOL-LC-GAA
Fab-FCOL-GAA
mAb-GAA

FIG. 4D

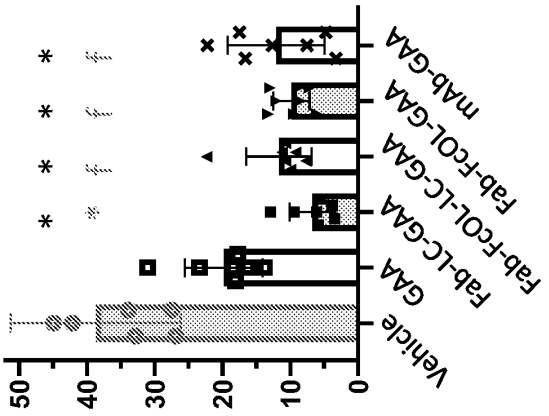
0
10
20
30
40
50
Vehicle
GAA
Fab-LC-GAA
Fab-FCOL-LC-GAA
Fab-FCOL-GAA
mAb-GAA

FIG. 4C

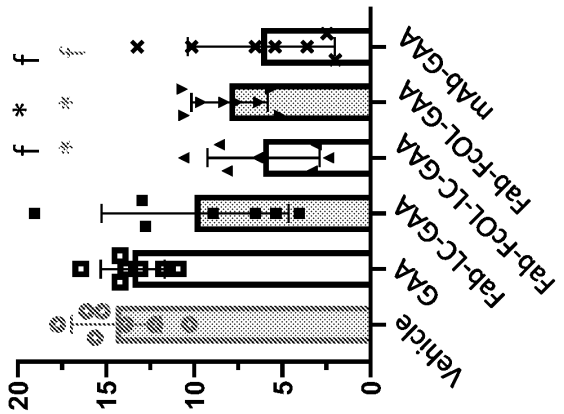

FIG. 4G

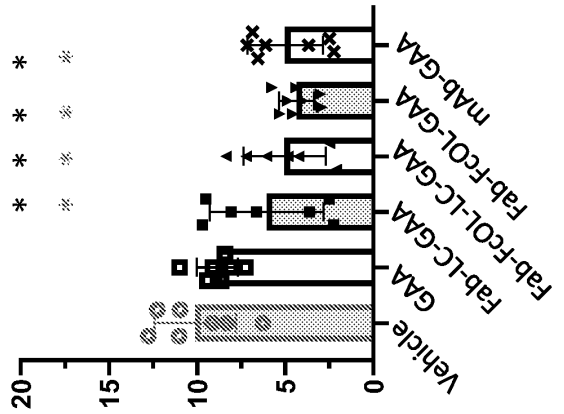

FIG. 4F

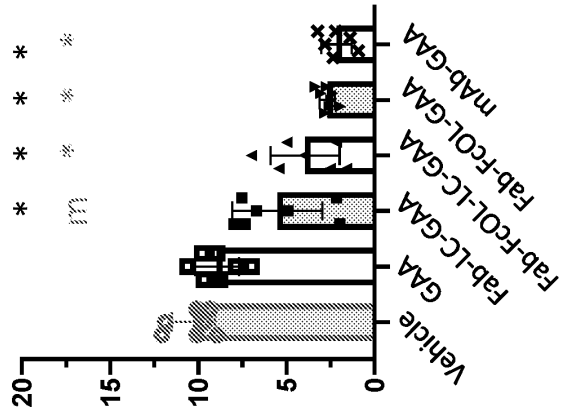

FIG. 4E

Fab-FcOL-GAA Light Chain:

DIQMTQSPSSLSASVGDRVTITCRAS**QDISSF**LNWYQQKPGKAPKLLIY**YTS**RLQSGVPSRFSGSGSGTDYTLTISSLQPEDFATYYC
QQGNTLPRTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:31)

Fab-FcOL-GAA Heavy Chain_HOLE

QVQLVQSGAEVKKPGASVKVSCKAS**GYTFTRYY**LNWVRQAPGQGLEWIGM**IDPSVSET**HYAQKFQGRATLTVDKSTSTAYMELSSLRS
EDTAVYYC**SQIRLPYYYAMDS**WGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC
VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNNASRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV***C***
TLPPSRDELTKNQVSL***S***C***A***VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL***V***SKLTVDKSRWQQGNVFSCSVMHEALHN**RF**T
QKSLSLSPG (SEQ ID NO:33)

Fab-FcOL-GAA FcOL_KNOB+GAA

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNNASRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP***C***RDELTKNQVSL***W***CLVKGFYPSDIAVEWESNGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGQQGASRPGPRDAQAHPGRPRAVPTQCDVPPNSRF
DCAPDKAITQEQCEARGCCYIPAKQGLQGAQMGQPWCFFPPSYPSYKLENLSSSEMGYTATLTRTTPTFFPKDILTLRLDVMMETENR
LHFTIKDPANRRYEVPLETPRVHSRAPSPLYSVEFSEEPFGVIVHRQLDGRVLLNTTVAPLFFADQFLQLSTSLPSQYITGLAEHLSP
LMLSTSWTRITLWNRDLAPTPGANLYGSHPFYLALEDGGSAHGVFLLNSNAMDVVLQPSPALSWRSTGGILDVYIFLGPEPKSVVQQY
LDVVGYPFMPPYWGLGFHLCRWGYSSTAITRQVVENMTRAHFPLDVQWNDLDYMDSRRDFTFNKDGFRDFPAMVQELHQGGRRYMMIV
DPAISSSGPAGSYRPYDEGLRRGVFITNETGQPLIGKVWPGSTAFPDFTNPTALAWWEDMVAEFHDQVPFDGMWIDMNEPSNFIRGSE
DGCPNNELENPPYVPGVVGGTLQAATICASSHQFLSTHYNLHNLYGLTEAIASHRALVKARGTRPFVISRSTFAGHGRYAGHWTGDVW
SSWEQLASSVPEILQFNLLGVPLVGADVCGFLGNTSEELCVRWTQLGAFYPFMRNHNSLLSLPQEPYSFSEPAQQAMRKALTLRYALL
PHLYTLFHQAHVAGETVARPLFLEFPKDSSTWTVDHQLLWGEALLITPVLQAGKAEVTGYFPLGTWYDLQTVPIEALGSLPPPPAAPR
EPAIHSEGQWVTLPAPLDTINVHLRAGYIIPLQGPGLTTTESRQQPMALAVALTKGGEARGELFWDDGESLEVLERGAYTQVIFLARN
NTIVNELVRVTSEGAGLQLQKVTVLGVATAPQQVLSNGVPVSNFTYSPDTKVLDICVSLLMGEQFLVSWC (SEQ ID NO:37)

FIG. 5

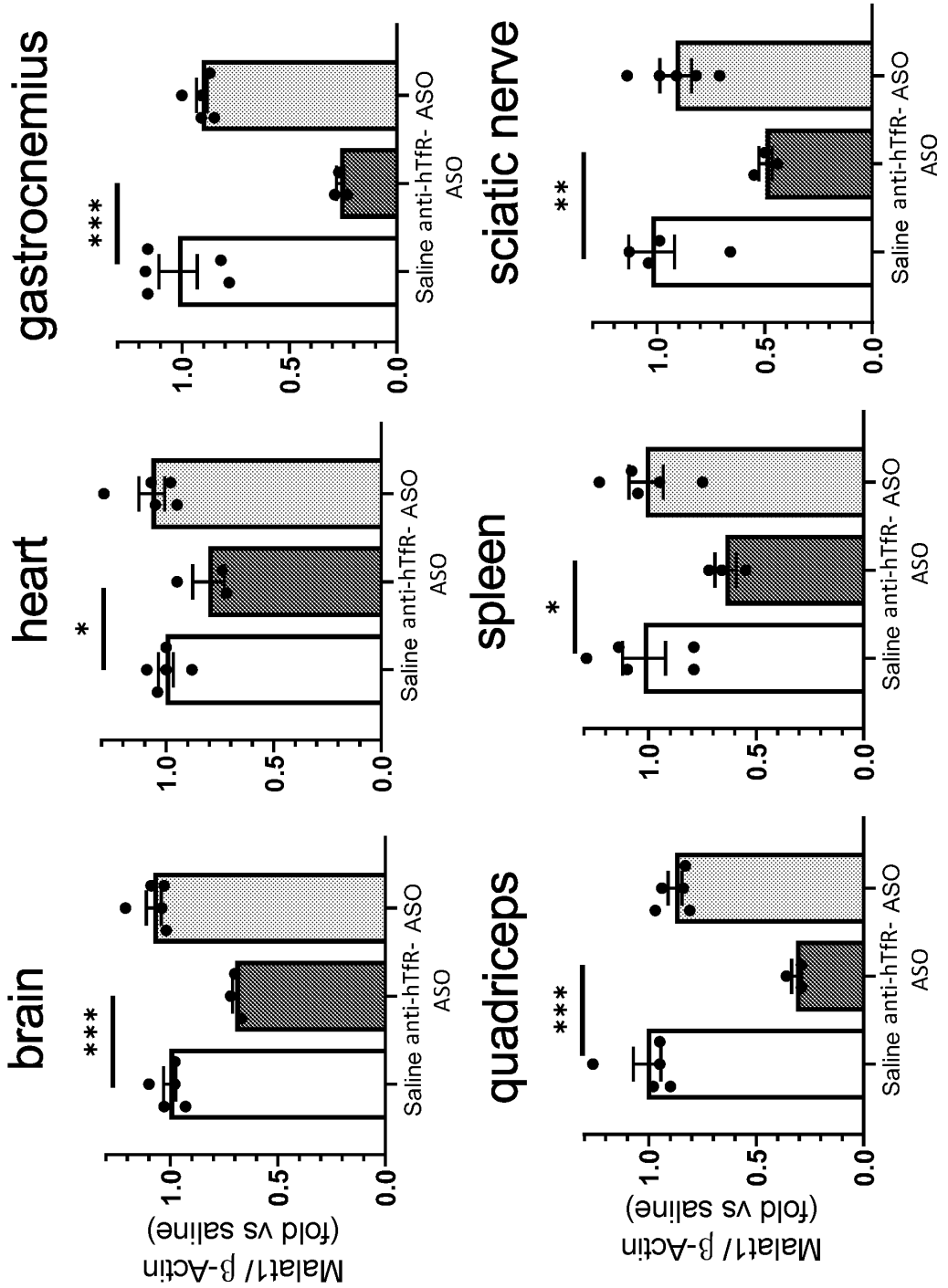
brain
heart
gastrocnemius
quadriceps
spleen
sciatic nerve
Malat1/ β-Actin
(fold vs saline)
1.0
0.5
0.0
***
*
**
Saline
anti-hTfR- ASO
ASO

FIG. 6