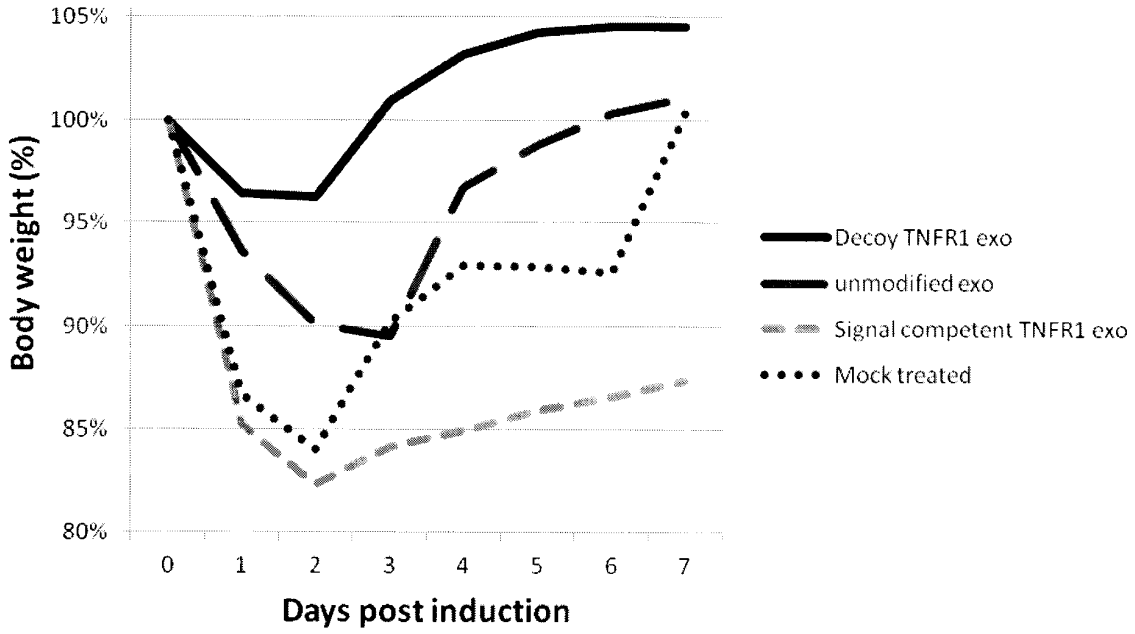

105%
100%
95%
90%
85%
80%
Body weight (%)
0
1
2
3
4
5
6
7
Days post induction
Decoy TNFR1 exo
unmodified exo
Signal competent TNFR1 exo
Mock treated

Figure 1.

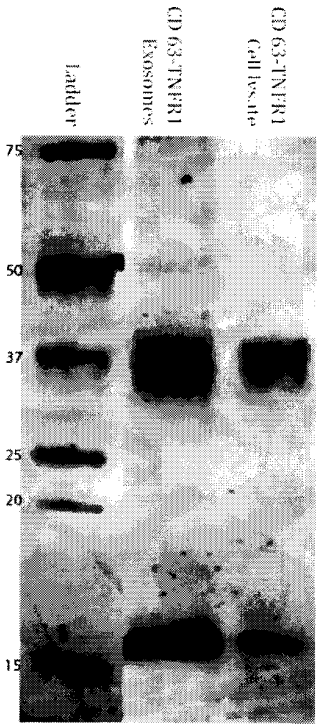

Ladder
CD 63-TNFR1 Exosomes
CD 63-TNFR1 Cell lysate
75
50
37
25
20
15

Figure 2.

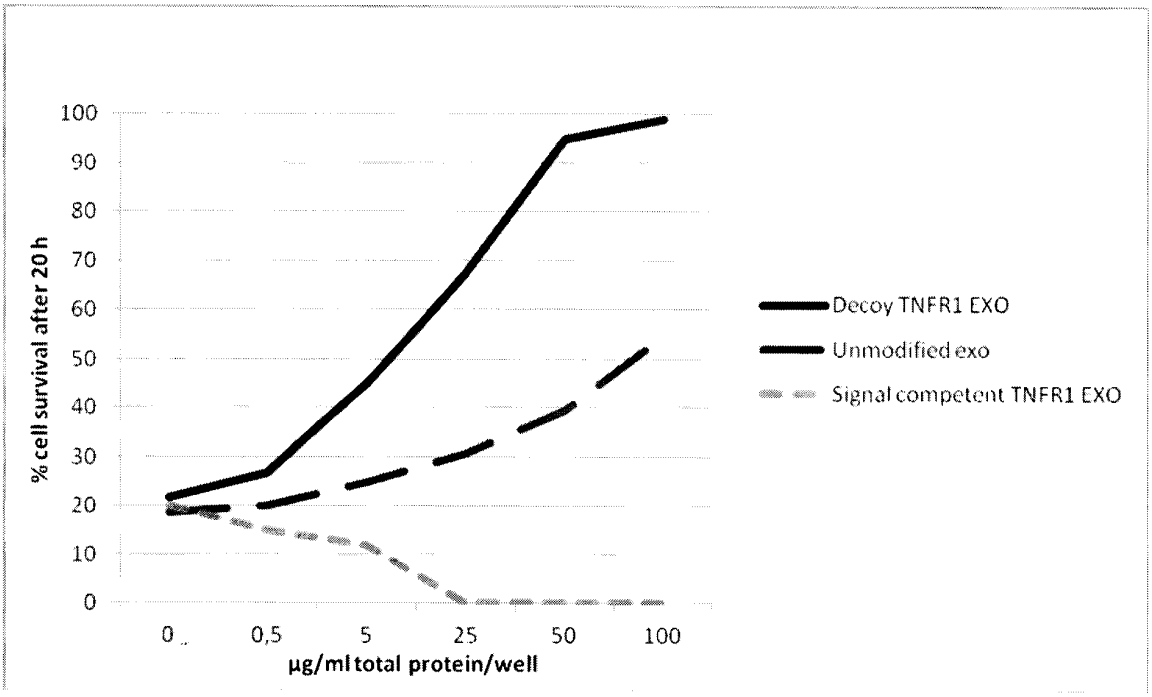

100
90
80
70
60
50
40
30
20
10
0
% cell survival after 20 h
0
0,5
5
25
50
100
µg/ml total protein/well
Decoy TNFR1 EXO
Unmodified exo
Signal competent TNFR1 EXO

Figure 3.

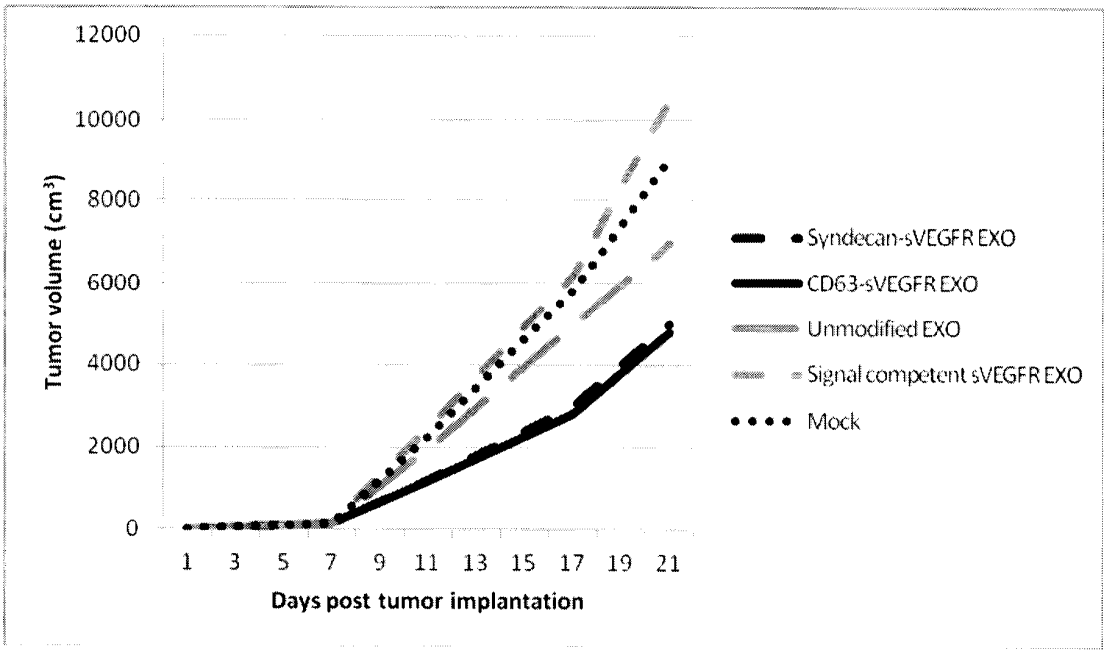

12000
10000
8000
6000
4000
2000
0
Tumor volume (cm³)
1 3 5 7 9 11 13 15 17 19 21
Days post tumor implantation
Syndecan-sVEGFR EXO
CD63-sVEGFR EXO
Unmodified EXO
Signal competent sVEGFR EXO
Mock

Figure 4.

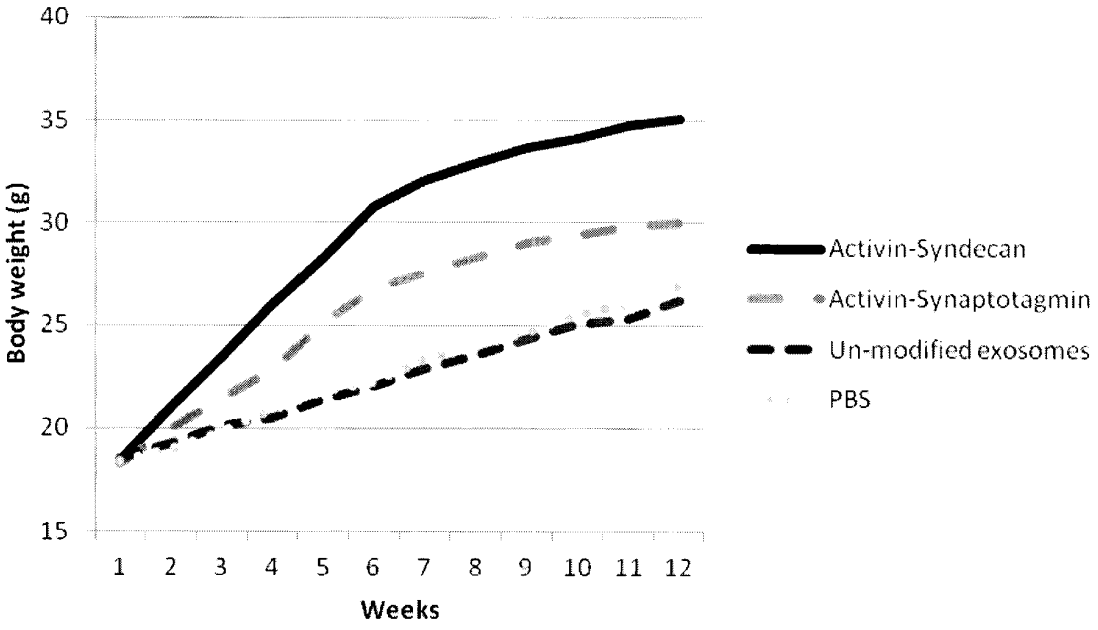

40
35
30
25
20
15
Body weight (g)
1
2
3
4
5
6
7
8
9
10
11
12
Weeks
Activin-Syndecan
Activin-Synaptotagmin
Un-modified exosomes
PBS

Figure 5.

>murine CD63 (bold are sequences removed from CD63 to insert the constructs)

MAVEGGMKCVKFLLVVLLAFCAGAVSLIACGAVQVVLNQAITEICARSLLFVQIIAVGAFLFLVAF
VGCCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSEFNKSFQQQMQNYLKDNKTATILDK
LQKENNCCGASNYTDWENIPGMAKDRVPDSCCINITVGCGNDFKESTITKGCVETIAKWLRKNILLVA
AAALGIAFVEVLGIIFSICLVNSIRSPEVM

Below all parts in bold represent the insert (i.e. either TNFR1 or ACVR2b)

>psTNFR1a-Syt7-His TNFR1-Synaptotagmin (with His tag)

MAPGIHPSGVTGLVPSLGDREKRDSLCPQGKYVHSKNNSICCTKCHKGTYLVSDCPSPGRDTVCRECEK
GTFTASQNYLRQCLSCKTCRKEMSQVEISPCQADKDTVCGCKENQFQRYLSETHFQCVDCSPCFNGTVT
IPCKETQNTVCNCHAGFFLRESECVPCSHCKKNEECMKLCLPPPLANVTNPQDSGTSGGAEWEMDFTFITVETTNQDNKTITIAVPIQATHDGSCGDPNA
SAKIMIQFGFAVSWAVNFTKEASHVSIHDITVLSVNTSDSTVFPGAVAMGVHTVNDPENFNVELDVTFHC
NGVLTDNLTPVVQKVWGIHLQAFVQNGTVSRNEQVCEEDQLPTTVAPIIHTTAPSTTTILTPDSIPTPT
PTPTPTVGNVSIRNGNTTCLLATMGLQLNITEEAVFFIVDNNPATTNFDGSCQPQSAQLRLNNSQIKVLD
IFIFAVDKEARFYLKEVKVDVYLLANGSAFVSMYVLSFWDAPLGSSVMQNKEQVLSVSPAFQDNEFNLN
VQFFNVTNGQVSTAQEDSLDDDTILIPITVGAGLSGLIIVIVIAYLIGRRKTYAGYQTL

>pmCD63-sTNFR1a
MAVEGGMKCVKFLLVVLLAFCAGAVSLIACGAVQVVLNQAITEICARSLLFVQIIAVGAFLFLVAF
VGCCGACKENYCLMITFAIFLSLIMLVEVAVAIAGYVFRDQVKSEFNKSFQQQMQNYLKDNKTATILDK
LQKENNCCGASNYTDWENIPGMAKDRVPDSCCINITVGCGNDFKESTITKGCVETIAKWLRKNILLVAAAALGIAFVEVLGIIFSICLV
KSIRSGYEVMD

>pSTNFR1a-Syt7-eGFP TNFR1-Synaptotagmin (with EGFP)
MARGIHPSGVTGLVPSLGDREKRDSLCPQGKYVHSKNNSICCTKCHKGTYLVSDCPSPGRDTVCRECEK
GTFTASQNYLRQCLSCKTCRKEMSQVEISPCQADKDTVCGCKENQFQRYLSETHFQCVDCSPCFNGTVT
IPCKETQNTVCNCHAGFFLRESECVPCSHCKKNEECMKLCLPPPLANVTNPQDSGTSGGGSMVRDPEAA
SPGAPTPDVLLVSALITVSLSVTIVLCGLCHWCQRKLGKRVKKSLETVGIEQLEVATMVSKGEELFTGV
VPILVELDGDVNGHKFSVSGEGEGDATYGKLTLKFICTTGKLPVPWPTLVTTLTYGVQCFSRYPDHMKQ
HDFFKSAMPEGYVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNILGHKLEYNYNSHN
VYIMADKQKNGIKVNFKIRHNIEDGSVQLADHYQQNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHM
VLLEFVTAAGITLGMDELYK

hACVR2b-Syndecan Activin-Syndecan construct
MRAPAFWVALALLWGSLCAGSGRGEAETRECIYYNANWELERTNQSGLERCEGEQDKRLHCYASWRNSSG
TIELVKKGCWLDDFNCYDRQECVATEENPQVYFCCCEGNFCNERFTHLPEAGGPEVTYEPPPTAPTLLT
VLAVSLLPIGGLSLIVLLAFWMYRHRKSGGKGDEGSVSLEEPKQANGGALMDETMQLEEPVAGGHH
HHHHEPSMGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLKFICTTGKLPVPWPTLVTTL
TYGVQCFSRYPDHMKQHDFFKSAMPEGYVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKED
GNILGHKLEYNYNSHNVYIMADKQKNGIKVNFKIRHNIEDGSVQLADHYQQNTPIGDGPVLLPDNHYLS
TQSALSKDPNEKRDHMVLLEFVTAAGITHGMDELYK

>pLamp2b-hACVR2b Lamp2b-Activin
MCLSFVNGAKLILIFLFLSAVQSNALIVNLTDSNGTCLYARGSGRGEAETRECIYYNANWELERTNQSG
LERCEGEQDKRLHCYASWRNSSGTIELVKKGCWLDDFNCYDRQECVATEENPQVYFCCCEGNFCNERFT
HLPEAGGPEVTYEPPPTAPTLLTSGGAEWEMDFTFITVETTNQDNKTITIAVPIQATHDGSCGDPNSA
SAKIMIQFGFAVSWAVNFTKEASHVSIHDITVLSVNTSDSTVFPGAVAMGVHTVNDPENFNVELDVTFHC
YLTYNLTPVVQKVWGIHLQAFVQNGTVSRNEQVCEEDQLPTTVAPIIHTTAPSTTTILTPDSIPTPTPT
PTPTVGNVSIRNGNTTCLLATMGLQLNITEEAVFFIVDNNPATTNFDGSCQPQSAQLRLNNSQIKVLDF
IFAVDKEARFYLKEVKVDVYLLANGSAFVSMYVLSFWDAPLGSSVMQNKEQVLSVSPAFQDNEFNLNVQ
FFNVTNGQVSTAQEDSLDDDTILIPITVGAGLSGLIIVIVIAYLIGRRKTYAGYQTL

>phACVR2b-Syt7-His Activin-Synaptotagmin
MARGSGRGEAETRECIYYNANWELERTNQSGLERCEGEQDKRLHCYASWRNSSGTIELVKKGCWLDDFN
CYDRQECVATEENPQVYFCCCEGNFCNERFTHLPEAGGPEVTYEPPPTAPTLLTSGGLYRDPEAASPGA
PTPDVLLVSALITVSLSVTIVLCGLCHWCQRKLGNRVKNSLETVGTPDSHHHHHHGNLVWI

Figure 6.

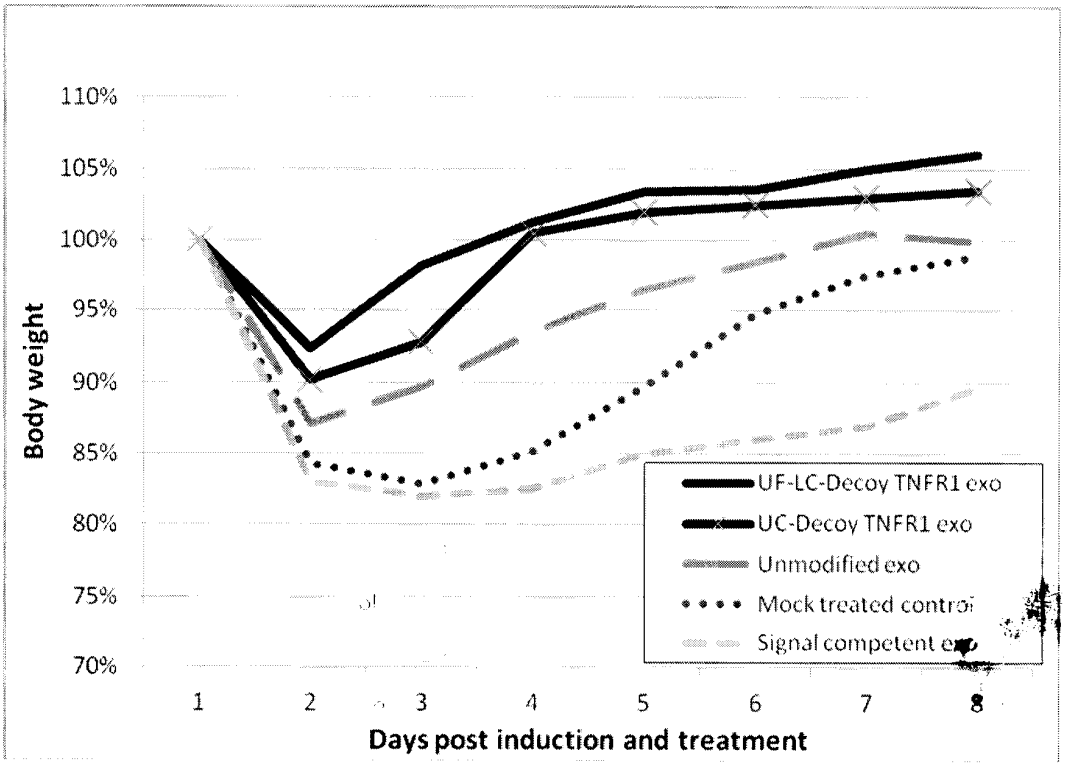

110%
105%
100%
95%
90%
85%
80%
75%
70%
Body weight
1
2
3
4
5
6
7
8
Days post induction and treatment
UF-LC-Decoy TNFR1 exo
UC-Decoy TNFR1 exo
Unmodified exo
Mock treated control
Signal competent exo

Figure 7.

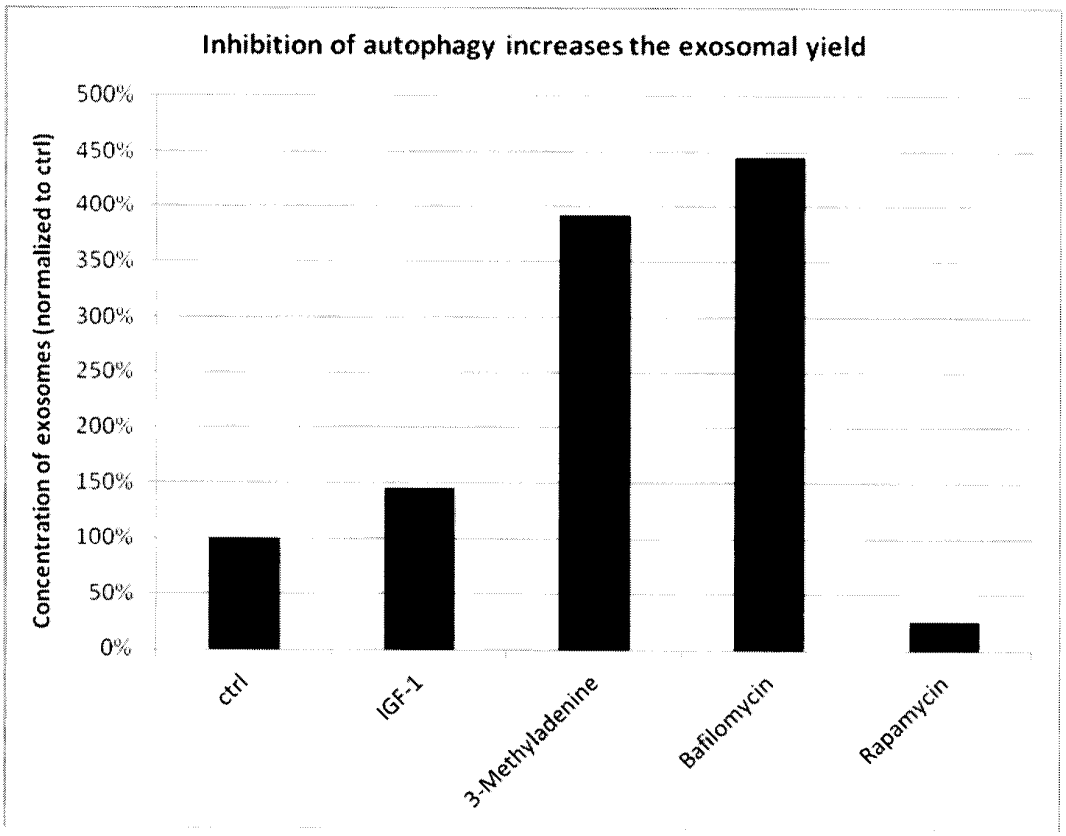

Inhibition of autophagy increases the exosomal yield
Concentration of exosomes (normalized to ctrl)
500%
450%
400%
350%
300%
250%
200%
150%
100%
50%
0%
ctrl
IGF-1
3-Methyladenine
Bafilomycin
Rapamycin

Figure 8.

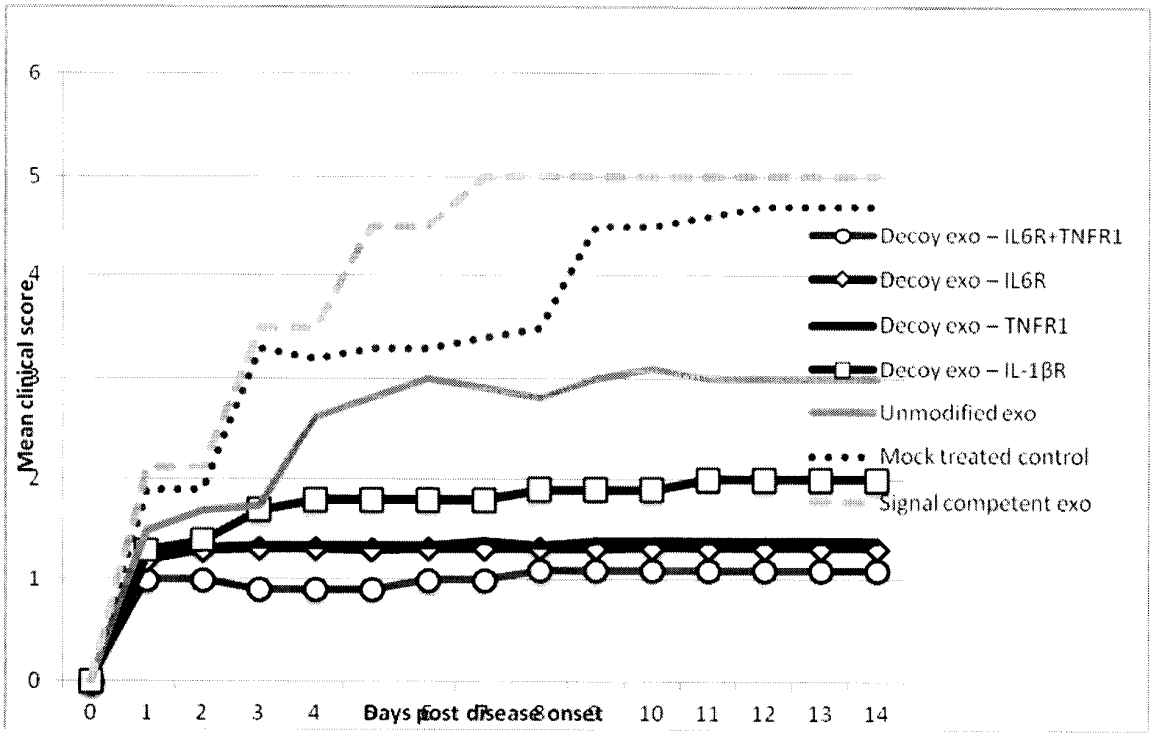

Mean clinical score
Days post disease onset
Decoy exo – IL6R+TNFR1
Decoy exo – IL6R
Decoy exo – TNFR1
Decoy exo – IL-1βR
Unmodified exo
Mock treated control
Signal competent exo

Figure 9.

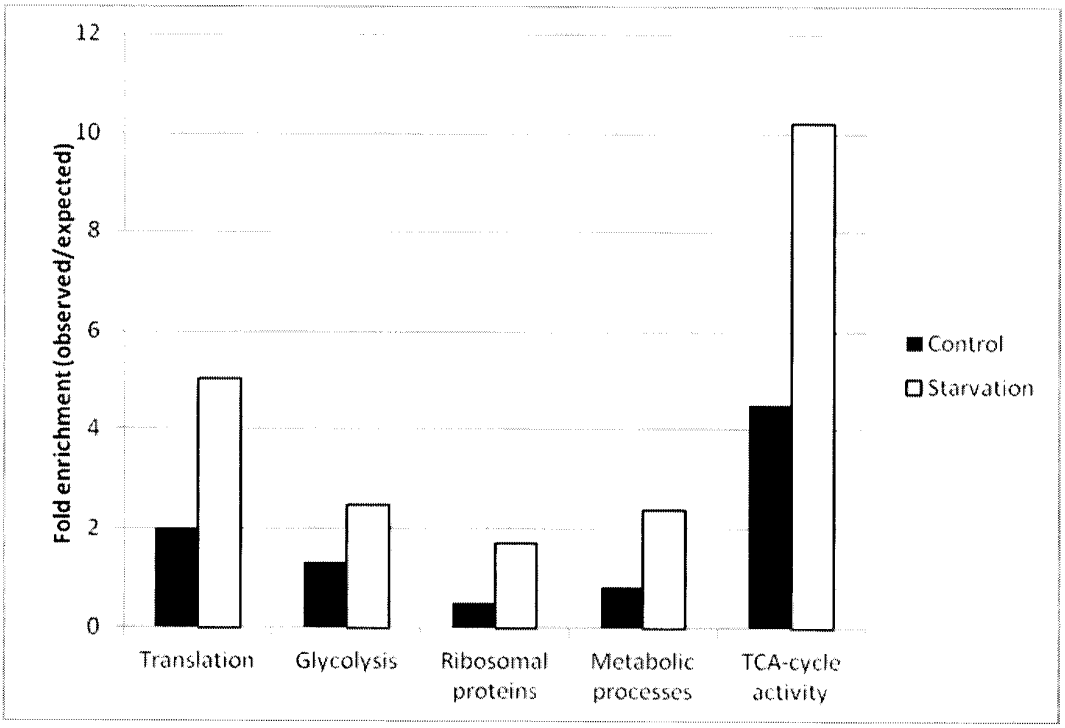

12
10
8
6
4
2
0
Fold enrichment (observed/expected)
Translation
Glycolysis
Ribosomal proteins
Metabolic processes
TCA-cycle activity
Control
Starvation

Figure 10.