

		H8-IL21-C01	H8-IL21-C03	H8-IL21-C04	H8-IL21-C06	H8-IL21-C07	H8-IL21-C08	H8-IL21-C11	H8-IL21-C13
	Ni-HisTrap	V	V	X	X	V	V	V	V
Expi293	Superdex 75 (SEC)	V	V	X	X	V	V	V	V
	Final SDS-PAGE	V	V	X	X	V	V	V	V
CHO-S	Ni-HisTrap	V	V	V	V	V	V	V	V
	Superdex 75 (SEC)	V	V	X	V	V	V	V	X
	Final SDS-PAGE	V	V	X	V	V	V	V	X

FIG. 1

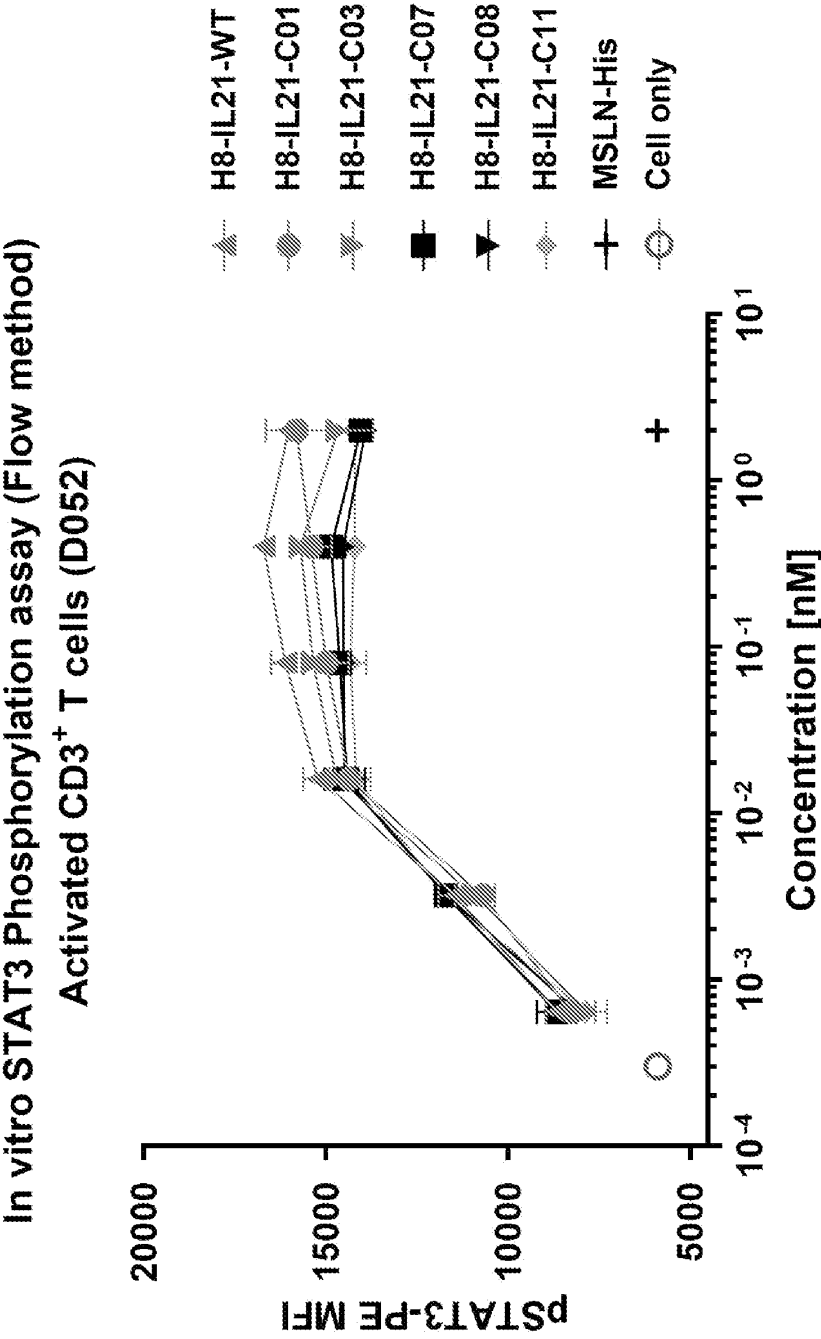


FIG. 2A

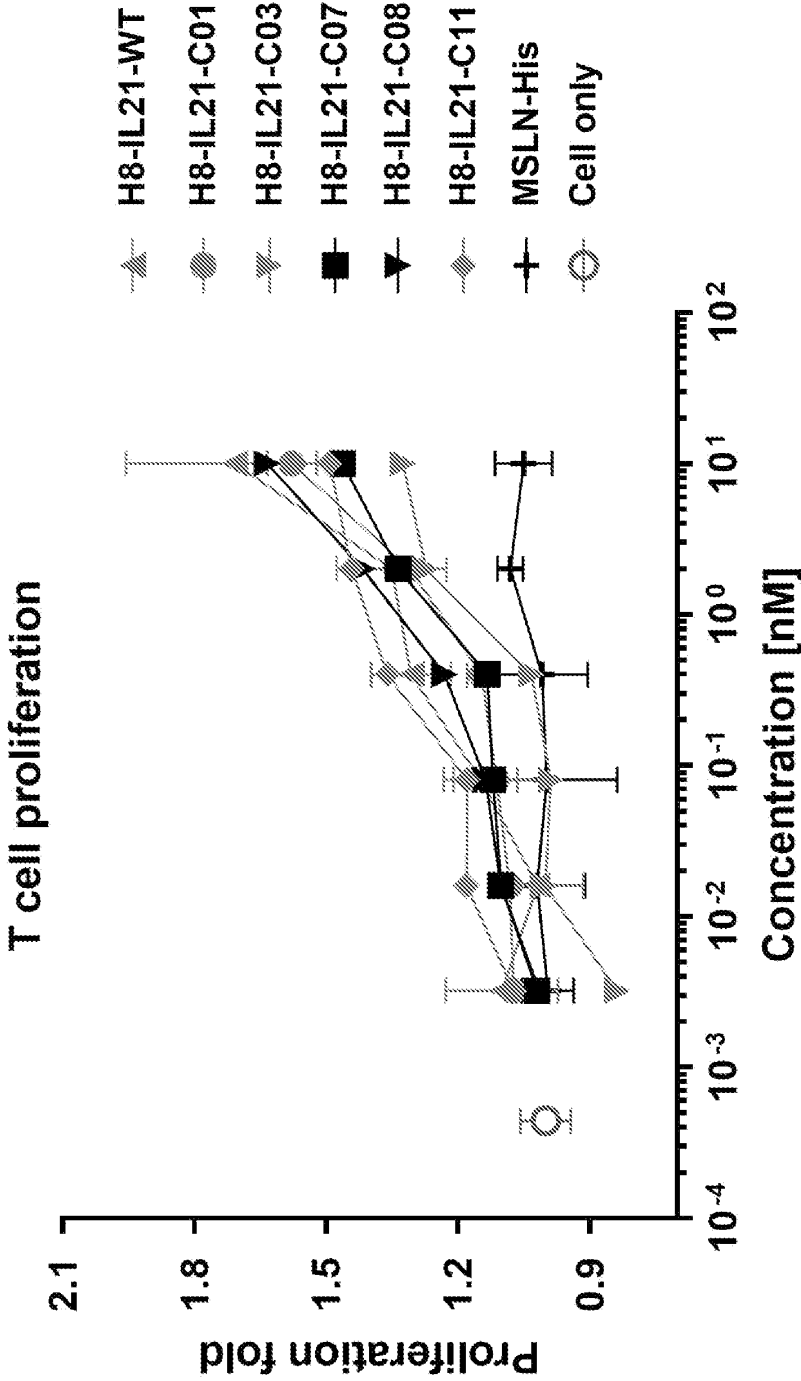


FIG. 2B

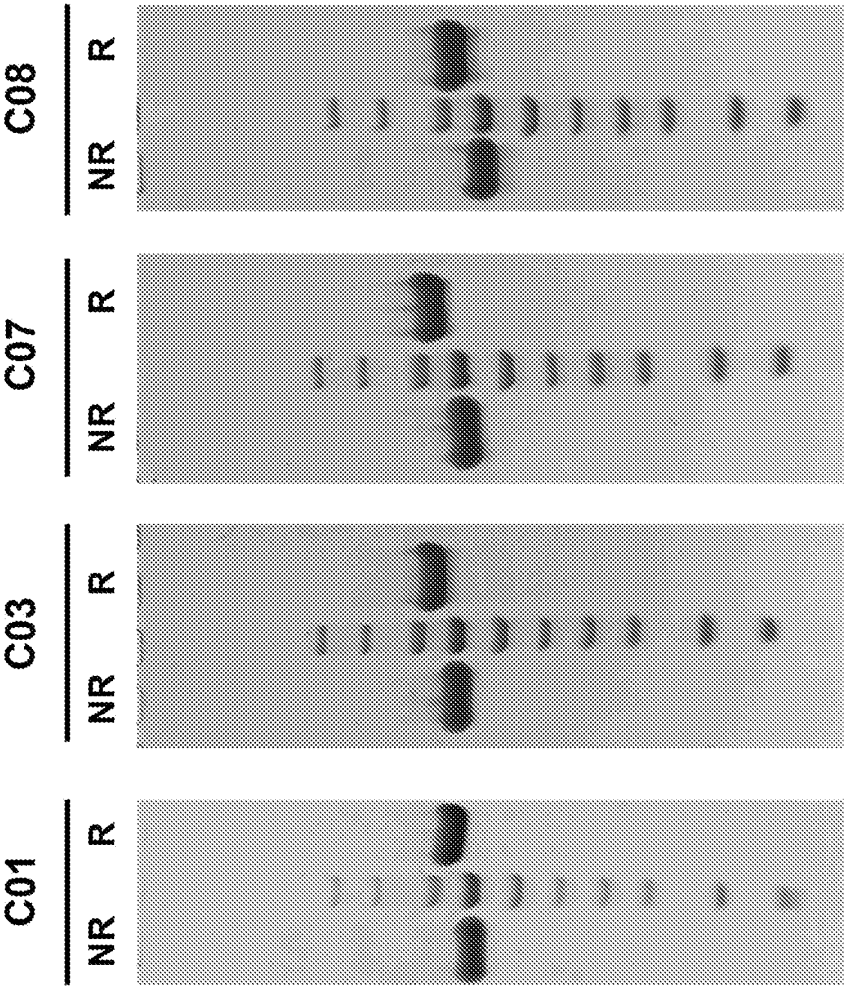


FIG. 3A

Protein	Theoretical M.W.	pI	HMW%	Major%	LMW%
HSA-IL21-WT (Expi293)	84,697	6.53	3.726	96.274	0.000
HSA-IL21-C01 (Expi293)	84,674	6.53	1.349	98.651	0.000
HSA-IL21-C03 (Expi293)	84,676	6.47	1.985	98.015	0.000
HSA-IL21-C07 (Expi293)	84,933	6.53	2.016	97.984	0.000
HSA-IL21-C08 (Expi293)	84,628	6.47	1.535	98.465	0.000

FIG. 3B

		ISOTHERMAL (25°C)				THERMO RAMP (25-85°C)			
Sample	No.	Radius (nm)	%PD	MW-S (kDa)	Radius (nm)	MW-S (kDa)	T _{agg} (°C)	T _{onset} (°C)	
	WT	5.29 ±0.06	27.4 ±9.22	87.8±5.14	6.74 ±0.02	96.7 ±2.83	56.23 ±1.01	59.44 ±0.09	
	C01	6.32 ±0.45	Multimodal	120.5 ±4.80	12.34 ±0.42	174.6 ±5.85	59.77 ±0.71	66.28 ±0.29	
	C03	4.71 ±0.04	19.6 ±1.09	75.9 ±2.11	5.65 ±0.05	81.7 ±9.86	61.09 ±0.12	62.51 ±1.55	
	C07	4.39 ±0.06	7.8 ±1.34	68.3 ±1.19	5.33 ±0.04	79.2 ±5.87	63.56 ±1.27	65.47 ±0.18	
	C08	4.50 ±0.00	12.0 ±1.77	70.6 ±1.44	5.56 ±0.08	82.0 ±2.03	61.02 ±0.87	63.92 ±0.09	

FIG. 3C

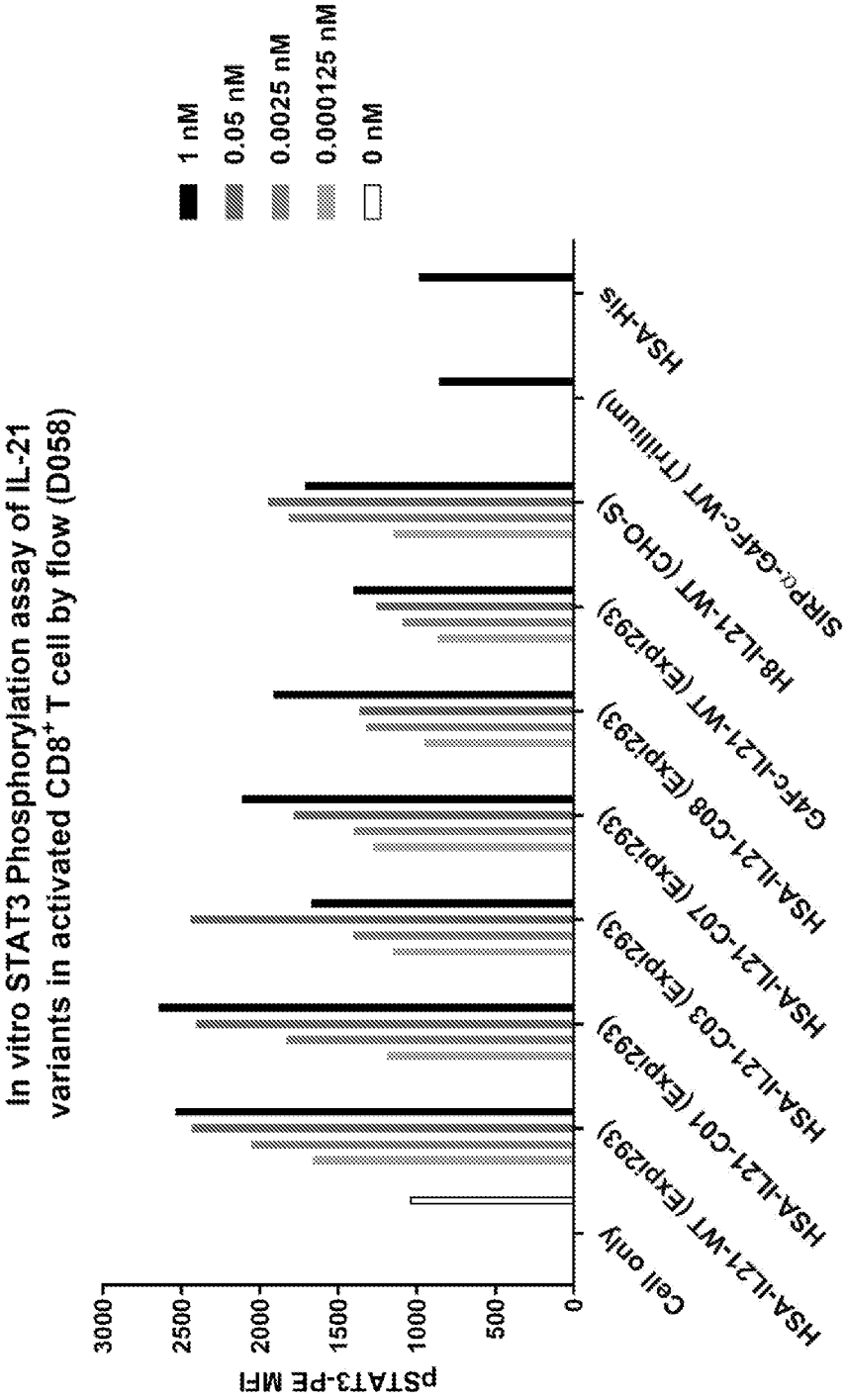


FIG. 4A

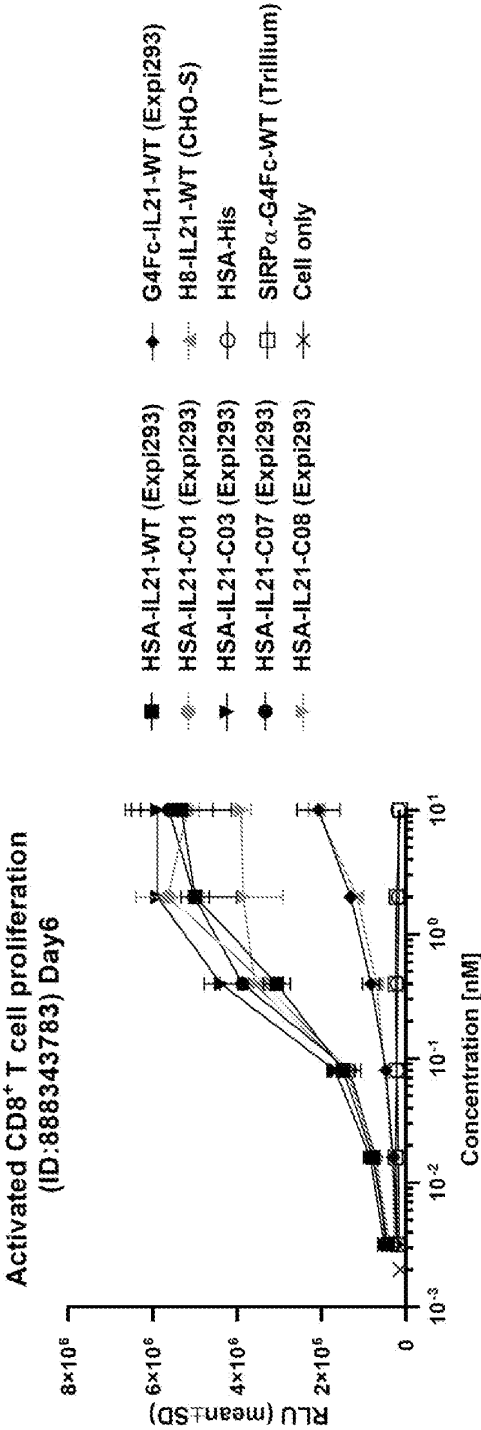


FIG. 4B

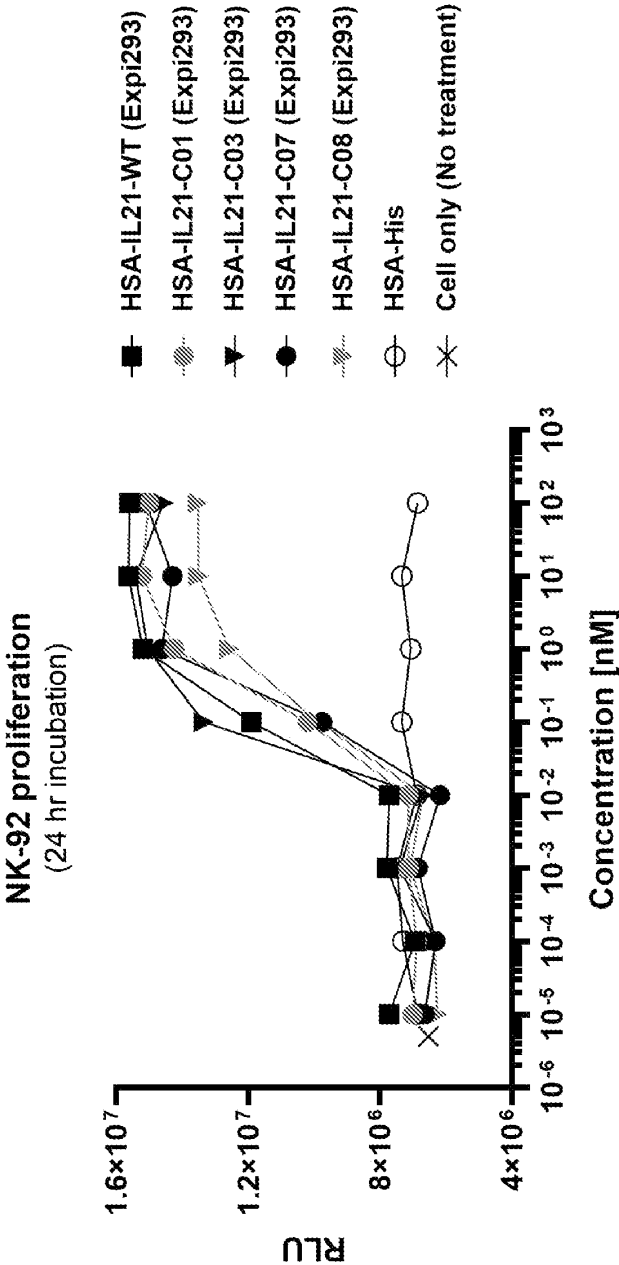


FIG. 5

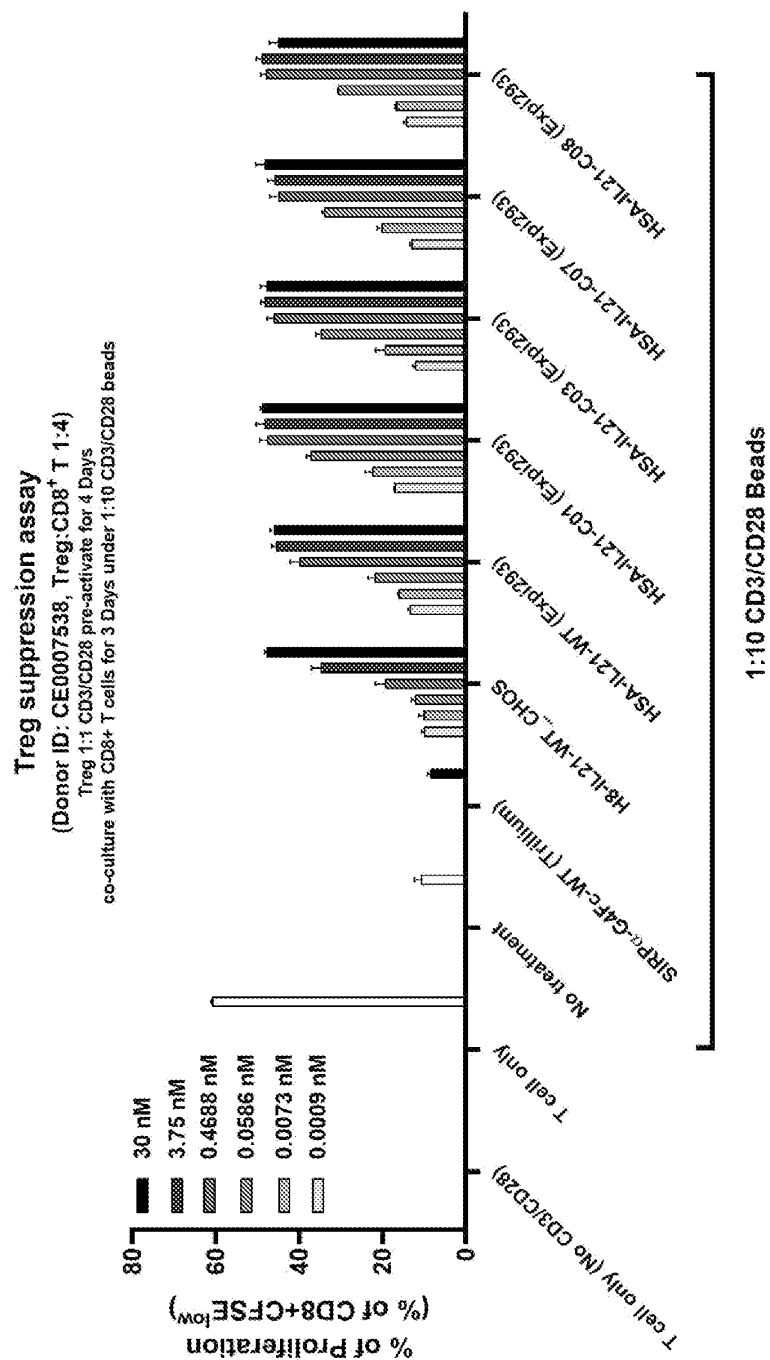


FIG. 6

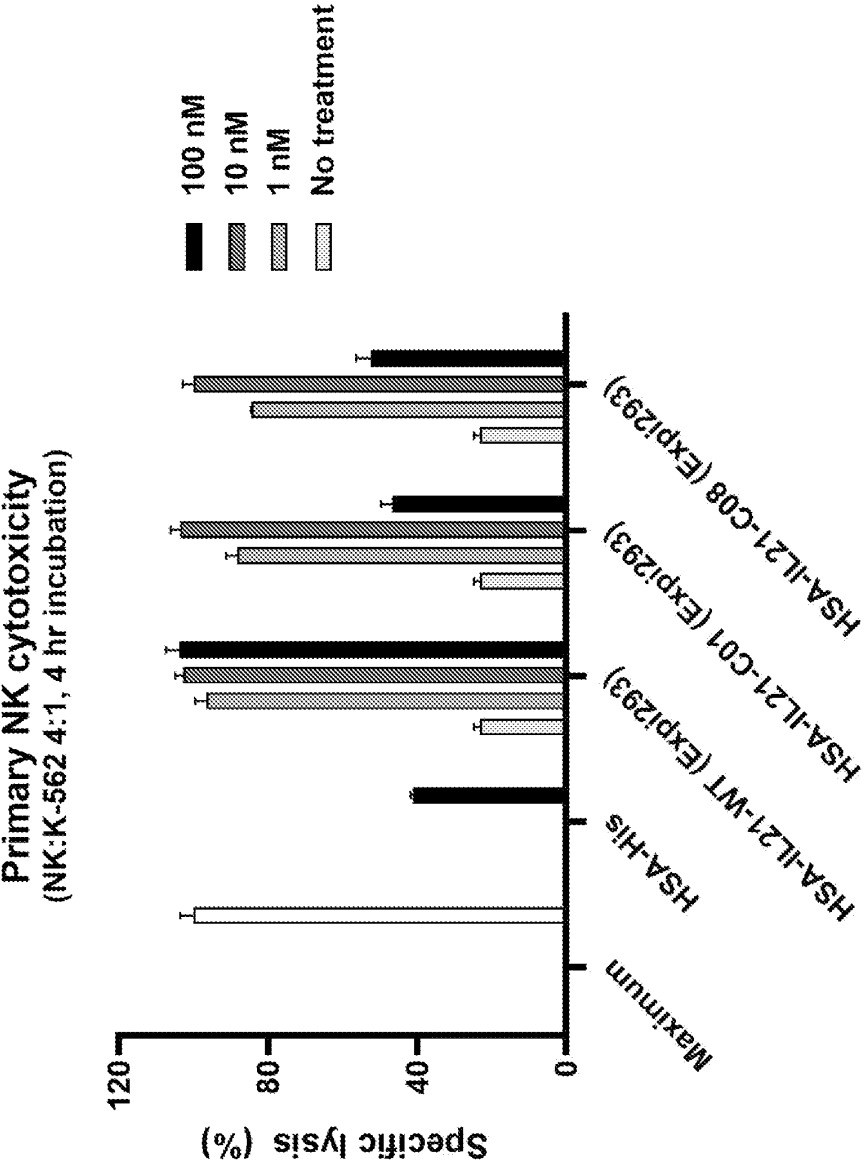


FIG. 7

Group	Animal	Target cell	Treatment agent	Dose	Treatment schedule
1	BALB/c female 5-6 wks old 10 mice/G 221108	CT26, Mouse colon ca. 2E5, s.c. With Matrigel 221117	Vehicle	10 mL/kg	Treatment starts when the tumor reaches 100-200 mm ³ (D4) 221121 i.P injection Twice a week for 3 weeks
2			HSA-IL21-WT	10 mg/kg	
3			HSA-IL21-C01	10 mg/kg	
4			HSA-IL21-C08	10 mg/kg	

FIG. 8A

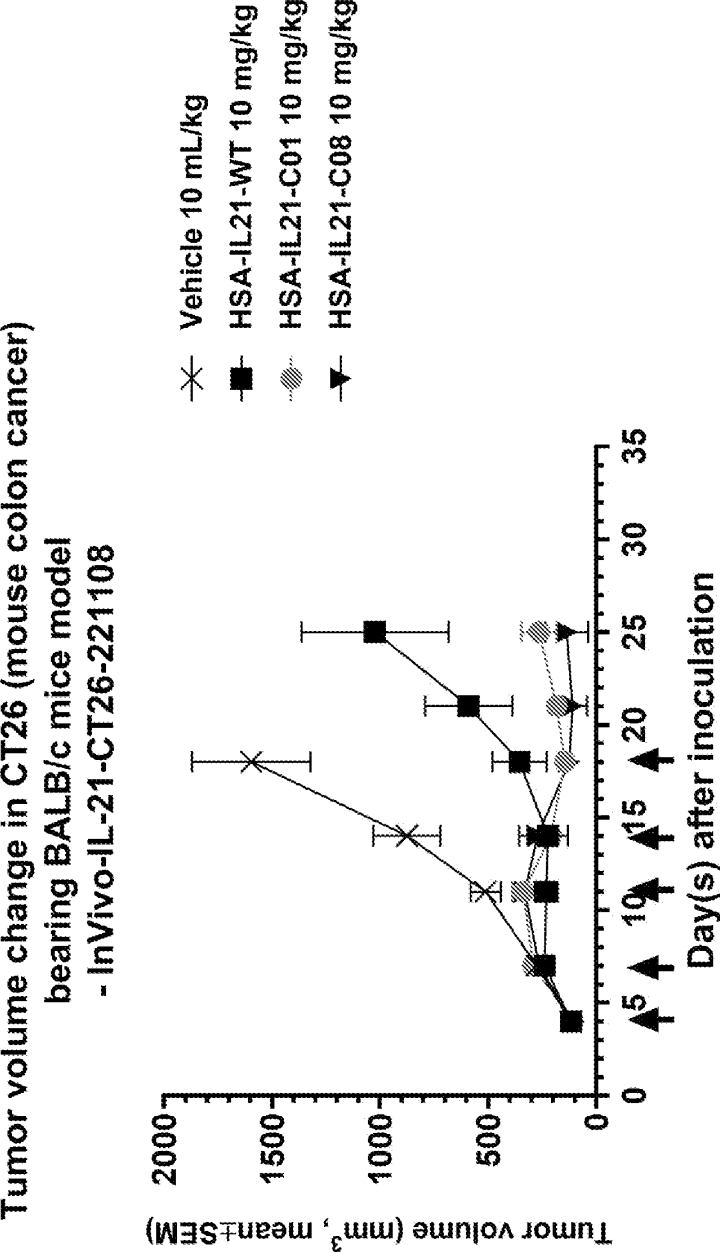


FIG. 8B

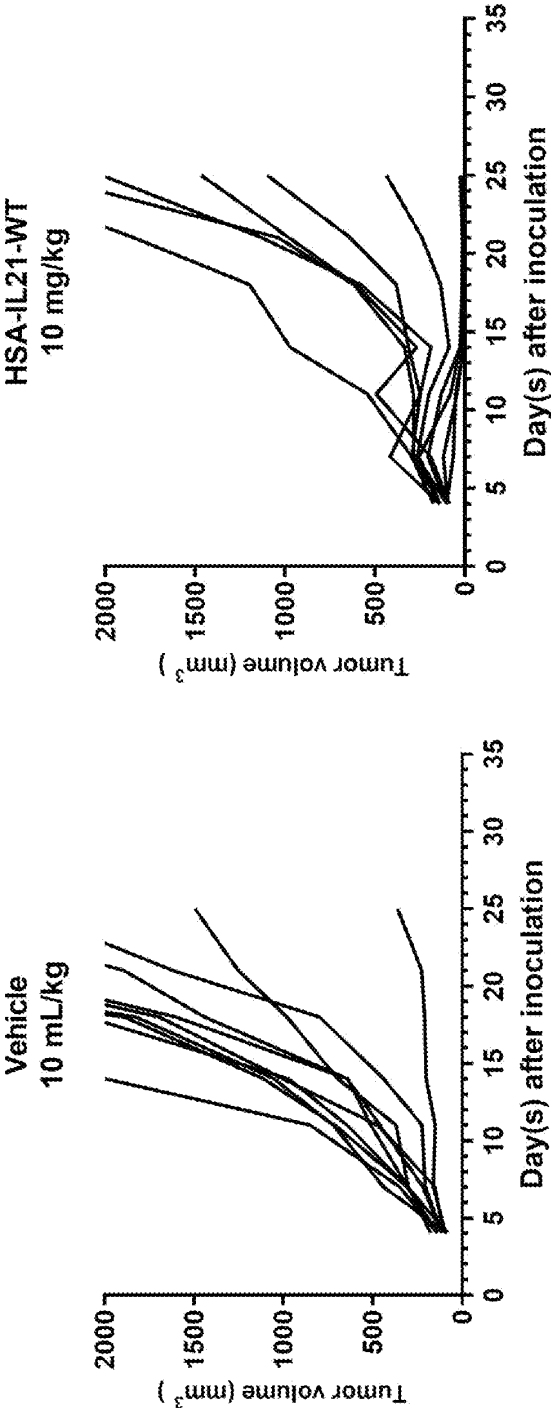


FIG. 8C

FIG. 8D

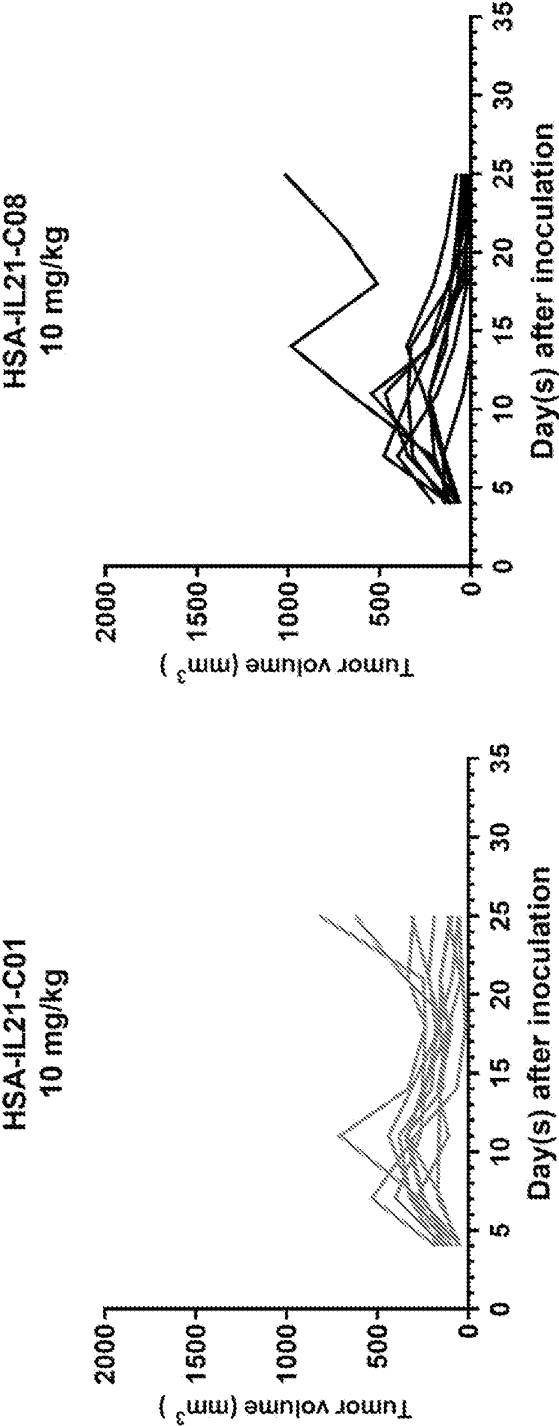


FIG. 8E

FIG. 8F

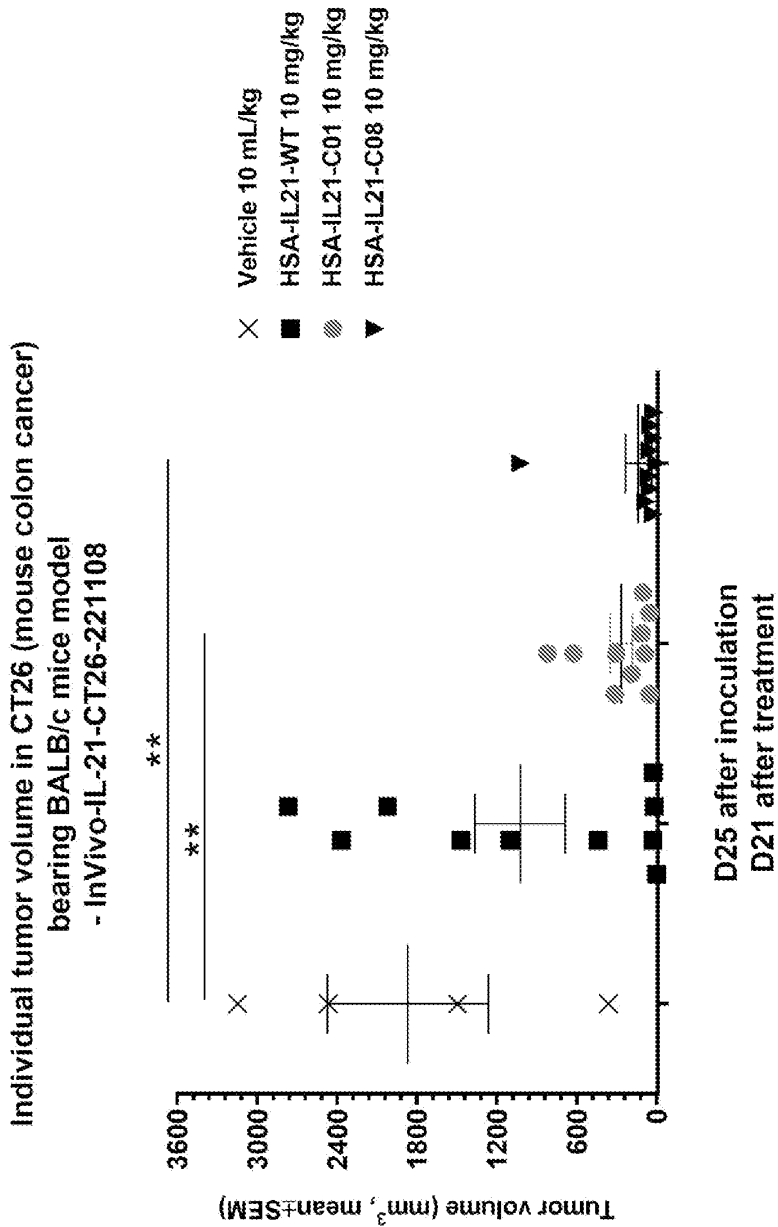


FIG. 8G

Body weight change in CT26 (mouse colon cancer)
bearing BALB/c mice model
- InVivo-IL-21-CT26-221108

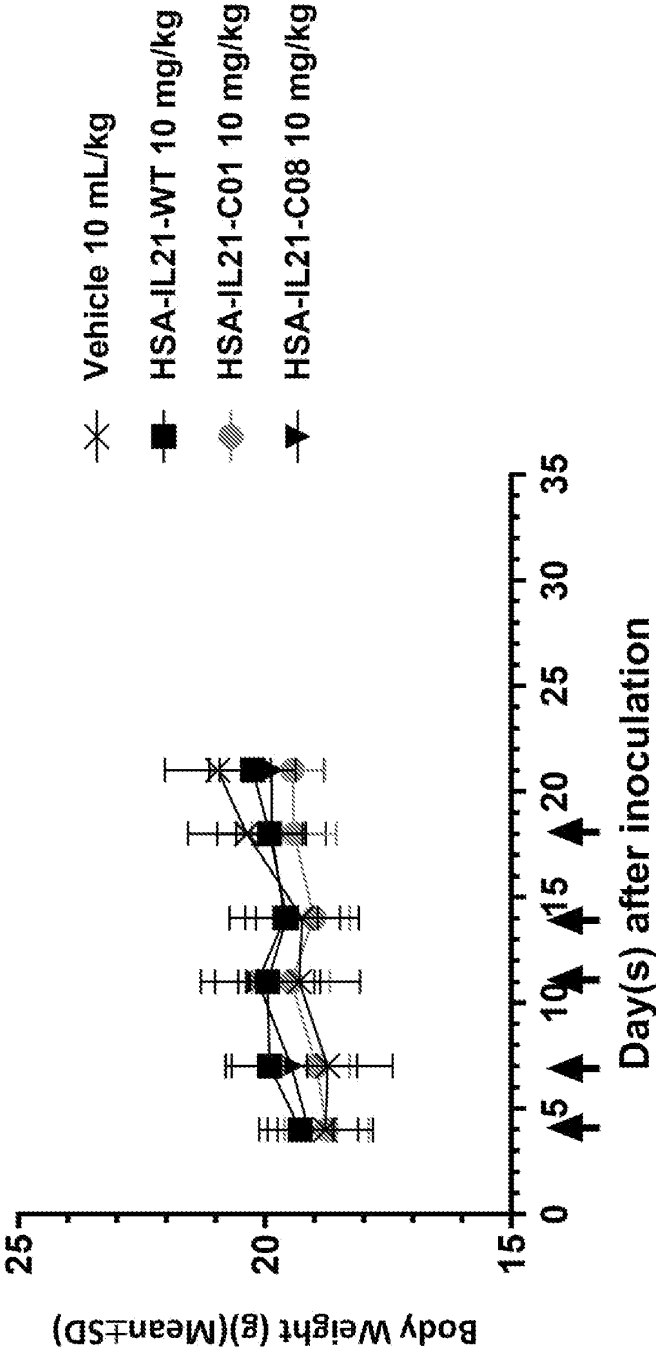


FIG. 8H

Treatment	TV (Mean±SEM)	TGI(%)	P value One-way ANOVA followed by Bonferroni's multiple comparisons test
Vehicle 10 mL/kg	1869±606	-	-
HSA-IL21-WT 10 mg/kg	1024±341	48	0.3731
HSA-IL21-C01 10 mg/kg	266±83	91	0.0056**
HSA-IL21-C08 10 mg/kg	137±99	99	0.0025**

FIG. 8I

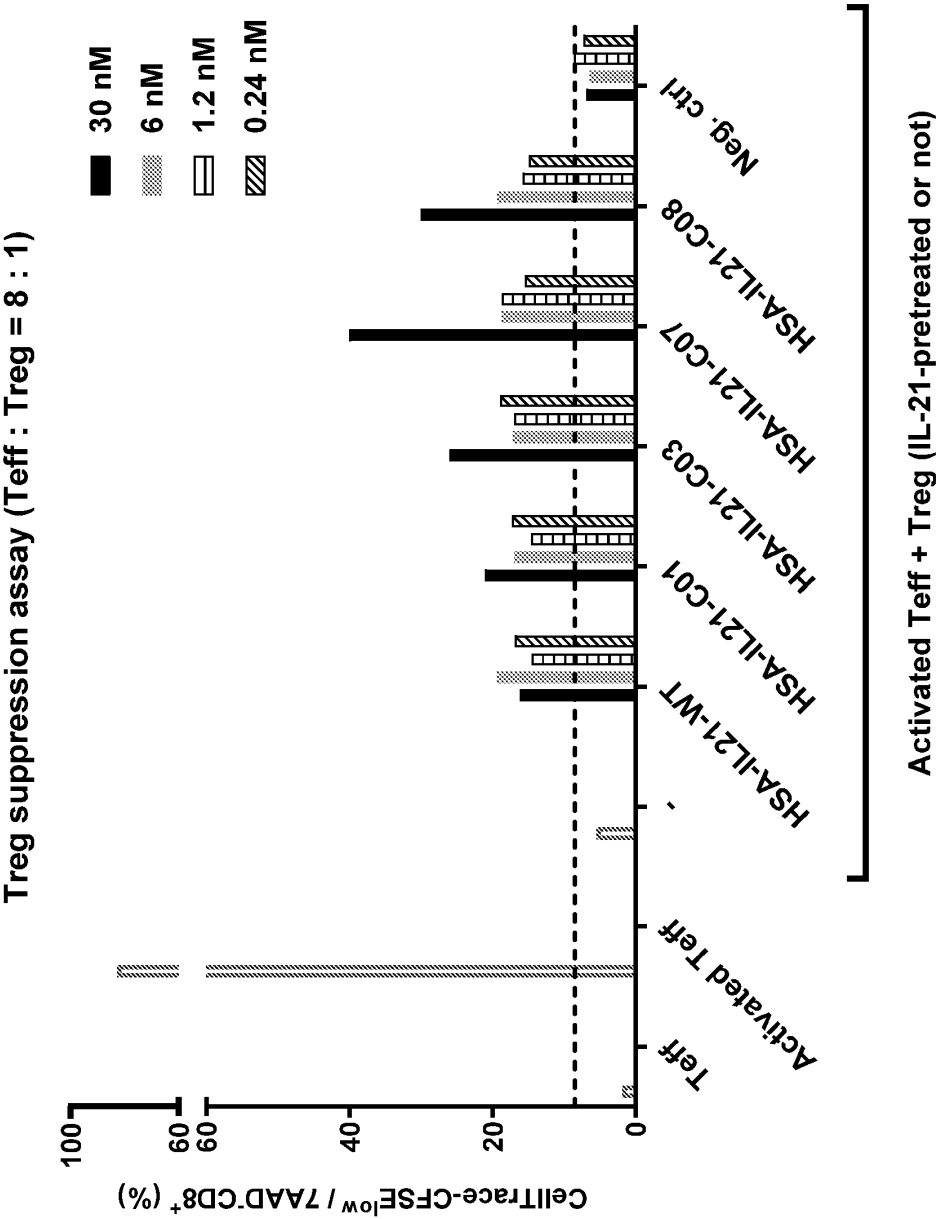


FIG. 9A

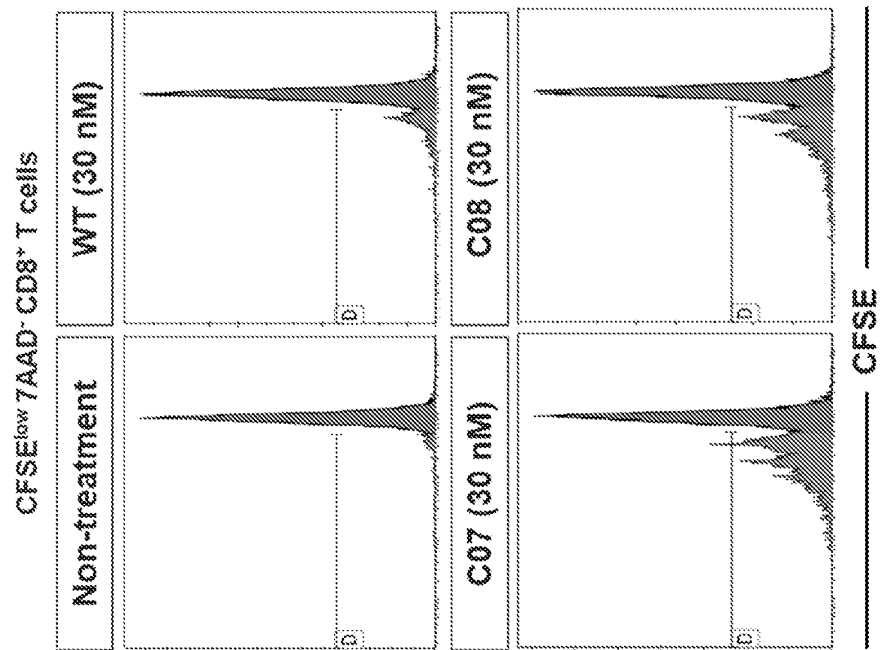


FIG. 9B

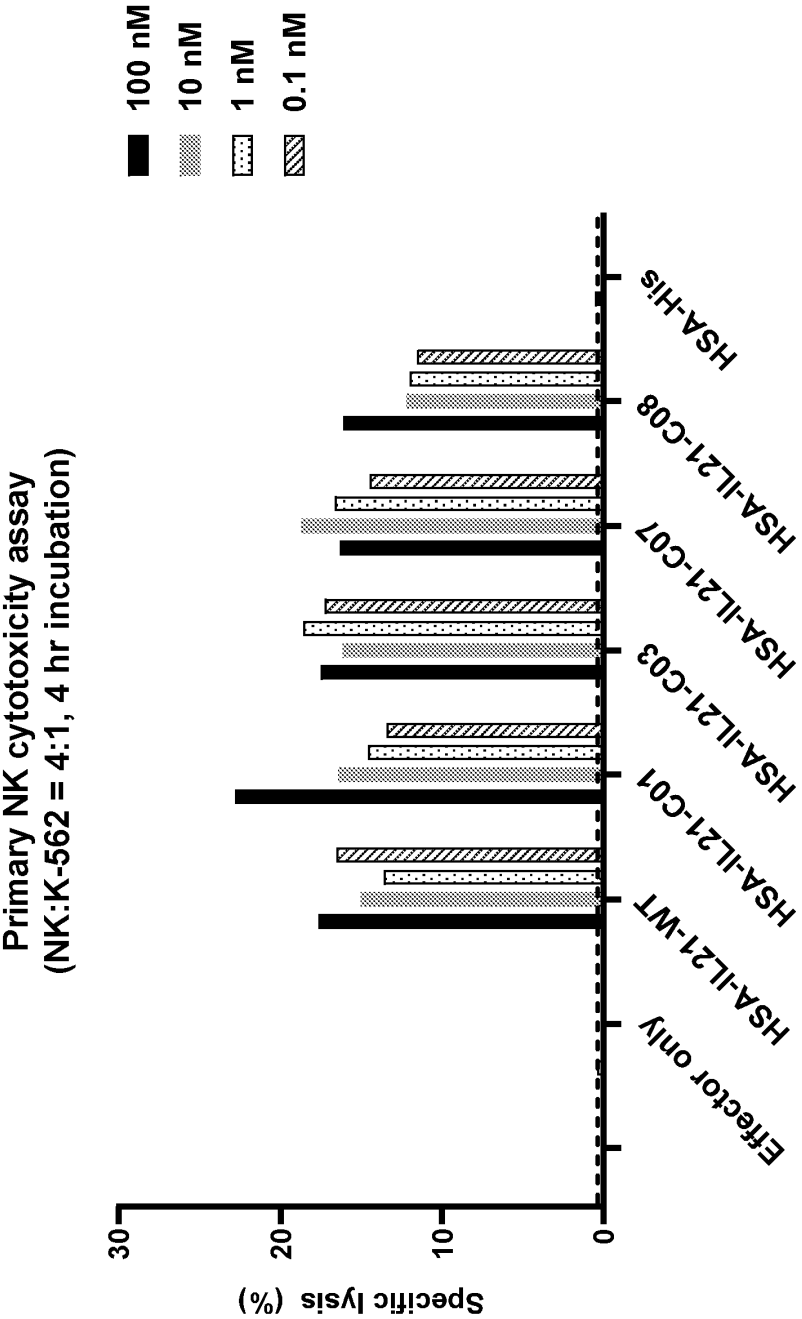


FIG. 10

Group	Animal	Target cell	Treatment agent	Dose	Treatment schedule
1	BALB/c female 5-6 wks old 8 mice/G1 16 mice/G2-G4	CT26, Mouse colon ca. 2E5, s.c. With Matrigel One-side	Vehicle	10 mL/kg	Treatment starts when the tumor reaches 100-200 mm ³ i.p. injection, Twice a week for 3 weeks
2			HSA-IL21-WT	10 mg/kg	
3			HSA-IL21-C01	10 mg/kg	
4			HSA-IL21-C08	10 mg/kg	

↓ Memory effect tests: CT26 rechallange of G3, G4 (mice with tumor size less than 50 mm³)

Group	Animal	Target cell	Group	Treatment schedule
3	BALB/c, female 5-6 wks old 10-11 mice/G3 and G4 6 mice/G5	CT26, Mouse colon ca. 2E5, s.c. With Matrigel The other side	HSA-IL21-C01	Inoculate 2E5 of CT26, s.c. with Matrigel on Day 40 after the initial inoculation (3 weeks later from 5 th dose)
4			HSA-IL21-C08	
5			Tumor only	

FIG. 11A

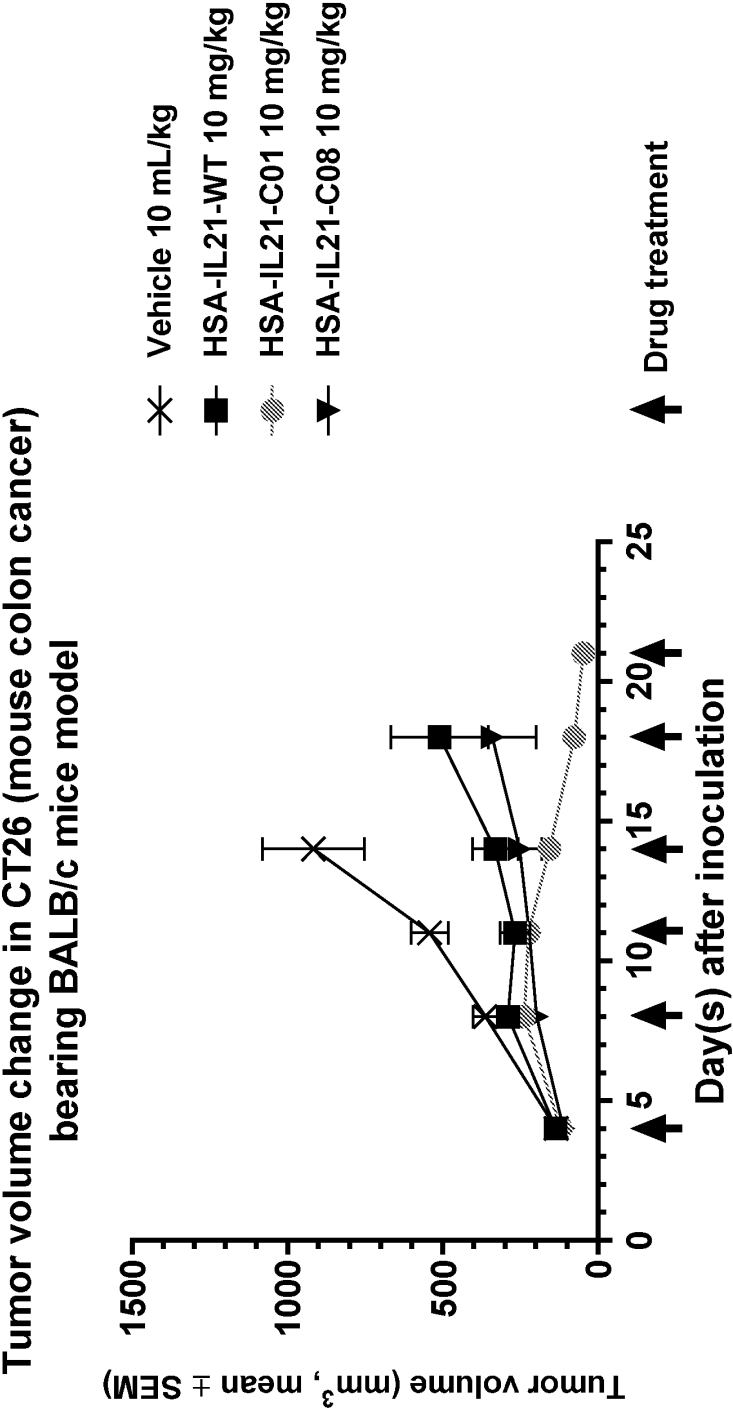


FIG. 11B

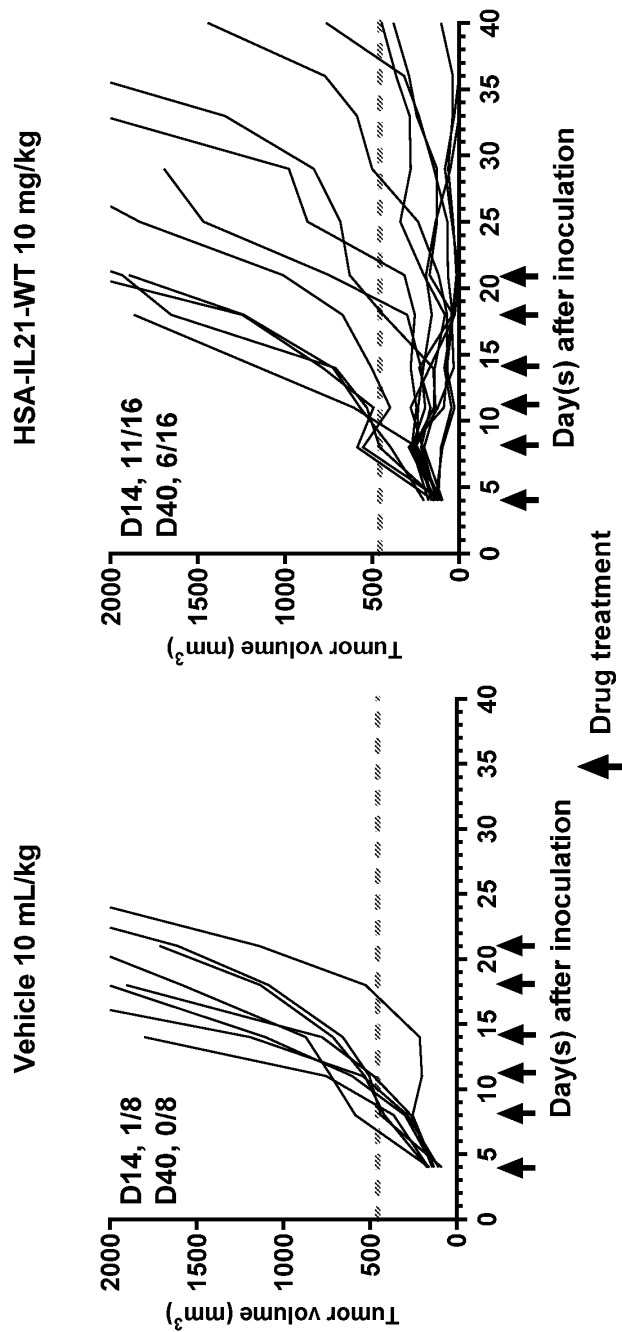
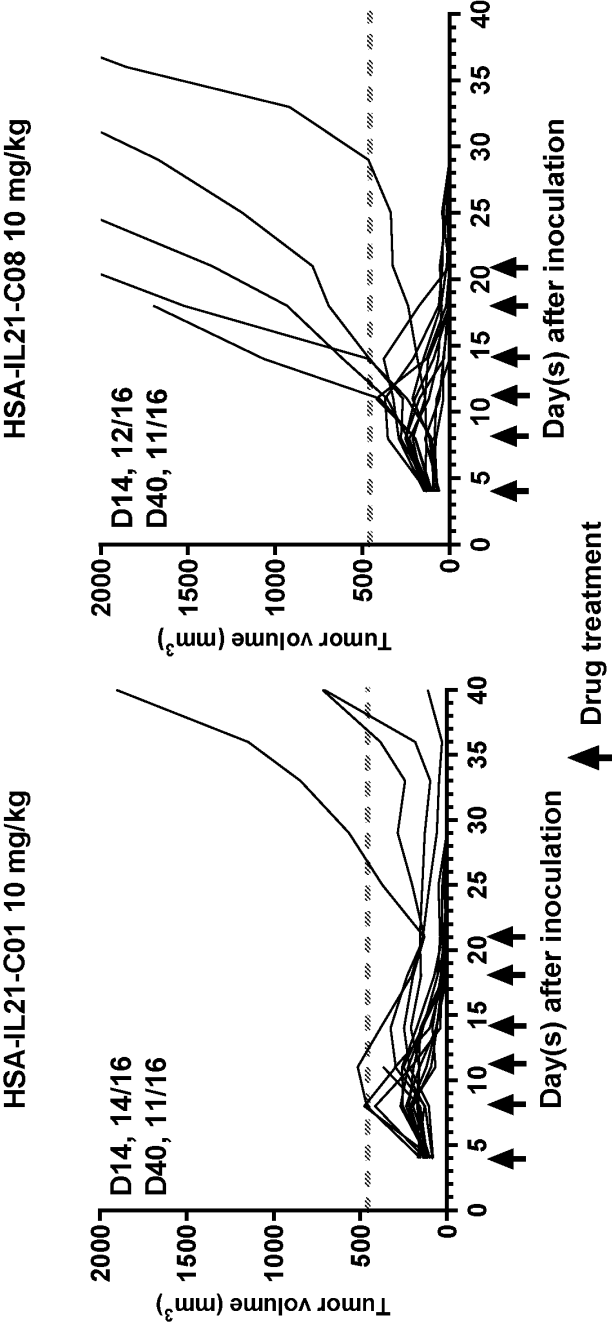


FIG. 11D

FIG. 11C



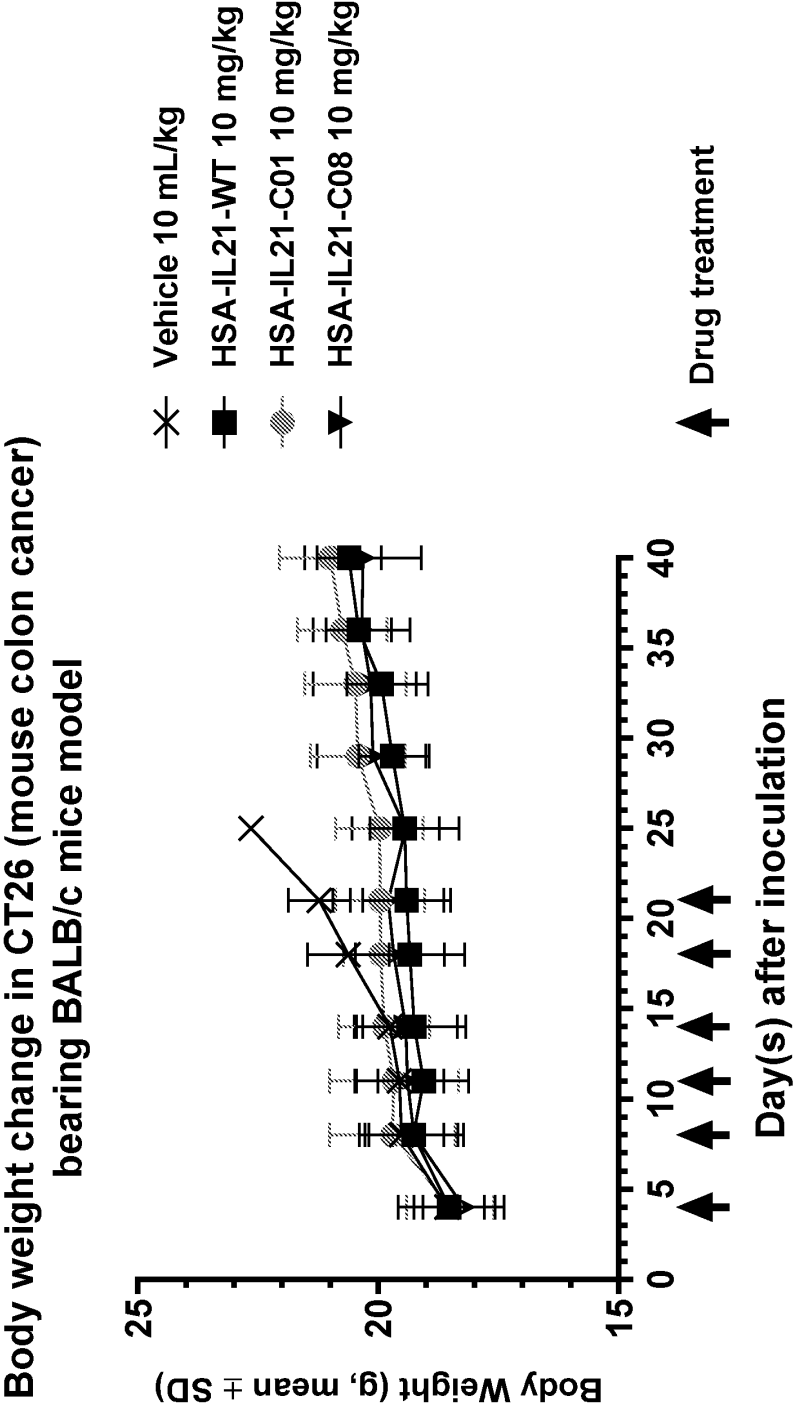


FIG. 11G

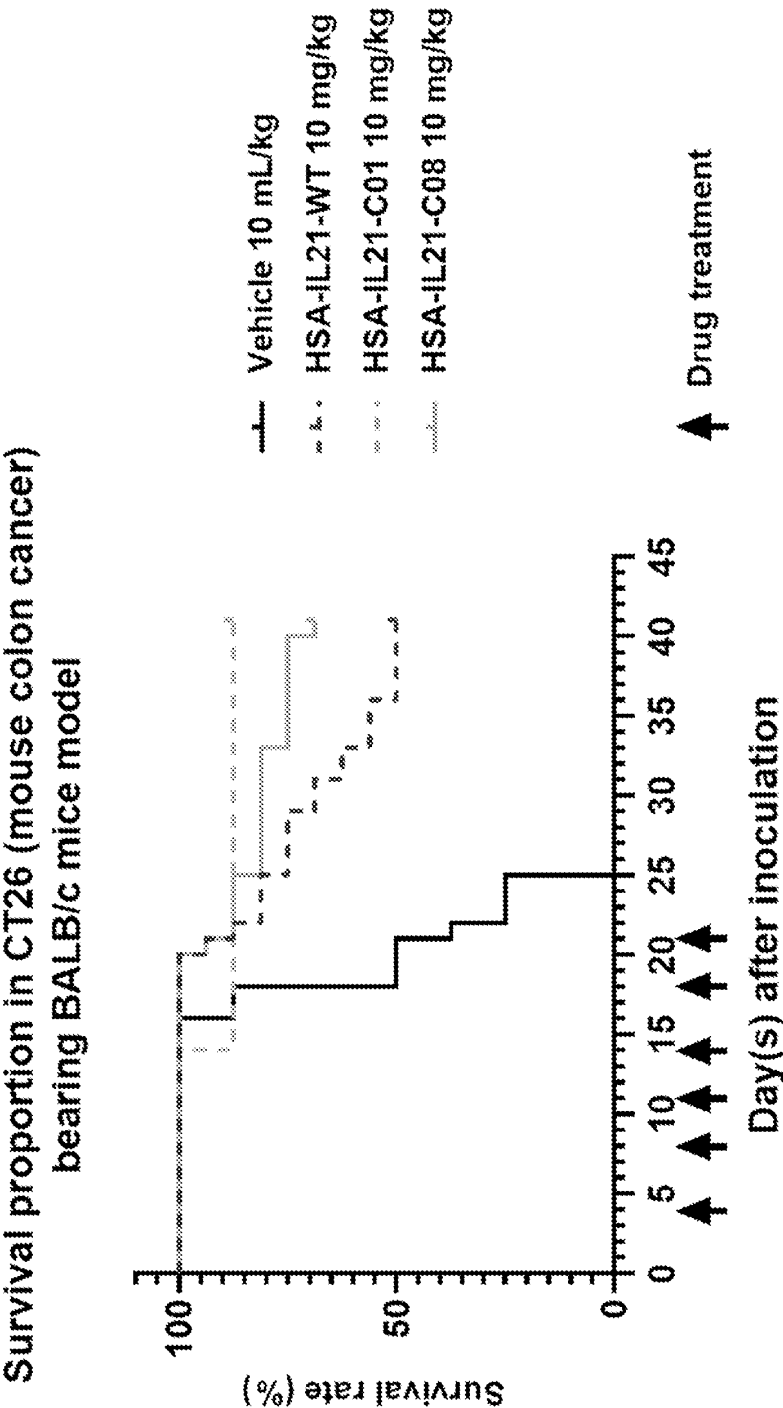


FIG. 11H

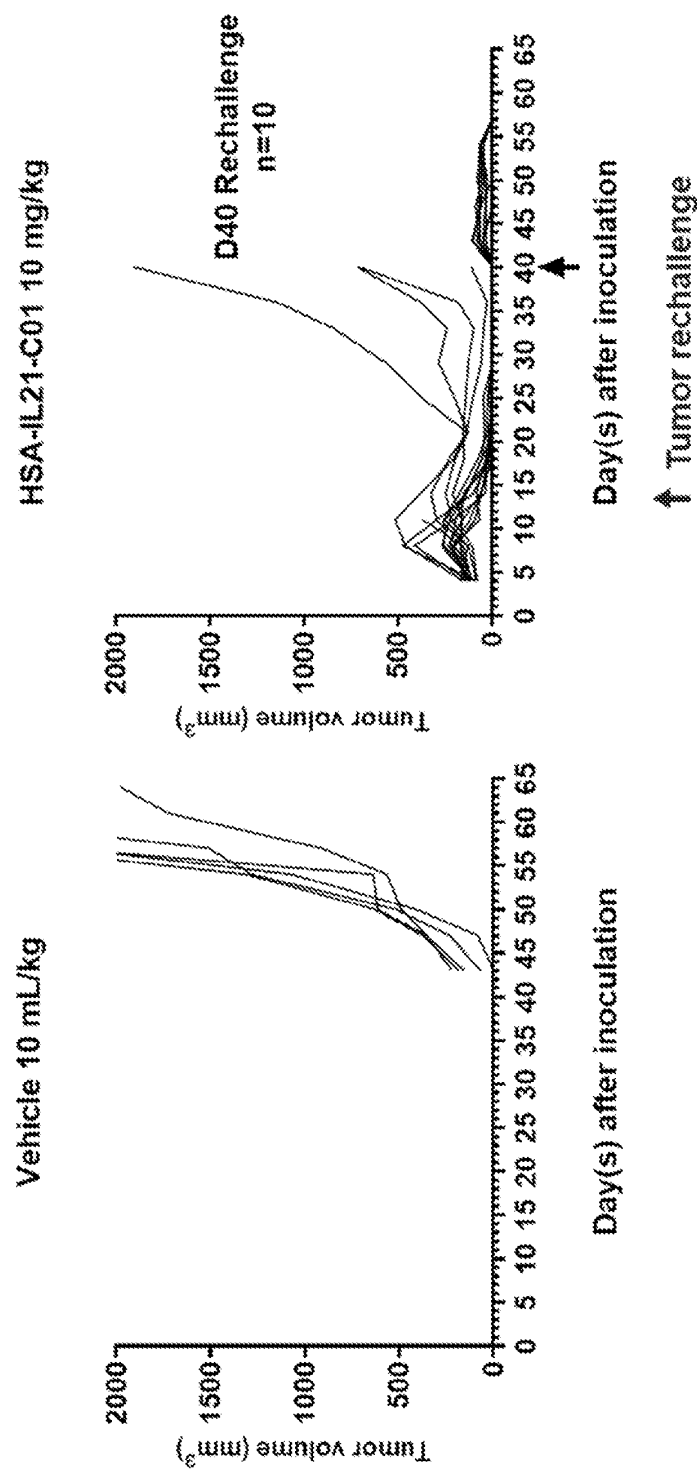


FIG. 11J

FIG. 11I

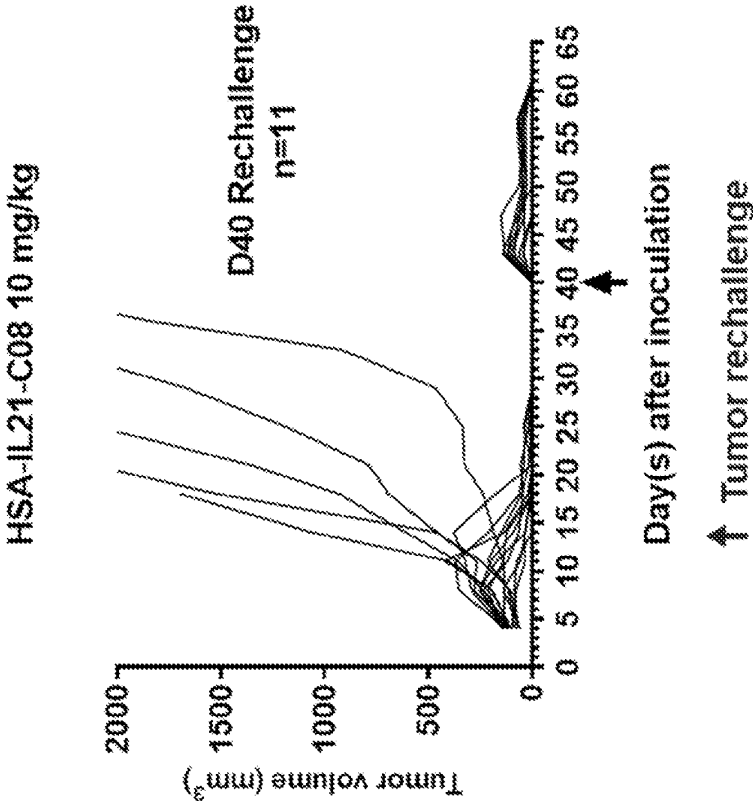


FIG. 11K

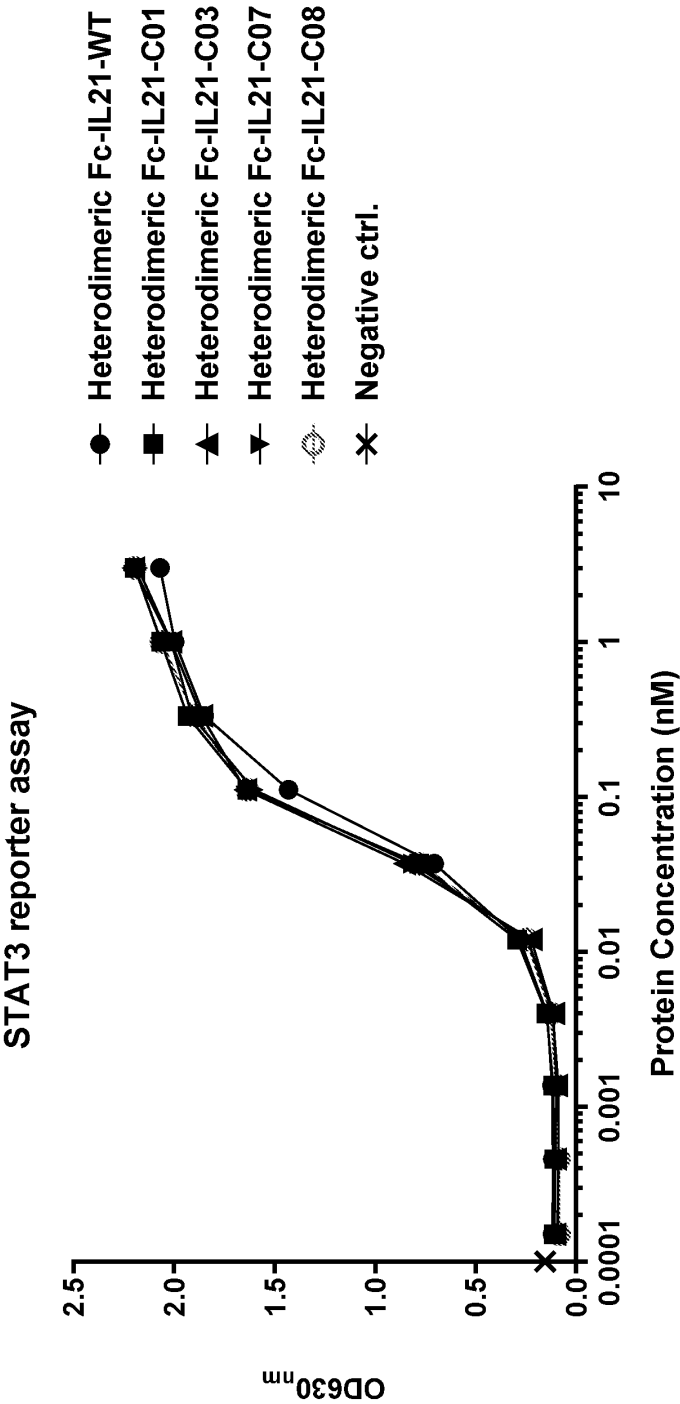


FIG. 12

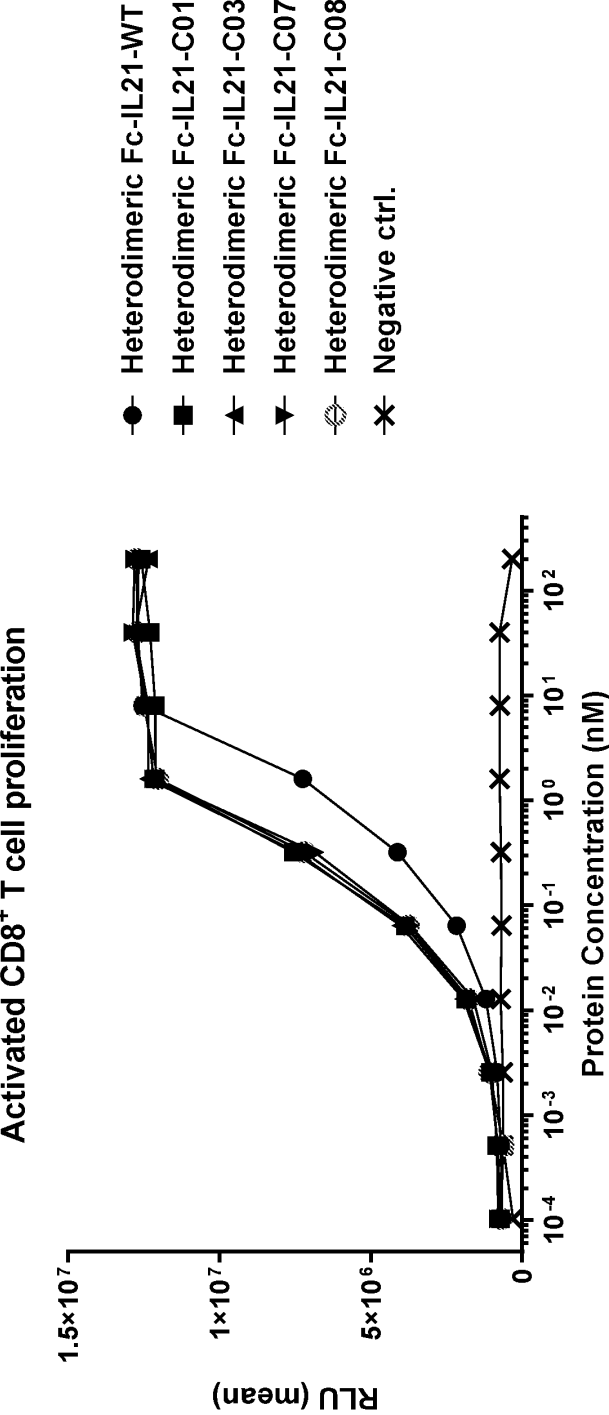


FIG. 13A

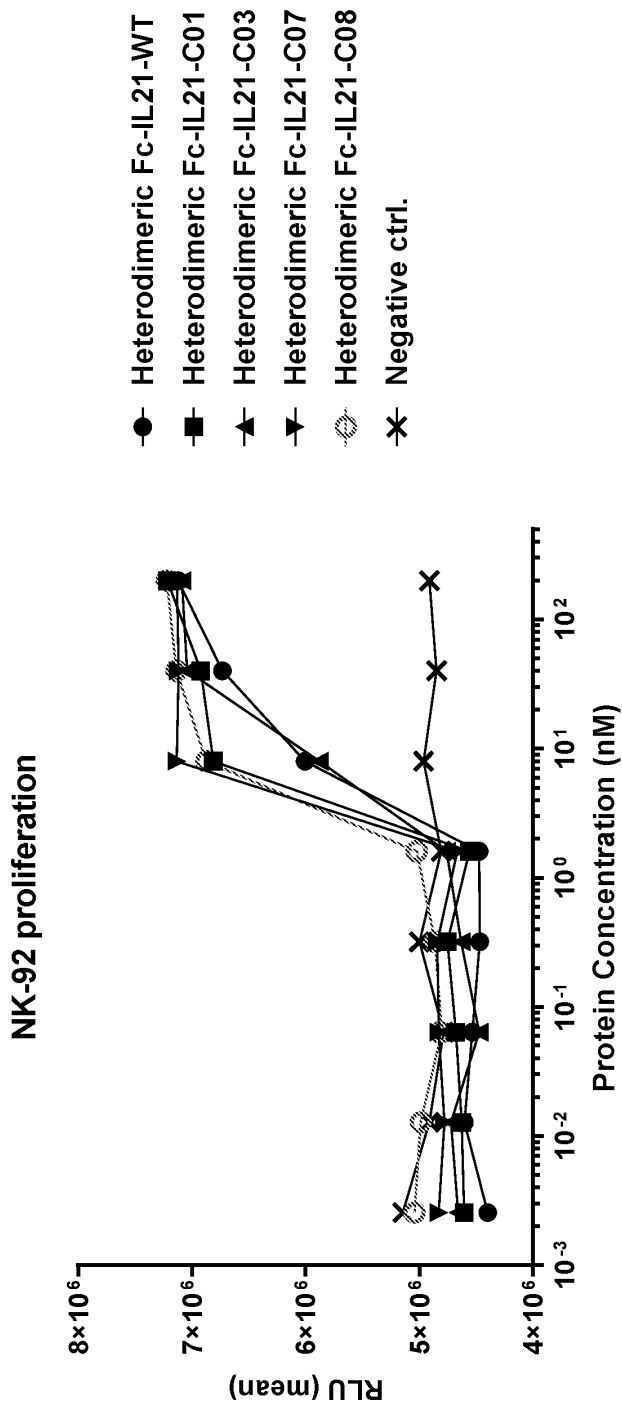


FIG. 13B

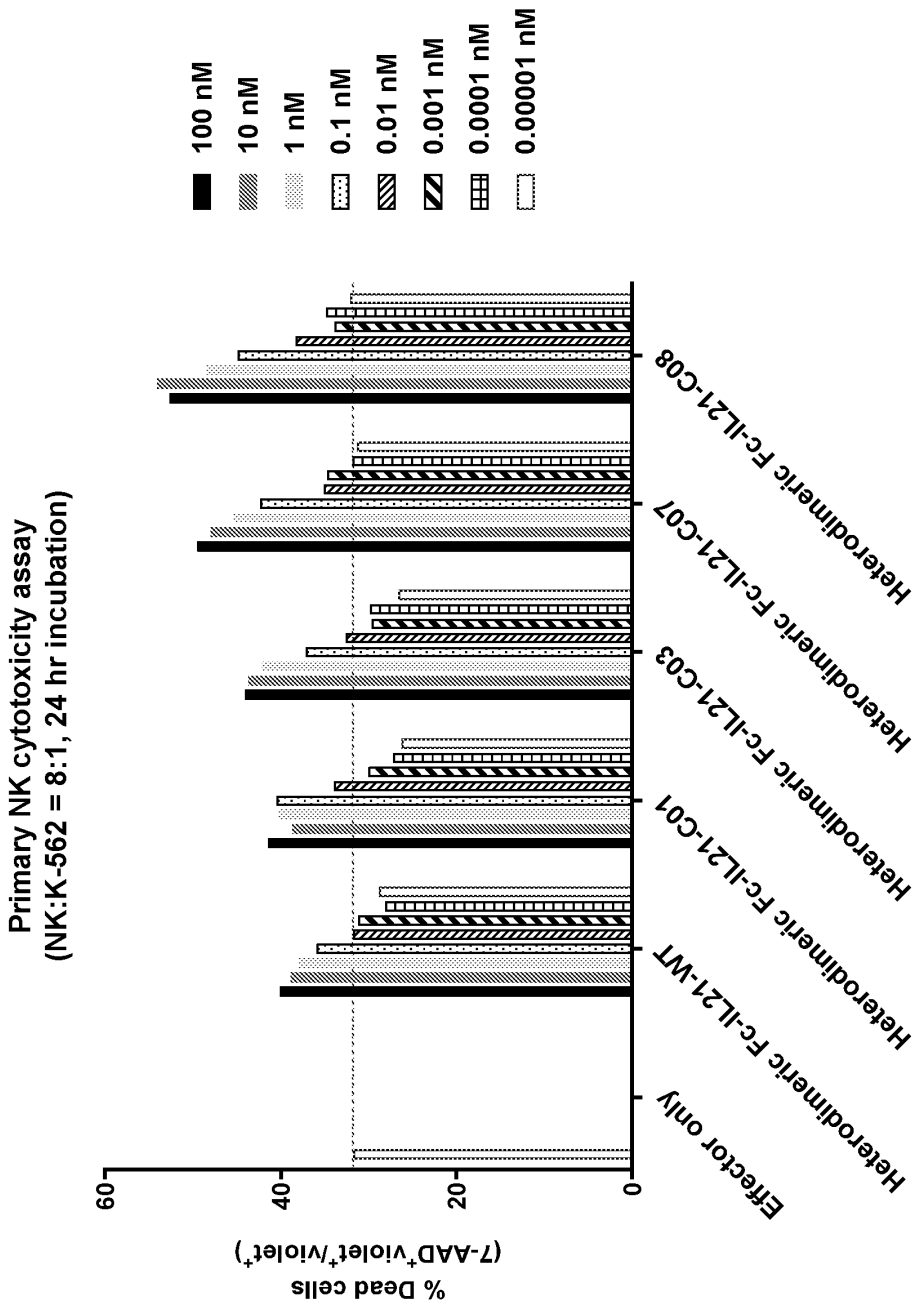
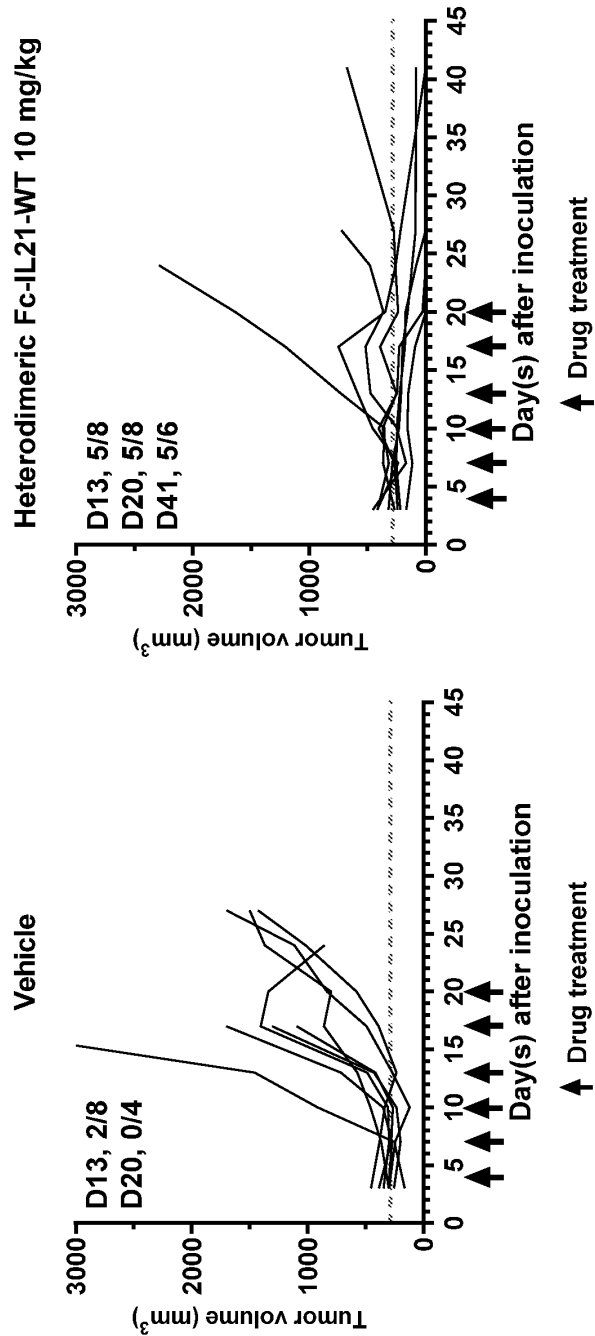


FIG. 14

Group	Animal	Target cell	Treatment agent	Dose	Treatment schedule
1	BALB/c female 5 wks old 8 mice/G1, G2 16 mice/G3-G6	CT26, Mouse colon ca. 2E5, s.c. With Matrigel One-side	Vehicle	10 mL/kg	Treatment starts on Day 4 after the tumor inoculation i.p. injection, Twice a week for 3 weeks
2			Heterodimeric Fc-IL21-WT	10 mg/kg	
3			Heterodimeric Fc-IL21-C01	10 mg/kg	
4			Heterodimeric Fc-IL21-C03	10 mg/kg	
5			Heterodimeric Fc-IL21-C07	10 mg/kg	
6			Heterodimeric Fc-IL21-C08	10 mg/kg	

FIG. 15A



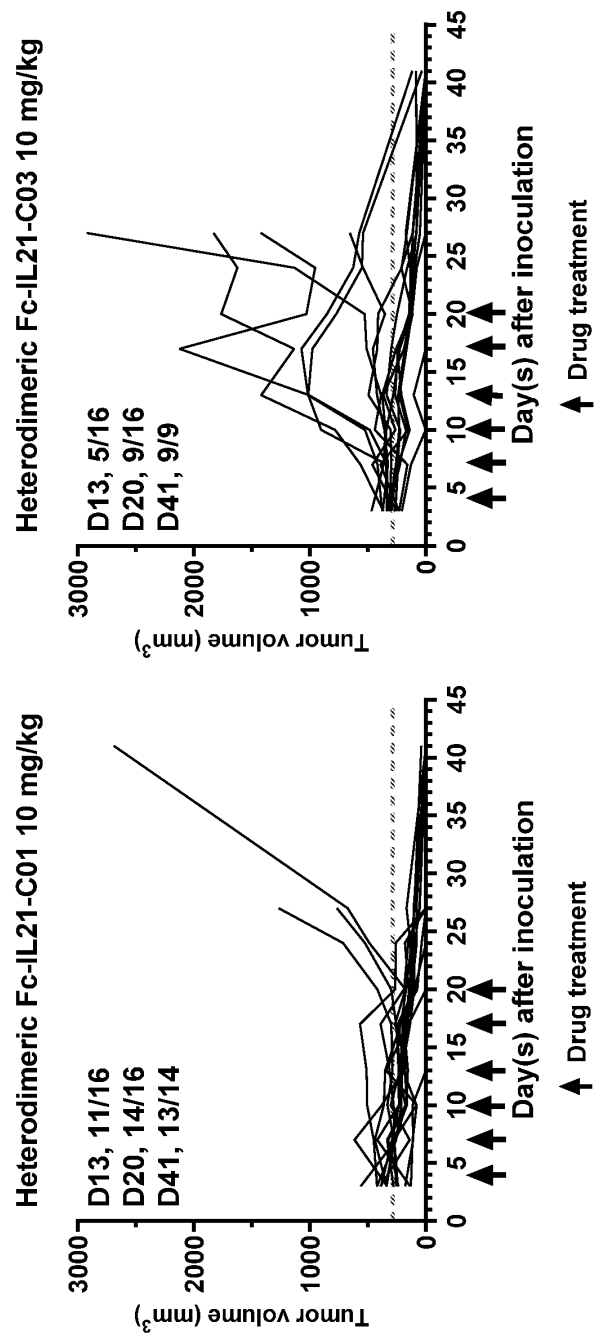


FIG. 15D

FIG. 15E

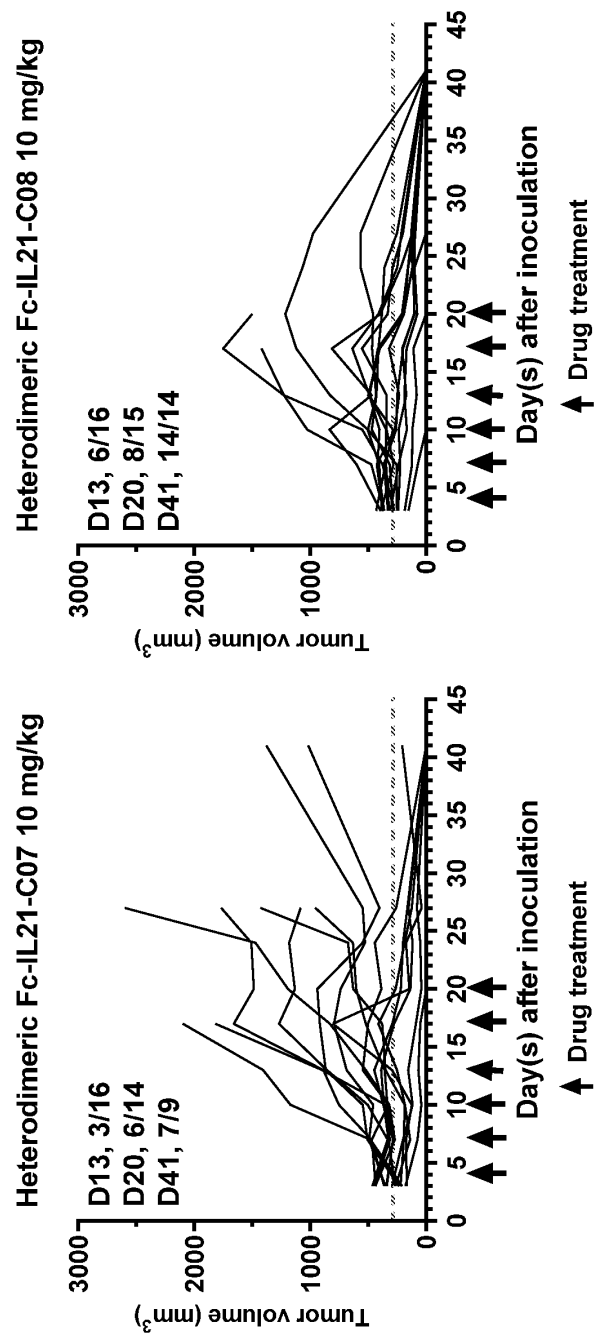


FIG. 15F

FIG. 15G

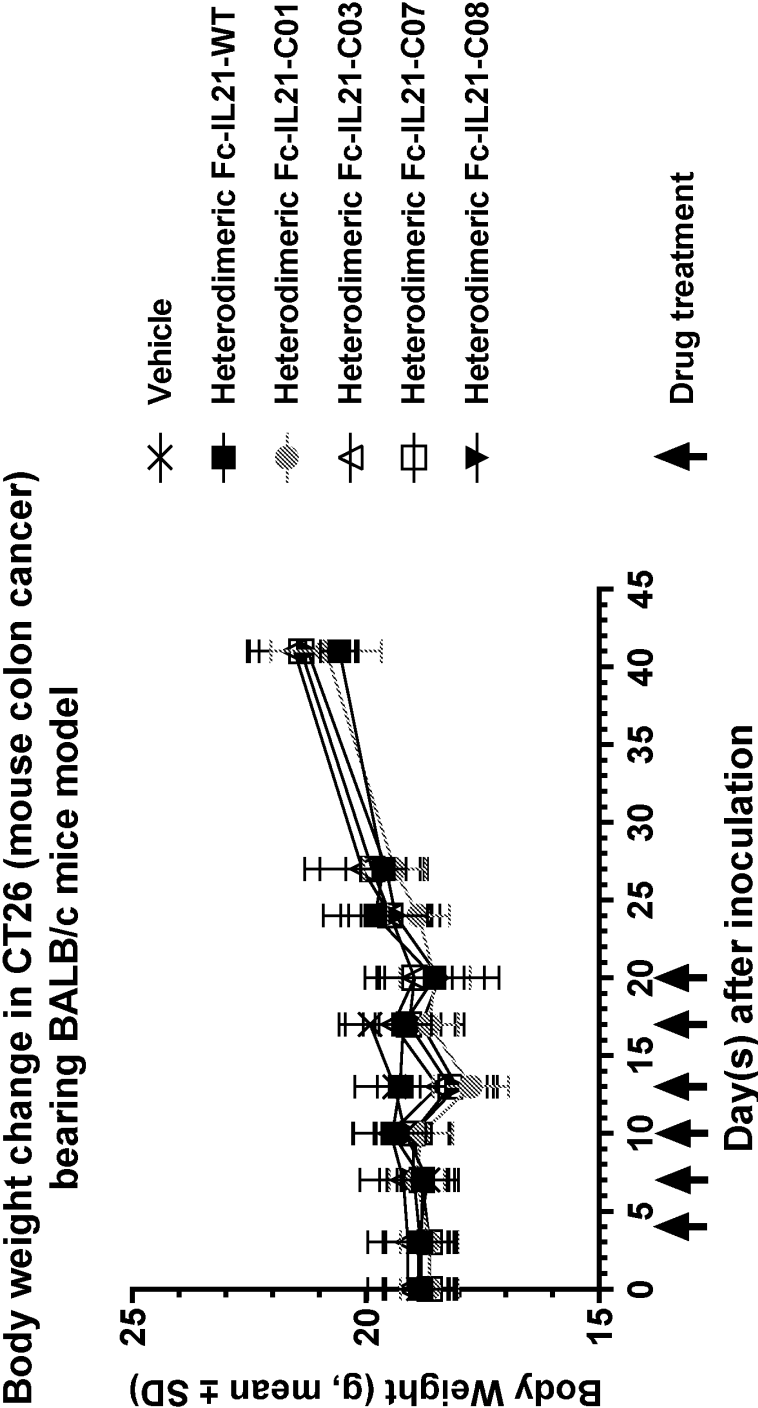


FIG. 15H

FIG. 16

Wild-type human IL21 (SEQ ID NO: 1)
MRSSPGNMERIVICLMVIFLGLTLVHKSSSQGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANT
GNNERIINVSIIKKLKRKPPSTNAGRQKHRLTCPCSDSYEKKPPKEFLERFKSLQKMIHQHLSRTHGSEDS

G4Fc-IL21-WT (SEQ ID NO: 16)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVWEESNGQPENNYKTTPP
VLDSGSGFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK
GGGGGGGGGGGGAS
HKSSSQGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSIIKKLKRKPPSTNAG
RRQKHRLTCPCSDSYEKKPPKEFLERFKSLQKMIHQHLSRTHGSEDS

HSA-IL21-WT (SEQ ID NO: 17)
HHHHHHHHGGGS
DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLQHKDDNPRLVRPEVDVMCTAFHDNEETFLKKYL YEIARRHPYFYAPELLFFAKRYKAAFTGCCQAADKAAACL
LPKLDELDEGKASSAKQRLKCSLQKFGERAFKAWAVARLSQRPKAEFAEVSKLVTDLTKVHTECCHGDILLECADDRADLAKYICEN
QDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLP SLAADFVESKDVCKNYAEAKDVLGMFLYEYARRHPDYSVVLLRLAKTYETT
LEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFNQALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCKHPEAKR
MPCAE DYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVK
HKPKATKEQLKAVMDDFAAFVEKCKADDKETCFAEEGKKLVAASQAALGL
GGGGGGGGGGGGAS
HKSSSQGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSIIKKLKRKPPSTNAG
RRQKHRLTCPCSDSYEKKPPKEFLERFKSLQKMIHQHLSRTHGSEDS

HSA-IL21-C01 (SEQ ID NO: 18)
HHHHHHHHGGGS
DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLQHKDDNPRLVRPEVDVMCTAFHDNEETFLKKYL YEIARRHPYFYAPELLFFAKRYKAAFTGCCQAADKAAACL
LPKLDELDEGKASSAKQRLKCSLQKFGERAFKAWAVARLSQRPKAEFAEVSKLVTDLTKVHTECCHGDILLECADDRADLAKYICEN
QDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLP SLAADFVESKDVCKNYAEAKDVLGMFLYEYARRHPDYSVVLLRLAKTYETT
LEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFNQALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCKHPEAKR

MPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETTFHADICTLSEKERQIKKQTALVELVK
HKPKATKEQLKAVMDDFAAFVEKCKCKADDKETCTFAEEGKKLVAAASQAALGL
GGGSGGGSGGGGAS
HKSSSQGQDR HMIRMRLQID IVDQLKNYVN DLVPEFLPAP EDVETNCEWS AFSCFQKAQL KSANTGNNER IINVSIIKKLK
RKPPSTNAGR RQKHRLTCPS CDSYEKKPPK EFLERFKSLL QKMIHQHLSS RTHGSEDS

HSA-IL21-C03 (SEQ ID NO: 19)
HHHHHHHHHGGG

DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKL VNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLQHKDDNPNL PRLVRPEVDVMCTAFHDNEETFLKKYL YEIARRHPYFYAPEL LFFAKRYKAAFTCCQAADKAAACL
LPKLDELDEGKASSAKQRLK CASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDILLECADDRADLAKYICEN
QDSISSKLECCCKPLLEKSHCIAEVENDEMPADLP SLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVL LRLAKTYETT
LEKCCAAADPHECYAKVDFE FKPLVEEPQNL IKQNCELFEQLGEYKFQNAL LVRYTKKVPQVSTPTLVEVSRNLGKVGSKCKKHPEAKR
MPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETTFHADICTLSEKERQIKKQTALVELVK
HKPKATKEQLKAVMDDFAAFVEKCKCKADDKETCTFAEEGKKLVAAASQAALGL
GGGSGGGSGGGGAS

HKSSSQGQDR HMIRMRLQID IVDQLKNYCN DLVPEFLPAP EDVETNCEWS AFSCFQKAQL KSANTGNNER IINVSIIKKLK
RKPPSTNAGR RQKHRLTCPS CDSYEKKPPC EFLERFKSLL QKMIHQHLSS RTHGSEDS

HSA-IL21-C07 (SEQ ID NO: 20)
HHHHHHHHHGGG

DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKL VNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLQHKDDNPNL PRLVRPEVDVMCTAFHDNEETFLKKYL YEIARRHPYFYAPEL LFFAKRYKAAFTCCQAADKAAACL
LPKLDELDEGKASSAKQRLK CASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDILLECADDRADLAKYICEN
QDSISSKLECCCKPLLEKSHCIAEVENDEMPADLP SLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVL LRLAKTYETT
LEKCCAAADPHECYAKVDFE FKPLVEEPQNL IKQNCELFEQLGEYKFQNAL LVRYTKKVPQVSTPTLVEVSRNLGKVGSKCKKHPEAKR
MPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETTFHADICTLSEKERQIKKQTALVELVK
HKPKATKEQLKAVMDDFAAFVEKCKCKADDKETCTFAEEGKKLVAAASQAALGL
GGGSGGGSGGGGAS

HKSSSQGQDR HMIRMRLQID IVDQLKNYVN DLVPEFLPAP EDVETNCEWS AFSCFQKAQL KSCNTGNNER IINVSIIKKLK
RKPPSTNAGR RQKHRLTCPS CDSYEKKPPK EFLERFKSLL QKMIHQHLSS RTHGSEDS

HSA-IL21-C08 (SEQ ID NO: 21)
HHHHHHHHHGGG

FIG. 16 Cont.

DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLOHKDDNPRLVRPEVDVMCTAFHDNEETFLKKYLIEIARRHPYFYAPELLFFAKRYKAAFTGCCQAADKAACL
LPKLDLDEDEGKASSAKQRLKCSLQKGERAFKAWAVARLSQRPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDDRADLAKYICEN
QDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVLGMFLYEARHPDYSVLLRLAKTYETT
LEKCCAAADPHECYAKVDFEFLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCKKHPEAKR
MPCAEYLSVVLNQLCVLHEKTPVSDRVTCKCTESLVNRRPCFSALEVDETYVPKEFNAETTFHADICTLSEKERQIKKQTALVELVK
HKPKATKEQLKAVMDDFAAFVEKCKCKADDKETCTFAEEGKKLVAAASQAALGL
GGGGSGGGSGGGAS
HKSSSQGQDR HMIRMRLQID IVDQLKNYVN DLVPECLPAP EDVETNCEWS AFSCFQKAQL KSANTGNNER IINVSICKLK
RKPPSTNAGR RQKHRLTCPS CDSYECKPPK EFLERFKSL QKMIHQHLSS RTHGSEDS

8XHis tag (SEQ ID NO: 22)
HHHHHHHHGG

SIRPα-G4Fc-WT (Trillium) (SEQ ID NO: 23)

EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGAPARELIYNQKEGHFPRVTVSESTKRENMDFSISISNITPADACTY
YCVKFRKGSPTDFKSGAGTELSVRAKPSKYGPPCPAPPEFLGGPSVFLFPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWY
VDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKGLPSSIEKTSKAGQPREPQVYTLPPSQEEMTKNQVSLTCL
LVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

H8-IL21-WT (SEQ ID NO: 24)
HHHHHHHHGG

HKSSSQGQDRHMIRMRLQIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERI INVSICKLKRKPPSTNAG
RQKHRLTCPS CDSYECKPPKEFLERFKSLQKMIHQHLSSRTHGSEDS

Linker (SEQ ID NO: 25)
GGGGSGGGSGGGAS

human serum albumin (HSA) (SEQ ID NO: 26)

DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLOHKDDNPRLVRPEVDVMCTAFHDNEETFLKKYLIEIARRHPYFYAPELLFFAKRYKAAFTGCCQAADKAACL
LPKLDLDEDEGKASSAKQRLKCSLQKGERAFKAWAVARLSQRPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDDRADLAKYICEN
QDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVLGMFLYEARHPDYSVLLRLAKTYETT
LEKCCAAADPHECYAKVDFEFLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCKKHPEAKR

FIG. 16 Cont.

MPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYPKEFNAETTFTHADICTLSEKERQIKKQTALVELVK
HKPKATKEQLKAVMDDFAAFVEKCKCKADDKETCFAEEGKKLVAAASQAALGL

Linker-2 (SEQ ID NO: 27)
GGGS

Human IgG4 hinge region and Fc region (SEQ ID NO: 28)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
VLDSGSGFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

IgG4 Hinge + IgG4Fc-Knob strand (SEQ ID NO: 29)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
VLDSGSGFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

IgG4 Hinge + IgG4Fc-Hole strand (SEQ ID NO: 30)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
VLDSGSGFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

IgG4 Hinge (SEQ ID NO: 31)
ESKYGPPCPPCP

IgG4Fc-Knob strand (SEQ ID NO: 32)
APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTSKAGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSGFFLYS
RLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

IgG4Fc-Hole strand (SEQ ID NO: 33)
APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTSKAGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSGFFLYS
RLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

FIG. 16 Cont.

Linker (SEQ ID NO: 34)
TGGGGGGGGSSAAA

IgG4Fc (Hole) - IL21-WT (SEQ ID NO: 35)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVCTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTP
VLDSGSFFLVSRLLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKTTGGGGSSAAAHKSSSQGQDRHMRQLIDVD
QLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSICKLKRKPPSTNAGRRQKHRLTCTPSCDSYEKKPPKEF
LERFKSLLQKMIHQHLLSSRTHGSEDS

IgG4Fc (Hole) - IL21-C01 (SEQ ID NO: 36)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVCTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTP
VLDSGSFFLVSRLLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKTTGGGGSSAAAHKSSSQGQDRHMRQLIDVD
QLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSICKLKRKPPSCNAGRRQKHRLTCTPSCDSYEKKPPKEF
LERFKSLLQKMIHQHLLSSRTHGSEDS

IgG4Fc (Hole) - IL21-C03 (SEQ ID NO: 37)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVCTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTP
VLDSGSFFLVSRLLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKTTGGGGSSAAAHKSSSQGQDRHMRQLIDVD
QLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSICKLKRKPPSTNAGRRQKHRLTCTPSCDSYEKKPPKEF
LERFKSLLQKMIHQHLLSSRTHGSEDS

IgG4Fc (Hole) - IL21-C07 (SEQ ID NO: 38)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVCTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTP
VLDSGSFFLVSRLLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKTTGGGGSSAAAHKSSSQGQDRHMRQLIDVD
QLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSICKLKRKPPSTNAGRRQKHRLTCTPSCDSYEKKPPKEF
LERFKSLLQKMIHQHLLSSRTHGSEDS

IgG4Fc (Hole) - IL21-C08 (SEQ ID NO: 39)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKGLPSSIEKTSKAGQPREPQVCTLPPSQEEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTP

FIG. 16 Cont.

VLDSDGSFFLVSRLLTVDKSRWQEGNVFSCVMHEALHNHYYTQKSLSLSLGTGGGGGGGGSSAAAHKSSSQGQDRHMIRMRLIDIVD
QLKNVNDLVPECLPAPEDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSIKKLKRKPPSTNAGRRQKHRLTCFSCDSYECKPPKEF
LERFKSLLQKMIHQHLLSSRTHGSEDS

Human IgG4 Fc region (SEQ ID NO: 40)
APEFLGGPSVFLFPPKPKDILMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTIISKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYS
RLTVDKSRWQEGNVFSCVMHEALHNHYYTQKSLSLSLGG

Linker (SEQ ID NO: 41)
GGGG

hSIRPα-Fc-mt10 (SEQ ID NO: 42)
EEELQVIQPDKSVSVAAGESAILTCTVTSLYPVGPIQWFRGAGPARELIYNQKRQTFPRVTTVSESTKRFNMDFSISISNITPADAGTY
YCVKFRKGSPTDFKSGAGTELSVRAKPSSESKYGPCCPAPAEFLGGPSVFLFPPKPKDILMISRTPEVTCVVVDVSQEDPEVQFNWY
VDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYYTQKSLSLSLGG

FIG. 16 Cont.