

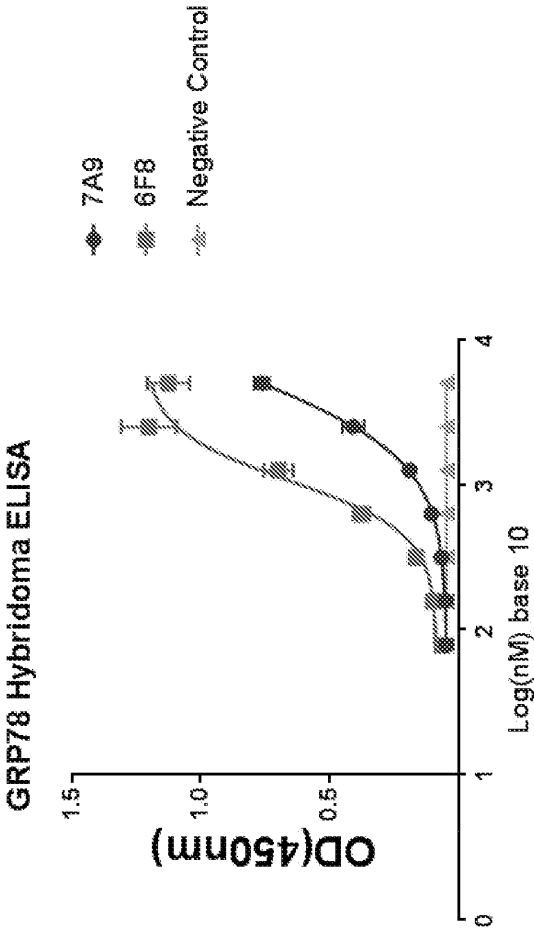


FIG. 1

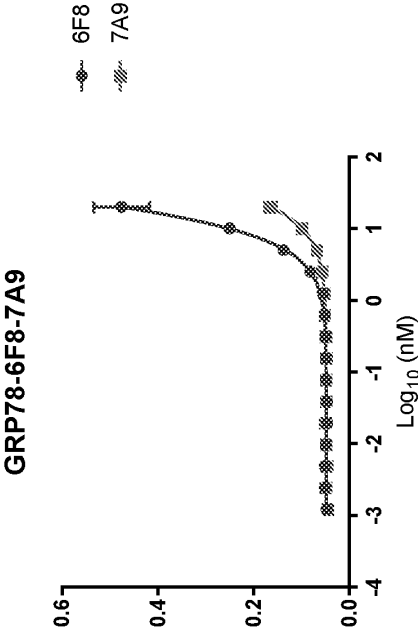


FIG. 2

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Cell surface binding of GRP78 antibodies on NSCLC

A549
4A4A4

4A6O9

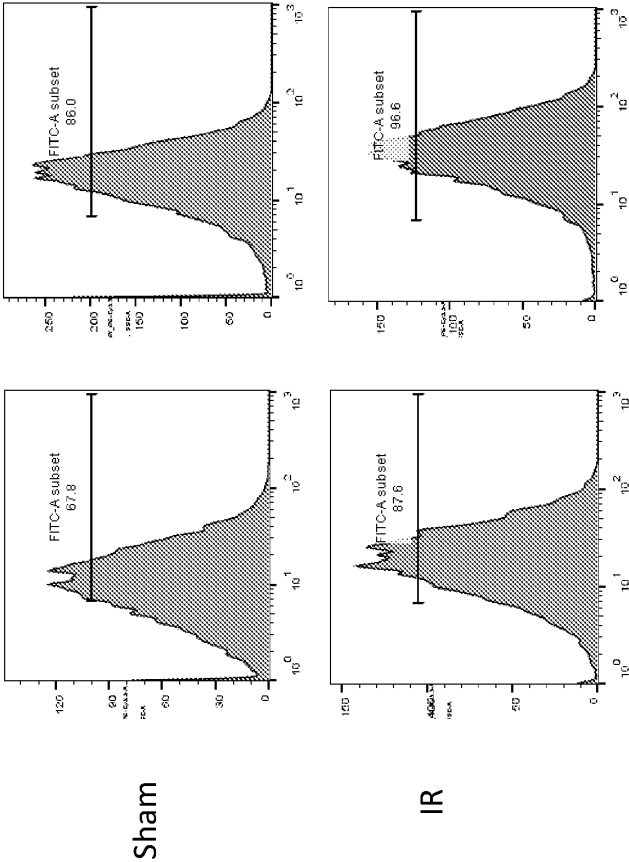


FIG. 3

Epitope mapping of GRP78 antibodies
7A9

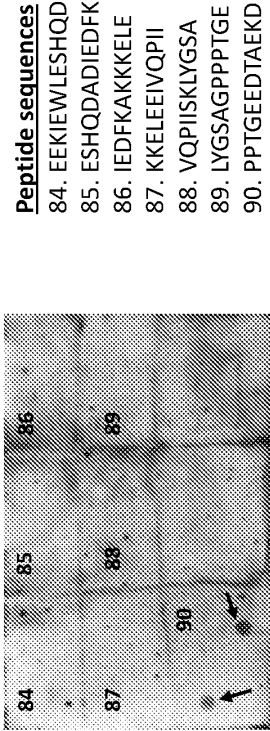


FIG. 4

Epitope mapping of GRP78 antibodies

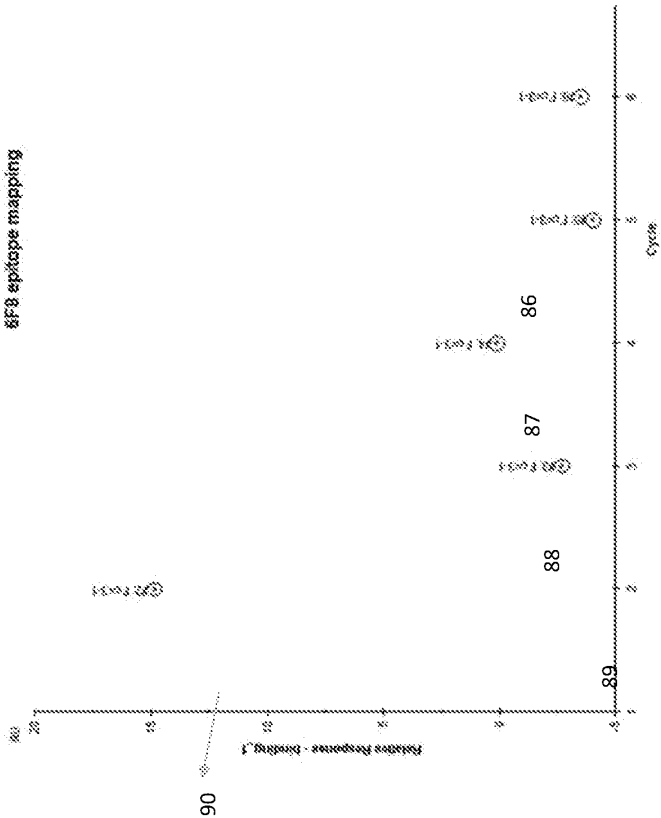
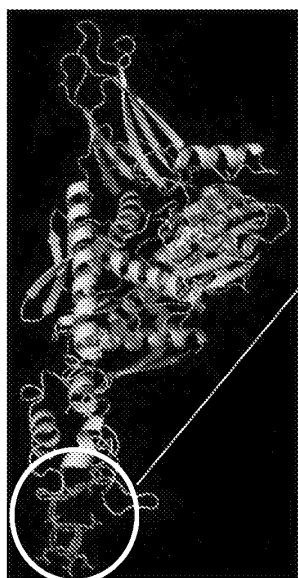


FIG. 5A

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6F8 epitope : PPTGEEDTAE

FIG. 5B

Epitope mapping of GRP78 antibodies

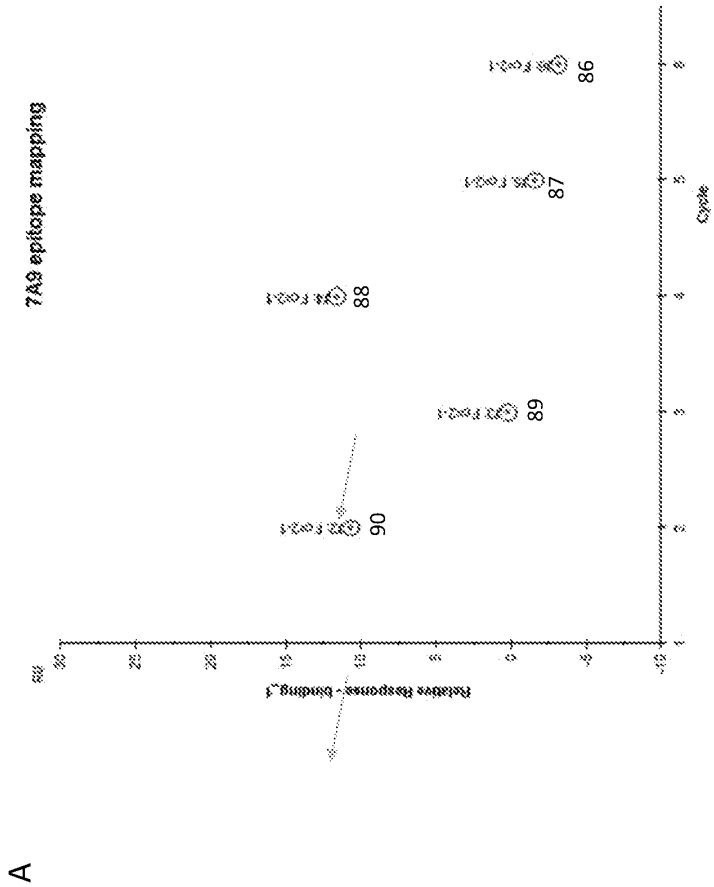
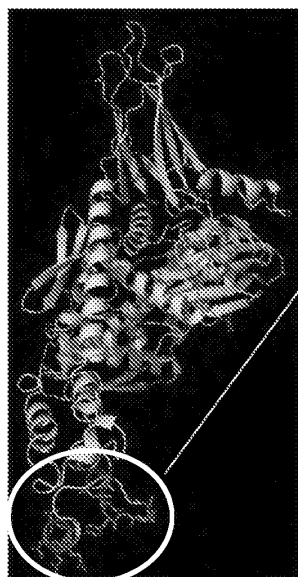


FIG. 6A

Epitope mapping of GRP78 antibodies



7A9 epitope : ISKLYGSA ..EDTAE

FIG. 6B

Flowcytometry for cell surface binding of GRP78 antibodies

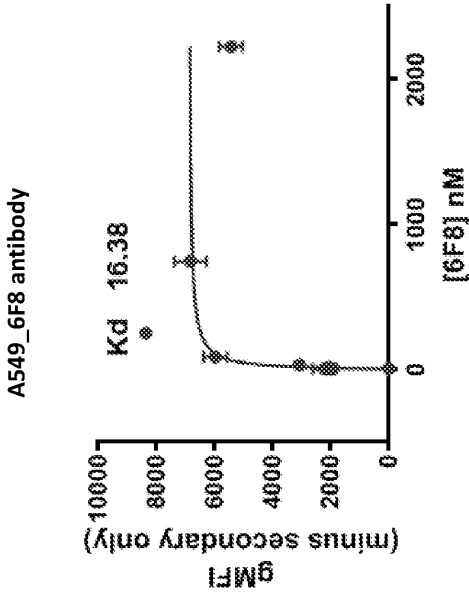


FIG. 7A

Flowcytometry for cell surface binding of GRP78 antibodies

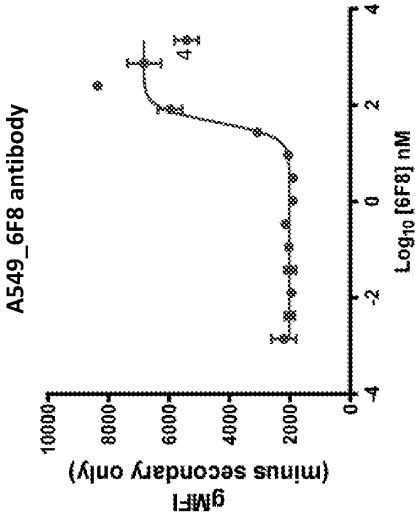


FIG. 7B

Flowcytometry for cell surface binding of 6F8 to A549 cells

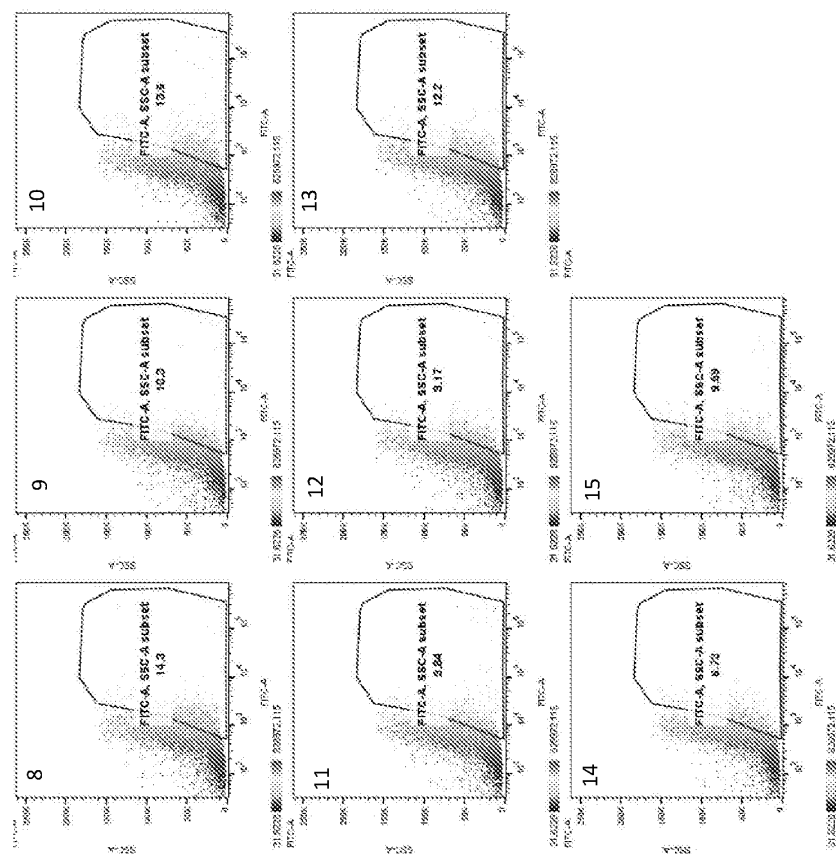


FIG. 8B

Flowcytometry for cell surface binding of 6F8 to H460 cells

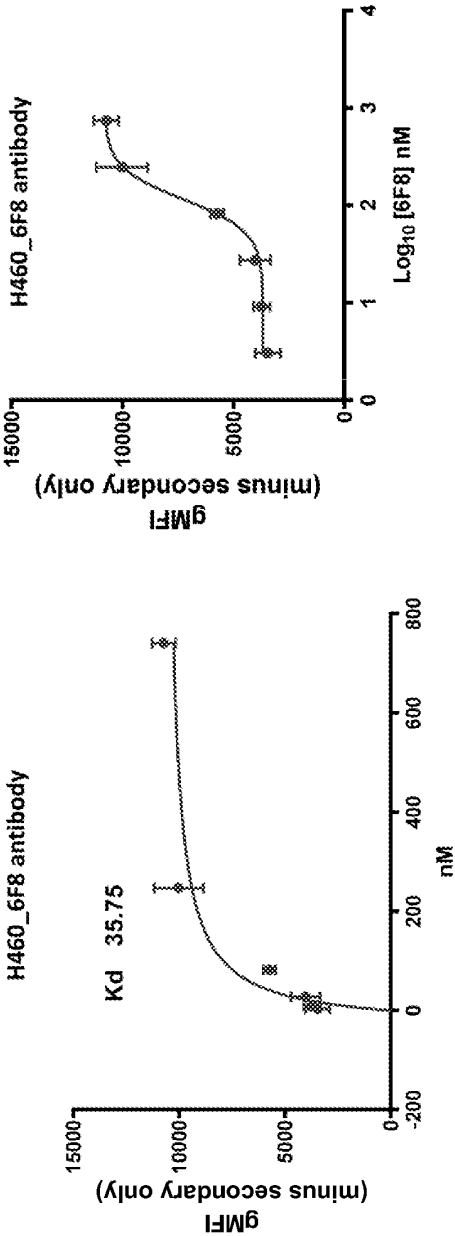


FIG. 9A-9B

Flowcytometry for cell surface binding of 6F8 to H460 cells

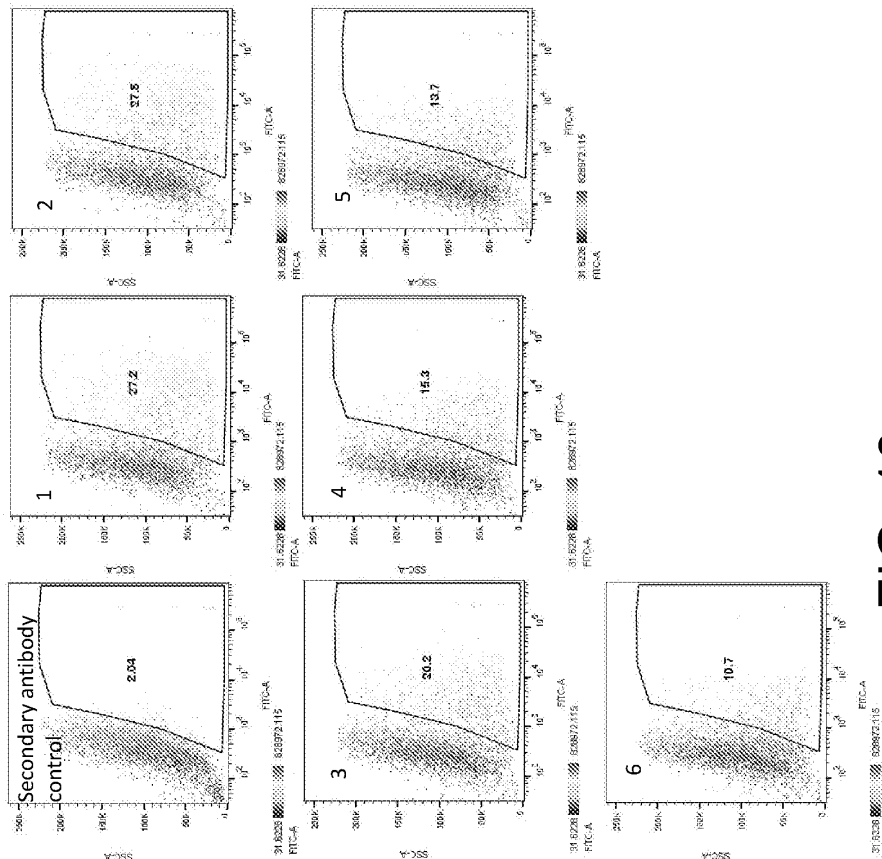


FIG. 10

Flow cytometry for cell surface binding of 7A9 antibody to H460 cells

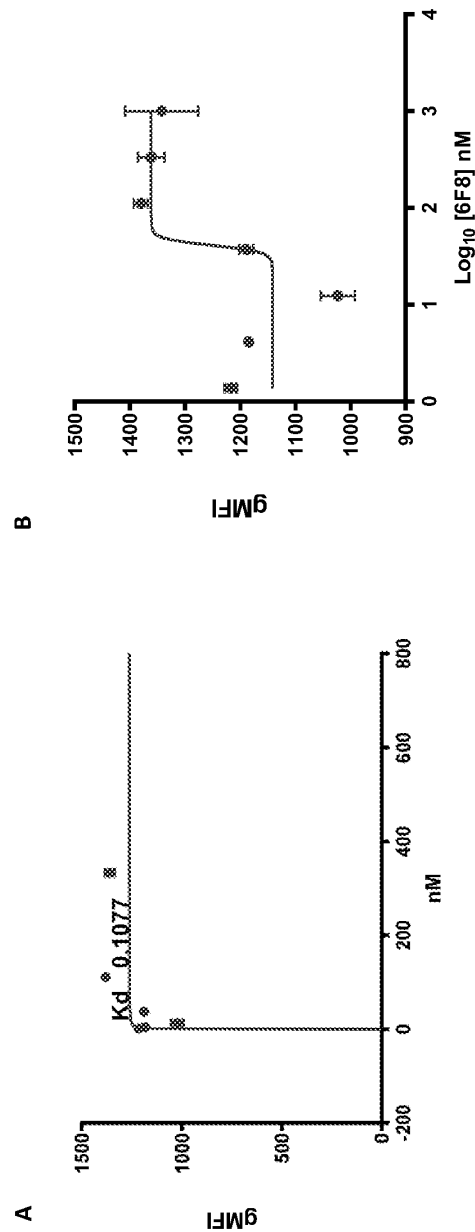


FIG. 11A-11B

Flow cytometry for cell surface binding of 7A9 antibody to H460 cells

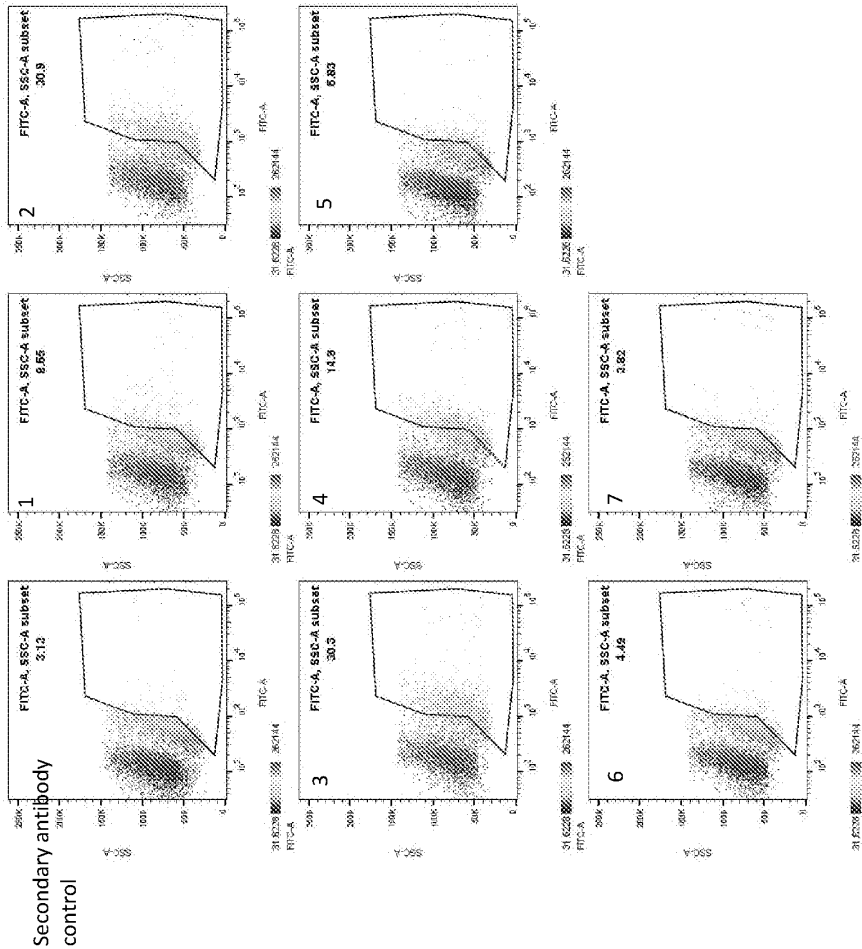


FIG. 12

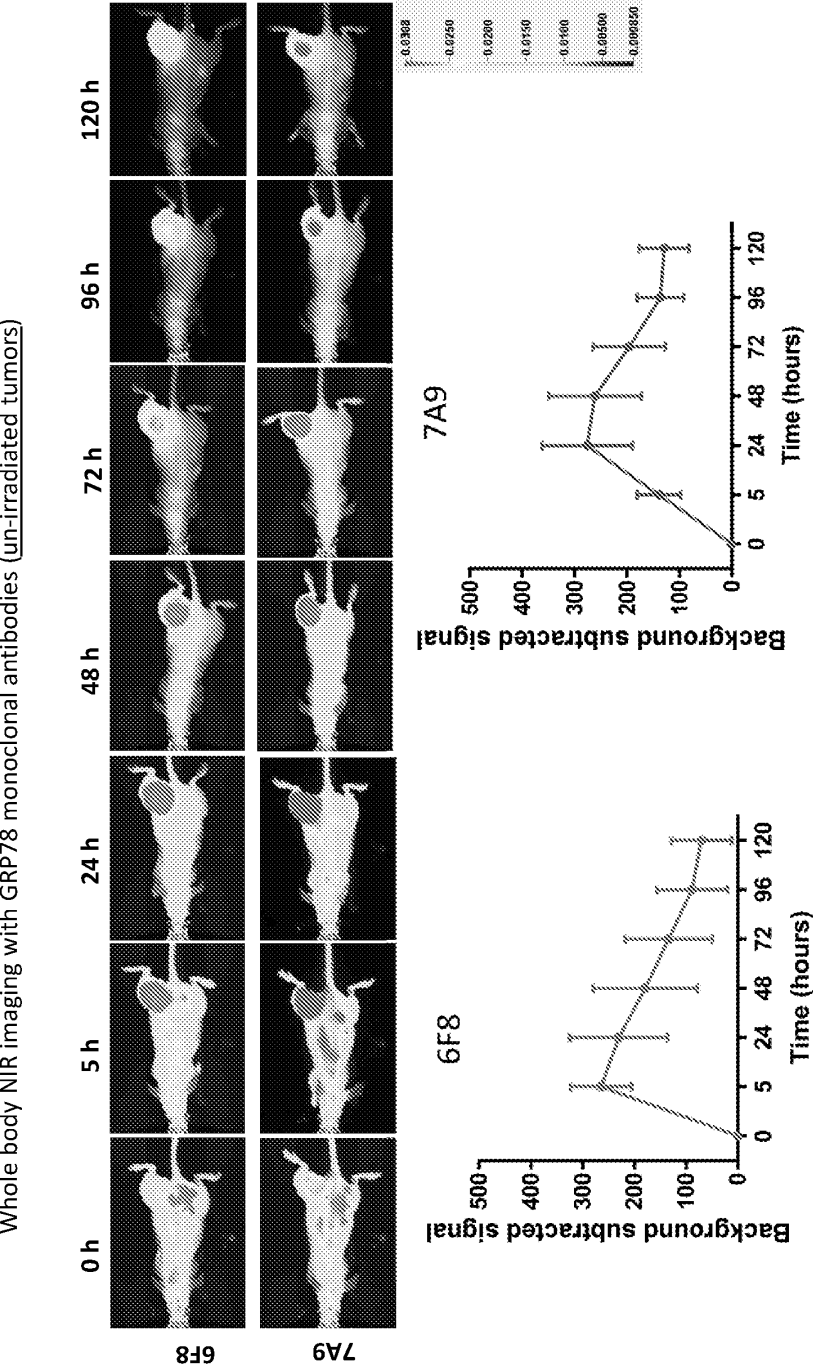


FIG. 13

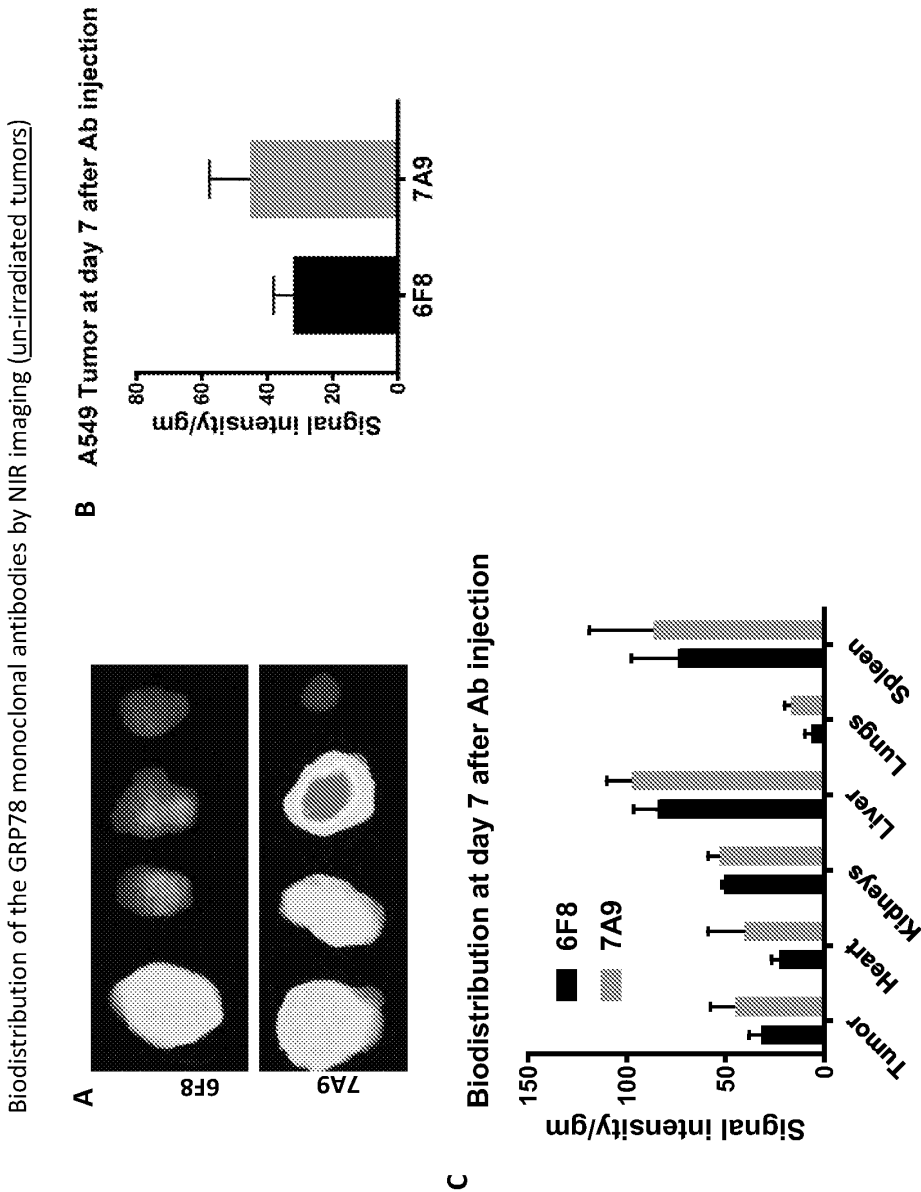


FIG. 14A-14C

Internalization of the GRP78 monoclonal antibodies in A549 cells

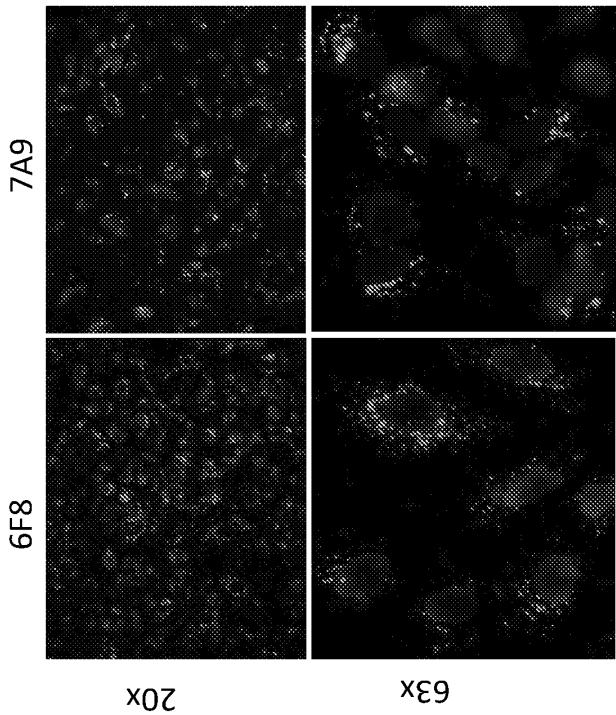


FIG. 15

Dot blot showing GRP78 scFv-Fc binding to GRP78 full length protein

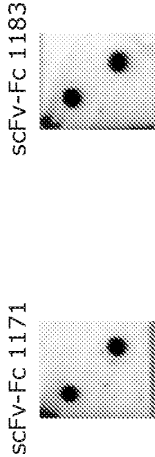
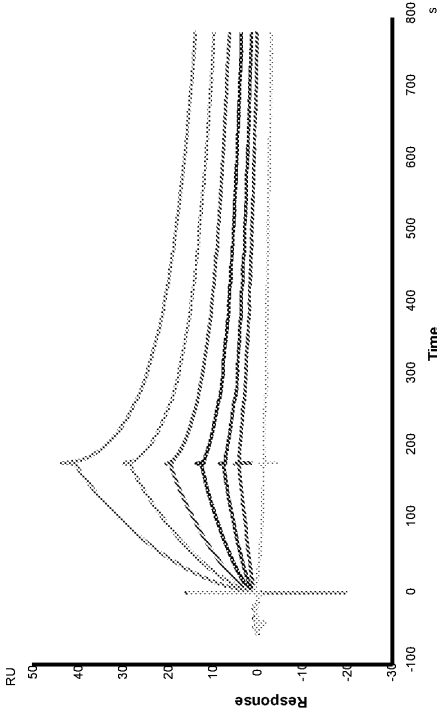


FIG. 16

scFv 1171-Fc



k_a (1/Ms)	k_d (1/s)	K_D (M)
6.79×10^5	3.24×10^{-3}	4.77×10^{-9}

FIG. 17

scFv 1183-Fc

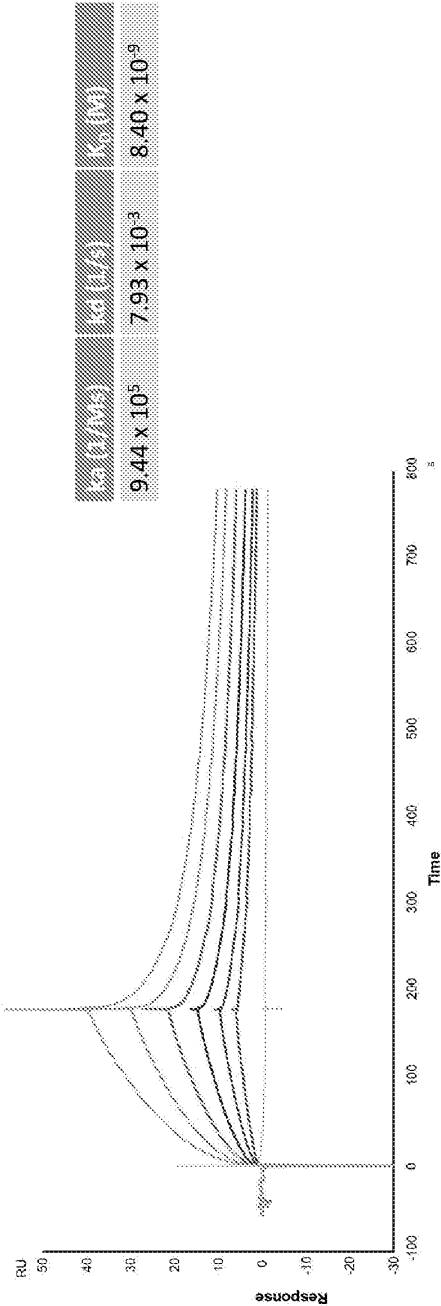


FIG. 18

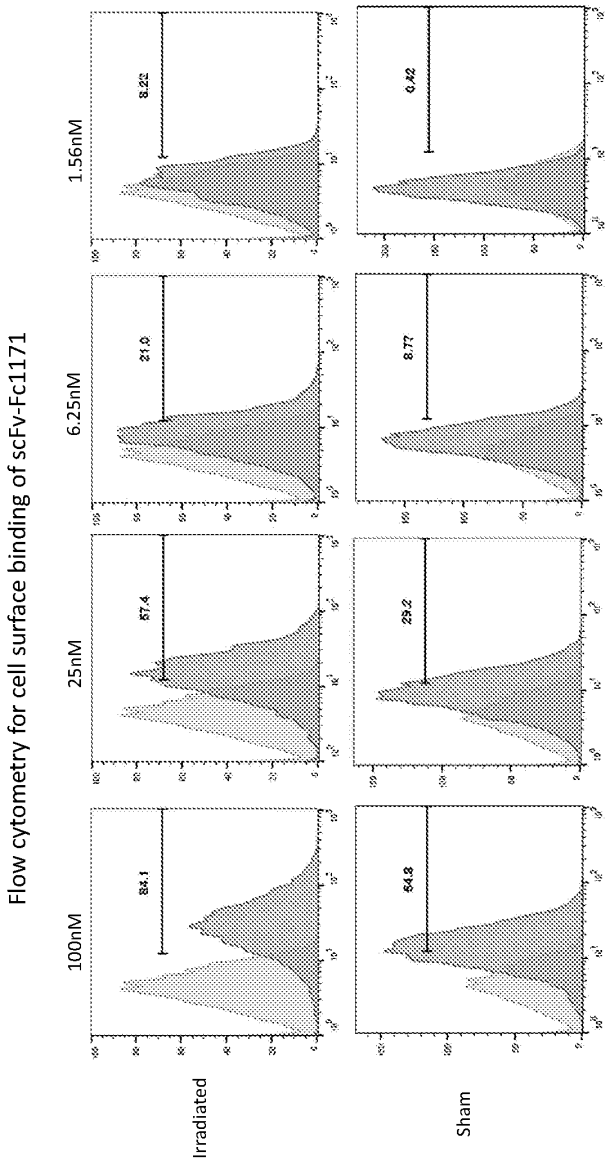


FIG. 19

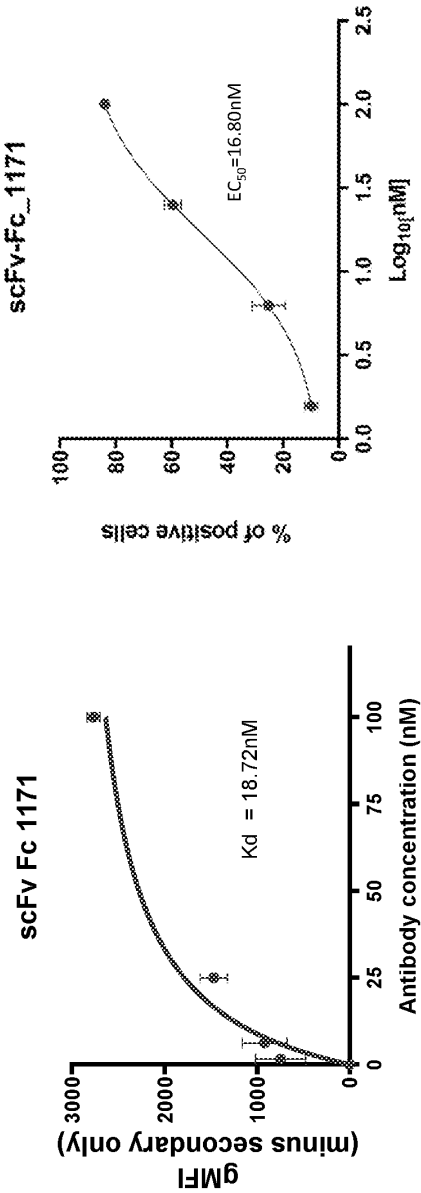


FIG. 20

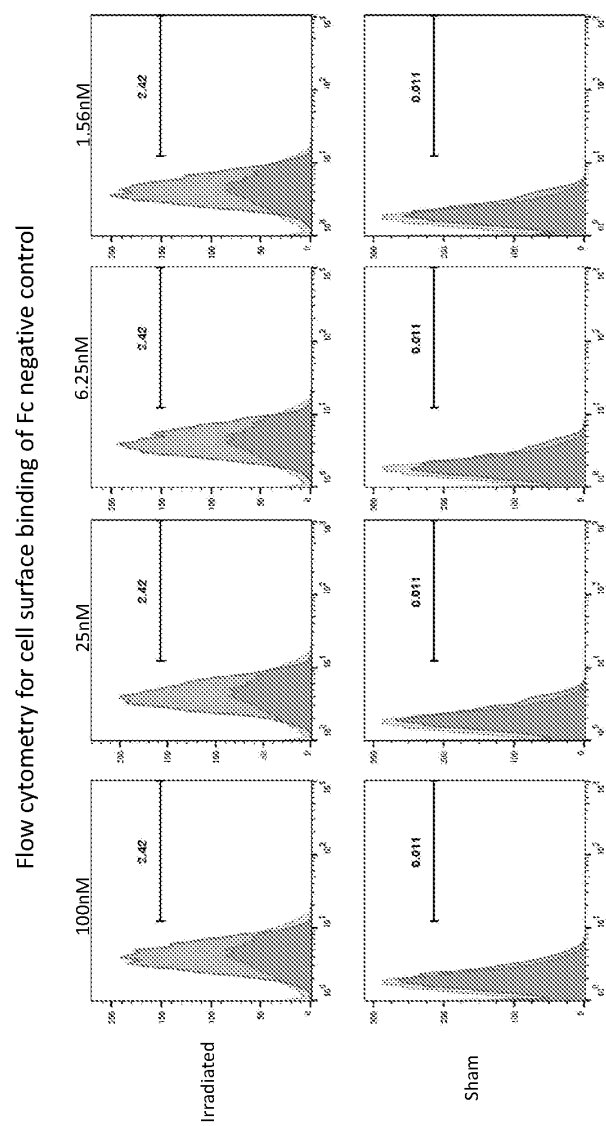


FIG. 21

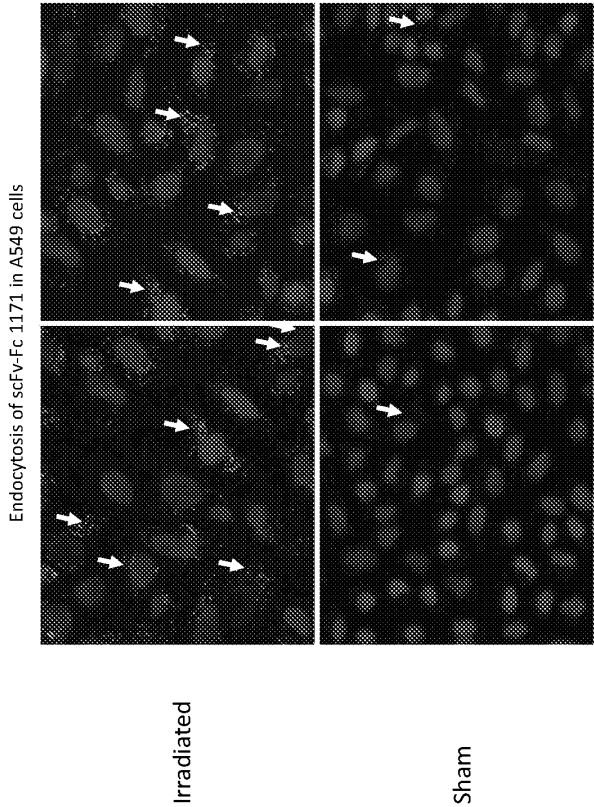


FIG. 22

Dose response of GRP78 scFv-Fc 1171 and Fc using colony formation assay

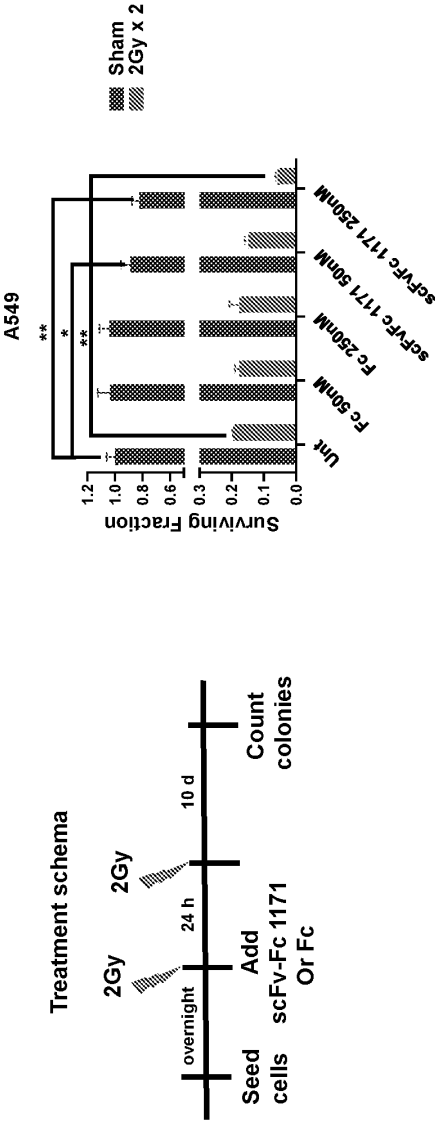


FIG. 23

Dose response of GRP78 scFv-Fc 1171 and Fc using colony formation assay on H460 cells

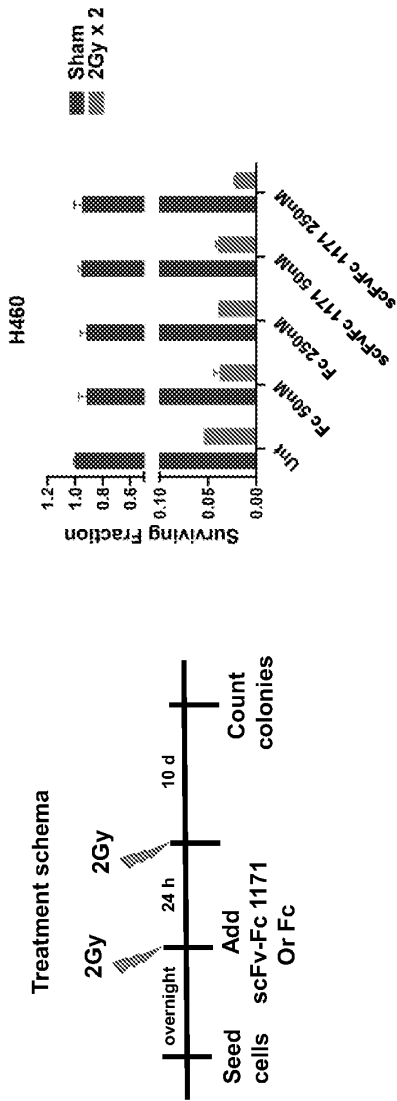


FIG. 24

GRP78 monoclonal antibody sequence
6F8

Heavy chain: DNA sequence (408 bp)

Signal sequence-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4

ATGCTGTTGGGGCTGAAGTGGTTTGCTTTGTTGTTTTTATCAAGGTGTGCATTGTGAGTGCAGCTTGT
TCAGTCTGGTGGAGGATTGGTGGGCTTAAAGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCAACC
TCATAACCTCCGCCATGAACCTGGTCCGCCAGGTTCCAGGAAAGGTTTGGAAATGGTTCGTCGATAAGA
AGTAAATAATTATAATATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTCAACATTTTCAGAGATGA
TTCCAAAAACAATGCTCTATCTGCATAATGAACAACCTTGAATACTGAGGACACAGCCATGTATTACTGTGTGA
GGCCCCCGGGTTTGCTTACTGGGGCCAAAGGACTCTGGTCACTGTCTCTGCA

Heavy chain: Amino acid sequence (136 aa)

Signal peptide-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4

MLLGLKWWCFVVFYQGVHCEVQVLESVGGGLVREPKGSLKLSCAAASGFTLNTSAMNWVRQVPGKGLEWVGRIR
SKNYNYATYYADSVKDRETLERDDSQNMILYLQNMNLKTEDTAMYICVRPPPGFAYWGQGLVTVSA

Light chain: DNA sequence (381 bp)

Signal sequence-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4

ATGAGGGTTCCTGCTCAGCTTTTGGCTTCTTGTCTGTTTCCAGGTACCAGATGTGACATCCAGAT
GACCCAGTCTCCATCCCTTATCTGCTCTCTGGGAGAAAGAGTCAGTCTCACTTGTTCGGACAAGTCAGG
AAATTAGTGGTCACTTAAGCTGGCTTCAGCAGAAACCAGATGGAACATAATAACGCTGATCTAAGCCGCA
TCCAGTTTAGATTCTGGTGTCCJAAAAAGGTTJAGTGCAGTAGGCTCTGGGTCAAGATTATCTCTCACCAT
CAGCAGCCTTGAGTCTGAAGATTTTGCAGACTATTACTGTCTACAATATTCTAGTTATCCCGTACACGTTCC
CAGGGGACCAAGCTGGAAATAAAA

Light chain: Amino acid sequence (127 aa)

Signal peptide-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4

MRVPAHVFGFLLLWFPGTGRCDIQMTQSPSSLSASLGERVSLTCTRTSQEISGHLNWLQKQPDGTIKRLLIYAA
SSLDSGVPRRTSGSRSGSDYSLTISLSESEDFADYYCLQYSSYPYTFGGGKLEIN

FIG. 25

GRP78 monoclonal antibody sequence

7A9

Heavy chain: DNA sequence (420 bp)
Signal sequence-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4
ATGCTGTTGGGCTGAAGTGGTCTTTCTTTGTTTATCAAGGTGTCATTGTGAGTGGCAGCTTGTTCAG
ACTGGTGGAGGATTTGGTGCAGCTTAAAGGGTCAATGAAGTCTCATGTGGCAGTCTCTGGAATCAATATC
AATGCCATGAACCTGGTCCGCCAGGCTCCAGAAAGGCTTGAATGGGTGCTCGCATAGAAGTAAAGTAAT
AATTATGCAACATATTATGCCGATTCAGTGAAGGACAGGCTCAACCATCCAGAGATGATTCACAAAGCATGCTC
TATCTGCAAAATGAACAACCTGAAACTGAGGACACAGCATGTAATTAATCTGTGTGAGAGATATAACTCGGCGCGGG
TACTTCGATGCTCGGGCCGAGGACACCGTCAACGCTCTCTCA

Heavy chain: Amino acid sequence (140 aa)
Signal peptide-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4
MLLGLKWFVFFVYQGVHCEVQLVETGGGLVQPKNSLKLSCAVSGITPENINAMNWRQAPGKGLEWVARIRKSN
NYATYYADSVKDRFTISRDDSQSMILYLQMMNLKTEETAMYYCVRDITPRAGYFDVWGAGTIVTVSS

Light chain: DNA sequence (384 bp)
Signal sequence-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4
ATGCATTTTCAAGTGCAGATTTTCAGCTTCCTGTAAATCAGTCCCTCAGTCATAATGTCCAGAGGACAAATTCCTT
CTCAACCCAGTCTCCAGCAATCATGCTCTGCATCTCAGGAGAGAGTCAACATAACTGAGTGGCCAGCTCAAGT
GTAAATTACATGCACCTGGTTCAGCAGACAGCAGCACTTCTCCAAACCTGTGATTTATAGCACAATCCCAACCTG
GCTTCTGGAGTCCCTGCTGGCTTLAGTGGCAGTGGATCTGGGACTCTTACTCTCTCACAATCAGCCGAATGGAG
GCTGAAGATGCTGCCACTTATTACTGCCAGAAAGCAGTAGTATCCGCTCAGCTTCGGTCTGGGACCAAGCTG
CAGCTGAAA

Light chain: Amino acid sequence (128 aa)
Signal peptide-FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4
MHFQVQIFSLILISAVIMSRGQIVLTQSPALMSAPGKVTITCSASSSVIYMHWFQOKPGTSPKLIWYSTSNL
ASGVPARFSGSGSGTSYSLTISRMEAEADAATYYCQRSSYLEFTFGAGTKLELK

FIG. 26

GRP78 scFV sequence

SCFV GRP78--1183

----CDR1---> <---CDR2--> <---CDR3-----

humIGLV048 SGSIASNY....__EDN.....__QSYDSTNGV

NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPSSPTTVYEDNQRPSPGVDPFRFSGSIDSSNSASLTISGLKTEDEADYYCQSY
DSTNGVFGGGTKLTVL

humIGHV182

----CDR1---> <--CDR2--> <---CDR3-----

GGTFSSYA....__ISAYNGNT..__ARDPPLRYFDWFRGSDWFDP

QMLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGGGLEWMGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSL
RSDDTAVYYCARDPPLRYFDWFRGSDWFDPWGGTLTVTS

FIG. 27

GRP78 scFV sequence
SCFV GRP78--1164
-----CDR1---> <--CDR2--> <---CDR3-----
humIGLV083 NIGSKN..... GDS..... QVWDSNSDHPFV
SYELMQPPSVSMAPGGQTARITCGGNIGSKKWHWYQQKSGQAPVLVHGDSDRPSGIPERISGRNFGNTATLTINRVEAGDEADYY
CCVWDSNSDHPFVFGTGKVTVL
humIGHV062 -----CDR1---> <--CDR2--> <---CDR3-----
GYTFTDYA.... INPGSGNT.. ARDRQGPDY
WVQLVESGPEVKKPGASVNVSCKASGYTFTDYAIHWVRQAPGQRPPEWMGW#PQSQNTIKYSQKFKQVRVTITRDTASATYAM
EMTSLRSEDTAIYYCARDROGPDYWGQGLVTVS

FIG. 28

GRP78 scFV sequence

SCFV GRP78--1171

-----CDR1----> <--CDR2--> <---CDR3-----

humIGKV120 QSISSY....._DAS....._QQYDNLALT

DIQLTQSPSSLSASVGDRTVTITCRASQSISSYLNWYQQKPGKAPKLLIYDASNILETGVPSPRFGSGSGTDFTFTISSLQPEDIATY
YCCQYDNLALTFFGGGTKVDIK

humIGHV237 -----CDR1----> <--CDR2--> <---CDR3-----

GGTFSNPV.....IITMIFGTT..... AKDPPMFDY

QVQLVQSGAEVKKPGSSVKVCKSSGGTFFSNPVISWVRQAPGGGLEWMGGHIMFGTTIYYGNSVGRFIVSRDNSKNMLFLQMNSLRAEDTAV
YYCAKQPPMFDYWGQGTLVTVS

FIG. 29

GRP78 scFV sequence

Scfv 1256

-----CDR1---> <--CDR2--> <---CDR3-----

humIGKV098

QGIRND.....__AAS.....__LQHNTYPWT

DIVMTQSPSSLSASVGDRTVTITCRASQGINNDLGWYQQKPGKAPKRLYAAASLQSGVPSRFSGSGTEFTLTISLQPEDFATYY
CLOHNTYPWTFGQGTVKVEIK

humIGHV062

-----CDR1---> <--CDR2--> <---CDR3-----

GGYIDRYE....__IYTSGR...__... ARDRQGPDY

EVQLVETGPGLVKPSQTLSTCSVSQGYIDRYFIHWVRQAPGQRPEWMGWYTSQRTKYSQKFQVRVTITRDTASATYMEM
TSLRSEDTAIYYCARDRQGPDYWGQGLTVTS

FIG. 30