

R175H

```

      10      20      30
M S D K I I H L T D D S F D T D V L K A D G A I L V D F W A
      40      50      60
E W C G P G S G S G Q H M T E V V R C P H H E R C S D G S
      70      80      90
G T E V V R C P H H E R G S G V R C P H H E R G S G S G
      100     110     120
P C K M I A P I L D E I A D E Y Q G K L T V A K L N I D Q N
      130     140     150
P G T A P K Y G I R G I P T L L L F K N G E V A A T K V G A
      160     170
L S K G Q L K E F L D A N L A G S G H H H H H H STOP

```

Figure 1A**R248Q**

```

M S D K I I H L T D D S F D T D V L K A D G A I L V D F W A
      40      50      60
E W C G P G S G S G S C M G G M N R P I L T I I T L E D G
      70      80      90
S G M G G M N R P I L T I I T L E D G S G N S S C M G G M
      100     110     120
N R P I L T G S G S G P C K M I A P I L D E I A D E Y Q G
      130     140     150
K L T V A K L N I D Q N E G T A P K Y G I R G I P T L L L F
      160     170     180
K N G E V A A T K V G A L S K G Q L K E F L D A N L A G S G
H H H H H H STOP

```

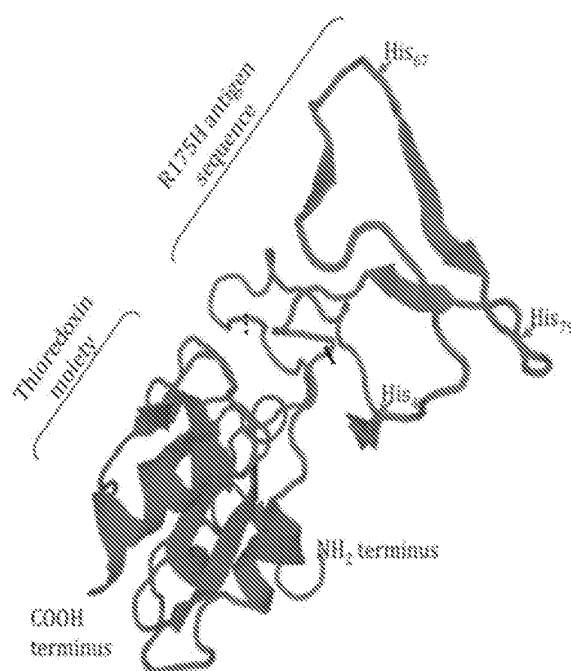
Figure 1B

R273H

```

      10              20              30
M S D K I I H L T D D S F D T D V L K A D G A I L V D F W A
      40              50              60
E W C G P G S G S G R N S F E V V C A G S G N L L G R N S
      70              80              90
F E V V C A C G S G G R N S F E V V C A C P G S G S G P
     100             110             120
C K M I A P I L D E I A D E Y Q G K L T V A K L N I D Q N P
     130             140             150
G T A P K Y G I R G I P T L L L F K N G E V A A T K V G A L
     160             170
S K G Q L K E F L D A N L A G S G H H H H H H STOP

```

Figure 1C**Figure 2A**

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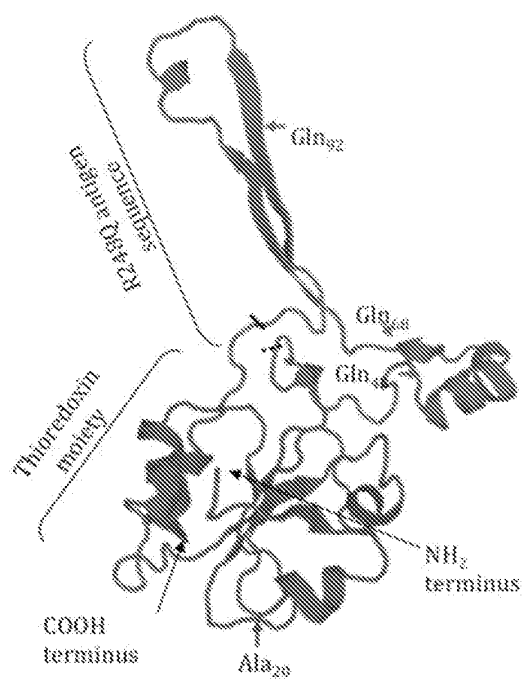


Figure 2B

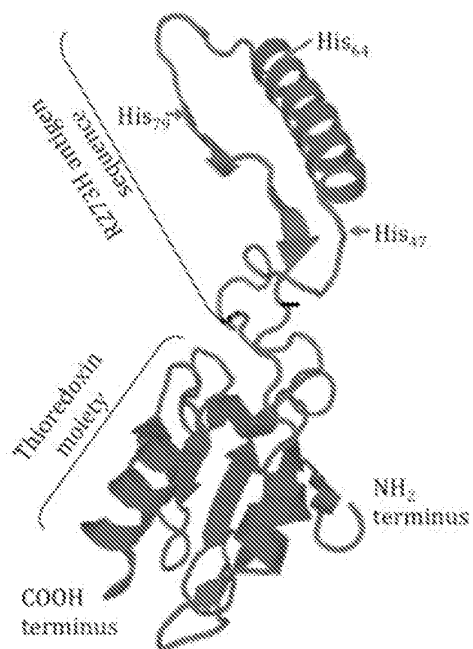


Figure 2C

R175H

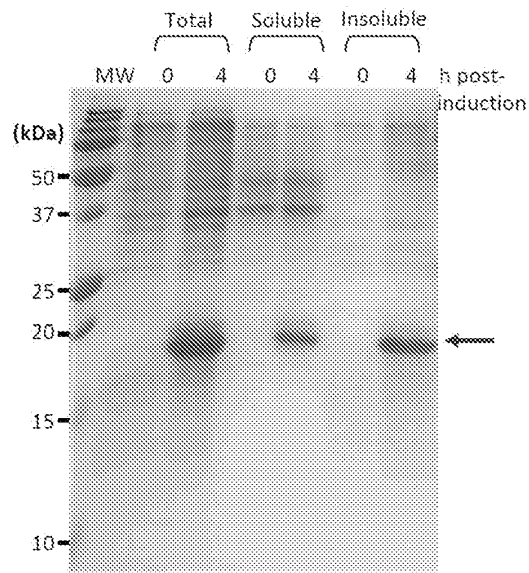


Figure 3A

R248Q

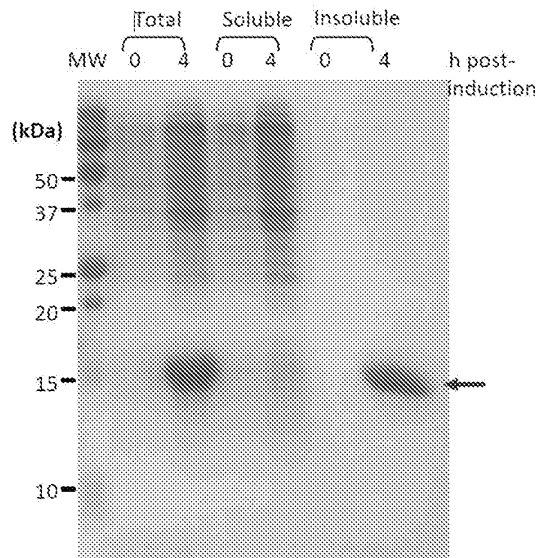


Figure 3B

R273H

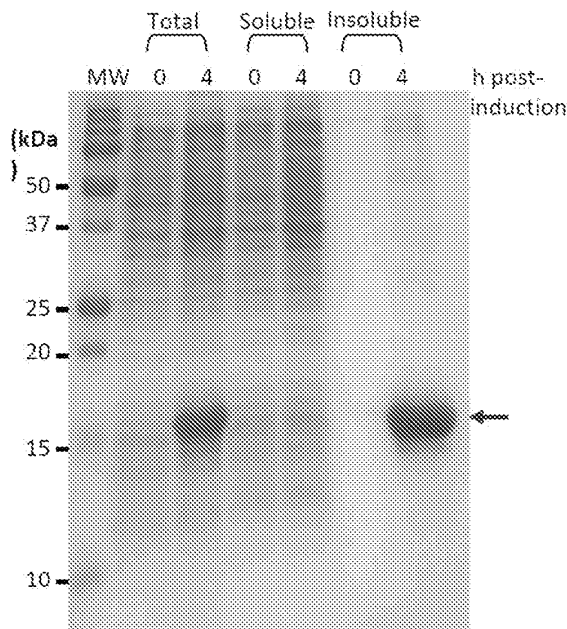


Figure 3C

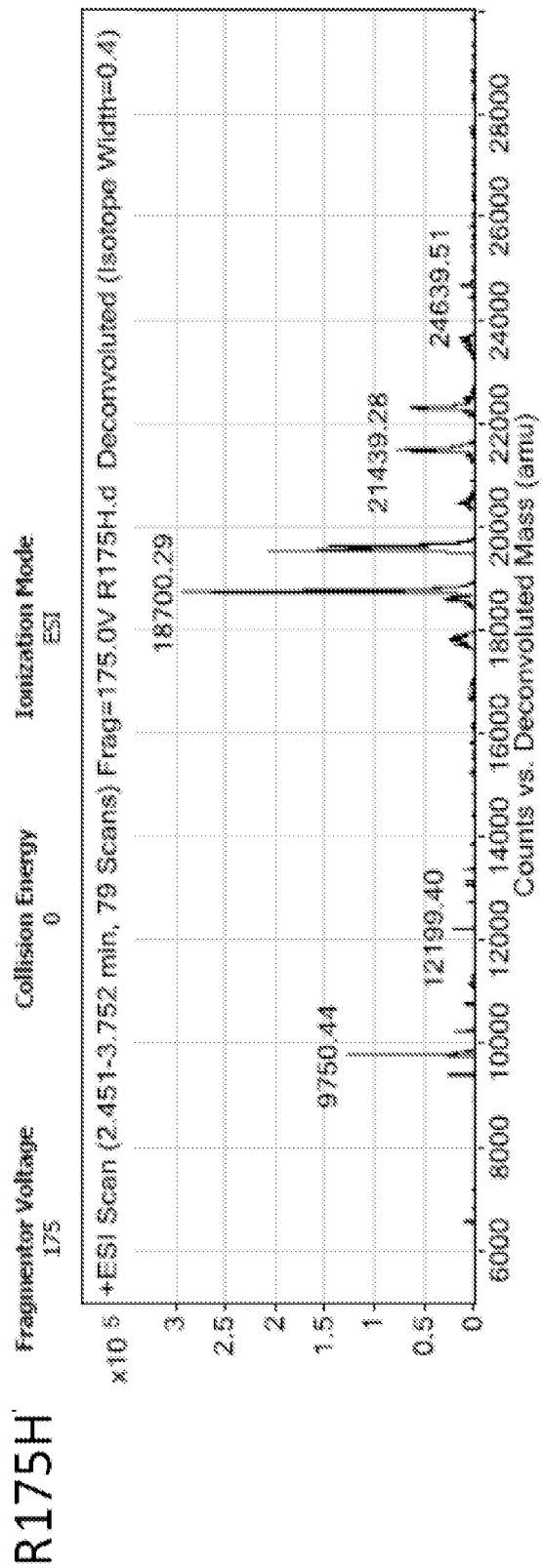


Figure 4A

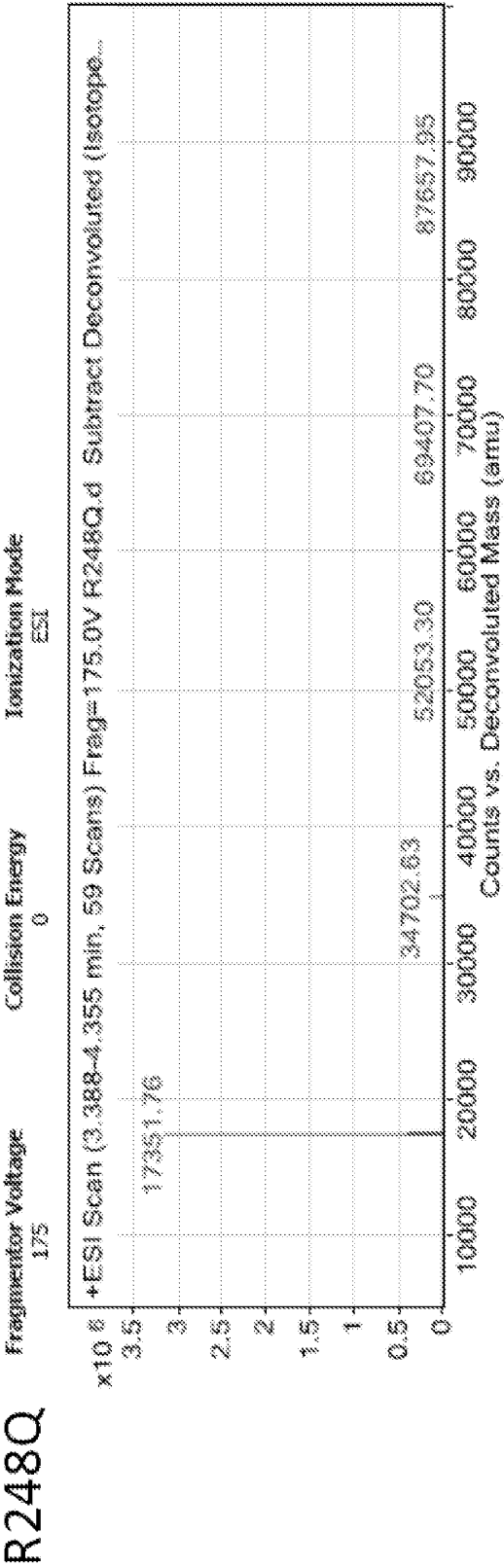


Figure 4B

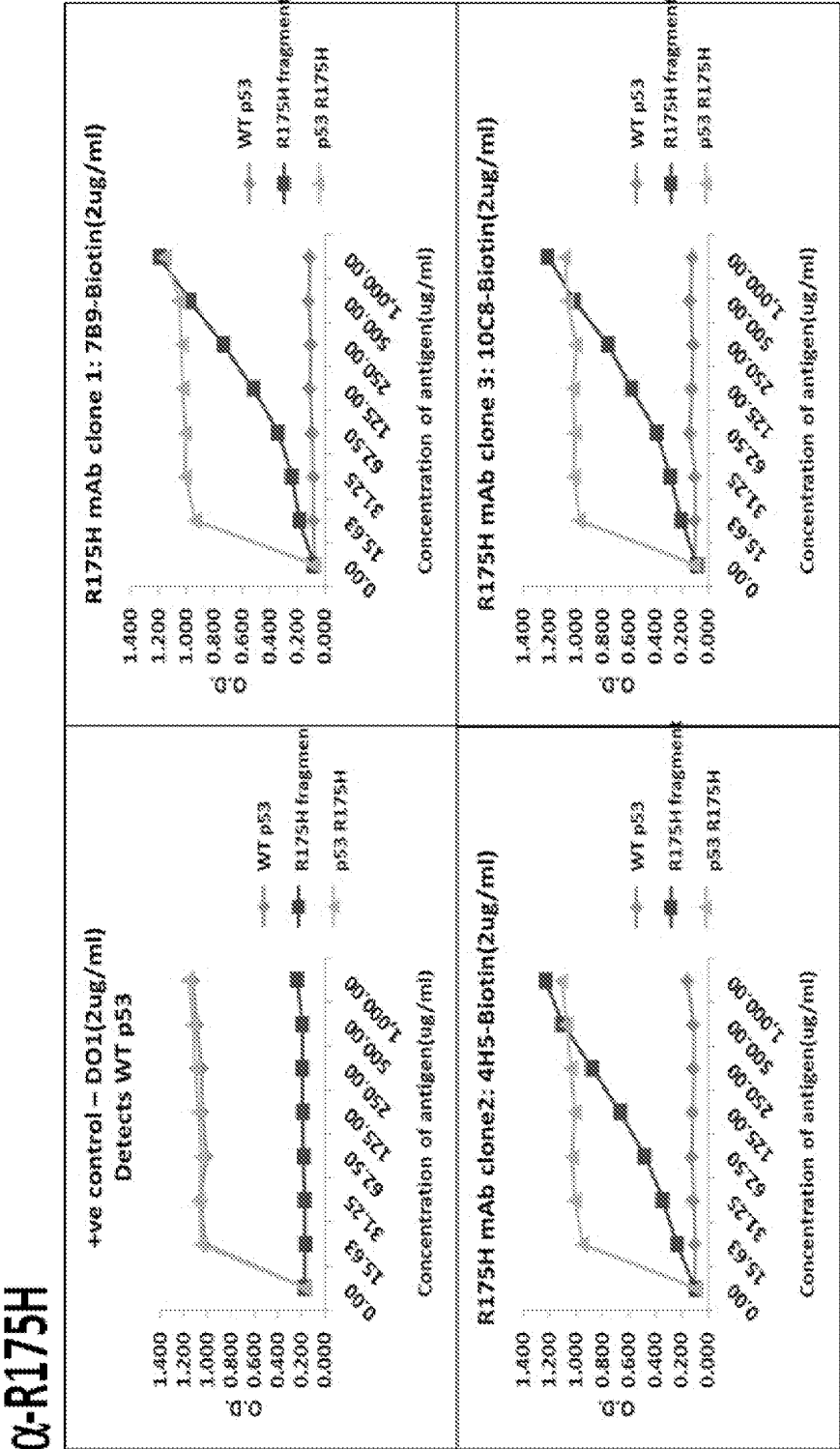


Figure 5A

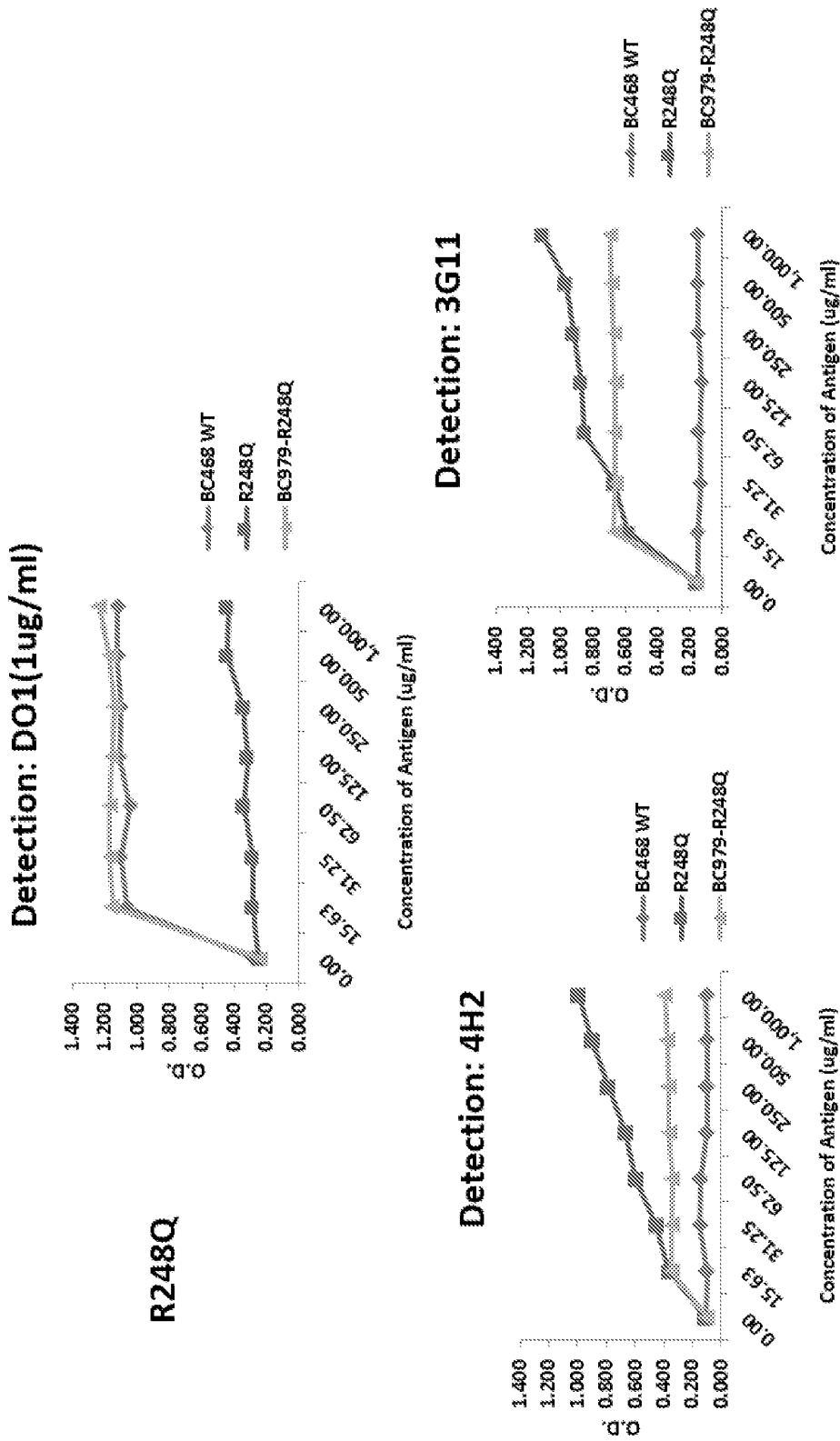


Figure 5B

R273H

Detection: DO1-Biotin(2ug/ml)

Detection: 13E4-Biotin (1ug/ml)

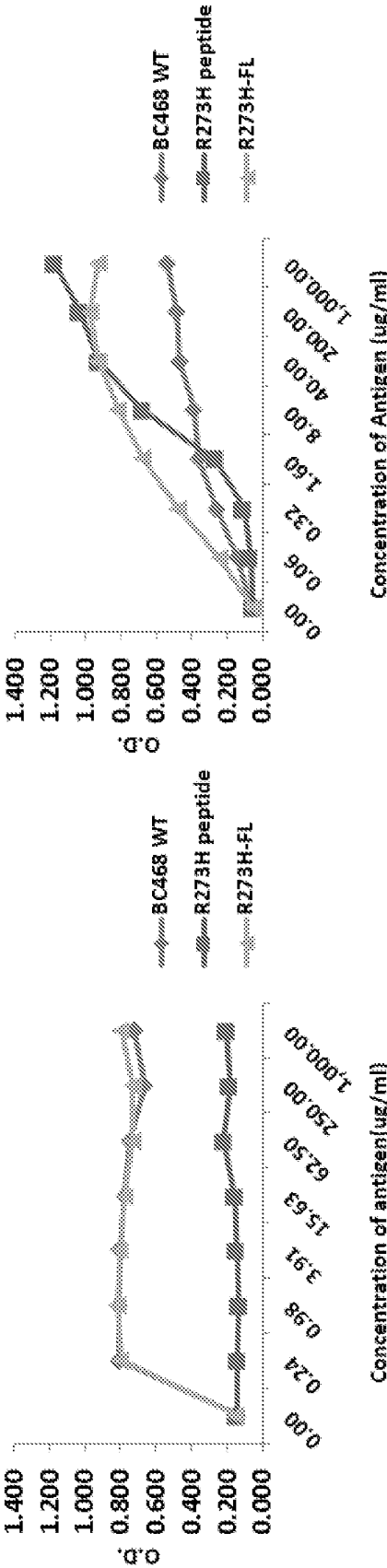


Figure 5C

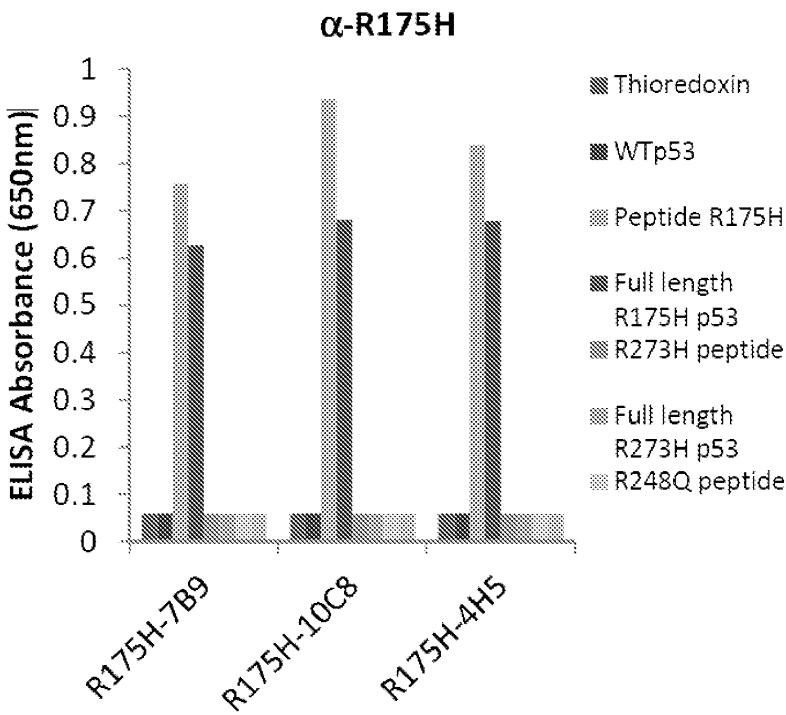


Figure 6A

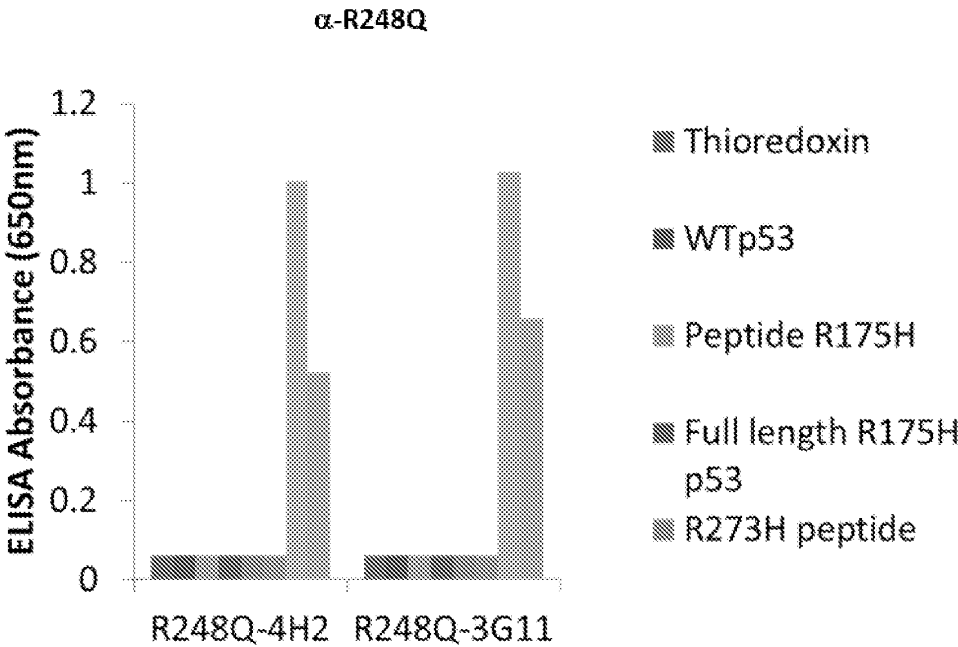


Figure 6B

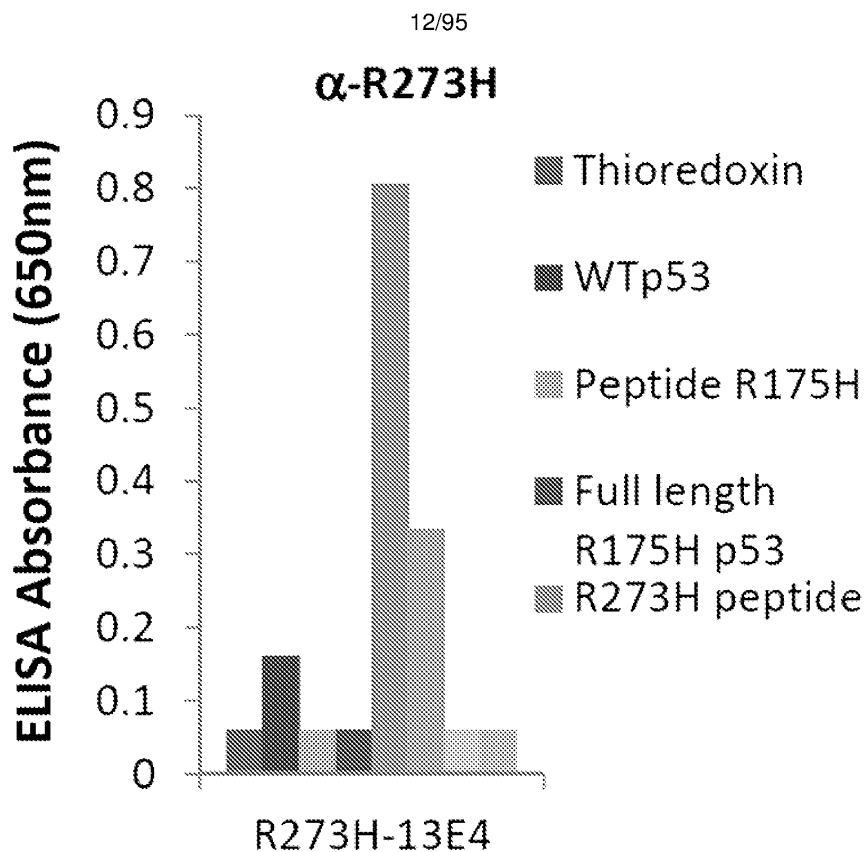


Figure 6C

Anti-R175H mAbs

10C8

WTp53	QHMTEVVRRCPPHHERCSD
R175H	QHMTEVVRHCPHHERCSD
6	---GGVLHLPHHTRN--
3	---ADNHEPHPLACD-
4	-----T-RHQPHHSLPPR
8	-----T-PHQPHHSFTPR
7	---VSTGVHYPHHSA----
2	---VDMHHYPHHYKD---
5	-----ILASHRPHHYGY-
1	---LCTPLLHPIHHL---

Consensus: **167QHMTEVVRHCPHHERCSD184**

10C8, 7B9, 4H5 epitope

Figure 7A

Anti-R248Q mAbs

4H2

WTp53	GMNRRPILTIITLED
R248Q	GMNQRPILTIITLED
1	-----ELWQNVRPFLWV-----
2	-----SRPADHWPRHNE----
3	-----SSRPMALHWPIKV-----
4	-----VSSRPSSHWPI-----
5	---SNTPHWPRGPGI-----
6	-----INTPRDWAYGGL-----
7	-----FNQPPRSGRVI-----

Consensus: **245** GMNQRP ILTIITLED **260**
4H2 epitope

Figure 7B

Anti-R273H mAb

13E4

WTp53	----GRNSFEVRVAC-----
R273 H	----GRNSFEVHVAC-----
4	----GK-TYSYHMQLYT-----
3	-----YHVGILGRLFM
5	-----YNTFPYHLGYTL-----
2	---DNASSKVHHGH-----
1	-----TFVHGNTWTIVN-
6	---TNTMHAVHHPL-----

Consensus: **267**RNSFEVHVACPGR**280**
13E4 epitope

Figure 7C

Anti-R175H mAbs

7B9		4H5	
WTp53	QHMTEVVRRCPPHERCSD	WTp53	QHMTEVVRRCPPHERCSD
R175H	QHMTEVVRHCPPHERCSD	R175H	QHMTEVVRHCPPHERCSD
4	----YNQTHHPHHQEY--	8	---VGSPQHHWPHHHSN---
9	---GAPEVHHPAHQA---	9	---VGSPQHHWPHHHCN---
7	----KTLS-HAPHHHSKE--	2	---VGSPQHHWPHHHSN---
8	----HSPV-HTPHGSGK--	7	---VGSPQHHWPHHHSN---
5	-----TPHQPHHSFTPR	1	---VGSPQHHWPHHHSK---
6	---DSHFLHYPHHHSN---	3	---LEVN-HWGHHYRT-
2	-----ESTGHSPHQHN---	5	---GGSG-HQSGGHRP----
3	----STPVHTPHHAHY--	6	----SLG-HKSHHFIAA----
1	----SGSLQHRPHPRN----	10	---FDLRDYMHHMPHH-----
Consensus: 167 QHMTEVVRHCPPHERCSD 184			
10C8, 7B9, 4H5 epitope			

Figure 8A

Anti-R248Q mAbs

3G11

WTp53	GMNRRPILTIITLED S
R248Q	GMNQRPILTIITLED S
1	----- SSTHYSWSLMDA
2	----- GPSCHYCF TGLP ----
3	----- GPSCHYCF TGLP ----
4	WSVPPGRHIHYS-----
5	WSVPPGRHIHYS-----
10	----- FSVPSG HYIRAN-----
8	----- FSVRPFHYAQDN-----
7	----- FSVPFDRIQETP-----
9	----- FSVRPYDPQIEN-----
6	----- HSVWYAN GSVKT -----

Consensus: **215SVVVPYEPPEVGSDCTTIHYN 235**
3G11 epitope

Figure 8B

4H5 Alanine Scan on R175H

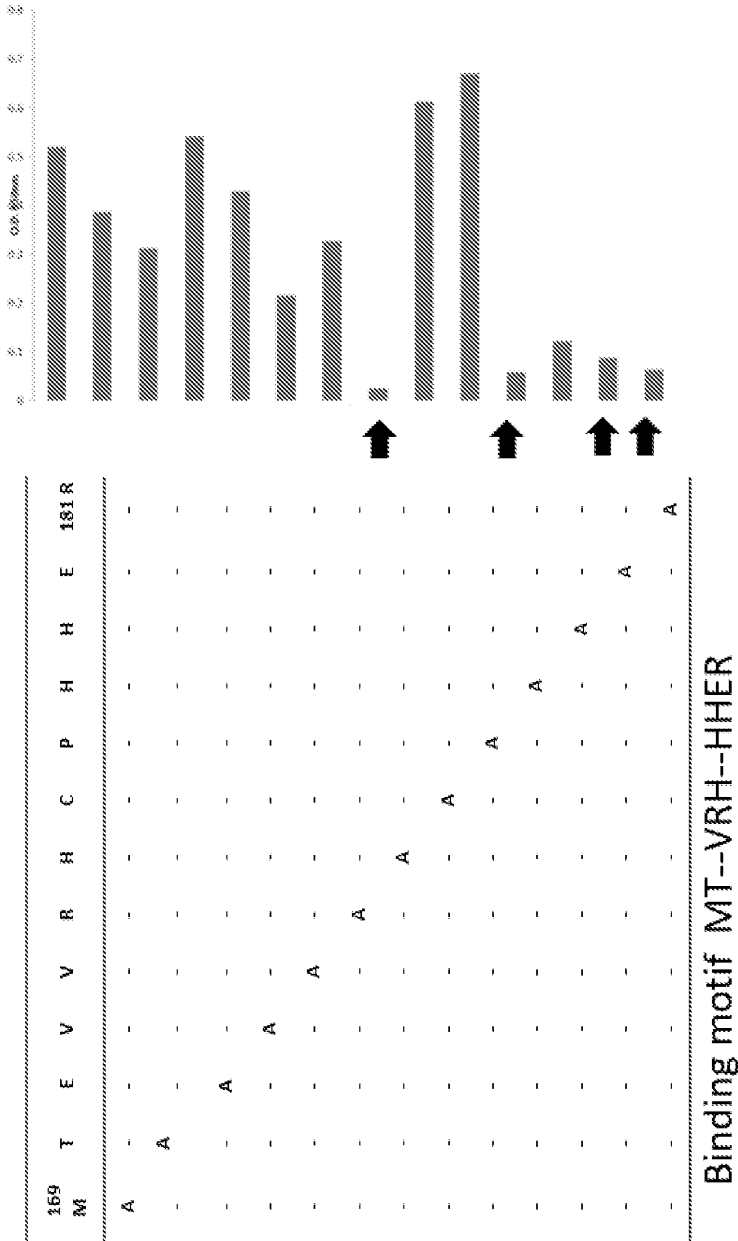


Figure 9A

7B9 Alanine Scan on R175H

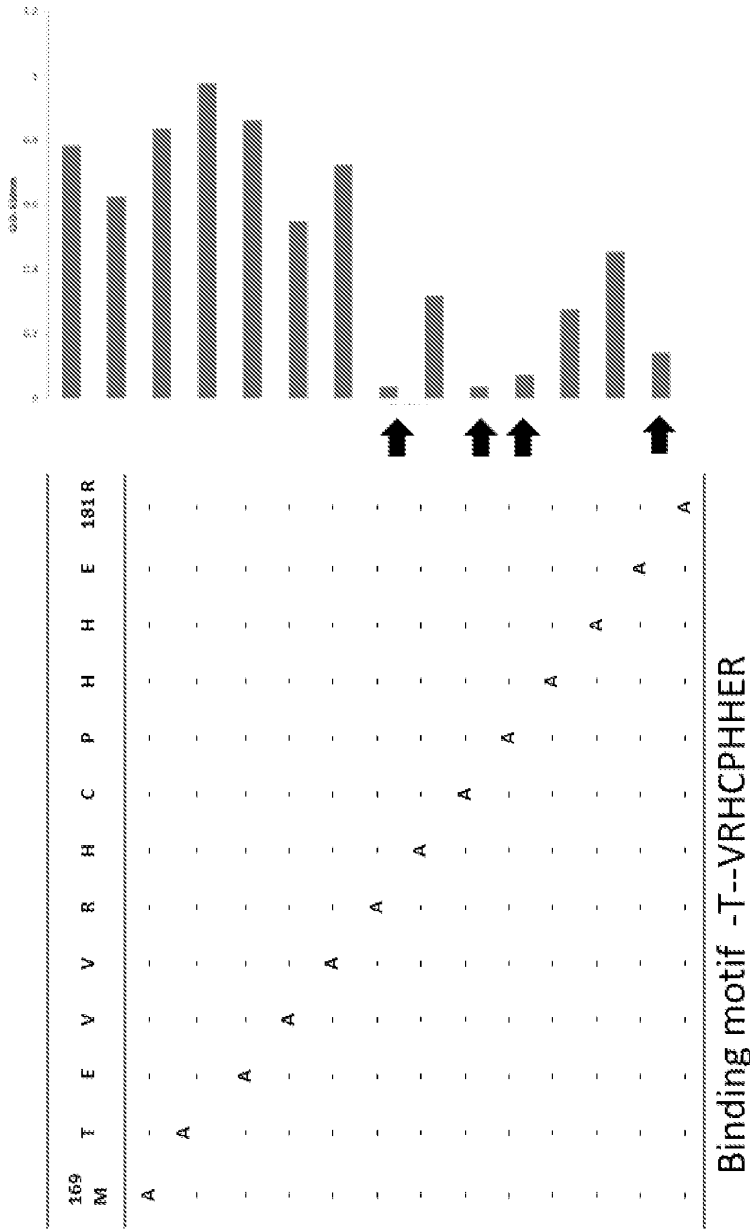


Figure 9B

10C8 Alanine Scan on R175H

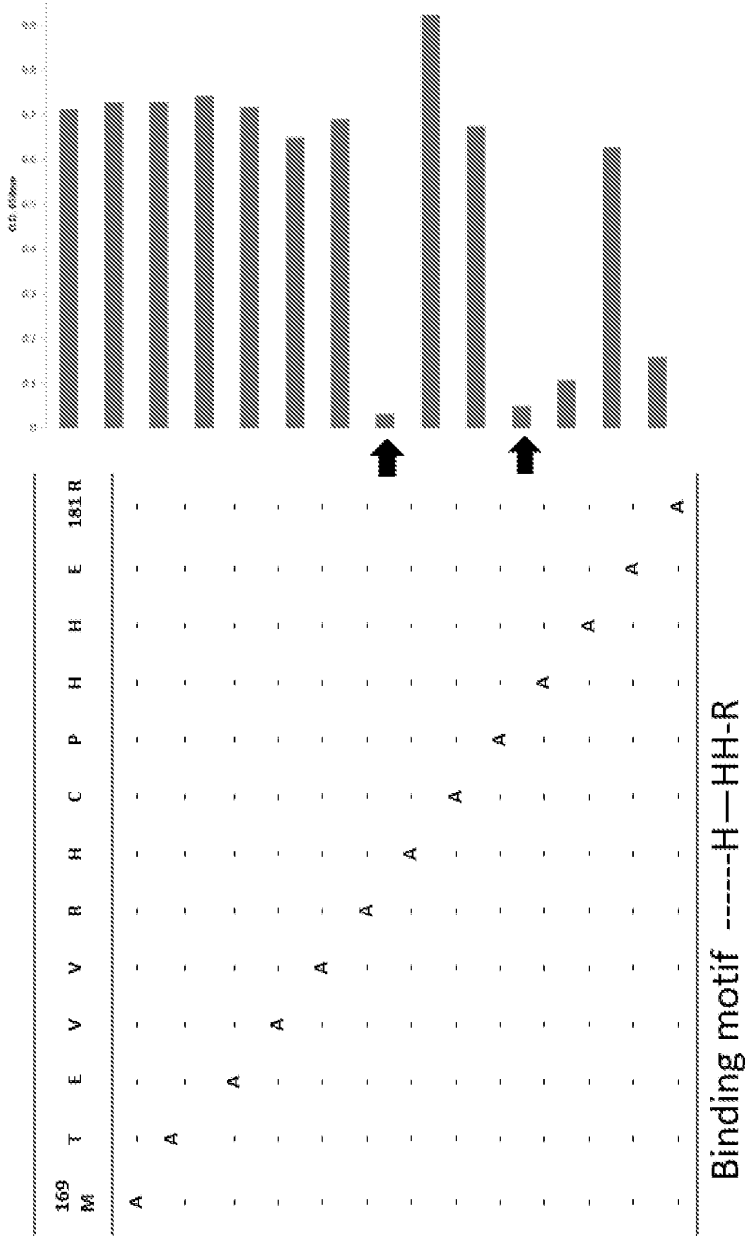


Figure 9C

13E4 Alanine Scan on R273H

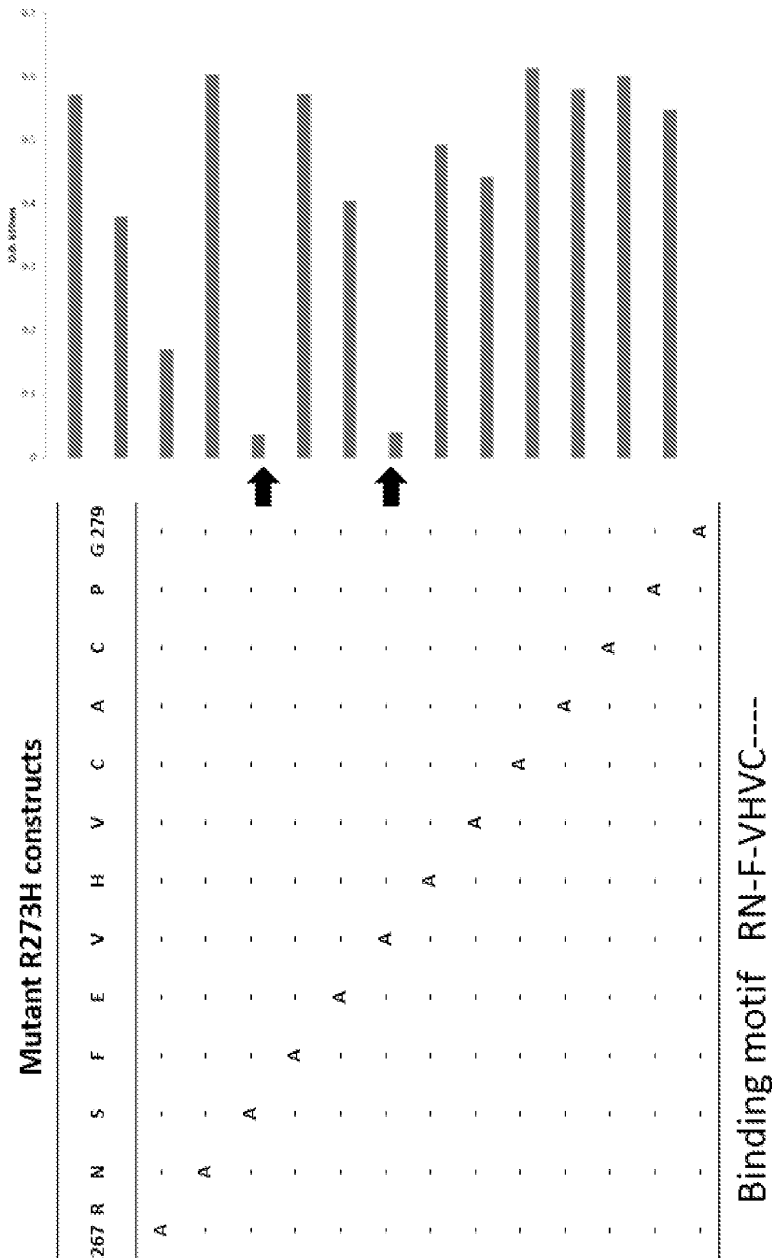


Figure 9D

MEEQSDPSV EPPLSQETES DLWKLLPENN VLSPLPSQAM DDIMLSPDDI EQWFTEDPGP DEAPRMPEAA PPVAPAPAAP TPAAPAPAPS WPLSSSVPSQ 100
KTYQGSYGER LGFLHSGTAK SVTCTYSPAL NKMFCQAKT CPVQLWVDST PPPGTRVRAM AIYKQSQHMT EVVR**R175H**RCSDSDGLAP PQHLIRVEGN 200
LRVEYLDNRN TFRHSVVVPPY EPPEVGS DCT TIHYNVMCNS SCMGGMNQRP ILTIITLED SGNLLGRNSF **R248Q****R273H**VCACPGR ORRTEENLR KKGEPHHELP 300
PGSTKRALPN NTSSSPQPKK KPLDGEYFTL QIRGRERFEM FRELNEALEL KDAQAGKEPG GSRAHSSHILK SKKGOSTSRH KKLMEKTEGP DSD 393

Figure 10

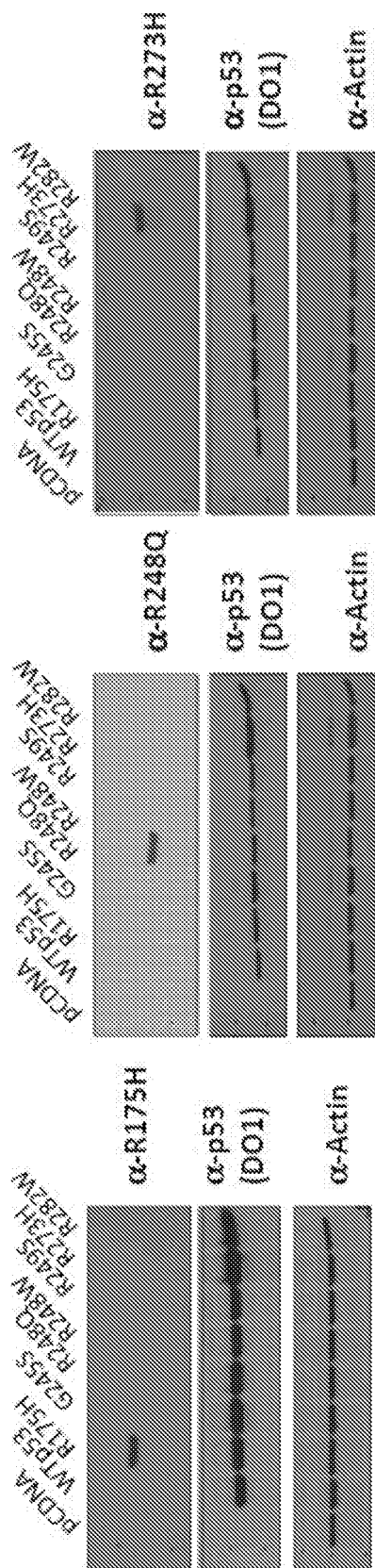
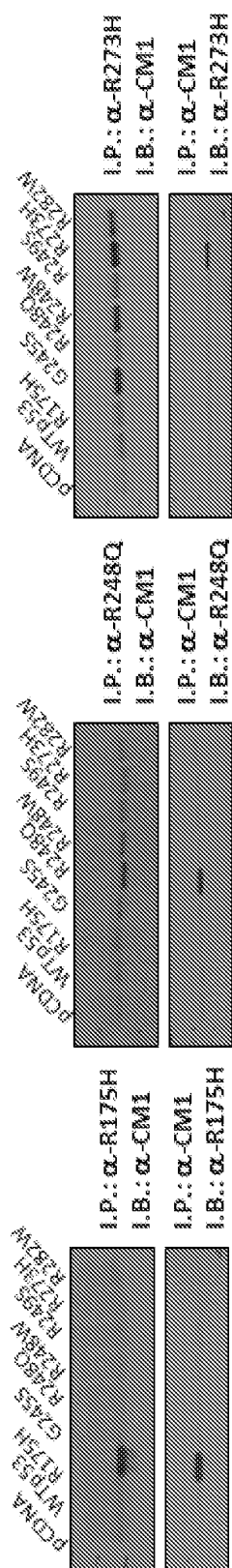


Figure 11



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Cell lines used in study	p53 status
A549, MCF-7, HCT116, MRC5, RKO, U2OS	Wild-type
AU565	R175H
SKBR3	R175H
HEC-1A	R248Q
RD	R248W
786-O	R248W
PLC-PRF/15	R249S
KNS-62	R249S
SW480	R273H
A431	R273H

Figure 13

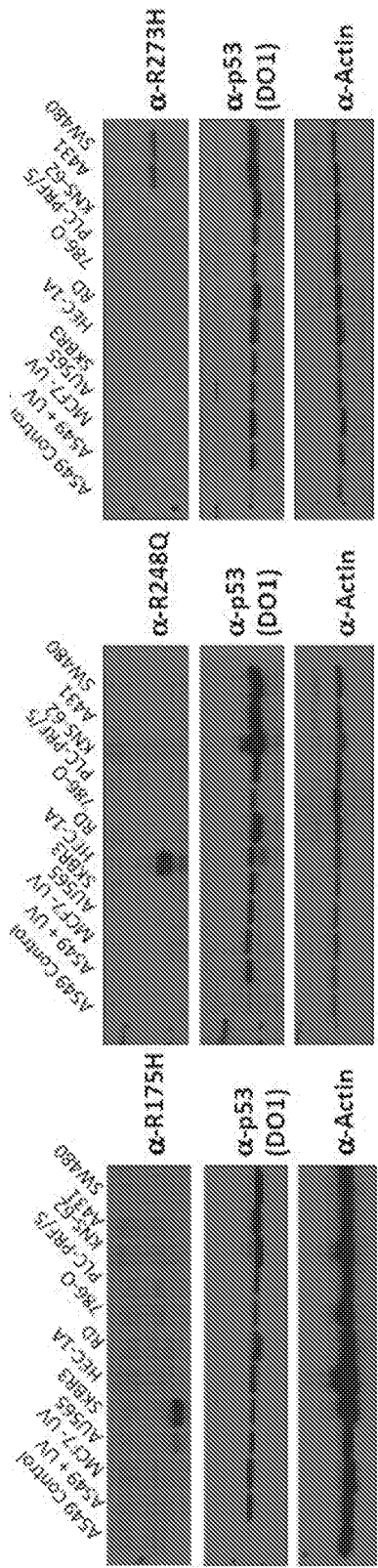
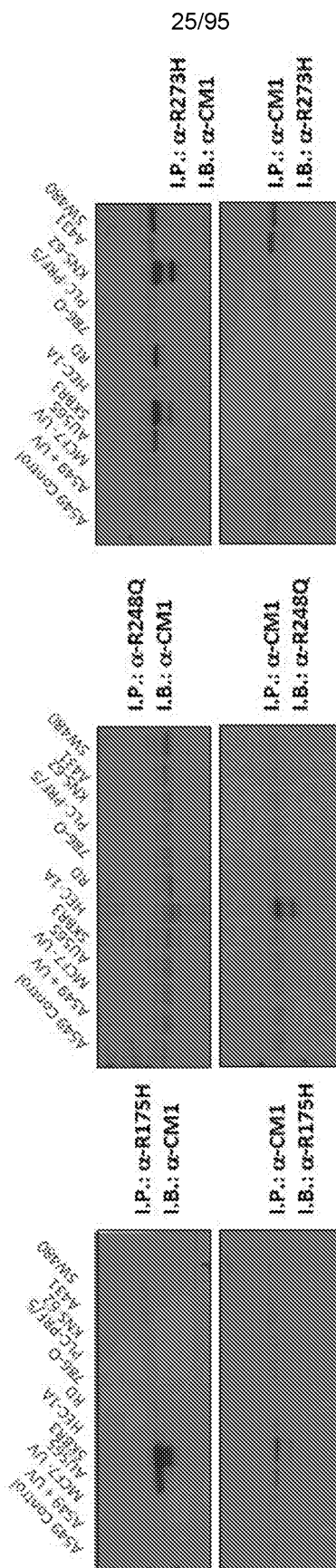


Figure 14





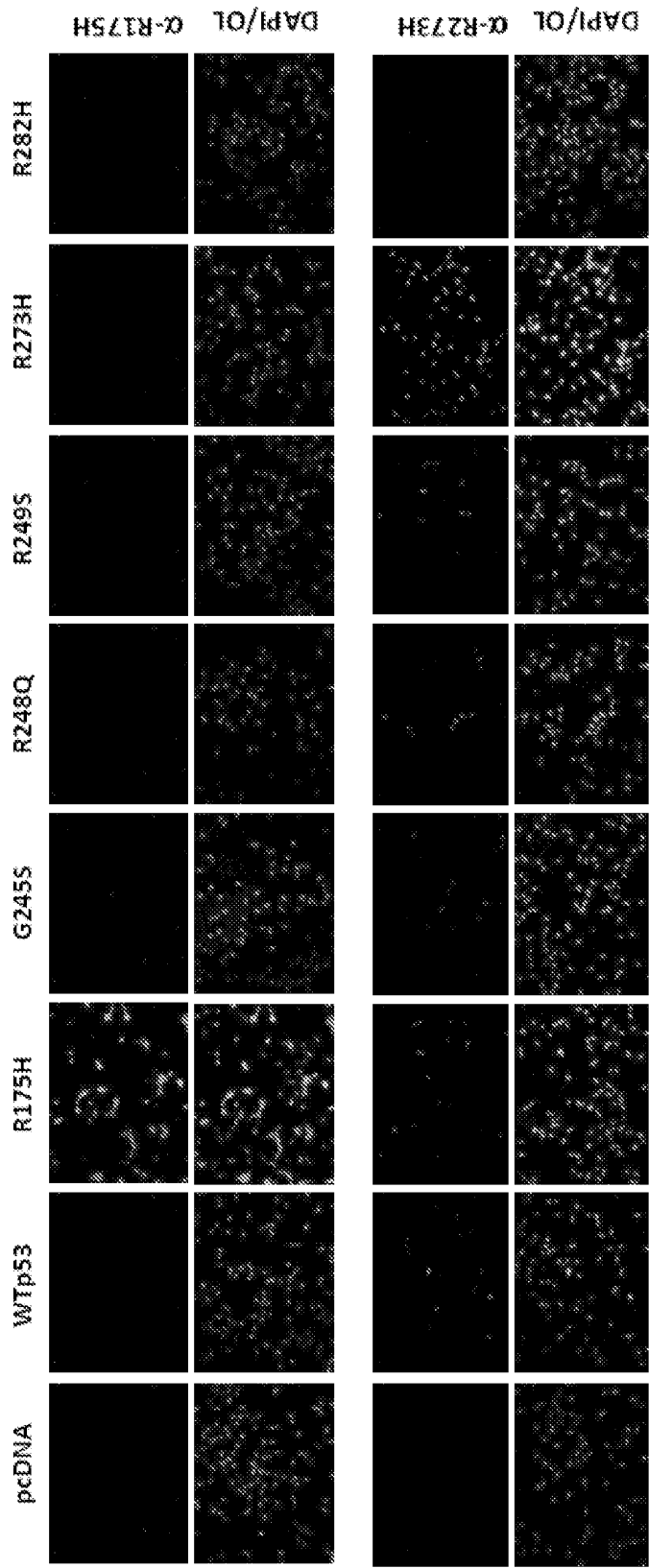


Figure 16 (cont.)

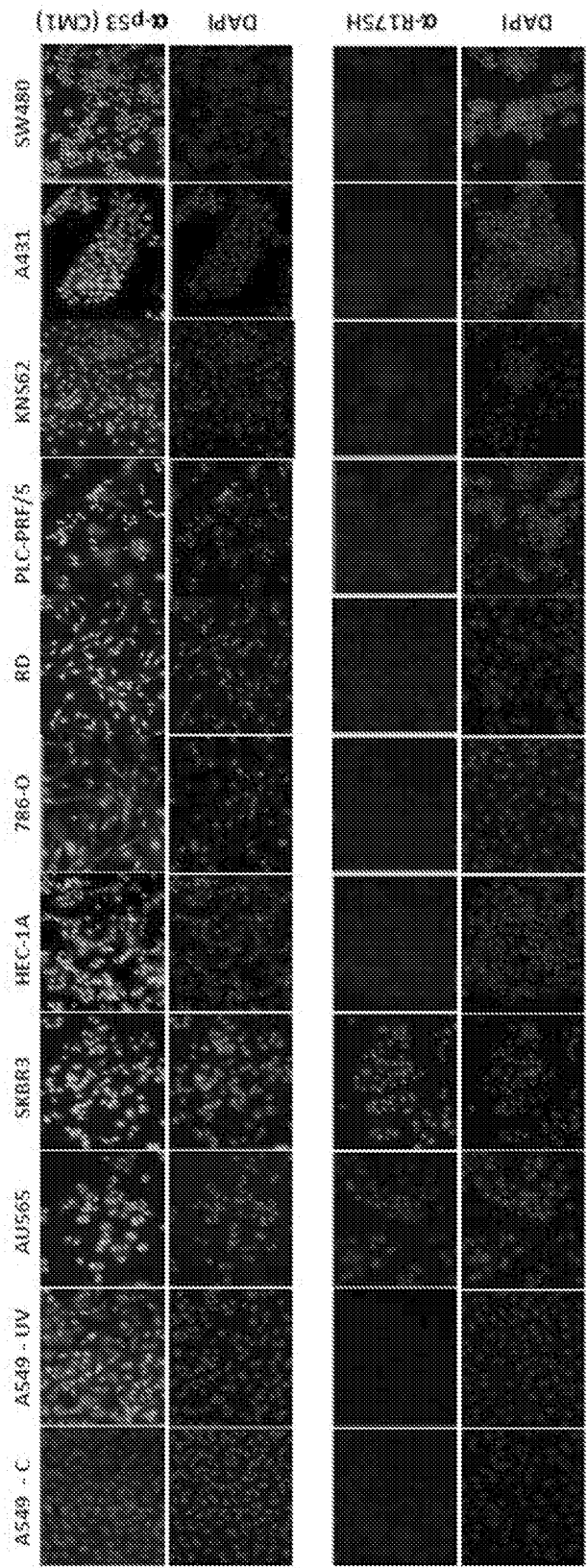


Figure 17A

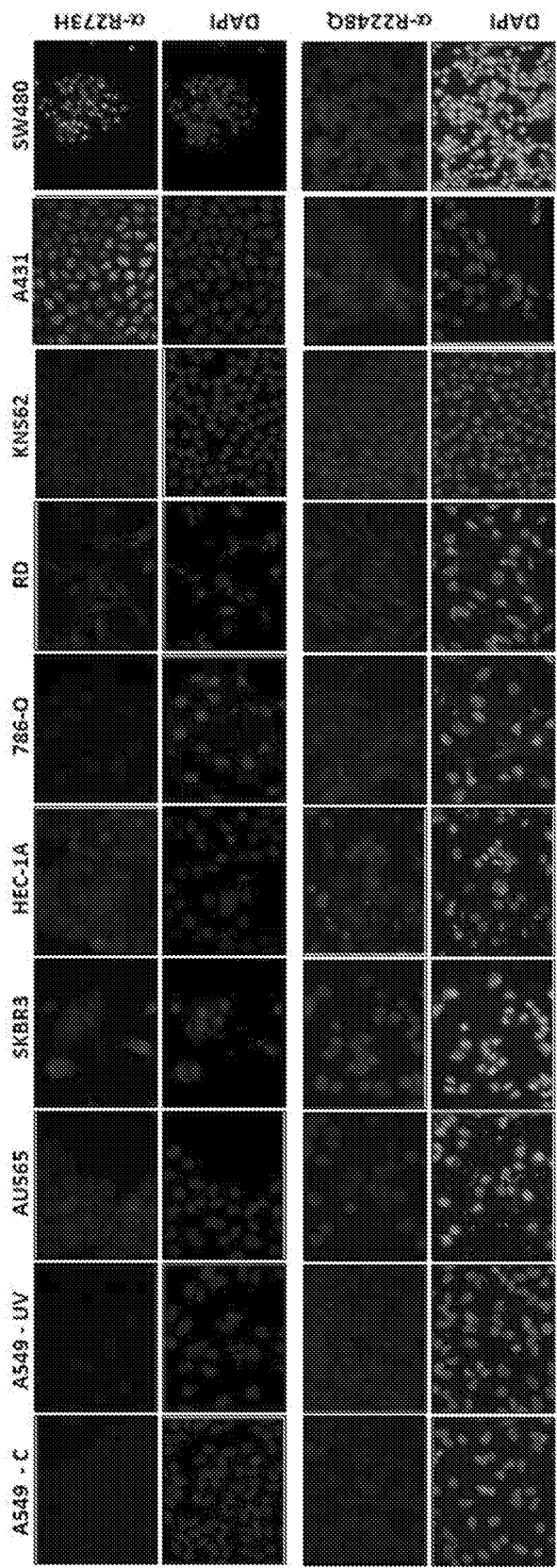


Figure 17A (cont.)

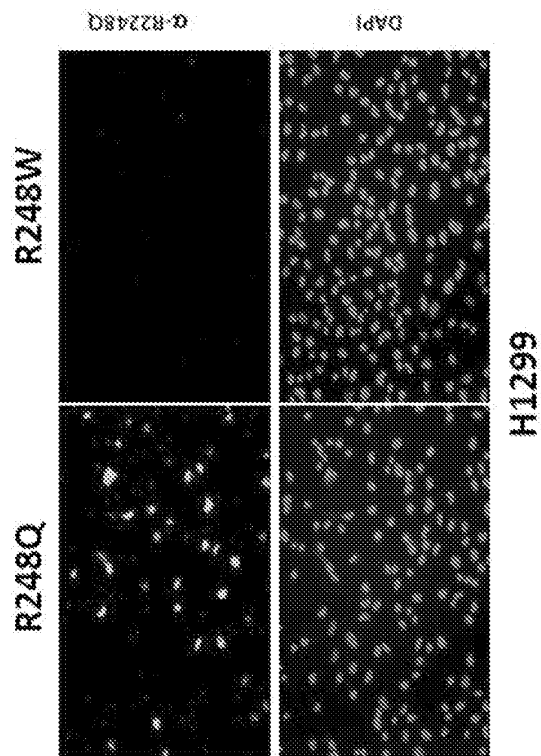


Figure 17B

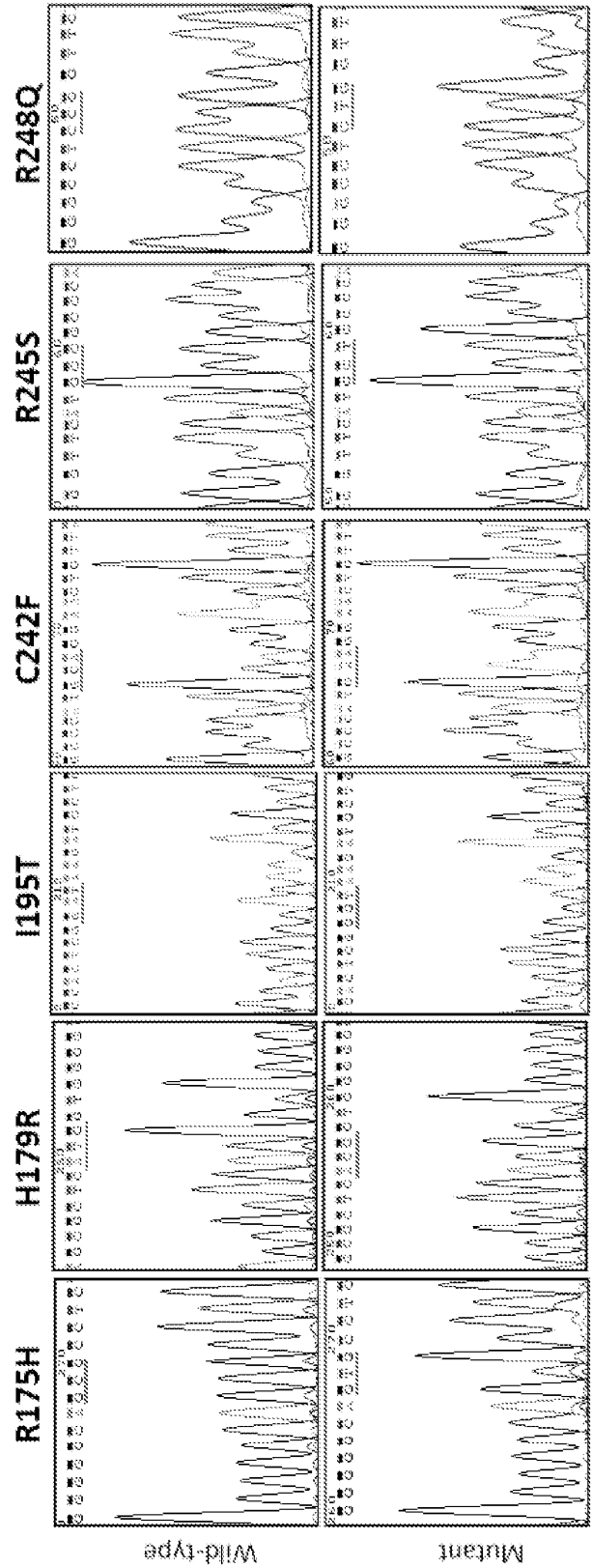


Figure 18A

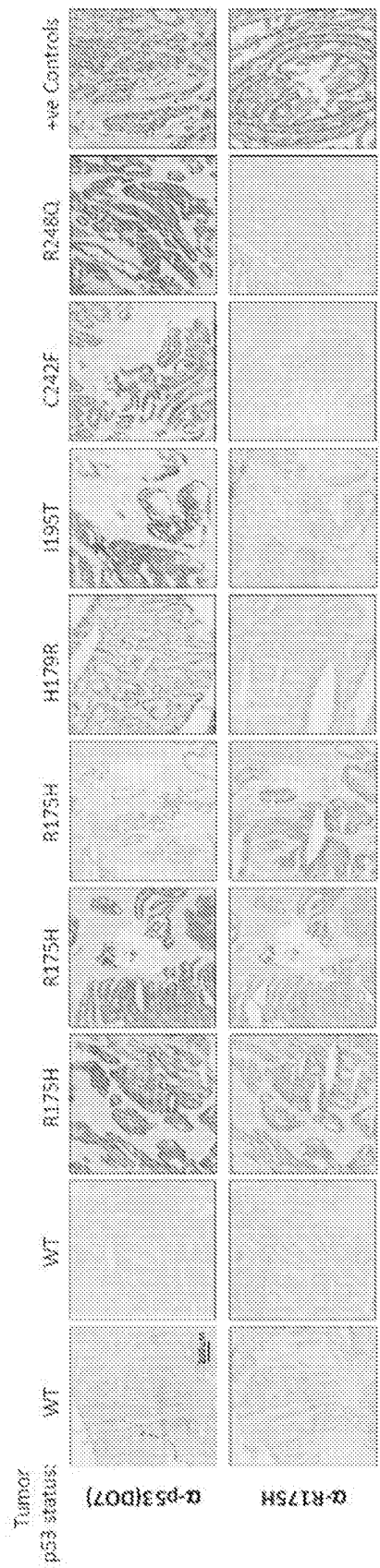


Figure 18B

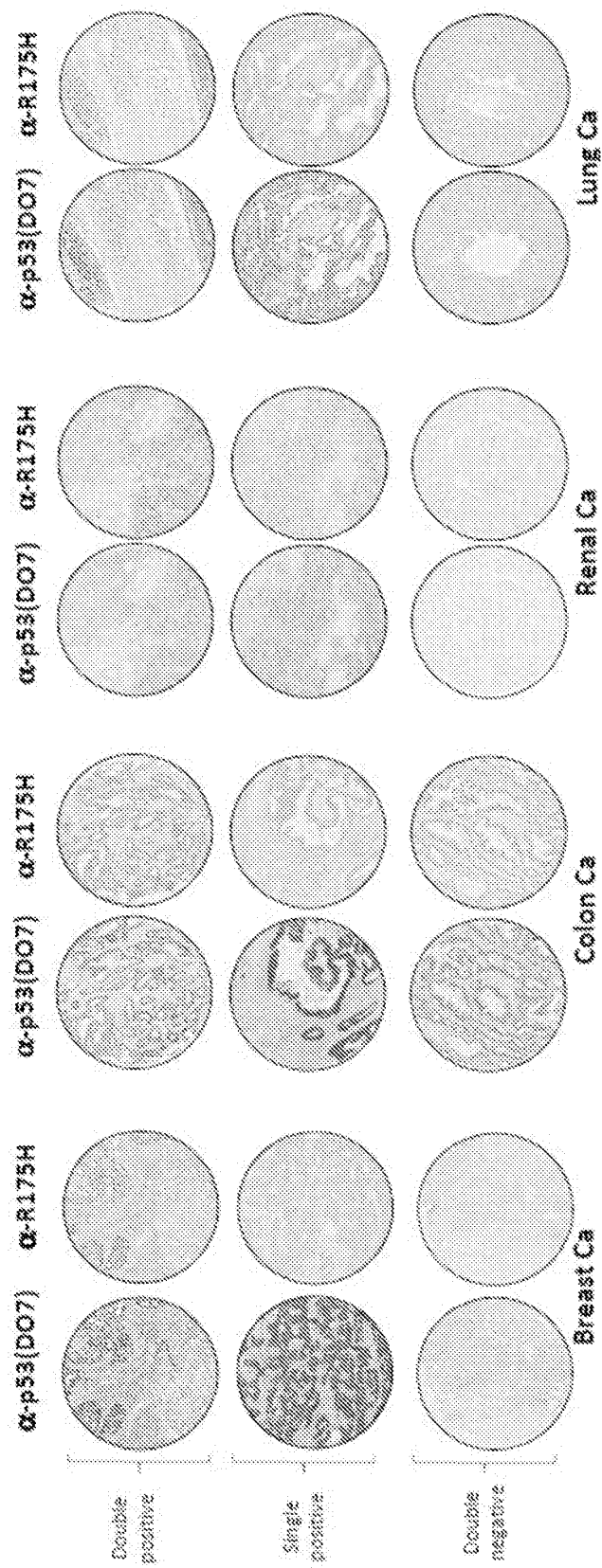


Figure 19

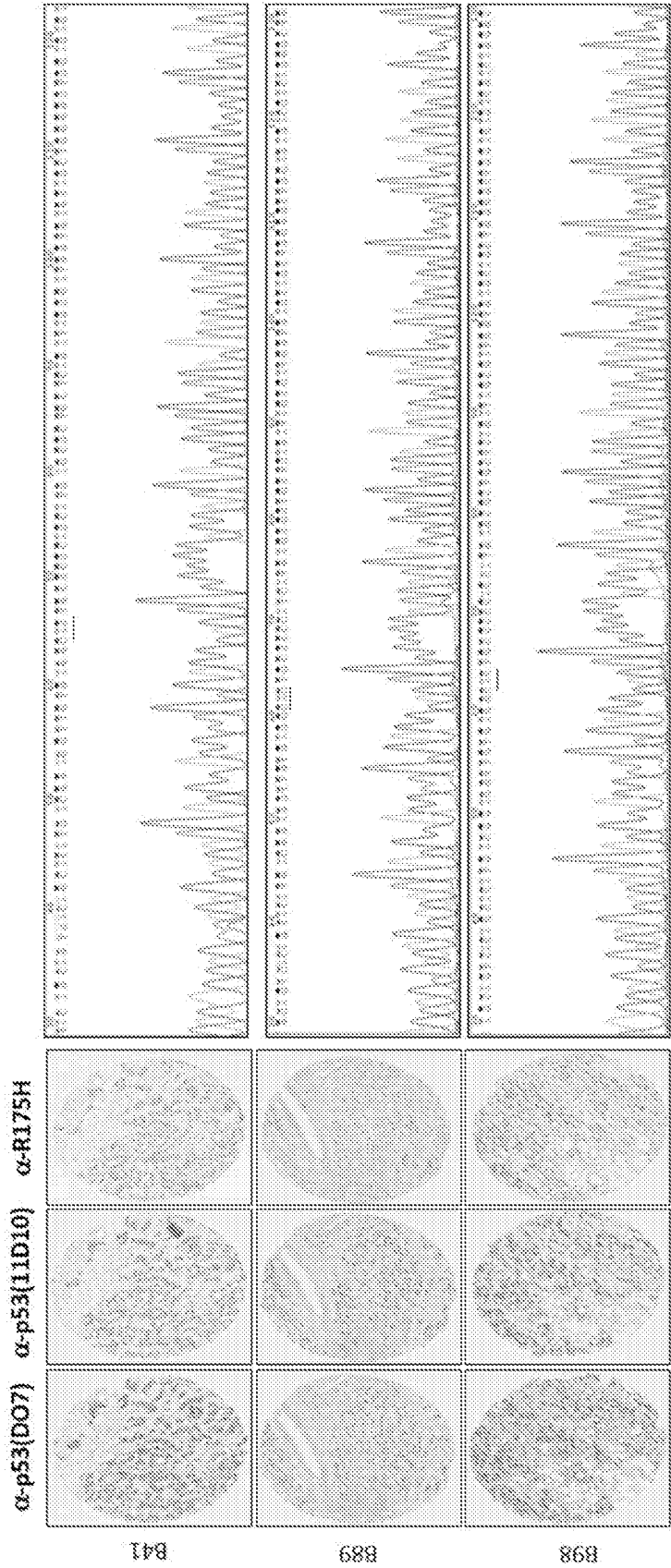


Figure 20A

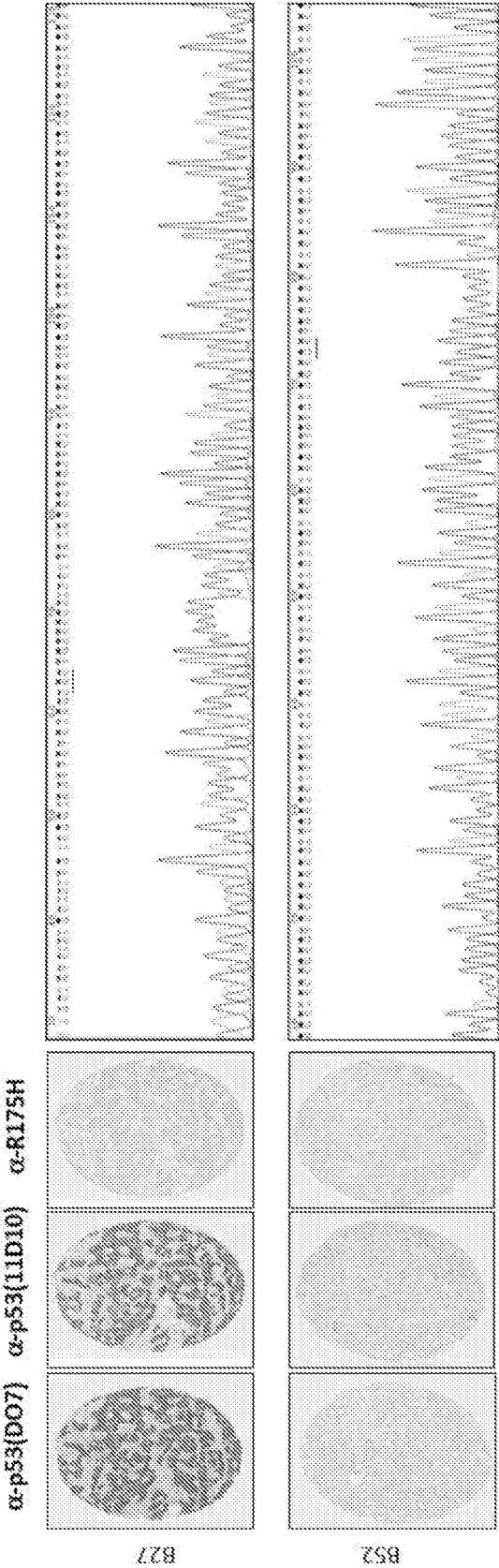


Figure 20B

Combined data from analysis of human tumor microarrays by immunohistochemistry

TMA ^s *	Total samples = n	α-pan-p53 ⁺ (DO7) n (%)	α-R175H ⁺ n (%)
Colon	99	60 (60)	5
Breast	102	72 (70)	5
Lung	169	114 (67)	8
Prostate	231	27 (11)	0
Renal	196	68 (34)	3

*: TMA: tumor microarray

Figure 21

R175		
	↓	
P53_HUMAN	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRVEYLLDDRNTFRHSVVVPYEPPEVG	226
P53_CERAE	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRVEYSDDRNTFRHSVVVPYEPPEVG	226
P53_MACMU	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRVEYSDDRNTFRHSVVVPYEPPEVG	226
P53_MACFU	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRVEYSDDRNTFRHSVVVPYEPPEVG	226
P53_MACFA	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRVEYSDDRNTFRHSVVVPYEPPEVG	226
P53_TUPGB	VTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLHAEYSDDRNTFRHSVVVPYEPPEVG	226
P53_MARMO	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	224
P53_RABIT	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	223
P53_DELLE	MTEVVRRCPPHHERCSDYSDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	220
P53_PIG	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	219
P53_CANFA	VTEVVRRCPPHHERCSDSSDG-LAPPQHLIRVEGNLRAKYLLDDRNTFRHSVVVPYEPPEVG	214
P53_FELCA	MTEVVRRCPPHHERCPDSSDG-LAPPQHLIRVEGNLHAKYLLDDRNTFRHSVVVPYEPPEVG	219
P53_CAVPO	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLHAEYVDDRNTFRHSVVVPYEPPEVG	224
P53_SHEEP	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYFDDRNTFRHSVVVPYEPPEVG	215
P53_MESAU	MTEVVRRCPPHHERSSE-GDG-LAPPQHLIRVEGNMHAEYLLDDRNTFRHSVVVPYEPPEVG	229
P53_CRIGR	MTEVVRRCPPHHERSSE-GDS-LAPPQHLIRVEGNLHAEYLLDDRNTFRHSVVVPYEPPEVG	226
P53_BOVIN	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	219
P53_BOSIN	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	219
P53_RAT	MTEVVRRCPPHHERCSD-GDG-LAPPQHLIRVEGNPYAEYLLDDRNTFRHSVVVPYEPPEVG	224
P53_MOUSE	MTEVVRRCPPHHERCSD-GDG-LAPPQHLIRVEGNLYPEYLLDDRNTFRHSVVVPYEPPEVG	220
P53_HORSE	MTEVVRRCPPHHERCSDSSDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	177
P53_EQUAS	MTEVVRRCPPHHERCSDSSDG-LAPPQHLIRVEGNLRAEYLLDDRNTFRHSVVVPYEPPEVG	102
P53_CHICK	VAEVRRCPPHHERCGGGTDG-LAPAQHLIRVEGNPQARYHDDTTKRHSVVVPYEPPEVG	212
P53_XENLA	VAEVRRCPPHHERSVEPGED-AAPPSHLMRVEGNLQAYYMEDVNSGRHSVCVYEPGPQVG	201
P53_ONCMY	VADVVRRCPPHHERSTSENNEG-PAPRGHLIRVEGNQRSEYMEDGNTLRHSVLVYEPGPQVG	215
P53_DANRE	VAEVRRCPPHHERTPDG-DN-LAPAGHLIRVEGNQRANREDNITLRHSVFPVYEPAPQLG	194
P53_ICTPU	VAEVRRCPPHHERSNDSSDG-PAPPGLLIRVEGNSRAVYQEDGNTQAHSVVVPYEPGPQVG	202
P53_XIPMA	VGEVVRRCPPHHQ-SEDLSDN-KS---HLIRVEGSLAQYFEDPNTRRHSVTVPYERPQLG	189
P53_XIPHE	VGEVVRRCPPHHQ-SEDLSDN-KS---HLIRVEGSLAQYFEDPNTRRHSVTVPYERPQLG	189

Figure 22

R273
↓

P53_HUMAN	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_CERAE	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MACMU	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MACFU	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MACFA	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_TUPGB	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MARMO	SECTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	284
P53_RABIT	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	283
P53_DELLE	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	280
P53_PIG	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_CANFA	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	274
P53_FELCA	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_CAVPO	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	284
P53_SHEEP	SECTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	275
P53_MESAU	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	289
P53_CRIGR	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_BOVIN	SECTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_BOSIN	SECTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_RAT	SDYTTIIHYKYMCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	284
P53_MOUSE	SEYTTIIHYKYMCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	280
P53_HORSE	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	237
P53_EQUAS	SDCTTIIHNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	162
P53_CHICK	SDCTTVLYNFMCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	272
P53_XENLA	TECTTVLYNFMCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	261
P53_ONCMY	SECTTVLYNFMCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	275
P53_DANRE	AEWTTVLLNYMCNSSCMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	254
P53_ICTPU	SQSTTVLYNFMCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	262
P53_XIPMA	SEMTTILLSFMCNCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	249
P53_XIPHE	SEMTTILLSFMCNCSNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	249

Figure 22 (cont.)

R248
↓

P53_HUMAN	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_CERAE	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MACMU	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MACFU	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MACFA	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_TUPGB	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MARMO	SECTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	284
P53_RABIT	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	283
P53_DELLE	SDCTTIHNYFMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	280
P53_PIG	SDCTTIHNYFMCNSSCMGNNRRPILTIITLEDASGNLLGRNSFEVRVACPGDRRTEE	279
P53_CANFA	SDYTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNVLRNSFEVRVACPGDRRTEE	274
P53_FELCA	SDCTTIHNYFMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	279
P53_CAVPO	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	284
P53_SHEEP	SECTTIHNYFMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	275
P53_MESAU	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDPSGNLLGRNSFEVRVACPGDRRTEE	289
P53_CRIGR	SDCTTIHNYMCNSSCMGNNRRPILTIITLEDPSGNLLGRNSFEVRVACPGDRRTEE	286
P53_BOVIN	SECTTIHNYFMCNSSCMGNNRRPILTIITLEDSCGNLLGRNSFEVRVACPGDRRTEE	279
P53_BOSIN	SECTTIHNYFMCNSSCMGNNRRPILTIITLEDSCGNLLGRNSFEVRVACPGDRRTEE	279
P53_RAT	SDYTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	284
P53_MOUSE	SEYTTIHNYMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	280
P53_HORSE	SDCTTIHNYFMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	237
P53_EQUAS	SDCTTIHNYFMCNSSCMGNNRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	162
P53_CHICK	SDCTTVLYNFMCNSSCMGNNRRPILTIITLEGPGQLLGRRCFEVRVACPGDRKIEE	272
P53_XENLA	TECTTVLYNFMCNSSCMGNNRRPILTIITLETQGLLLGRRCFEVRVACPGDRRTEE	261
P53_ONCMY	SECTTVLYNFMCNSSCMGNNRRPILTIITLETQEGQLLGRRSFEVRVACPGDRKTEE	275
P53_DANRE	AEWTTVLLNYMCNSSCMGNNRRPILTIITLETQEGQLLGRRSFEVRVACPGDRKTEE	254
P53_ICTPU	SQSTTVLYNFMCNSSCMGNNRRPILTIITLETQDGHLLGRRTFEVRVACPGDRKTEE	262
P53_XIPMA	SEMTTILLSFMCNSSCMGNNRRPILTIITLETTEGEVLGRRCFEVRVACPGDRKTEE	249
P53_XIPHE	SEMTTILLSFMCNSSCMGNNRRPILTIITLETTEGEVLGRRCFEVRVACPGDRKTEE	249

Figure 22 (cont.)

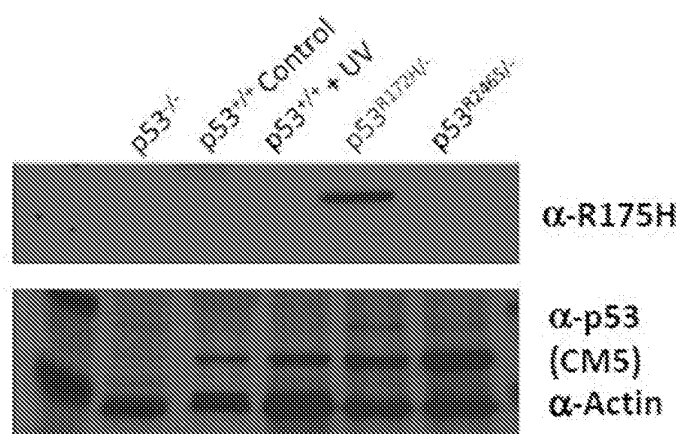


Figure 23A

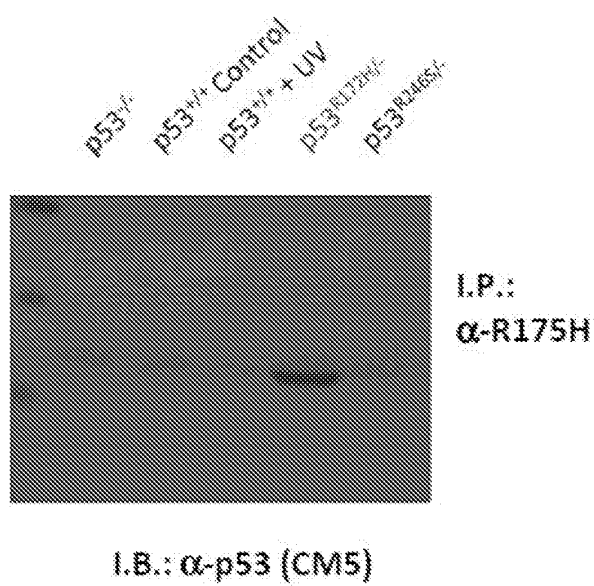


Figure 23B

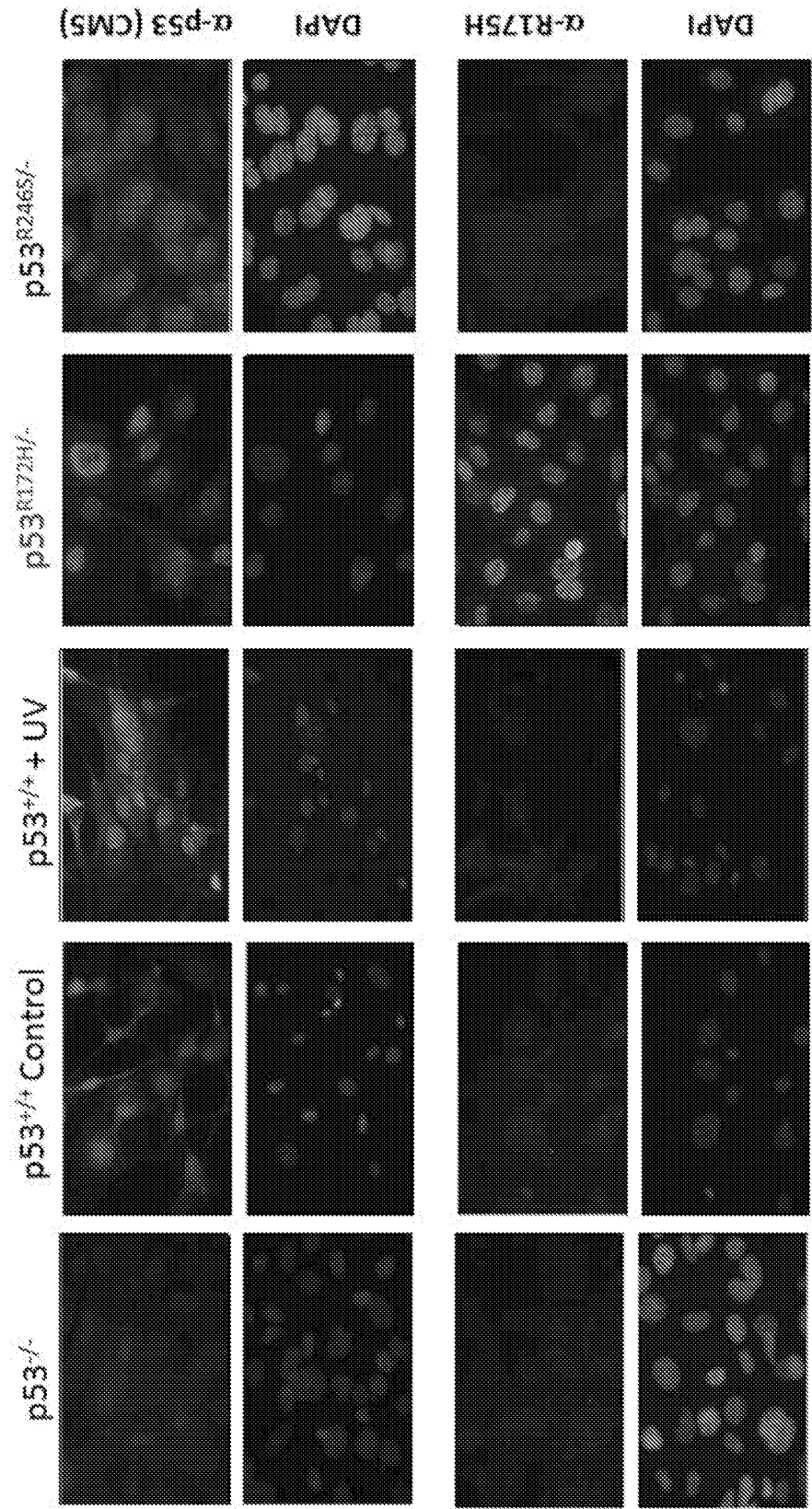


Figure 23C

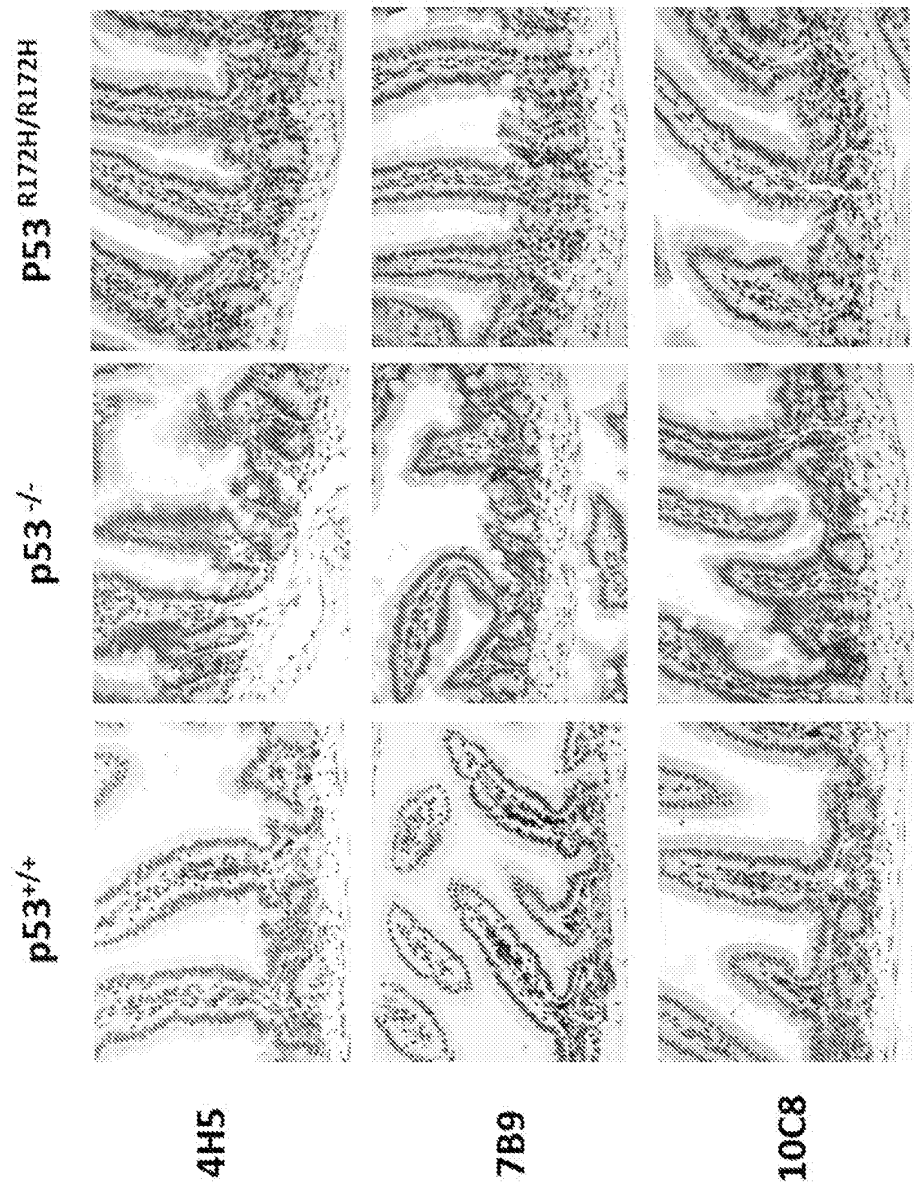


Figure 23D

Anti-R175H clone 4H5

DIVLTQSTSSLSVSAGERVTLSCCKSSQSLNLSGNQKSYLAWYQQKPGQPPKLLIYGASTRE
SGVPDRFTGSGSETDFTLTISVQPEDLAVYYCQNDHSYPLTFGAGTKLELK (SEQ ID
NO:18)

LC-CDR1: QSLNLSGNQKSY (SEQ ID NO:19)
LC-CDR2: GAS (SEQ ID NO:20)
LC-CDR3: QNDHSYPLT (SEQ ID NO:21)

Anti-R175H clone 7B9

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK (SEQ ID
NO:22)

LC-CDR1: QSLNLSGNQKSN (SEQ ID NO:23)
LC-CDR2: GAS (SEQ ID NO:20)
LC-CDR3: QNDHSYPLT (SEQ ID NO:21)

Anti-R175H clone 10C8

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK (SEQ ID
NO:22)

LC-CDR1: QSLNLSGNQKSN (SEQ ID NO:23)
LC-CDR2: GAS (SEQ ID NO:20)
LC-CDR3: QNDHSYPLT (SEQ ID NO:21)

Figure 24

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Anti-R175H clone 4H5

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVT
VY NQKFVKATLTVDSSSTAYLELRSLTSEDSAVYYCARWGGDYVTGGGTTLTVSS (SEQ ID NO:24)

HC-CDR1: GFTFTEYT (SEQ ID NO:25)

HC-CDR2: IDPNNGVT (SEQ ID NO:26)

HC-CDR3: ARWGGDYV (SEQ ID NO:27)

Anti-R175H clone 7B9

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGT
VY NQKFVKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLTVSS (SEQ ID NO:28)

HC-CDR1: GYTFTEYT (SEQ ID NO:29)

HC-CDR2: INPYSGGT (SEQ ID NO:30)

HC-CDR3: ARWGGDYV (SEQ ID NO:27)

Anti-R175H clone 10C8

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGT
VY NQKFVKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLTVSS (SEQ ID NO:28)

HC-CDR1: GYTFTEYT (SEQ ID NO:29)

HC-CDR2: INPYSGGT (SEQ ID NO:30)

HC-CDR3: ARWGGDYV (SEQ ID NO:27)

Figure 25

Anti R175H Clone	CDR 1	CDR 2	CDR 3
Light Chain			
4H5	QSLNLSGNQKSY (SEQ ID NO:19)	GAS (SEQ ID NO:20)	QNDHSYPLT (SEQ ID NO:21)
7B9	QSLNLSGNQKSN (SEQ ID NO:23)	GAS (SEQ ID NO:20)	QNDHSYPLT (SEQ ID NO:21)
10C8	QSLNLSGNQKSN (SEQ ID NO:23)	GAS (SEQ ID NO:20)	QNDHSYPLT (SEQ ID NO:21)
Consensus	QSLNLSGNQKSX ₁ (SEQ ID NO:31) where X ₁ = Y or N	GAS (SEQ ID NO:20)	QNDHSYPLT (SEQ ID NO:21)
Heavy Chain			
4H5	GFTFTEYT (SEQ ID NO:25)	IDPNNGVT (SEQ ID NO:26)	ARWGGDYV (SEQ ID NO:27)
7B9	GYTFTEYT (SEQ ID NO:29)	INPYSGGT (SEQ ID NO:30)	ARWGGDYV (SEQ ID NO:27)
10C8	GYTFTEYT (SEQ ID NO:29)	INPYSGGT (SEQ ID NO:30)	ARWGGDYV (SEQ ID NO:27)
Consensus	GX ₂ TFTEYT (SEQ ID NO:32) where X ₂ = F or Y	IX ₃ PX ₄ X ₅ GX ₆ T (SEQ ID NO:33) where X ₃ = D or N; X ₄ = N or Y; X ₅ = N or S; and X ₆ = V or G	ARWGGDYV (SEQ ID NO:27)

Figure 26

Light chain variable domains**Anti-R175H clone 4H5**

>4H5_aa_L

DIVLTQSTSSLSVSAGERVTLSCCKSSQSLNLSGNQKSYLAWYQQKPGQPPKLLIYGASTRE
SGVPDRFTGSGSETDFTLTISVQPEDLAVYYCQNDHSYPLTFGAGTKLELK [SEQ ID
NO:18]

>4H5_ntd_L

GATATTGTGCTACCCCAATCTACATCCTCCCTGAGTGTGTCAGCTGGAGAGAGGGTCA
CTTTGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAATCAAAAGAGTTACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAACTGTTGATCTACGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGGATCTGAAACCGATTTAC
TCTTACCATCAGCAGTGTGCAGCCTGAAGACCTGGCAGTTTATTATTGTCAGAATGATC
ATAGTTATCCGCTCACGTTCCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 34]

Anti-R175H clone 7B9

>7B9_aa_L

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK [SEQ ID
NO:22]

>7B9_ntd_L

GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAATCAAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 35]

Anti-R175H clone 10C8

>10C8_aa_L

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK [SEQ ID
NO: 22]

>10C8_ntd_L

GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAATCAAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 36]

Figure 27

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Heavy chain variable domains**Anti-R175H clone 4H5**

>4H5_aa_H

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVTVY
NQKFKVKATLTVDRSSSTAYLELRSLTSEDSAVYYCARWGGDYVTGGGTTLVSS [SEQ ID
NO: 24]

>4H5_ntd_H

GAGGTTTCAGCTGCAGCAGTCTGGACCTGAAGTGGTGAAGCCTGGGGCTTCAGTGAAGA
TATCTTGCAAGACTTCCGGATTACATTCAGTGAATACACCATGCACTGGATGAAACAG
AGCCATGGAAGGAGCCTTGAGTGGATCGGACGTATTGATCCTAACAATGGTGTACTGT
TTATAACCAGAAGTTCAAGGTCAAGGCCACATTGACTGTGGACAGGTCCTCCAGCACA
GCCTATCTGGAGCTCCGCAGTCTGACGTCTGAGGACTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTACTACGTCACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO: 37]

Anti-R175H clone 7B9

>7B9_aa_H

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLVSS [SEQ
ID NO: 28]

>7B9_ntd_H

GAGGTCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATATCCTGCAAGACTTCTGGCTACACTTTCACTGAATACACCATGCACTGGATGAAGCA
GAGCCATGGAAGAGCCTTGAGTGGATTGGACGTATTAATCCTTATAGTGGTGGTACTG
TCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACTGTGGACAAGTCCTCCAGCAC
AGCCTATATGGAGCTCCGCAGCCTGACATCTGATGATTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTACTACGTCACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO: 38]

Anti-R175H clone 10C8

>10C8_aa_H

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLVSS [SEQ
ID NO: 28]

>10C8_ntd_H

GAGGTGCAGCTTCAGCAGTCCGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATATCCTGCAAGACTTCTGGCTACACTTTCACTGAATACACCATGCACTGGATGAAGCA
GAGCCATGGAAGAGCCTTGAGTGGATTGGACGTATTAATCCTTATAGTGGTGGTACTG
TCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACTGTGGACAAGTCCTCCAGCAC
AGCCTATATGGAGCTCCGCAGCCTGACATCTGATGATTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTACTACGTCACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO: 39]

Figure 27 (cont.)

Anti-R248Q clone 3G11

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGSPKRLIYLVSKLDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK (SEQ ID NO:40)

LC-CDR1: QSLLYSDGKTY (SEQ ID NO:41)
LC-CDR2: LVS (SEQ ID NO:42)
LC-CDR3: WQGTHFPLT (SEQ ID NO:43)

Anti-R248Q clone 4H2

DIVITQSPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGSPKRLIYLVSELDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK (SEQ ID NO:44)

LC-CDR1: QSLLYSDGKTY (SEQ ID NO:41)
LC-CDR2: LVS (SEQ ID NO:42)
LC-CDR3: WQGTHFPLT (SEQ ID NO:43)

Figure 28

Anti-R248Q clone 3G11

DVQLQQSGPELVKPGASVKMSCKASGYTFTDYYVKWVKQSPGQSLEWIGDIIHPKNGGTN
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAAKMGGYDDYWGQGTTTLTVSS
(SEQ ID NO:45)

HC-CDR1: GYTFTDYY (SEQ ID NO:46)

HC-CDR2: IHPKNGGT (SEQ ID NO:47)

HC-CDR3: AKMGGYDDY (SEQ ID NO:48)

Anti-R248Q clone 4H2

QVQLKQSGPELVKPGASVKMSCKASGYTFTDYYLKWVRQSHGKSLEWIGDIIDPKNGGTNY
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAAKQGGFDDYWGQGTTTLTVSS (SEQ
ID NO:49)

HC-CDR1: GYTFTDYY (SEQ ID NO:46)

HC-CDR2: IDPKNGGT (SEQ ID NO:50)

HC-CDR3: AKQGGFDDY (SEQ ID NO:51)

Figure 29

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Anti-R248Q Clone	CDR 1	CDR 2	CDR 3
Light Chain			
3G11	QSLLYSDGKTY (SEQ ID NO:41)	LVS (SEQ ID NO:42)	WQGTHFPLT (SEQ ID NO:43)
4H2	QSLLYSDGKTY (SEQ ID NO:41)	LVS (SEQ ID NO:42)	WQGTHFPLT (SEQ ID NO:43)
Consensus	QSLLYSDGKTY (SEQ ID NO:41)	LVS (SEQ ID NO:42)	WQGTHFPLT (SEQ ID NO:43)
Heavy Chain			
3G11	GYTFTDYY (SEQ ID NO:46)	IHPKNGGT (SEQ ID NO:47)	AKMGGYDDY (SEQ ID NO:48)
4H2	GYTFTDYY (SEQ ID NO:46)	IDPKNGGT (SEQ ID NO:50)	AKQGGFDDY (SEQ ID NO:51)
Consensus	GYTFTDYY (SEQ ID NO:46)	IX ₇ PKNGGT (SEQ ID NO:52) where X ₇ = H or D	AKX ₈ GGX ₉ DDY (SEQ ID NO:53) where X ₈ = M or Q; and X ₉ = Y or F

Figure 30

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Light chain variable domains**Anti-R248Q clone 3G11**

>3G11_aa_L

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVS KLDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:40]

>3G11_ntd_L

GATATTGTGCTGACACAGACTCCACTCACTTTGTCGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAAATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GTTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTAAACTGG
ACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTACACTGAA
AATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACATT
TTCCTCTCACGTTCCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 54]**Anti-R248Q clone 4H2**

>4H2_aa_L

DIVITQSPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVS ELDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:44]

>4H2_ntd_L

GACATTGTGATCACACAGTCTCCACTCACTTTGTCGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAGATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GCTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTGAACTG
GACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTACACTGA
AAATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACAT
TTTCCTCTCACGTTCCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 55]**Figure 31**

Heavy chain variable domains**Anti-R248Q clone 3G11**

>3G11_aa_H

DVQLQQSGPELVKPGASVKMSCKASGYTFDYYVKWVKQSPGQSLEWIGDIHPKNGGTN
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAKMGGYDDYWGGQTTLTVSS
[SEQ ID NO:45]

>3G11_ntd_H

GATGTGCAGCTTCAGCAGTCAGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGA
TGTCCTGTAAGGCTTCTGGATACACATTCAGTACTACTATGTGAAGTGGGTGAAGCAG
AGTCCTGGACAGAGCCTTGAGTGGATTGGAGATATTCATCCTAAGAACGGTGGTACTAA
CTACAACCAGAAGTTCAAGGGCAAGGCCGCATTGACTGTGGACAAATCCTCCAGCACA
GCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTTCTGTGCAA
AATGGGAGGCTACGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[SEQ ID NO: 56]

Anti-R248Q clone 4H2

>4H2_aa_H

QVQLKQSGPELVKPGASVKMSCKASGYTFDYYLKWVRQSHGKSLEWIGDIDPKNGGTNY
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAKQGGFDDYWGGQTTLTVSS [SEQ
ID NO:49]

>4H2_ntd_H

CAGGTGCAGCTGAAGCAGTCAGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATGTCCTGTAAGGCTTCTGGATACACATTCAGTACTACTATCTGAAGTGGGTGAGGCA
GAGTCATGGAAAGAGCCTTGAGTGGATTGGAGATATAGATCCCAAGAATGGTGGTACT
AATTACAACCAGAAGTTTAAGGGCAAGGCCACATTGACTGTGGACAAATCCTCCAGCAC
AGCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTAAGTGTGCAA
AACAGGGGGGGTTTCGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[SEQ ID NO: 57]

Figure 31 (cont.)

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Anti-R273H clone 13E4

DIVMTQSPLSLPVNLGDQVSLSCRSSQSIVHNNGDTYLEWYLQKPGQSPKLLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHLPLTFGSGTKLELK (SEQ ID NO:58)

LC-CDR1:	QSIVHNNGDTY	(SEQ ID NO:59)
LC-CDR2:	KVS	(SEQ ID NO:60)
LC-CDR3:	FQGSHLPLT	(SEQ ID NO:61)

Figure 32**Anti-R273H clone 13E4**

EVQLLETGGDLVTPGGSLKLSCAASGFSFSDYYMYWVRQTPEKRLEWVATISVGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYYCVRDGNDGKFLGYWGQGTFTVTV
S (SEQ ID NO:62)

HC-CDR1:	GFSFSDYY	(SEQ ID NO:63)
HC-CDR2:	ISVGGTYT	(SEQ ID NO:64)
HC-CDR3:	VRDGNDGKFLG	(SEQ ID NO:65)

Figure 33

Anti-R273H clone 13E4**Light chain variable domain**

>13E4_aa_L
DIVMTQSPLSLPVNLGDQVSLSCRSSQSIVHNNGDTYLEWYLQKPGQSPKLLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHLPLTFGSGTKLELK [SEQ ID NO:58]

>13E4_ntd_L
GATATTGTGATGACACAATCTCCACTCTCCCTGCCTGTCAATCTTGGAGATCAAGTCTC
CCTCTCTTGCAGATCTAGTCAGAGCATTGTACATAATAATGGAGACACCTATTTAGAATG
GTACCTACAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGAT
TTTCTGGGGTCCCAGACAGGTTTCAGTGGCAGTGGATCAGGGACAGATTTCACTCAA
GATCAGCAGAGTGGAGGCTGAGGATCTGGGAATTTATTACTGCTTTCAAGGTTACATC
TTCCGCTCACGTTTCGGTTCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 66]

Heavy chain variable domain

>13E4_aa_H
EVQLLETGGDLVTPGGSCLKLSAASGFESFSDYYMYWVRQTPEKRLEWVATISVGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYYCVRDGN DGKFLGYWGQGTFTVTV
S [SEQ ID NO:62]

>13E4_ntd_H
GAAGTGCAGCTGTTGGAGACTGGGGGAGACTTAGTGACGCCTGGAGGGTCCCTGAAA
CTCTCCTGTGCAGCCTCTGGATTGAGCTTCAGTGACTATTATATGTATTGGGTTCGCCA
GACTCCGGAAGAGAGGCTGGAGTGGGTCGCAACTATTAGTGTTGGTGGTACATACACC
TTCTATTCAGACAATGTGAAGGGGAGATTTCGTCTCCTCAGAGACAATGCCAGGAAAAA
TCTGCATCTGGAAATGAACAGTCTGAAGTCTGAGGACGCAGCCATGTATTACTGTGTAA
GAGATGGCAACGATGGAAAATTTCTTGGGTACTGGGGCCAGGGGACTTTCGTCACTGT
CACT [SEQ ID NO: 67]

Figure 34

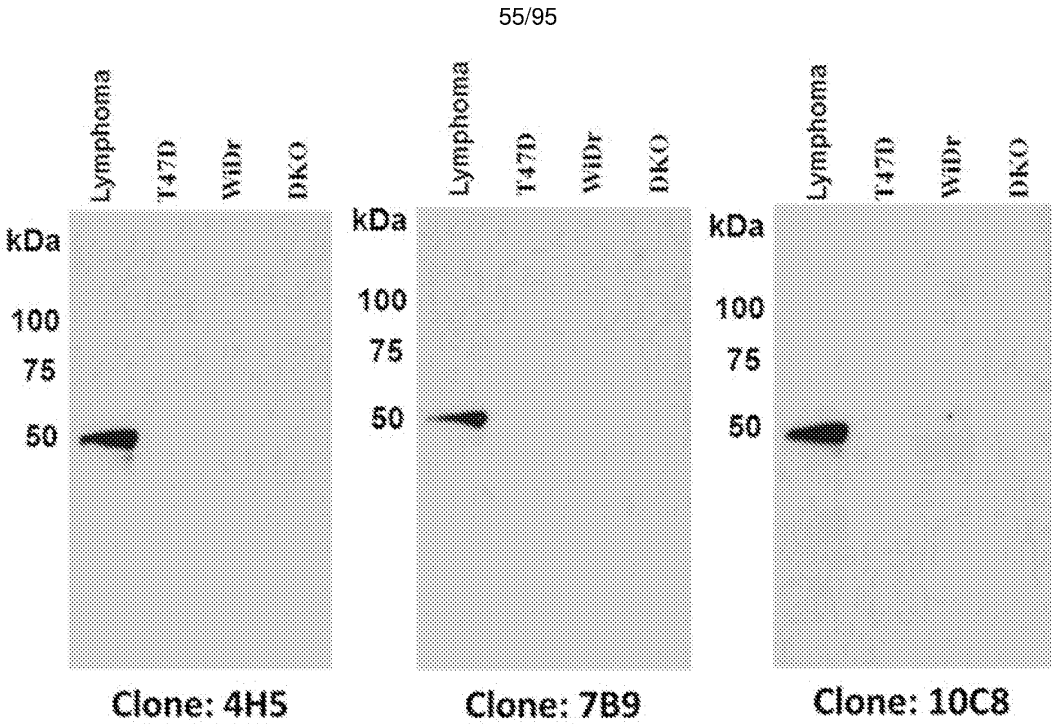


Figure 35

Clone: 4H5

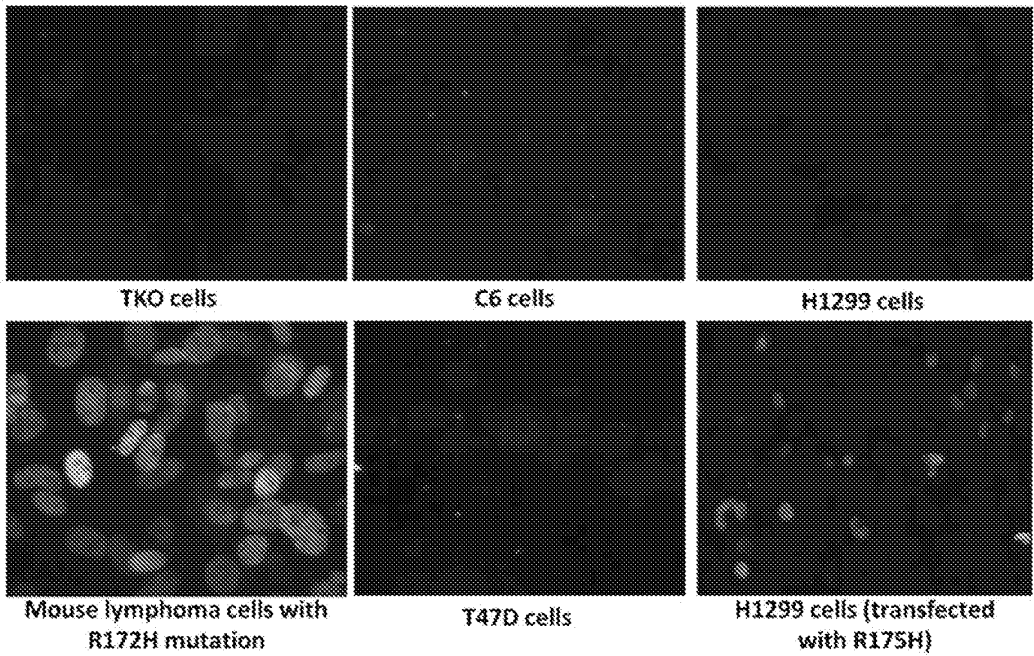


Figure 36A

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Clone: 7B9

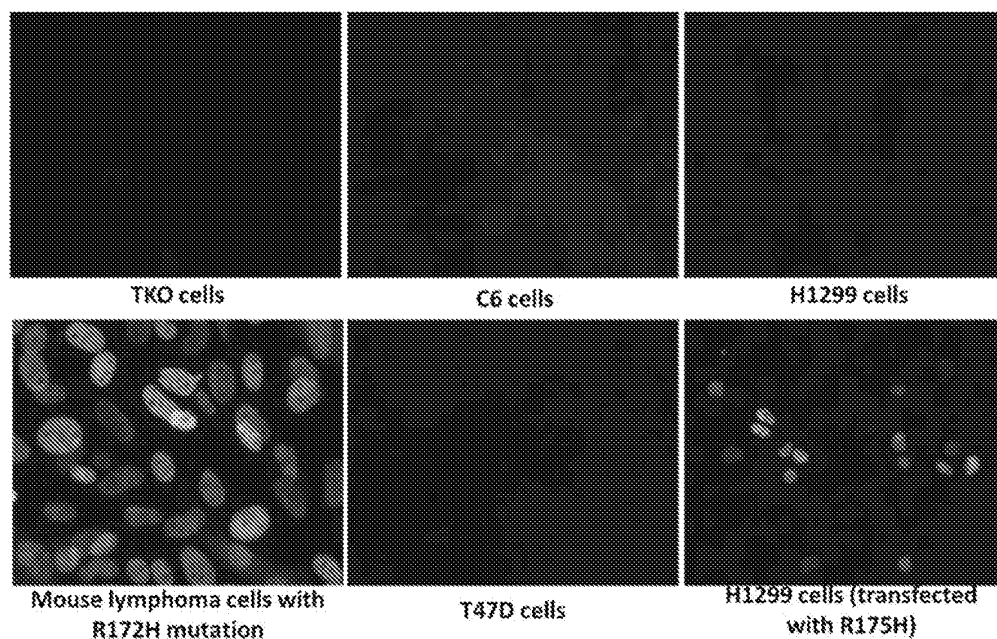


Figure 36B

Clone: 10C8

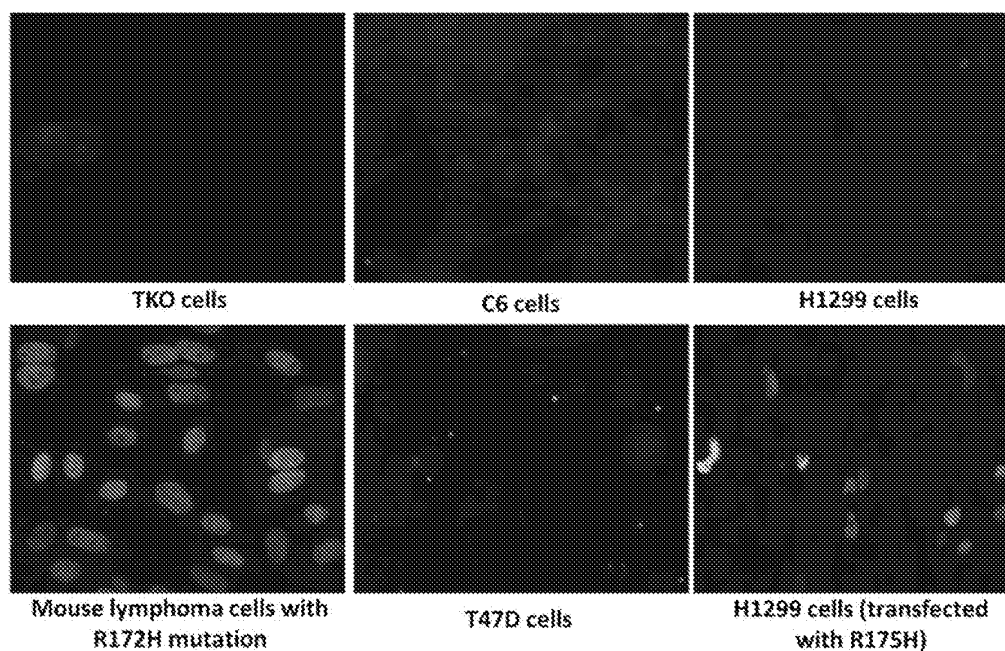


Figure 36C

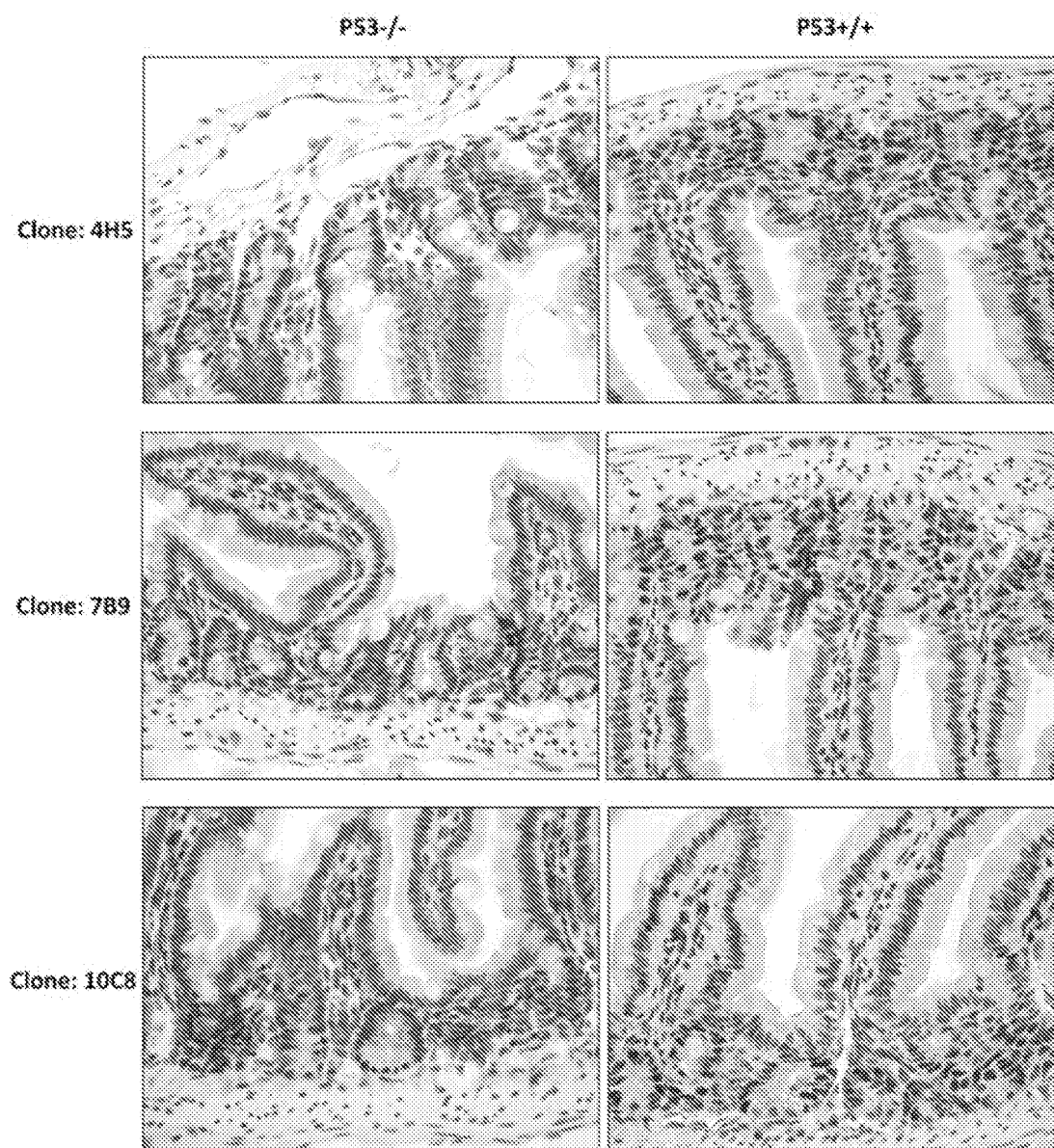


Figure 37

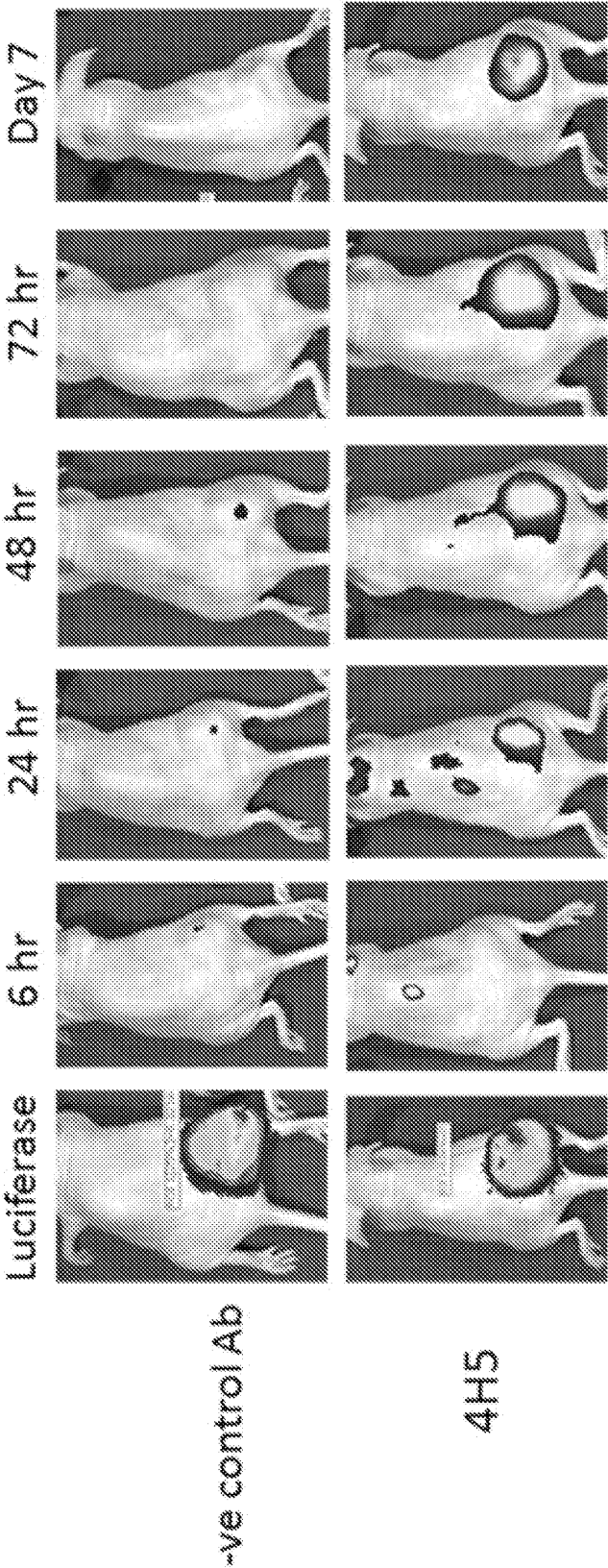


Figure 38

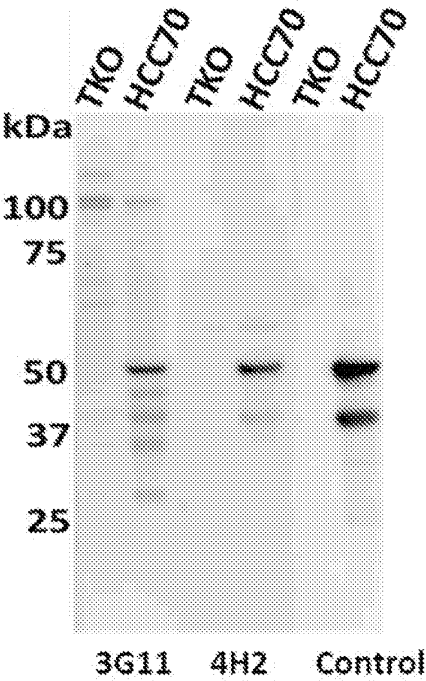


Figure 39

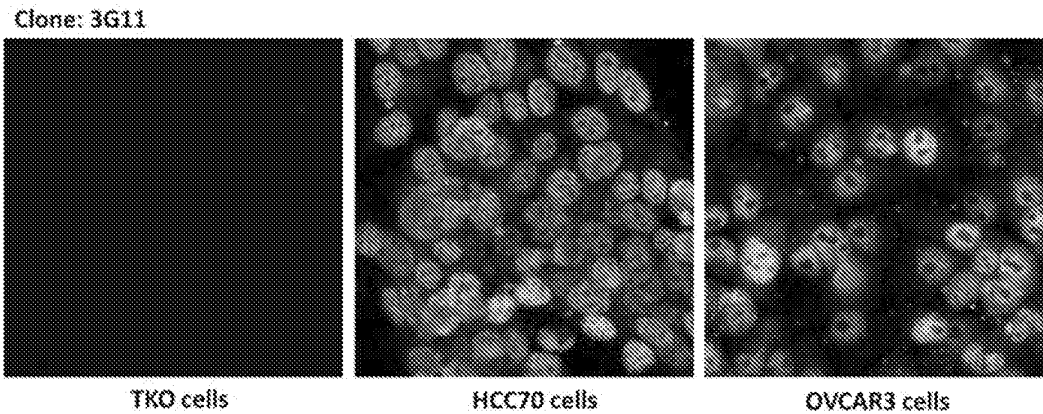


Figure 40A

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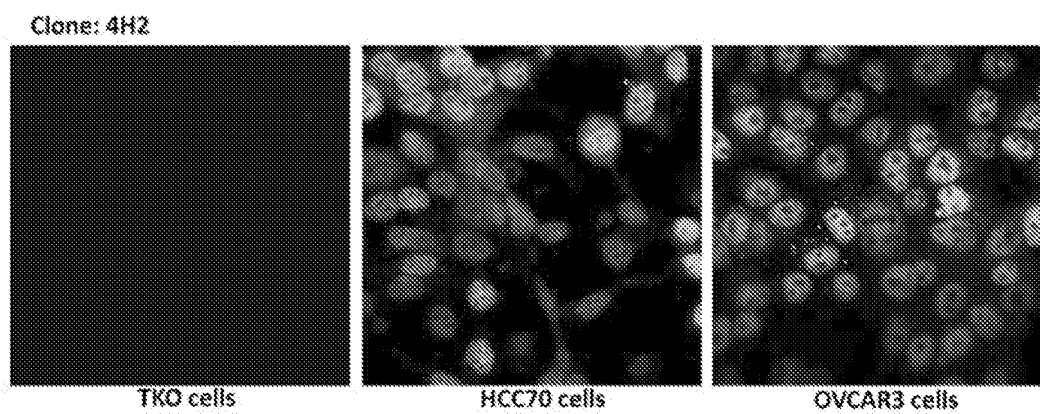


Figure 40B

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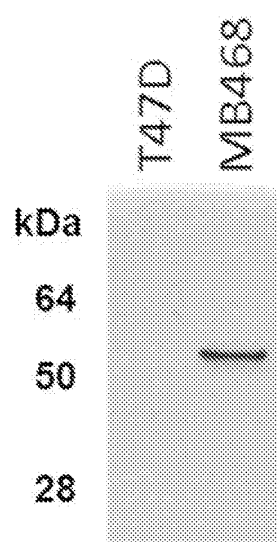


Figure 41

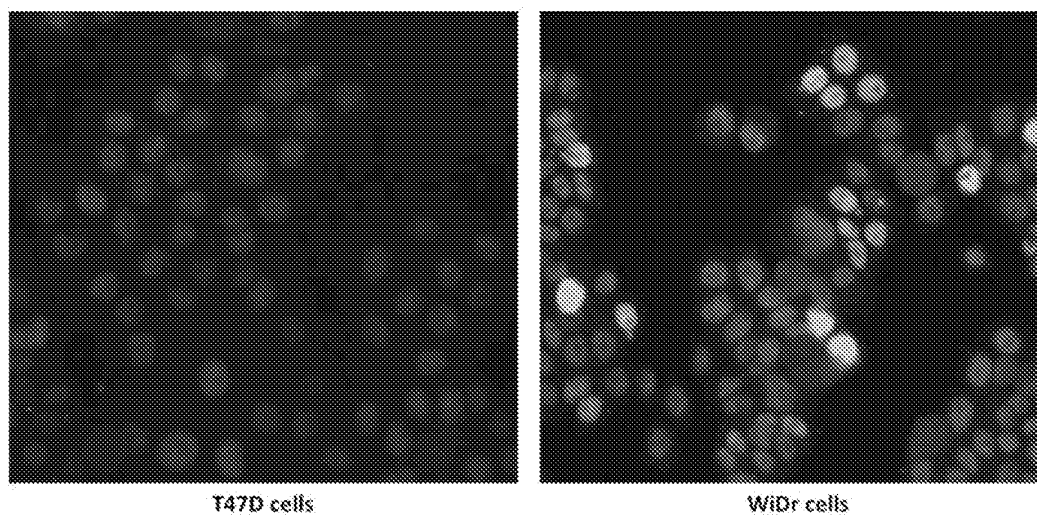


Figure 42

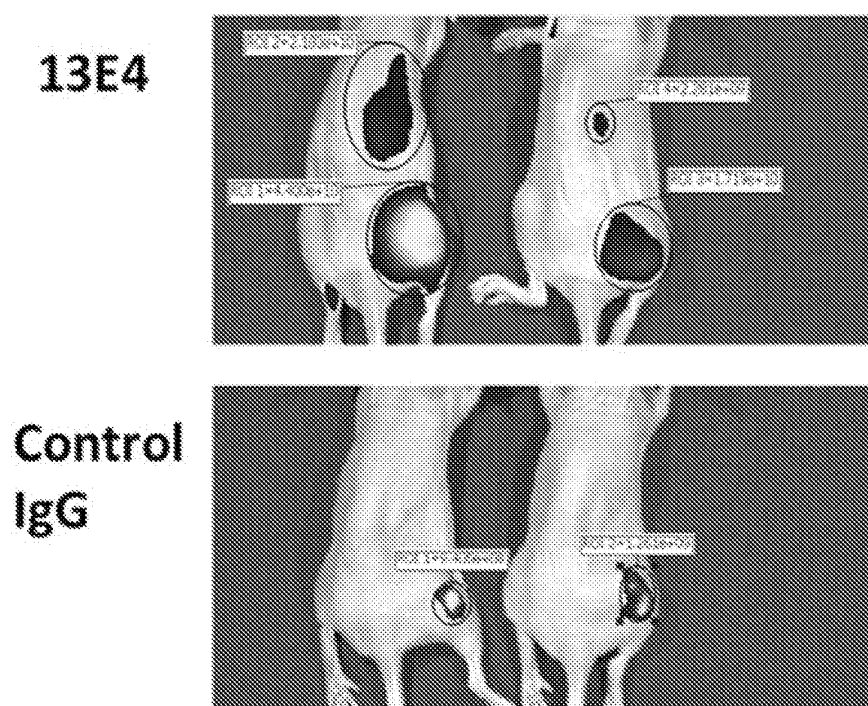


Figure 43

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p53 +/+

Clone: 4H5



Clone: 7B9



Clone: 10C8

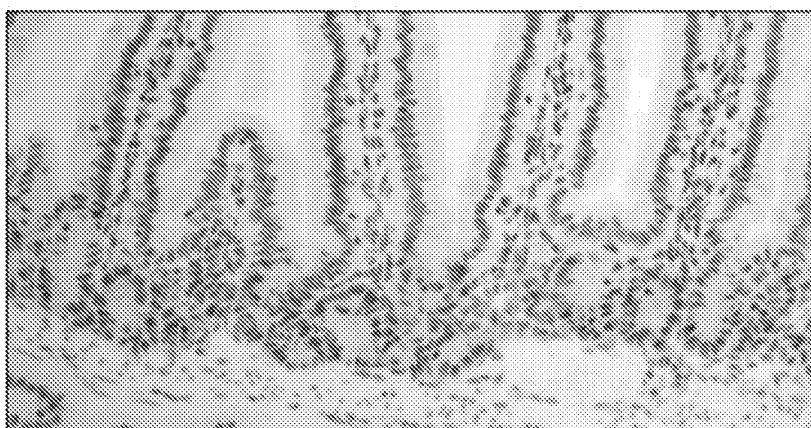


Figure 44

SKBR(R175H cell line tumor): anti-R175H a/b vs IgG control

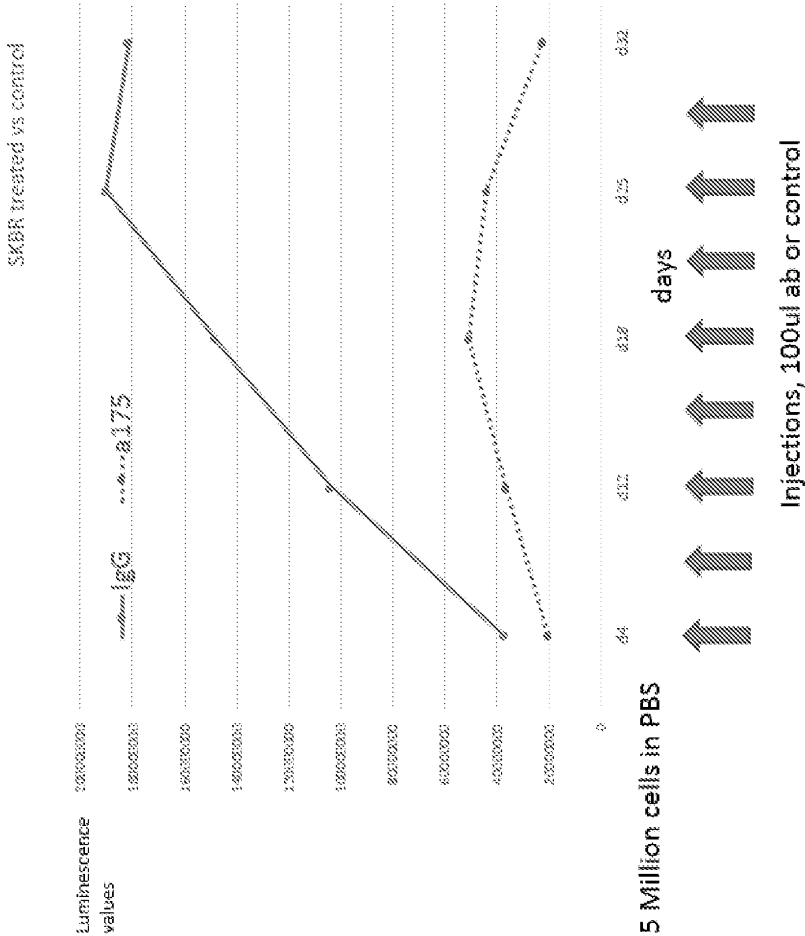


Figure 45

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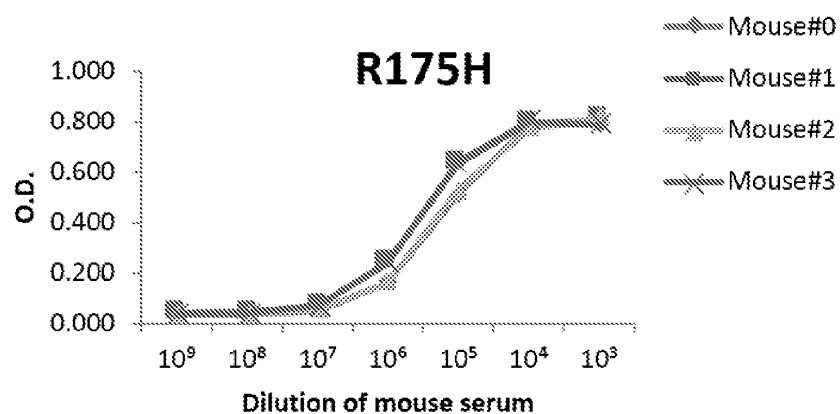


Figure 46A

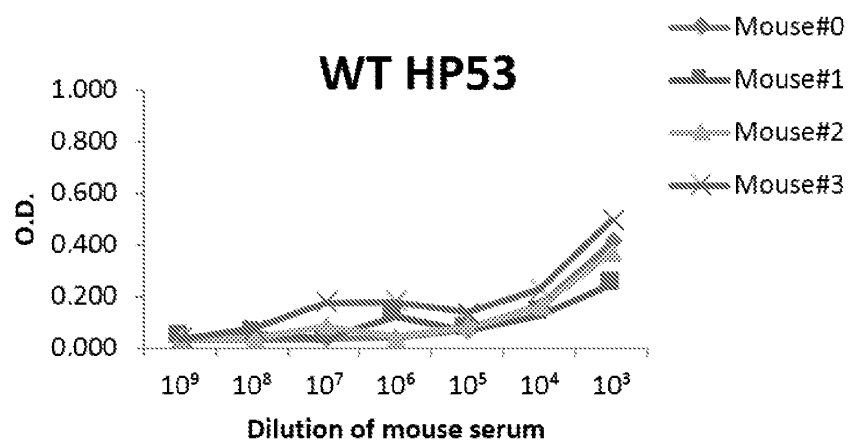


Figure 46B

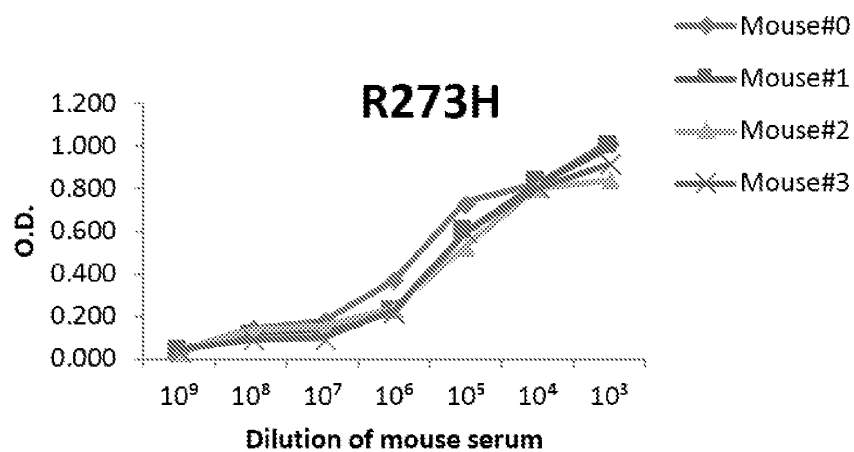


Figure 46C

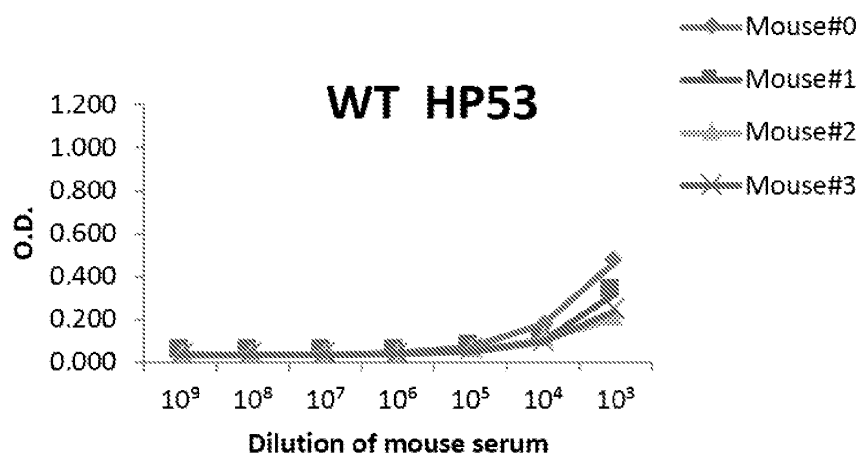


Figure 46D

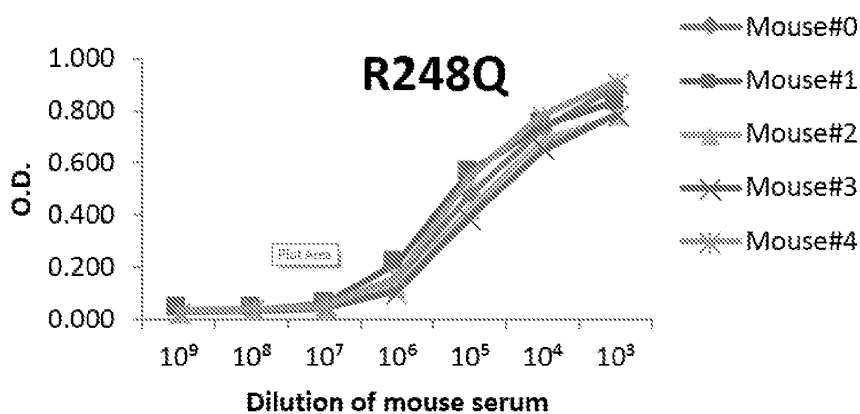


Figure 46E

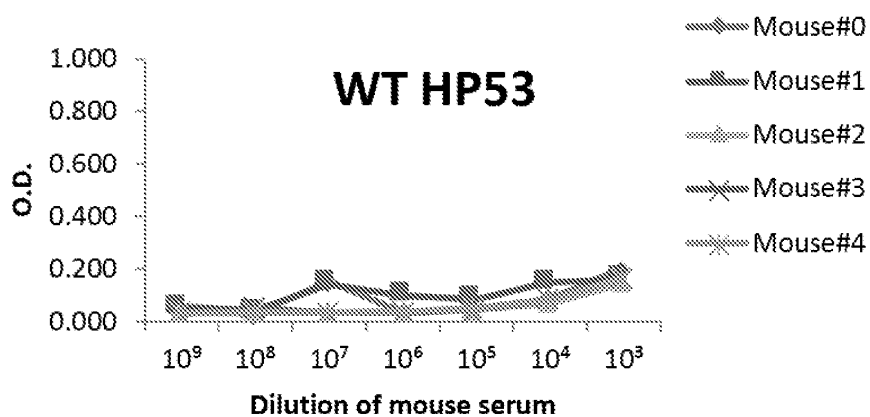
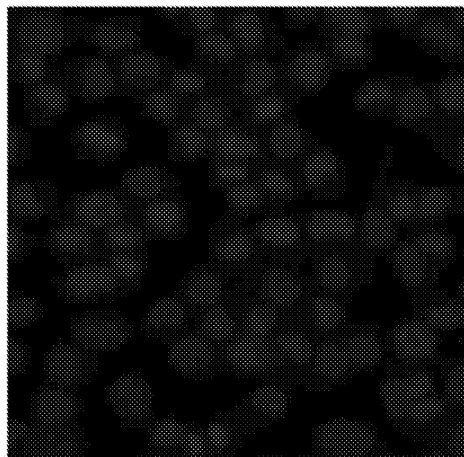
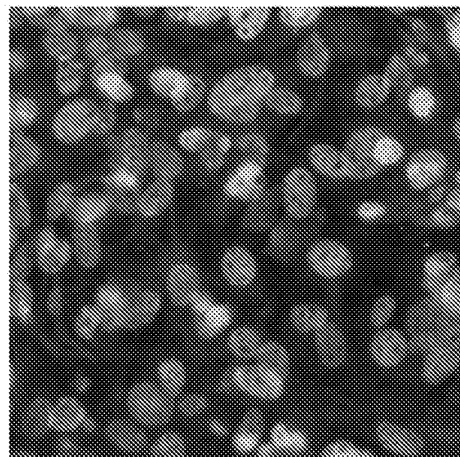


Figure 46F

R175H



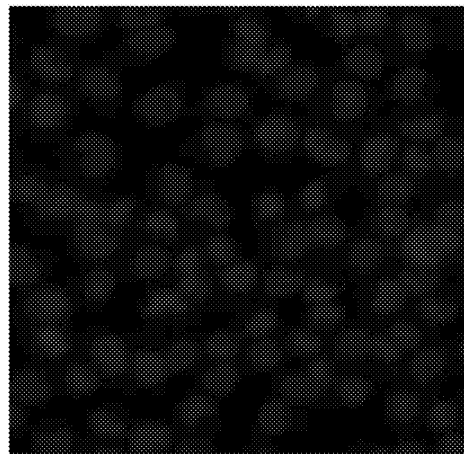
Normal mouse serum on
R175H positive cells



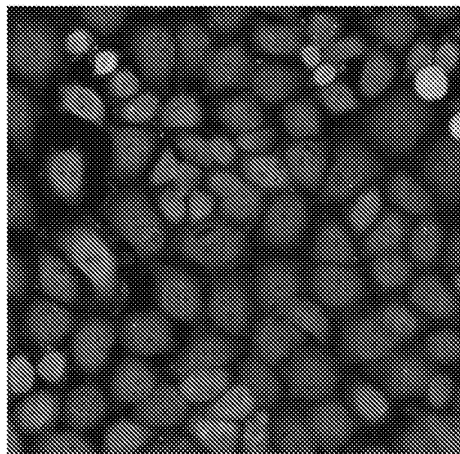
R175H Mouse serum
on R175H positive
cells

Figure 47A

R248Q



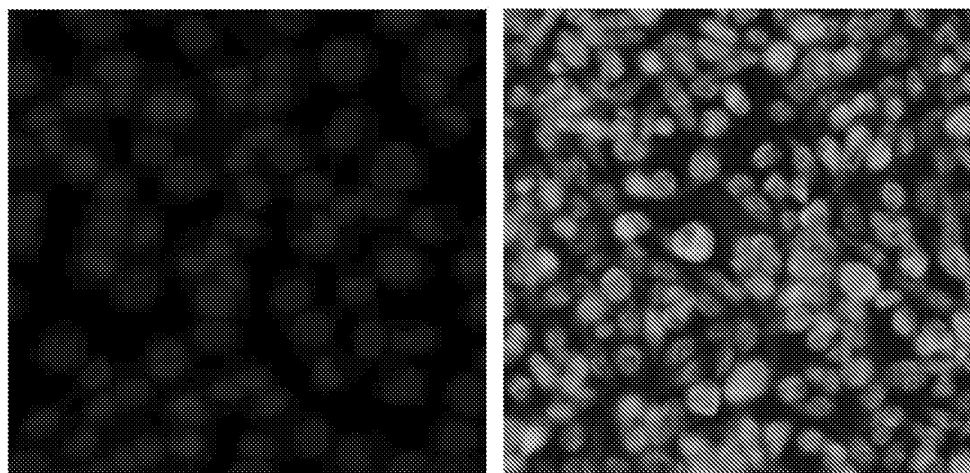
Normal mouse serum on
R248Q positive cells



R248Q Mouse serum on
R248Q positive cells

Figure 47B

R273H



Normal mouse serum on R273H positive cells

R273H Mouse serum on R273H positive cells

Figure 47C

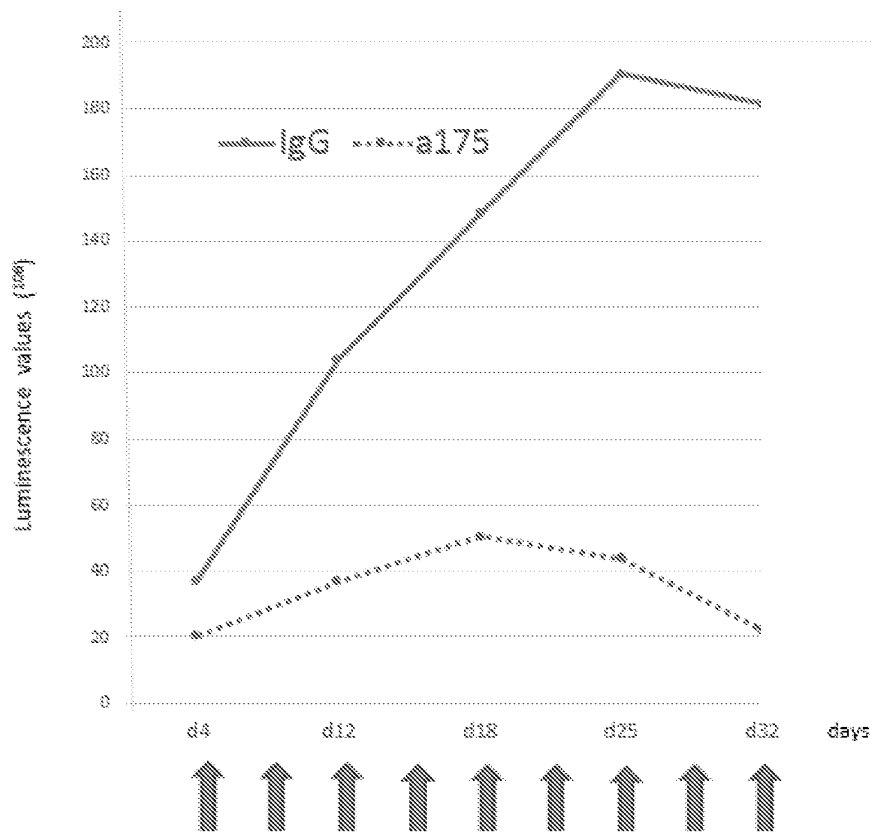


Figure 48

Mouse-human chimeric anti-R175H clone 4H5

DIVLTQSTSSLSVSAGERVTLSCCKSSQSLNLSGNQKSYLAWYQQKPGQPPKLLIYGASTRE
SGVPDRFTGSGSETDFTLTISVQPEDLAVYYCQNDHSYPLTFGAGTKLELK (SEQ ID
NO:237)

LC-CDR1: QSLNLSGNQKSY (SEQ ID NO:19)

LC-CDR2: GAS (SEQ ID NO:20)

LC-CDR3: QNDHSYPLT (SEQ ID NO:21)

Mouse-human chimeric anti-R175H clone 7B9

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGTKLELK (SEQ ID
NO:238)

LC-CDR1: QSLNLSGNQKSN (SEQ ID NO:23)

LC-CDR2: GAS (SEQ ID NO:20)

LC-CDR3: QNDHSYPLT (SEQ ID NO:21)

Mouse-human chimeric anti-R175H clone 10C8

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGTKLELK (SEQ ID
NO:238)

LC-CDR1: QSLNLSGNQKSN (SEQ ID NO:23)

LC-CDR2: GAS (SEQ ID NO:20)

LC-CDR3: QNDHSYPLT (SEQ ID NO:21)

Figure 49

Mouse-human chimeric anti-R175H clone 4H5

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVTVY
NQKFKVKATLTVDRSSSTAYLELRSLTSEDSAVYYCARWGGDYVTGGGTTLTVSS (SEQ ID
NO:239)

HC-CDR1: GFTFTEYT (SEQ ID NO:25)

HC-CDR2: IDPNNGVT (SEQ ID NO:26)

HC-CDR3: ARWGGDYV (SEQ ID NO:27)

Mouse-human chimeric anti-R175H clone 7B9

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLTVSS (SEQ
ID NO:240)

HC-CDR1: GYTFTEYT (SEQ ID NO:29)

HC-CDR2: INPYSGGT (SEQ ID NO:30)

HC-CDR3: ARWGGDYV (SEQ ID NO:27)

Mouse-human chimeric anti-R175H clone 10C8

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLTVSS (SEQ
ID NO:241)

HC-CDR1: GYTFTEYT (SEQ ID NO:29)

HC-CDR2: INPYSGGT (SEQ ID NO:30)

HC-CDR3: ARWGGDYV (SEQ ID NO:27)

Figure 50

Light chain variable domains**Mouse-human chimeric anti-R175H clone 4H5**

>MH 4H5_aa_L
DIVLTQSTSSLSVSAGERVTLSCCKSSQSLLNSGNQKSYLAWYQQKPGQPPKLLIYGASTRE
SGVPDRFTGSGSETDFTLTISVQPEDLAVYYCQNDHSYPLTFGAGTKLELK [SEQ ID
NO:237]

>MH 4H5_ntd_L
GATATTGTGcTCaCCCaATCTACATCCTCCCTGAGTGTGTGTCAGCTGGAGAGAGGGTCAC
TTTGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAAATCAAAAGAGTTACTTGG
CCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAACTGTTGATCTACGGGGCATCCAC
TAGGGAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGGATCTGAAACCGATTTCAC
CTTACCATCAGCAGTGTGCAGCCTGAAGACCTGGCAGTTTATTATTGTCAGAATGATCA
TAGTTATCCGCTCACGTTCCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:242]

Mouse-human chimeric anti-R175H clone 7B9

>MH 7B9_aa_L
DIVMTQSPSSLSVSGGEKVTMSCKSSQSLLNSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGTKLELK [SEQ ID
NO:238]

>MH 7B9_ntd_L
GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAAATCAAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTCAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:243]

Mouse-human chimeric anti-R175H clone 10C8

>MH 10C8_aa_L
DIVMTQSPSSLSVSGGEKVTMSCKSSQSLLNSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGTKLELK [SEQ ID
NO:238]

>MH 10C8_ntd_L
GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAAATCAAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTCAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:243]

Figure 51

Heavy chain variable domains**Mouse-human chimeric anti-R175H clone 4H5**

>MH 4H5_aa_H
EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVTVY
NQKFKVKATLTVDKSSSTAYLELRSLTSEDSAVYYCARWGGDYVTGGGTTLTVSS [SEQ
ID NO:239]

>MH 4H5_ntd_H
GAGGTTCAAGTGCAGCAGTCTGGACCTGAAGTGGTGAAGCCTGGGGCTTCAGTGAAGA
TATCTTGCAAGACTTCCGGATTACATTCACTGAATACACCATGCACTGGATGAAACAG
AGCCATGGAAGGAGCCTTGAGTGGATCGGACGTATTGATCCTAACAATGGTGTACTGT
TTATAACCAGAAGTTCAAGGTCAAGGCCACATTGACTGTGGACAGGTCCTCCAGCACA
GCCTATCTGGAGCTCCGCAGTCTGACGTCTGAGGACTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO:244]

Mouse-human chimeric anti-R175H clone 7B9

>MH 7B9_aa_H
EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLTVSS [SEQ
ID NO:240]

>MH 7B9_ntd_H
GAGGTCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATATCCTGCAAGACTTCTGGCTACACTTTCACTGAATACACCATGCACTGGATGAAGCA
GAGCCATGGAAAGAGCCTTGAGTGGATTGGACGTATTAATCCTTATAGTGGTGGTACTG
TCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACTGTGGACAAGTCCTCCAGCAC
AGCCTATATGGAGCTCCGCAGCCTGACATCTGATGATTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO:245]

Mouse-human chimeric anti-R175H clone 10C8

>MH 10C8_aa_H
EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDSAVYYCARWGGDYVTGGGTTLTVSS [SEQ
ID NO:241]

>MH 10C8_ntd_H
GAGGTGCAGCTTCaGCAGTCGGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATATCCTGCAAGACTTCTGGCTACACTTTCACTGAATACACCATGCACTGGATGAAGCA
GAGCCATGGAAAGAGCCTTGAGTGGATTGGACGTATTAATCCTTATAGTGGTGGTACTG
TCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACTGTGGACAAGTCCTCCAGCAC
AGCCTATATGGAGCTCCGCAGCCTGACATCTGATGATTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO:246]

Figure 52

Mouse-human chimeric anti-R273H clone 13E4

DIVMTQSPLSLPVNLGDQVSLSCRSSQQSIVHNNGDTYLEWYLQKPGQSPKLLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHLPLTFGSGTKLELK (SEQ ID
NO:247)

LC-CDR1:	QSIVHNNGDTY	(SEQ ID NO:59)
LC-CDR2:	KVS	(SEQ ID NO:60)
LC-CDR3:	FQGSHLPLT	(SEQ ID NO:61)

Figure 53**Mouse-human chimeric anti-R273H clone 13E4**

EVQLLETGGDLVTPGGSLKLSCAASGFSFSDYYMYWVRQTPEKRLEWVATISVGGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYYCVRDGNDGKFLGYWGGTFVTVTV
S (SEQ ID NO:248)

HC-CDR1:	GFSFS	(SEQ ID NO:63)
HC-CDR2:	ISVG	(SEQ ID NO:64)
HC-CDR3:	VRDGNDGKFLG	(SEQ ID NO:65)

Figure 54

Mouse-human chimeric anti-R273H clone 13E4 light chain variable domain

>MH 13E4_aa_L
DIVMTQSPLSLPVNLGDQVSLSCRSSQSIVHNNGDTYLEWYLQKPGQSPKLLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHLPLTFGSGTKLELK [SEQ ID
NO:247]

>MH 13E4_ntd_L
GATATTGTGATGACACAATCTCCACTCTCCCTGCCTGTCAATCTTGAGATCAAGTCTC
CCTCTCTTGCAGATCTAGTCAGAGCATTGTACATAATAATGGAGACACCTATTTAGAATG
GTACCTACAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGAT
TTTCTGGGGTCCCAGACAGGTTCAAGTGGCAGTGGATCAGGGACAGATTTCACTCAA
GATCAGCAGAGTGGAGGCTGAGGATCTGGGAATTTATTACTGCTTTCAAGGTTACATC
TTCCGCTCACGTTTCGGTTCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:249]

Figure 55**Mouse-human chimeric anti-R273H clone 13E4 heavy chain variable domain**

>MH 13E4_aa_H
EVQLLETGGDLVTPGGSLKLSCAASGFSFSDYYMYWVRQTPEKRLEWVATISVGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYVCVRDGNDGKFLGYWGQGTFTVTV
S [SEQ ID NO:248]

>MH 13E4_ntd_H
GAAGTGCAGCTGTTGGAGACTGGGGGAGACTTAGTGACGCCTGGAGGGTCCCTGAAA
CTCTCCTGTGCAGCCTCTGGATTCACTTCAGTGACTATTATATGTATTGGGTTCCGCA
GACTCCGGAAGAGGCTGGAGTGGGTCGCACTATTAGTGTTGGTGGTACATACACC
TTCTATTCAGACAATGTGAAGGGGAGATTCGTCATCTCCAGAGACAATGCCAGGAAAAA
TCTGCATCTGGAAATGAACAGTCTGAAGTCTGAGGACGCAGCCATGTATTACTGTGTAA
GAGATGGCAACGATGGAAAATTTCTTGGGTACTGGGGCCAGGGGACTTTCGTCACTGT
CACTGTCTCT [SEQ ID NO:250]

Figure 56

Mouse-human chimeric anti-R248Q clone 3G11

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGSPKRLIYLVSKLDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK (SEQ ID NO:251)

LC-CDR1: QSLLYSDGKTY (SEQ ID NO:41)

LC-CDR2: LVS (SEQ ID NO:42)

LC-CDR3: WQGTHFPLT (SEQ ID NO:43)

Mouse-human chimeric anti-R248Q clone 4H2

DIVITQSPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGSPKRLIYLVSELDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK (SEQ ID NO:252)

LC-CDR1: QSLLYSDGKTY (SEQ ID NO:41)

LC-CDR2: LVS (SEQ ID NO:42)

LC-CDR3: WQGTHFPLT (SEQ ID NO:43)

Figure 57

Mouse-human chimeric anti-R248Q clone 3G11

DVQLQQSGPELVKPGASVKMSCKASGYTFTDYYVKWVKQSPGQSLEWIGDIHPKNGGTN
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAKMGGYDDYWGGQTTLTVSS
(SEQ ID NO:253)

HC-CDR1: GYTFTDYY (SEQ ID NO:46)

HC-CDR2: IHPKNGGT (SEQ ID NO:47)

HC-CDR3: AKMGGYDDY (SEQ ID NO:48)

Mouse-human chimeric anti-R248Q clone 4H2

QVQLKQSGPELVKPGASVKMSCKASGYTFTDYYLKWVRQSHGKSLEWIGDIDPKNGGTNY
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAKQGGFDDYWGGQTTLTVSS (SEQ
ID NO:254)

HC-CDR1: GYTFTDYY (SEQ ID NO:46)

HC-CDR2: IDPKNGGT (SEQ ID NO:50)

HC-CDR3: AKQGGFDDY (SEQ ID NO:51)

Figure 58

Mouse-human chimeric anti-R248Q clone 3G11 light chain variable domain

>MH 3G11_aa_L

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGSPKRLIYLVSKLDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:251]

>MH 3G11_ntd_L

GATATTGTGCTGACACAGACTCCACTCACTTTGTCGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAAATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GTTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTAAACTGG
ACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTACACTGAA
AATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACATT
TTCCTCTCACGTTTCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:255]**Mouse-human chimeric anti-R248Q clone 4H2 light chain variable domain**

>MH 4H2_aa_L

DIVITQSPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGSPKRLIYLVSELD SGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:252]

>MH 4H2_ntd_L

GACATTGTGATCACACAGTCTCCACTCACTTTGTCGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAGATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GCTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTGAACTG
GACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTACACTGA
AAATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACAT
TTTCCTCTCACGTTTCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:256]**Figure 59**

Mouse-human chimeric anti-R248Q clone 3G11 heavy chain variable domain

>MH 3G11_aa_H
DVQLQQSGPELVKPGASVKMSCKASGYTFTDYYVKWVKQSPGQSLEWIGDIHPKNGGTN
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAKMGGYDDYWGGQTTLTVSS
[SEQ ID NO:253]

>MH 3G11_ntd_H
GATGTGCAGCTTCAGCAGTCAGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGA
TGTCCTGTAAGGCTTCTGGATACACATTCACTGACTACTATGTGAAGTGGGTGAAGCAG
AGTCCTGGACAGAGCCTTGAGTGGATTGGAGATATTCATCCTAAGAACGGTGGTACTAA
CTACAACCAGAAGTTCAAGGGCAAGGCCGATTGACTGTGGACAAATCCTCCAGCAC
GCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTTCTGTGCAA
AATGGGAGGCTACGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[SEQ ID NO:257]

Mouse-human chimeric anti-R248Q clone 4H2 heavy chain variable domain

>MH 4H2_aa_H
QVQLKQSGPELVKPGASVKMSCKASGYTFTDYYLKWVRQSHGKSLEWIGDIDPKNGGTNY
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAKQGGFDDYWGGQTTLTVSS [SEQ
ID NO:254]

>MH 4H2_ntd_H
CAGGTGCAGCTGAAGCAGTCAGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATGTCCTGTAAGGCTTCTGGATACACATTCACTGACTACTATCTGAAGTGGGTGAGGCA
GAGTCATGGAAAGAGCCTTGAGTGGATTGGAGATATAGATCCCAAGAATGGTGGTACT
AATTACAACCAGAAGTTTAAGGGCAAGGCCACATTGACTGTGGACAAATCCTCCAGCAC
AGCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAA
AACAGGGGGGGTTTCGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[SEQ ID NO:258]

Figure 60

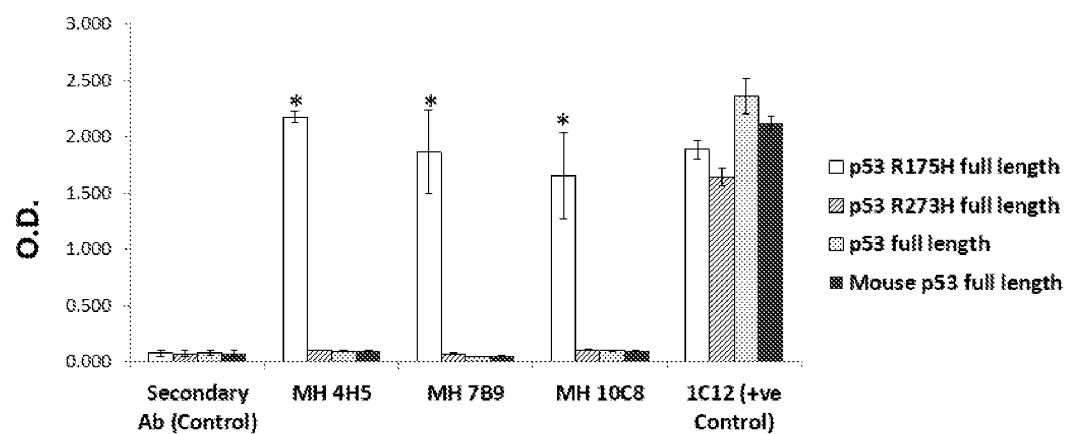


Figure 61

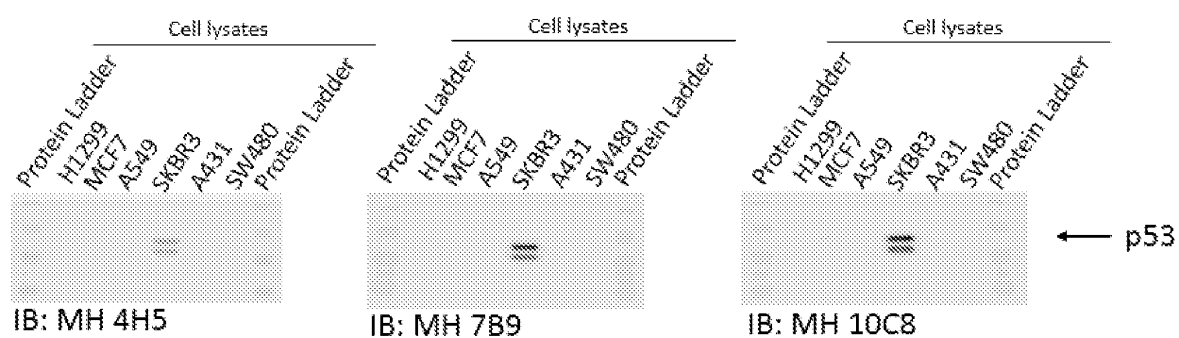


Figure 62

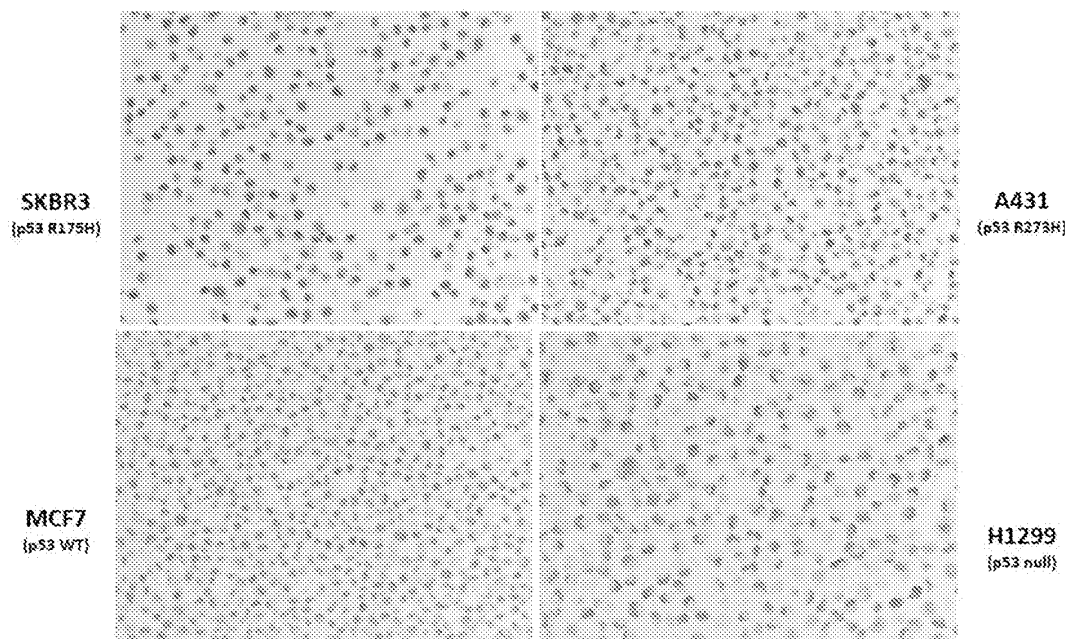


Figure 63

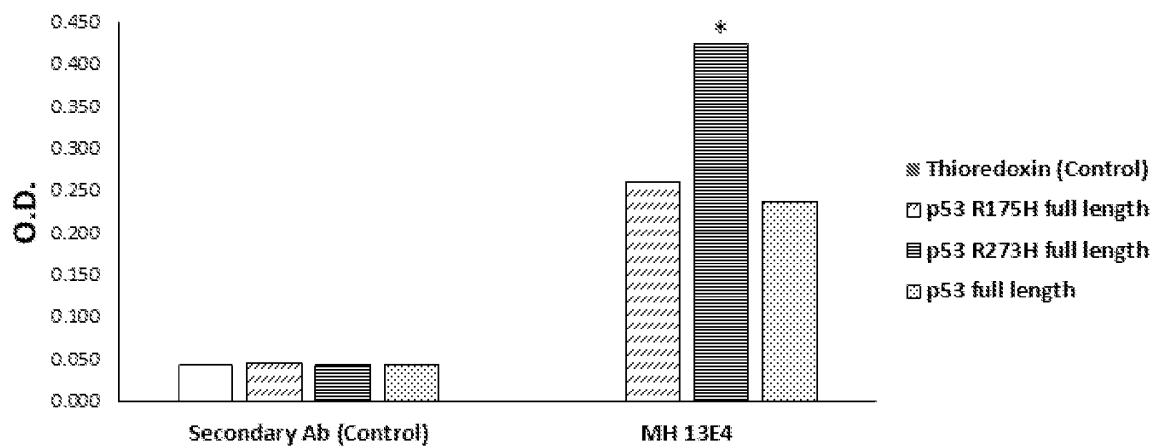


Figure 64

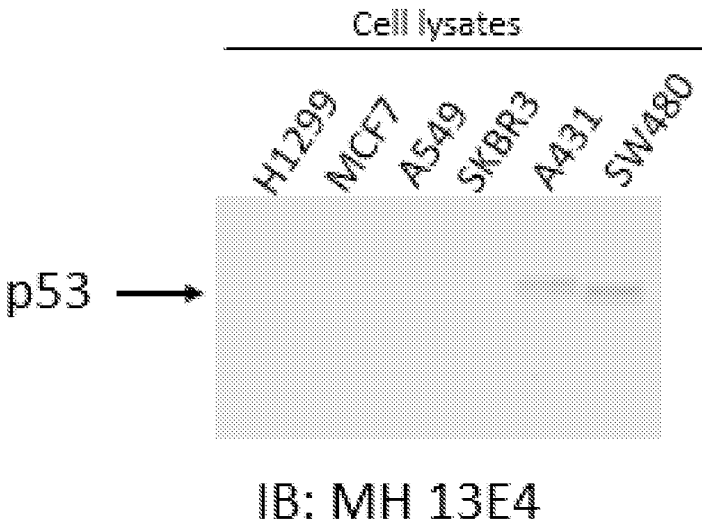


Figure 65

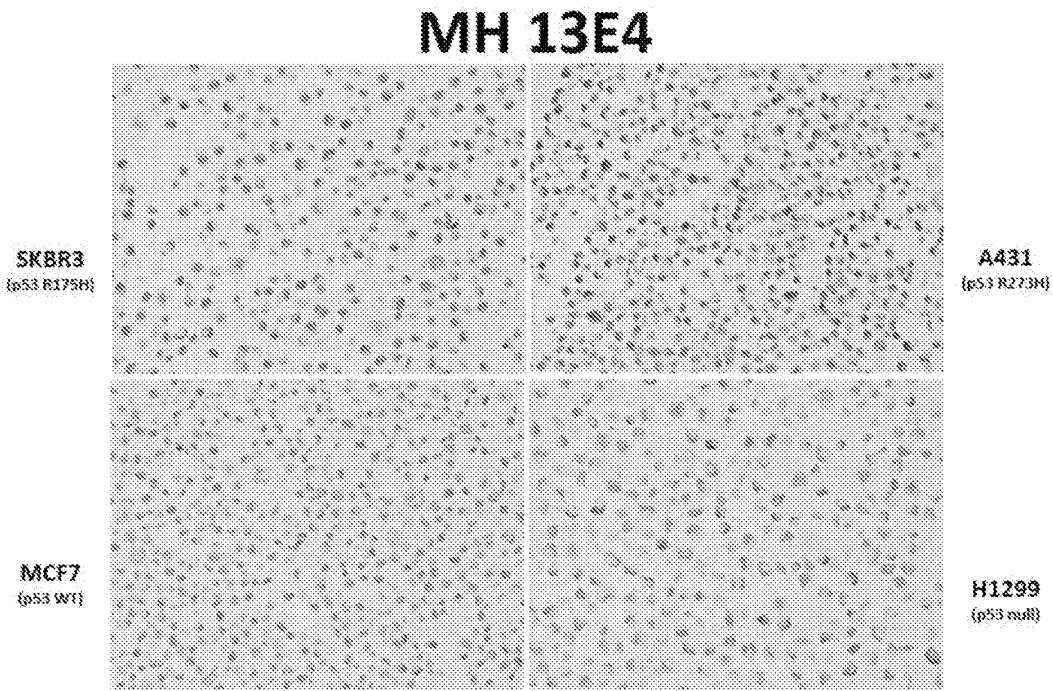
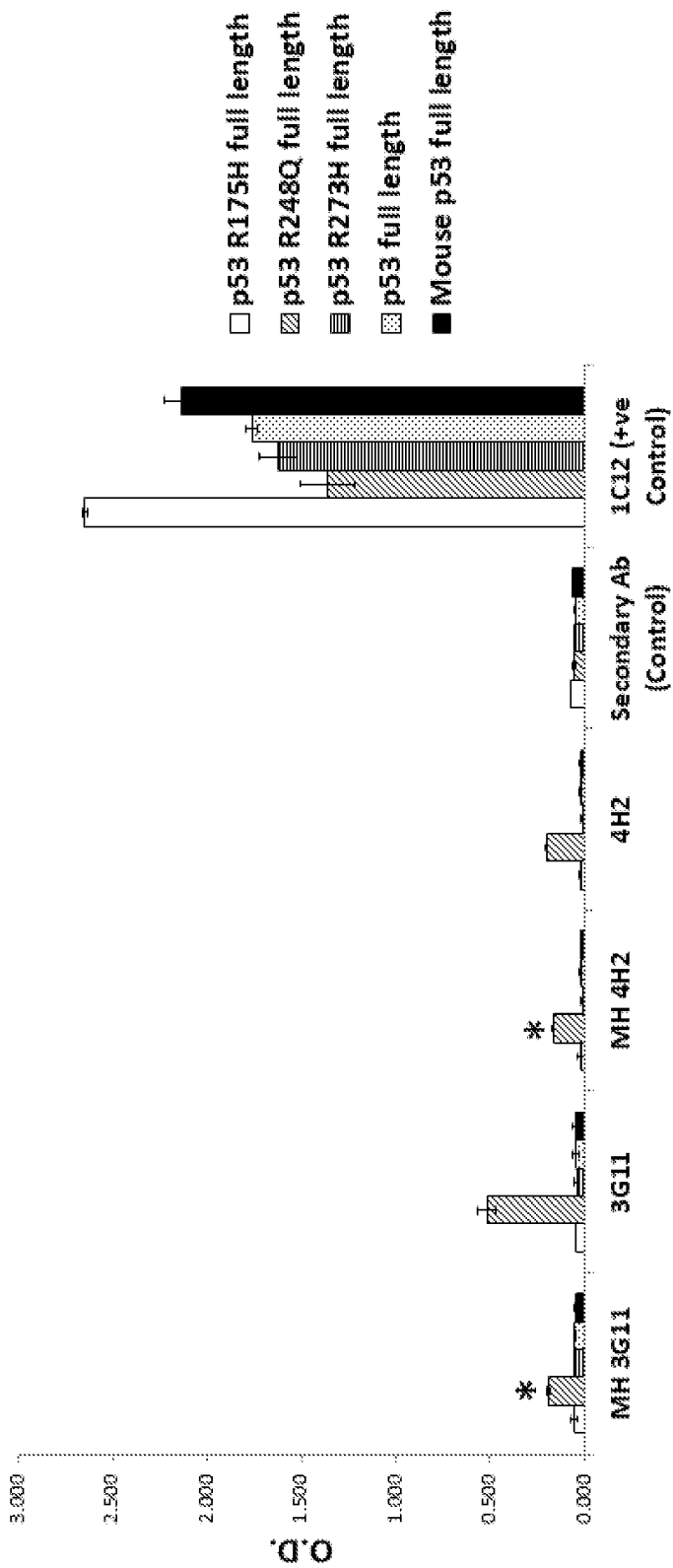


Figure 66



Note: "MH 3G11" refers to chimeric 3G11 antibody, "MH 4H2" refers to chimeric 4H2 antibody

Figure 67

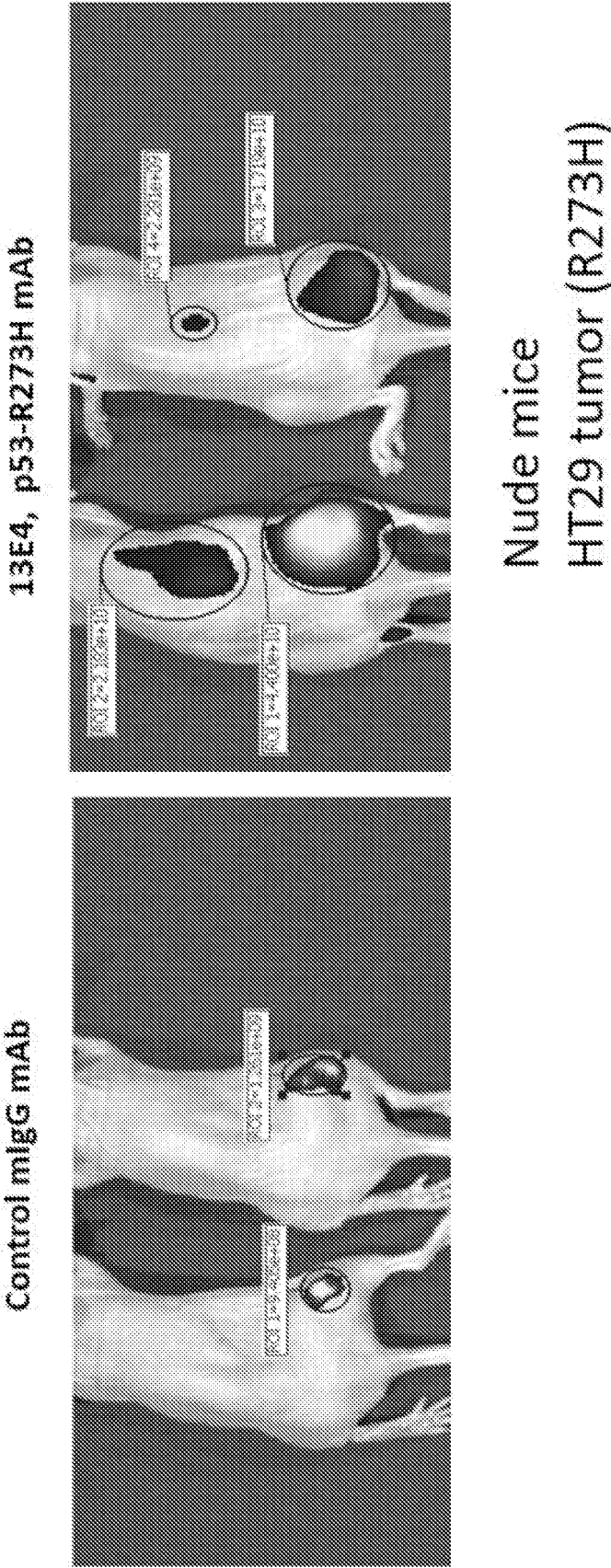


Figure 68

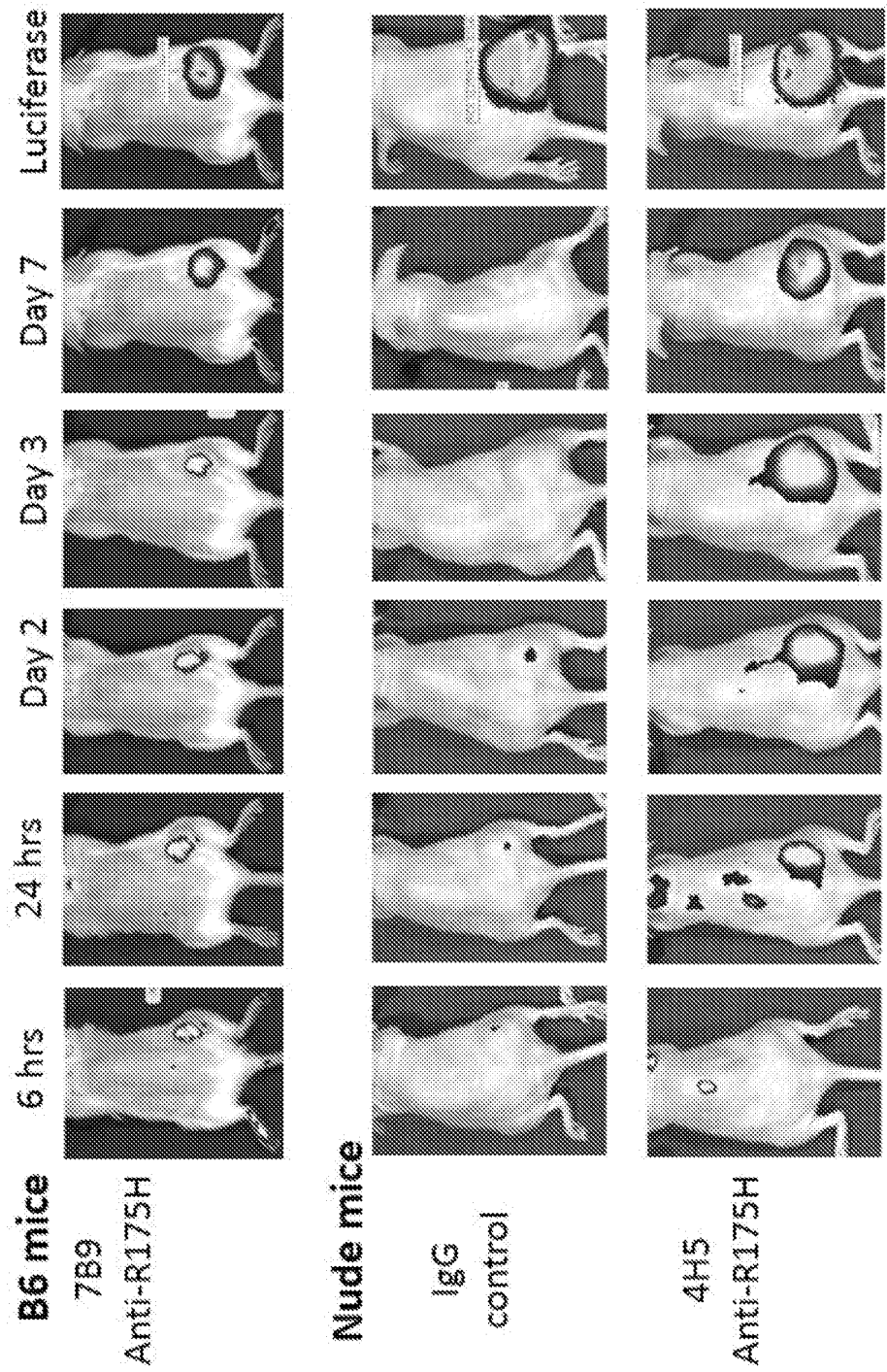


Figure 69

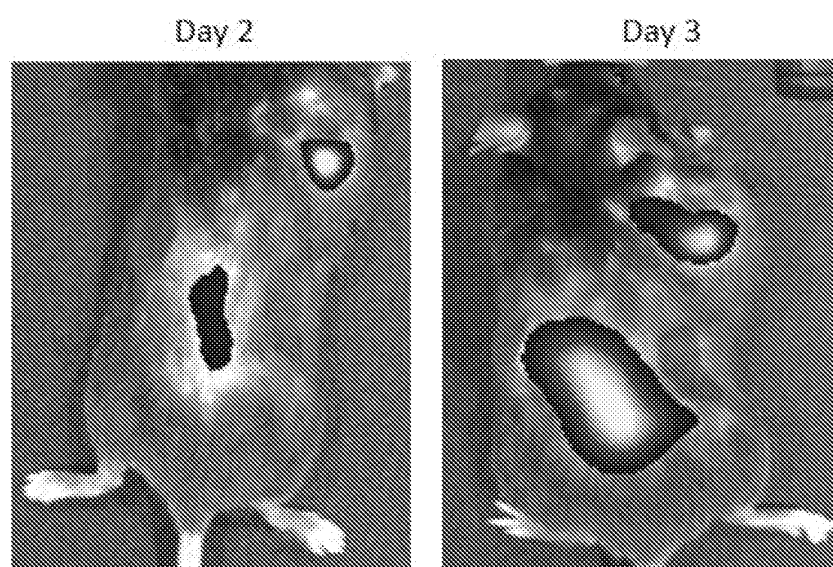


Figure 70

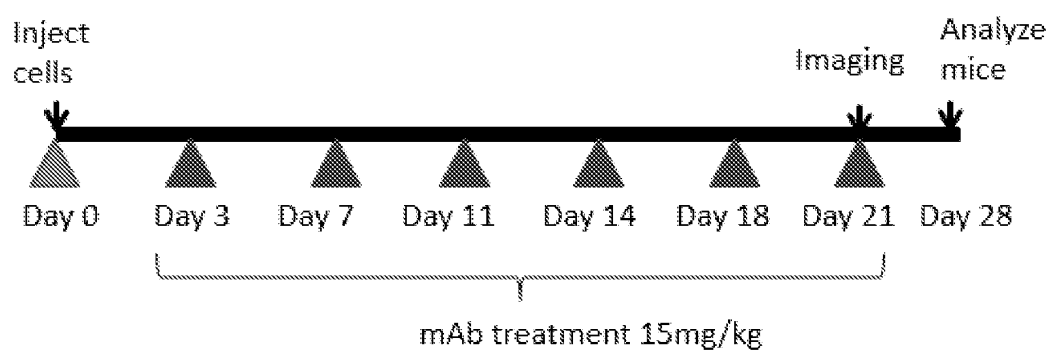
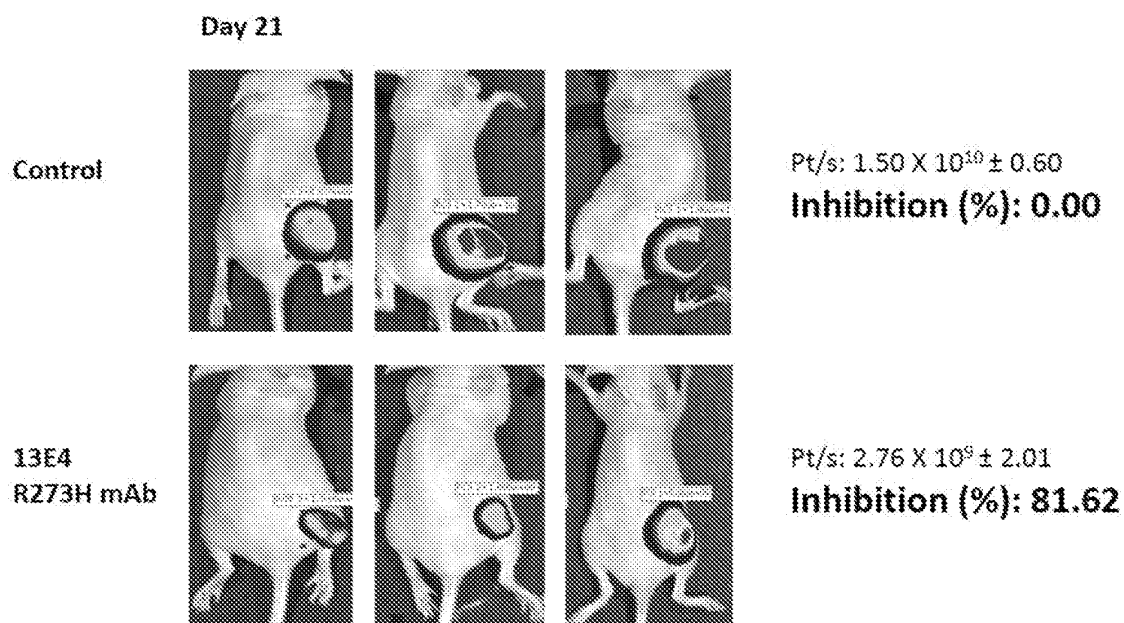
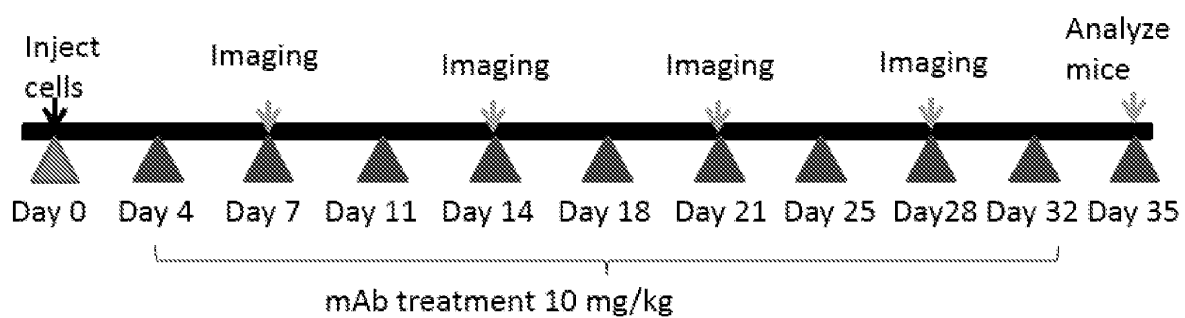


Figure 71A

**Figure 71B****Figure 72A**

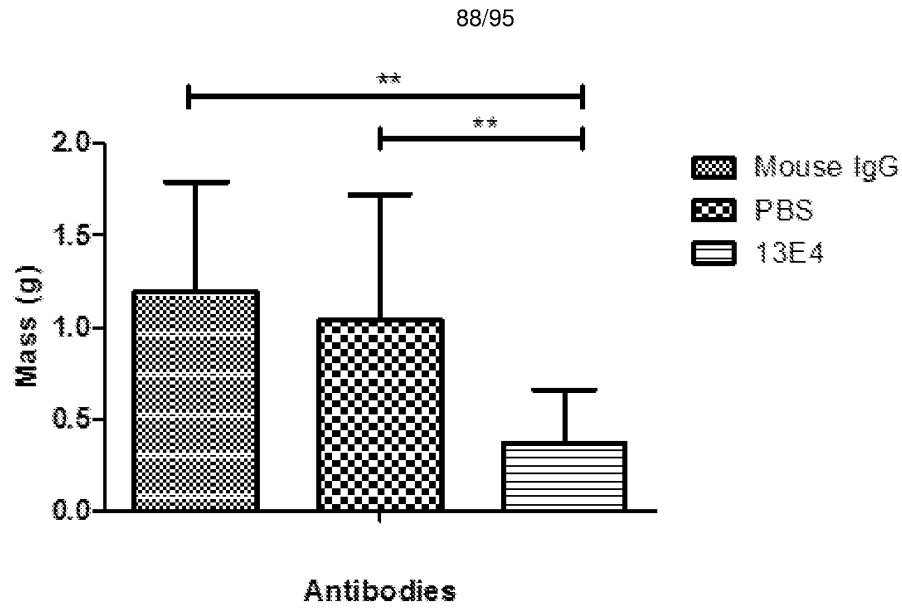


Figure 72B

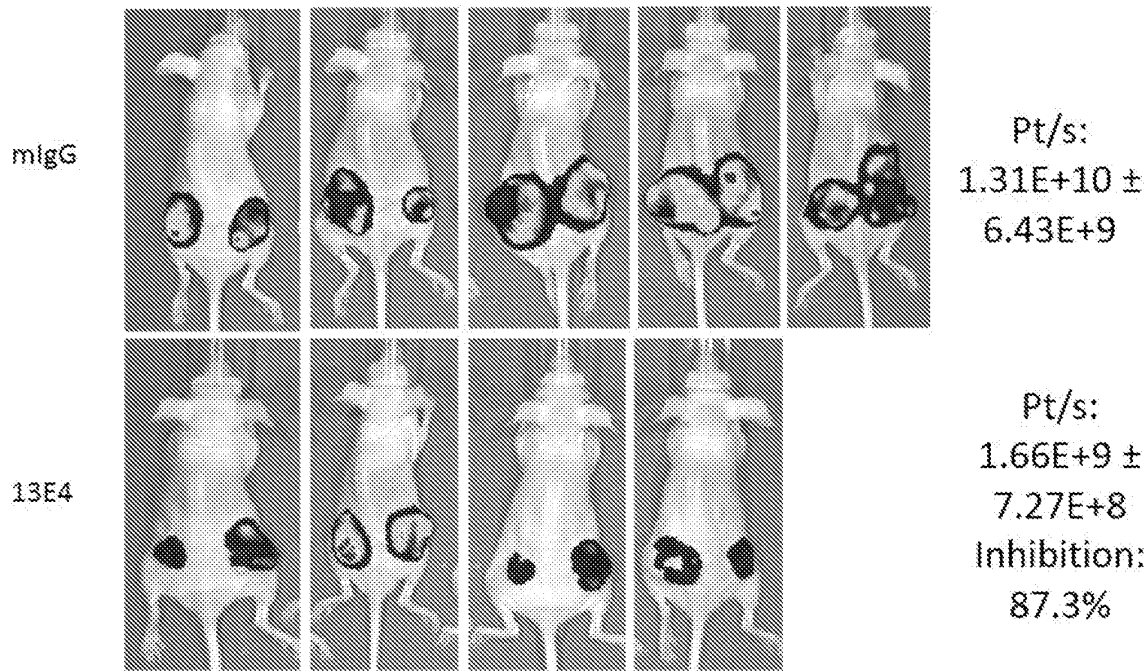


Figure 72C

Tumour growth curve

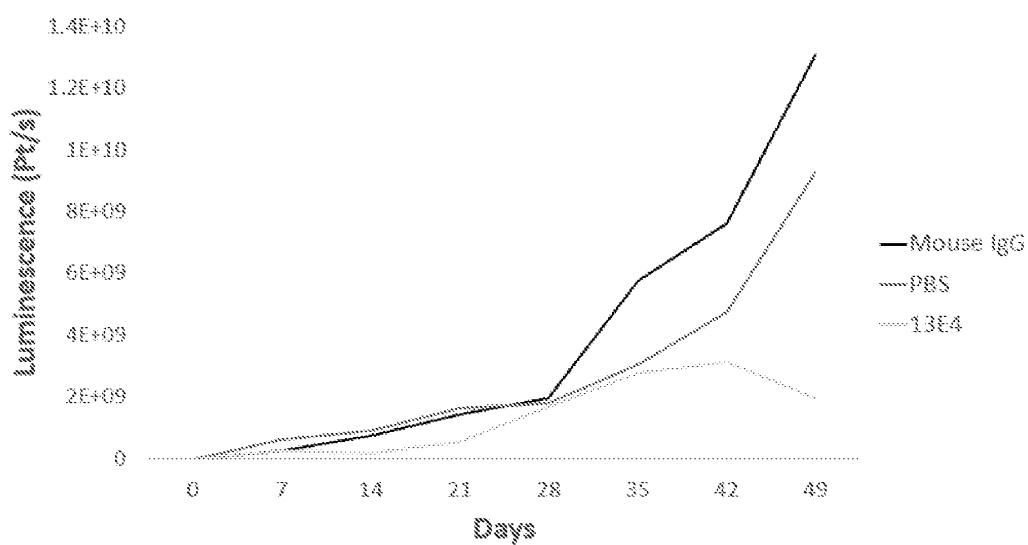
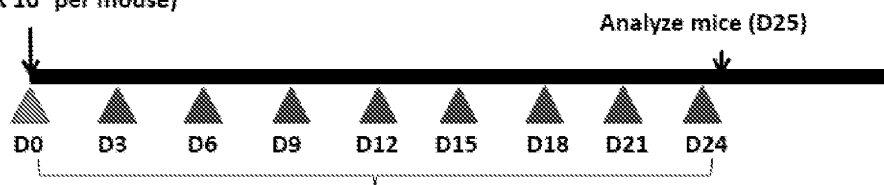


Figure 72D

Inject B6 mouse with p53^{R175H} mouse
tumor cells, clone 32
(3 X 10⁶ per mouse)



mAb treatment; 100 ug of
ascites was i.v. injected into
mouse on Day 3, 6, 9, 12, 15, 18,
21 and Day 24. Mice were
sacrificed on Day 25 and tumor
weight was measured.

Figure 73A

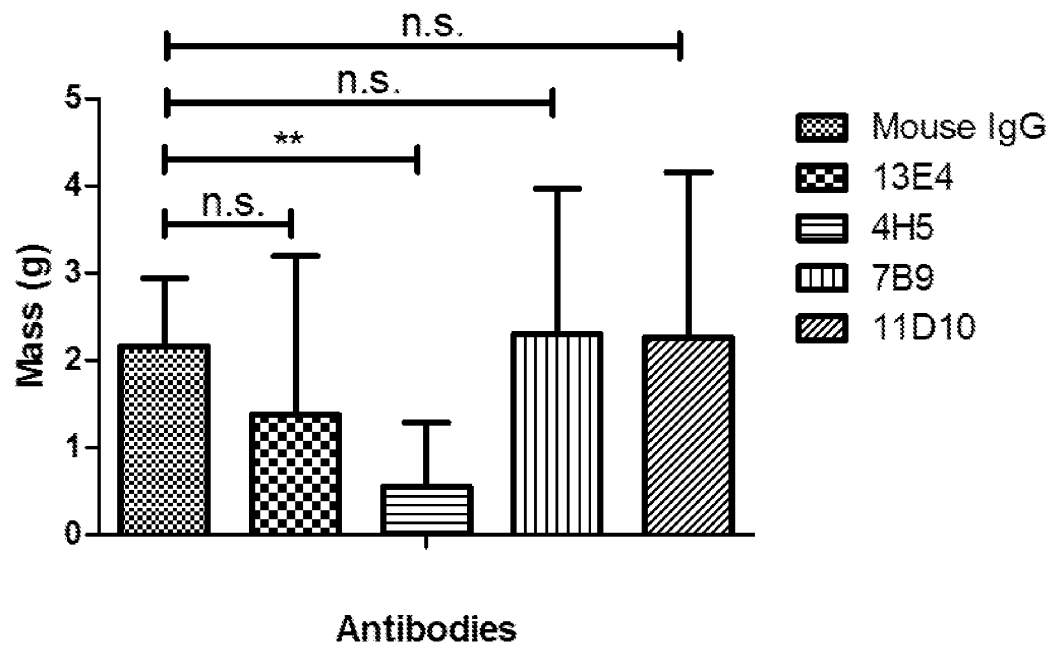


Figure 73B

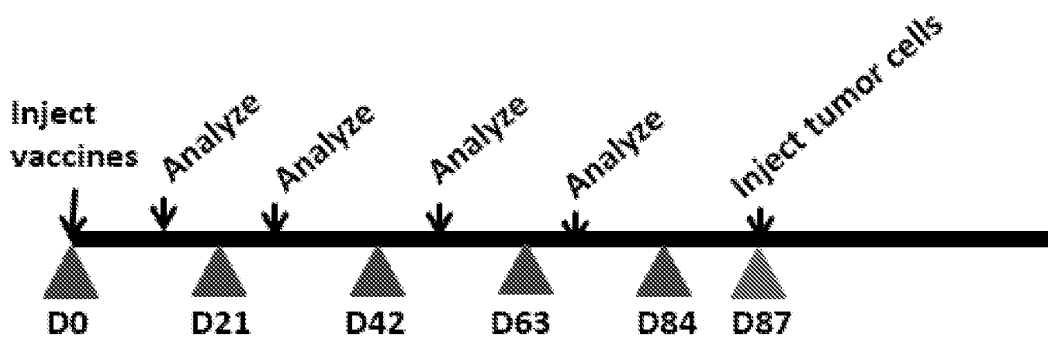


Figure 74A

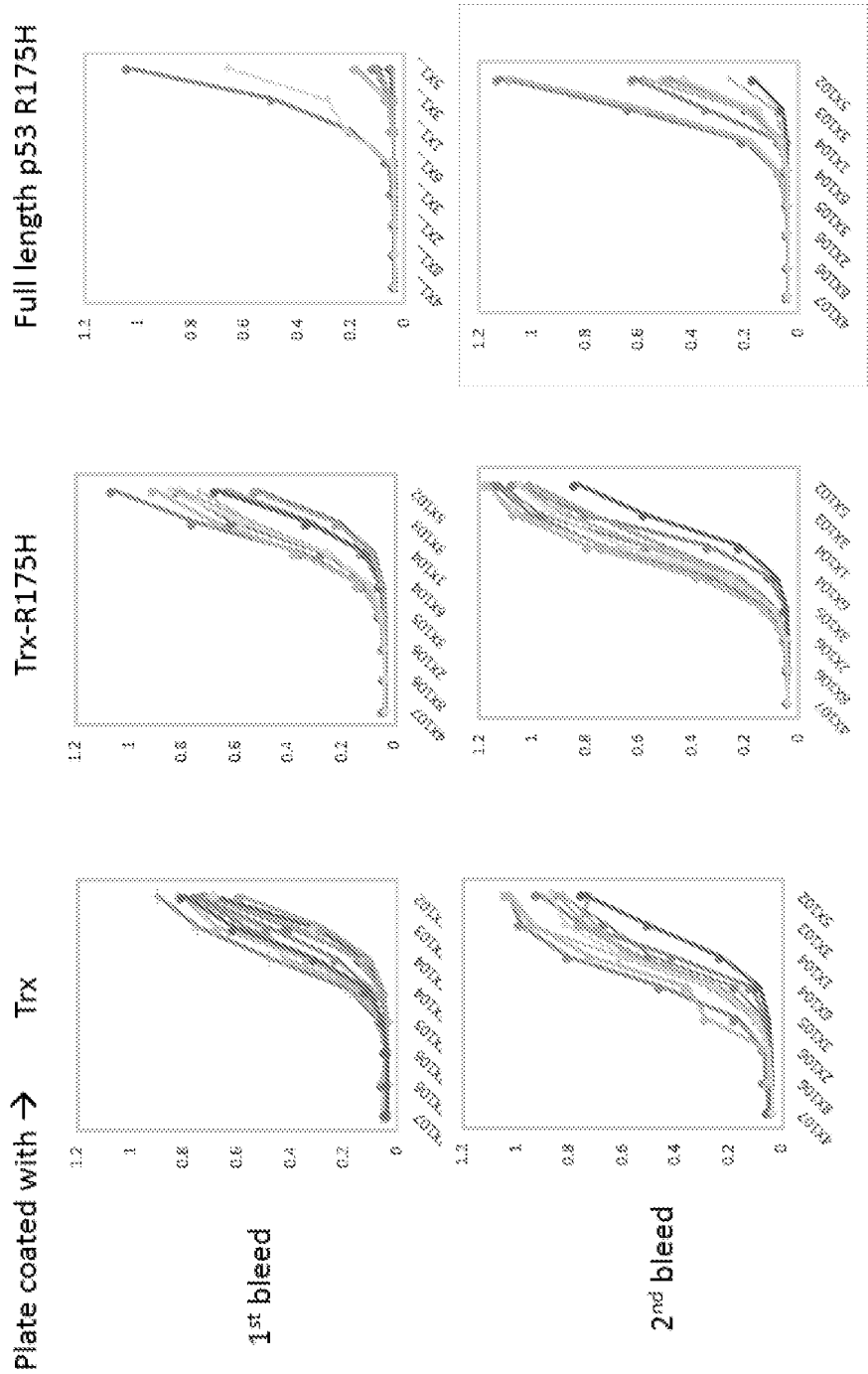


Figure 74B

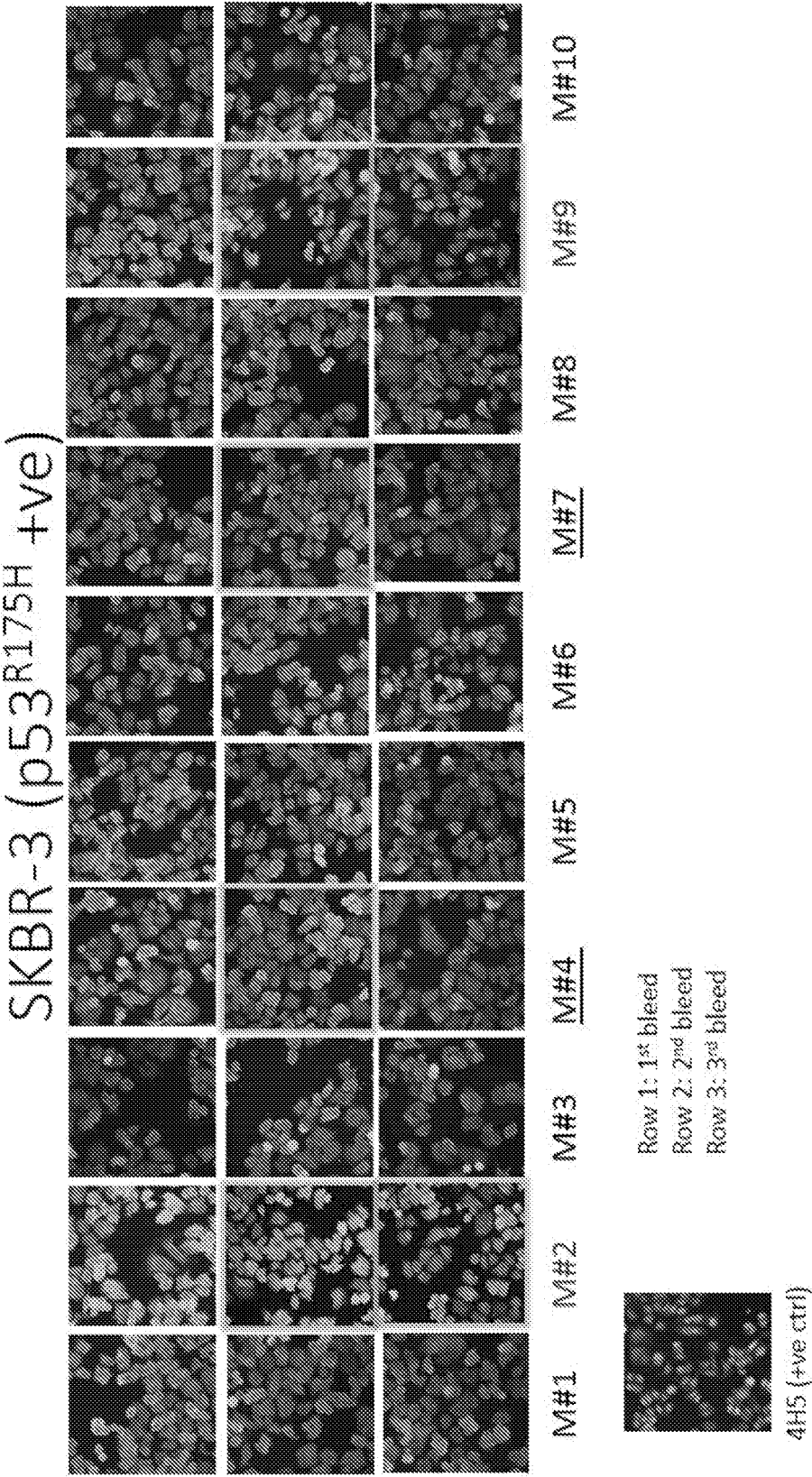


Figure 74C

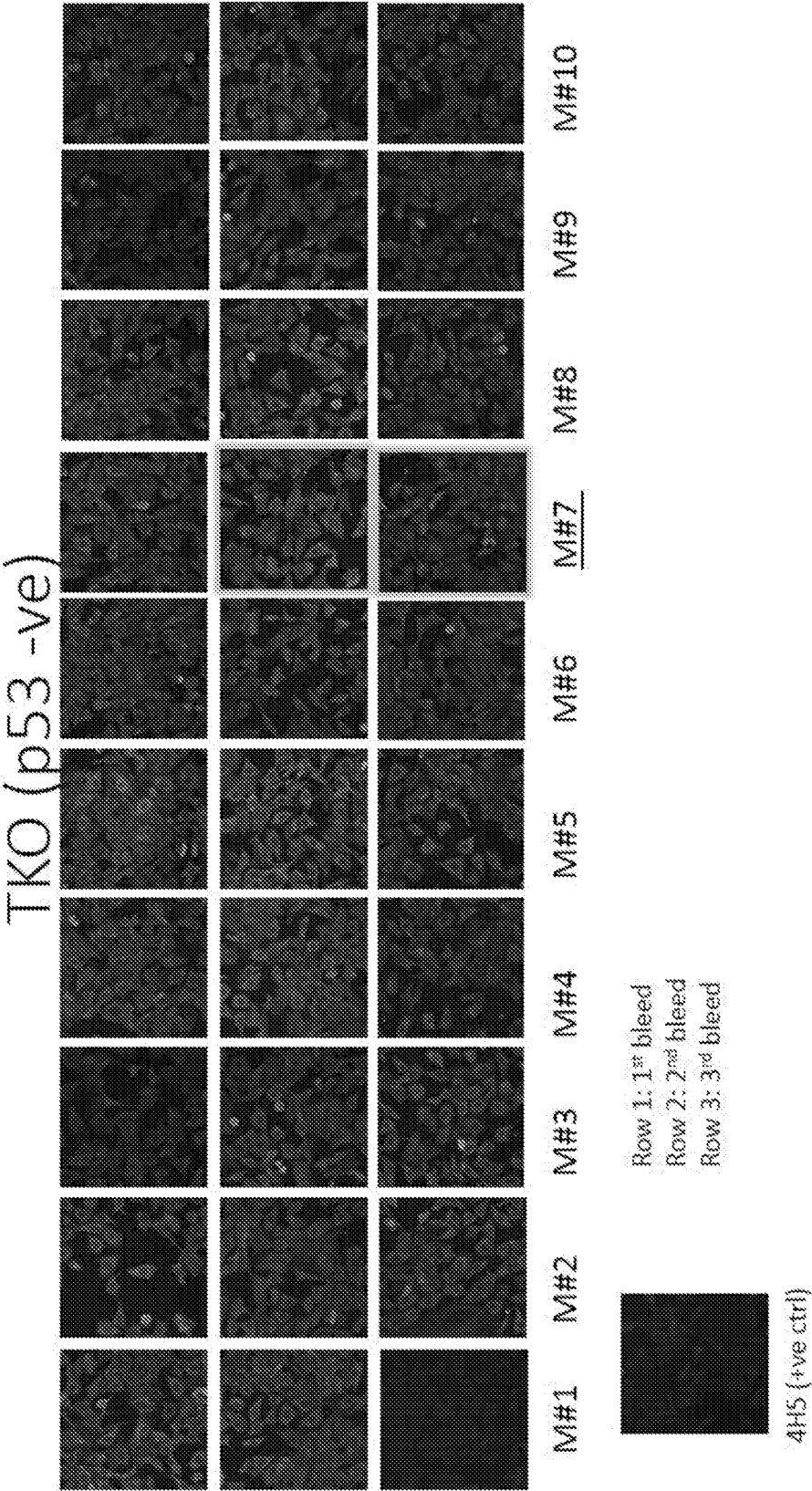


Figure 74D

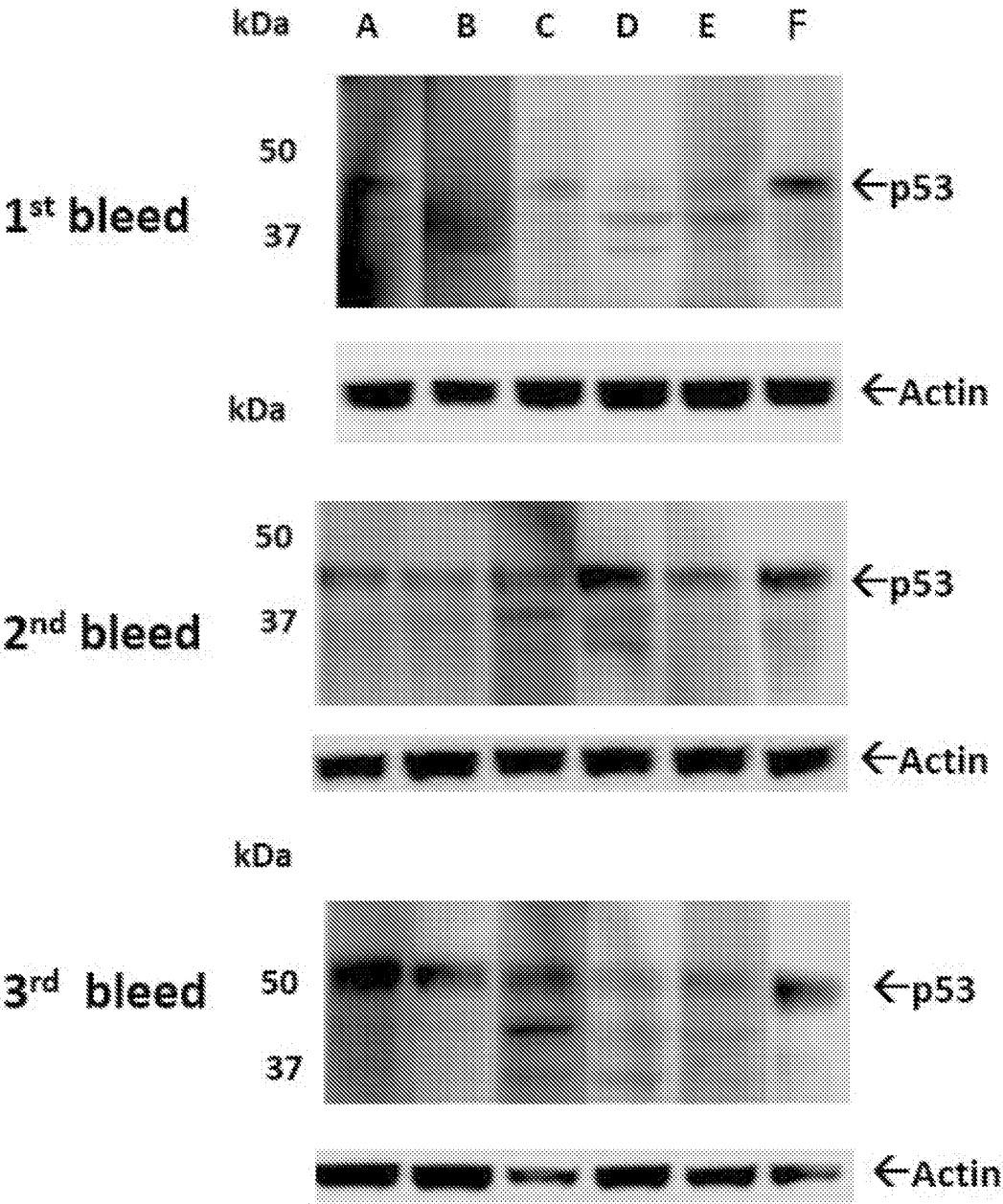


Figure 74E

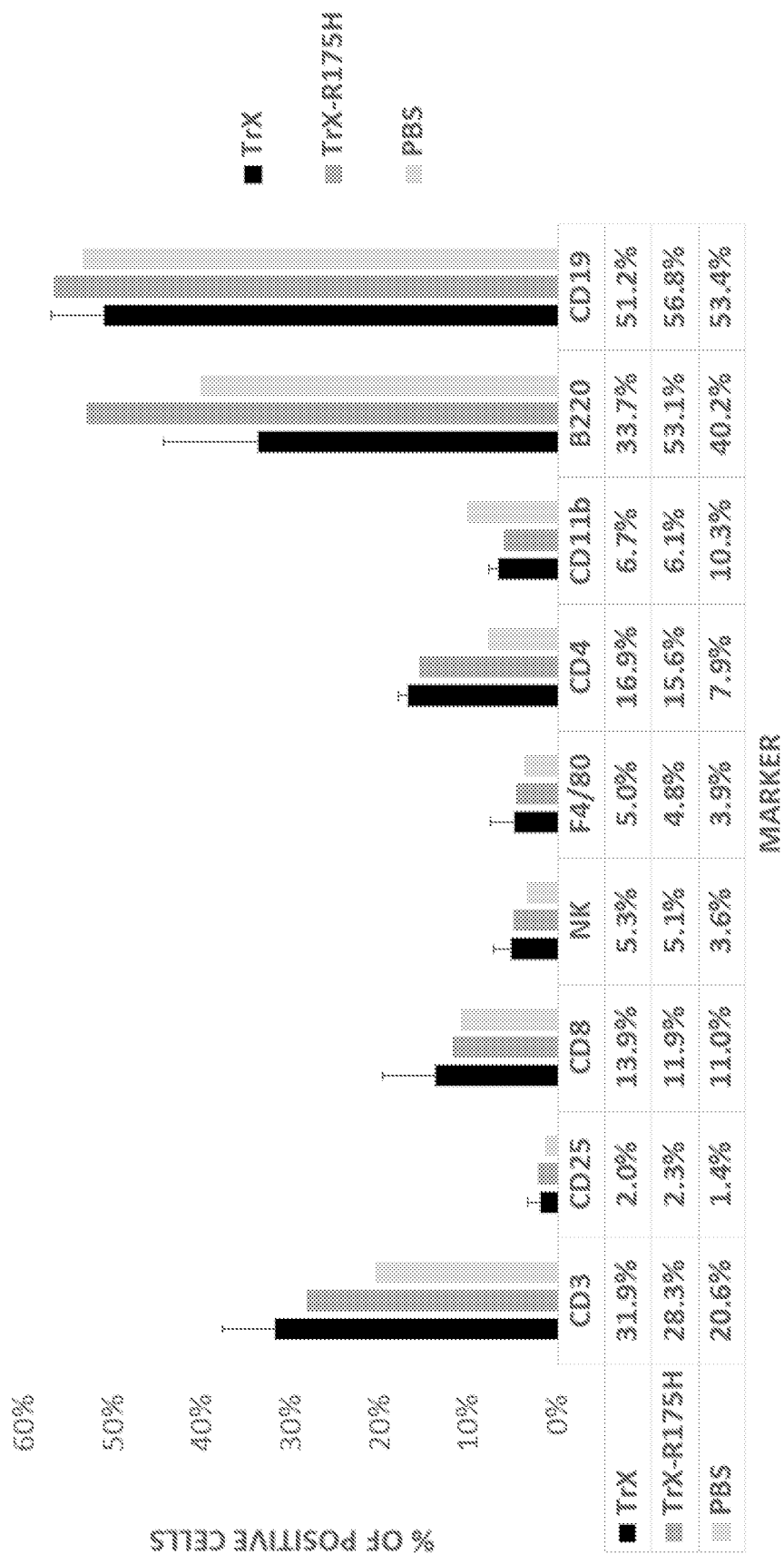


Figure 74F