

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 P 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

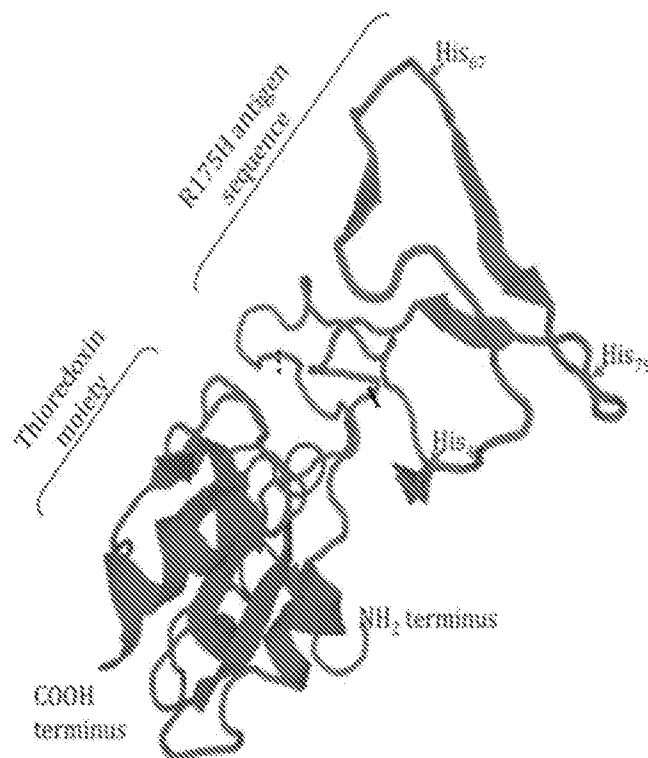
Figure 1B

R273H

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      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 H STOP

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Figure 1C**Figure 2A**

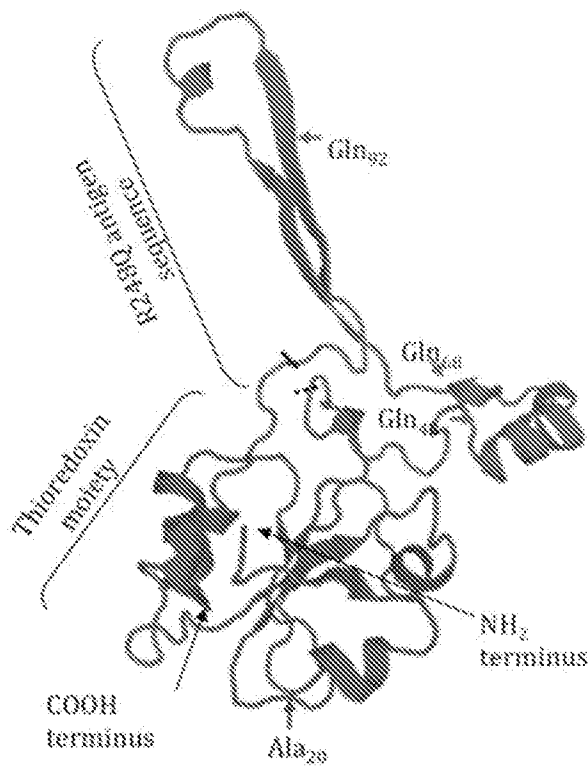


Figure 2B

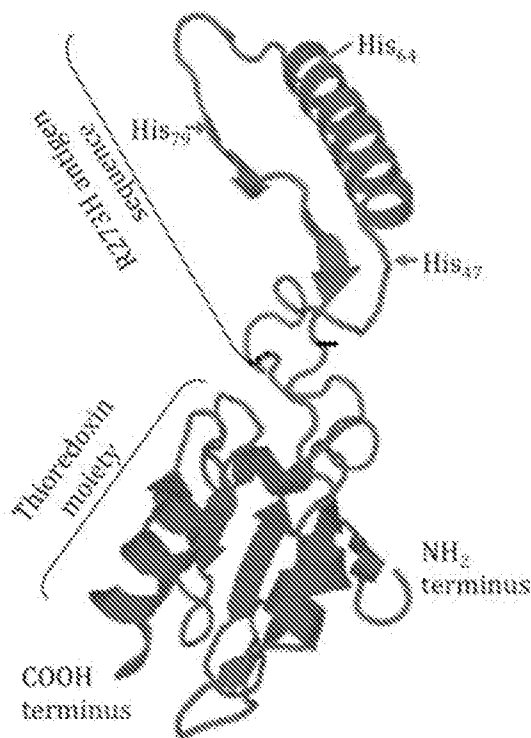


Figure 2C

R175H

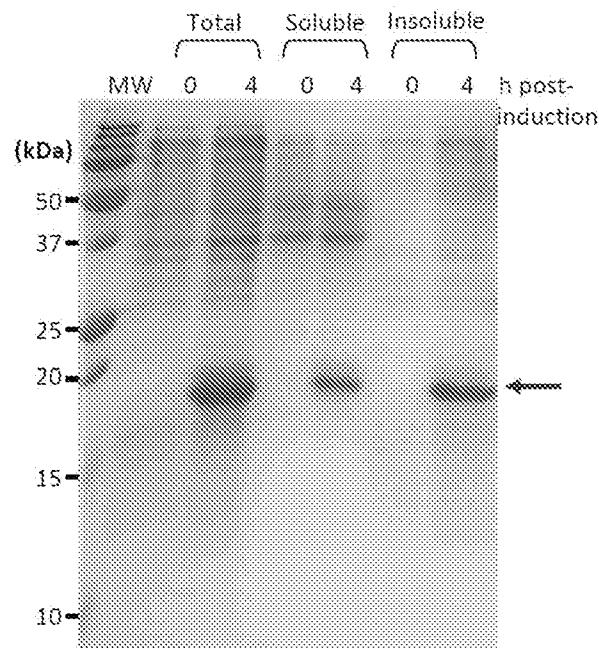


Figure 3A

R248Q

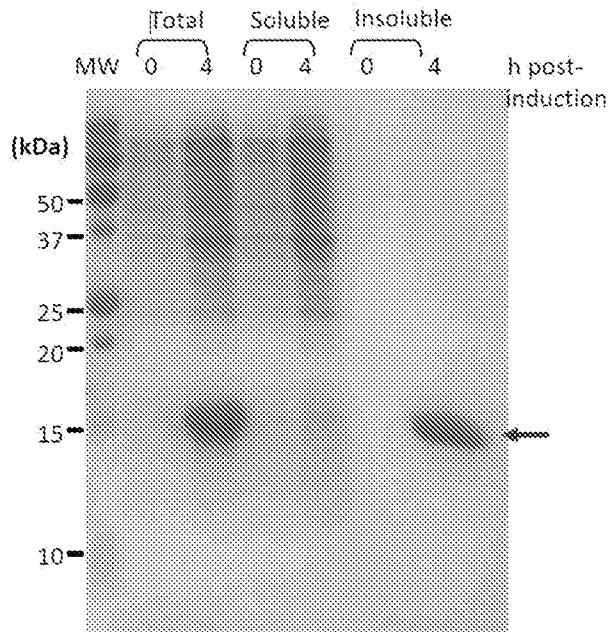


Figure 3B

R273H

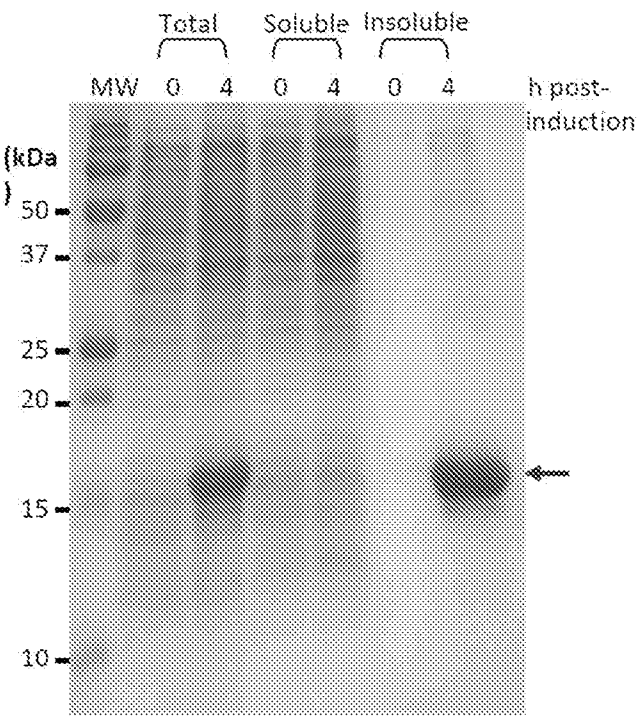


Figure 3C

R175H

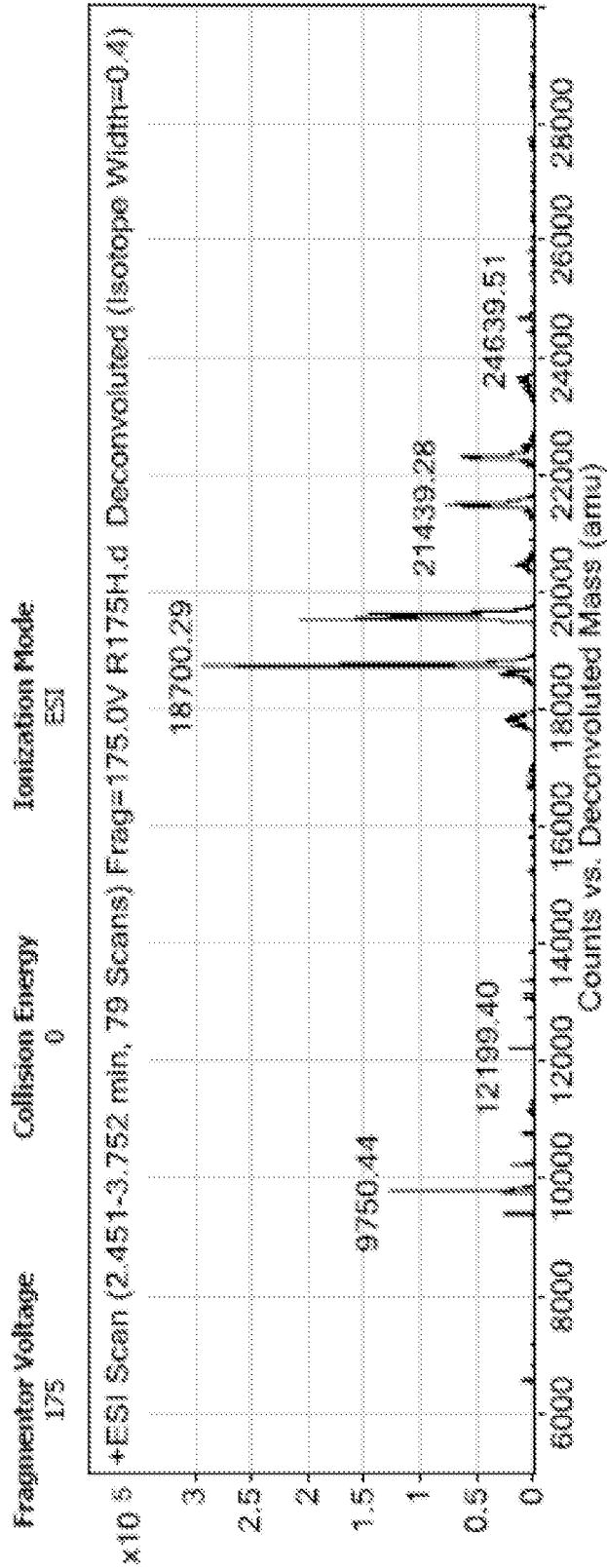


Figure 4A

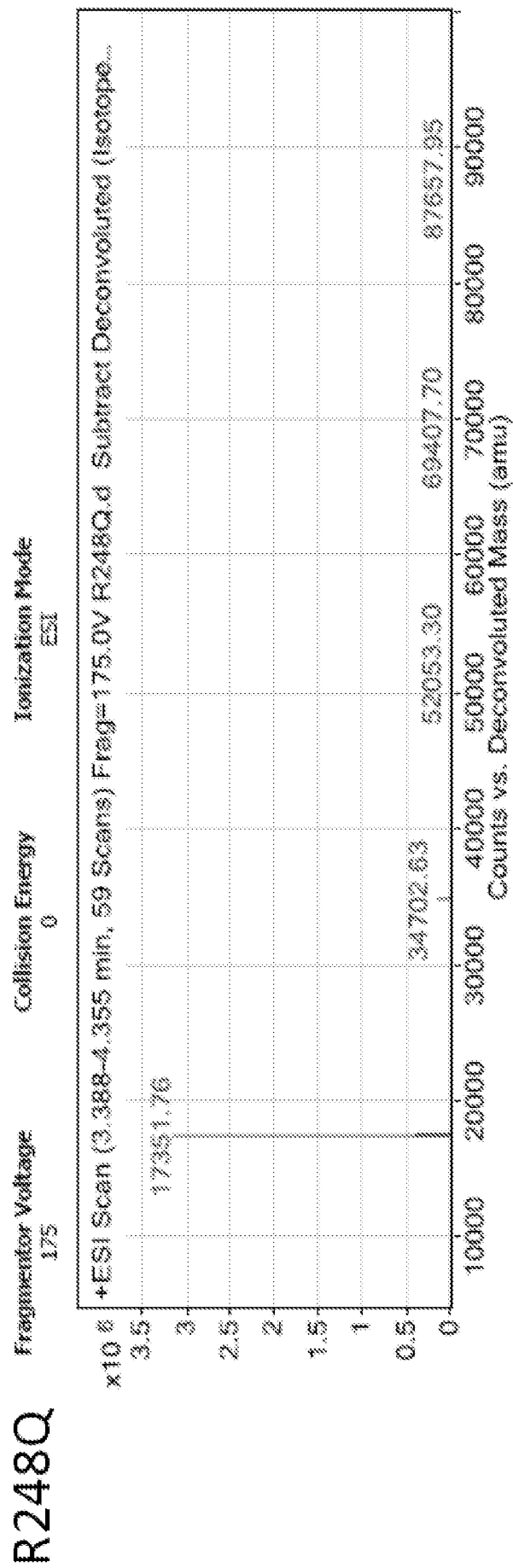


Figure 4B

α-R175H

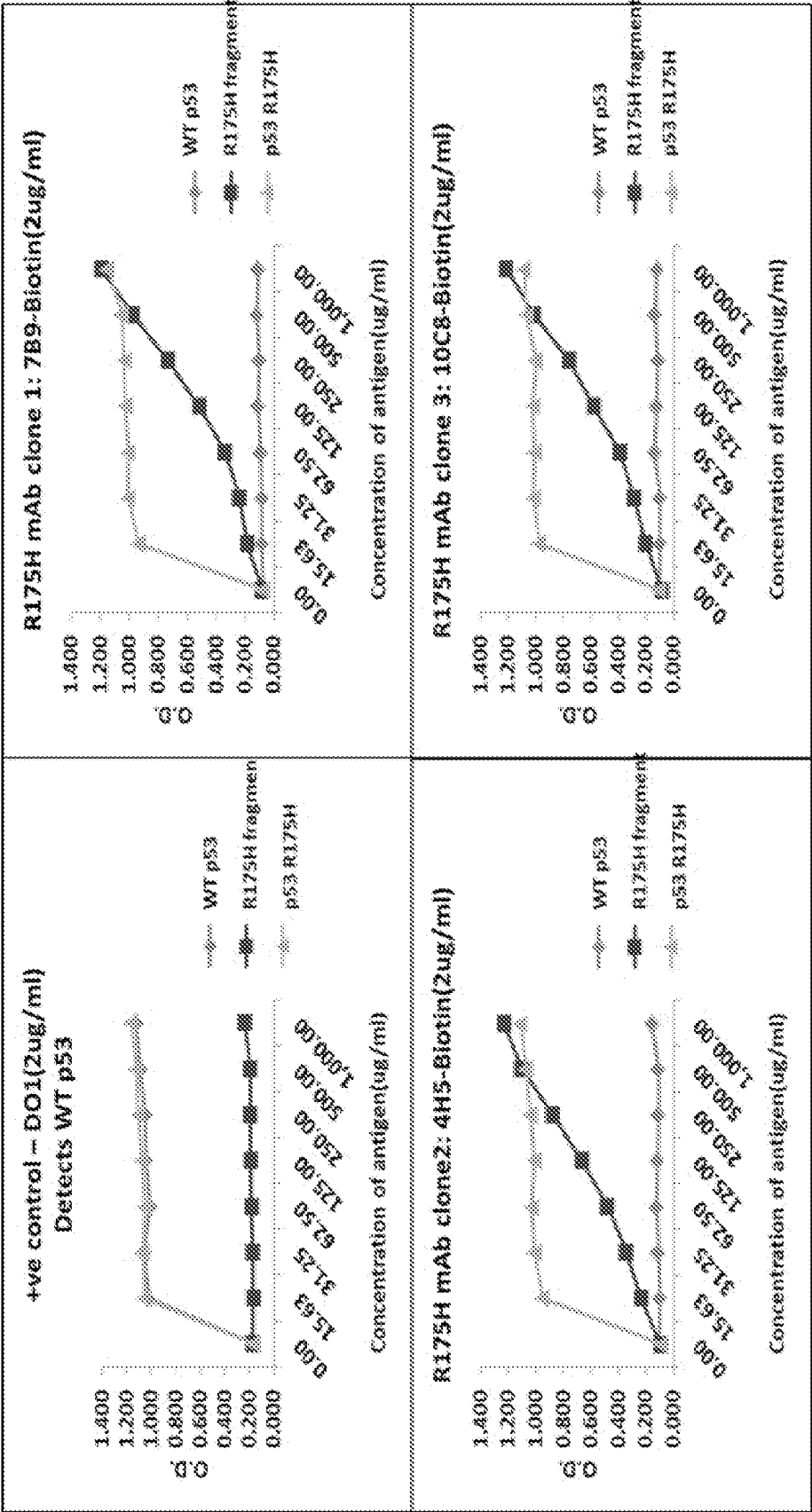


Figure 5A

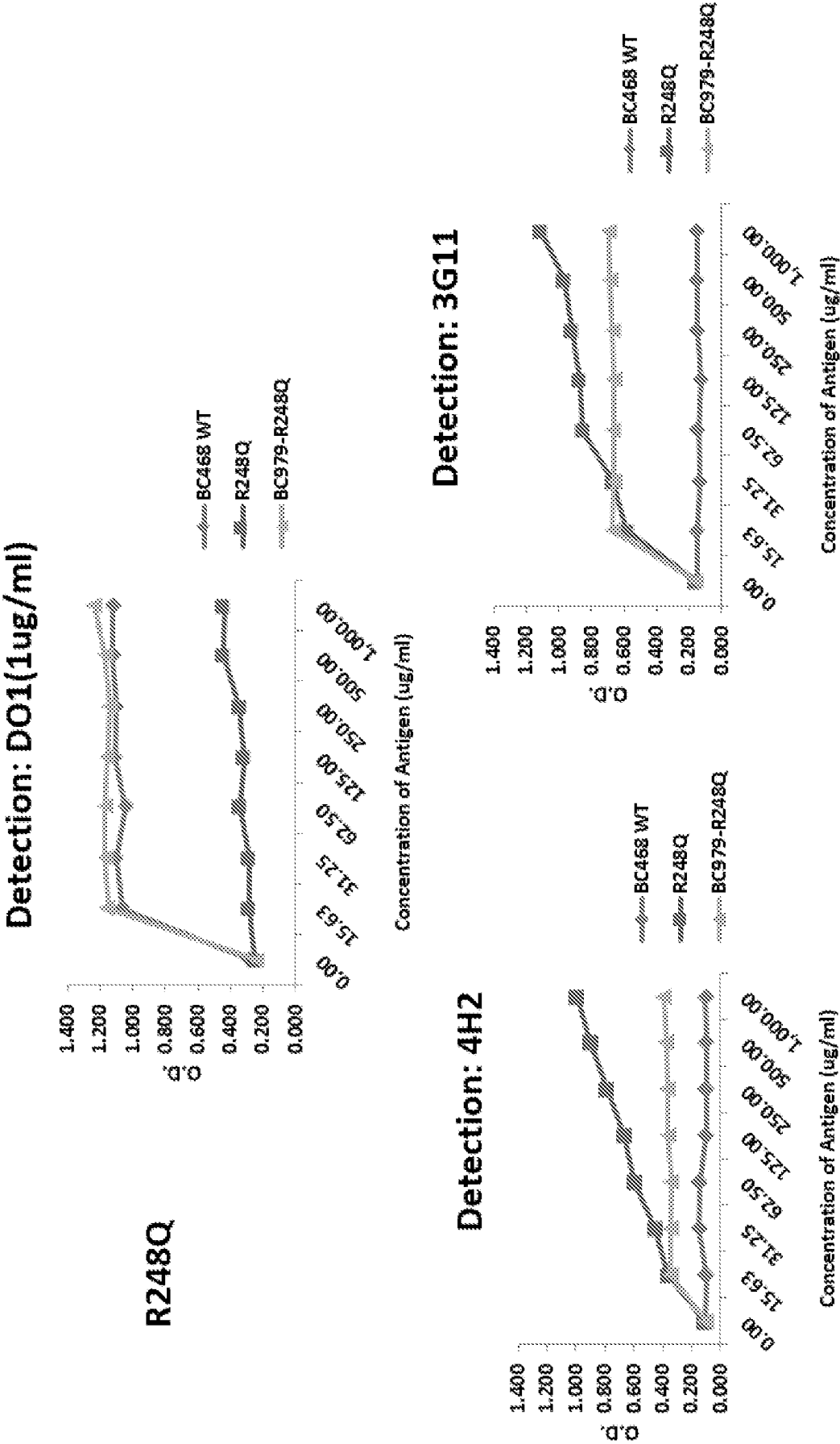
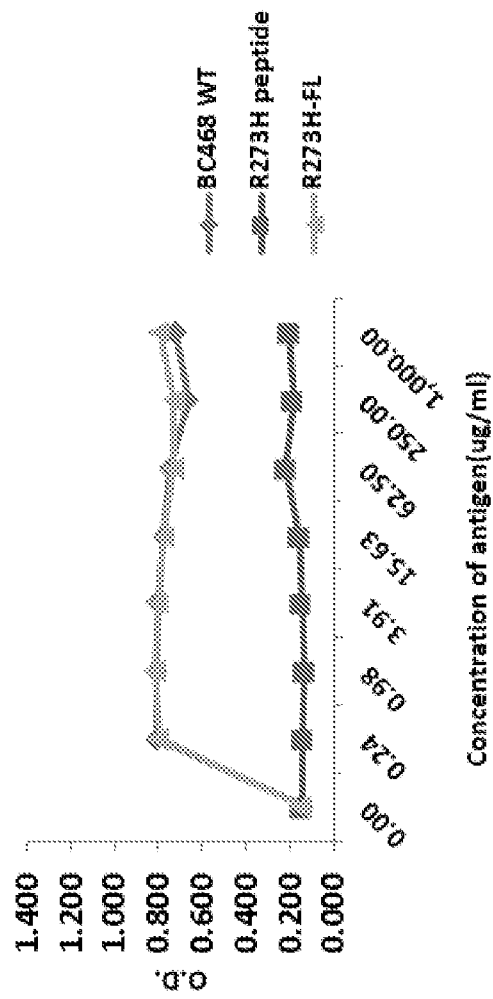


Figure 5B

R273H

Detection: DO1-Biotin(2ug/ml)



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

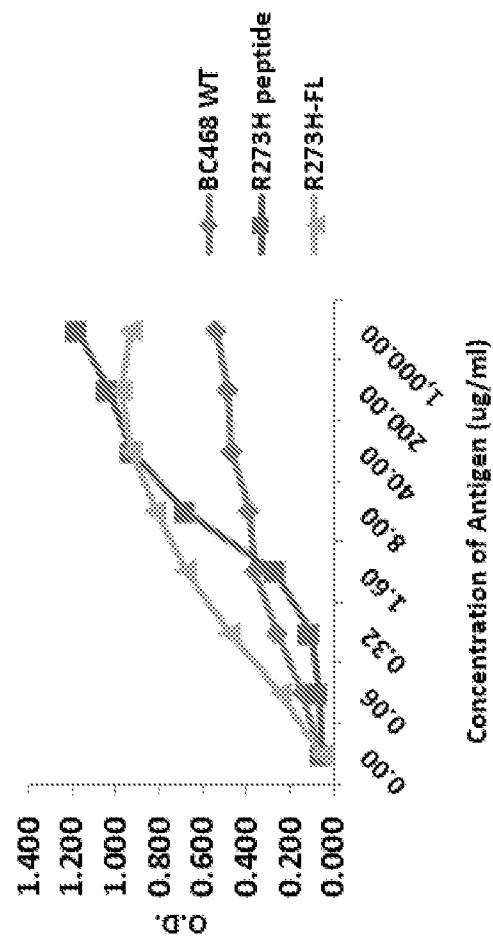


Figure 5C

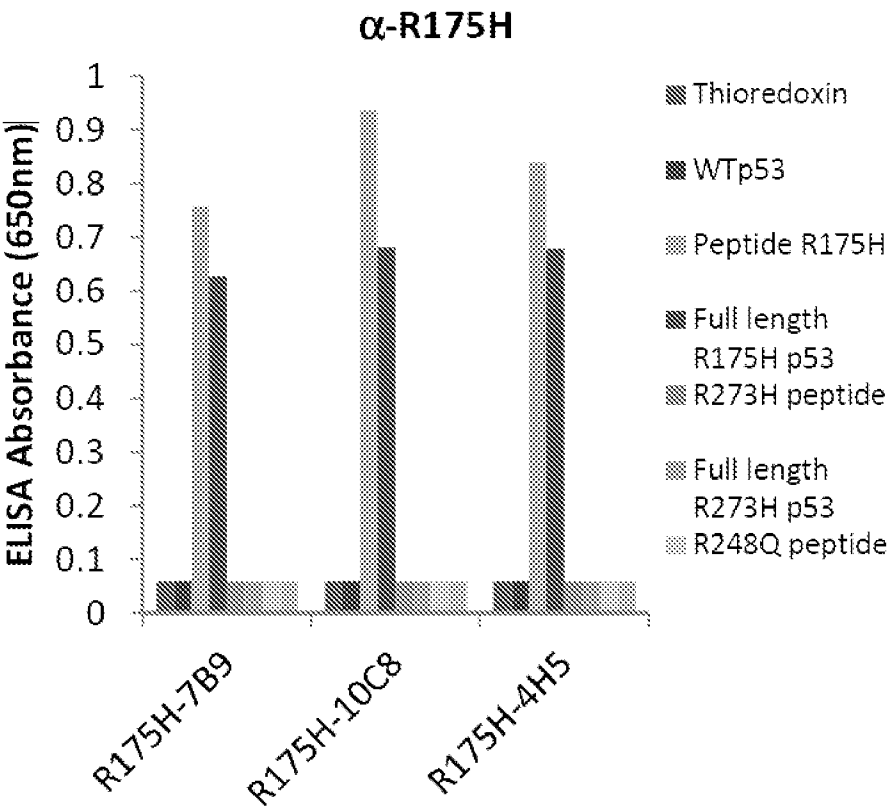


Figure 6A

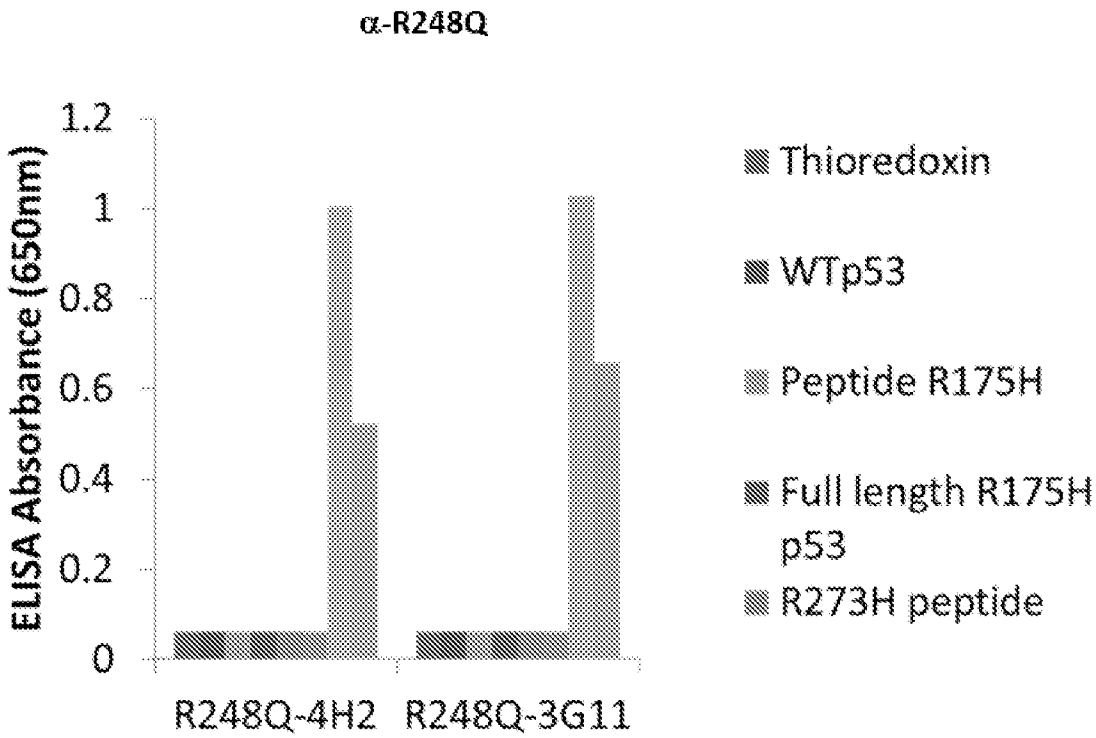


Figure 6B

12/95

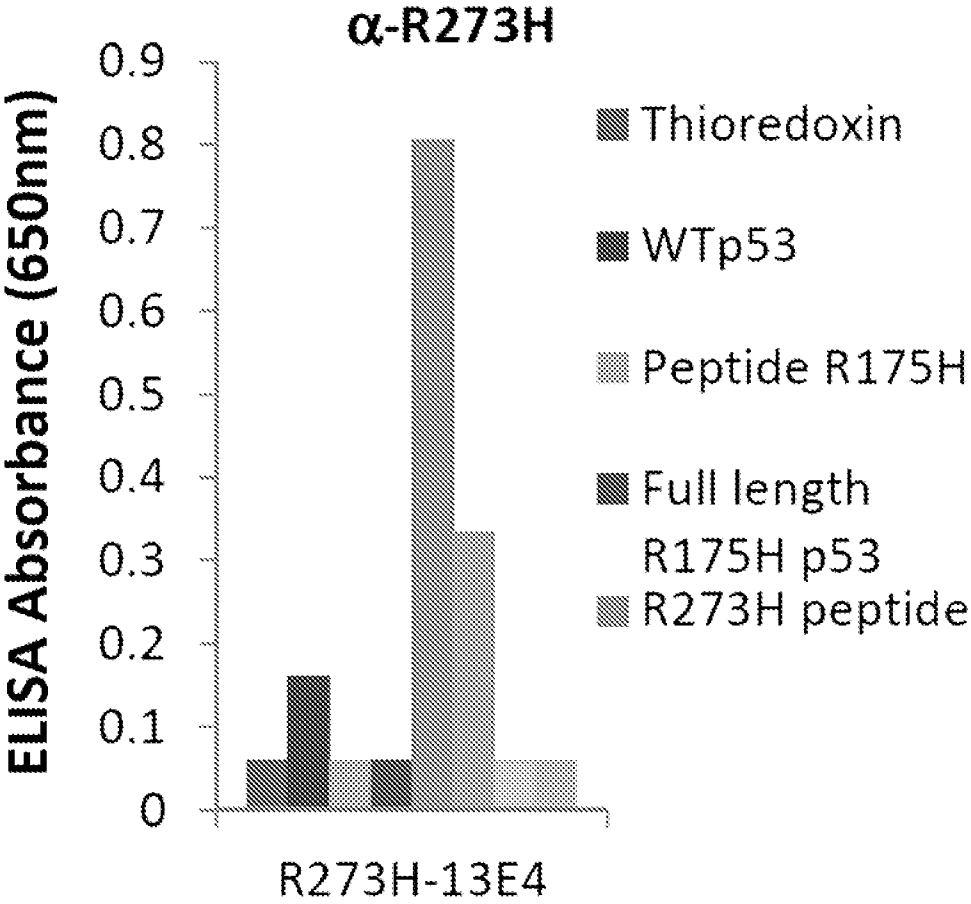


Figure 6C

Anti-R175H mAbs

10C8

WTp53	QHMTEVVRRCPHHERCSD
R175H	QHMTEVVRRHCPHHERCSD
6	---GGVLHLPHHTRN--
3	----ADNHEPHPLACD-
4	-----T-RHQPHHSLPPR
8	-----T-PHQPHHSFTPR
7	---VSTGVHYPHHSA-----
2	---VDMHHYPHHYKD---
5	-----ILASHRPHHYGY-
1	---LCTPLLHPHHHL---

Consensus: **167QHMTEVVRRHCPHHERCSD184**

10C8, 7B9, 4H5 epitope

Figure 7A

Anti-R248Q mAbs

4H2

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

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

Figure 7B

Anti-R273H mAb

13E4

WTp53	----GRNSFEVRVCAC-----
R273H	----GRNSFEVHVCAC-----
4	----GK-TYSYHMQLYT-----
3	-----YHVGGILGRLFM-----
5	-----YNTFPYHLGYTL-----
2	---DNASSKVVHGH-----
1	-----TFVHGNWTIVN-----
6	---TNTMHAHVHPL-----

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

Figure 7C

Anti-R175H mAbs

7B9		4H5	
WTp53	QHMTEVRRCPHHERCSD	WTp53	QHMTEVRRCPHHERCSD
R175H	QHMTEVVRHCPHHERCSD	R175H	QHMTEVVRHCPHHERCSD
4	----YNQTHHPHHQEY--	8	---VGSPQHWPHHSN---
9	---GAPEVHHPAHQQA---	9	---VGSPQHWPHHCN---
7	----KTLS-HAPHHHSKE--	2	---VGSPQHWPHHSN---
8	----HSPV-HTPHGSGK--	7	---VGSPQHWPHHSN---
5	-----TPHQPHHSFTPR	1	---VGSPQHWPHHSK---
6	---DSHFLHYPHHSN----	3	---LEVN-HWGHHYRT-
2	-----ESTGHSPPHQHN---	5	---GGSG-HQSGHRP----
3	-----STPVHTPPHHAHY--	6	----SLG-HKSHHFIAA----
1	----SGSLQHRPPHPRN----	10	---FDLRDYMHPHH-----
Consensus: 167 QHMTEVVRHCPHHERCSD 184			

10C8, 7B9, 4H5 epitope

Figure 8A

Anti-R248Q mAbs

3G11

WTp53	GMNRRPILTIITLED S
R248Q	GMNQRPILTIITLED S
1	----- SSTHYSW SLMDA
2	----- GPSCHYCFTGLP----
3	----- GPSCHYCFTGLP----
4	WSVPPGRHIHYS-----
5	WSVPPGRHIHYS-----
10	----- FSVPSG HYIRAN-----
8	----- FSVRPFHYAQDN-----
7	----- FSVPDFRIQETP-----
9	----- FSVRPYDPQIEN-----
6	----- HSVWYAN GSVKT -----

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

Figure 8B

159 M	T	E	V	V	R	H	C	P	H	H	E	181R
A	-	-	-	-	-	-	-	-	-	-	-	-
-	A	-	-	-	-	-	-	-	-	-	-	-
-	-	A	-	-	-	-	-	-	-	-	-	-
-	-	-	A	-	-	-	-	-	-	-	-	-
-	-	-	-	A	-	-	-	-	-	-	-	-
-	-	-	-	-	A	-	-	-	-	-	-	-
-	-	-	-	-	-	A	-	-	-	-	-	-
-	-	-	-	-	-	-	A	-	-	-	-	-
-	-	-	-	-	-	-	-	A	-	-	-	-
-	-	-	-	-	-	-	-	-	A	-	-	-
-	-	-	-	-	-	-	-	-	-	A	-	-
-	-	-	-	-	-	-	-	-	-	-	A	-

Binding motif MT--VRH--HHER

Figure 9A

7B9 Alanine Scan on R175H

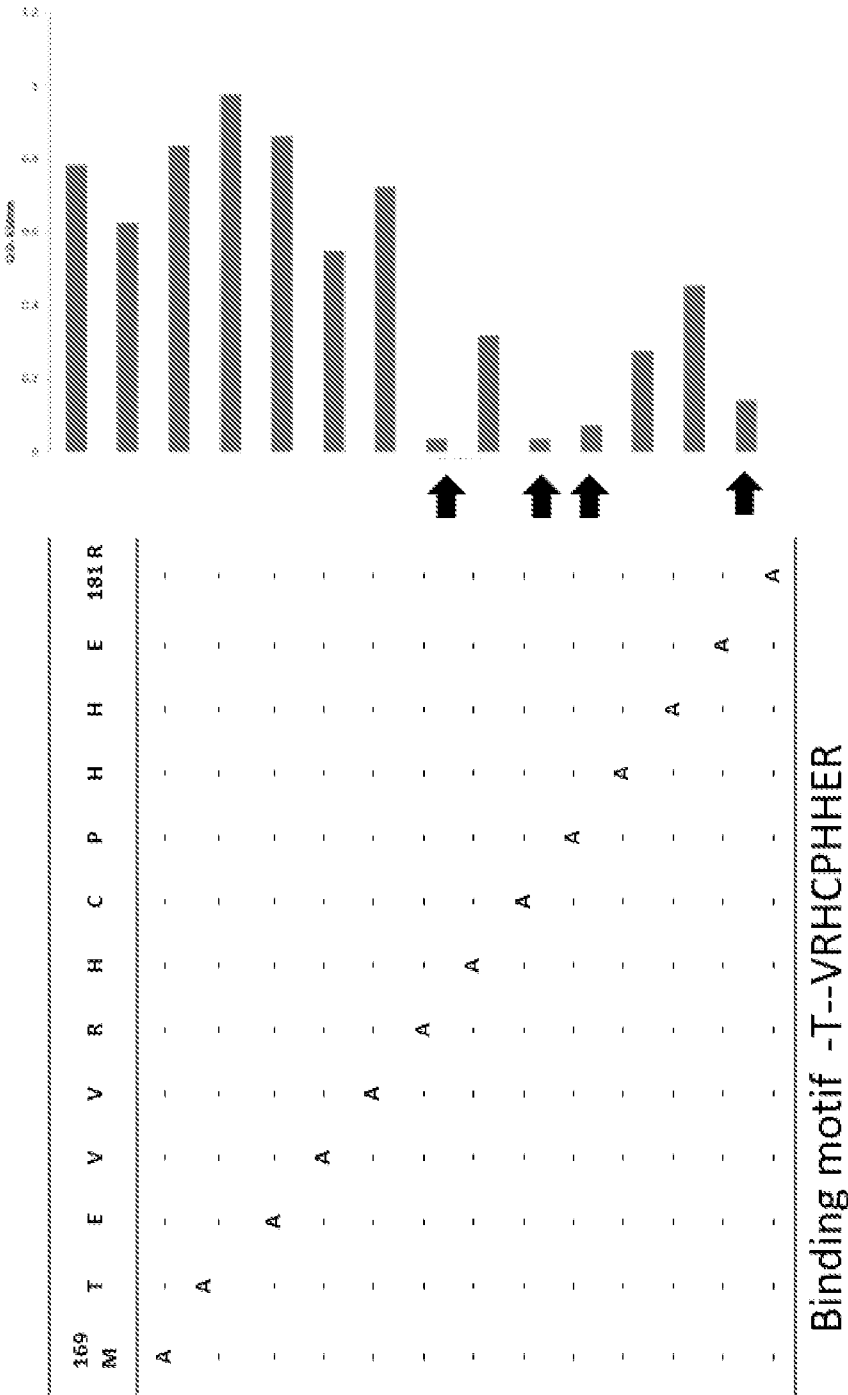


Figure 9B

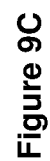


Figure 9C

13E4 Alanine Scan on R273H

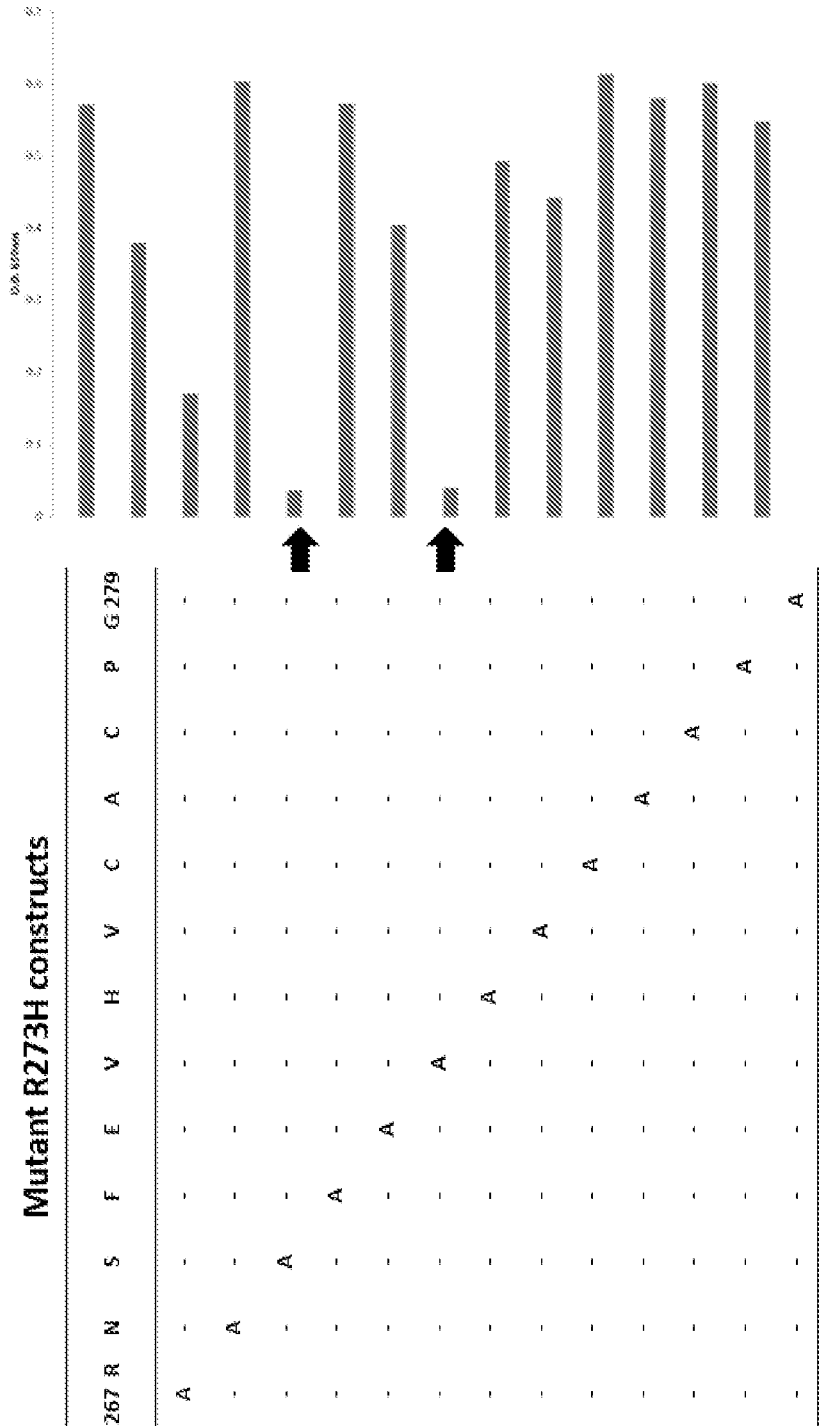


Figure 9D

MEE PQSDPSV EPPLSQETFS DLWKLLPENN VLSPLPSQAM DDLMILSPDDI EQWFTEDPGP DEAPRMPEAA PPVAPAPAAP TPAAPAPAPS WPLSSSVPSQ 100
KTYQGSYGR LGFLHSGTAK SVTCTYSPAL NKMECOLAKT CPVQLWVDST PPPGTRVRAM AYNKQSQHMT EVVR**R175H**RCSDSDGLAP PQHLIRVEGN 200
LRVEYLDNRN TFRHSVVVPPY EPPEVGSDCT TIHYNMYMCNS SCMGGMNQRP ILTITLED SGNLLGRNSF EV**R273H**VCACPGR DRRTEENLR KKGEPHHELP 300
PGSTKRALPN NTSSSPQPKK KPLDGEYFTL QIRGRERFEM FRELNEALEL KDAQAGKEPG GSRAHSSHILK SKKGOSTSRH KKLMEFKTEGP DSD 393

Figure 10

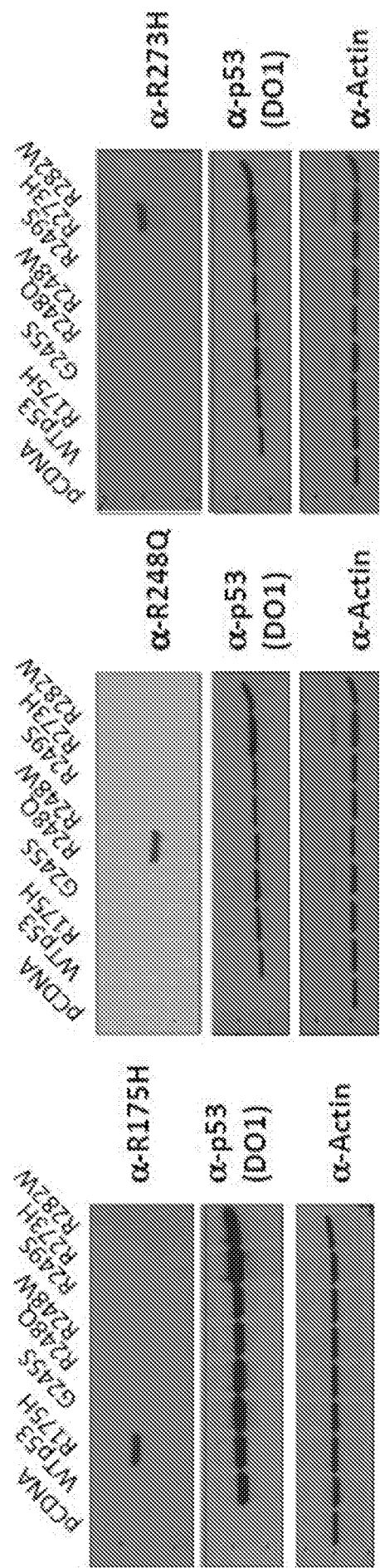


Figure 11

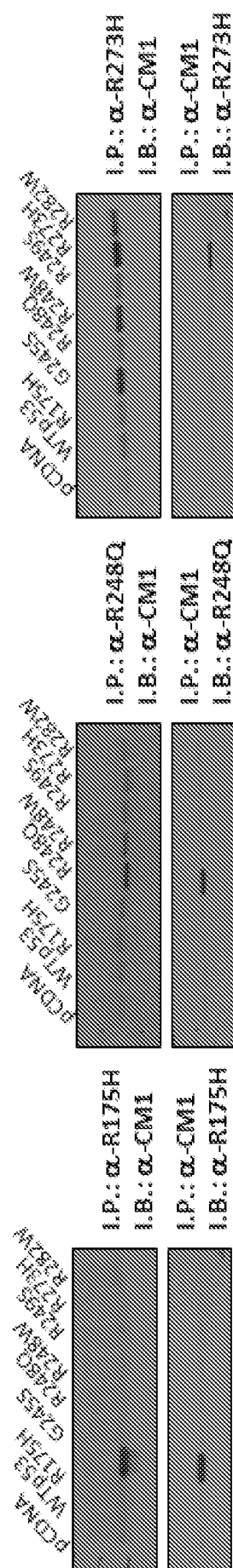


Figure 12

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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

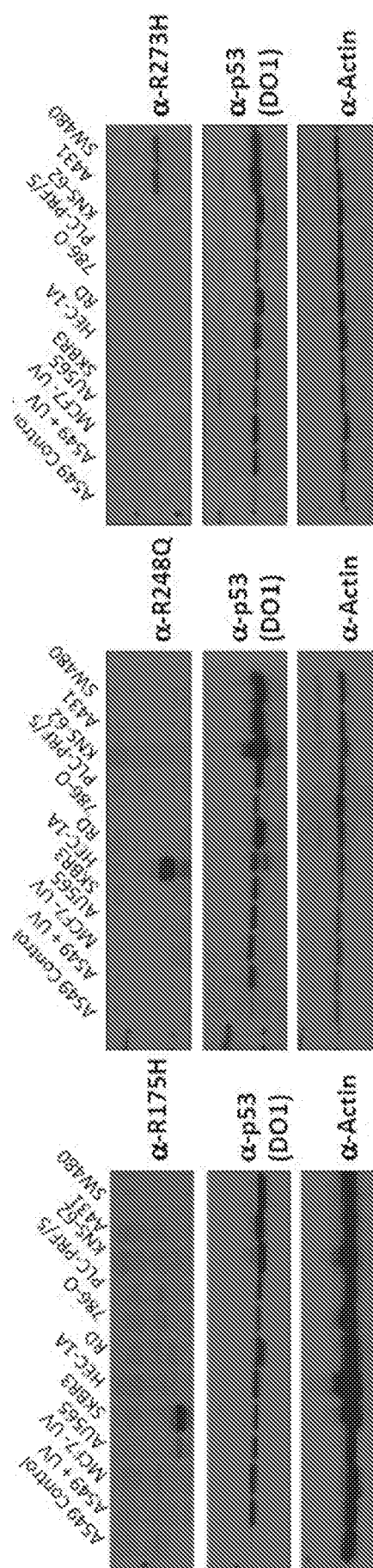


Figure 14

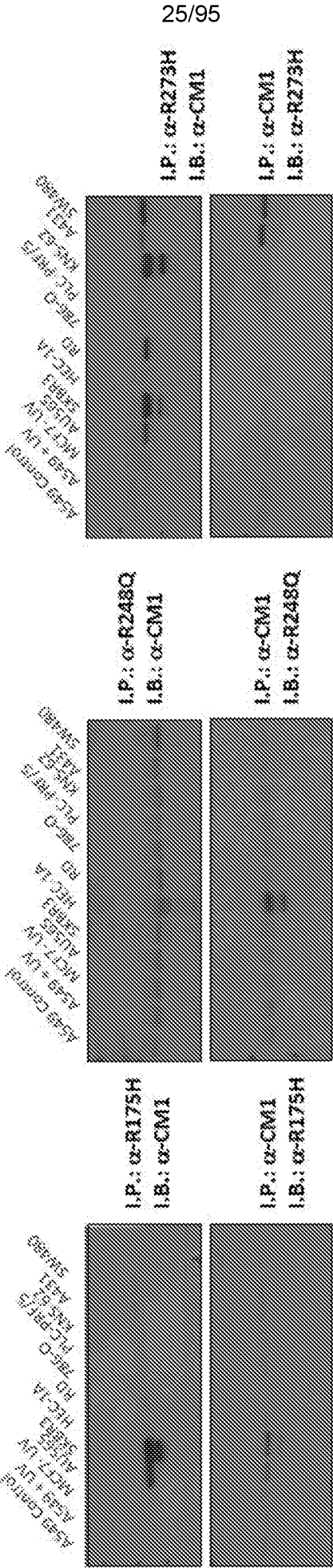


Figure 15

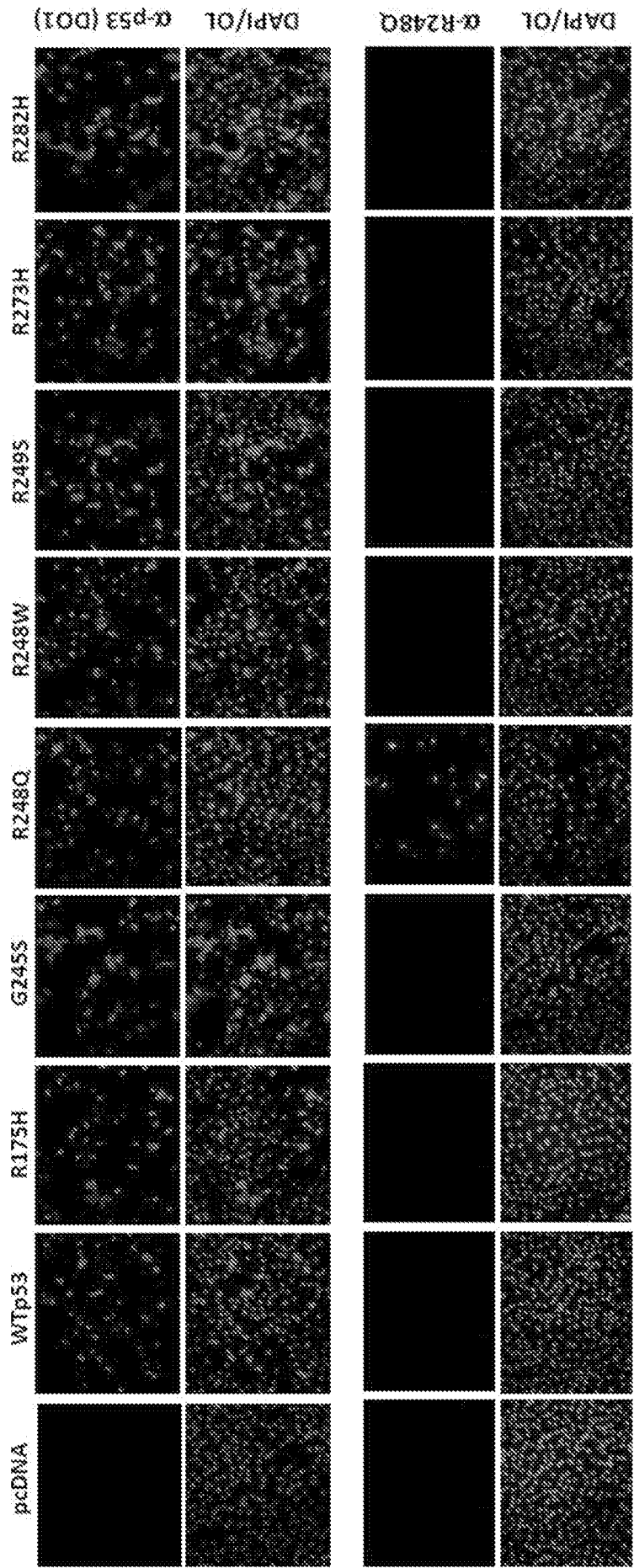


Figure 16

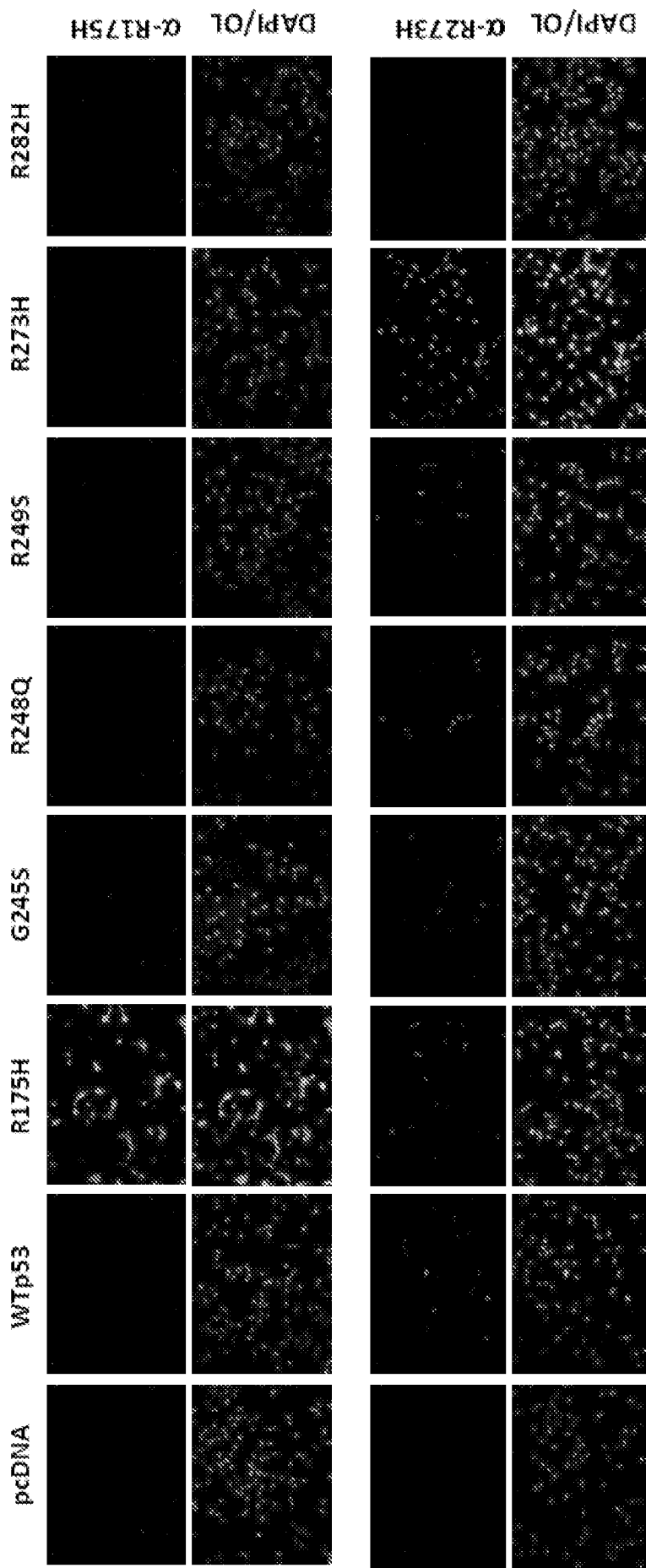


Figure 16 (cont.)

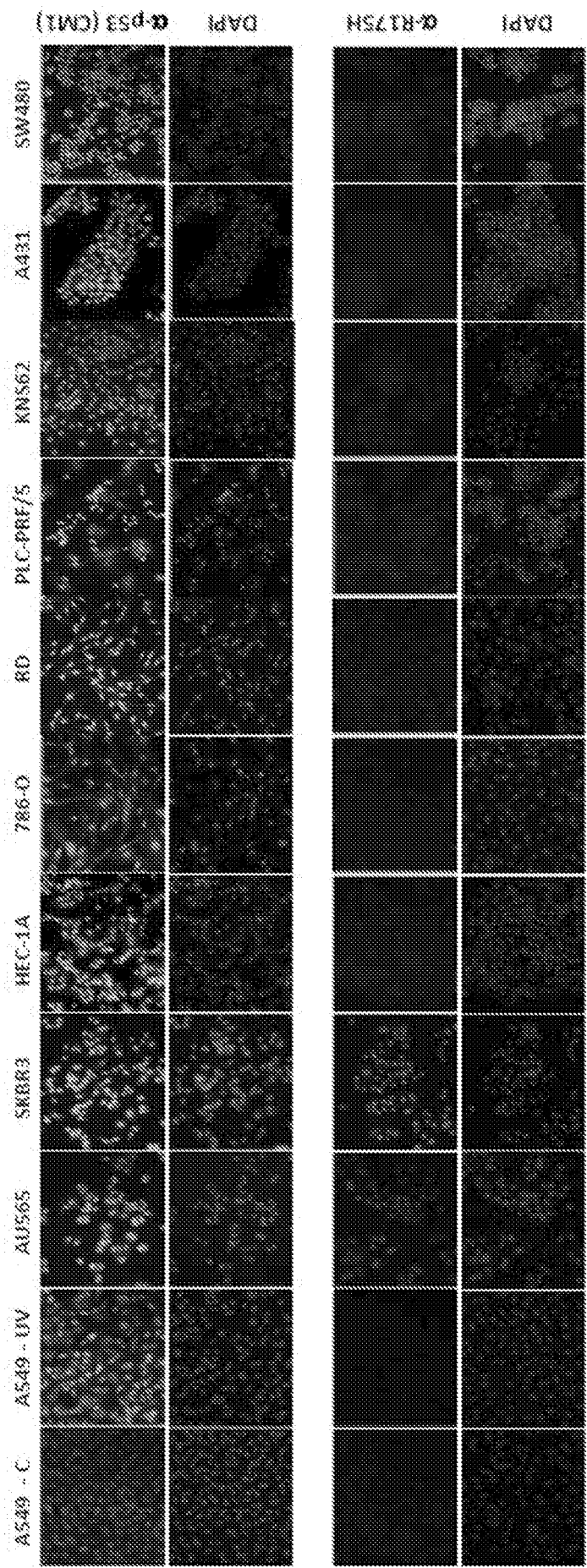


Figure 17A

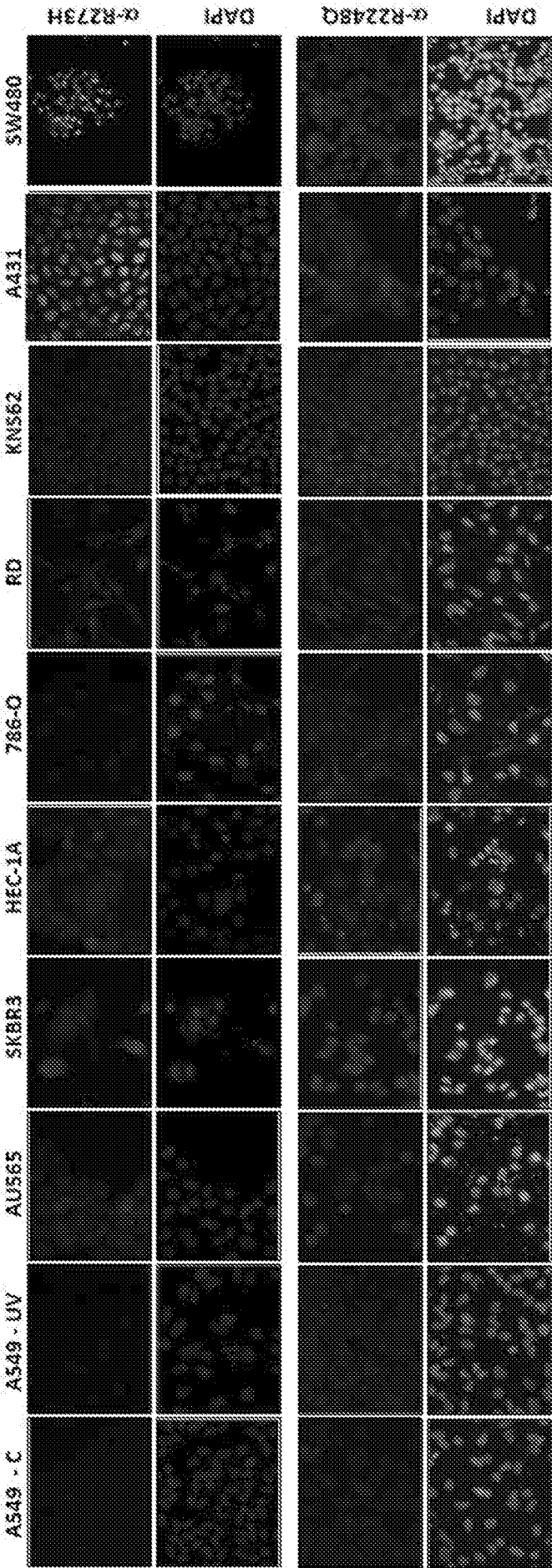


Figure 17A (cont.)

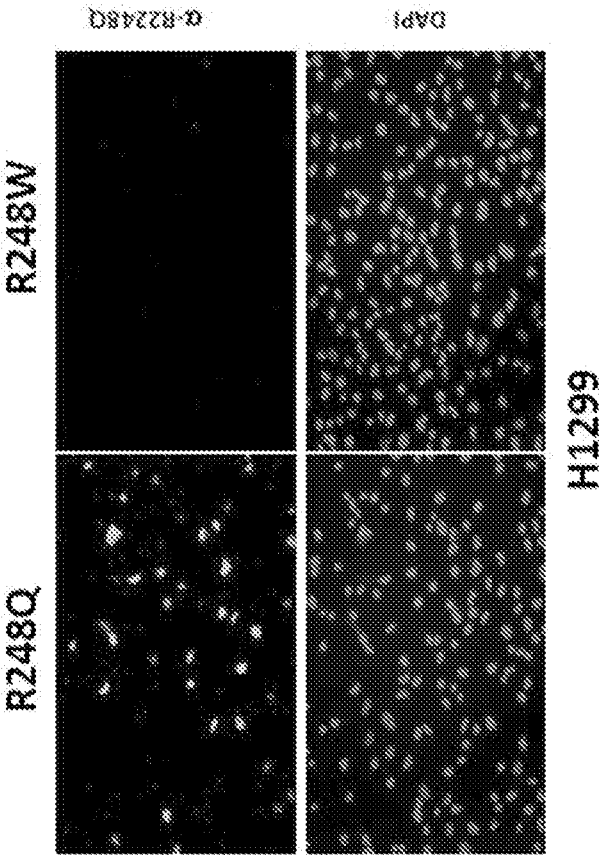


Figure 17B

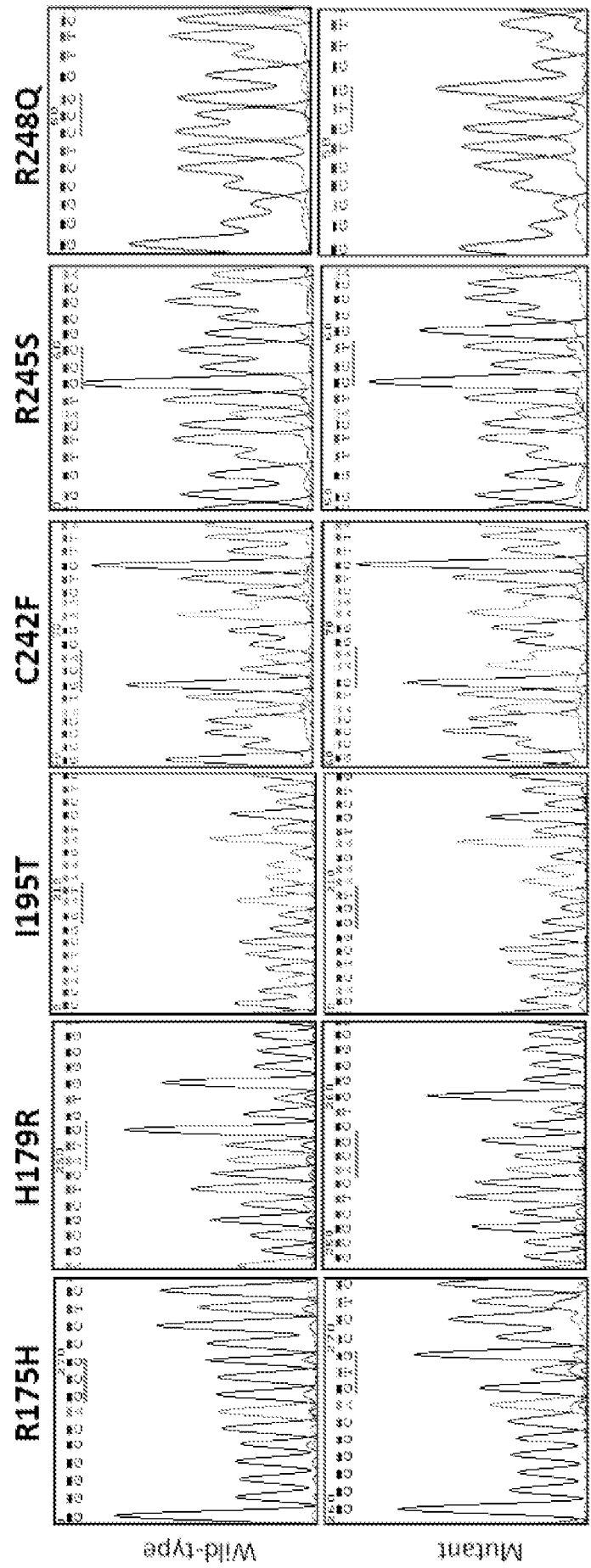


Figure 18A

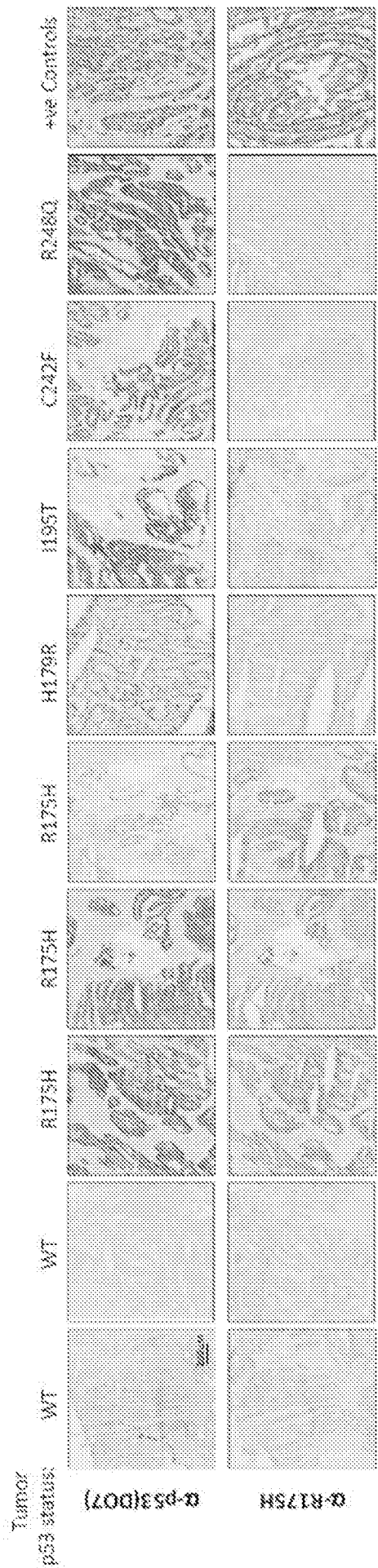


Figure 18B

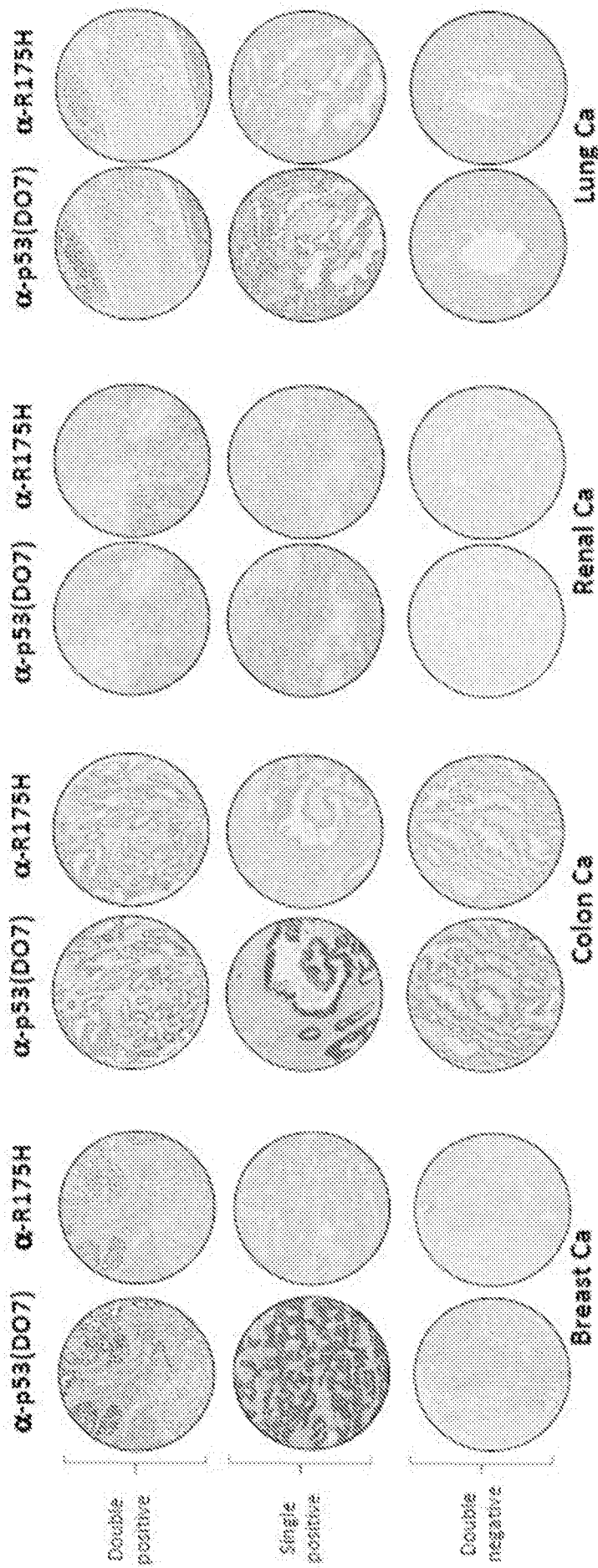


Figure 19

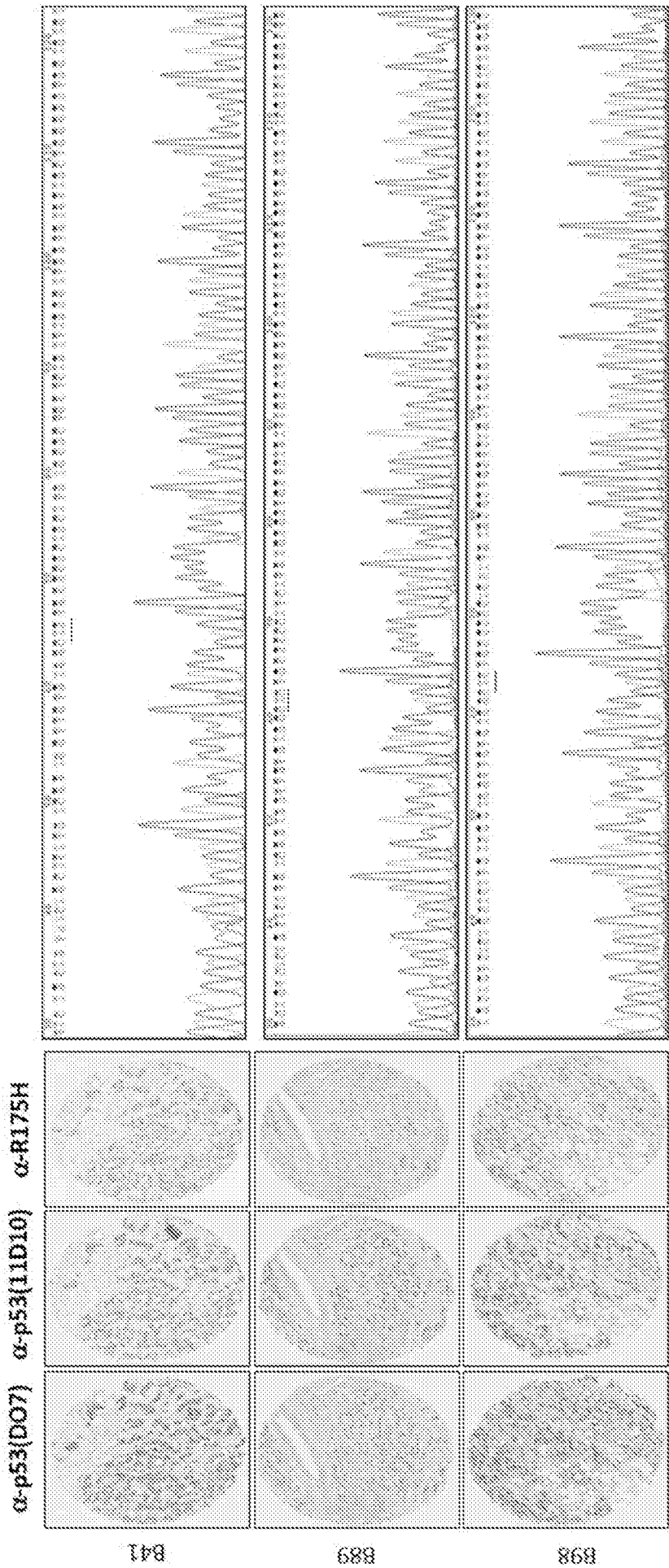


Figure 20A

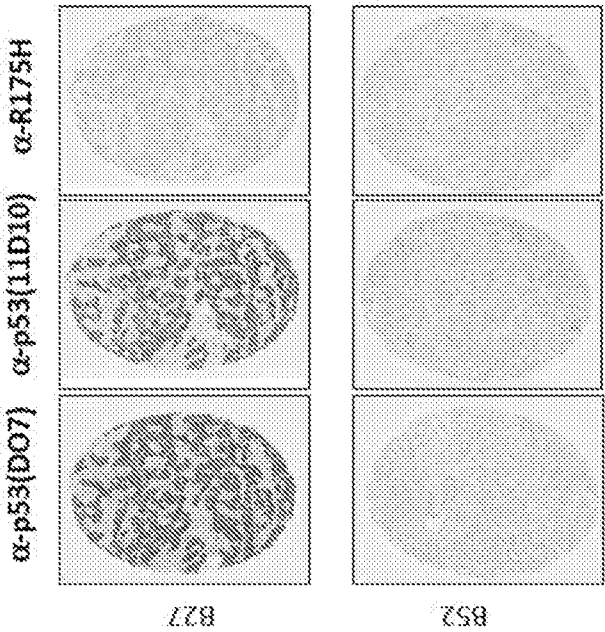


Figure 20B

Combined data from analysis of human tumor microarrays by immunohistochemistry

TMA's *	Total samples = n	α-pan- p53 ⁺ (D07) 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		
	↓	
IP53_HUMAN	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	226
IP53_CERAE	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYSDNRNTFRHSVVVPYEPPEVG	226
IP53_MACMU	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYSDNRNTFRHSVVVPYEPPEVG	226
IP53_MACFU	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYSDNRNTFRHSVVVPYEPPEVG	226
IP53_MACFA	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYSDNRNTFRHSVVVPYEPPEVG	226
IP53_TUPGB	VTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYSDNRNTFRHSVVVPYEPPEVG	226
IP53_MARMO	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	224
IP53_RABIT	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	223
IP53_DELLE	MTEVVRRCPPHHERCSDYSDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	220
IP53_PIG	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	219
IP53_CANFA	VTEVVRRCPPHHERCSDSDG-LAPPQHLIRVEGNLRAKYLDNRNTFRHSVVVPYEPPEVG	214
IP53_FELCA	MTEVVRRCPPHHERCSDSDG-LAPPQHLIRVEGNLHAKYLDNRNTFRHSVVVPYEPPEVG	219
IP53_CAVPO	MTEVVRRCPPHHERCSD-SDG-LAPPQHLIRVEGNLRAEYVDDRNTFRHSVVVPYEPPEVG	224
IP53_SHEEP	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYFDDRNTFRHSVVVPYEPPEVG	215
IP53_MESAU	MTEVVRRCPPHHERSSE-GDG-LAPPQHLIRVEGNMHAELDDKQTFRHSVVVPYEPPEVG	229
IP53_CRIGR	MTEVVRRCPPHHERSSE-GDS-LAPPQHLIRVEGNLHAEYLDKQTFRHSVVVPYEPPEVG	226
IP53_BOVIN	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	219
IP53_BOSIN	MTEVVRRCPPHHERSSDYSDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	219
IP53_RAT	MTEVVRRCPPHHERCSD-GDG-LAPPQHLIRVEGNPYAEYLDNRQTFRHSVVVPYEPPEVG	224
IP53_MOUSE	MTEVVRRCPPHHERCSD-GDG-LAPPQHLIRVEGNLYPEYLEDNRQTFRHSVVVPYEPPEAG	220
IP53_HORSE	MTEVVRRCPPHHERCSDSDG-LAPPQHLIRVEGNLRAEYLDNRNTFRHSVVVPYEPPEVG	177
IP53_EQUAS	MTEVVRRCPPHHERCSDSDG-LAPPQHLIRVEGNLRAEYLDNRNTLRHSVVVPYEPPEVG	102
IP53_CHICK	VAEVVRRCPPHHERCGGTDG-LAPAQHLIRVEGNPQARYHDDETTFRHSVVVPYEPPEVG	212
IP53_XENLA	VAEVVRRCPPHHERSVPEGED-AAPPSHLMRVEGNLQAYYMEDVNSGRHSVCVPEGPPQVG	201
IP53_ONCMY	VADVVRRCPPHHQSTSENNEG-PAPRGHLVRVEGNQRSEYMEDGNTLRHSVLVPYEPPPQVG	215
IP53_DANRE	VAEVVRRCPPHHERTPDG-DN-LAPAGHLIRVEGNQRANREDNITLRHSVFPVPEAPQLG	194
IP53_ICTPU	VAEVVRRCPPHHERSNDSSDG-PAPPGHLLRVEGNSRAVYQEDGNTQAHSVVVPYEPPPQVG	202
IP53_XIPMA	VGEEVVRRCPPHHQ-SEDLSDN-KS---HLIRVEGSQAQYFEDPNTRRHSTVTPYERPQLG	189
IP53_XIPHE	VGEEVVRRCPPHHQ-SEDLSDN-KS---HLIRVEGSQAQYFEDPNTRRHSTVTPYERPQLG	189

Figure 22

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P53_HUMAN	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_CERAE	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MACMU	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MACFU	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MACFA	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_TUPGB	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_MARMO	SECTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	284
P53_RABIT	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	283
P53_DELLE	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	280
P53_PIG	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_CANFA	SDYTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNVLRNSFEVRVCACPGDRRTEE	274
P53_FELCA	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_CAVPO	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	284
P53_SHEEP	SECTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	275
P53_MESAU	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	289
P53_CRIGR	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	286
P53_BOVIN	SECTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_BOSIN	SECTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	279
P53_RAT	SDYTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	284
P53_MOUSE	SEYTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	280
P53_HORSE	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	237
P53_EQUAS	SDCTTIHYNMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	162
P53_CHICK	SDCTTVLYNFMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	272
P53_XENLA	TECTTVLYNFMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	261
P53_ONCMY	SECTTVLYNFMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	275
P53_DANRE	AEWTTVLLNFMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	254
P53_ICTPU	SQSTTVLYNFMNCSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	262
P53_XIPMA	SEMTTILLSFMCNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	249
P53_XIPHE	SEMTTILLSFMCNCSMGGMNRPPILTIITLEDSSGNLLGRNSFEVRVCACPGDRRTEE	249

Figure 22 (cont.)

R248
↓

P53_HUMAN	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_CERAE	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MACMU	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MACFU	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MACFA	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_TUPGB	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_MARMO	SECTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	284
P53_RABIT	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	283
P53_DELLE	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	280
P53_PIG	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	279
P53_CANFA	SDYTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	274
P53_FELCA	SDCTT IHYNM CNSSCMGGMRRRPITITILEDSSGNLLGRNSFEVRVACPGDRRTEE	279
P53_CAVPO	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	284
P53_SHEEP	SECTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	275
P53_MESAU	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	289
P53_CRIGR	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	286
P53_BOVIN	SECTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	279
P53_BOSIN	SECTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	279
P53_RAT	SDYTT IHYKYM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	284
P53_MOUSE	SEYTT IHYKYM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	280
P53_HORSE	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	237
P53_EQUAS	SDCTT IHYNM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	162
P53_CHICK	SDCTTVLYNFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	272
P53_XENLA	TECTTVLYNFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	261
P53_ONCMY	SECTTVLYNFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	275
P53_DANRE	AEWTTVLLNFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	254
P53_ICTPU	SQSTTVLYNFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	262
P53_XIPMA	SEMTT ILLSFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	249
P53_XIPHE	SEMTT ILLSFM CNSSCMGGMRRRPILTIITLEDSSGNLLGRNSFEVRVACPGDRRTEE	249

Figure 22 (cont.)

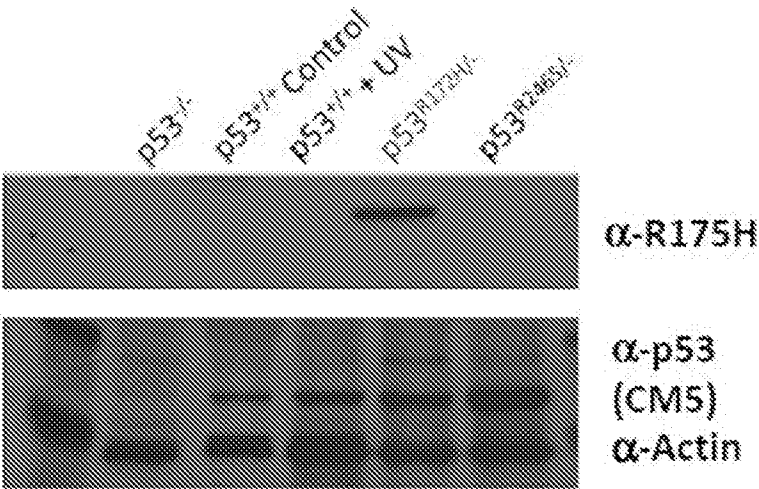


Figure 23A

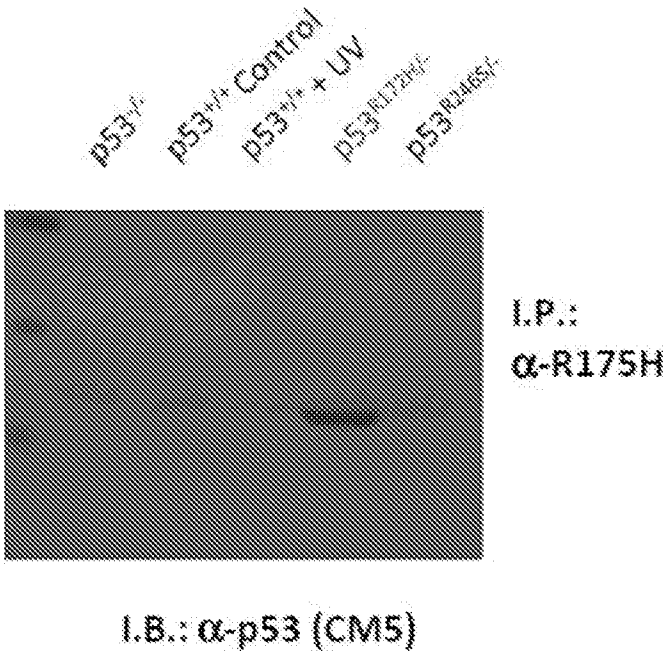


Figure 23B

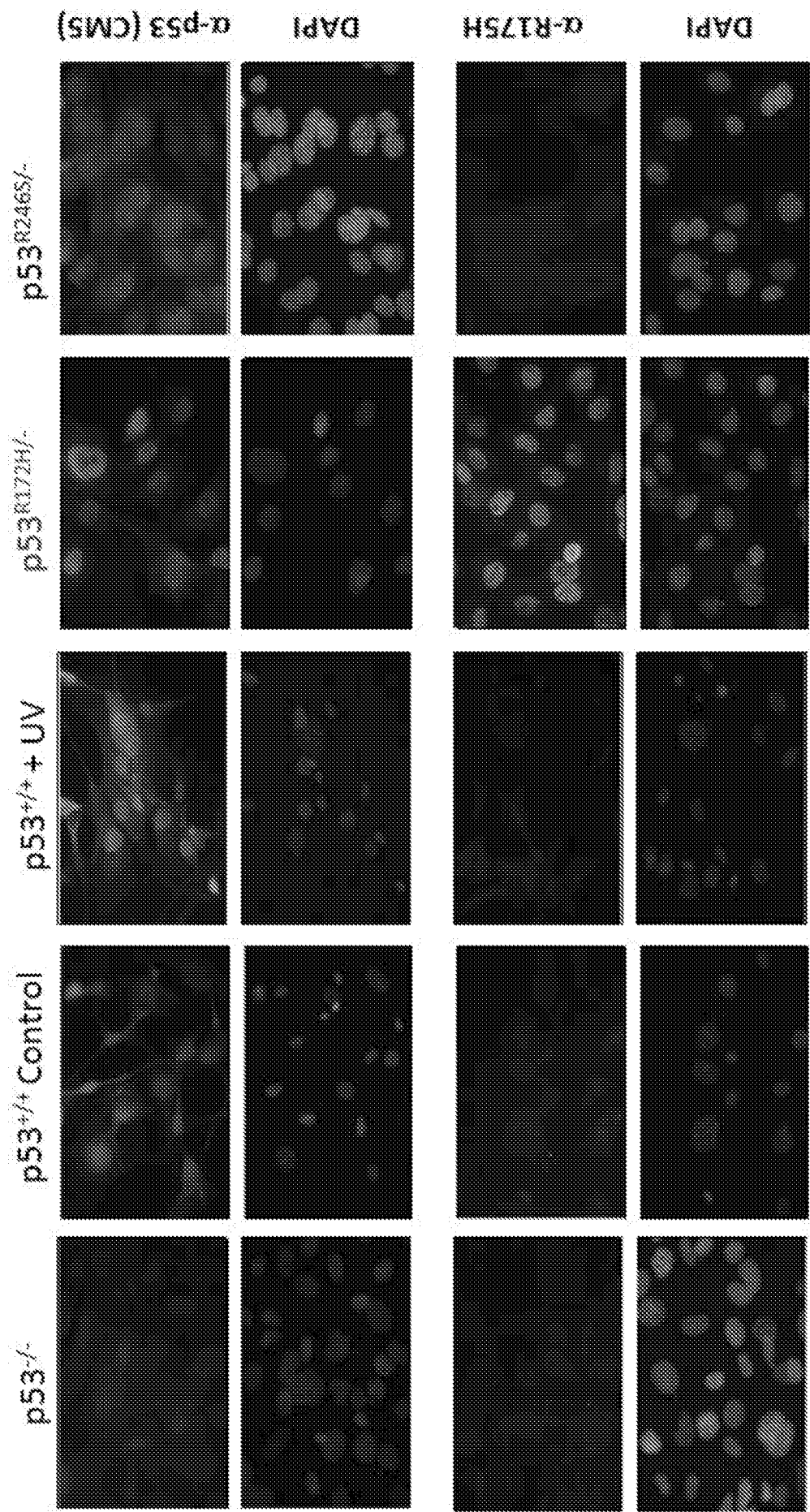


Figure 23C

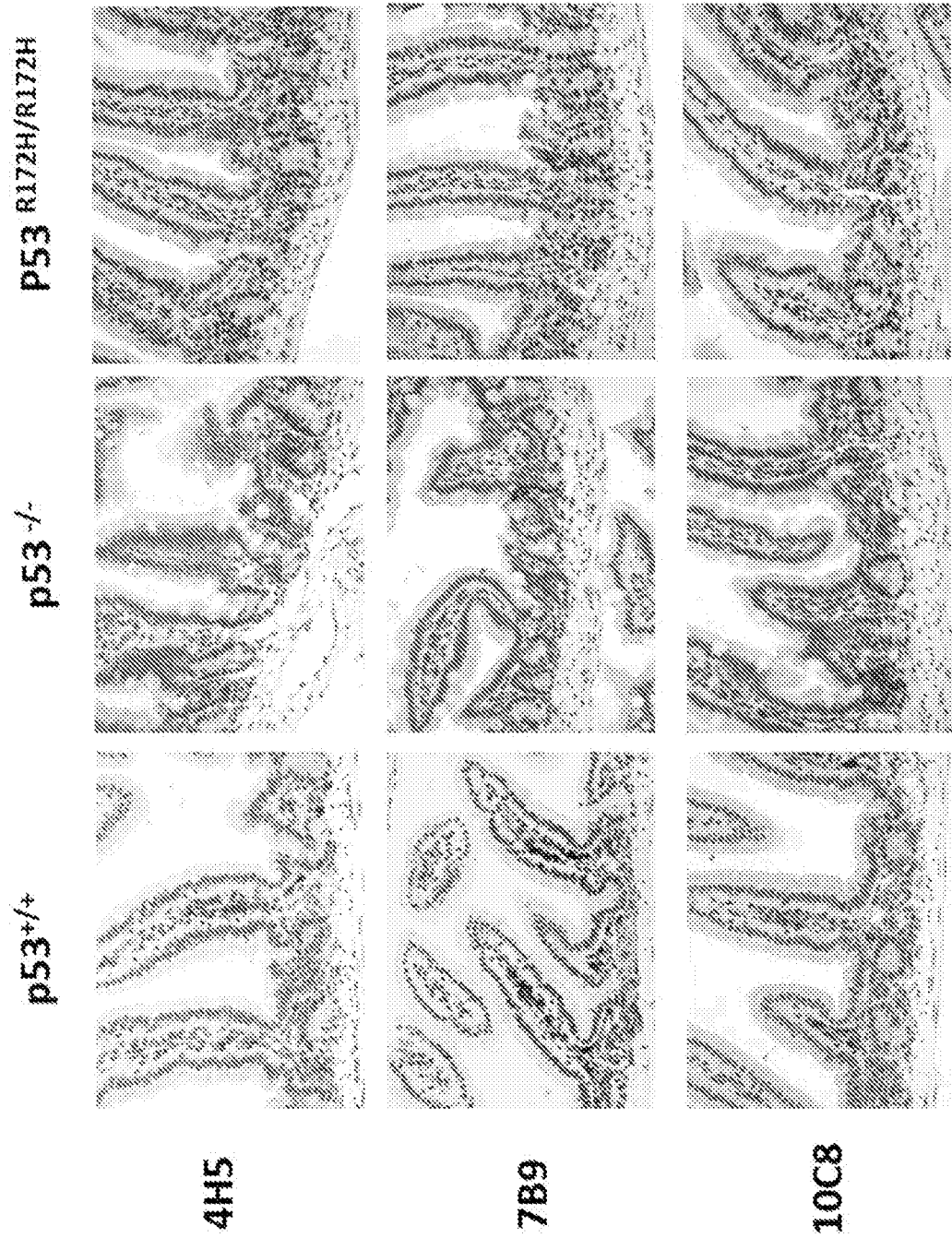


Figure 23D

Anti-R175H clone 4H5

DIVLTQSTSSLSVSAGERVTLSCCKSSQSLNSGNQKSYLAWYQQKPGQPPKLLIYGASTRE
SGVPDRFTGSGSETDFTLTISVQPEDLAVYYCQNDHSYPLTFGAGTKLELK (SEQ ID
NO:18)

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

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

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

Anti-R175H clone 7B9

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGTKLELK (SEQ ID
NO:22)

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

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

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

Anti-R175H clone 10C8

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGTKLELK (SEQ ID
NO:22)

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

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

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

Figure 24

Anti-R175H clone 4H5

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVTIVY
NQKFKVKATLTVDRSSSTAYLELRSLTSEDSAVYYCARWGGDYVTGGGTTLTVSS (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

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTIVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDDSAVYYCARWGGDYVTGGGTTLTVSS (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

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTIVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDDSAVYYCARWGGDYVTGGGTTLTVSS (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

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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
SGVPDRFTGSGSETDFTLTISSVQPEDLAVYYCQNDHSYPLTFGAGTKLELK [SEQ ID
NO:18]

>4H5_ntd_L

GATATTGTGCTCACCCAATCTACATCCTCCCTGAGTGTGTCAGCTGGAGAGAGGGTCA
CTTTGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAAATCAAAGAGTTACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAACTGTTGATCTACGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGGATCTGAAACCGATTTTAC
TCTTACCATCAGCAGTGTGCAGCCTGAAGACCTGGCAGTTTATTATTGTCAGAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 34]

Anti-R175H clone 7B9

>7B9_aa_L

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISSVQAEDLAVYYCQNDHSYPLTFGGGKLELK [SEQ ID
NO:22]

>7B9_ntd_L

GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAAATCAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTTAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 35]

Anti-R175H clone 10C8

>10C8_aa_L

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISSVQAEDLAVYYCQNDHSYPLTFGGGKLELK [SEQ ID
NO: 22]

>10C8_ntd_L

GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAAATCAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTTAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 36]

Figure 27

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

>4H5_aa_H

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVTIVY
NQKFKVKATLTVDRSSSTAYLELRLSLTSEDSAVYYCCARWGGDYVTGGGTTLTVSS [SEQ
ID NO: 24]

>4H5_ntd_H

GAGGTTCAGCTGCAGCAGTCTGGACCTGAACTGGTGAAGCCTGGGGCTTCAGTGAAGA
TATCTTGCAAGACTTCCGGATTCACATTCAGTGAATACACCATGCACTGGATGAAACAG
AGCCATGGAAGGAGCCTTGAGTGGATCGGACGTATTGATCCTAACAAATGGTGTTACTGT
TTATAACCAGAAGTTCAAGGTCAAGGCCACATTGACTGTGGACAGGTCCTCCAGCACA
GCCTATCTGGAGCTCCGCAGTCTGACGTCTGAGGACTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTCACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO: 37]**Anti-R175H clone 7B9**

>7B9_aa_H

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTIVY
NQKFKGKATLTVDKSSSTAYMELRLSLTSDDSAVYYCCARWGGDYVTGGGTTLTVSS [SEQ
ID NO: 28]

>7B9_ntd_H

GAGGTCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATATCCTGCAAGACTTCTGGCTACACTTTCACTGAATACACCATGCACTGGATGAAGCA
GAGCCATGGAAGAGAGCCTTGAGTGGATTGGACGTATTAATCCTTATAGTGGTGGTACTG
TCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACTGTGGACAAGTCCTCCAGCAC
AGCCTATATGGAGCTCCGCAGCCTGACATCTGATGATTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTCACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO: 38]**Anti-R175H clone 10C8**

>10C8_aa_H

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTIVY
NQKFKGKATLTVDKSSSTAYMELRLSLTSDDSAVYYCCARWGGDYVTGGGTTLTVSS [SEQ
ID NO: 28]

>10C8_ntd_H

GAGGTGCAGCTTCAGCAGTCGGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATATCCTGCAAGACTTCTGGCTACACTTTCACTGAATACACCATGCACTGGATGAAGCA
GAGCCATGGAAGAGAGCCTTGAGTGGATTGGACGTATTAATCCTTATAGTGGTGGTACTG
TCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACTGTGGACAAGTCCTCCAGCAC
AGCCTATATGGAGCTCCGCAGCCTGACATCTGATGATTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTCACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO: 39]**Figure 27 (cont.)**

Anti-R248Q clone 3G11

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVSKLDSGV
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

DIVITQSPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVSELDSGV
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

DVQLQQSGPELVKPGASVKMSCKASGYTFTDYYVKWVKQSPGQSLEWIGDIHPKNGGTN
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAKMGGYDDYWGGGTTTLTVSS
(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

QVQLKQSGPELVKPGASVKMSCKASGYTFTDYYLKWVRQSHGKSLEWIGDIDPKNGGTNY
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAKQGGFDDYWGGGTTTLTVSS (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

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

>3G11_aa_L

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVS KLDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:40]

>3G11_ntd_L

GATATTGTGCTGACACAGACTCCACTCACTTTGTGCGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAAATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GTTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTAAACTGG
ACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTCACTGAA
AATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACATT
TTCCTCTCACGTTCCGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 54]**Anti-R248Q clone 4H2**

>4H2_aa_L

DIVITQSPPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVS ELDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:44]

>4H2_ntd_L

GACATTGTGATCACACAGTCTCCACTCACTTTGTGCGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAGATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GCTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTGAACTG
GACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTCACTGAA
AAATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACAT
TTTCCTCTCACGTTCCGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 55]**Figure 31**

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

>3G11_aa_H

DVQLQQSGPELVKPGASVKMSCKASGYTFTDYYVKWVKQSPGQSLEWIGDIHPKNGGTN
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAKMGGYDDYWGGTTLTVSS
[SEQ ID NO:45]

>3G11_ntd_H

GATGTGCAGCTTCAGCAGTCAGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGA
TGTCTGTGAAGGCTTCTGGATACACATTCAGTACTACTATGTGAAGTGGGTGAAGCAG
AGTCCTGGACAGAGCCTTGAGTGGATTGGAGATATTCATCCTAAGAACGGTGGTACTAA
CTACAACCAGAAAGTTCAAGGGCAAGGCCGCATTGACTGTGGACAAATCCTCCAGCACA
GCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTTCTGTGCAAA
AATGGGAGGCTACGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[SEQ ID NO: 56]

Anti-R248Q clone 4H2

>4H2_aa_H

QVQLKQSGPELVKPGASVKMSCKASGYTFTDYYLKWVRQSHGKSLEWIGDIDPKNGGTNY
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAKQGGFDDYWGGTTLTVSS [SEQ
ID NO:49]

>4H2_ntd_H

CAGGTGCAGCTGAAGCAGTCAGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAG
ATGTCCTGTGAAGGCTTCTGGATACACATTCAGTACTACTATCTGAAGTGGGTGAGGCA
GAGTCATGGAAAGAGCCTTGAGTGGATTGGAGATATAGATCCCAAGAATGGTGGTACT
AATTACAACCAGAAAGTTTAAAGGGCAAGGCCACATTGACTGTGGACAAATCCTCCAGCAC
AGCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAA
AACAGGGGGGGTTCGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[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
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYYCVRDGNDGKFLGYWGQGTFVTVTV
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

DIVMTQSPLSLPVNLGDQVSLSCRSSQSIVHNNGDTYLEWYLQKPGQSPKLLIYK^{VS}NRFS
GVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHLPLTFGSGTKLELK [SEQ ID NO:58]

>13E4_ntd_L

GATATTGTGATGACACAATCTCCACTCTCCCTGCCTGTCAATCTTGGAGATCAAGTCTC
CCTCTCTTGACAGATCTAGTCAGAGCATTGTACATAATAATGGAGACACCTATTTAGAATG
GTACCTACAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGAT
TTTCTGGGGTCCCAGACAGGTTCAAGTGGCAGTGGATCAGGGACAGATTTCACTCAA
GATCAGCAGAGTGGAGGCTGAGGATCTGGGAATTTATTACTGCTTTCAAGGTTACATC
TTCCGCTCACGTTCCGTTCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO: 66]**Heavy chain variable domain**

>13E4_aa_H

EVQLLETTGGDLVTPGGSLKLSCAASGFSFSDYYMYWVRQTPEKRLEWVATISVGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYCYVRDGDNDGKFLGYWGQGTFTVTV
S [SEQ ID NO:62]

>13E4_ntd_H

GAAGTGCAGCTGTTGGAGACTGGGGGAGACTTAGTGACGCCTGGAGGGTCCCTGAAA
CTCTCCTGTGCAGCCTCTGGATTCAGCTTCAGTGACTATTATATGTATTGGGTTCGCCA
GACTCCGGAAAAGAGGCTGGAGTGGGTCGCAACTATTAGTGTTGGTGGTACATACACC
TTCTATTCAGACAATGTGAAGGGGAGATTTCGTCATCTCCAGAGACAATGCCAGGAAAAA
TCTGCATCTGGAAATGAACAGTCTGAAGTCTGAGGACGCAGCCATGTATTACTGTGTAA
GAGATGGCAACGATGGAAAATTTCTTGGGTACTGGGGCCAGGGGACTTTCGTCACCTGT
CACT [SEQ ID NO: 67]**Figure 34**

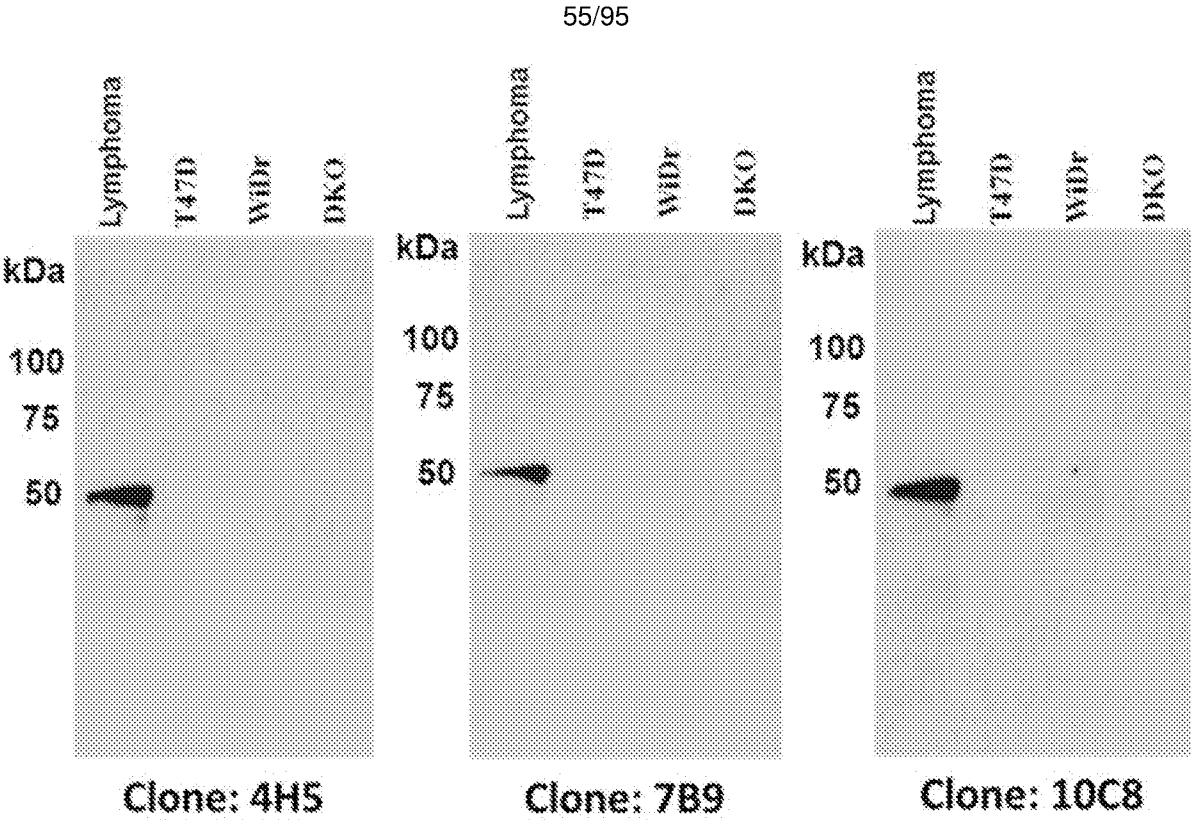


Figure 35

Clone: 4H5

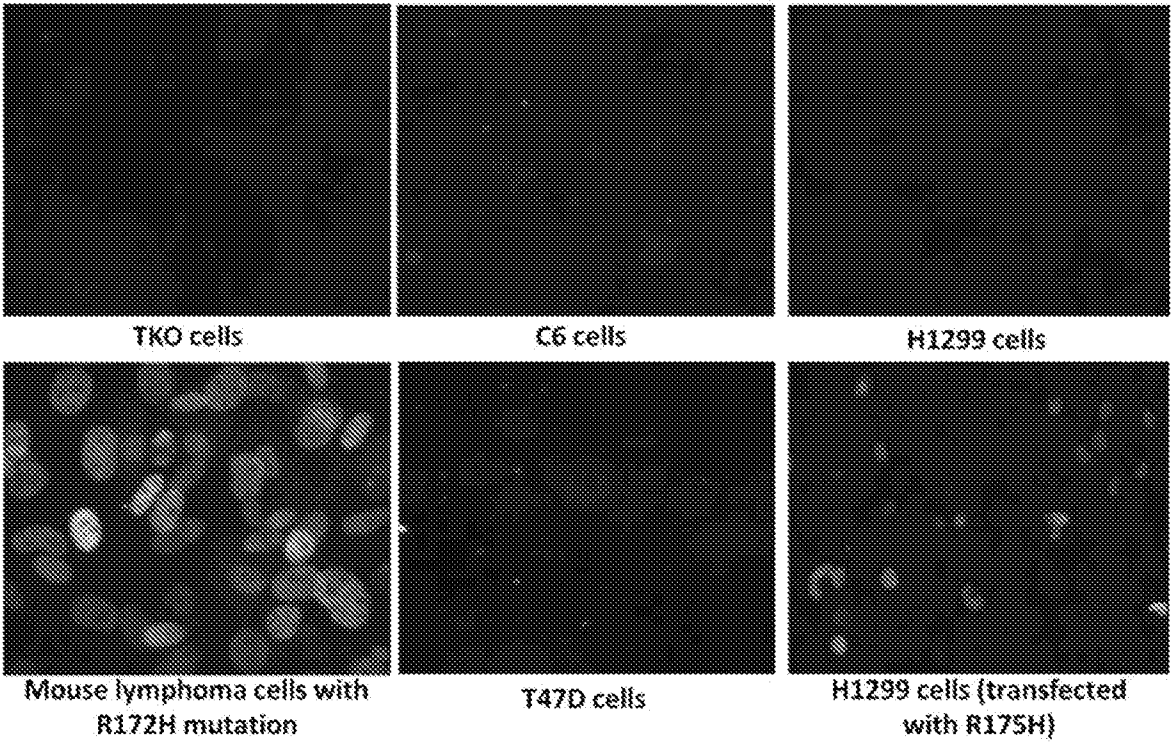


Figure 36A

Clone: 7B9

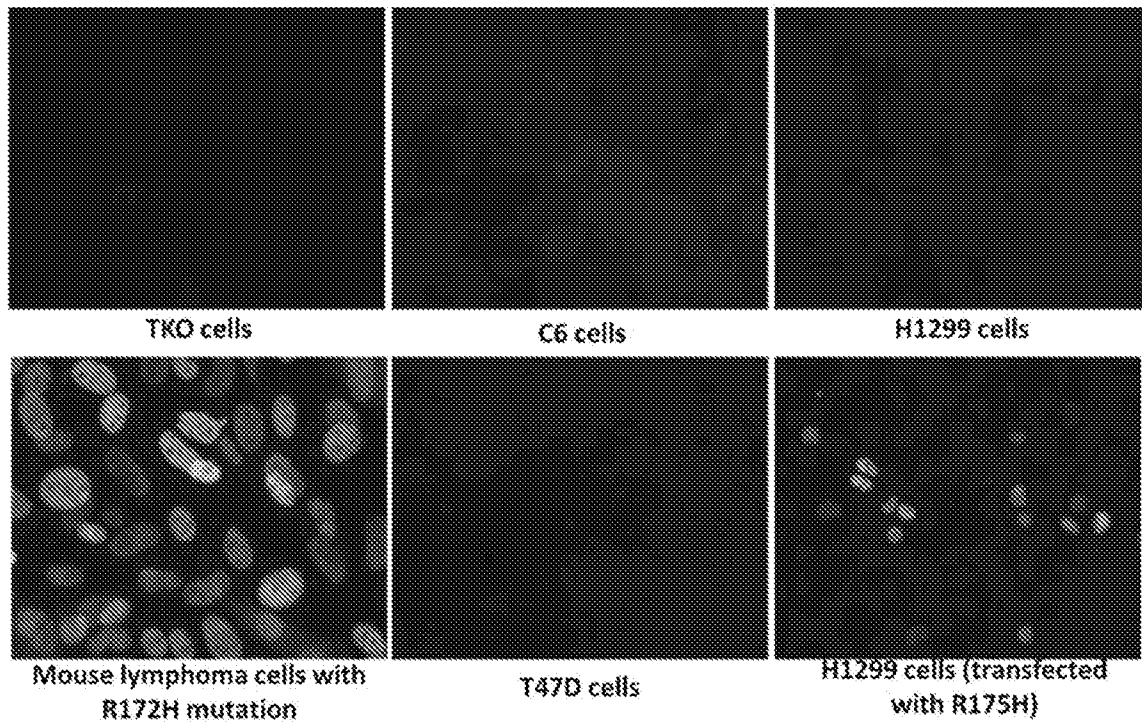


Figure 36B

Clone: 10C8

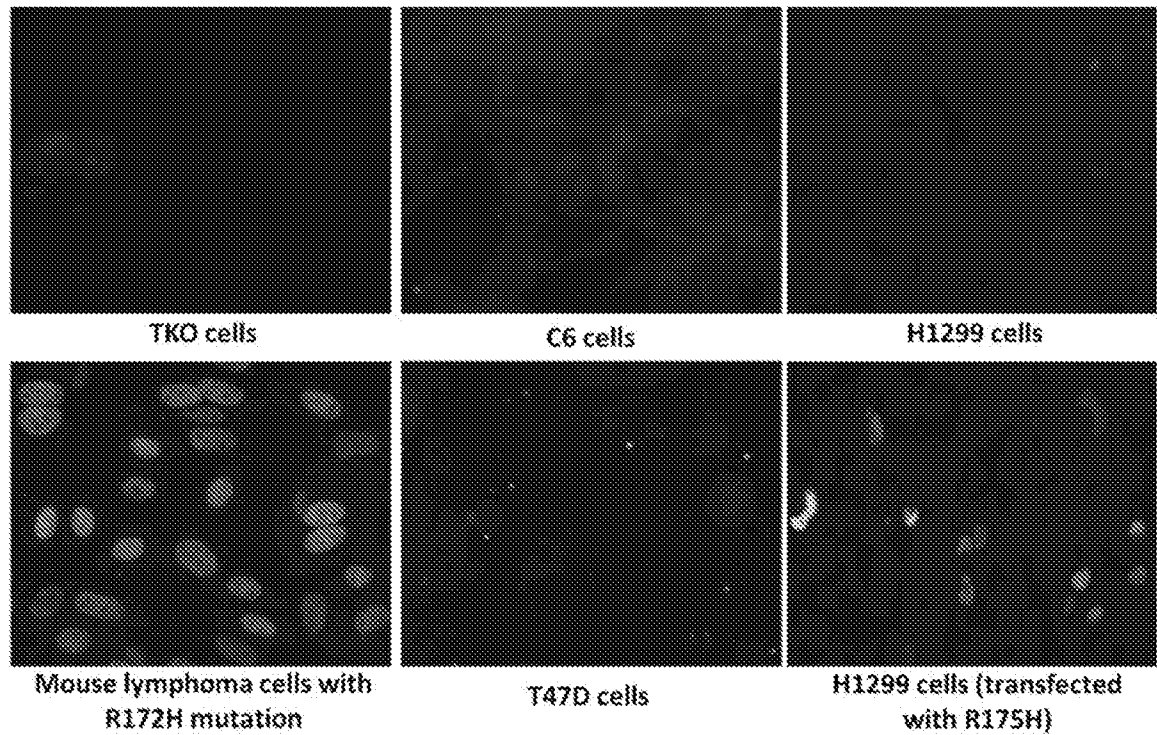


Figure 36C

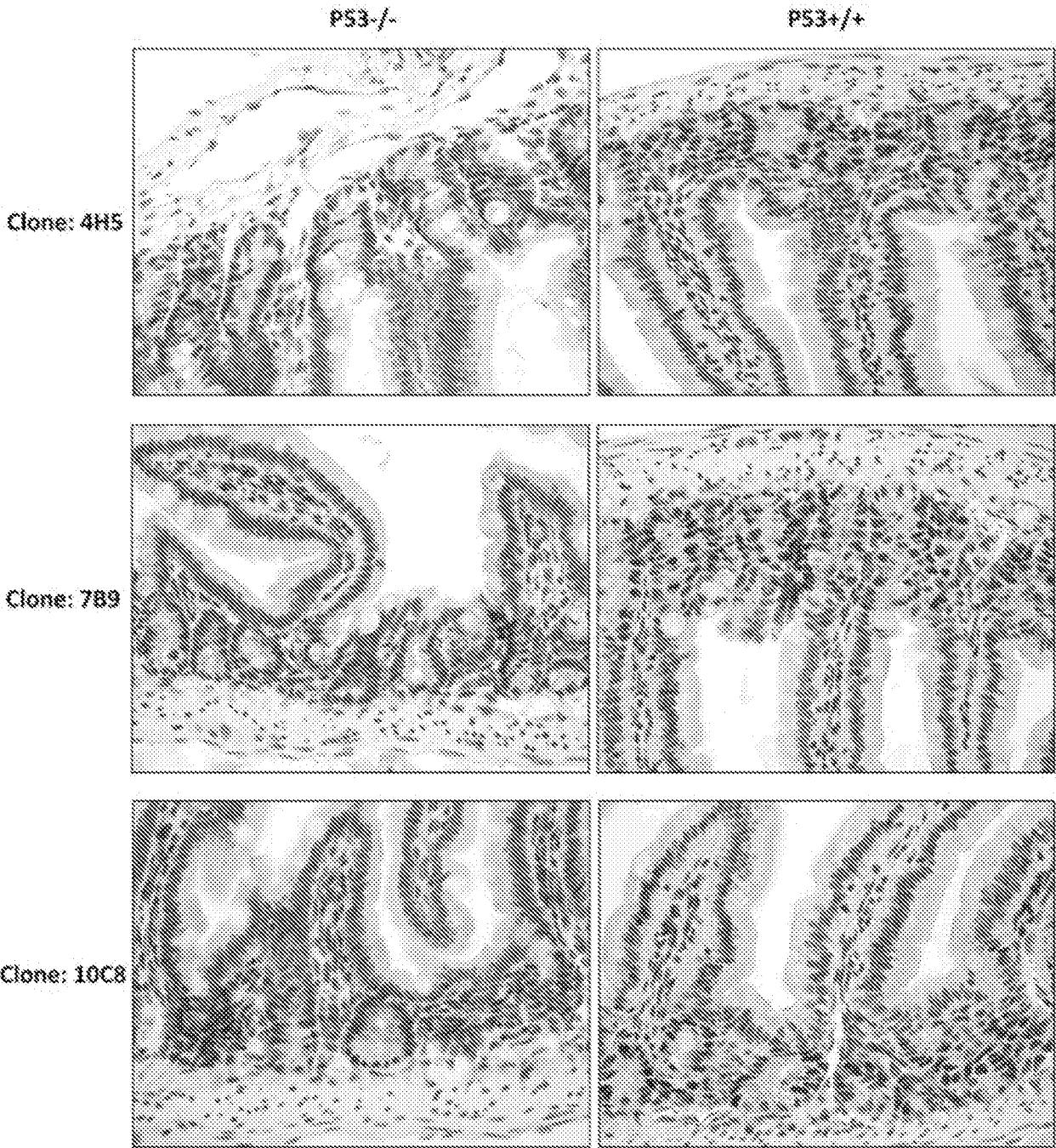


Figure 37

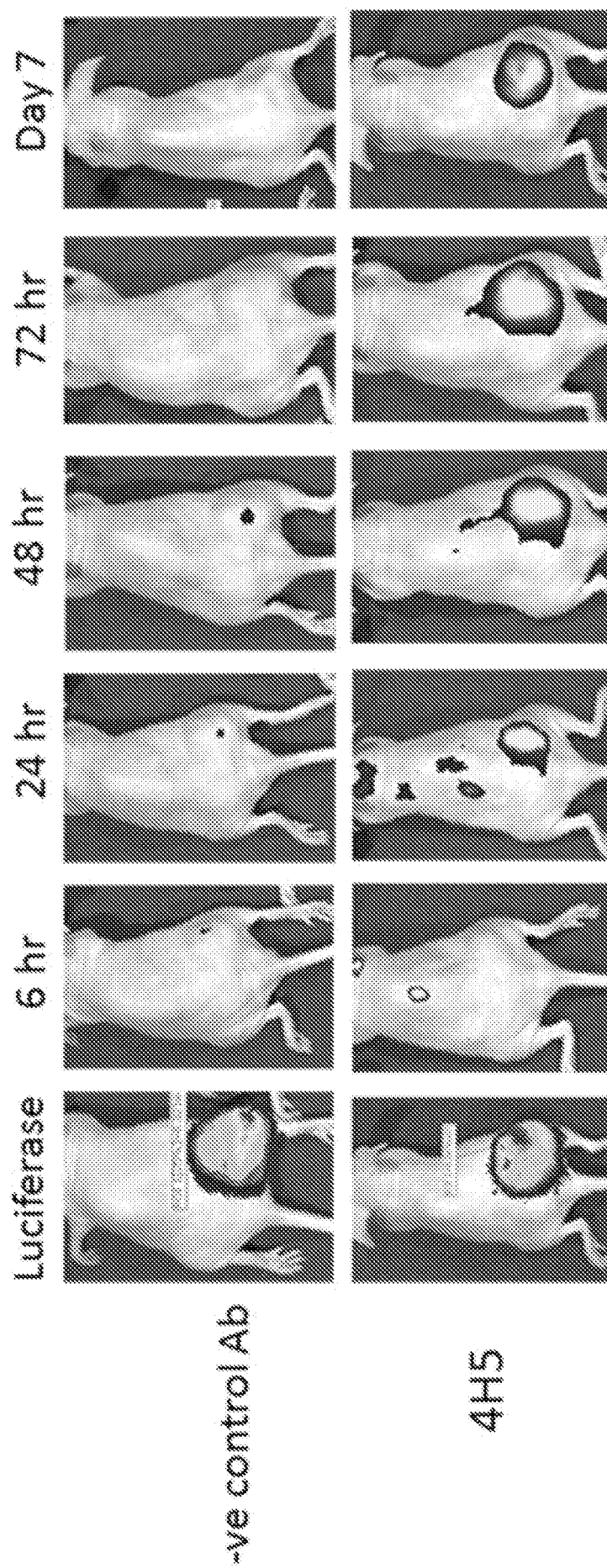


Figure 38

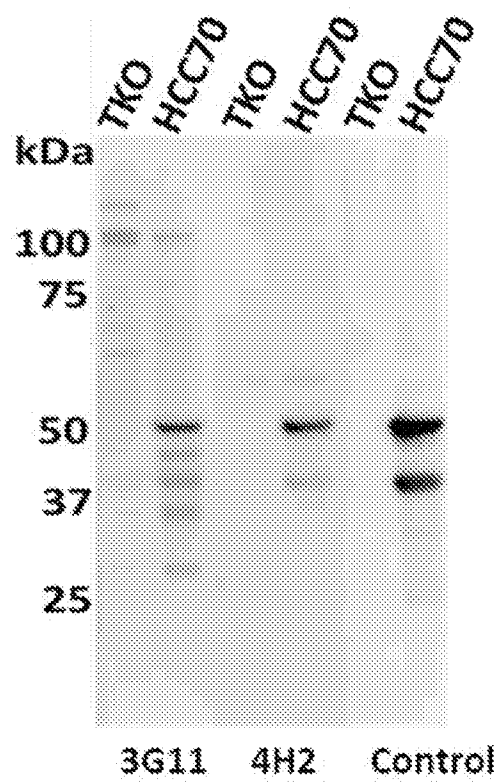


Figure 39

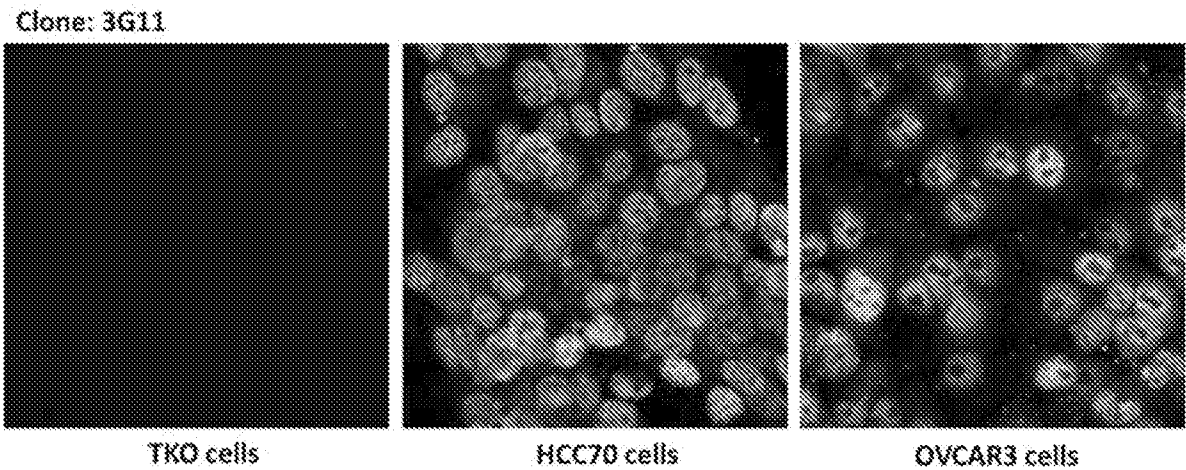


Figure 40A

60/95

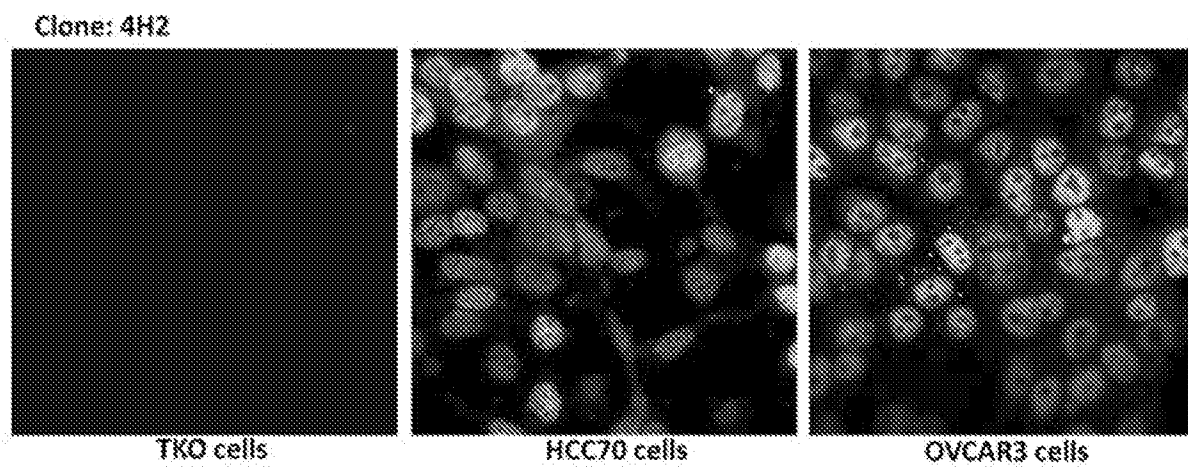


Figure 40B

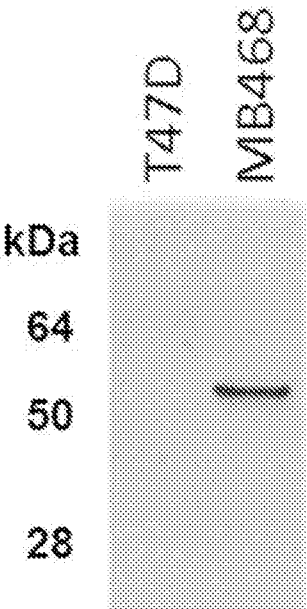


Figure 41

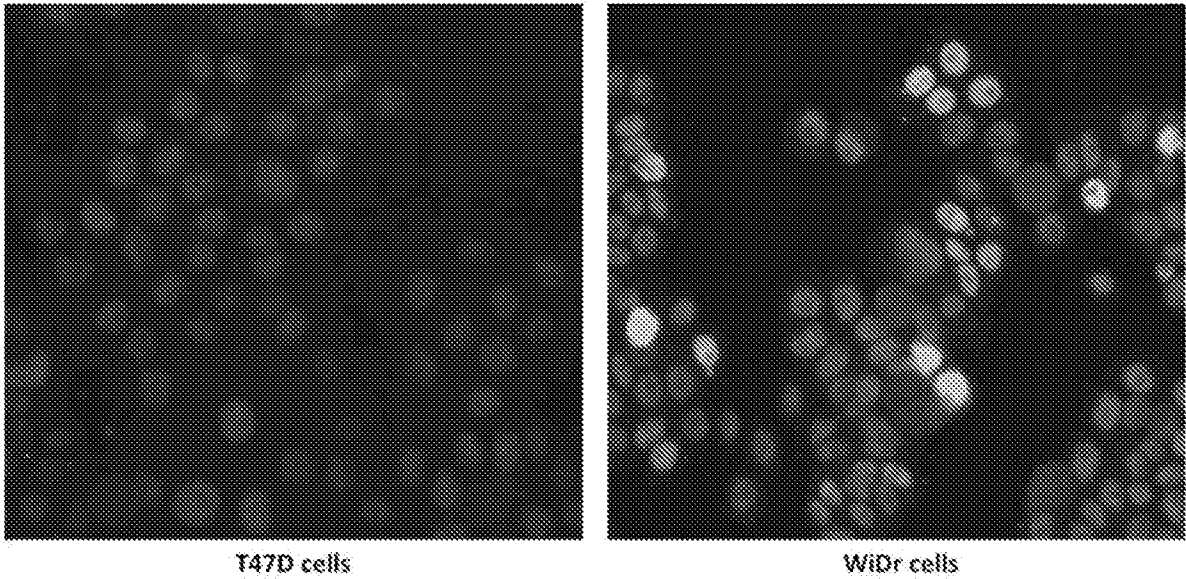


Figure 42

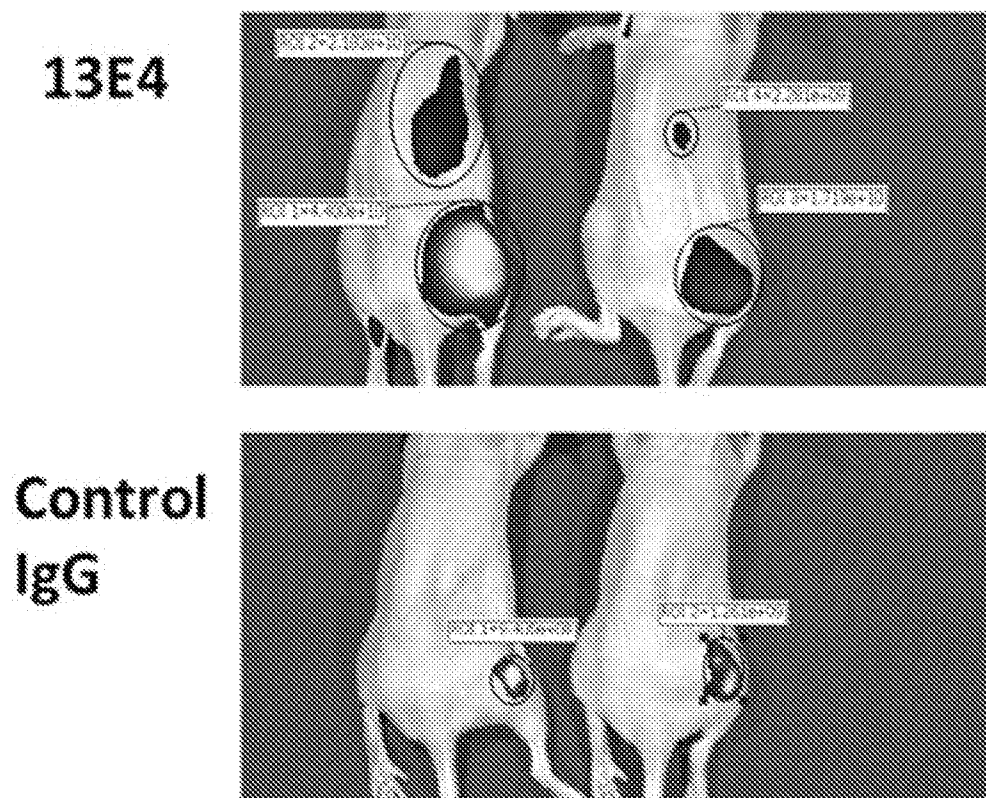


Figure 43

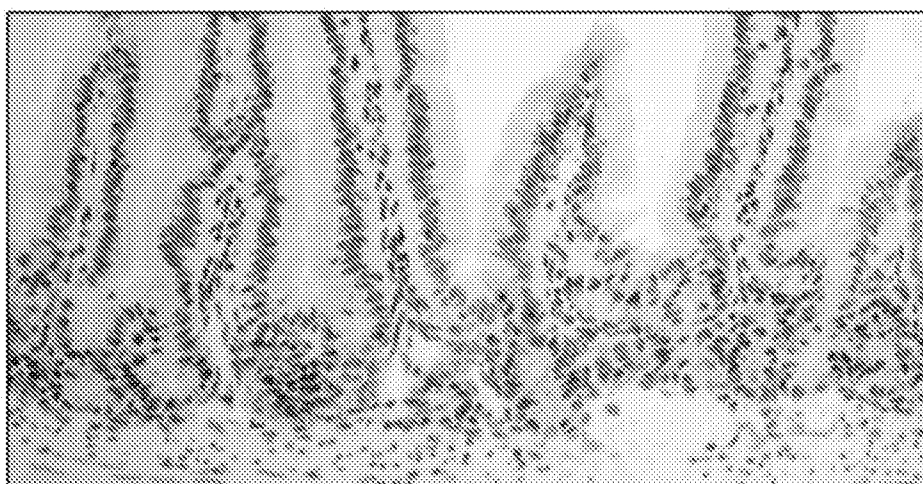
63/95

p53 +/+

Clone: 4H5



Clone: 7B9



Clone: 10C8

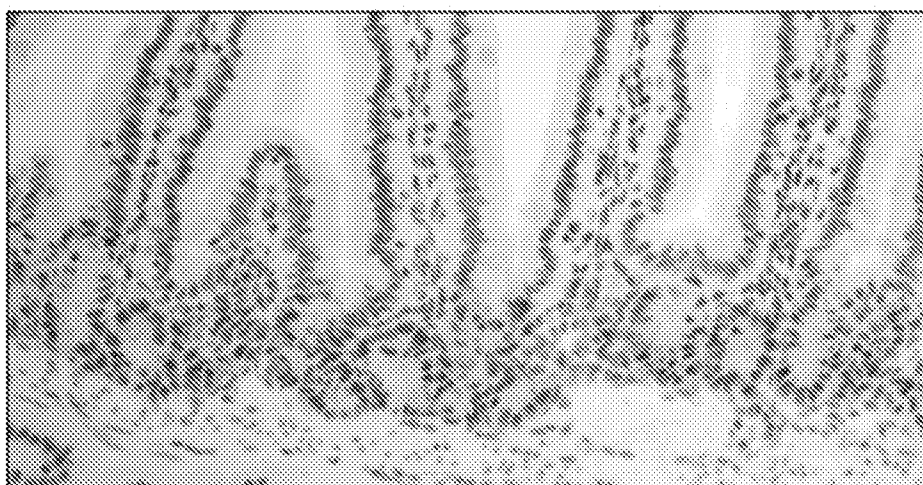


Figure 44

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

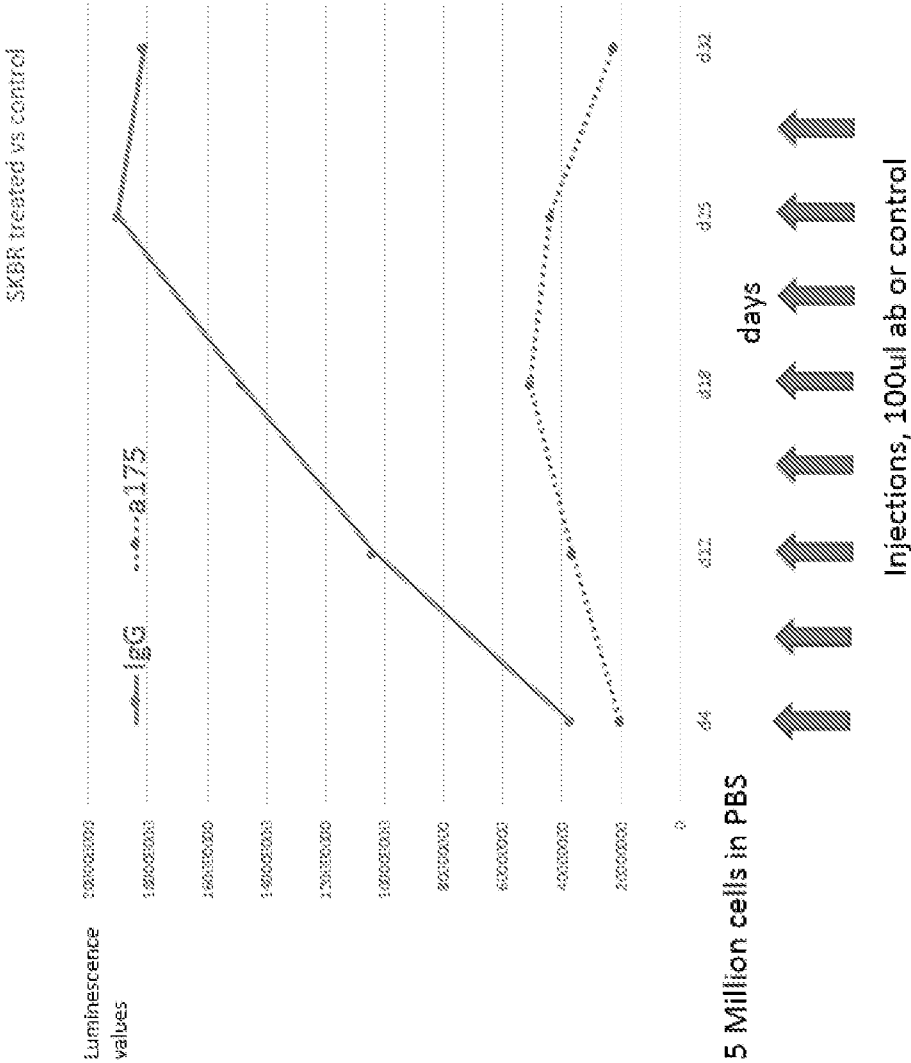


Figure 45

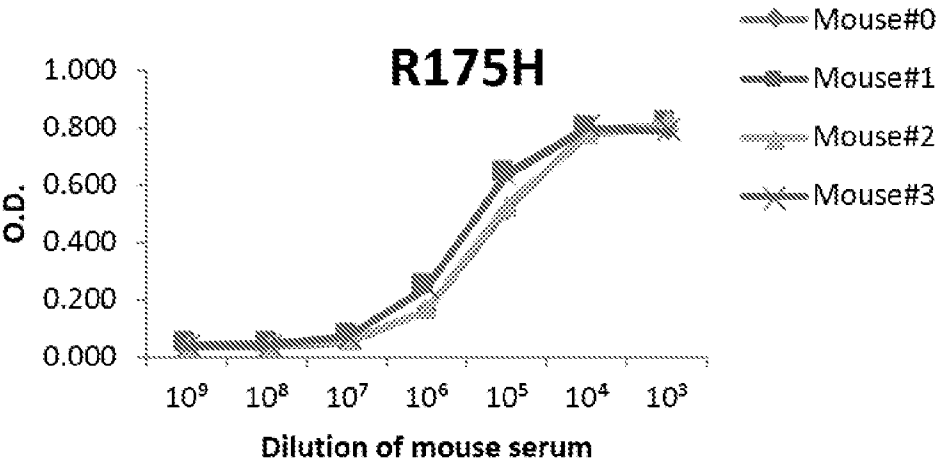


Figure 46A

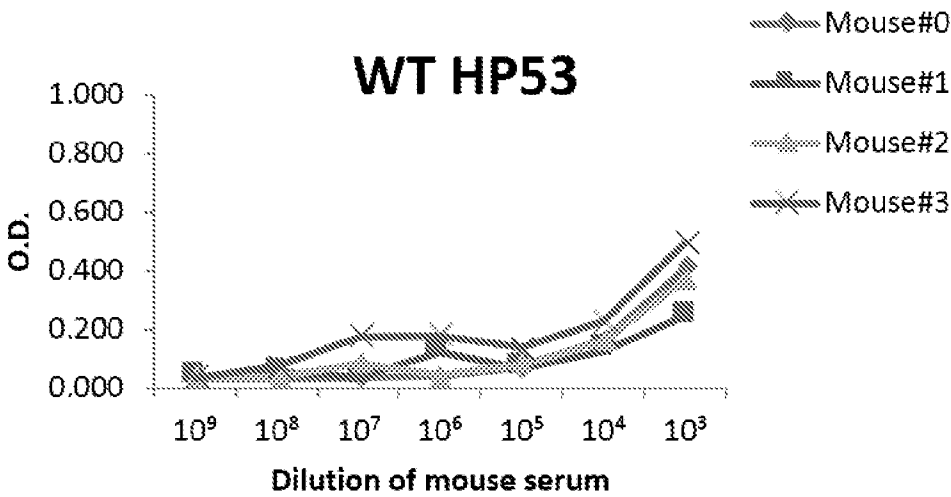


Figure 46B

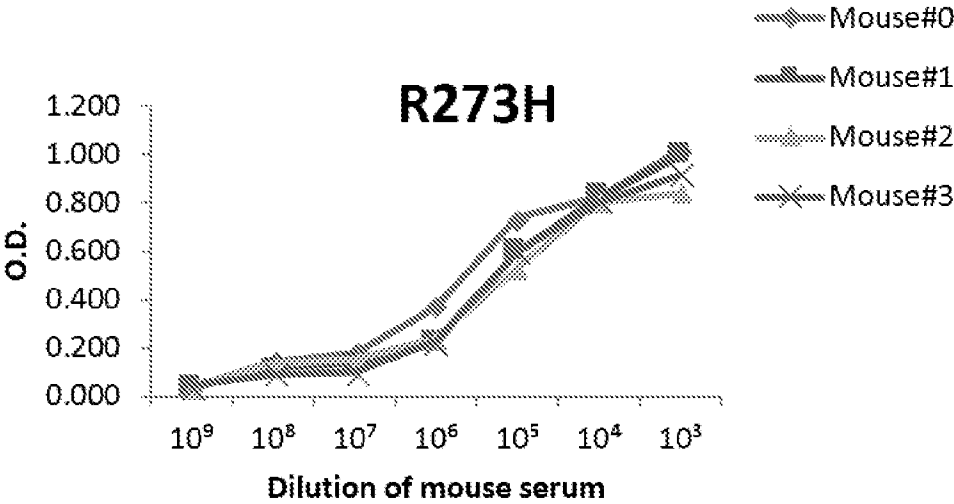


Figure 46C

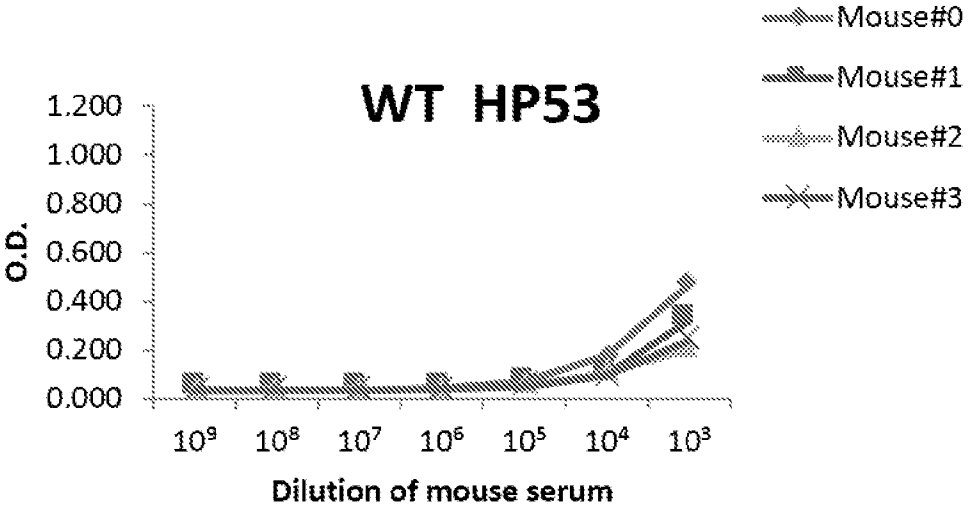


Figure 46D

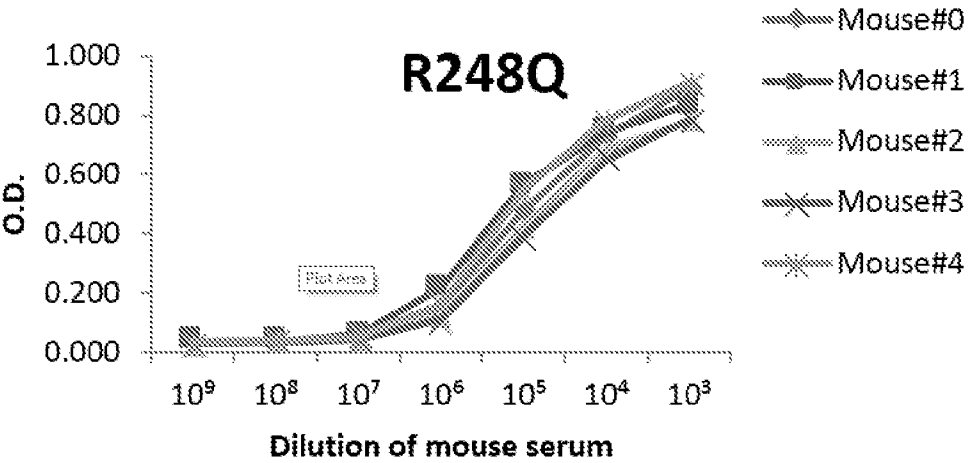


Figure 46E

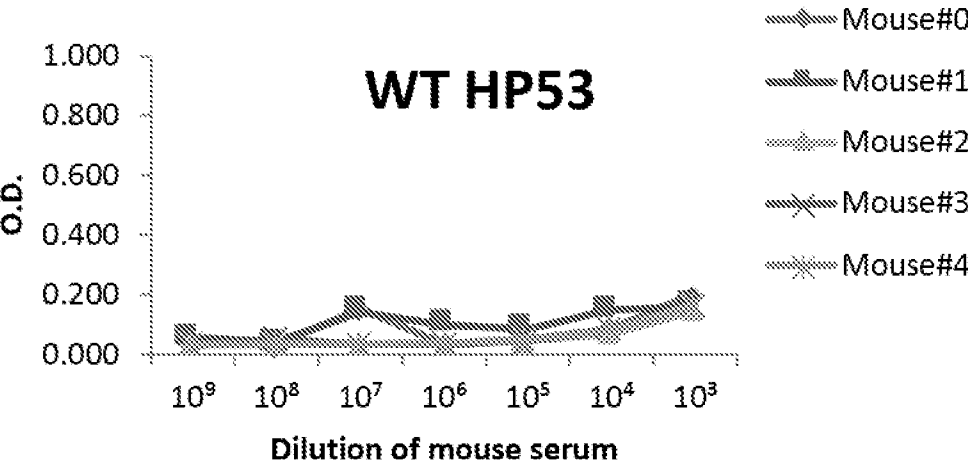
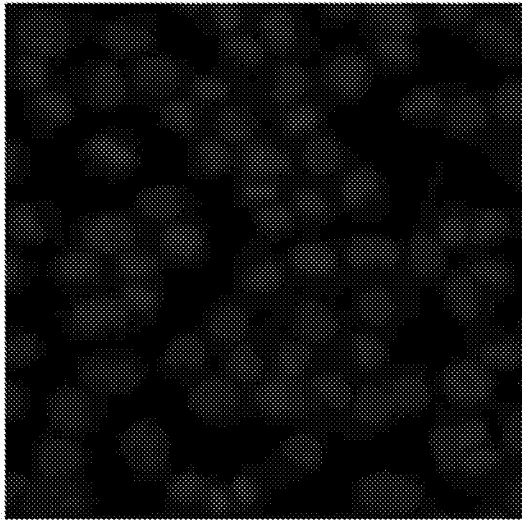
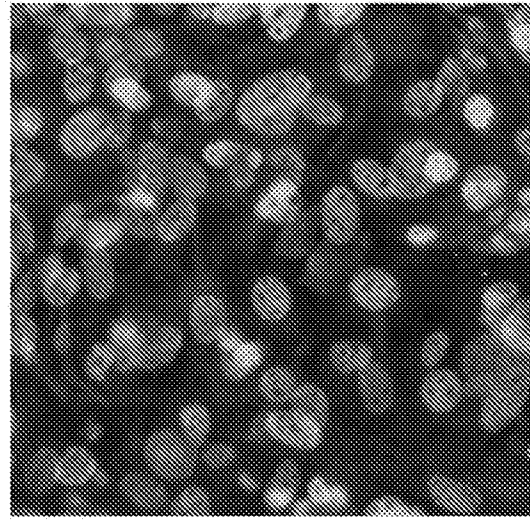


Figure 46F

R175H



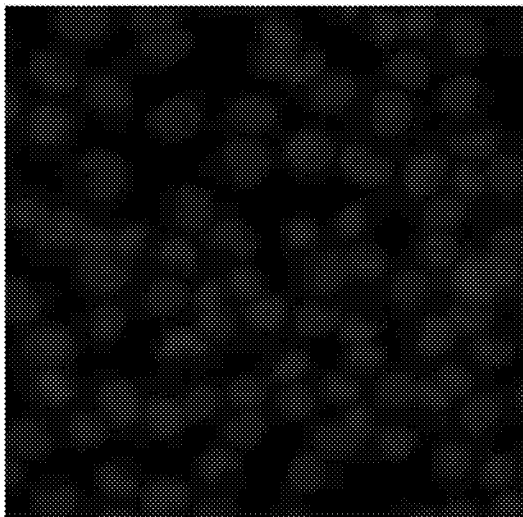
Normal mouse serum on
R175H positive cells



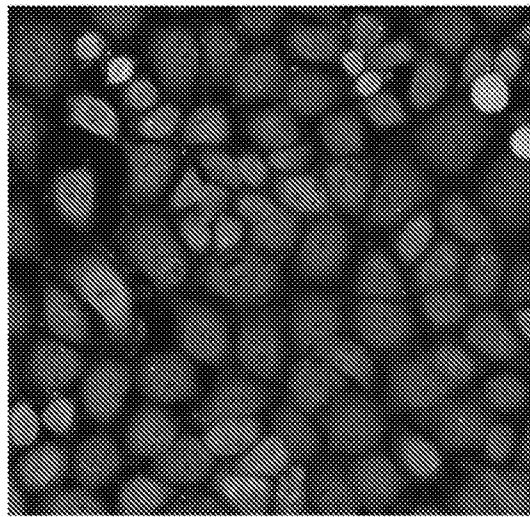
R175H Mouse serum
on R175H positive
cells

Figure 47A

R248Q



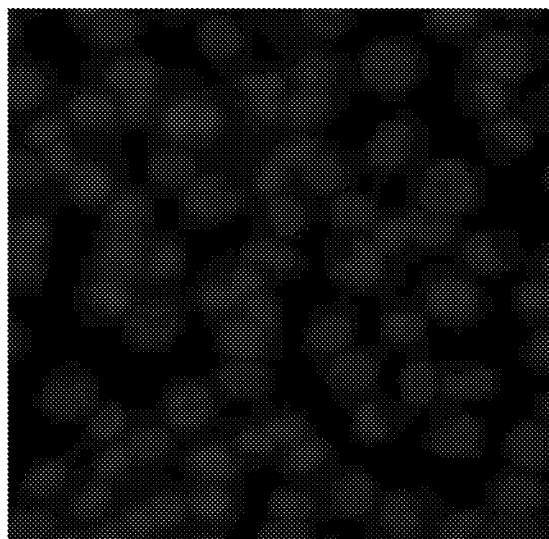
Normal mouse serum on
R248Q positive cells



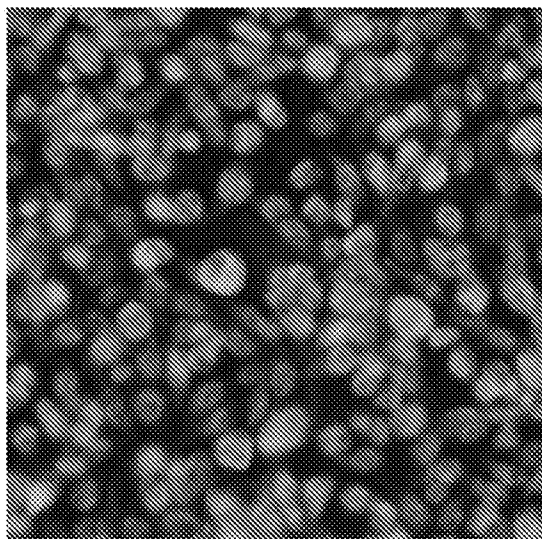
R248Q Mouse serum on
R248Q positive cells

Figure 47B

R273H



Normal mouse serum on R273H positive cells



R273H Mouse serum on R273H positive cells

Figure 47C

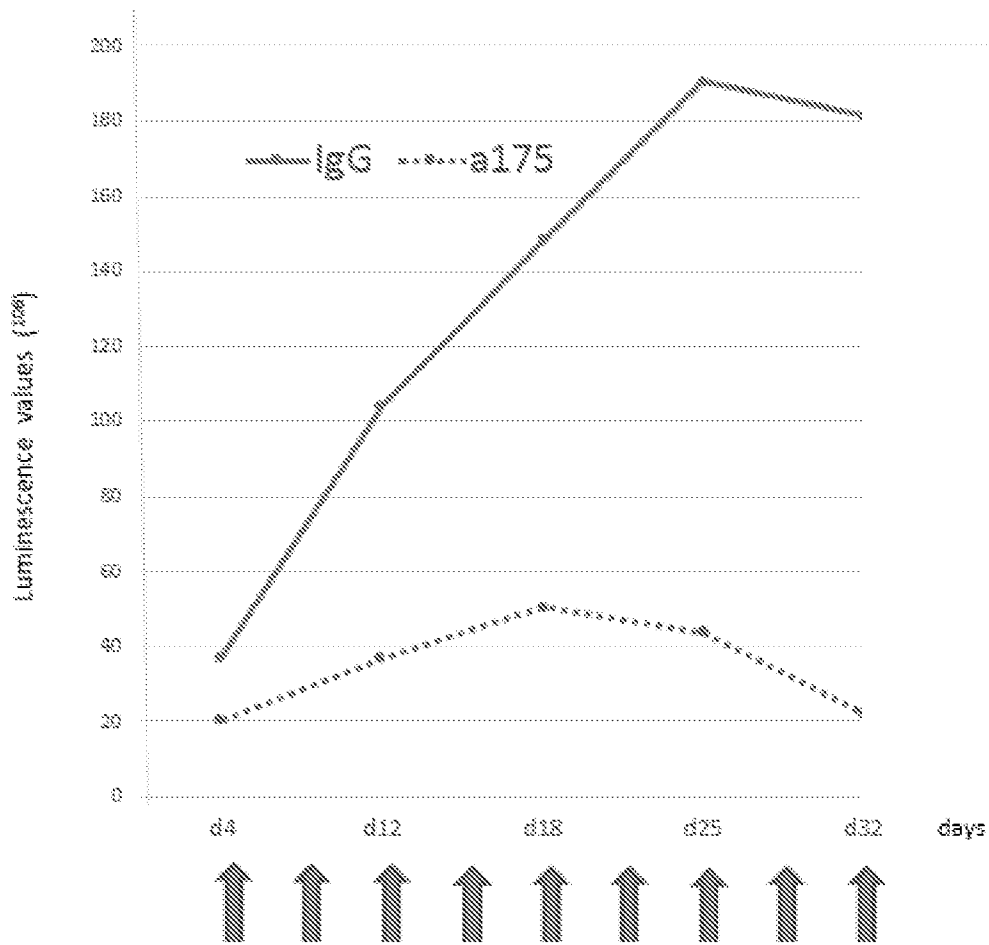


Figure 48

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
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK (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
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK (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

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVT
VY 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

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGT
TVY NQKFKGKATLTVDKSSSTAYMELRSLTSDDSAVYYCARWGGDYVTGGGTTLTVSS (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

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGT
TVY NQKFKGKATLTVDKSSSTAYMELRSLTSDDSAVYYCARWGGDYVTGGGTTLTVSS (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

DIVLTQSTSSLSVSAGERVTLSCCKSSQSLNLSGNQKSYLAWYQQKPGQPPKLLIYGASTRE
SGVPDRFTGSGSETDFTLTISVQPEDLAVYYCQNDHSYPLTFGAGTKLELK [SEQ ID
NO:237]

>MH 4H5_ntd_L

GATATTGTGcTCaCCCaATCTACATCCTCCCTGAGTGTGTCAGCTGGAGAGAGGGTCAC
TTTGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAATCAAAAGAGTTACTTGG
CCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAACTGTTGATCTACGGGGCATCCAC
TAGGGAATCTGGGGTCCCTGATCGCTTACAGGCAGTGGATCTGAAACCGATTTCAC
CTTACCATCAGCAGTGTGCAGCCTGAAGACCTGGCAGTTTATTATTGTCAGAATGATCA
TAGTTATCCGCTCACGTTCCGGTGCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:242]

Mouse-human chimeric anti-R175H clone 7B9

>MH 7B9_aa_L

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK [SEQ ID
NO:238]

>MH 7B9_ntd_L

GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAATCAAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTCAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:243]

Mouse-human chimeric anti-R175H clone 10C8

>MH 10C8_aa_L

DIVMTQSPSSLSVSGGEKVTMSCKSSQSLNLSGNQKSNLAWYQQKPGQPPKLLIYGASTR
ESGVPDRFAGSGSGTDFTLTISVQAEDLAVYYCQNDHSYPLTFGGGKLELK [SEQ ID
NO:238]

>MH 10C8_ntd_L

GATATTGTGATGACCCAGTCTCCATCCTCCCTGAGTGTGTCAGGAGGAGAGAAGGTCA
CTATGAGCTGCAAGTCCAGTCAGAGTCTGTAAACAGTGGAATCAAAAGAGCAACTTG
GCCTGGTACCAGCAGAAACCAGGGCAGCCTCCTAAATTGTTGATCTATGGGGCATCCA
CTAGGGAATCTGGGGTCCCTGATCGCTTCGCAGGCAGTGGATCTGGAACCGATTTCAC
TCTTACCATCAGCAGTGTGCAGGCTGAAGACCTGGCAGTTTATTACTGTCAAAATGATC
ATAGTTATCCGCTCACGTTCCGGTGGTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:243]

Figure 51

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

>MH 4H5_aa_H

EVQLQQSGPELVKPGASVKISCKTSGFTFTEYTMHWMKQSHGRSLEWIGRIDPNNGVTVY
NQKFKVKATLTVDKSSSTAYLELRSLTSEDSAVYYCARWGGDYVTGGGTTTLTVSS [SEQ
ID NO:239]

>MH 4H5_ntd_H

GAGGTTCAGCTGCAGCAGTCTGGACCTGAACTGGTGAAGCCTGGGGCTTCAGTGAAGA
TATCTTGCAAGACTTCCGGATTACATTCACTGAATACACCATGCACTGGATGAAACAG
AGCCATGGAAGGAGCCTTGAGTGGATCGGACGTATTGATCCTAACAAATGGTGTTACTGT
TTATAACCAGAAGTTCAAGGTCAAGGCCACATTGACTGTGGACAGGTCCTCCAGCACA
GCCTATCTGGAGCTCCGCAGTCTGACGTCTGAGGACTCTGCAGTCTATTACTGTGCAA
GATGGGGTGGTGACTACGTACGGGGGGAGGCACCACTCTCACAGTCTCCTCA [SEQ
ID NO:244]**Mouse-human chimeric anti-R175H clone 7B9**

>MH 7B9_aa_H

EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWMKQSHGKSLEWIGRINPYSGGTVY
NQKFKGKATLTVDKSSSTAYMELRSLTSDDSAVYYCARWGGDYVTGGGTTTLTVSS [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
NQKFKGKATLTVDKSSSTAYMELRSLTSDDSAVYYCARWGGDYVTGGGTTTLTVSS [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

DIVMTQSPLSLPVNLGDQVSLSCRSSQSIVHNNGDTYLEWYLQKPGQSPKLLIYKVSNRFS
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**

EVQLLETGGDLVTPGGSLKLSCAASGFSFSDYYMYWVRQTPEKRLEWVATISVGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYYCVRDGNDGKFLGYWGQGTFVTVTV
S (SEQ ID NO:248)

HC-CDR1:	GFSFSDYY	(SEQ ID NO:63)
HC-CDR2:	ISVGGTYT	(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

DIVMTQSPLSLPVNLGDQVSLSCRSSQSIVHNNNGDTYLEWYLQKPGQSPKLLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDLGIYYCFQGSHLPLTFGSGTKLELK [SEQ ID
NO:247]

>MH 13E4_ntd_L

GATATTGTGATGACACAATCTCCACTCTCCCTGCCTGTCAATCTTGGAGATCAAGTCTC
CCTCTCTTGCAGATCTAGTCAGAGCATTGTACATAATAATGGAGACACCTATTTAGAATG
GTACCTACAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGAT
TTTCTGGGGTCCCAGACAGGTTCAAGTGGCAGTGGATCAGGGACAGATTTCACTCAA
GATCAGCAGAGTGGAGGCTGAGGATCTGGGAATTTATTACTGCTTTCAAGGTTACATC
TTCCGCTCACGTTCCGTTCTGGGACCAAGCTGGAGCTGAAA [SEQ ID NO:249]**Figure 55****Mouse-human chimeric anti-R273H clone 13E4 heavy chain variable domain**

>MH 13E4_aa_H

EVQLLETGGDLVTPGGSLKLSAASGFSFSDYYMYWVRQTPEKRLEWVATISVGGTYTFY
SDNVKGRFVISRDNARKNLHLEMNSLKSEDAAMYVCVRDGDGKFLGYWGQGTFVTVTV
S [SEQ ID NO:248]

>MH 13E4_ntd_H

GAAGTGCAGCTGTTGGAGACTGGGGGAGACTTAGTGACGCCTGGAGGGTCCCTGAAA
CTCTCCTGTGCAGCCTCTGGATTCAGCTTCAGTGAATATTATATGTATTGGGTTCCGCA
GACTCCGGAAAAAGAGGCTGGAGTGGGTCGCAACTATTAGTGTTGGTGGTACATACACC
TTCTATTCAGACAATGTGAAGGGGAGATTTCGTCATCTCCAGAGACAATGCCAGGAAAAA
TCTGCATCTGGAAATGAACAGTCTGAAGTCTGAGGACGCAGCCATGTATTACTGTGTAA
GAGATGGCAACGATGGAAAATTTCTTGGGTACTGGGGCCAGGGGACTTTTCGTCACTGT
CACTGTCTCT [SEQ ID NO:250]**Figure 56**

Mouse-human chimeric anti-R248Q clone 3G11

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVSKLDSGV
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

DIVITQSPLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVSELD SGV
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
YNQKFKGKAALTVDKSSSTAYMQLNSLTSEDSAVYFCAKMGGYDDYWGGGTTTLTVSS
(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
NQKFKGKATLTVDKSSSTAYMQLNSLTSEDSAVYYCAKQGGFDDYWGGGTTTLTVSS (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

DIVLTQTPLTSLVTIGQPASISCKSNQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVSKLDSGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:251]

>MH 3G11_ntd_L

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

>MH 4H2_aa_L

DIVITQSPSLTSLVTIGQPASISCKSDQSLLYSDGKTYLNWLLQRPQGQSPKRLIYLVSELD SGV
PDRFTGSGSGTDFTLKISRVEAEDLGLYYCWQGTHFPLTFGAGTKLELK [SEQ ID NO:252]

>MH 4H2_ntd_L

GACATTGTGATCACACAGTCTCCACTCACTTTGTCTGGTTACCATTGGACAACCAGCCTC
CATCTCTTGCAAGTCAGATCAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTG
GCTATTACAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTGAACTG
GACTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTCACTGAA
AAATCAGCAGAGTGGAGGCTGAGGATTTGGGACTTTATTATTGCTGGCAAGGTACACAT
TTTCCTCTCACGTTCTGGTGCTGGGACCAAGCTGGAGCTGAAA [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
TGTCTGTGAAGGCTTCTGGATACACATTCACTGACTACTATGTGAAGTGGGTGAAGCAG
AGTCCTGGACAGAGCCTTGAGTGGATTGGAGATATTCATCCTAAGAACGGTGGTACTAA
CTACAACCAGAAGTTCAAGGGCAAGGCCGCATTGACTGTGGACAAATCCTCCAGCACA
GCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTTCTGTGCAAA
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
ATGTCCTGTGAAGGCTTCTGGATACACATTCACTGACTACTATCTGAAGTGGGTGAGGCA
GAGTCATGGAAAGAGCCTTGAGTGGATTGGAGATATAGATCCCAAGAATGGTGGTACT
AATTACAACCAGAAGTTTAAGGGCAAGGCCACATTGACTGTGGACAAATCCTCCAGCAC
AGCCTACATGCAGCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAA
AACAGGGGGGGTTTCGACGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
[SEQ ID NO:258]

Figure 60

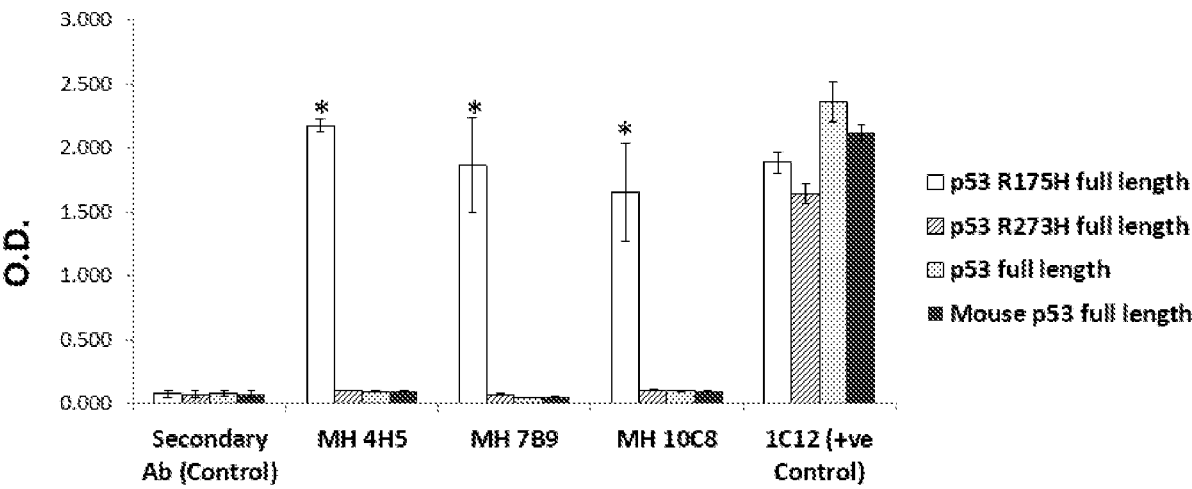


Figure 61

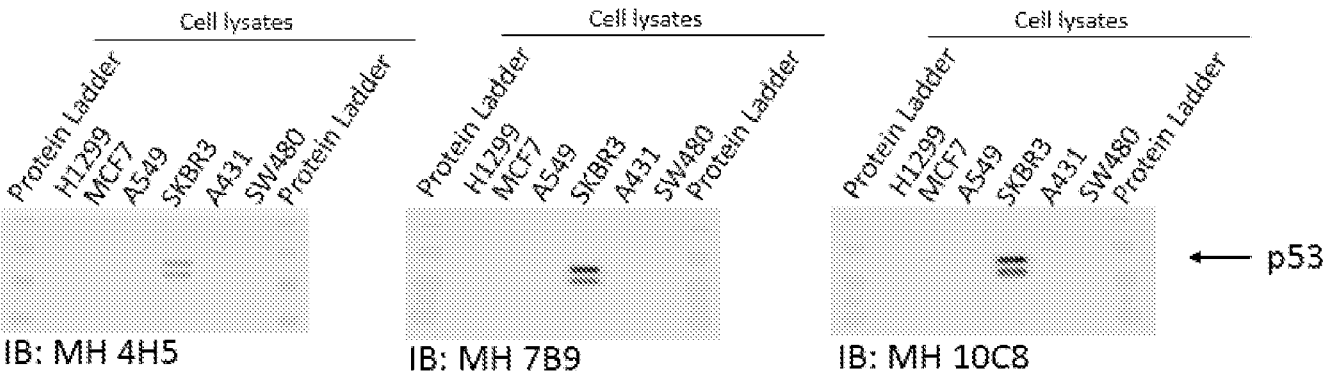


Figure 62

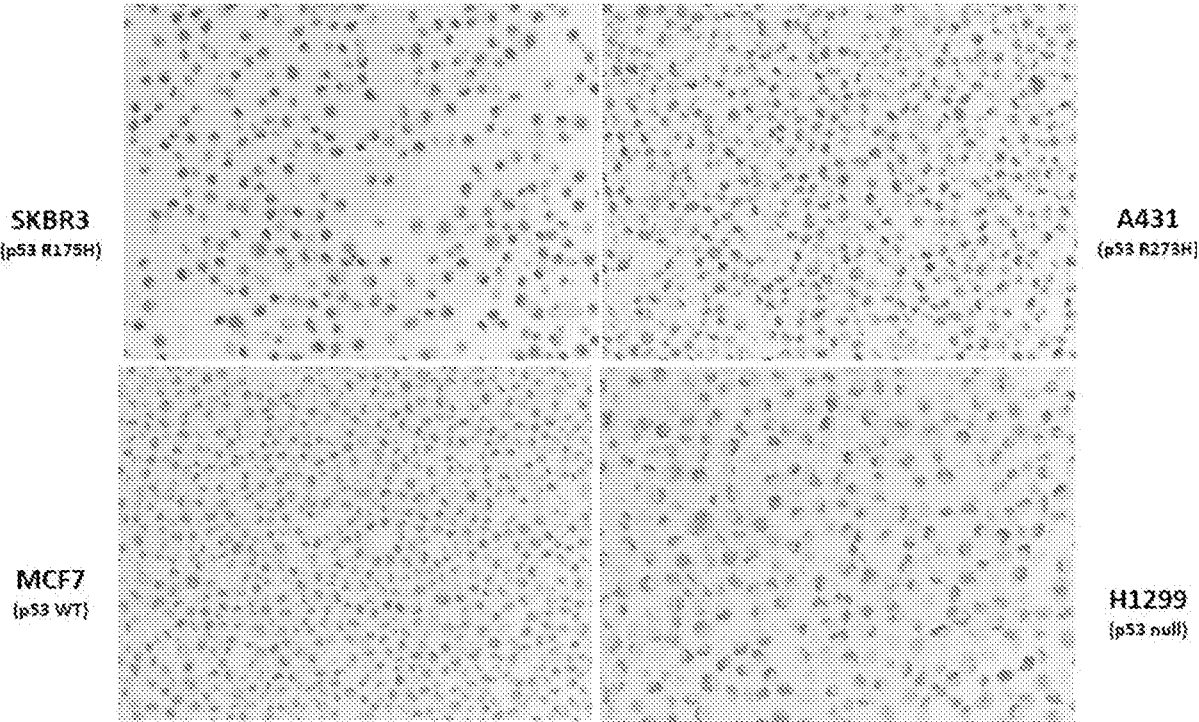


Figure 63

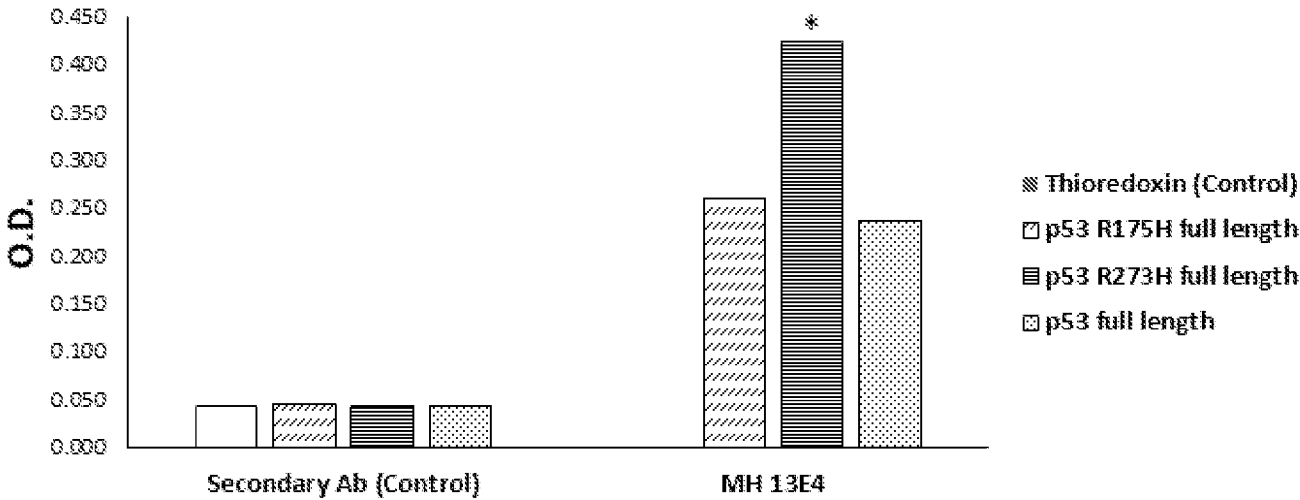


Figure 64

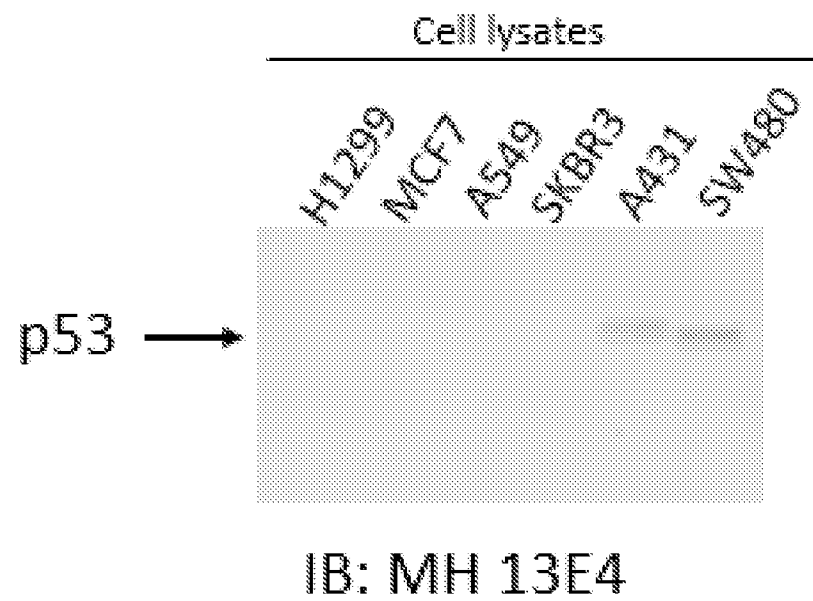


Figure 65

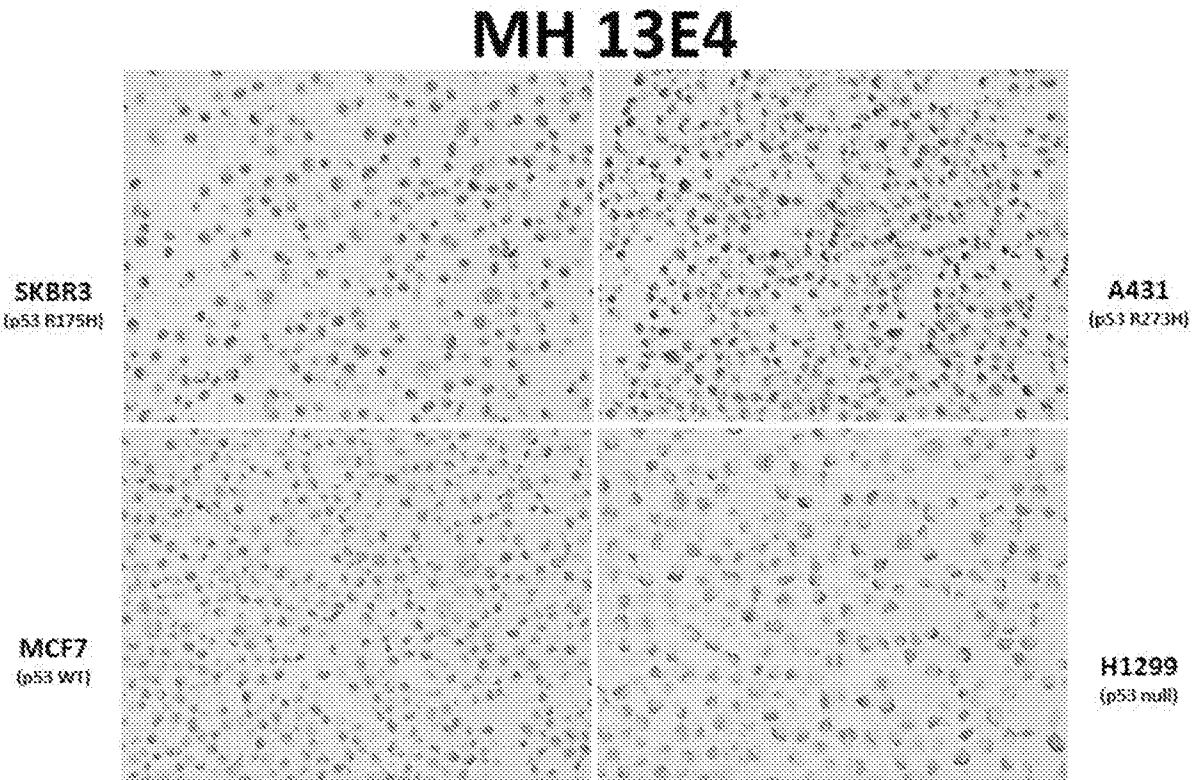
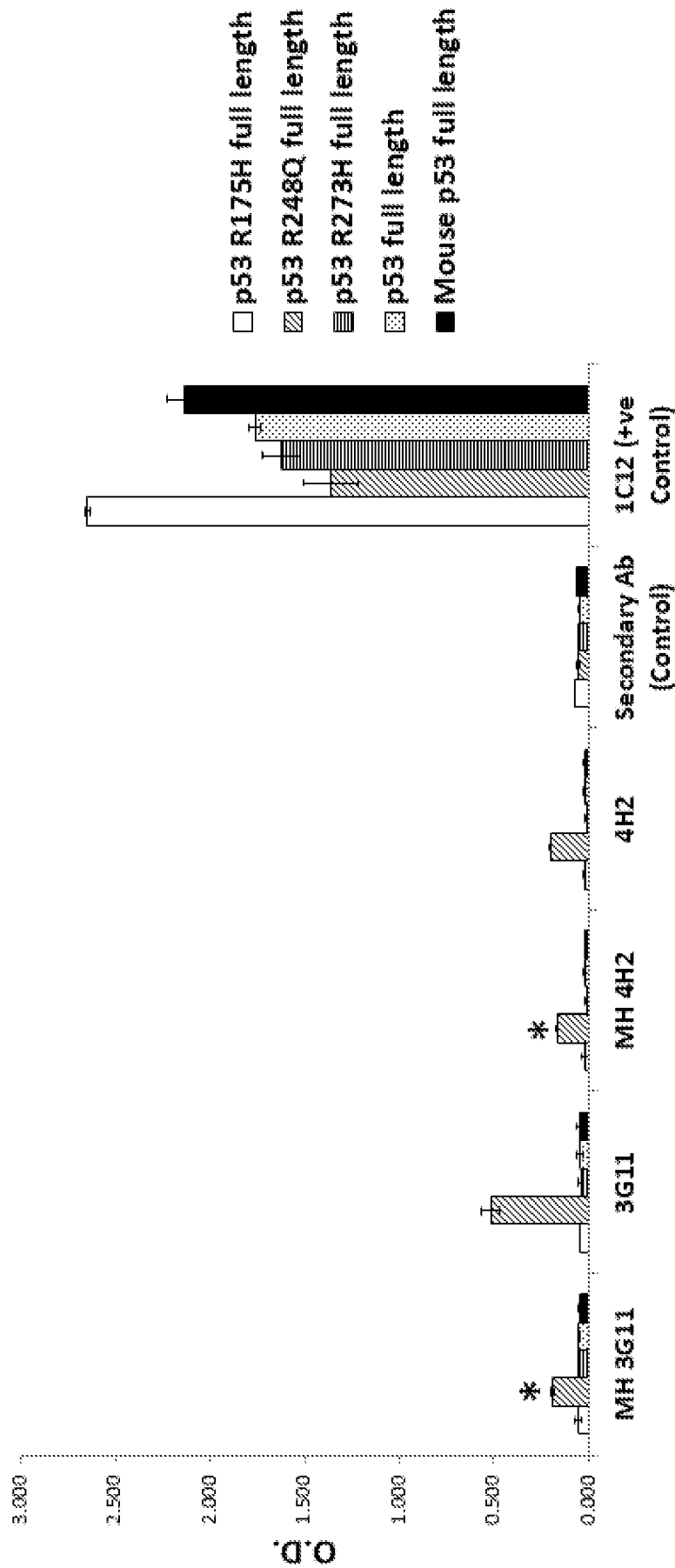


Figure 66

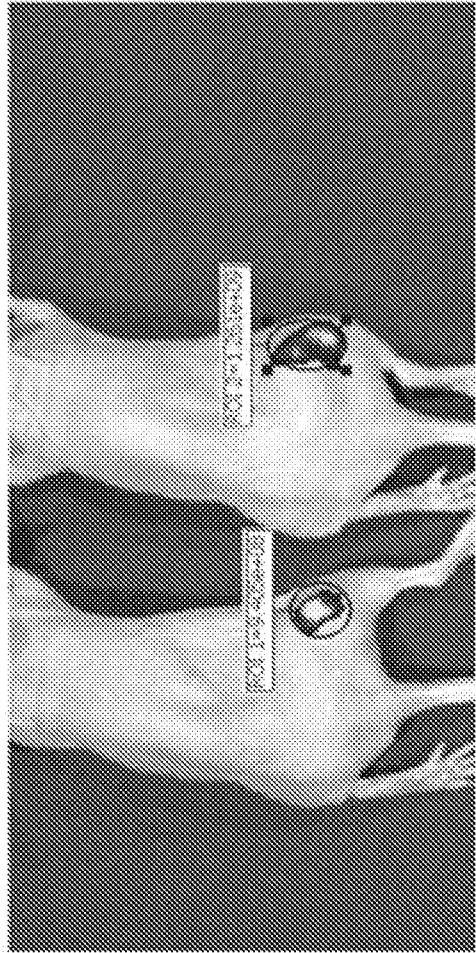
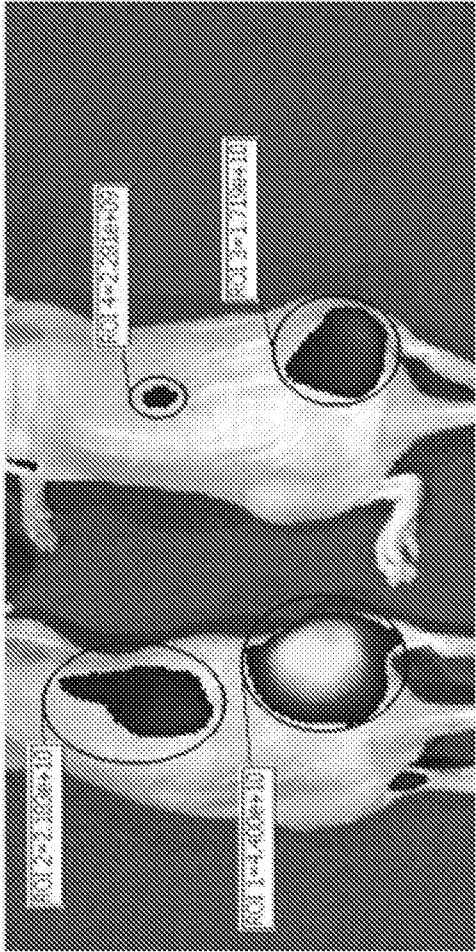


Note: "MH 3G11" refers to chimeric 3G11 antibody, "MH 4H2" refers to chimeric 4H2 antibody

Figure 67

Control mlgG mAb

13E4, p53-R273H mAb



Nude mice
HT29 tumor (R273H)

Figure 68

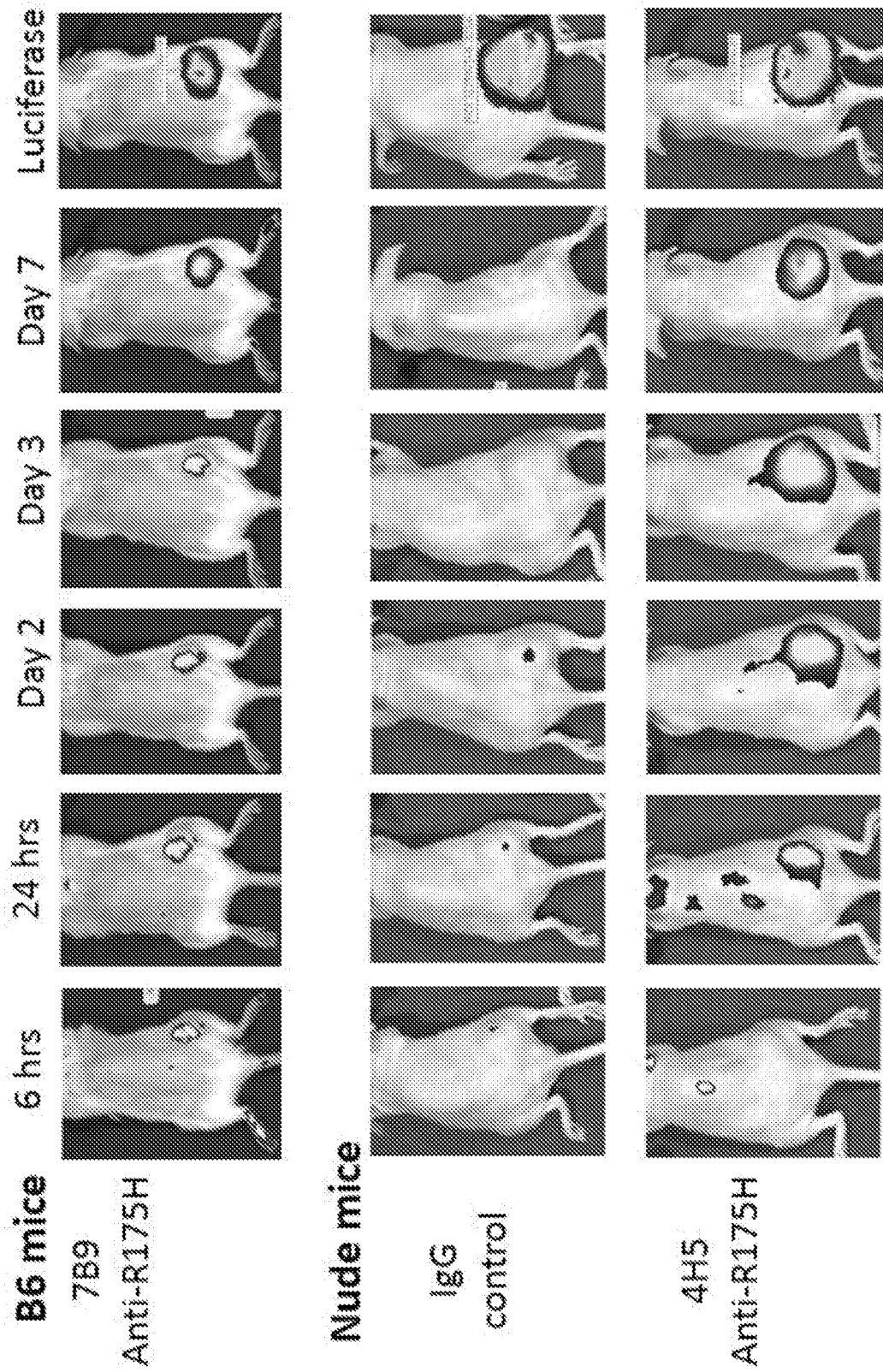


Figure 69

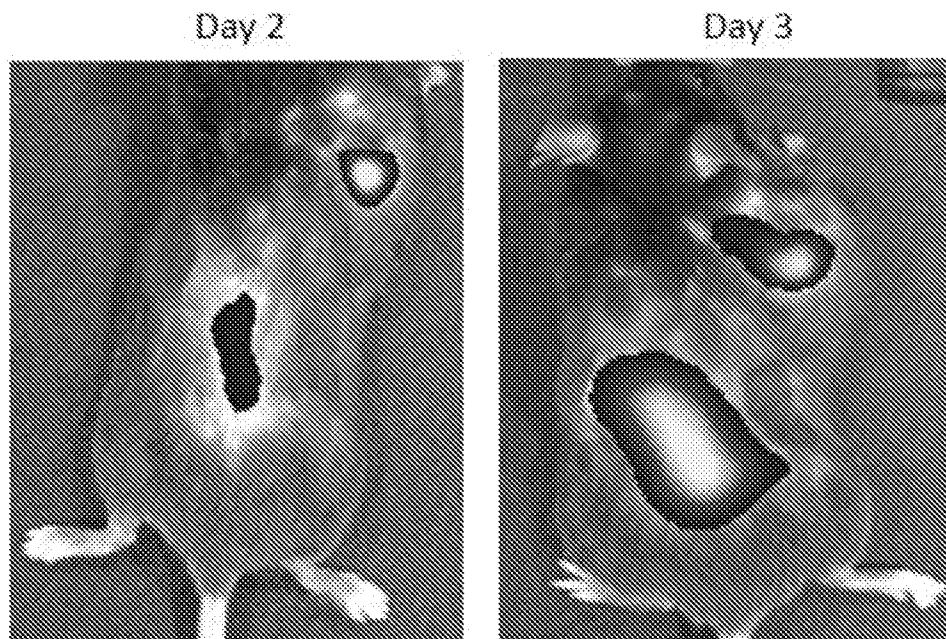


Figure 70

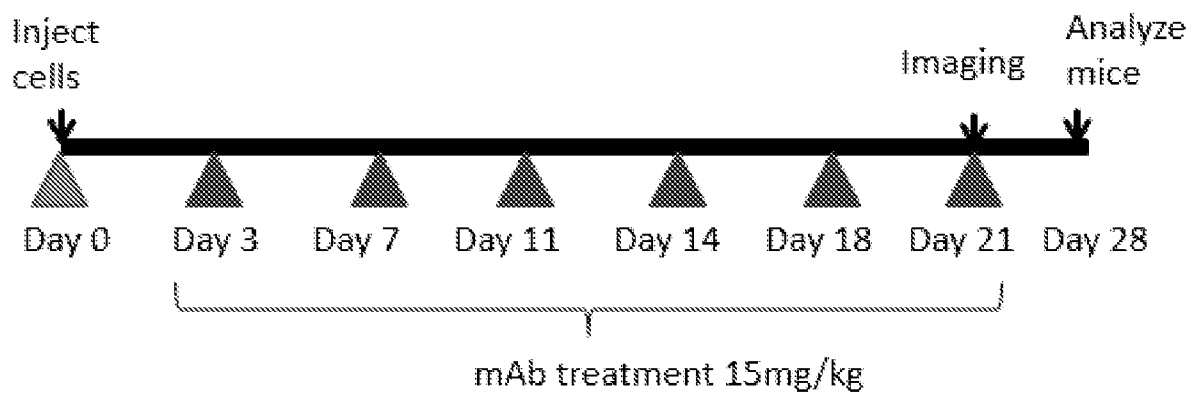


Figure 71A

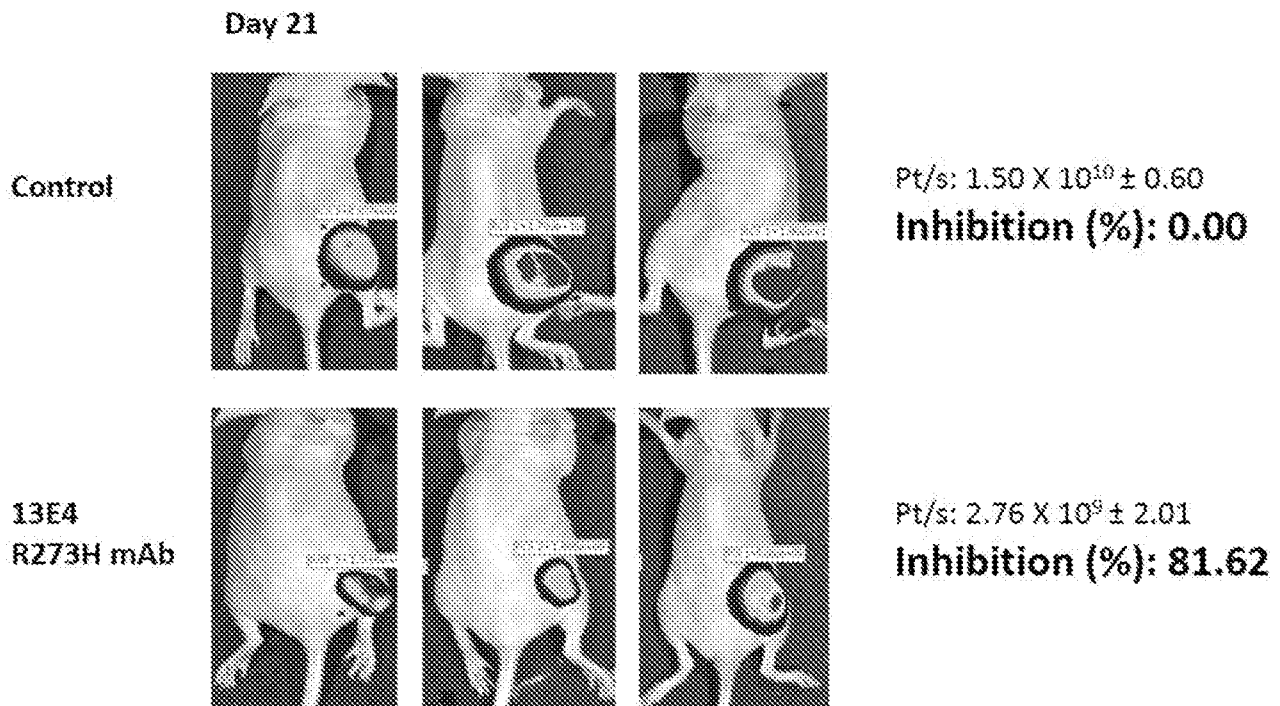


Figure 71B

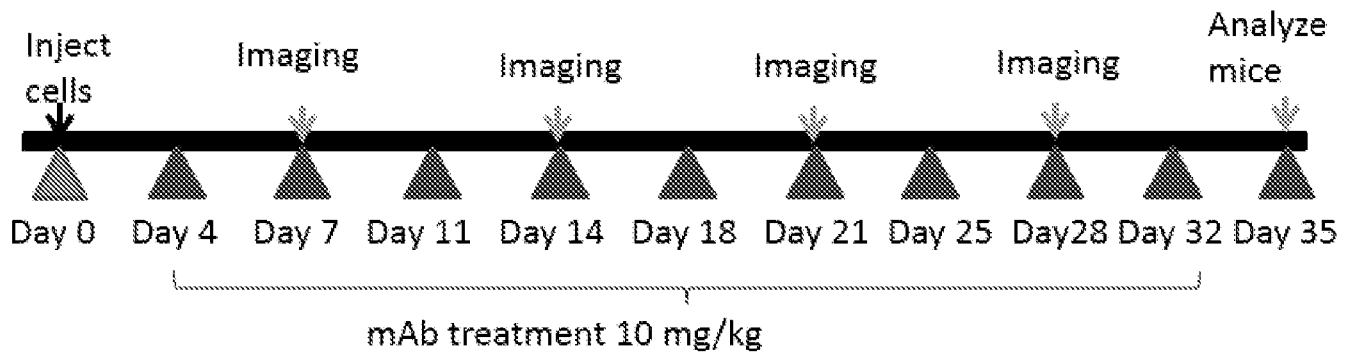


Figure 72A

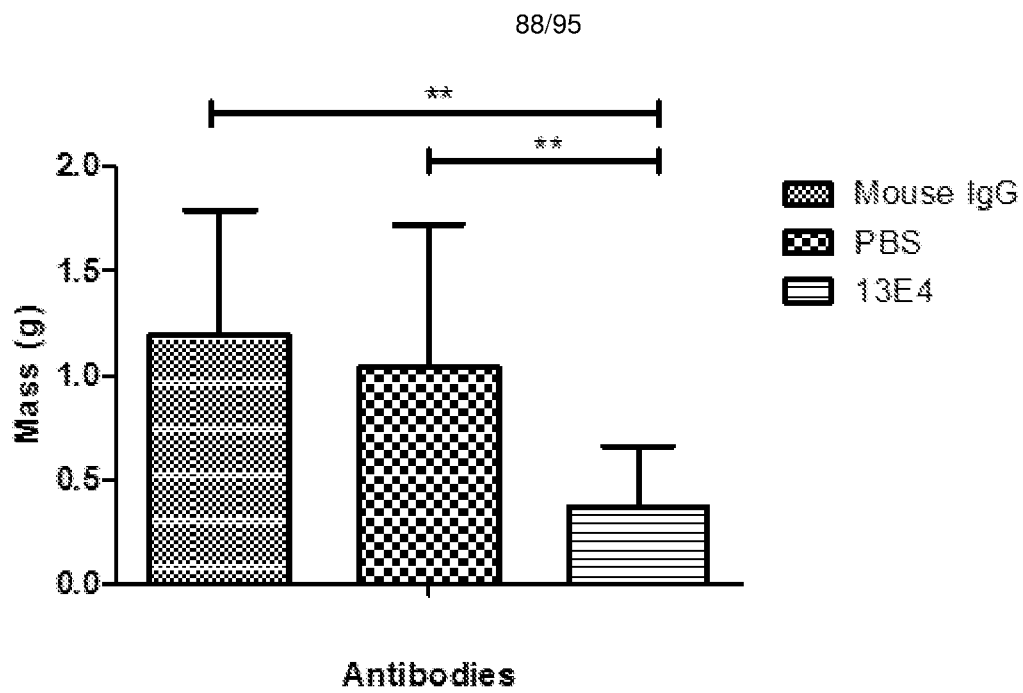


Figure 72B

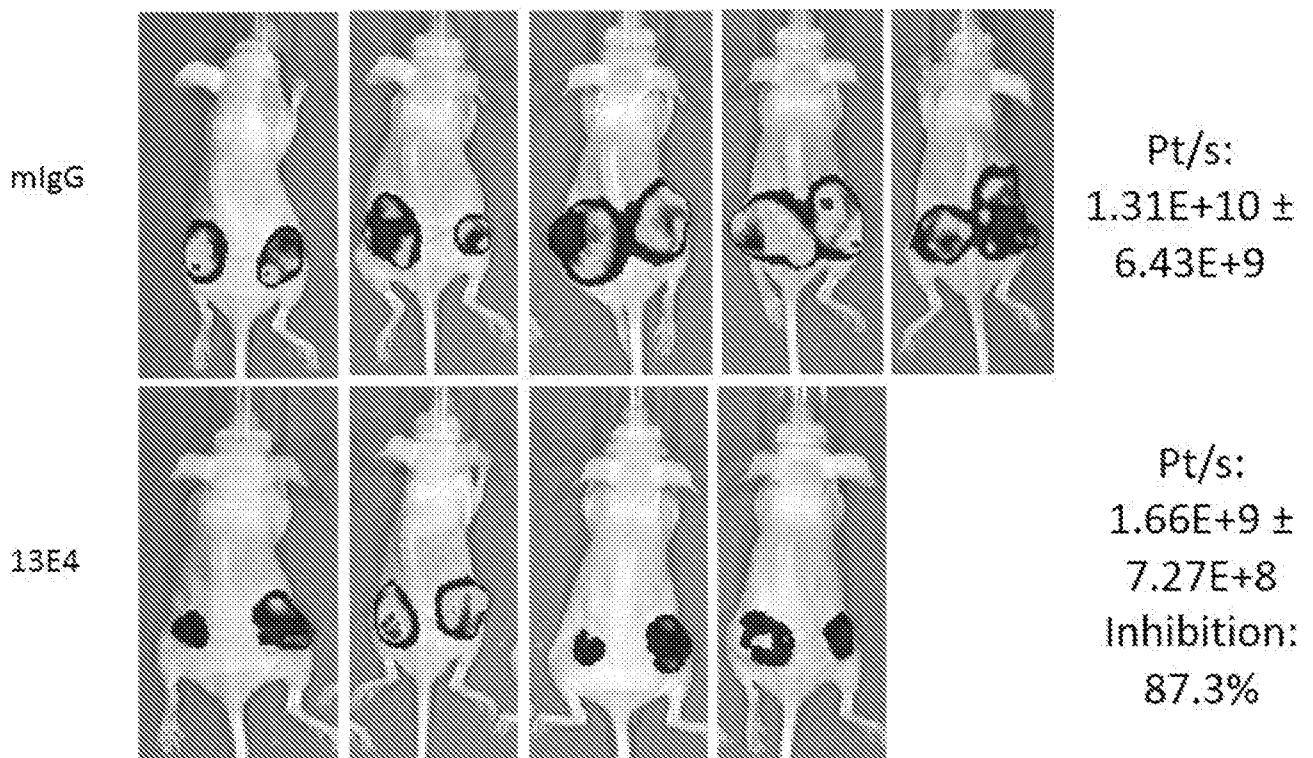


Figure 72C

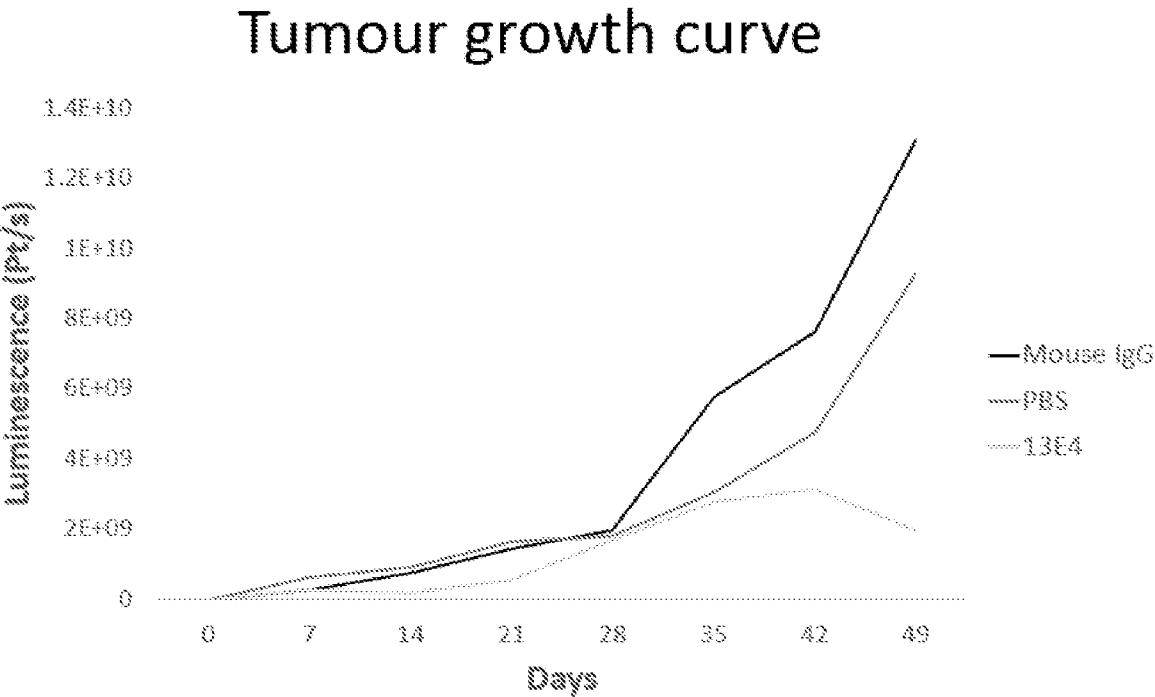


Figure 72D

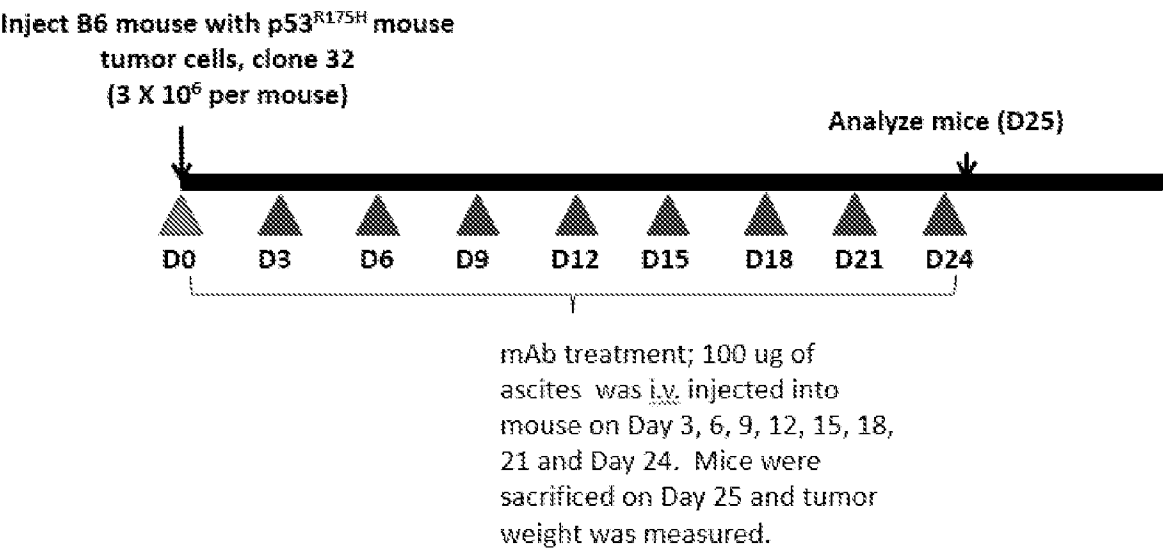


Figure 73A

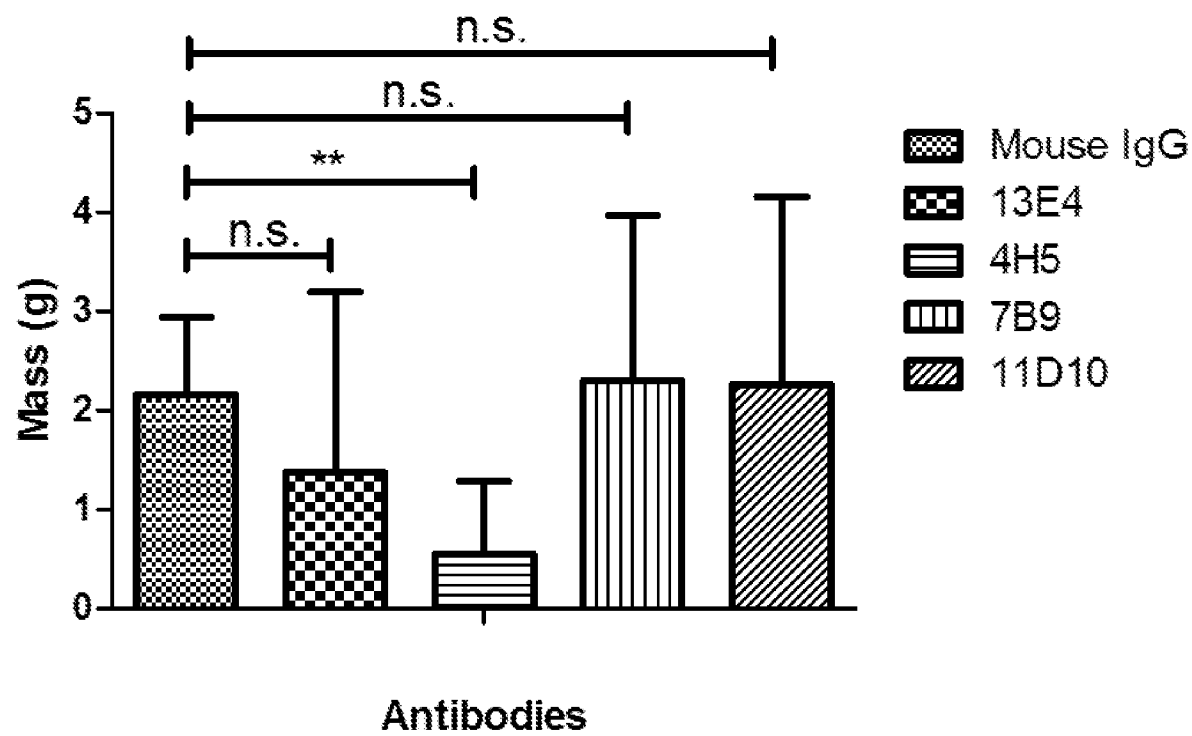


Figure 73B

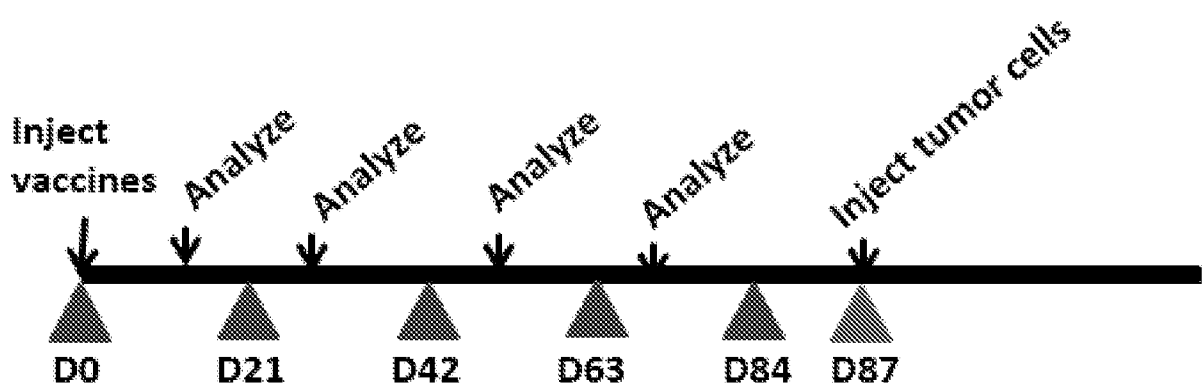


Figure 74A

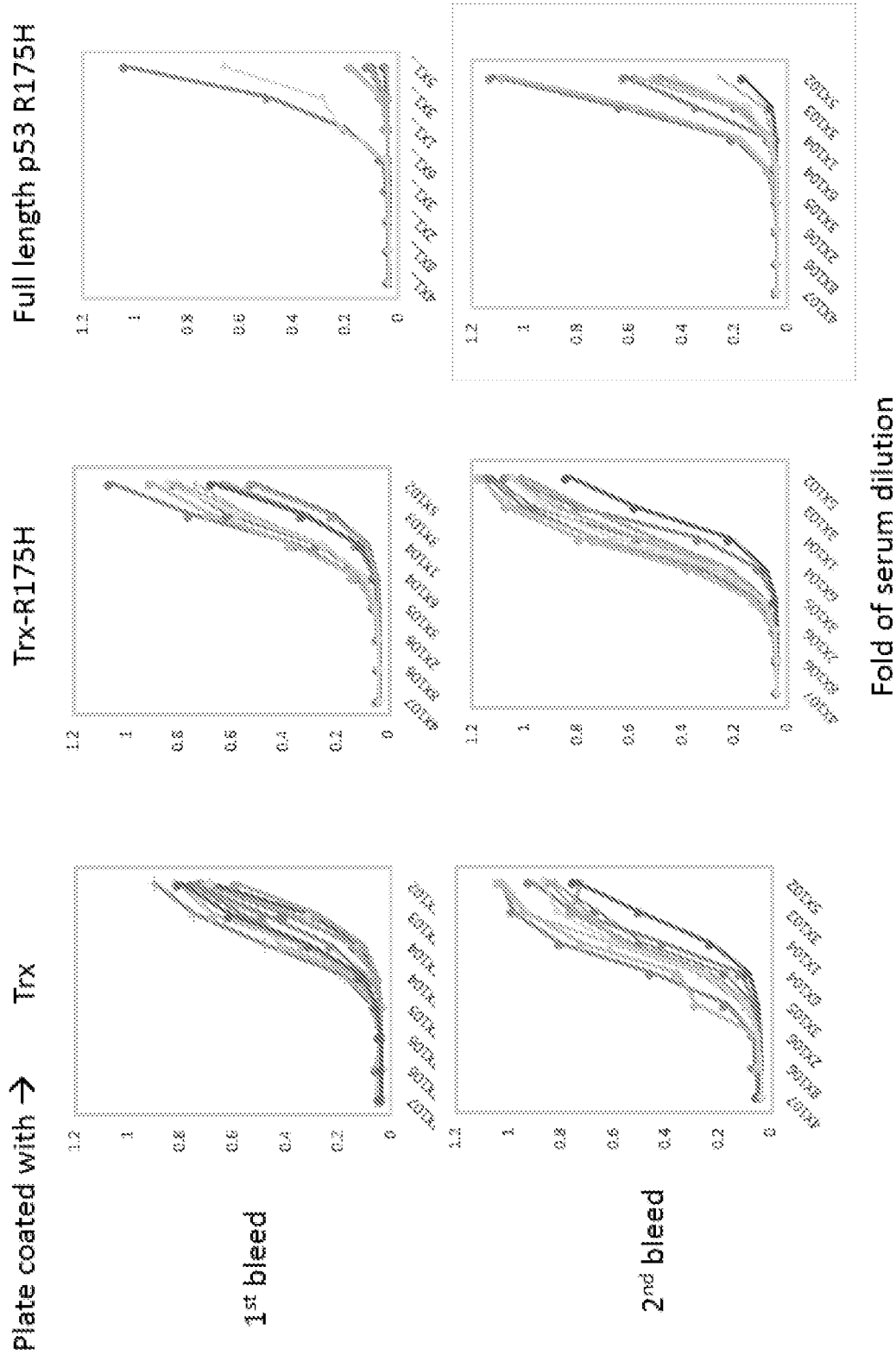


Figure 74B

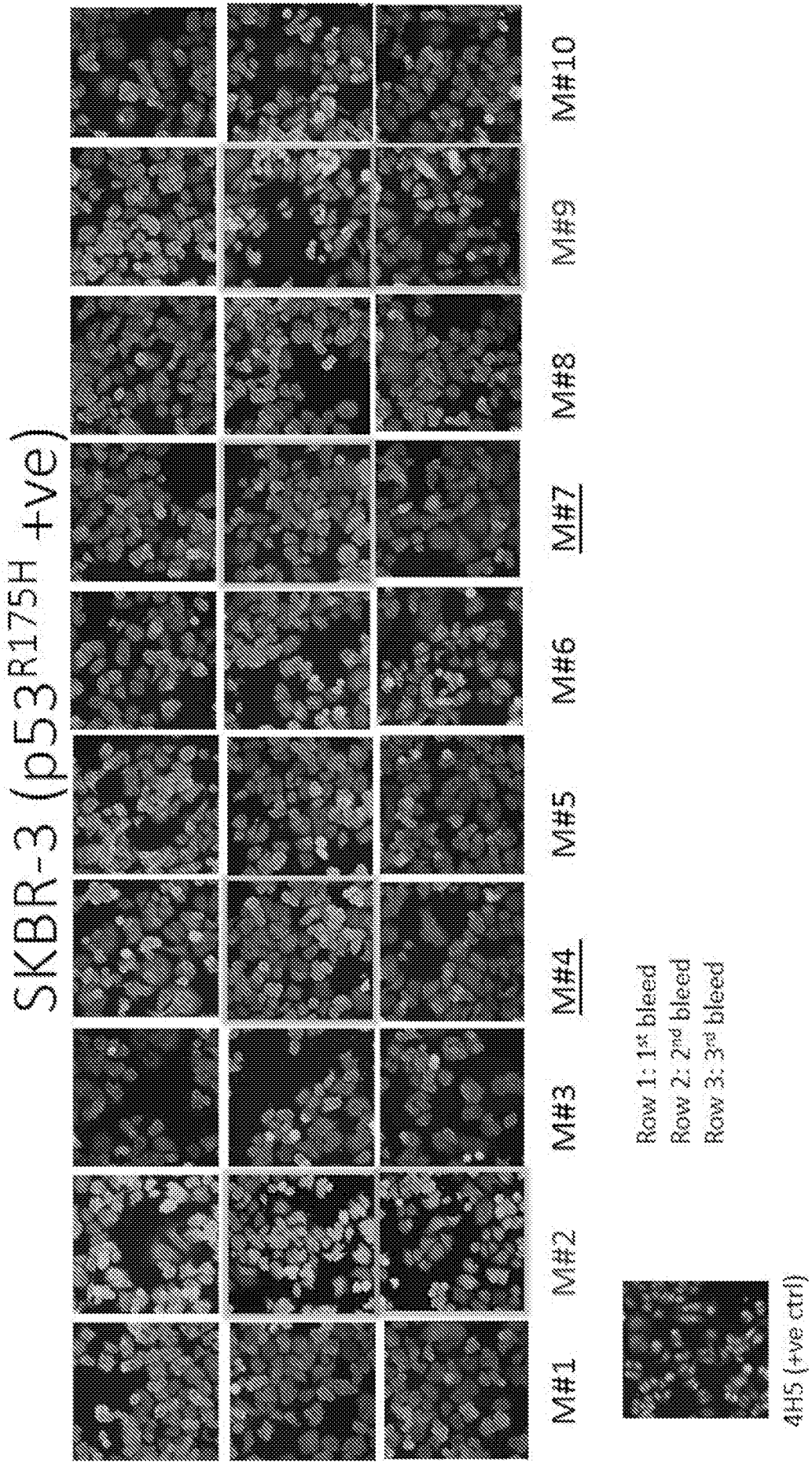


Figure 74C

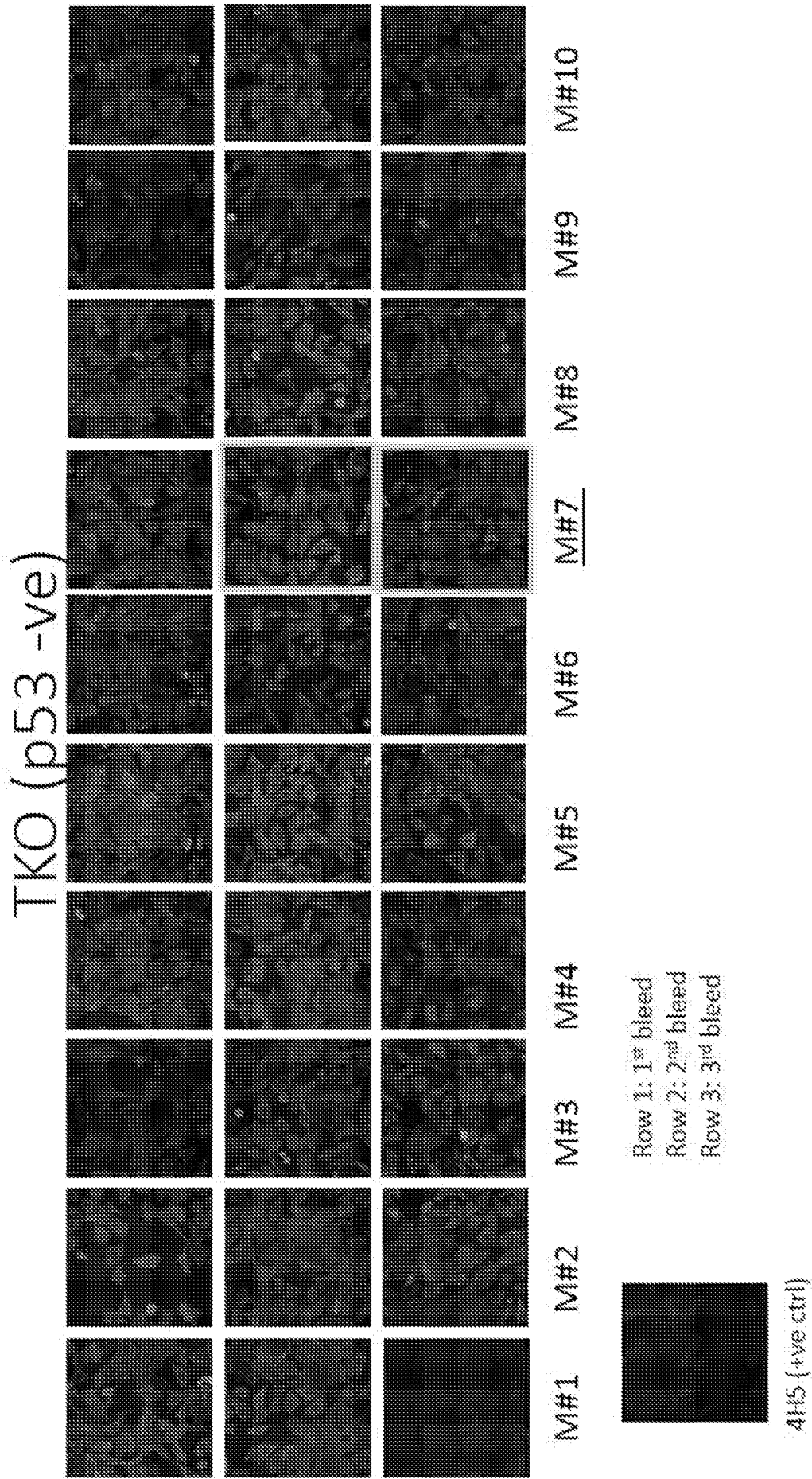


Figure 74D

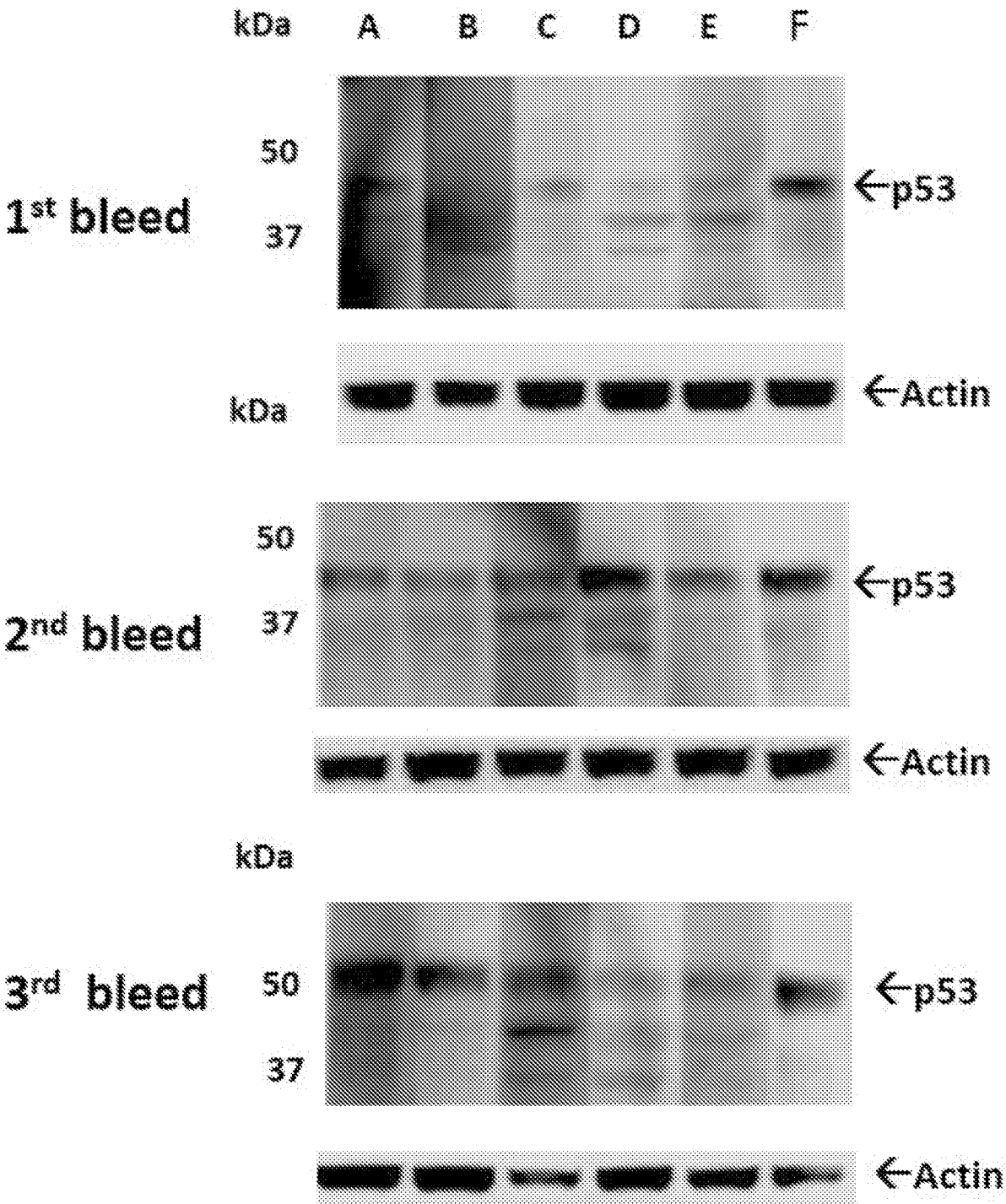


Figure 74E

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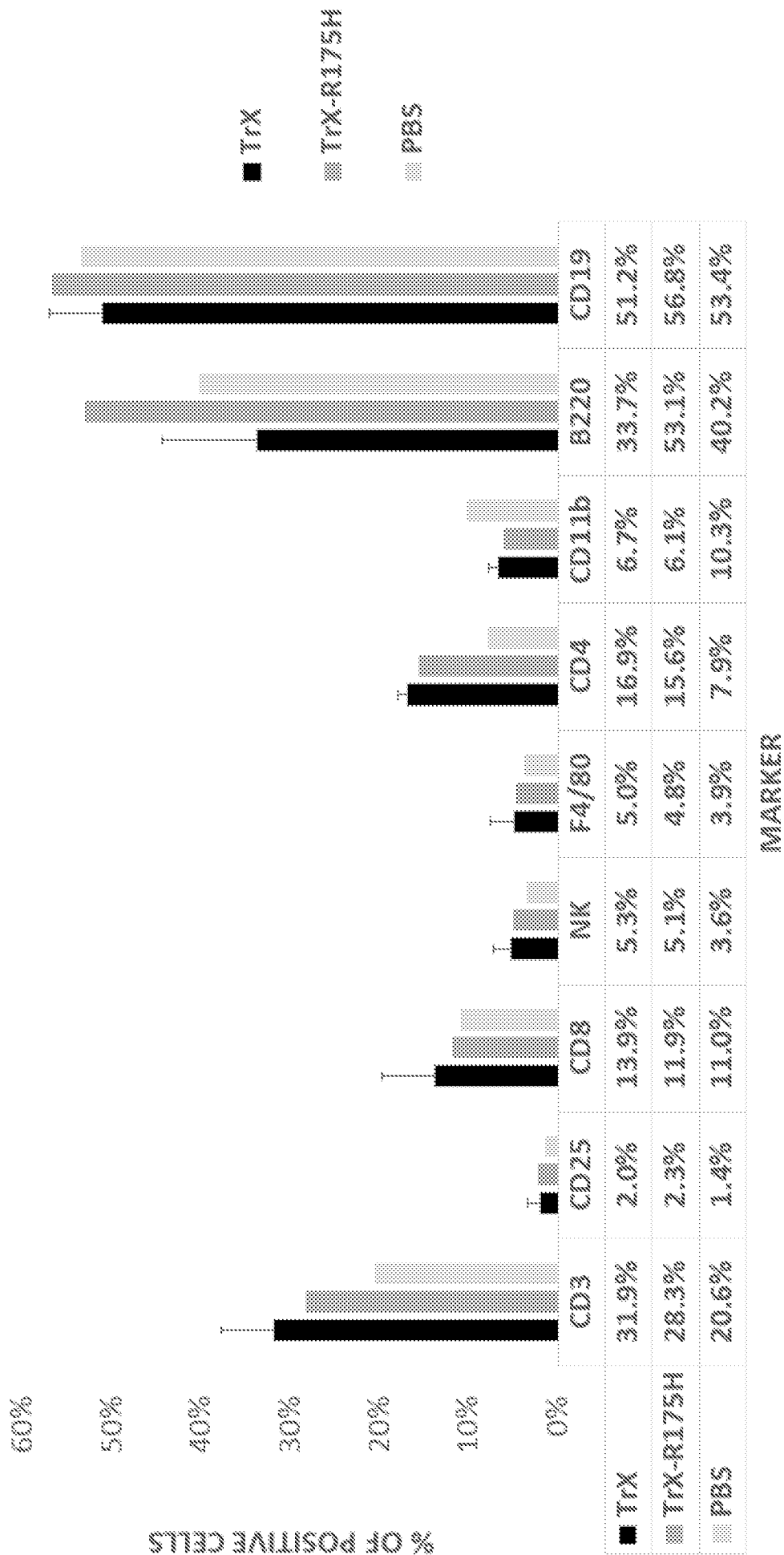


Figure 74F