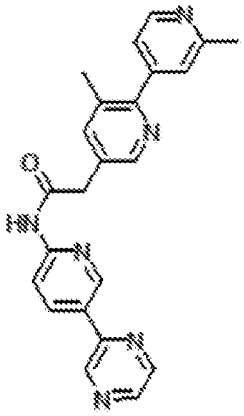
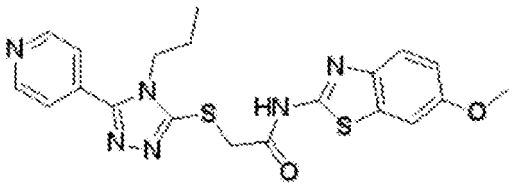
FIGURE 1

1A



COMPOUND A

1B



COMPOUND B

FIGURE 2

Figure 2A

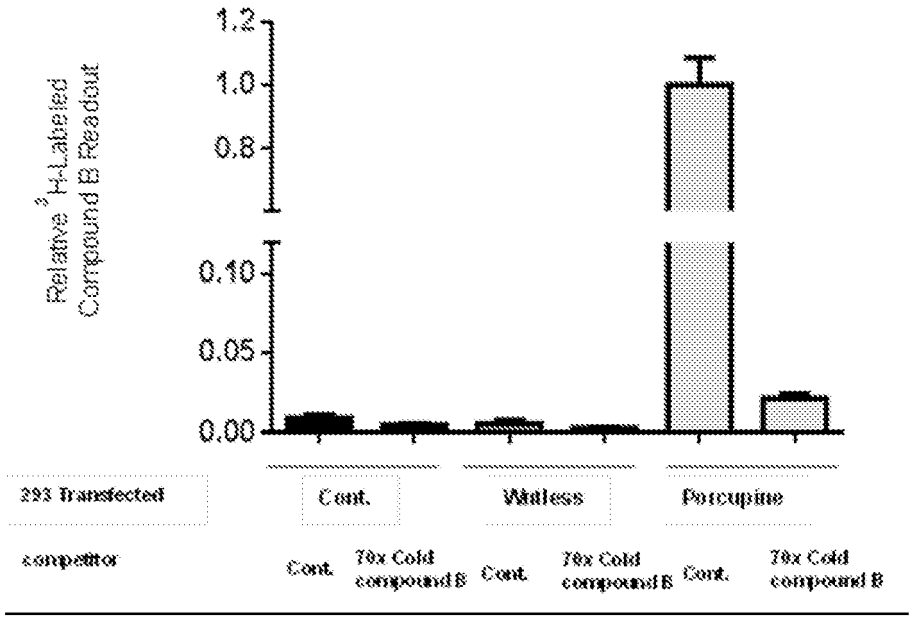


Figure 2B

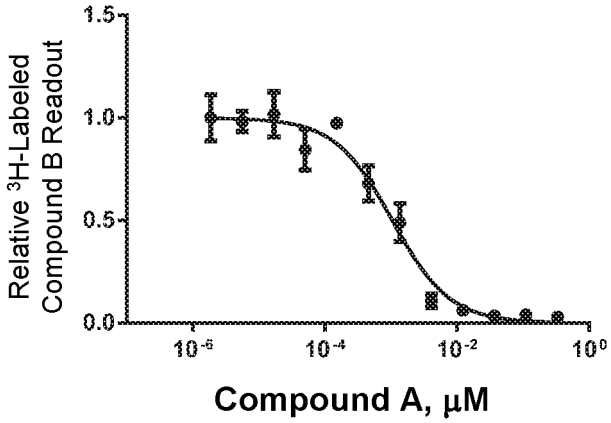


FIGURE 3

Figure 3A

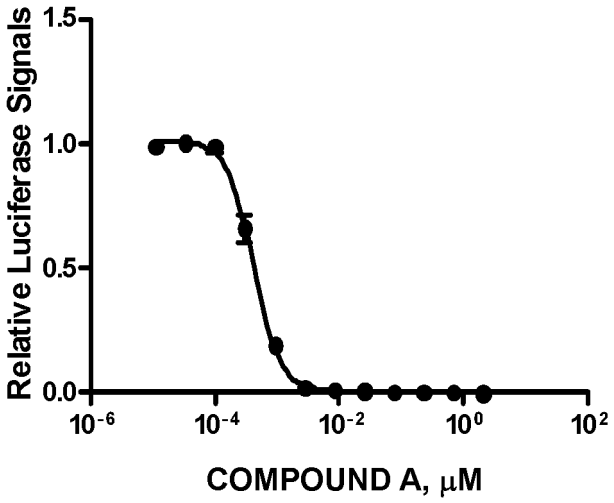


Figure 3B

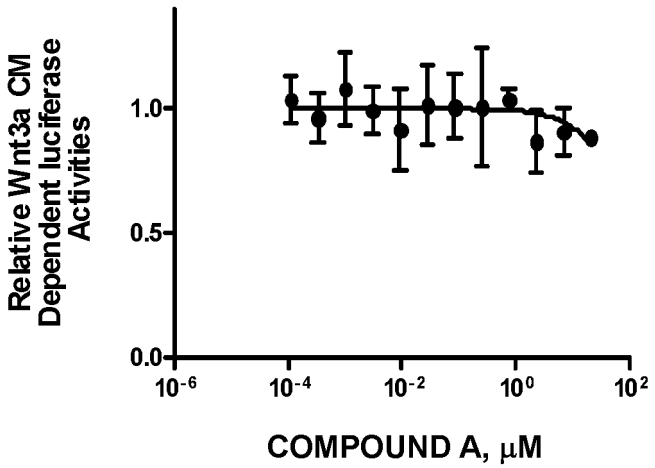


FIGURE 4

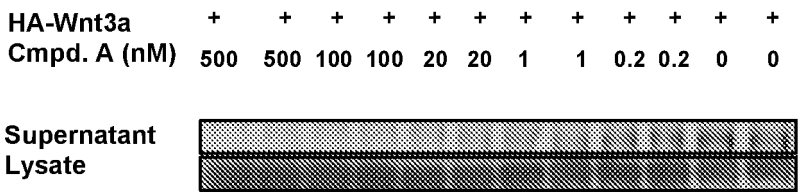

HA-Wnt3a + + + + + + + + + + + +
Cmpd. A (nM) 500 500 100 100 20 20 1 1 0.2 0.2 0 0
Supernatant
Lysate

FIGURE 5

Figure 5A

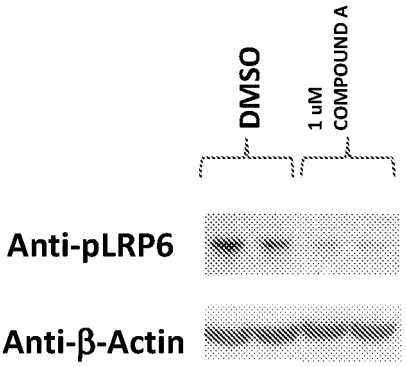


Figure 5B

```
WN10A_H   CHGTSGSCQLKTCW
WN10B_H   CHGTSGSCQFKTCW
WNT6_HU   CHGLSGSCALRTCW
WNT3_HU   CHGLSGSCEVKTCW
WNT3A_H   CHGLSGSCEVKTCW
WNT1_HU   CHGMSGSCTVRTCW
WNT4_HU   CHGVSGSCEVKTCW
WNT7A_H   CHGVSGSCTTKTCW
WNT7B_H   CHGVSGSCTTKTCW
WNT16_H   CHGVSGSCAVKTCW
WNT2_HU   CHGVSGSCTLRTCW
WNT2B_H   CHGVSGSCTLRTCW
WNT5A_H   CHGVSGSCSLKTCW
WNT5B_H   CHGVSGSCSLKTCW
WNT8A_H   CHGISGSCSIQTCW
WNT8B_H   CHGVSGSCTTQTCW
WNT11_H   CHGVSGSCSIRTCW
WNT9A_H   CHGVSGSCTVRTCW
WNT9B_H   CHGVSGSCAVRTCW
          *** ***    ***
```

Figure 5C

Assay	COMPOUND A IC_{50} (nM)
Wnt1 (RGA)	1.1
Wnt2 (RGA)	0.2
Wnt3 (RGA)	0.6
Wnt3a (RGA)	0.9
Wnt6 (RGA)	0.2
Wnt7a (RGA)	2.4
Wnt9a (RGA)	0.05

FIGURE 6

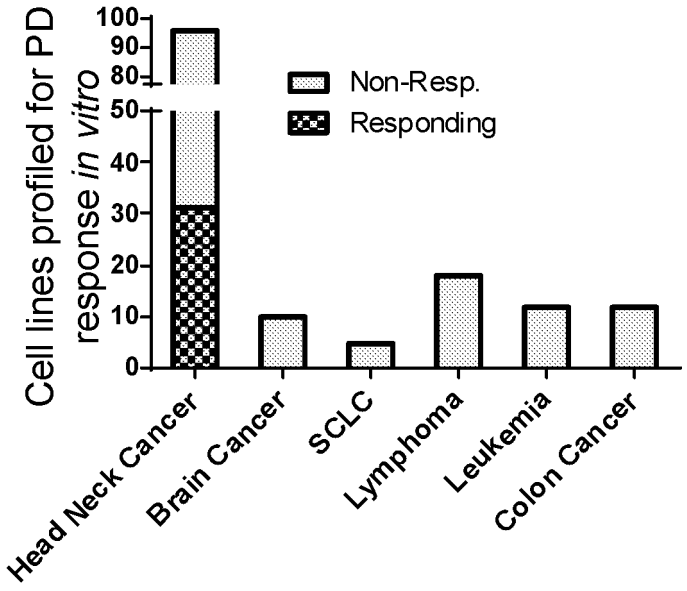

Cell lines profiled for PD response *in vitro*
100
90
80
50
40
30
20
10
0
Non-Resp.
Responding
Head Neck Cancer
Brain Cancer
SCLC
Lymphoma
Leukemia
Colon Cancer

FIGURE 7

No	Head neck cancer cell line names	Axin2 reduction response	Axin2 inhibition (1-treated/control)	No	Head neck cancer cell line names	Axin2 reduction response	Axin2 inhibition (1-treated/control)
1	A-253	No	0	21	UMSCC 10A	Yes	0.5
2	CAL27	Yes	0.7	22	UMSCC 10B	No	0.3
3	Detroit 562	No	0.2	23	UMSCC 11A	Yes	0.6
4	FaDu	No	0	24	UMSCC 11B	Yes	0.6
5	HN30	Yes	0.9	25	UMSCC 12	No	0.4
6	Hs 840.T	No	0	26	UMSCC 13	Yes	0.9
7	SCC-4	No	0.4	27	UMSCC 14A	No	0.0
8	SCC-9	No	0	28	UMSCC 14B	Yes	0.5
9	SCC-25	No	0.1	29	UMSCC 14C	Yes	0.7
10	SNU-1066	No	0.3	30	UMSCC 16	No	0.3
11	SNU-1076	Yes	0.9	31	UMSCC 17A	No	0.3
12	UMSCC 1	Yes	0.9	32	UMSCC 17B	Yes	0.6
13	UMSCC 2	No	0.2	33	UMSCC 19	Yes	0.5
14	UMSCC 3	No	0.0	34	UMSCC 21A	No	0.1
15	UMSCC 4	No	0.3	35	UMSCC 22A	No	0.3
16	UMSCC 5	No	0.3	36	UMSCC 22B	No	0.0
17	UMSCC 6	Yes	0.9	37	UMSCC 23	No	0.3
18	UMSCC 7	No	0.4	38	UMSCC 25	Yes	0.9
19	UMSCC 8	No	0.4	39	UMSCC 26	No	0.3
20	UMSCC 9	Yes	0.8	40	UMSCC 28	Yes	0.7

FIGURE 7 – cont.

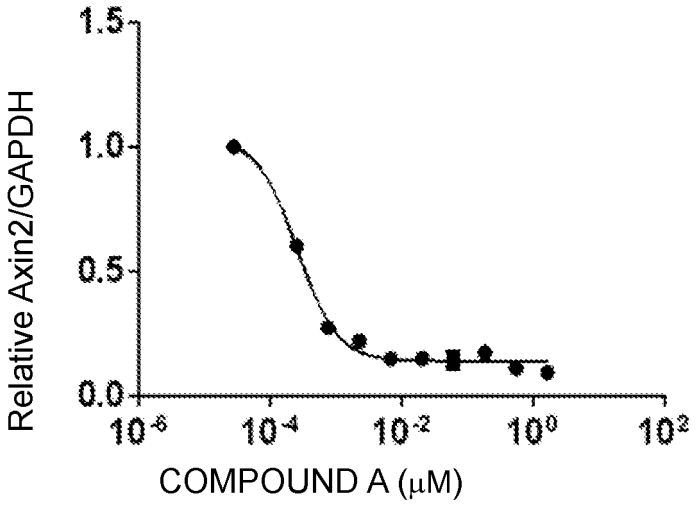
No	Head neck cancer cell line names	Axin2 reduction response	Axin2 inhibition (1-treated/control)	No	Head neck cancer cell line names	Axin2 reduction response	Axin2 inhibition (1-treated/control)
41	UMSCC 29	Yes	0.7	63	UMSCC 53	No	0.1
42	UMSCC 30	No	0.3	64	UMSCC 55	No	0.0
43	UMSCC 31	No	0	65	UMSCC 58	No	0.4
44	UMSCC 33	No	0.2	66	UMSCC 59	Yes	0.7
45	UMSCC 34	Yes	0.9	67	UMSCC 60	No	0.2
46	UMSCC 35	Yes	0.6	68	UMSCC 62	No	0.3
47	UMSCC 36	No	0.0	69	UMSCC 63	Yes	0.8
48	UMSCC 37	No	0.0	70	UMSCC 67	No	0.2
49	UMSCC 38	Yes	0.5	71	UMSCC 69	No	0.4
50	UMSCC 39	No	0.0	72	UMSCC 70	No	0.3
51	UMSCC 40	No	0.3	73	UMSCC 71	No	0.2
52	UMSCC 41	Yes	0.6	74	UMSCC 73B	No	0.4
53	UMSCC 42	No	0.3	75	UMSCC 74A	No	0.0
54	UMSCC 43	Yes	0.7	76	UMSCC 74B	No	0.0
55	UMSCC 44	No	0.0	77	UMSCC 76	Yes	0.7
56	UMSCC 45	Yes	0.5	78	UMSCC 77	No	0.2
57	UMSCC 46	Yes	0.5	79	UMSCC 78	No	0.0
58	UMSCC 47	No	0.3	80	UMSCC 80	No	0.0
59	UMSCC 49	No	0.2	81	UMSCC 81A	No	0.0
60	UMSCC 50	No	0.1	82	UMSCC 81B	No	0.3
61	UMSCC 51	No	0.4	83	UMSCC 83A	No	0.2
62	UMSCC 52	No	0.2	84	UMSCC 83B	No	0.4

FIGURE 7 – cont.

No	Head neck cancer cell line names	Axin2 reduction response	Axin2 inhibition (1-treated/control)	No	Head neck cancer cell line names	Axin2 reduction response	Axin2 inhibition (1-treated/control)
85	UMSCC 85	No	0.0	91	UMSCC 98	No	0.1
86	UMSCC 90	Yes	0.5	92	UMSCC 103	No	0.0
87	UMSCC 92	Yes	0.9	93	UMSCC 104	No	0.0
88	UMSCC 93	Yes	0.6	94	UMSCC 105	No	0.3
89	UMSCC 94	No	0.3	95	UMSCV 1A	No	0.0
90	UMSCC 97	Yes	0.8	96	UMSCV 6	No	0.1

FIGURE 8

8A



8B

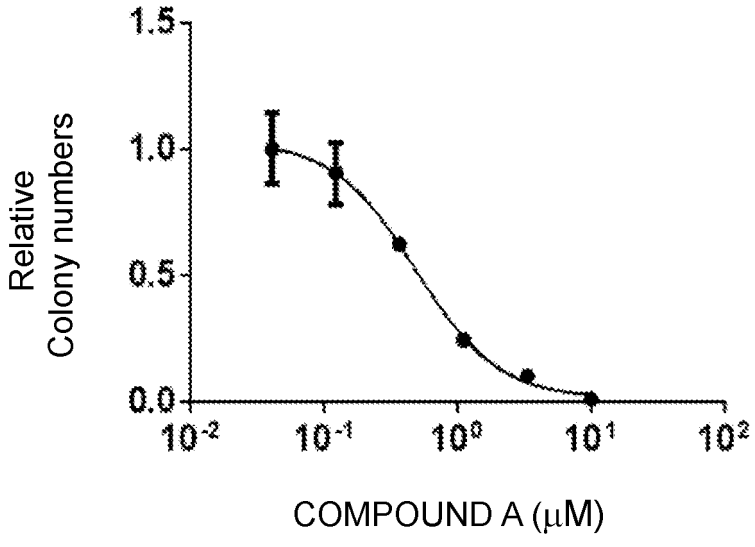
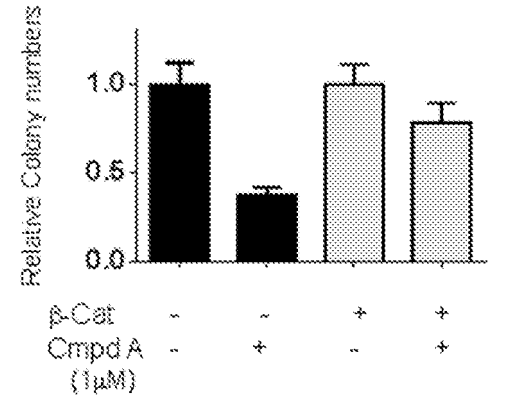
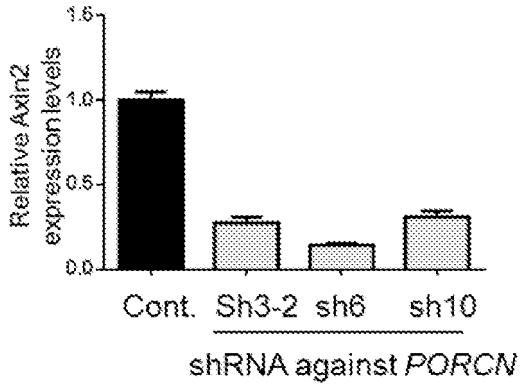


FIGURE 9

9A



9B



9C

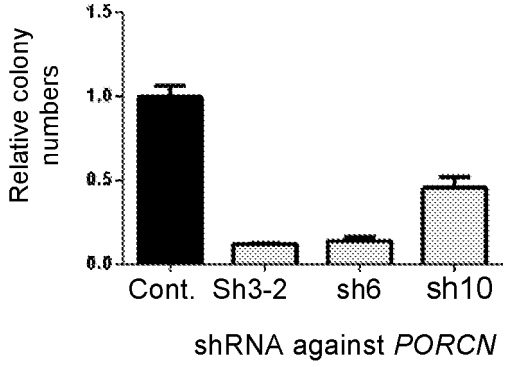
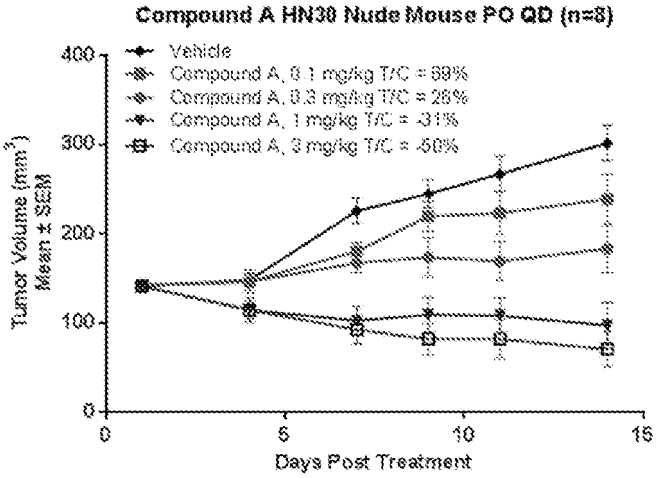
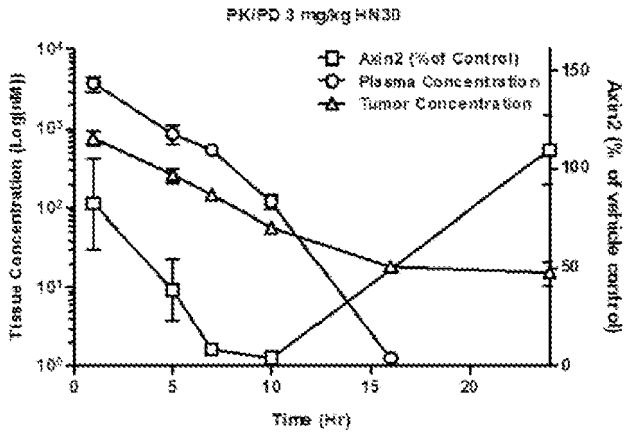


FIGURE 10

10A



10B



10C

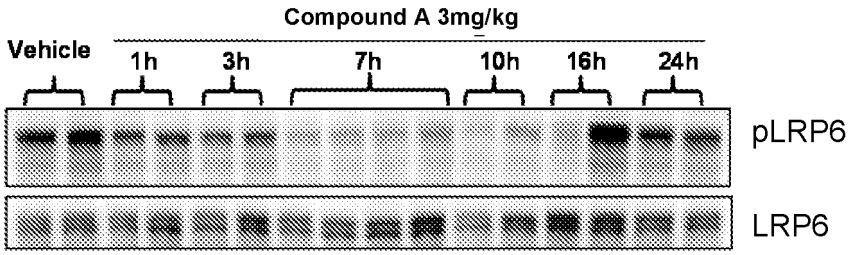


FIGURE 11

Genes	Mutation Occurrence
TP53	27/40 (68%)
CDKN2A	7/40 (18%)
Notch1	10/40 (25%)
PTEN	1/40 (3%)
HRAS	5/40 (13%)
PIK3CA	5/40 (13%)
Notch2	5/40 (13%)
Notch3	2/40 (5%)

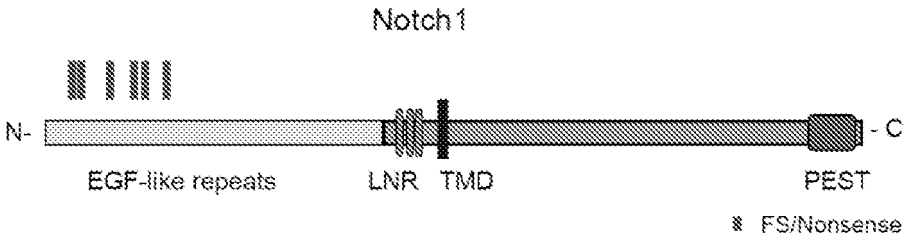
FIGURE 12

Gene	Genomic Change	Amino Acid change	Responsive Mutants	Resistant Mutants	Enrichment Factor
FAM58A	g.chrX:152864477G>GC|g.chrX:152858079GC>G|g.chrX:152864513G>GC	A18fs, A181fs, A6fs	11	1	6.6
FLJ43860	g.chr8:142459777C>CA	L850fs	7	1	4.2
NOTCH1	g.chr9:139411813AC>A|g.chr9:139411793TG>T|g.chr9:139410488C>CT|g.chr9:139417470C>A|g.chr9:139412259CTGGCACGG>C|g.chr9:139417398C>A	E488fs, G192X, E216X, K538fs, A495fs, P460fs,	5	1	3.0
OR7G3	g.chr19:9236916AG>A	A237fs	8	2	2.4
CCDC168	g.chr13:103386417C>A|g.chr13:103384147C>T	E5544X, W6300X	4	1	2.4
ZNF527	g.chr19:37879852C>CTGTG|g.chr19:37879854AT>A	P301fs, Y302fs	7	2	2.1
CDKN2A	g.chr9:21971123TGA>T|g.chr9:21968242C>T|g.chr9:21971186G>A|g.chr9:21971028C>T|g.chr9:21971120G>A	S78fs, W110X, R58X, R80X	4	0	NA

fs: frameshift; X: nonsense mutations

FIGURE 13

13A



13B

Cell Line	Responsive to COMPOUND A	Notch1 mutation
UMSCC 25	Yes	E488fs
UMSCC 28	Yes	A495fs
UMSCC 29	Yes	K538fs
UMSCC 47	No	G192X
UMSCC 59	Yes	P460fs
UMSCC 76	Yes	E216X

13C

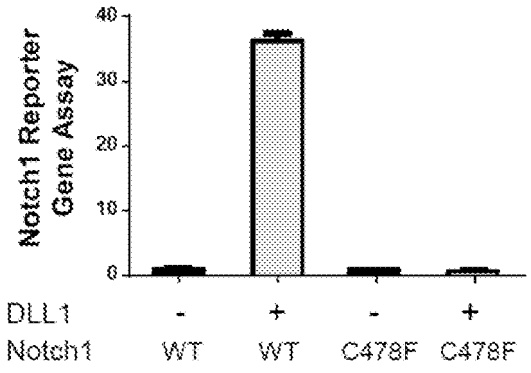
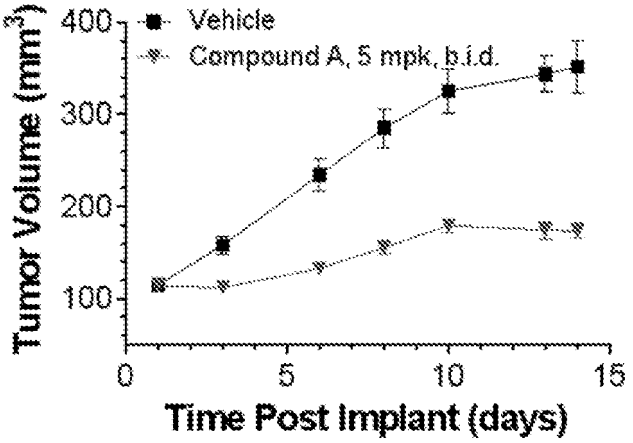


FIGURE 14

14A



14B

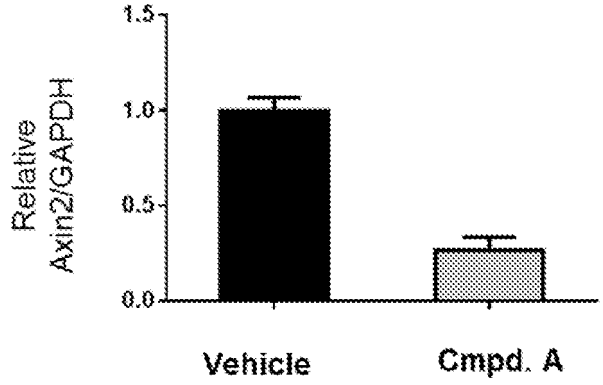


Figure 15

Cell Line	Responsive to COMPOUND A	FAT1 mutation
UMSCC 63	Yes	P2559S
UMSCC 11A	Yes	D4109G
UMSCC 41	Yes	G4147C
UMSCC 35	Yes	P2559L
UMSCC-25	Yes	N524fs
UMSCC-43	Yes	M1150fs
UMSCC 8	No	Q3887X

Figure 16

Cell Line	Responsive to COMPOUND A	HRAS mutation
UMSCC 17B	Yes	Q61L
UMSCC 43	Yes	G12V
UMSCC 63	Yes	G13D
UMSCC 17A	No	Q61L
HN30	Yes	G12D