

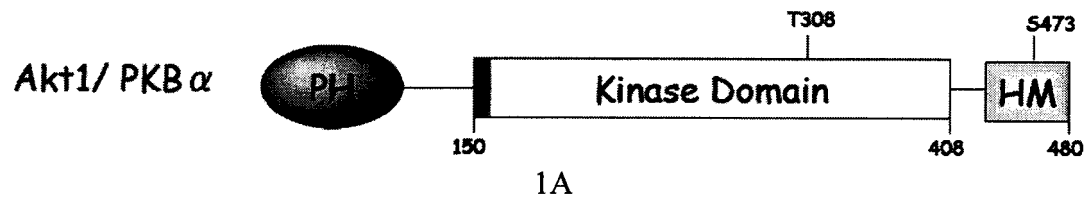
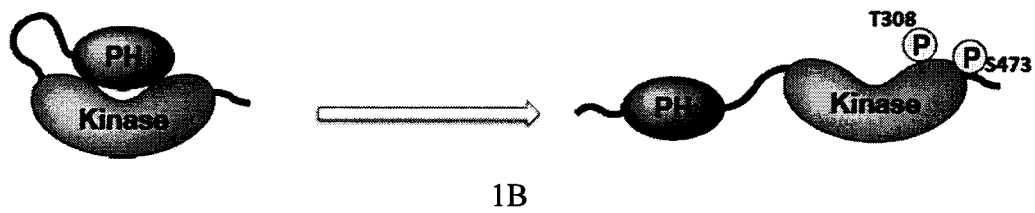
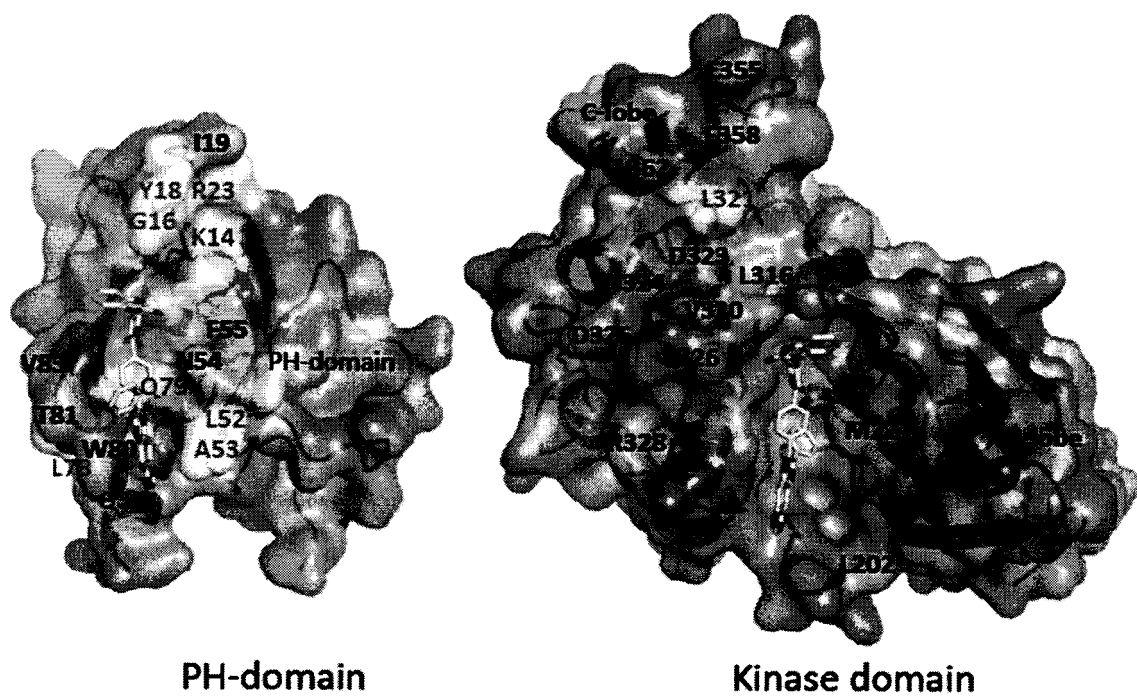


FIG 1

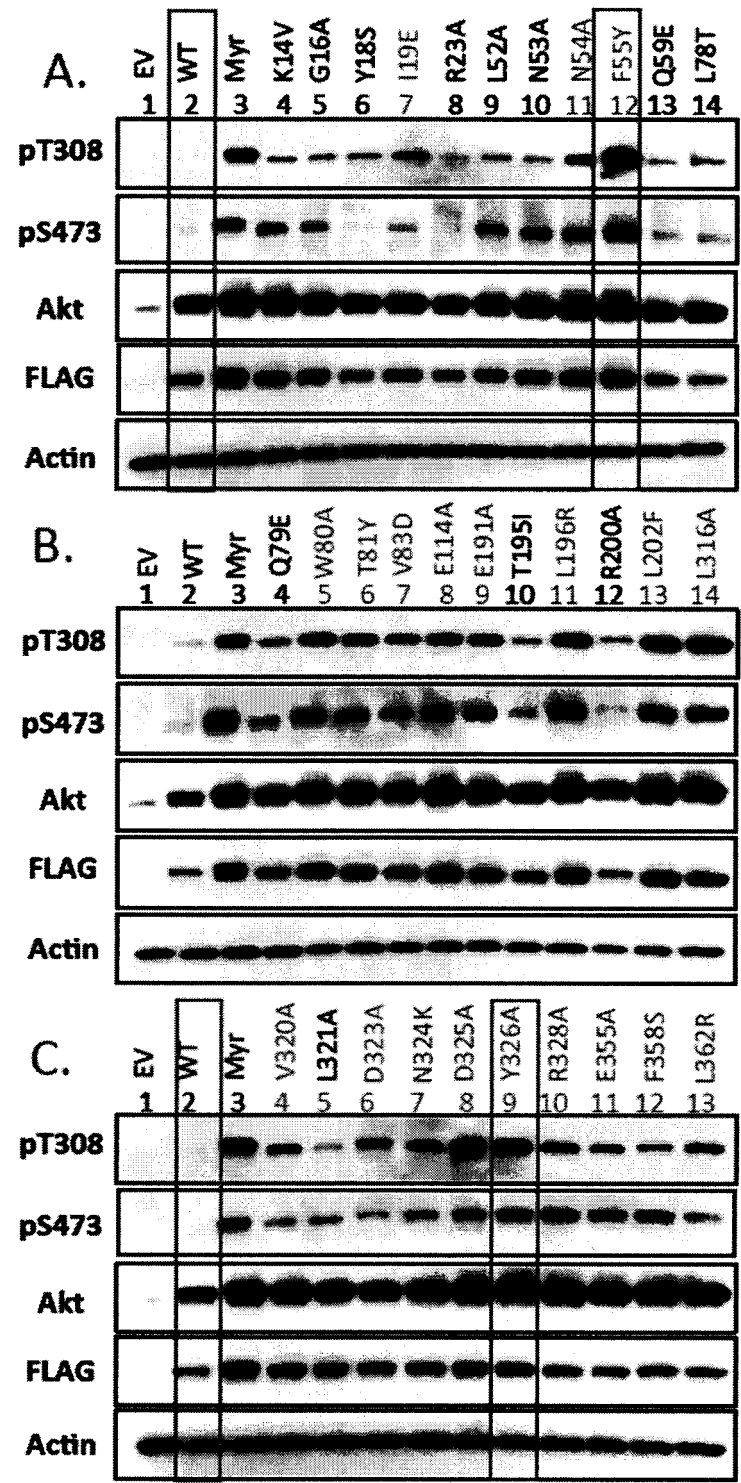


FIG 2

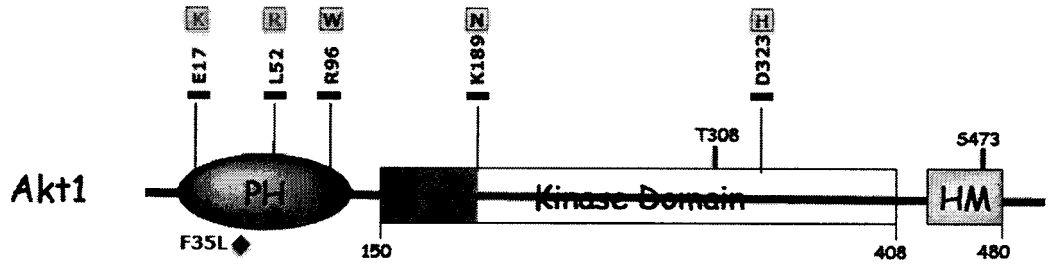


FIG 3

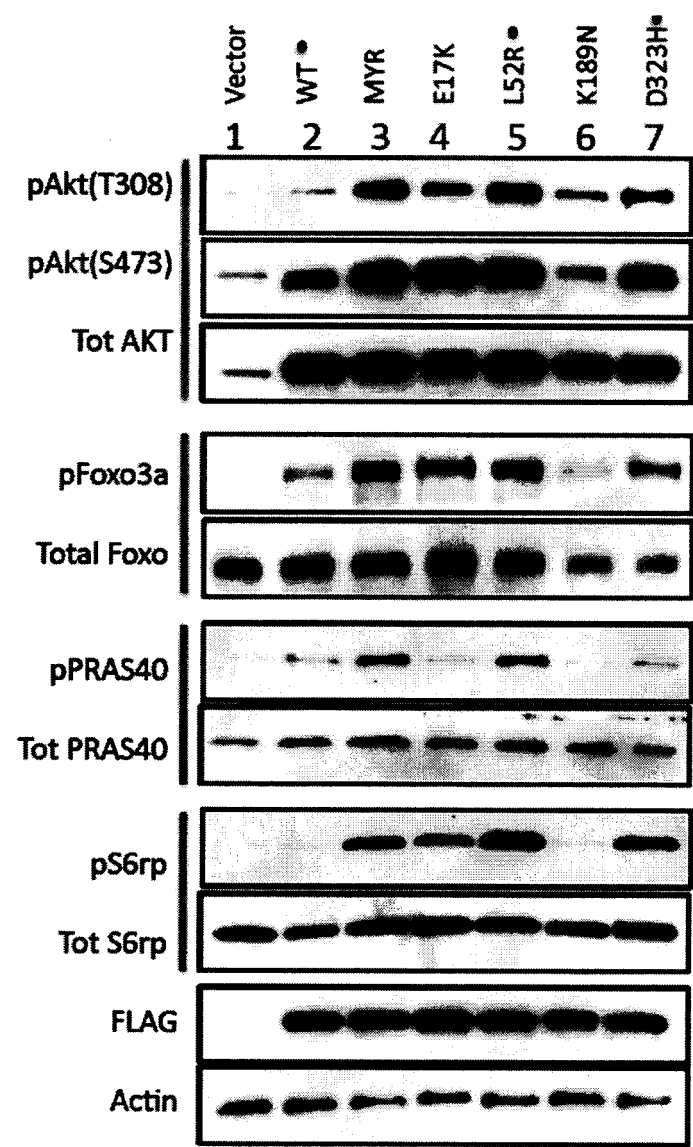


FIG 4

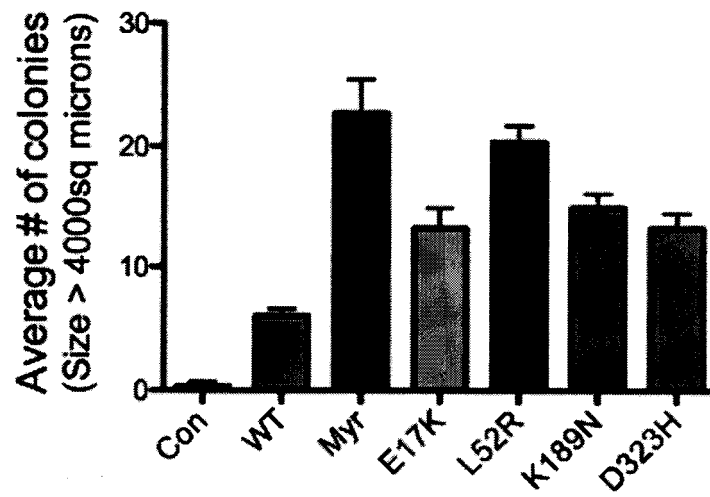


FIG 5

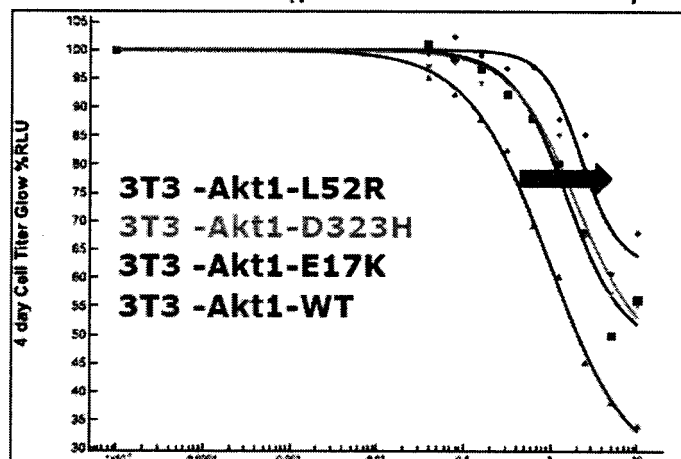
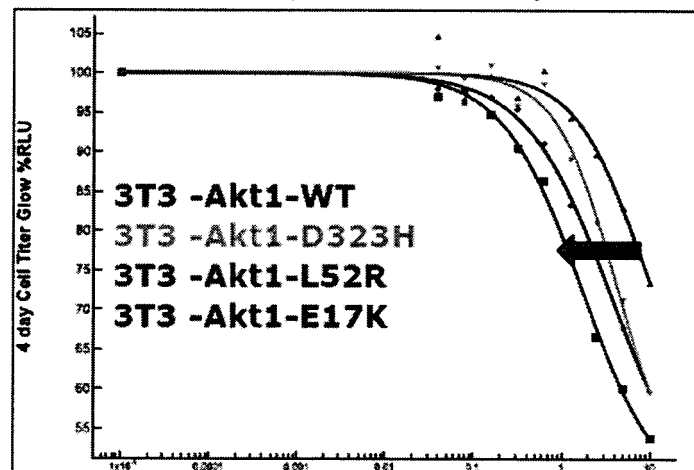
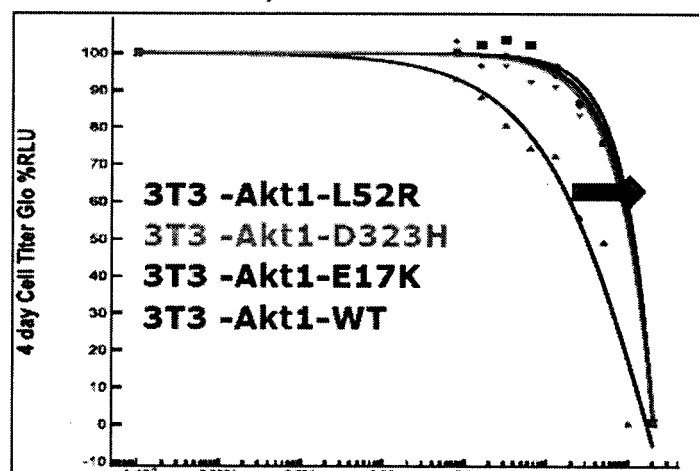
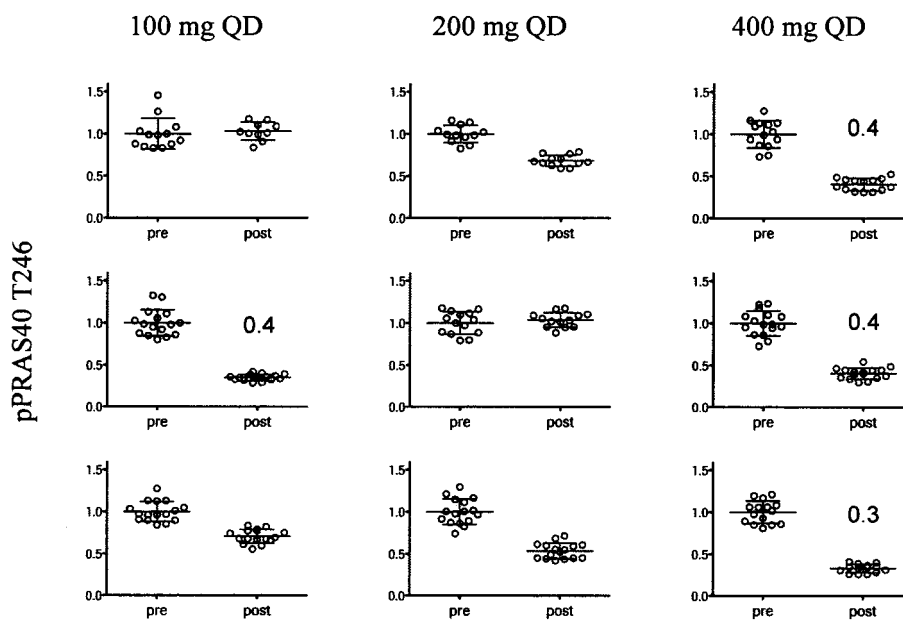
A. GDC-0941 (pan-PI3K inhibitor)**B. GDC-0068 (Akt ATP comp inhibitor)****C. MK2206 (Akt Allosteric inhibitor)**

FIG 6

Changes in pPRAS40 T246 in tumors from treated patients

• All 3 patients in 400 mg cohort show >60% inhibition.

FIG 7

Tumors with activated PI3K/AKT pathway

	Pathway Drivers																		
	BC	NSCLC	Prostate	HNSCC	Gastric	CRC	PDAC	Mela	HCC	Renal	Ovarian	Endo	Bladder	Meso	SCLC	GBM	AML	NHL	MM
PI3K Mut	28%	3%	2%	11%	8%	14-30%			35%	3%	6%	35%	12%			6%			
PI3K Amp		73% sq 24% ad		37%	36%	30%					30%	10%	10-50%						
PTEN Loss	30%	24%	75-100%	29%	40%	10-20%	20-75%	30%	16-40%	35%	50% endo 25% ser	30-80%	40%	0-62%	10-20%	70-90%	4%	5%	6%
AKT Amp.	3%			17-30%AKT2	20%AKT1		20% AKT2				12%								
AKT Mut.	2-8%	1%				1%					2%								
LKB1 Mut		15%																	
KRAS		20%				40%	~90%												
BRAF						15%	2%	50%											
NRAS								15%											

- PTEN loss numbers are from IHC, FISH, aCGH, mutations.
 - Need to be confirmed using validated in-house assays.
- PTEN loss typically associated with advanced disease, poor prognosis (prostate, BrCa, gastric, except ovarian)

FIG 8

High AKT activity predicts sensitivity to GDC-0068

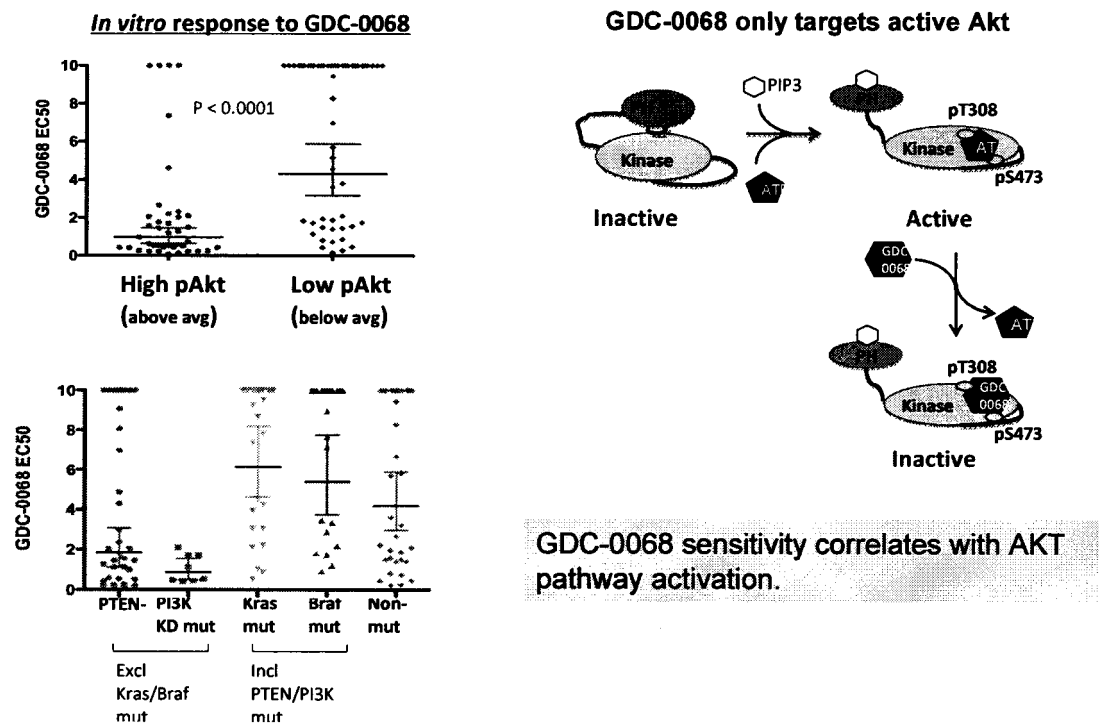


FIG 9

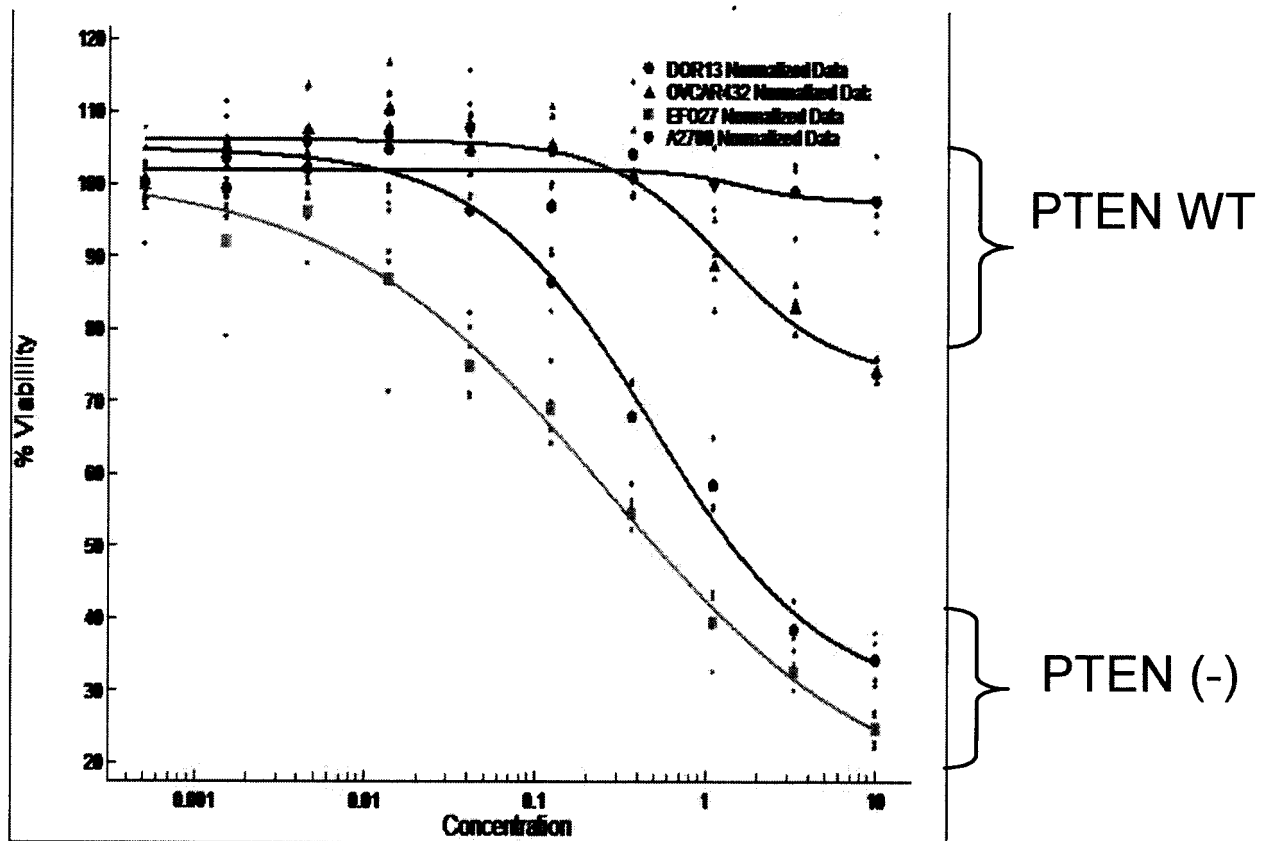


FIG 10

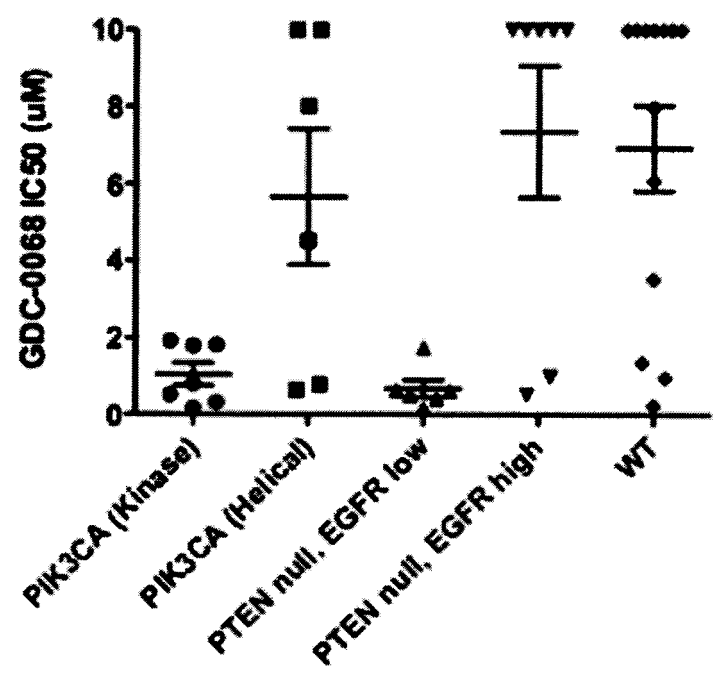


FIG 11

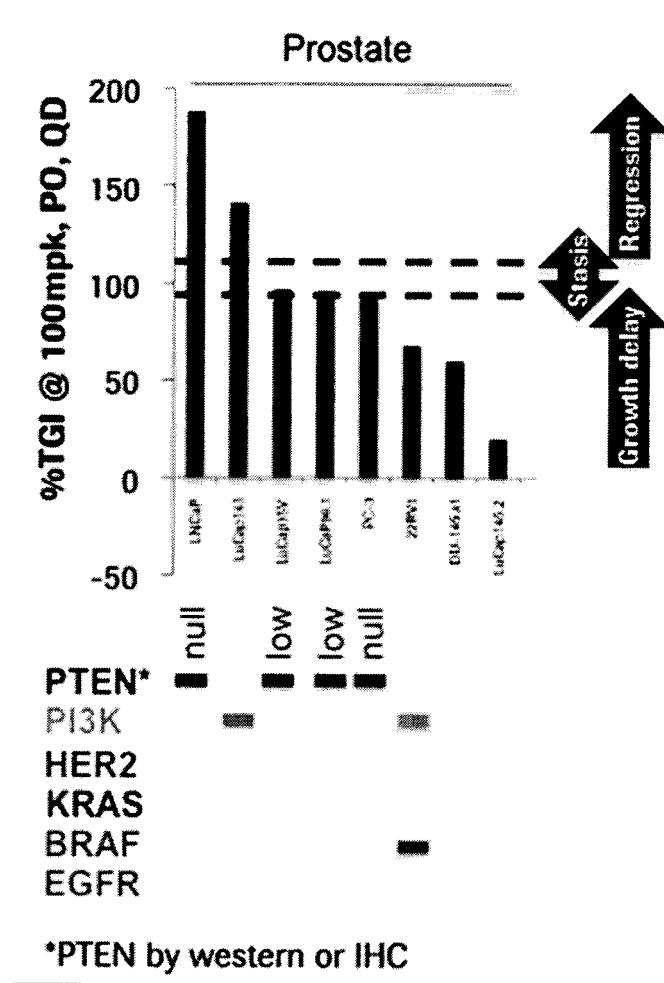


FIG 12A

☐ Robust efficacy(stasis/regression):

- ✓ LnCaP Prostate
- ✓ PC3 Prostate
- ✓ LuCaP35v Prostate (1° tumor)
- ✓ LuCaP141 Prostate (1° tumor)
- ✓ LuCaP96.1 Prostate (1° tumor)
- ✓ U87MG Glioblastoma
- ✓ IGROV-1 Ovarian
- ✓ SKOV3 Ovarian
- ✓ TOV-21G-X1 Ovarian
- ✓ BT474M1 Breast
- ✓ KPL4 Breast
- ✓ MCF7.1 Breast
- ✓ HCC1954.x1 Breast
- ✓ HM7 Colon
- ✓ 537Mel Melanoma
- ✓ HGC-27 Gastric
- MAXF401 Breast (1° tumor)
- Fo5 Breast (Tg Her2+ mouse allograft)

☐ Modest efficacy (growth delay):

- ✓ LuCaP145.2 Prostate (1° tumor)
- ✓ LuCaP77 Prostate (1° tumor)
- ✓ OVCAR3 Ovarian
- ✓ A2058.x1 Melanoma
- ❖ Lovo Colon
- DoHH2 NHL

☐ Little/No activity:

- ❖ Panc-1 Pancreatic
- ❖ NCI H2122 NSCLC
- ❖ MDA-MB-231 Breast

- ✓ PI3K mutation/amplification or PTEN mutation
- ❖ KRas or BRAf mutation

FIG 12B

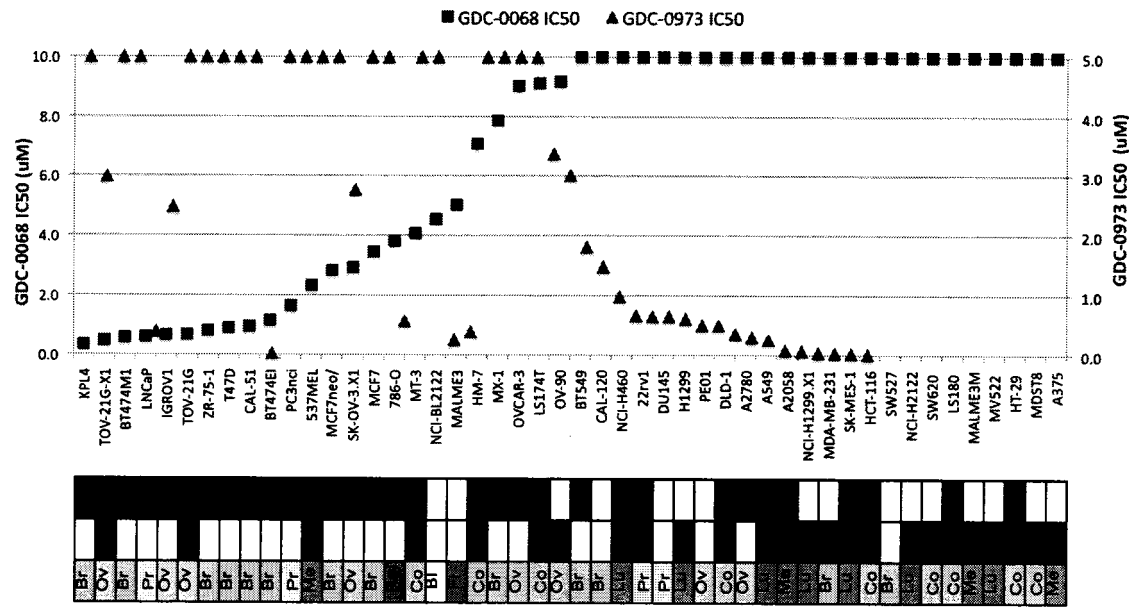


FIG 13

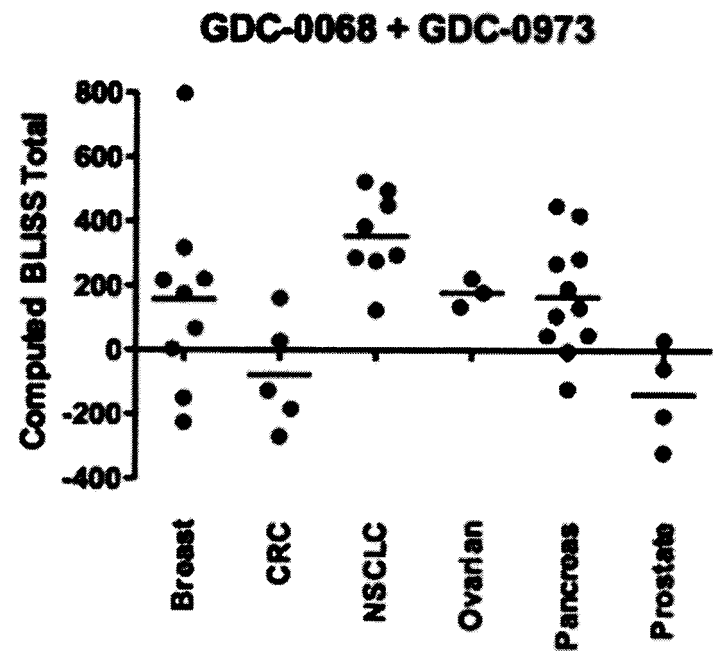


FIG 14

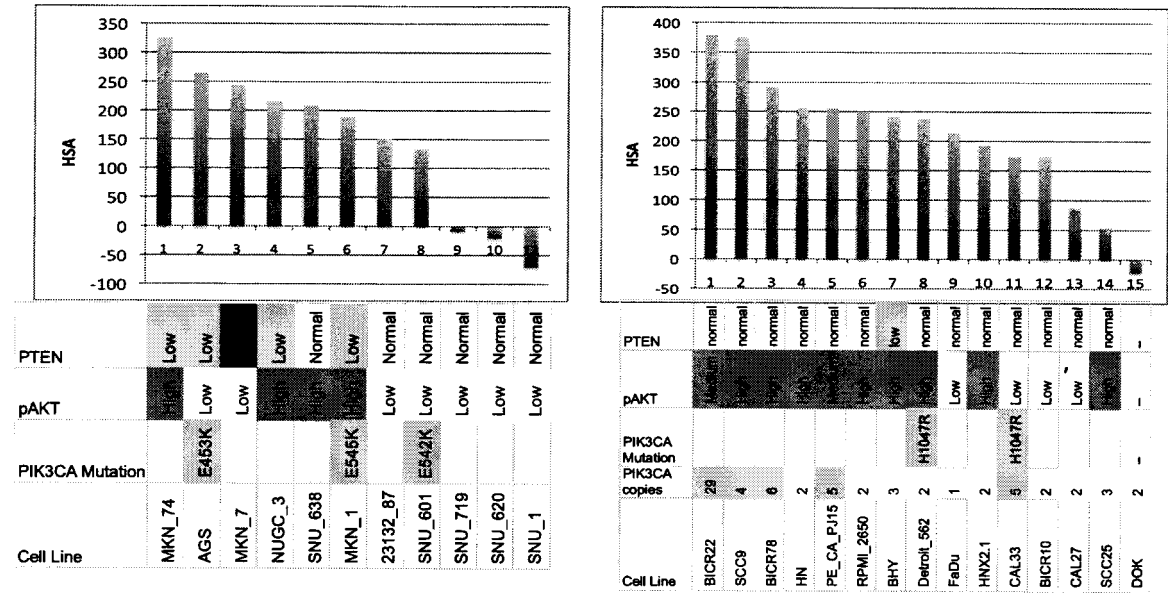


FIG 15

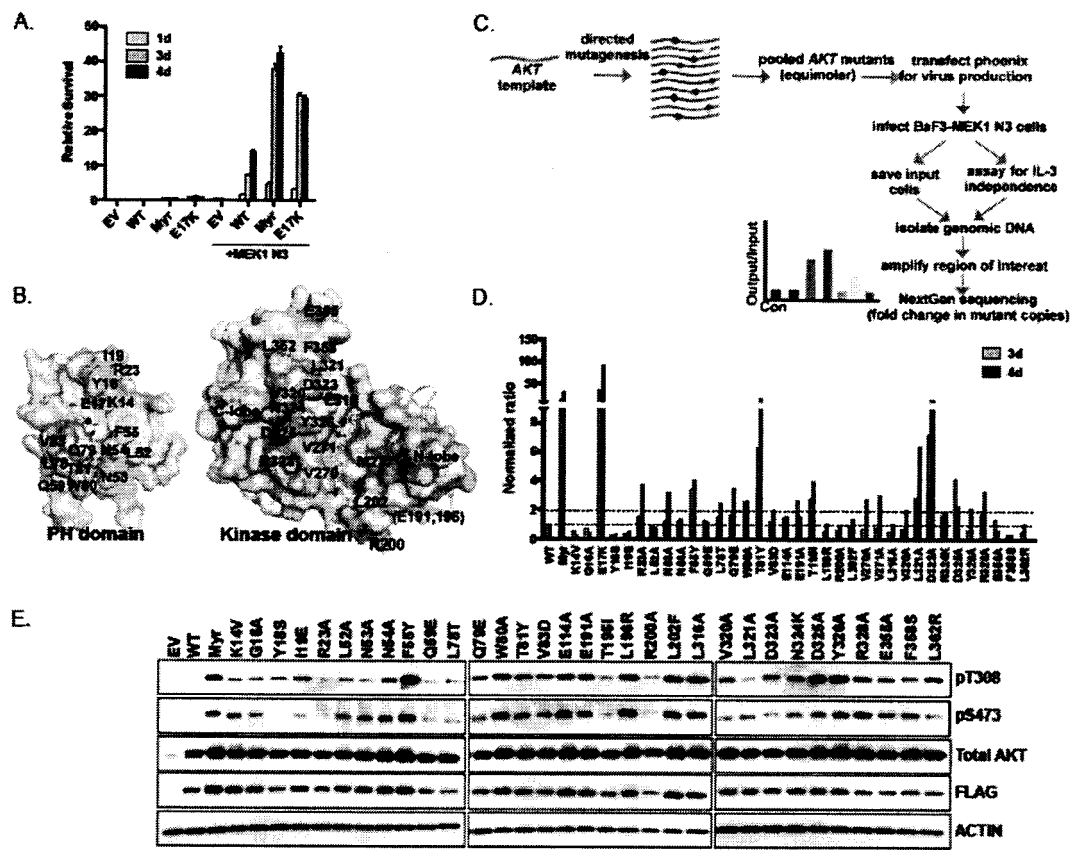


FIG 16

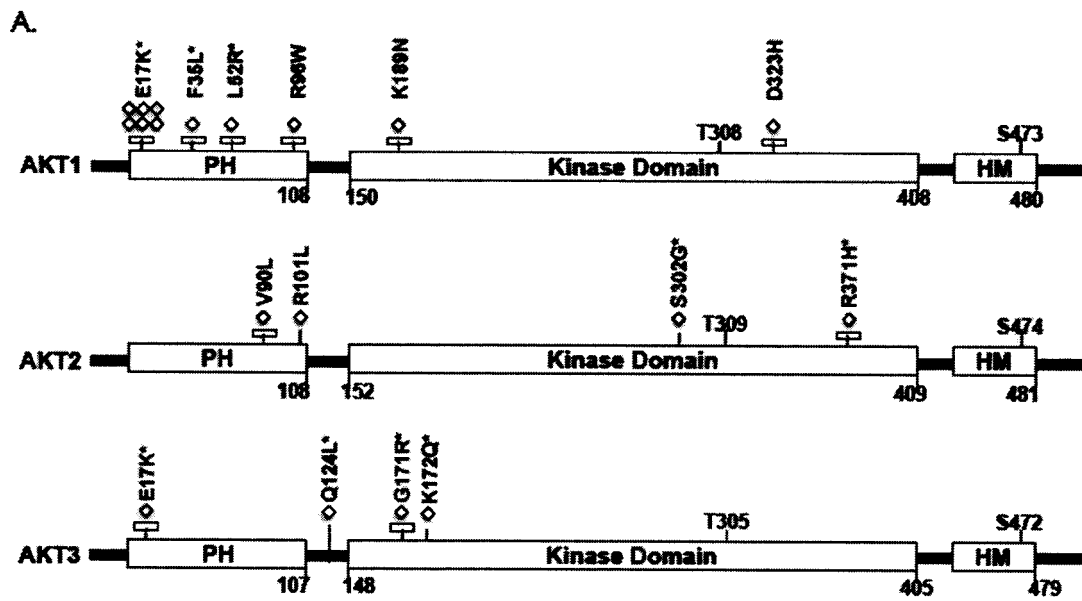


FIG 17