

Supplementary Information

Targeting the Akt/mTOR pathway in Brca1-deficient cancers

Tao Xiang¹, Yunhe Jia¹, David Sherris², Shunqiang Li³, Hanlin Wang⁴, Dongsu Lu⁵ and Qin Yang^{1*}

¹Department of Radiation Oncology, ³Department of Medicine and Siteman Cancer Center, ⁵Department of Pathology and Immunology, Washington University School of Medicine, Saint Louis, MO 63108; ²Paloma Pharmaceuticals, Jamaica Plain, MA; ⁴Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, CA 90048.

Supplementary Table 1. pAkt^{S473} and Brca1 expression in breast cancer samples with clinical-pathological features

	pAkt ^{S473}		Brca1	
	Positive (%)	Negative (%)	Negative (%)	Positive (%)
Total (n=101)	62 (61.39)	39 (38.61)	70 (69.31)	31 (30.69)
Grade				
T1 (n=69)	39 (56.52)	30 (43.48)	46 (66.67)	23 (33.33)
T2 (n=20)	15 (75.00)	5 (25.00)	17 (85.00)	3 (15.00)
T3 (n=12)	8 (66.67)	4 (33.33)	7 (58.33)	5 (41.67)
Tissue type				
Ductal CA (n=75)	45 (60.00)	30 (40.00)	53 (70.67)	22 (29.33)
Lobular CA (15)	10 (66.67)	5 (33.33)	10 (66.67)	5 (33.33)
Mammary CA (n=11)	7 (63.64)	4 (36.36)	5 (45.45)	6 (54.55)
Lymph node metastasis				
None (n=58)	34 (58.62)	24 (41.38)	39 (67.24)	19 (32.76)
Some (n=43)	28 (65.12)	15 (34.88)	31 (72.09)	12 (27.91)
Age				
<59 (n=53)	32 (60.38)	21 (39.62)	34 (64.15)	19 (35.85)
>60 (n=48)	30 (62.50)	18 (37.50)	36 (75.00)	12 (25.00)

Supplementary Table 2. pAkt^{S473} and Brca1 expression in relation to *PIK3CA* mutation and Ki67 expression

N=101	BRCA1			pAKT			BRCA1-negative pAKT-positive		
	n	Positive	Negative	Positive	Negative	P	50	P	
<i>PIK3CA</i>									
Wild-type	55	12	43	26	29	0.08	26	0.8	
Mutant	44	19	25	34	10		23		
Unknown	2		2	2			1		
<i>Ki67</i>									
Positive	61	14	47	43	18	0.06	30	0.06	
Negative	36	16	20	17	19		18		
Unknown	4	1	3	2	2		2		

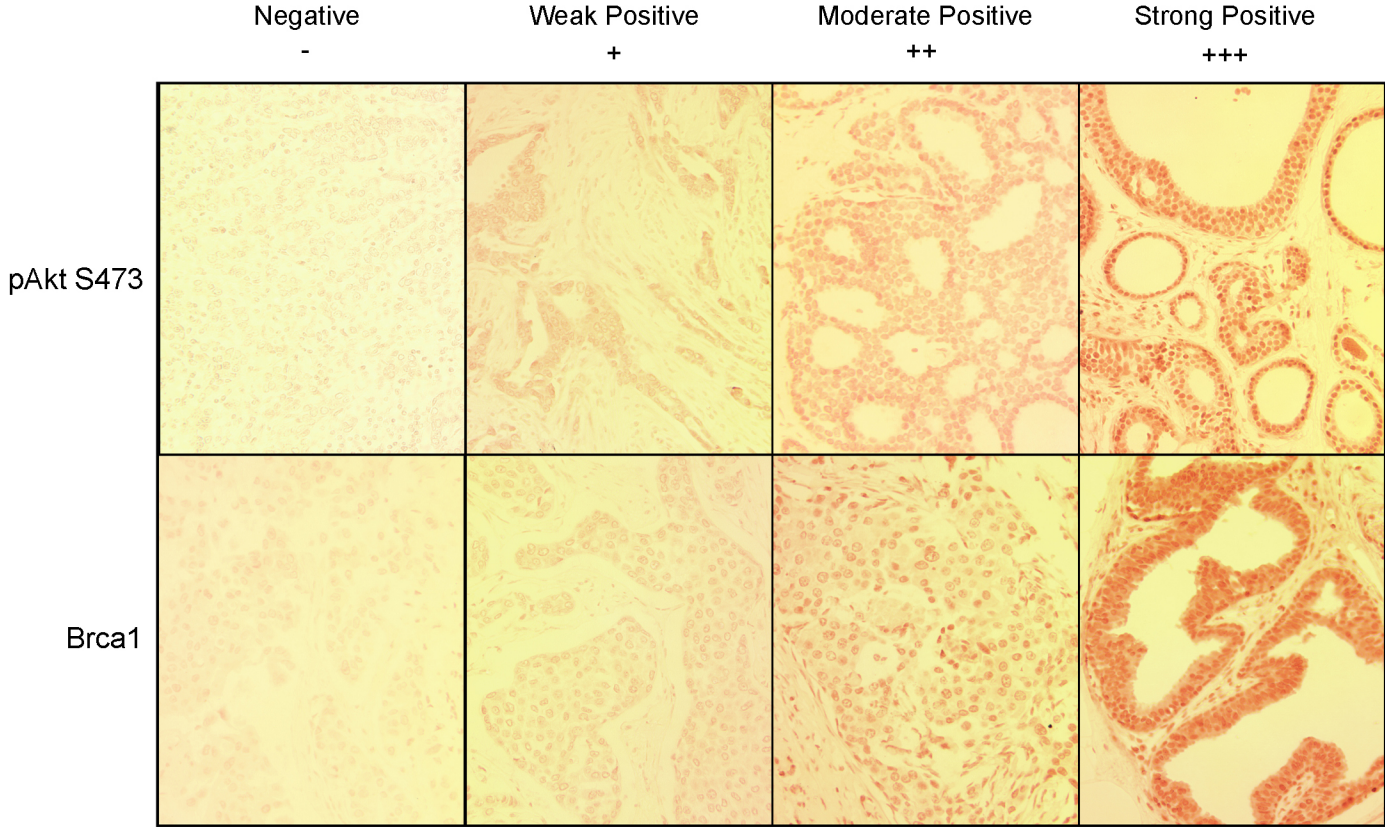
Supplementary figure legends

Supplementary Figure 1. Immunohistochemistry staining of pAkt (S473) and Brca1 in breast cancer tissue samples. Upper panel showed the different intensity of pAkt (S473) and lower panel for Brca1. Original magnification 200×.

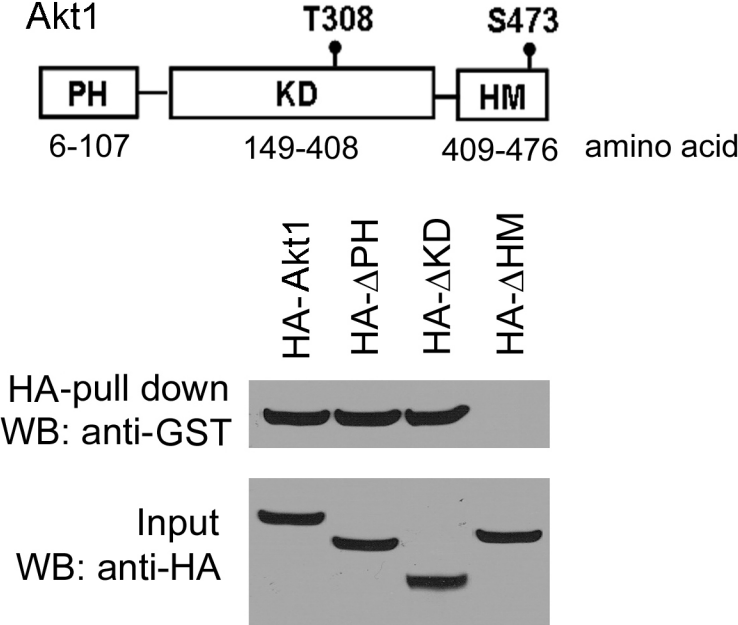
Supplementary Figure 2. Mapping the Brca1 binding domains of Akt1. MEFs were transfected with HA-tagged full-length or deletion fragments from three functional domains of Akt1. The cell lysates were incubated with GST-Brca1 BRCT protein. The complex was eluted and analyzed by Western blotting (WB) with anti-GST or anti-HA antibody.

Supplementary Figure 3. Haematoxylin and Eosin stain for *Brca1^{tr/tr}* MEF graft tumors in mice. The xenograft tumors were stained as homogeneous cell mass. The tumor phenotypes did not show difference in *Brca1^{tr/tr}* and *Brca1^{tr/tr}* with shAkt expression xenograft tumors.

Supplementary Fig. 1



Supplementary Fig. 2



Supplementary Fig.3

