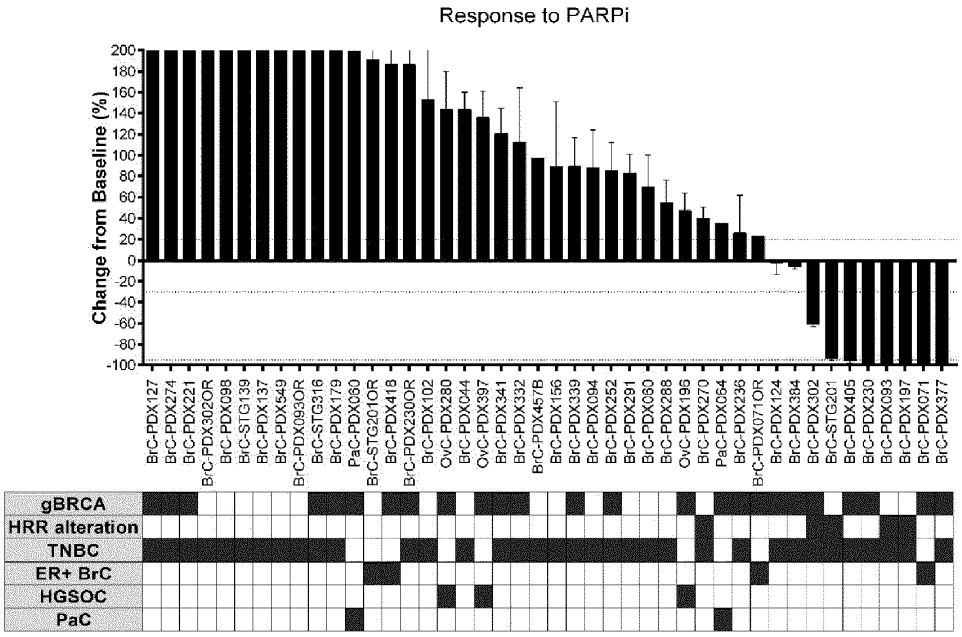

Response to PARPi
Change from Baseline (%)
200
180
160
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
BrC-PDX127
BrC-PDX274
BrC-PDX221
BrC-PDX302OR
BrC-PDX098
BrC-STG139
BrC-PDX137
BrC-PDX549
BrC-PDX093OR
BrC-STG316
BrC-PDX179
PaC-PDX060
BrC-STG201OR
BrC-PDX418
BrC-PDX230OR
BrC-PDX102
OvC-PDX280
BrC-PDX044
OvC-PDX397
BrC-PDX341
BrC-PDX332
BrC-PDX457B
BrC-PDX156
BrC-PDX339
BrC-PDX094
BrC-PDX252
BrC-PDX291
BrC-PDX060
BrC-PDX288
OvC-PDX196
BrC-PDX270
PaC-PDX064
BrC-PDX236
BrC-PDX071OR
BrC-PDX124
BrC-PDX384
BrC-PDX302
BrC-STG201
BrC-PDX405
BrC-PDX230
BrC-PDX093
BrC-PDX197
BrC-PDX071
BrC-PDX377
gBRCA
HRR alteration
TNBC
ER+ BrC
HGSOC
PaC

Fig. 1

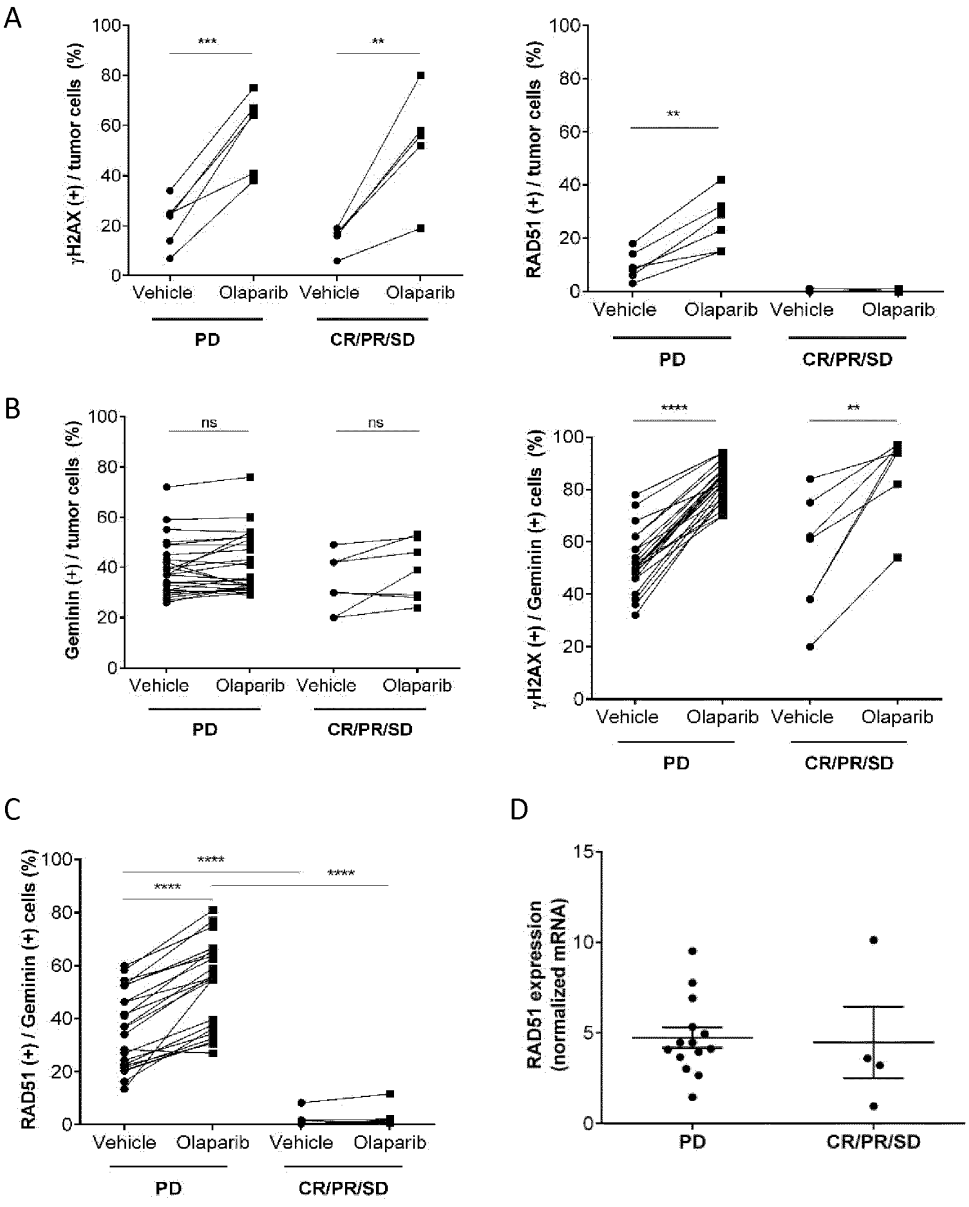

A
γH2AX (+) / tumor cells (%)
***
**
Vehicle
Olaparib
Vehicle
Olaparib
PD
CR/PR/SD
RAD51 (+) / tumor cells (%)
**
B
Geminin (+) / tumor cells (%)
ns
ns
γH2AX (+) / Geminin (+) cells (%)
****
**
C
RAD51 (+) / Geminin (+) cells (%)
****
****
****
D
RAD51 expression (normalized mRNA)

Fig. 2

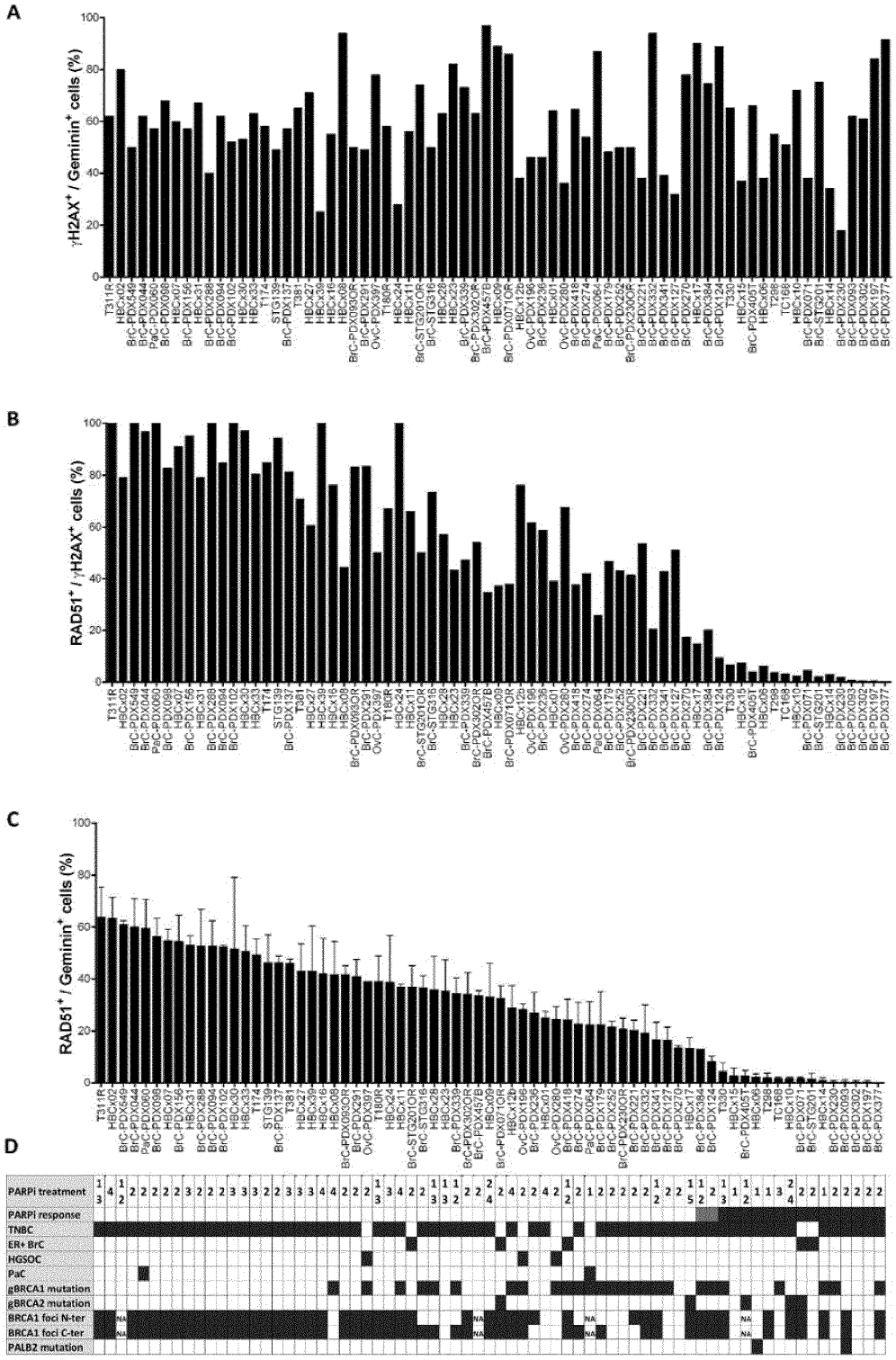

A
γH2AX+ / Geminin+ cells (%)
B
RAD51+ / γH2AX+ cells (%)
C
RAD51+ / Geminin+ cells (%)
D
PARPi treatment
PARPi response
TNBC
ER+ BrC
HGSOC
PaC
gBRCA1 mutation
gBRCA2 mutation
BRCA1 foci N-ter
BRCA1 foci C-ter
PALB2 mutation

Fig. 3

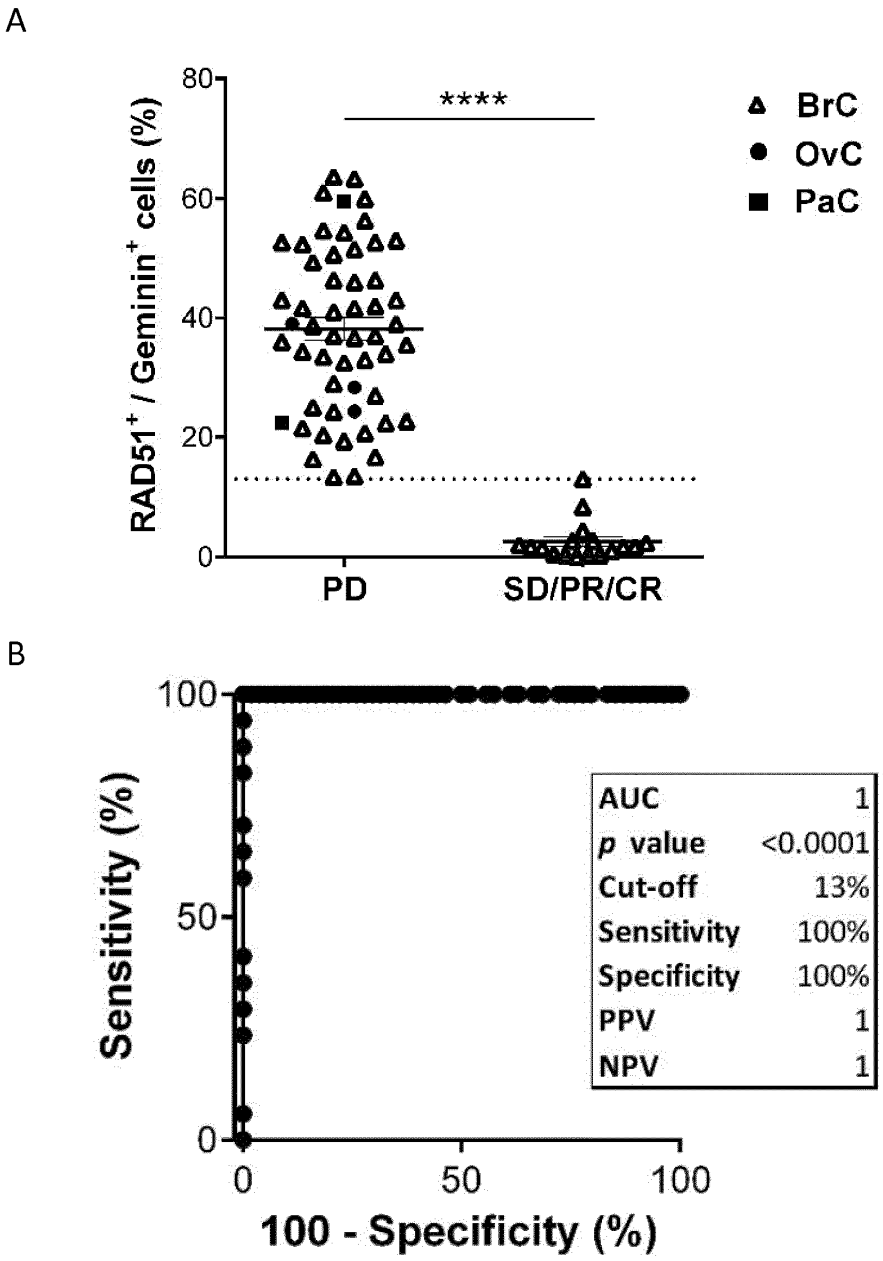

A
80
60
40
20
0
RAD51+ / Geminin+ cells (%)
****
BrC
OvC
PaC
PD
SD/PR/CR
B
100
50
0
Sensitivity (%)
0
50
100
100 - Specificity (%)
AUC 1
p value <0.0001
Cut-off 13%
Sensitivity 100%
Specificity 100%
PPV 1
NPV 1

Fig. 4

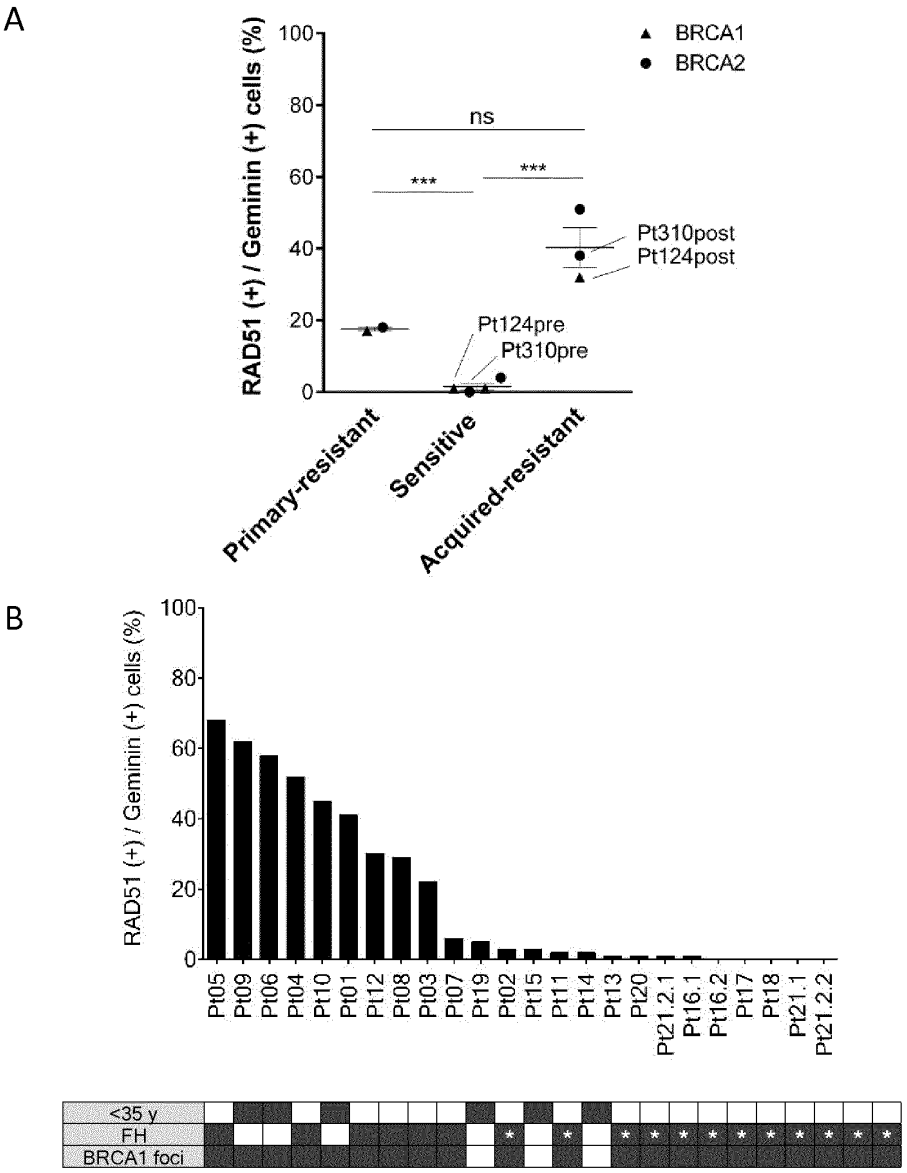
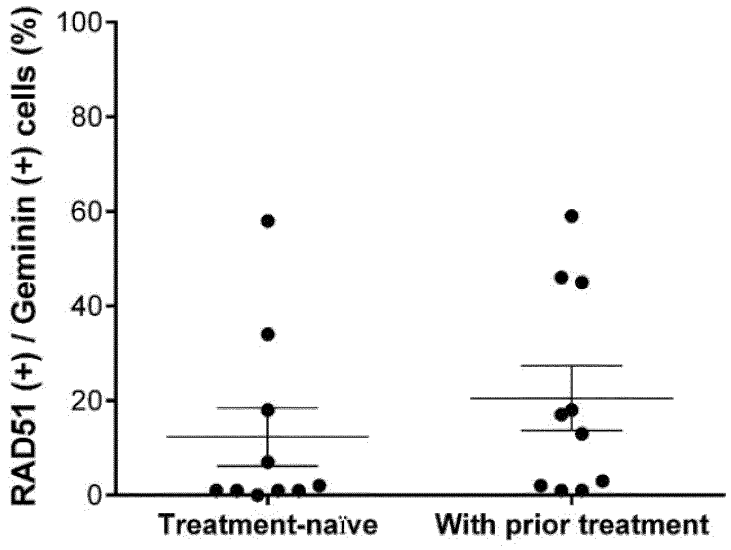

A
RAD51 (+) / Geminin (+) cells (%)
100
80
60
40
20
0
BRCA1
BRCA2
ns
***
***
Pt310post
Pt124post
Pt124pre
Pt310pre
Primary-resistant
Sensitive
Acquired-resistant
B
RAD51 (+) / Geminin (+) cells (%)
100
80
60
40
20
0
Pt05
Pt09
Pt06
Pt04
Pt10
Pt01
Pt12
Pt08
Pt03
Pt07
Pt19
Pt02
Pt15
Pt11
Pt14
Pt13
Pt20
Pt21.2.1
Pt16.1
Pt16.2
Pt17
Pt18
Pt21.1
Pt21.2.2
<35 y
FH
BRCA1 foci

Fig. 5

C


RAD51 (+) / Geminin (+) cells (%)
100
80
60
40
20
0
Treatment-naïve
With prior treatment

D

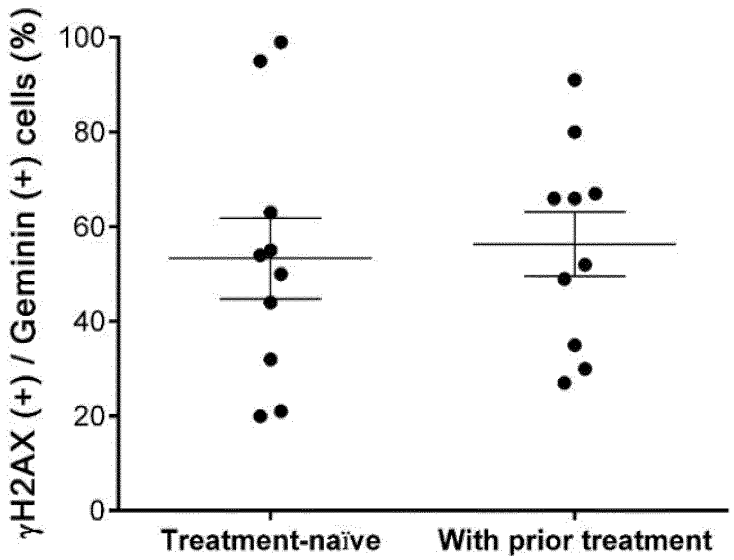
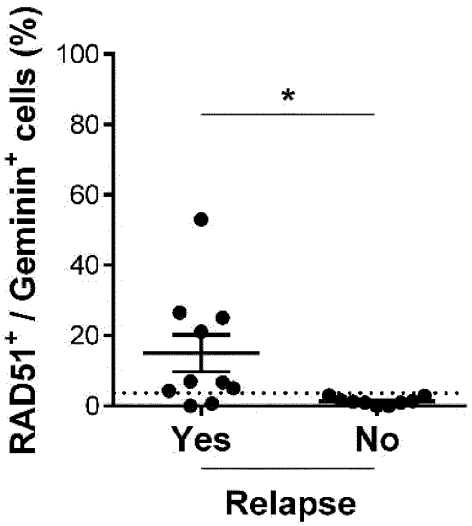

γH2AX (+) / Geminin (+) cells (%)
100
80
60
40
20
0
Treatment-naïve
With prior treatment

Fig. 5 (cont.)

A


RAD51+ / Geminin+ cells (%)
100
80
60
40
20
0
*
Yes
No
Relapse

B

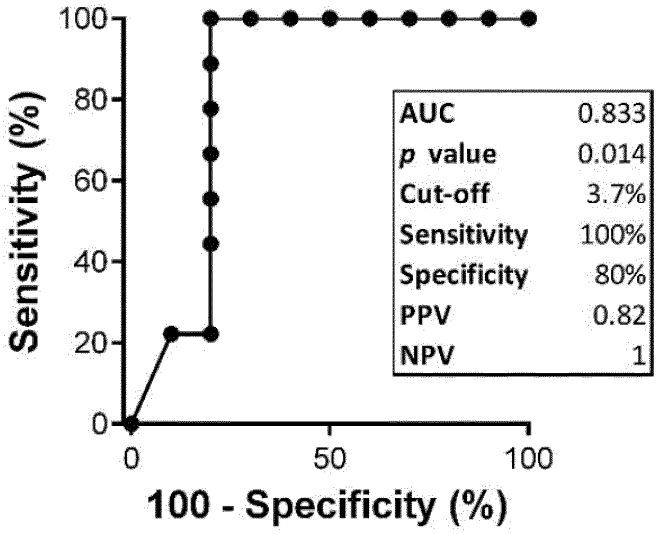

Sensitivity (%)
100
80
60
40
20
0
0
50
100
100 - Specificity (%)
AUC 0.833
p value 0.014
Cut-off 3.7%
Sensitivity 100%
Specificity 80%
PPV 0.82
NPV 1

Fig. 6

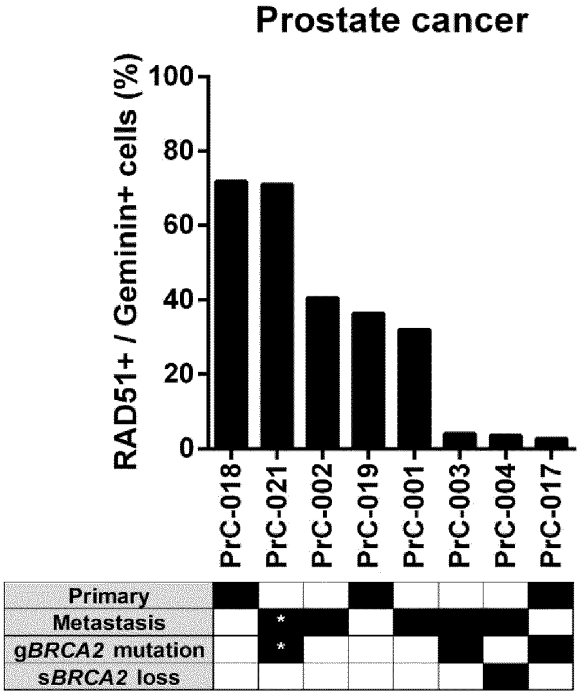

Prostate cancer
RAD51+ / Geminin+ cells (%)
100
80
60
40
20
0
PrC-018
PrC-021
PrC-002
PrC-019
PrC-001
PrC-003
PrC-004
PrC-017
Primary
Metastasis
gBRCA2 mutation
sBRCA2 loss
*
*

Fig. 7

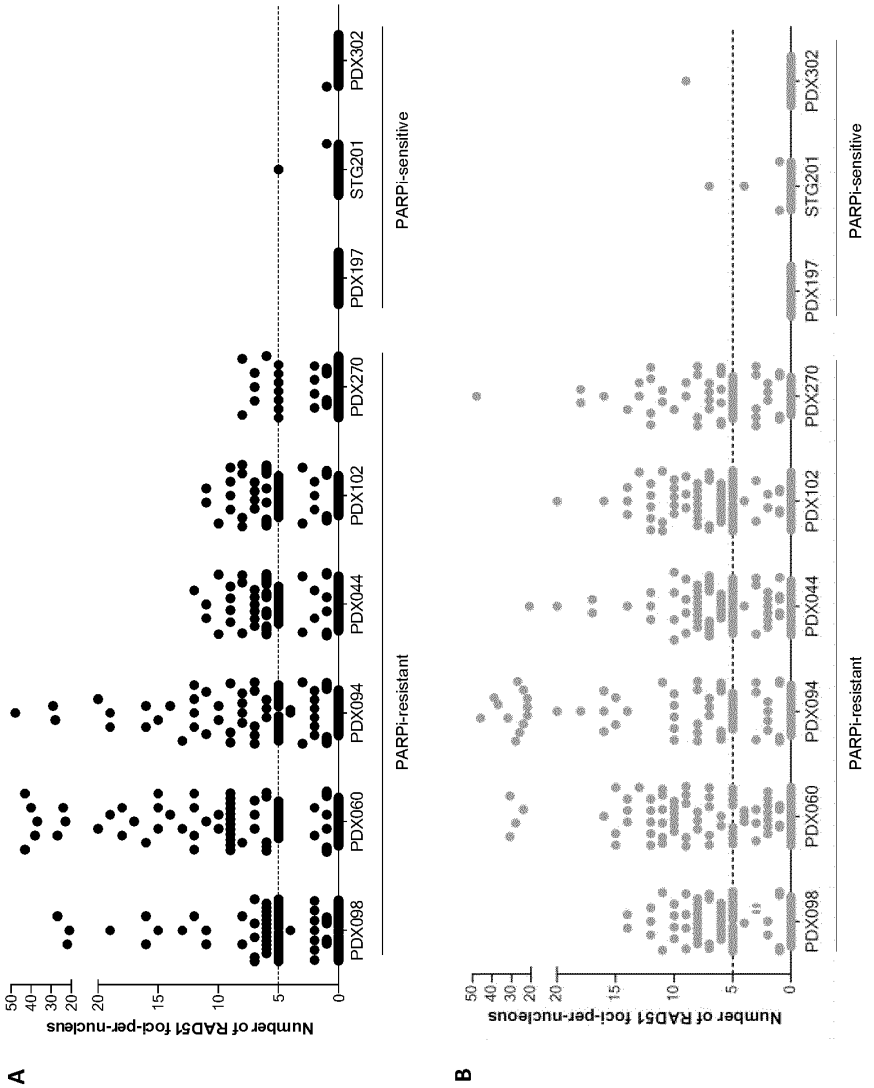
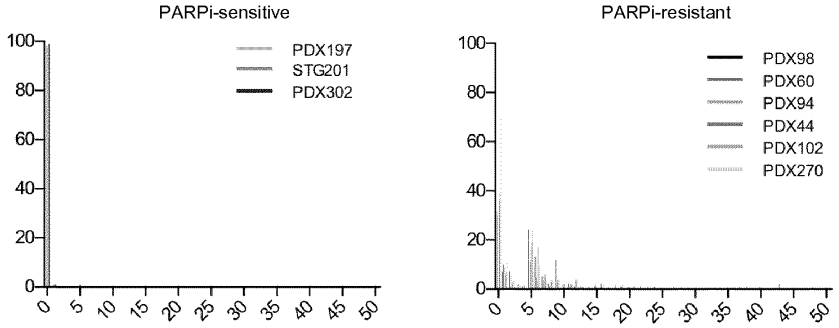

A
Number of RAD51 foci-per-nucleus
50
40
30
20
20
15
10
5
0
PDX098
PDX060
PDX094
PDX044
PDX102
PDX270
PDX197
STG201
PDX302
PARPi-resistant
PARPi-sensitive
B
Number of RAD51 foci-per-nucleus
50
40
30
20
20
15
10
5
0
PDX098
PDX060
PDX094
PDX044
PDX102
PDX270
PDX197
STG201
PDX302
PARPi-resistant
PARPi-sensitive

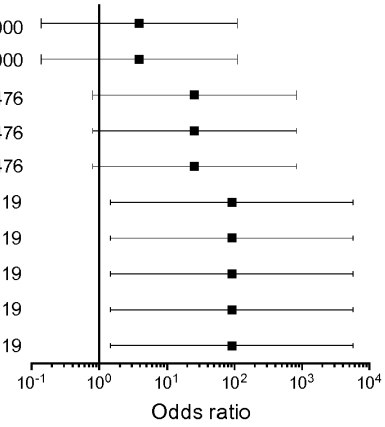
Fig. 8

C



D

	OR	95% CI	*p* value
> 10 foci-per-nucleus	3.889	0.1374 to 110.1	0.5000
> 9 foci-per-nucleus	3.889	0.1374 to 110.1	0.5000
> 8 foci-per-nucleus	25.67	0.7981 to 825.4	0.0476
> 7 foci-per-nucleus	25.67	0.7981 to 825.4	0.0476
> 6 foci-per-nucleus	25.67	0.7981 to 825.4	0.0476
> 5 foci-per-nucleus	91.00	1.462 to 5662	0.0119
> 4 foci-per-nucleus	91.00	1.462 to 5662	0.0119
> 3 foci-per-nucleus	91.00	1.462 to 5662	0.0119
> 2 foci-per-nucleus	91.00	1.462 to 5662	0.0119
> 1 foci-per-nucleus	91.00	1.462 to 5662	0.0119



E

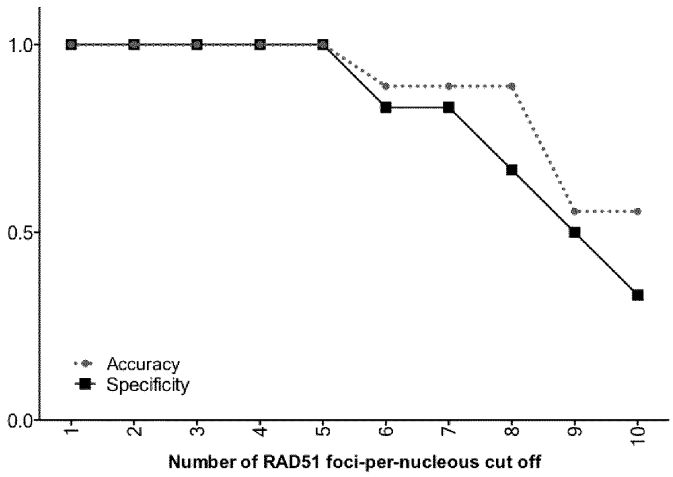
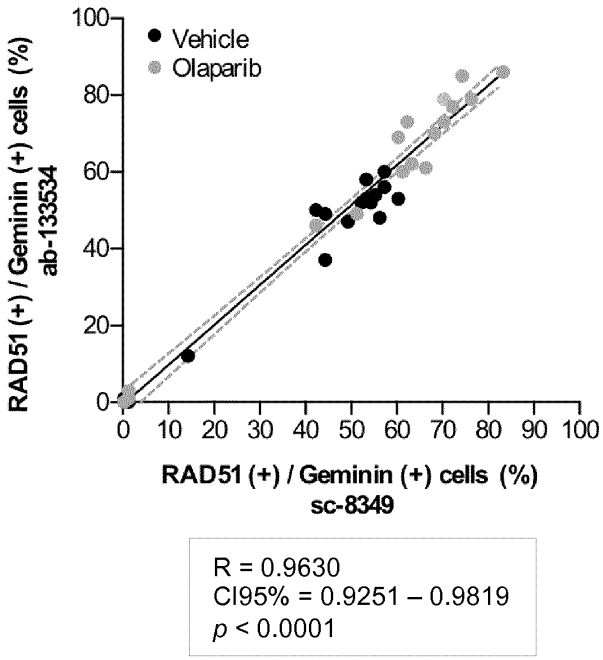


Fig. 8 (cont.)

A



R = 0.9630
CI95% = 0.9251 – 0.9819
$p < 0.0001$

B

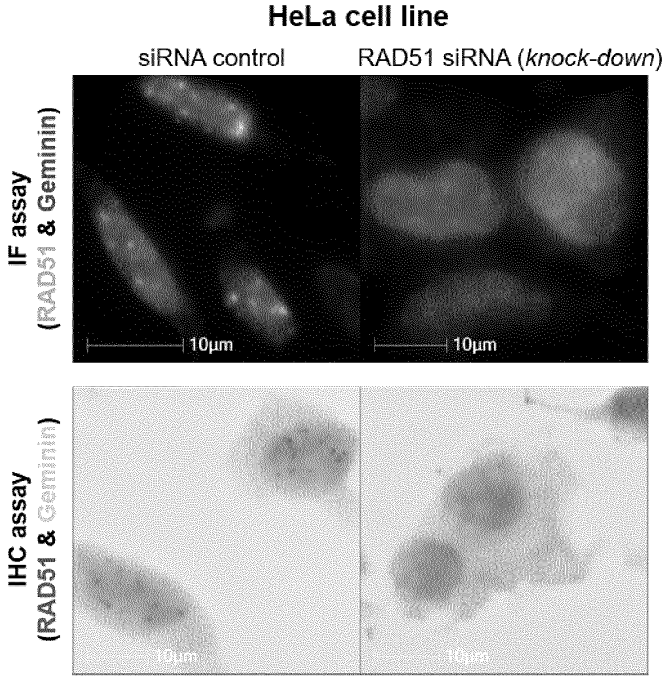


Fig. 9

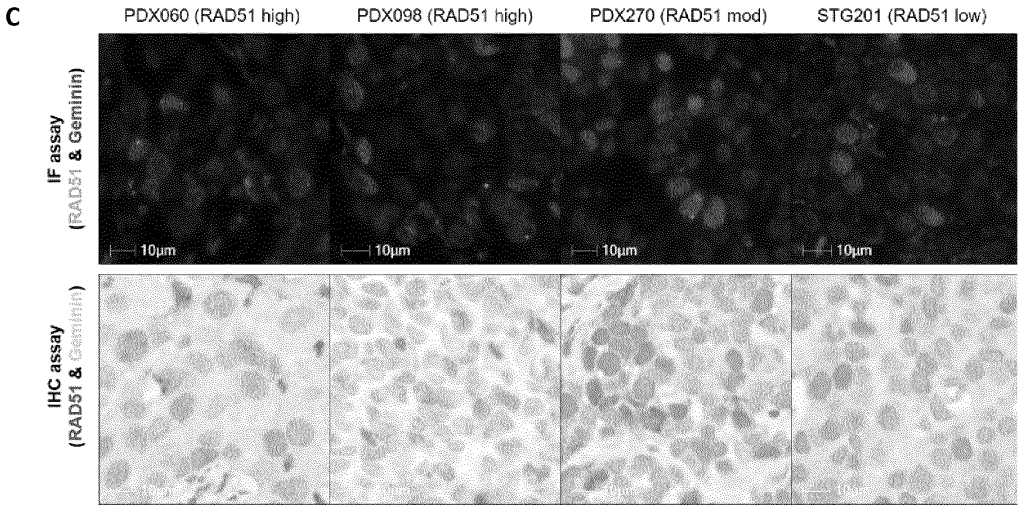

C
PDX060 (RAD51 high)
PDX098 (RAD51 high)
PDX270 (RAD51 mod)
STG201 (RAD51 low)
IF assay
(RAD51 & Geminin)
IHC assay
(RAD51 & Geminin)
10µm
10µm
10µm
10µm

Fig. 9 (cont.)

A

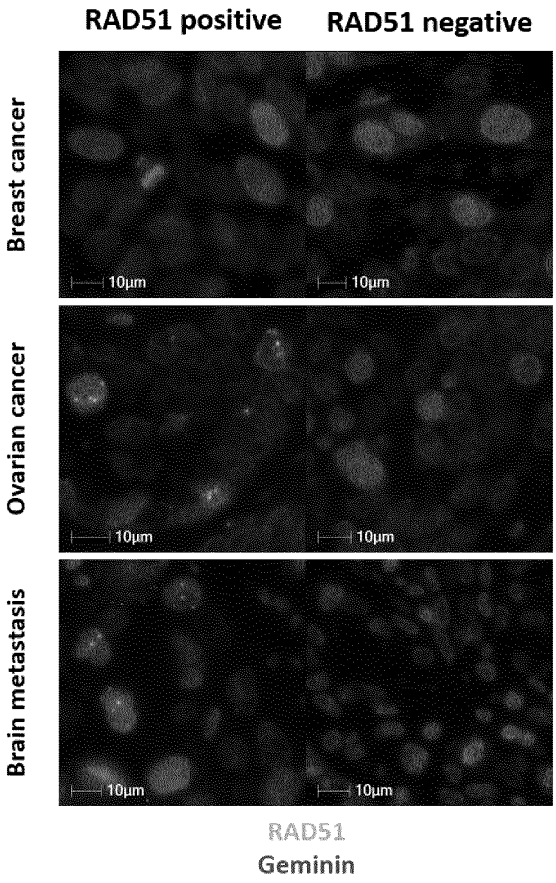

RAD51 positive
RAD51 negative
Breast cancer
Ovarian cancer
Brain metastasis
10µm
10µm
10µm
10µm
10µm
10µm
RAD51
Geminin

Fig. 10

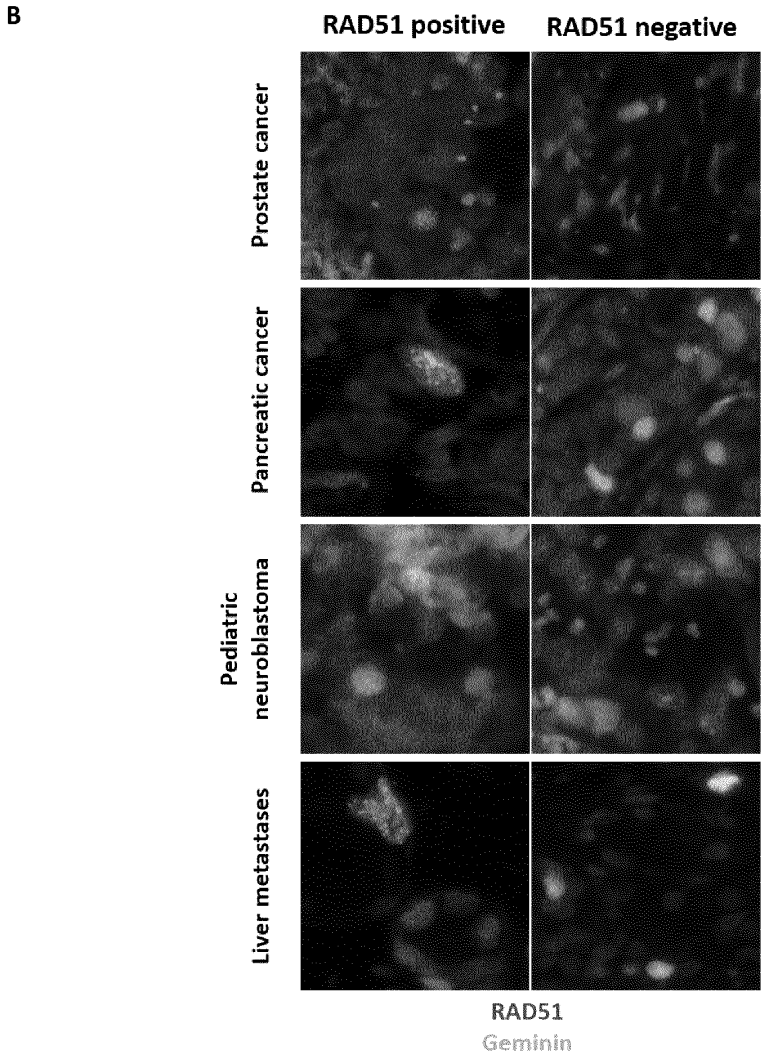

B
RAD51 positive
RAD51 negative
Prostate cancer
Pancreatic cancer
Pediatric neuroblastoma
Liver metastases
RAD51
Geminin

Fig. 10 (cont.)