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Title	Inhibition of the endosomal recycling pathway downregulates HER2 activation and overcomes resistance to tyrosine kinase inhibitors in HER2-positive breast cancer
Authors	Mishra, Anurag;Hourigan, David;Lindsay, Andrew J.
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Figure S1
a

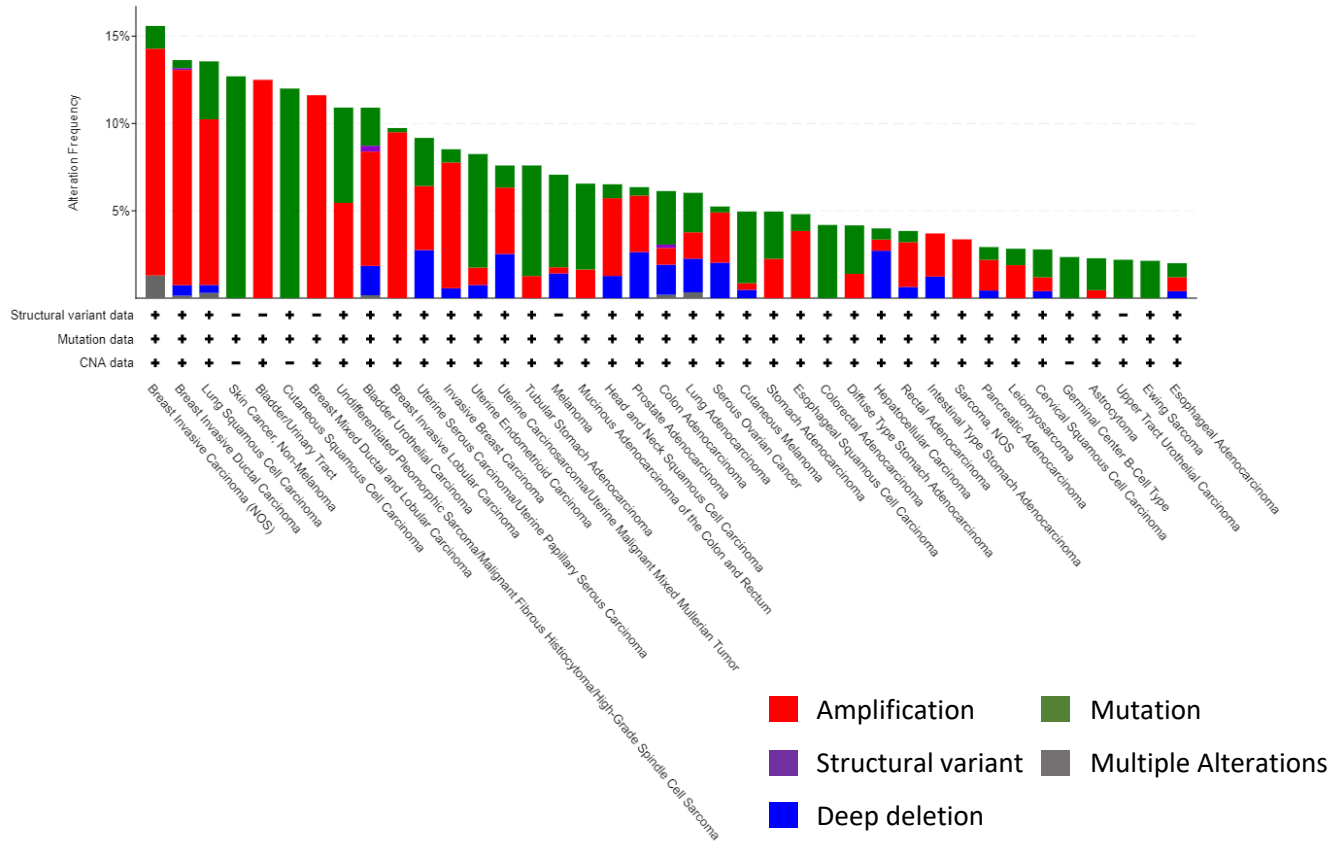
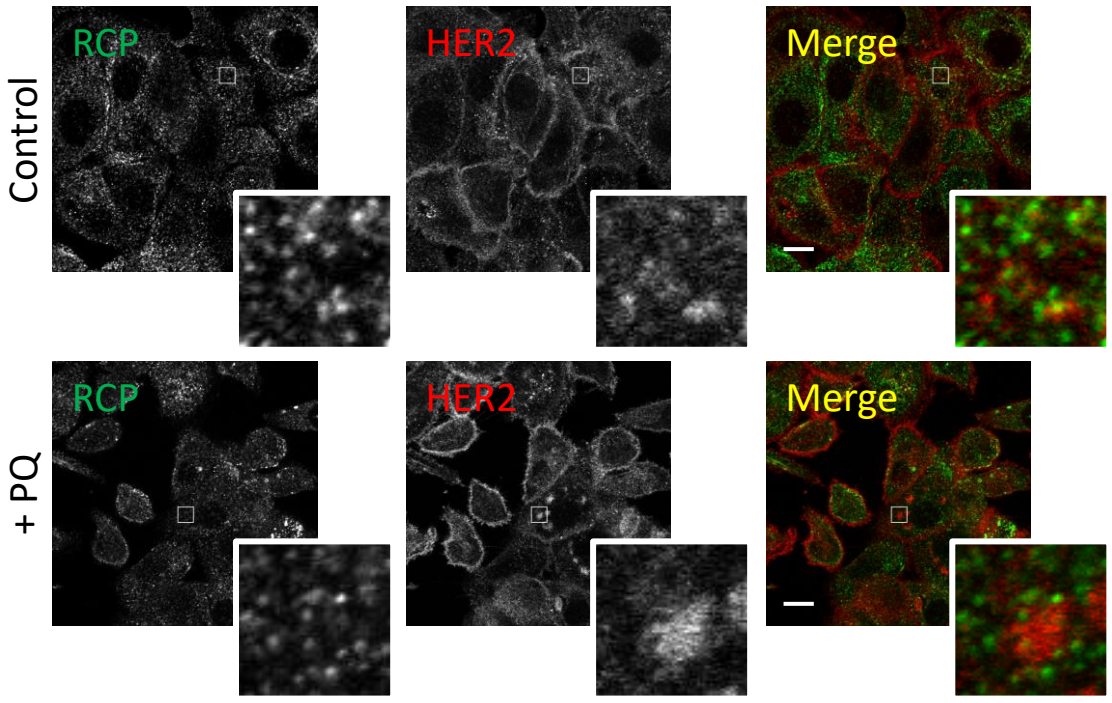
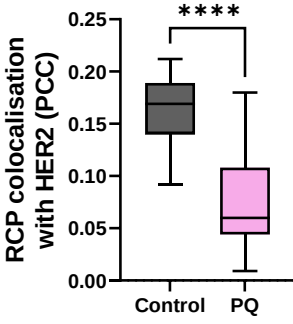

15%
10%
5%
Alteration Frequency
Structural variant data
Mutation data
CNA data
Breast Invasive Carcinoma (NOS)
Breast Invasive Ductal Carcinoma
Lung Squamous Cell Carcinoma
Skin Cancer, Non-Melanoma
Bladder/Urinary Tract
Cutaneous Squamous Cell Carcinoma
Breast Mixed Ductal and Lobular Carcinoma
Undifferentiated Pleomorphic Sarcoma/Malignant Fibrous Histiocytoma/High-Grade Spindle Cell Sarcoma
Bladder Urothelial Carcinoma
Uterine Serous Carcinoma/Uterine Papillary Serous Carcinoma
Breast Invasive Lobular Carcinoma
Invasive Breast Carcinoma
Uterine Endometrioid Carcinoma
Tubular Stomach Adenocarcinoma
Melanoma
Mucinous Adenocarcinoma of the Colon and Rectum
Head and Neck Squamous Cell Carcinoma
Prostate Adenocarcinoma
Colon Adenocarcinoma
Lung Adenocarcinoma
Serous Ovarian Cancer
Cutaneous Melanoma
Stomach Adenocarcinoma
Esophageal Squamous Cell Carcinoma
Colorectal Adenocarcinoma
Diffuse Type Stomach Adenocarcinoma
Hepatocellular Carcinoma
Rectal Adenocarcinoma
Intestinal Type Stomach Adenocarcinoma
Sarcoma, NOS
Pancreatic Adenocarcinoma
Leiomyosarcoma
Cervical Squamous Cell Carcinoma
Germinal Center B-Cell Type
Astrocytoma
Upper Tract Urothelial Carcinoma
Ewing Sarcoma
Esophageal Adenocarcinoma
Amplification
Mutation
Structural variant
Multiple Alterations
Deep deletion

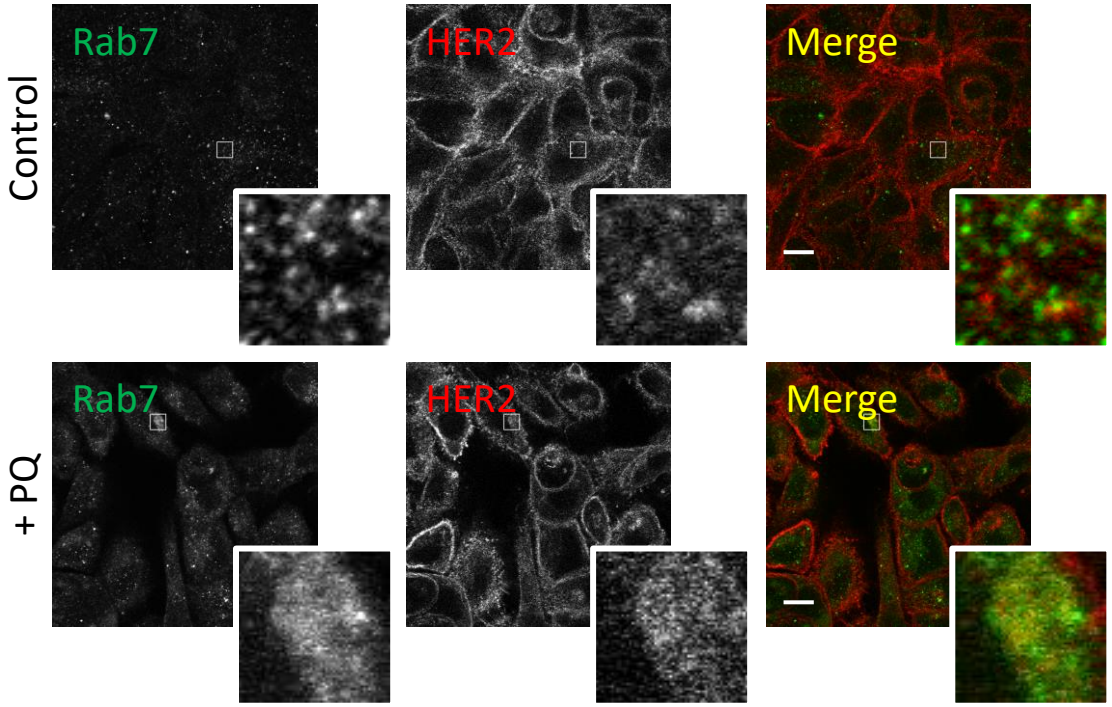
Figure S2

a


Control
+ PQ
RCP
HER2
Merge


RCP colocalisation with HER2 (PCC)
0.25
0.20
0.15
0.10
0.05
0.00
****
Control
PQ

b


Control
+ PQ
Rab7
HER2
Merge

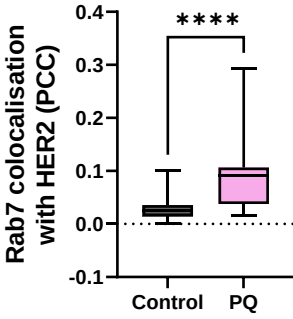

Rab7 colocalisation with HER2 (PCC)
0.4
0.3
0.2
0.1
0.0
-0.1
****
Control
PQ

Figure S3

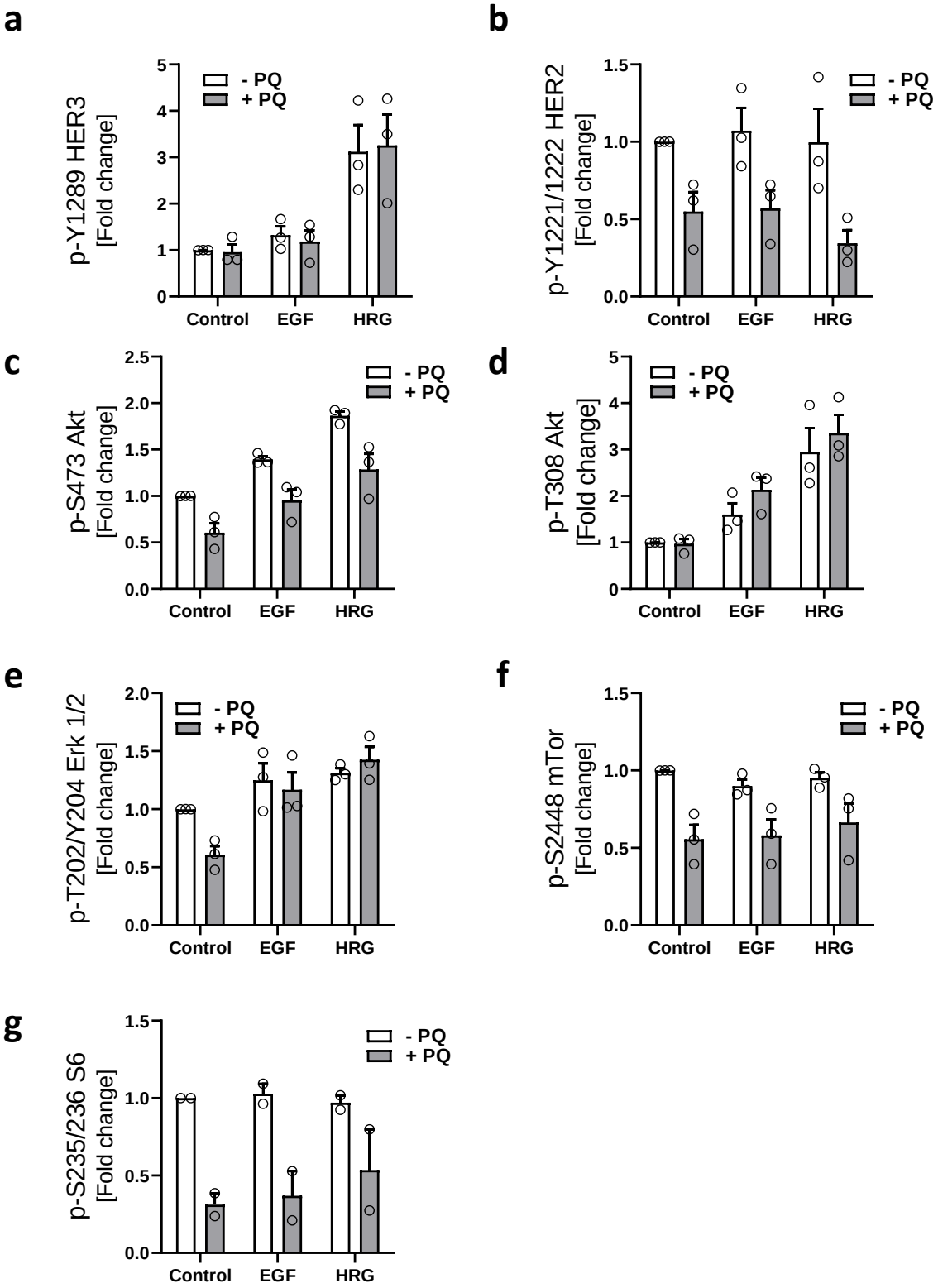
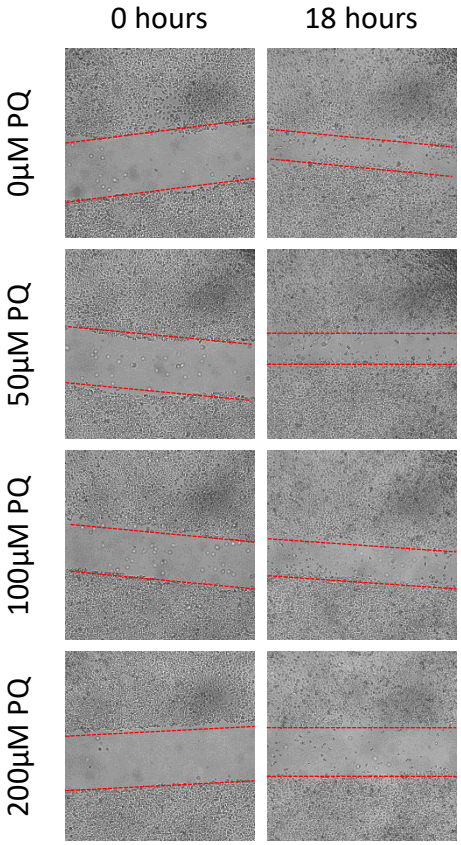
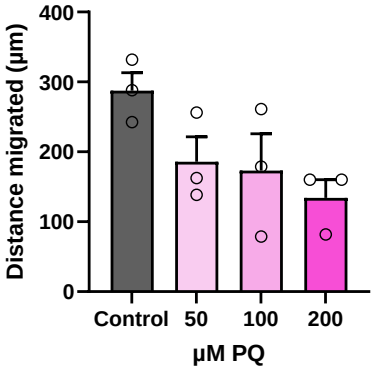

a
p-Y1289 HER3
[Fold change]
- PQ
+ PQ
Control
EGF
HRG
b
p-Y1221/1222 HER2
[Fold change]
c
p-S473 Akt
[Fold change]
d
p-T308 Akt
[Fold change]
e
p-T202/Y204 Erk 1/2
[Fold change]
f
p-S2448 mTor
[Fold change]
g
p-S235/236 S6
[Fold change]

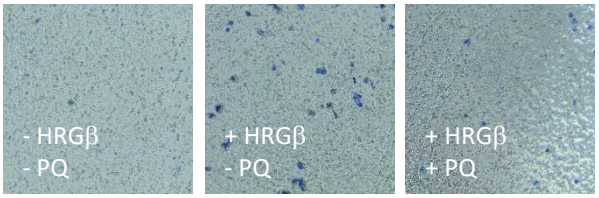
Figure S4

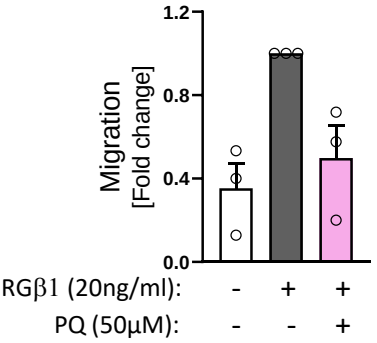
a



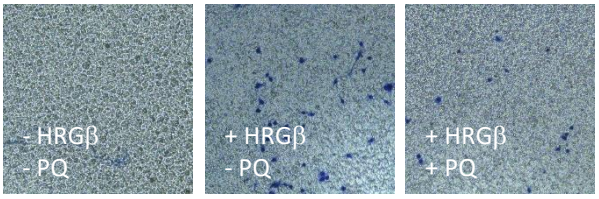


b





c



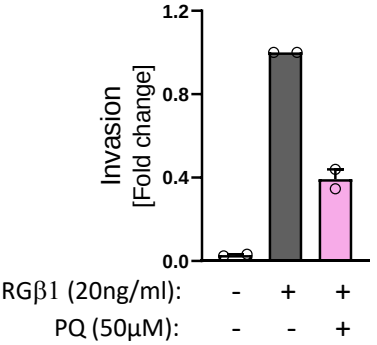


Figure S5

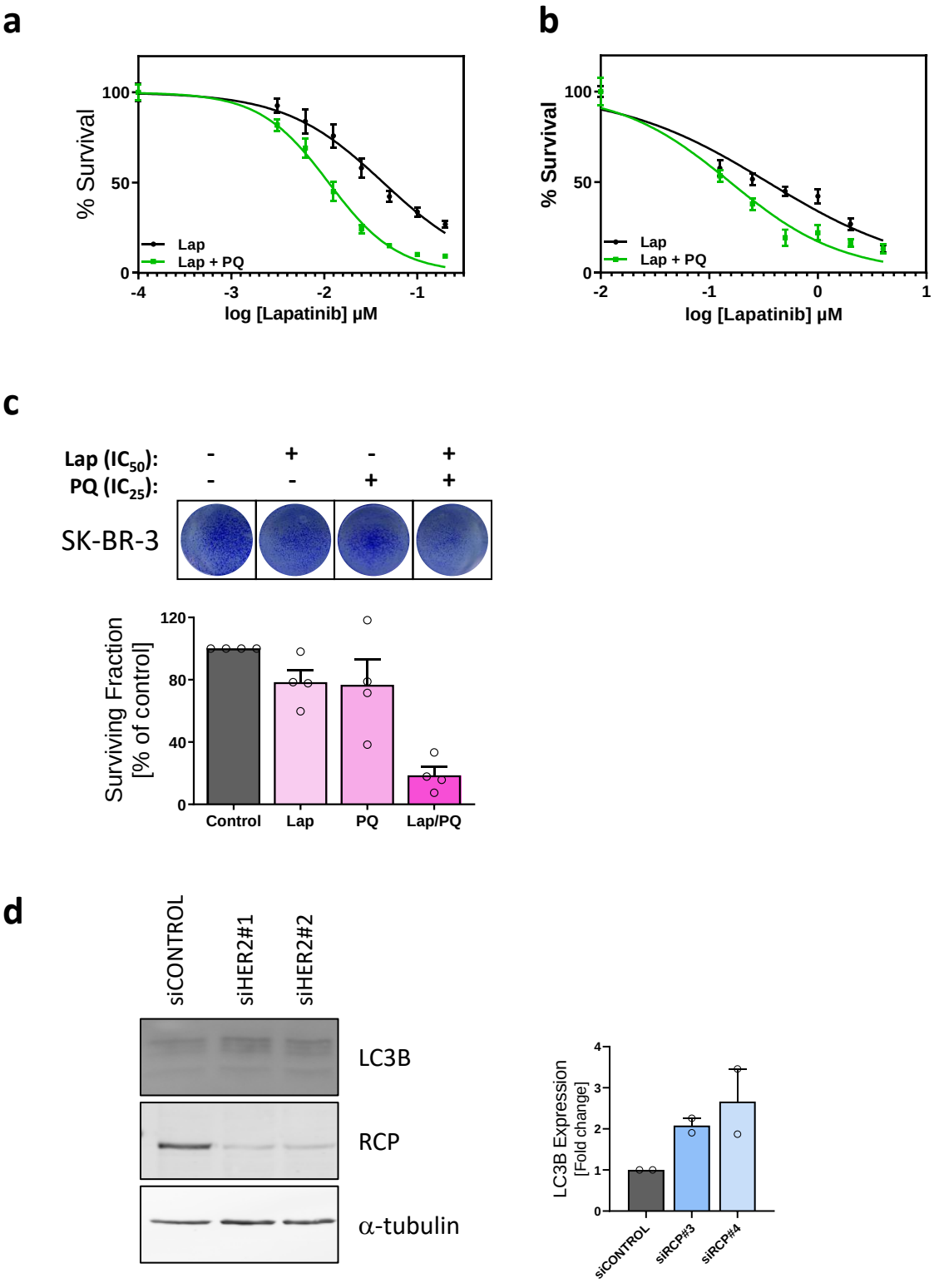

a
% Survival
100
50
0
-4
-3
-2
-1
log [Lapatinib] µM
Lap
Lap + PQ
b
% Survival
100
50
0
-2
-1
0
1
log [Lapatinib] µM
Lap
Lap + PQ
c
Lap (IC50):
PQ (IC25):
SK-BR-3
Surviving Fraction [% of control]
120
80
40
0
Control
Lap
PQ
Lap/PQ
d
siCONTROL
siHER2#1
siHER2#2
LC3B
RCP
α-tubulin
LC3B Expression [Fold change]
4
3
2
1
0
siCONTROL
siRCP#3
siRCP#4

Figure S6

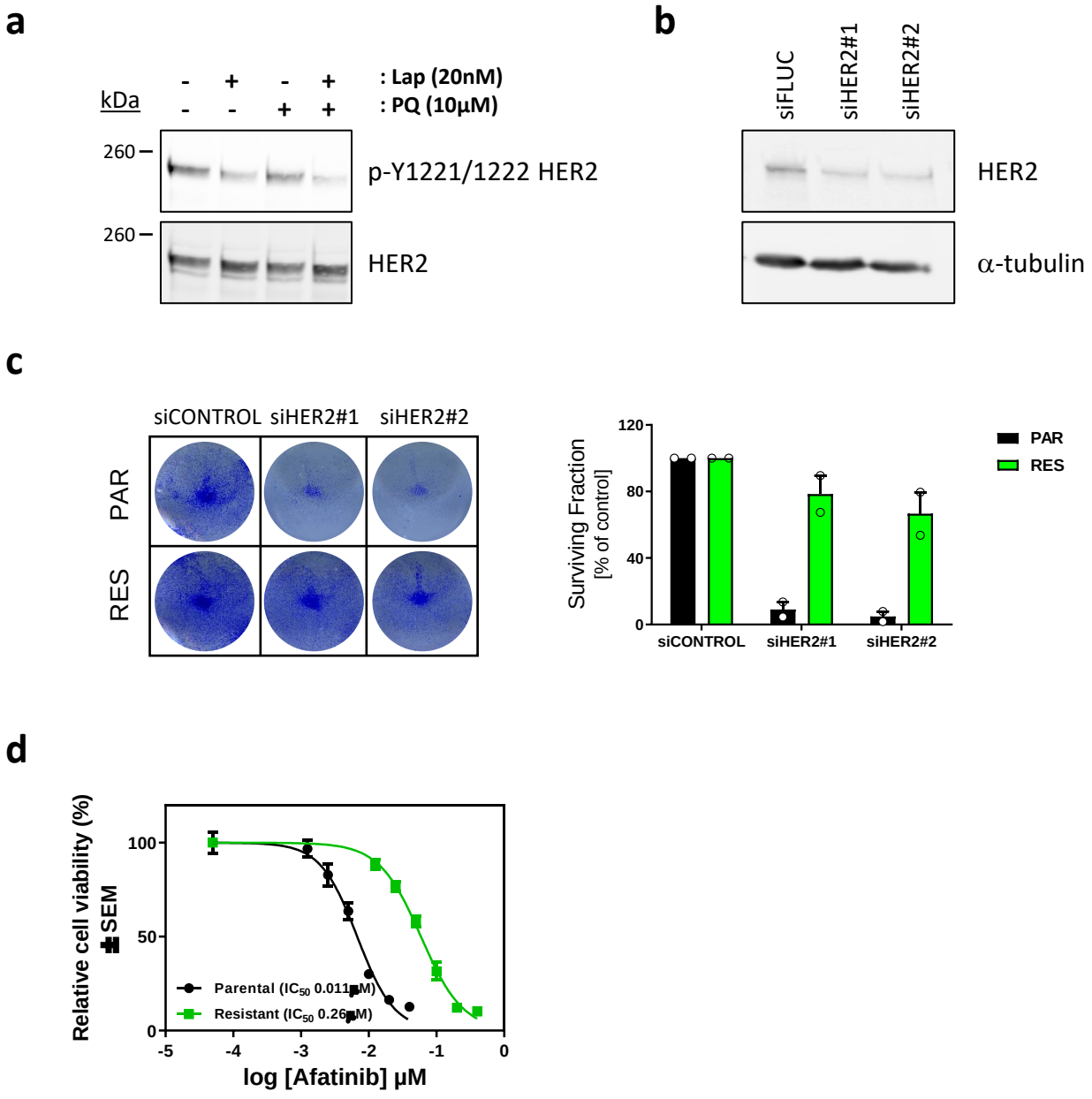
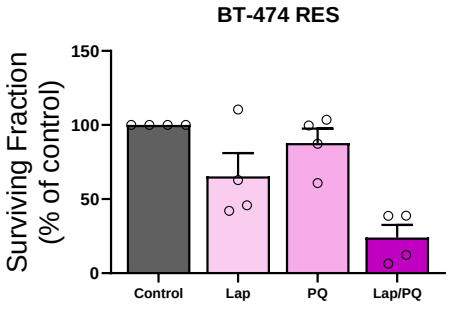
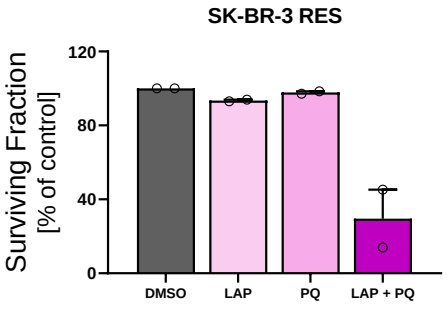

a
kDa
- + - + : Lap (20nM)
- - + + : PQ (10µM)
260
p-Y1221/1222 HER2
260
HER2
b
siFLUC
siHER2#1
siHER2#2
HER2
α-tubulin
c
siCONTROL siHER2#1 siHER2#2
PAR
RES
Surviving Fraction [% of control]
120
80
40
0
siCONTROL
siHER2#1
siHER2#2
PAR
RES
d
Relative cell viability (%) ± SEM
100
50
0
-5 -4 -3 -2 -1 0
log [Afatinib] µM
Parental (IC50 0.011µM)
Resistant (IC50 0.26µM)

Figure S7

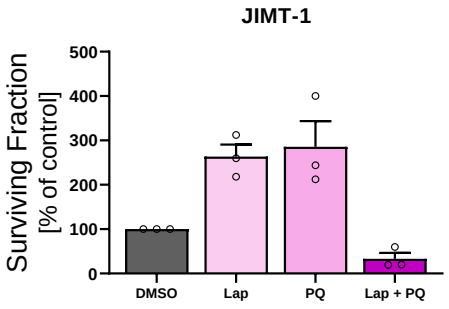
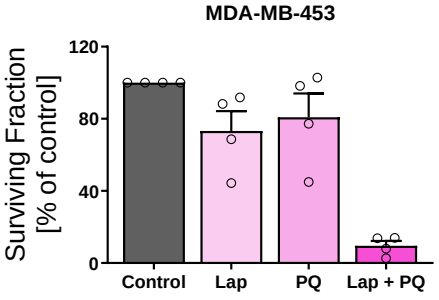
a



b



c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