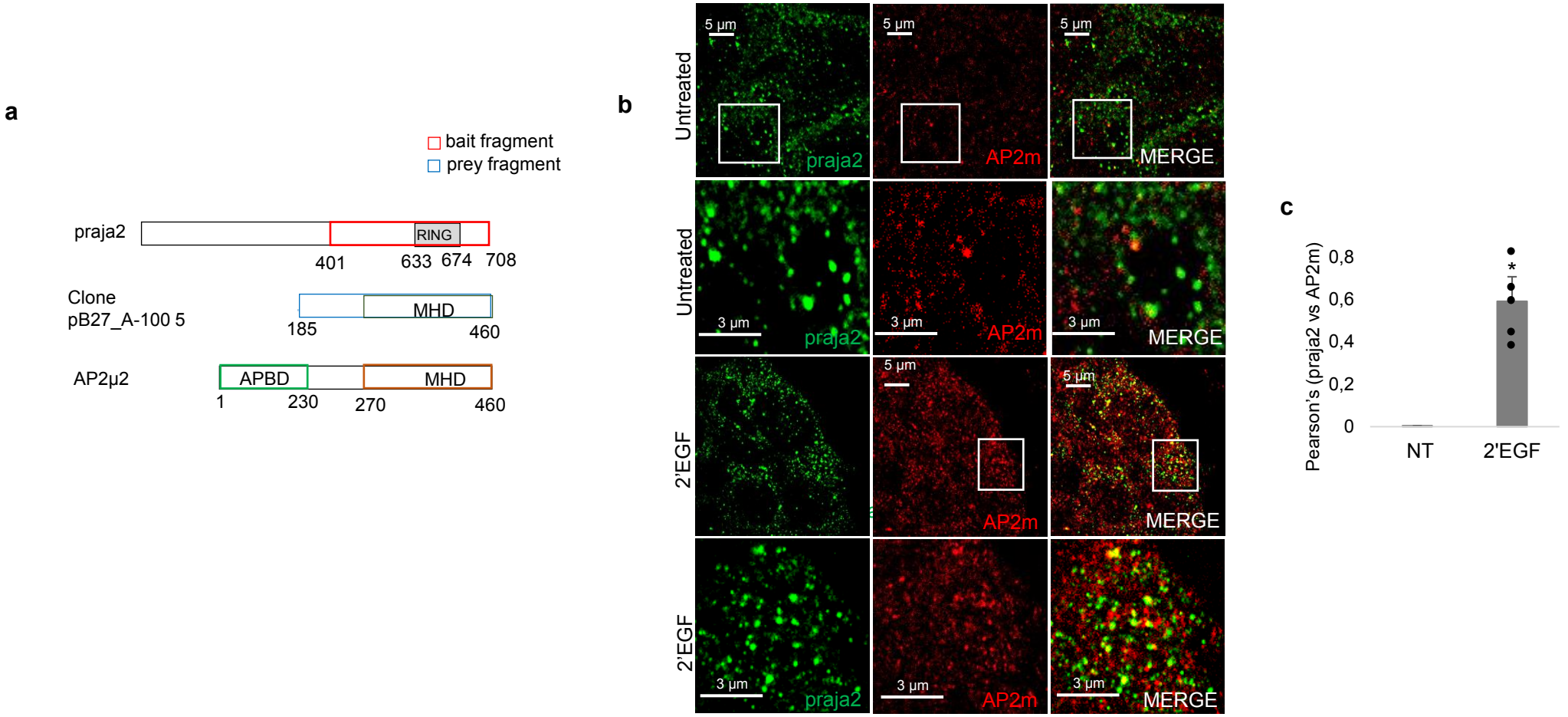
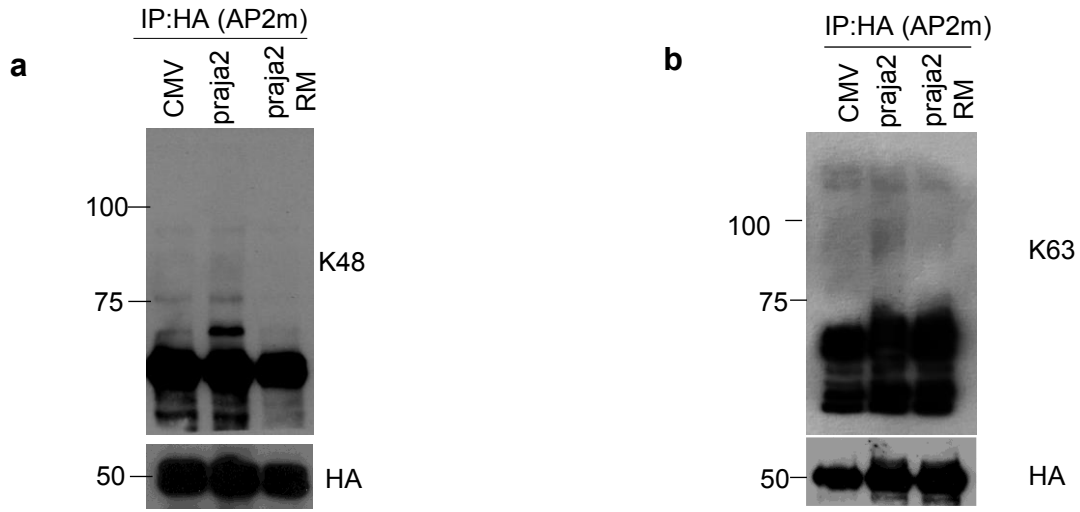


S1. (a) Schematic representation of praja2 domains. Highlighted in red is the bait fragment used for the yeast 2-hybrid screening. The prey fragment spanning residues 185-460 of AP-2 mu subunit is highlighted in blu.
(b) HeLa cells, left untreated or treated with EGF, were PFA-fixed and immunostained for praja2 and AP2m. Representative confocal images are shown. Scale bar (5 µM). **(c)** Pearson's coefficient and quantitative analysis of the experiments shown in c. A mean value of three independent experiments ± SD is shown. *P=0,014

Supplementary Figure 1

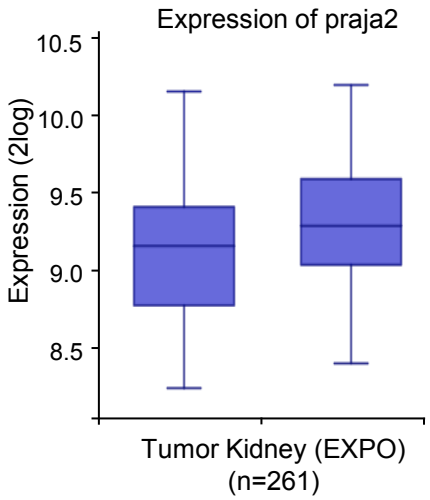


S2. (a) Immunoprecipitation of AP2m-HA from HEK293 cell lysates expressing AP2m-HA, Myc-ubiquitin and FLAG-praja2 or FLAG-praja2RM (inactive mutant). Precipitates were immunoblotted with anti-K8 (ubiquitinated AP2m) and anti-HA antibodies. **(b)**Immunoprecipitation of AP2m-HA from HEK293 cell lysates expressing AP2m-HA, Myc-ubiquitin and FLAG-praja2 or FLAG-praja2RM (inactive mutant). Precipitates were immunoblotted with anti-K63 (ubiquitinated AP2m) and anti-HA antibodies.

Supplementary Figure 2

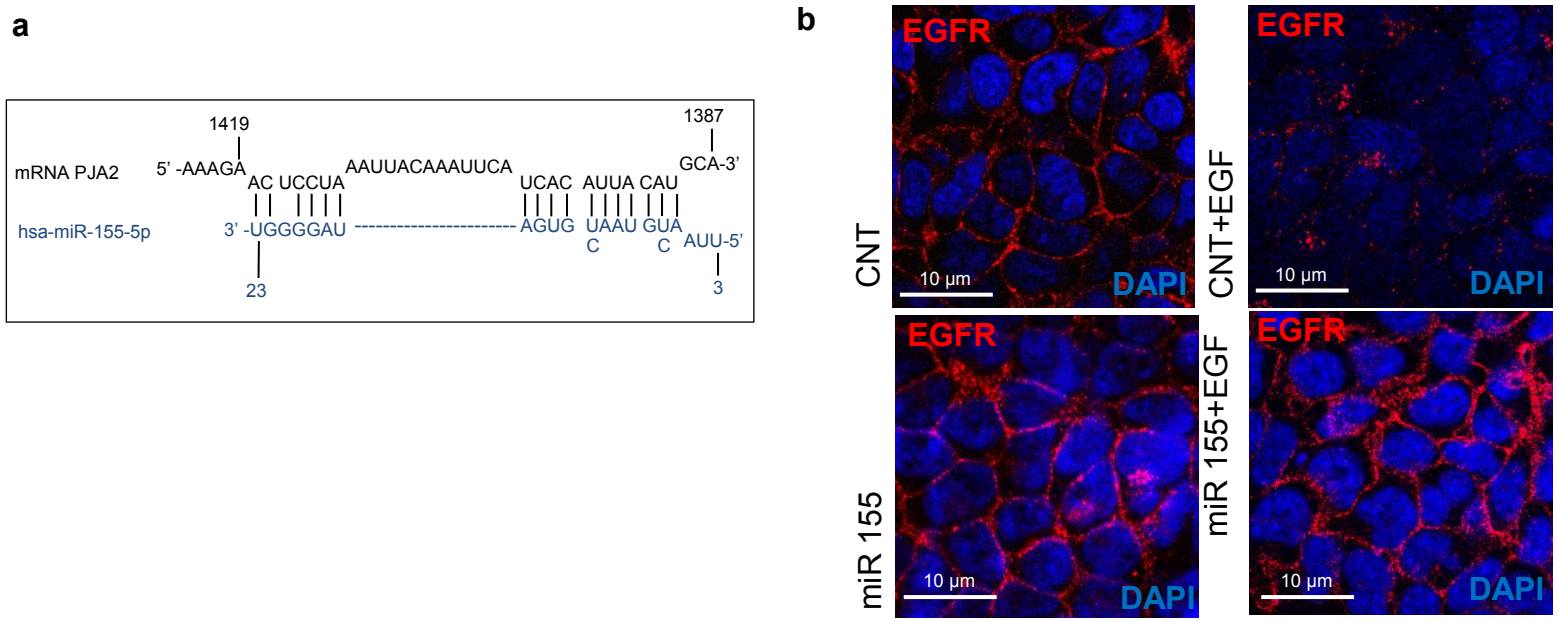
S3. a. HK2 cells were transfected with siRNAs (control or targeting praja2), serum-deprived overnight and treated with EGF (10 ng/ml) for indicated times. Lysates were immunoblotted for EGFR and praja2.
b. HeLa cells were transfected with siRNAs (control or targeting praja2), serum-deprived overnight and treated with transferrin (Tf, 2 µg/ml) up to 60 minutes. Lysates were immunoblotted for TfR and praja2.

Supplementary Figure 3



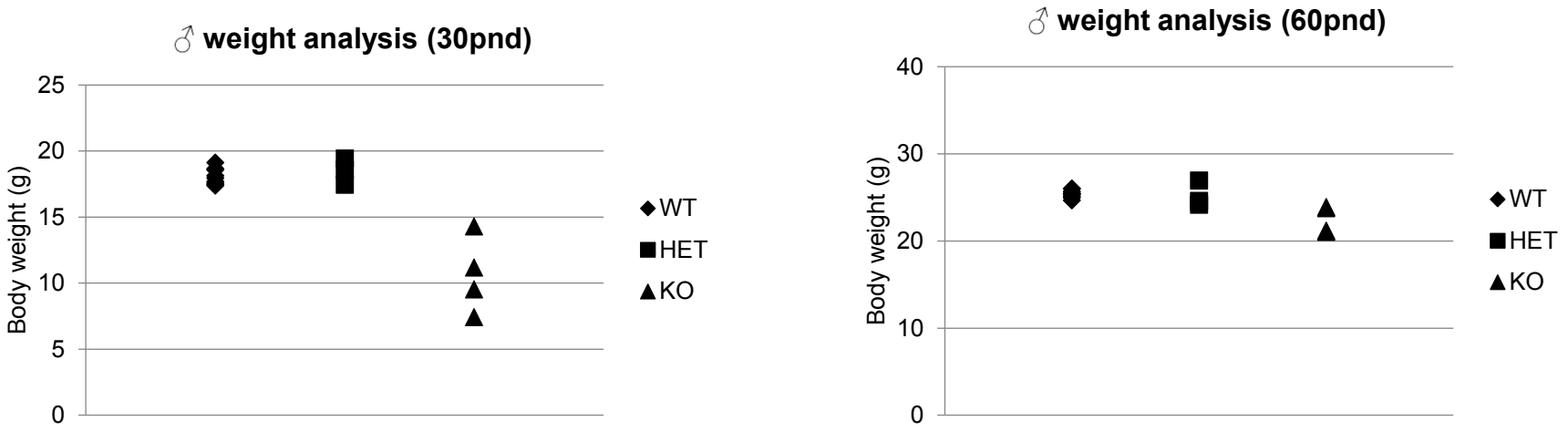
S4. Box plot showing relative expression (2log) of praja2 in normal (GSE18674) and tumors kidney tissues (GSE2109). Data were analyzed using "R2: Genomics Analysis and Visualization Platform" and one-way ANOVA test was performed ($p > 0.01$) for statistical analysis.

Supplementary Figure 4



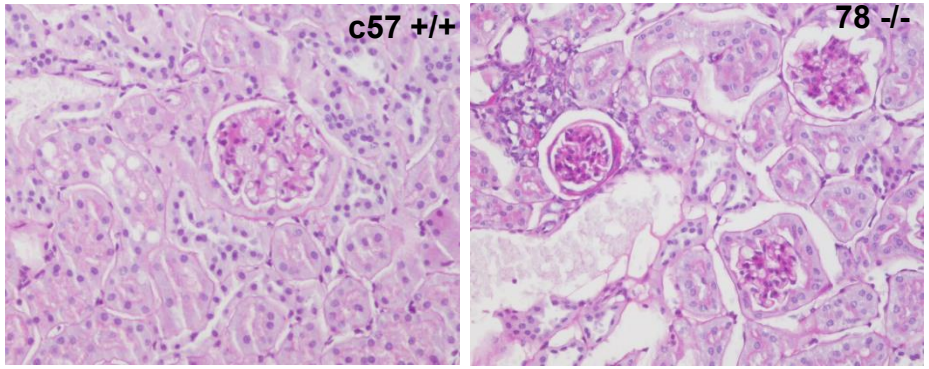
S5. (a) Hsa-miR-155-5p was predicted by target prediction programs intaRNA to align to positions 1387-1419 on the PJA2 3′UTR. Paired sequence alignment is marked by continuous lines. **(b)** HEK293 cells were transfected with miRNAs (control or 155), serum deprived and treated with EGF (10ng/µl) for 90 minutes. Cells were fixed and immunostained with anti EGFR antibody and DAPI. Representative confocal image are shown

Supplementary Figure 5



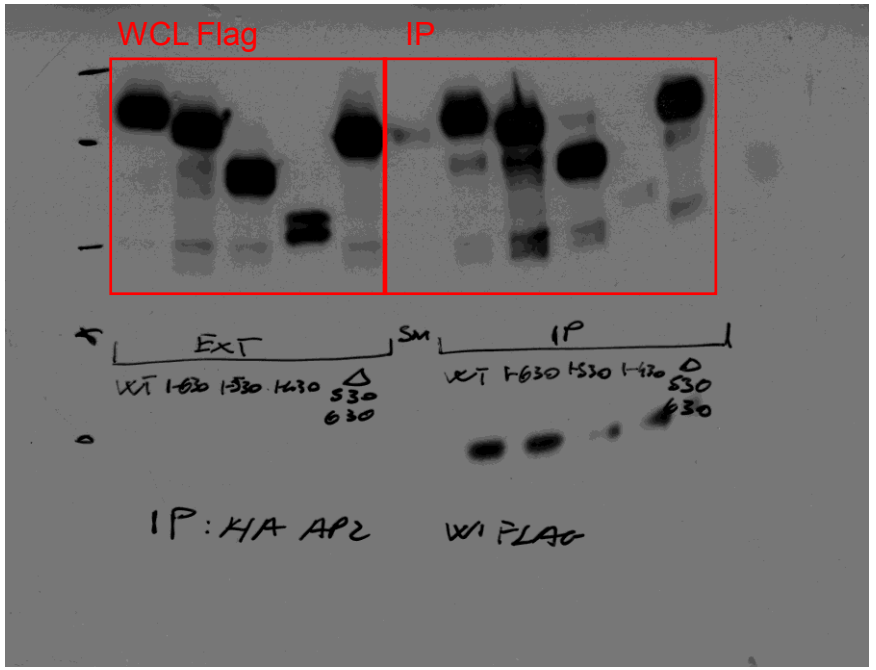
S6. Body weight of males Praja2 +/- , Praja2 -/- and control mice at 30 and 60 days after birth (n = 4 for each group)

Supplementary Figure 6



S7. Histological examination of kidney, mouse. Mild increase of PAS-positive mesangial matrix. Periodic acid – Schiff, 40x.

Fig1b



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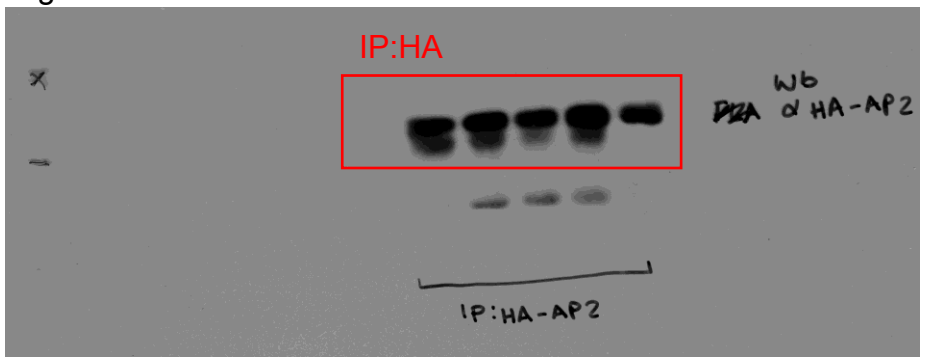

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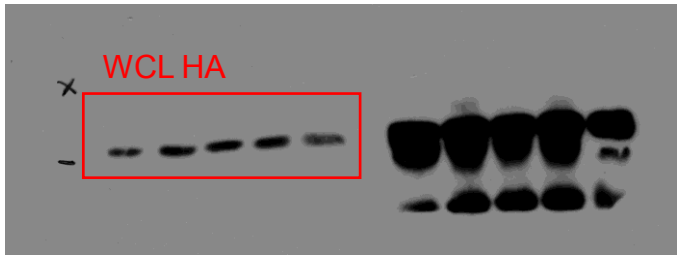

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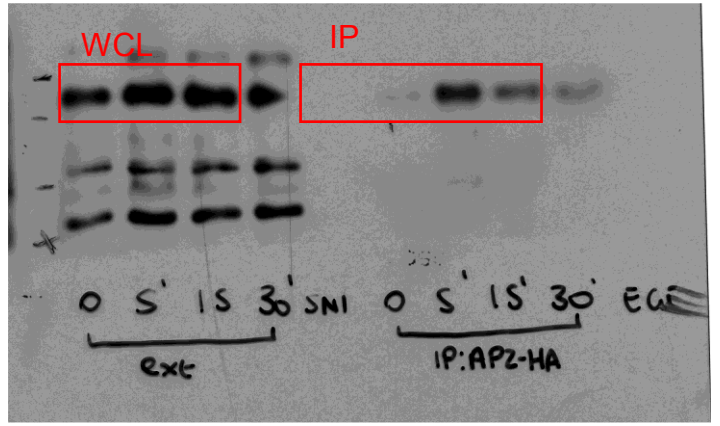

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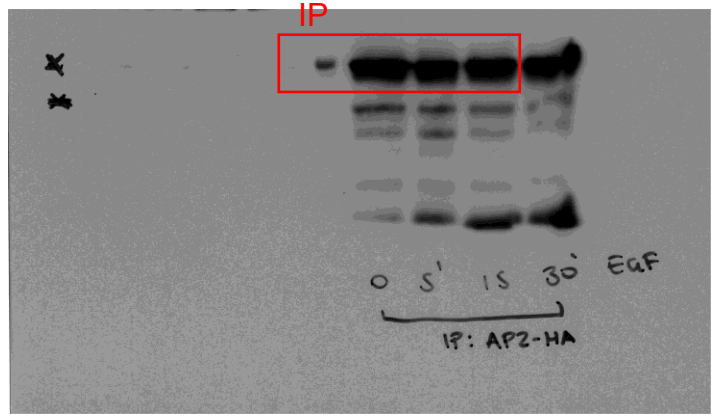

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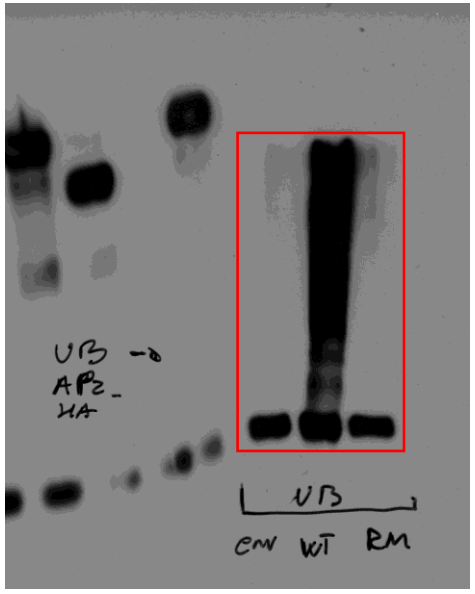

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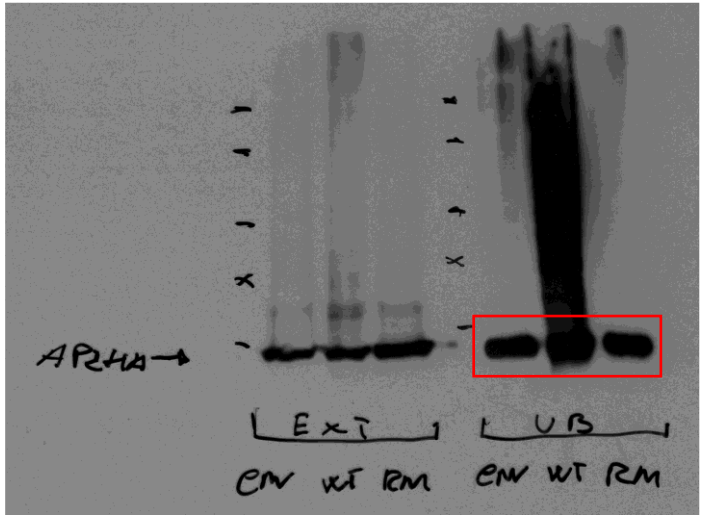

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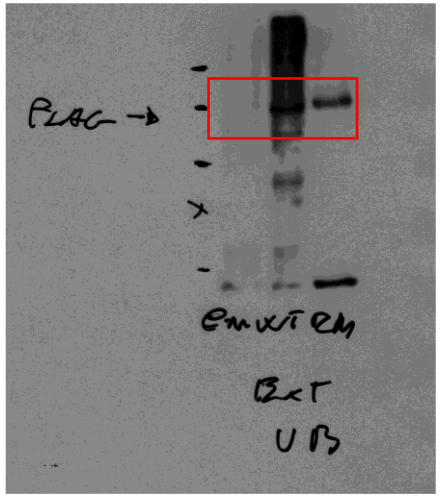

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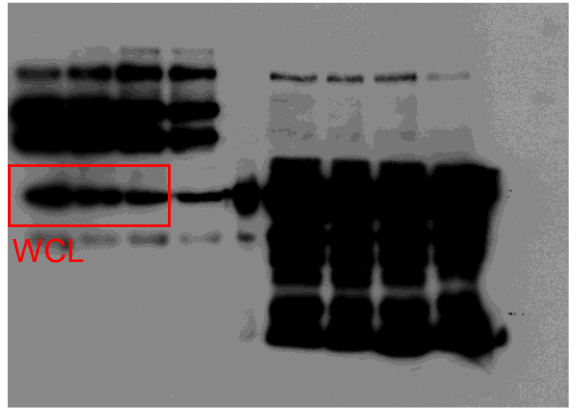
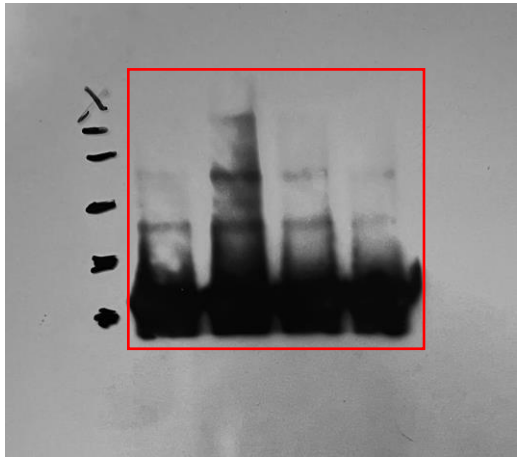


S8. Uncropped gels of the figures presented in Main and Supplementary Figures

Supplementary Figure 8

Fig1h



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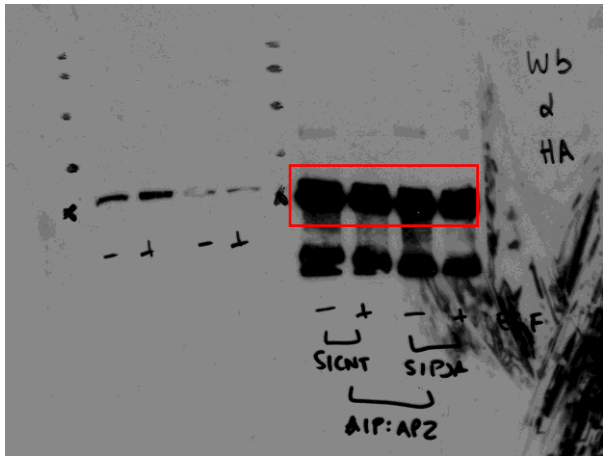

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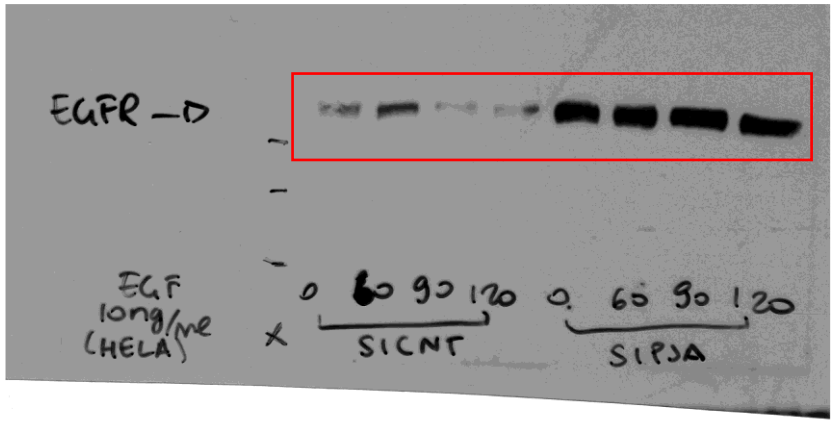

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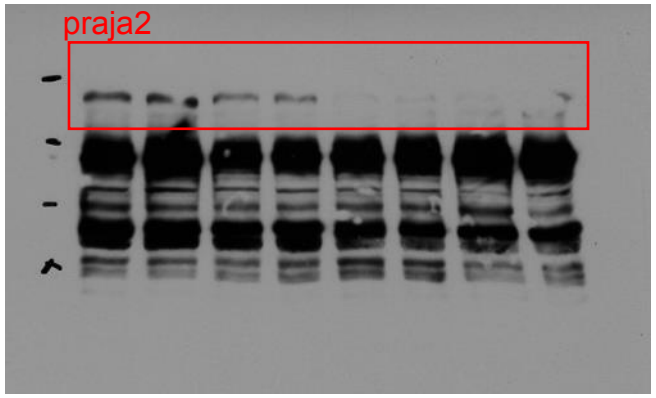

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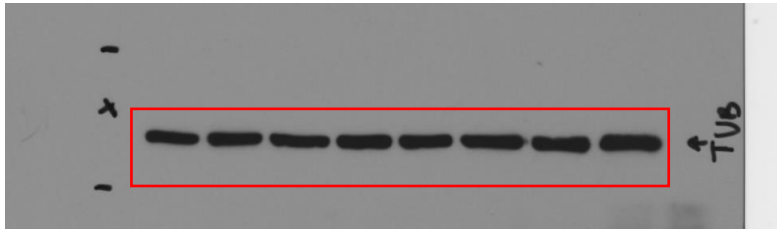

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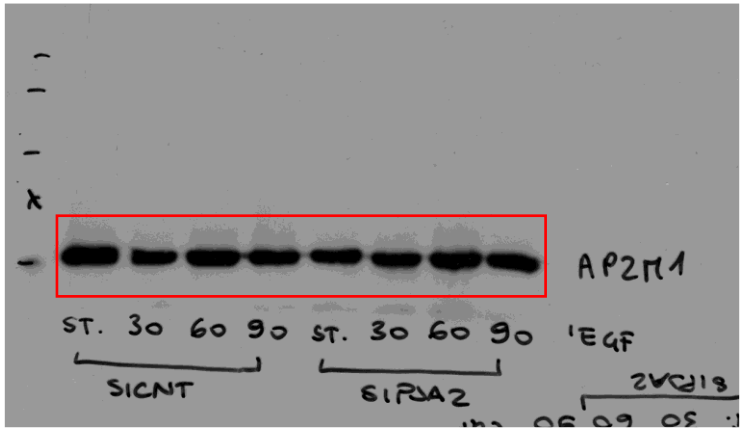

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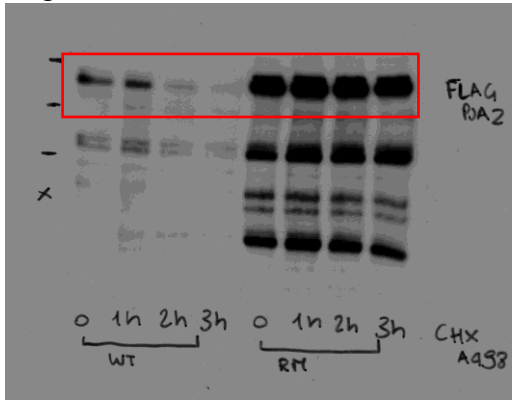

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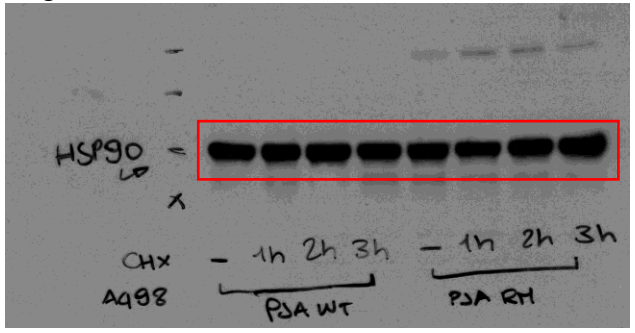

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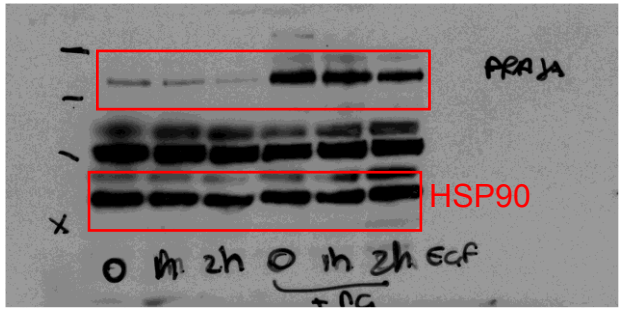
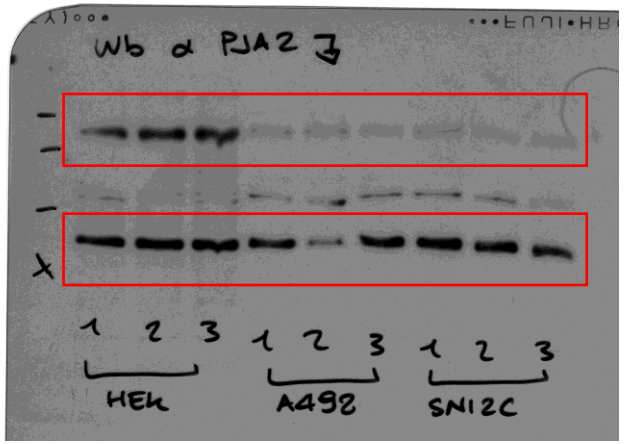


S8. Uncropped gels of the figures presented in Main and Supplementary Figures

Supplementary Figure 8

Fig3e



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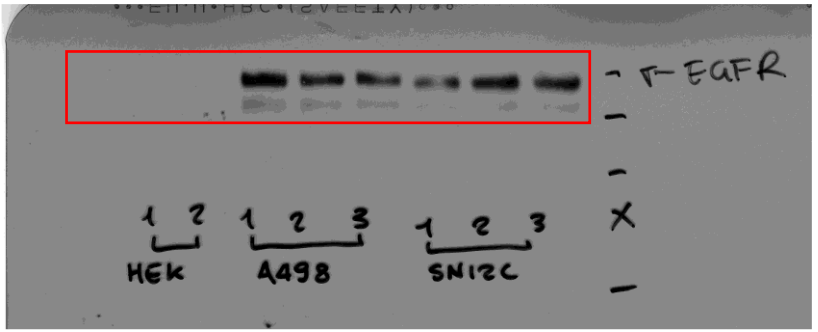

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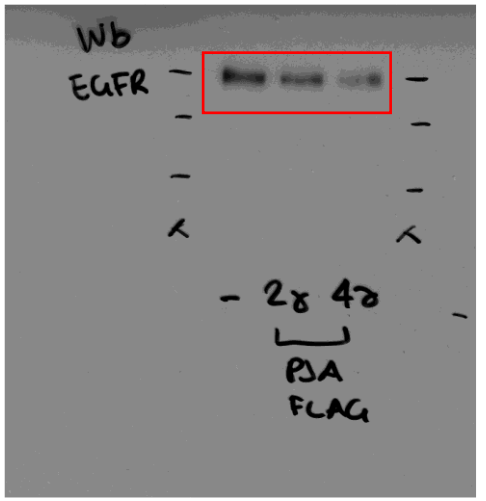

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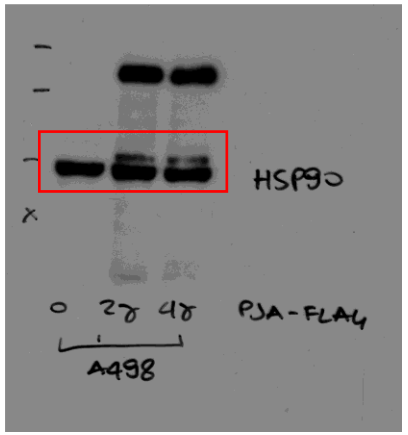

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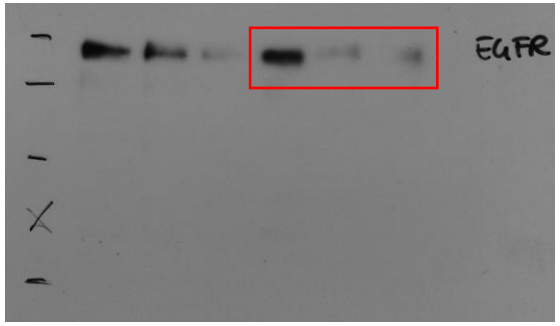

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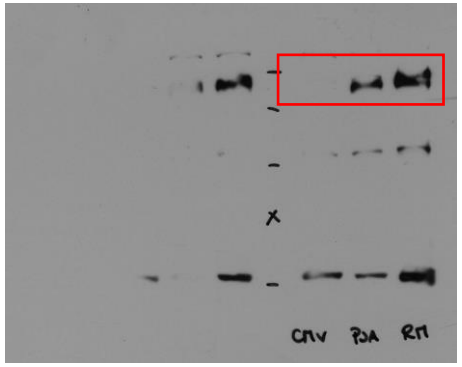

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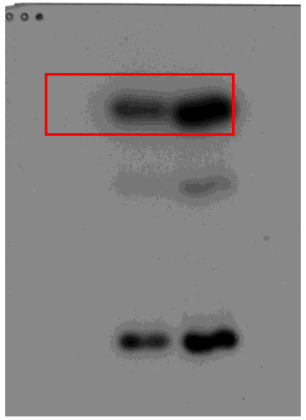
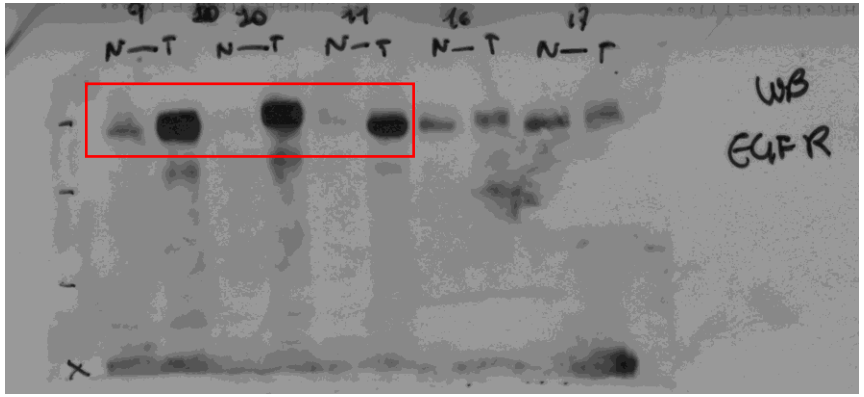


S8. Uncropped gels of the figures presented in Main and Supplementary Figures

Supplementary Figure 8

Fig4d



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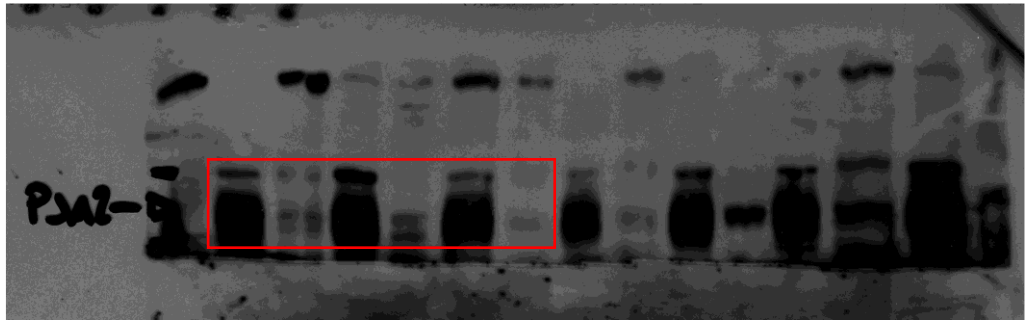

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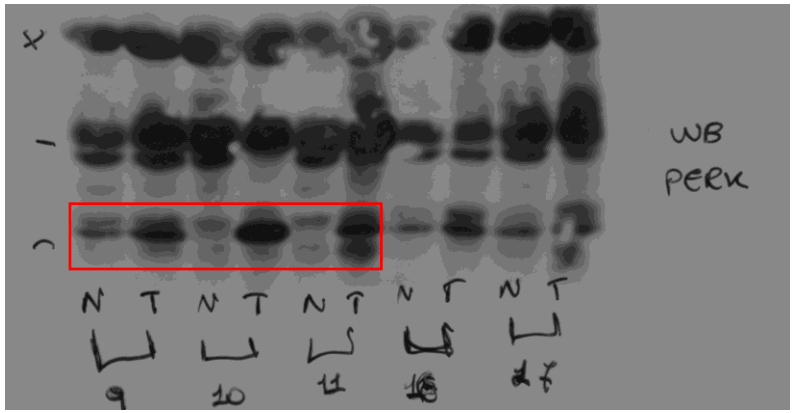

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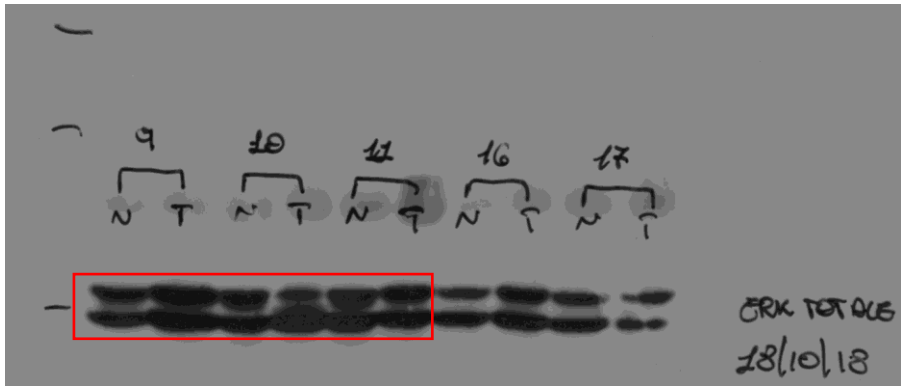

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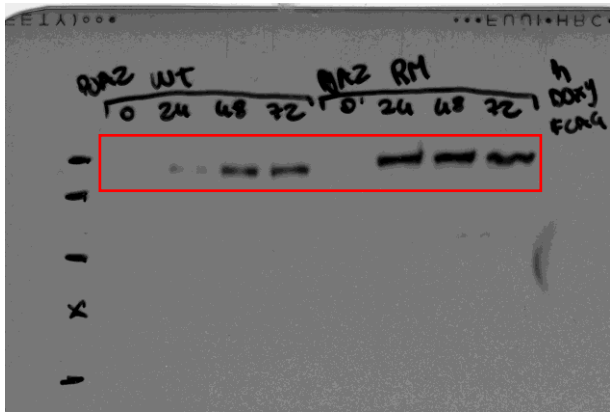

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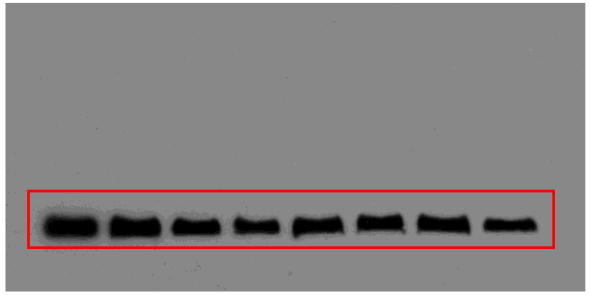

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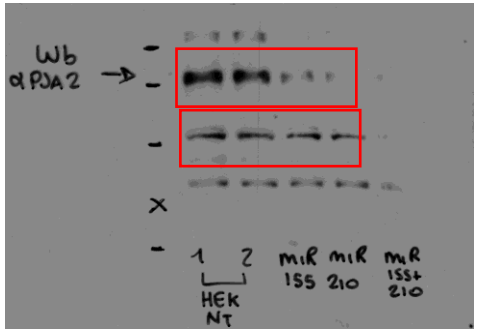

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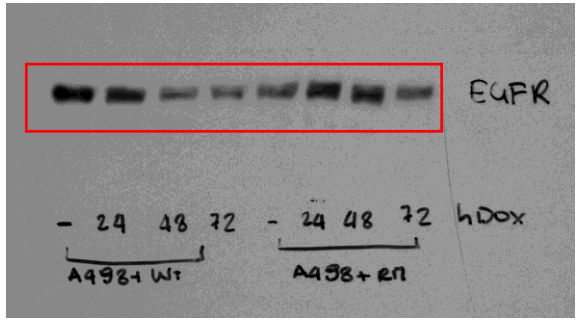
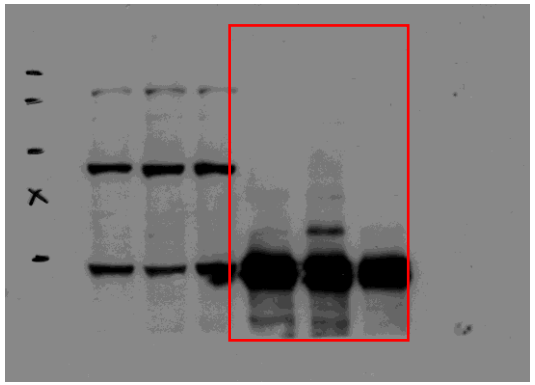


S8. Uncropped gels of the figures presented in Main and Supplementary Figures

Supplementary Figure 8

Fig S2a



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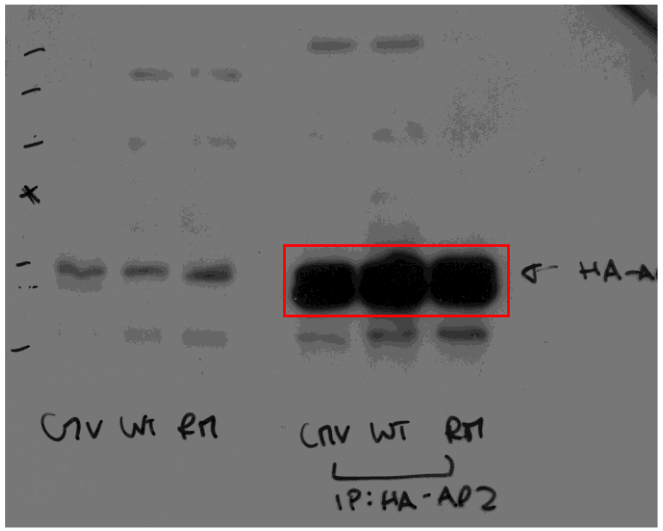

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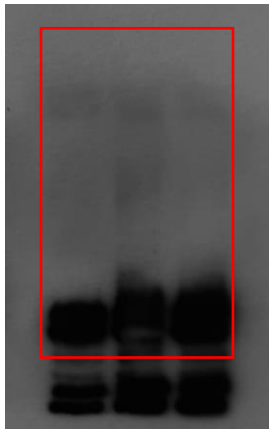

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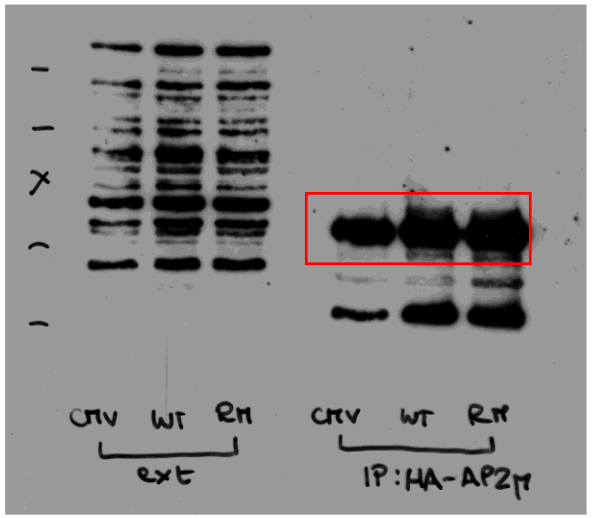

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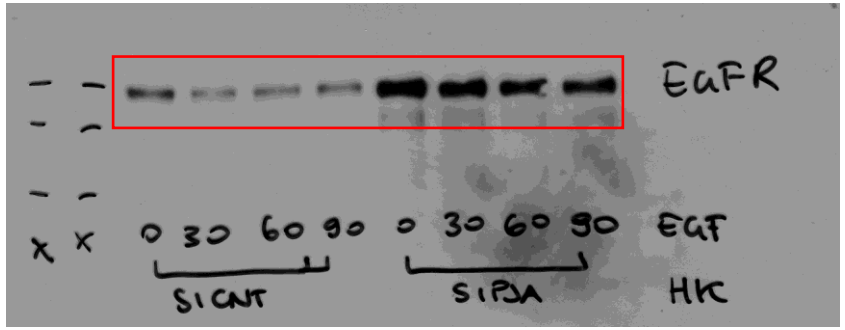

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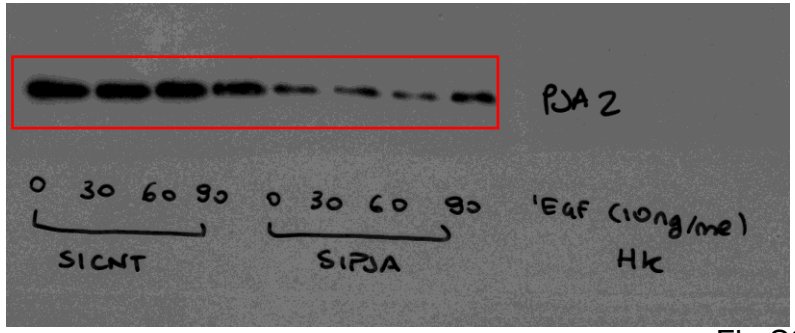

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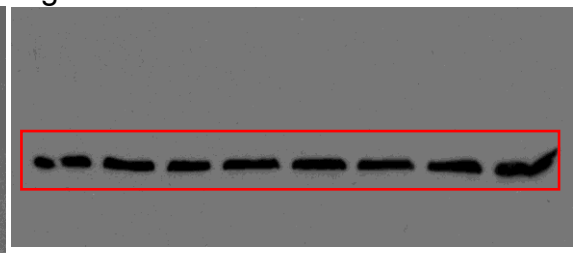

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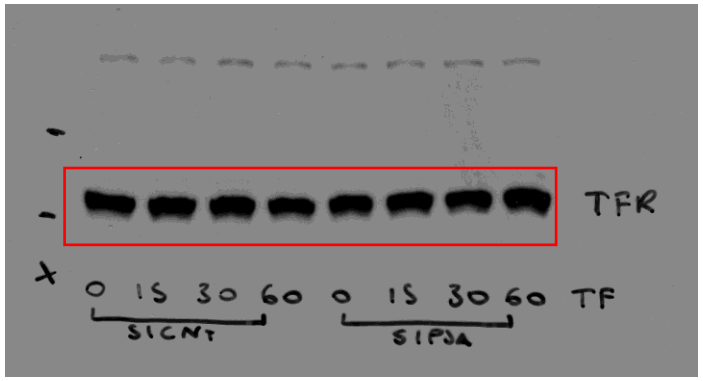

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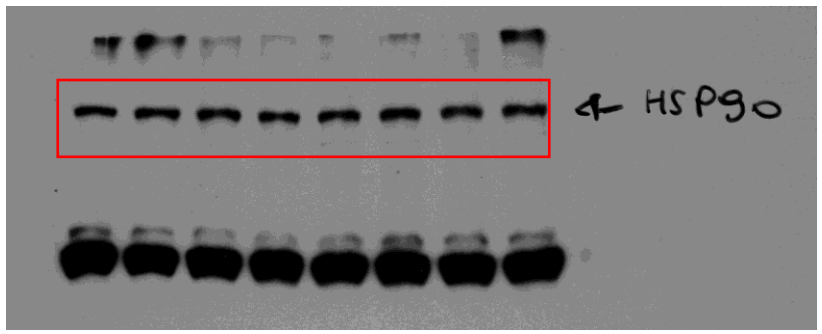

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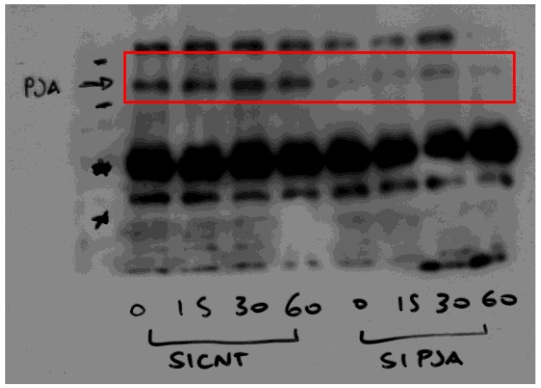
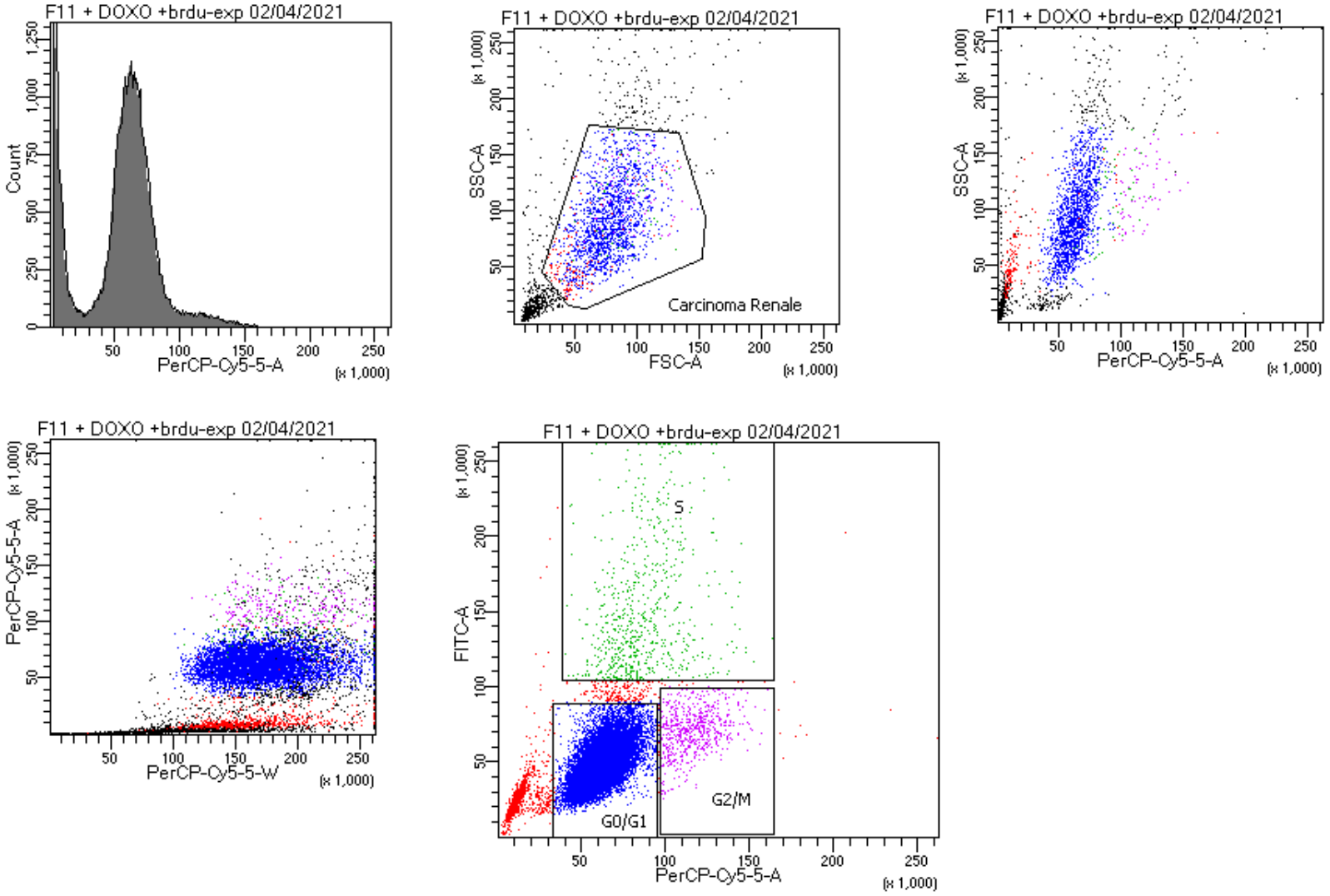


S8. Uncropped gels of the figures presented in Main and Supplementary Figures

Supplementary Figure 8



Supplementary Figure 9

S9. Gating strategy (FACS) data

Tube: exp 02/04/2021

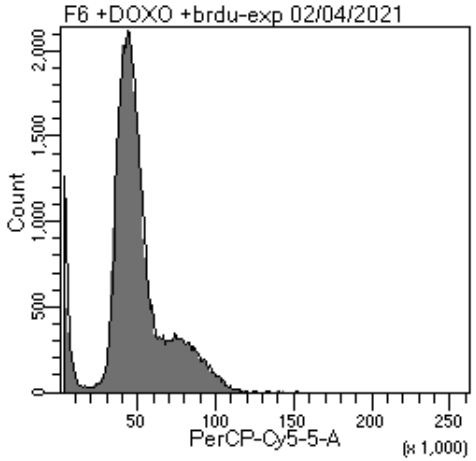
Population	#Events	%Parent	%Total
All Events	49,010	####	100.0
Carcinoma Renale	34,454	70.3	70.3
S	1,302	3.8	2.7
G0/G1	28,693	83.3	58.5
G2/M	1,159	3.4	2.4

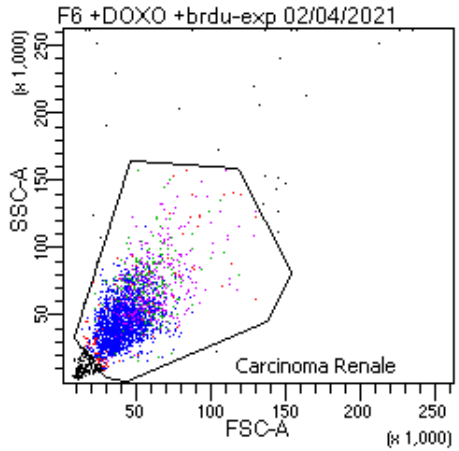
Experiment Name:	Cloni in Carcinoma Renale ...
Specimen Name:	F11 + DOXO +brdu
Tube Name:	exp 02/04/2021
Record Date:	Apr 2, 2021 3:59:52 PM
$OP:	Administrator
GUID:	80a139ae-978c-4433-8bc4...

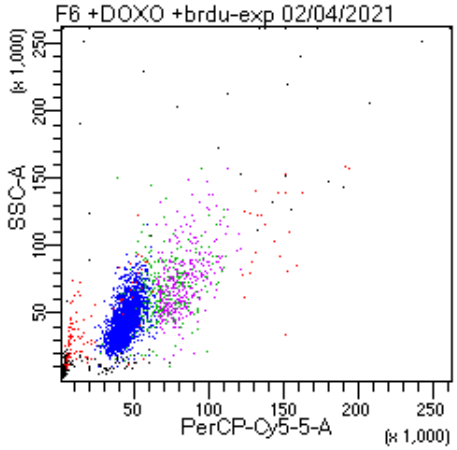
Population	#Events	%Parent	FITC-A Mean	PerCP-... Mean
Carcinoma Renale	34,454	70.3	52,153	60,177
S	1,302	3.8	153,945	86,960
G0/G1	28,693	83.3	49,040	61,302
G2/M	1,159	3.4	69,652	115,011

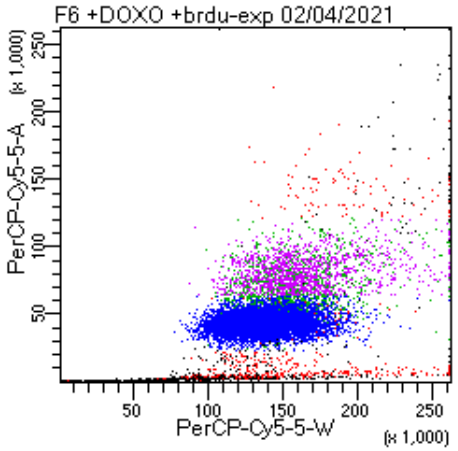
S9. Gating strategy (FACS) data

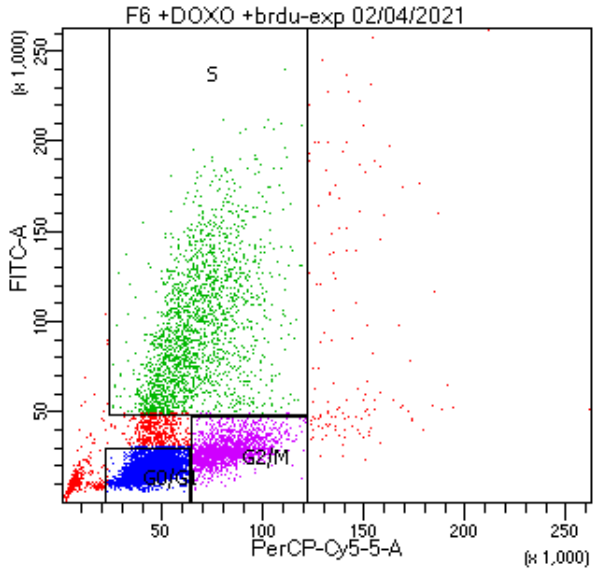
Supplementary Figure 9











S9. Gating strategy (FACS) data

Supplementary Figure 9

Tube: exp 02/04/2021

Population	#Events	%Parent	%Total
All Events	55,851	####	100.0
Carcinoma Renale	51,617	92.4	92.4
S	7,758	15.0	13.9
G0/G1	33,966	65.8	60.8
G2/M	5,904	11.4	10.6

Experiment Name:	Cloni in Carcinoma Renale ...
Specimen Name:	F6 +DOXO +brdu
Tube Name:	exp 02/04/2021
Record Date:	Apr 2, 2021 4:12:42 PM
$OP:	Administrator
GUID:	0faef819-00f4-4b2b-9187-f...

Population	#Events	%Parent	FITC-A Mean	PerCP-... Mean
Carcinoma Renale	51,617	92.4	31,468	50,455
S	7,758	15.0	96,418	66,368
G0/G1	33,966	65.8	16,708	42,158
G2/M	5,904	11.4	28,355	81,925

S9. Gating strategy (FACS) data

Supplementary Figure 9