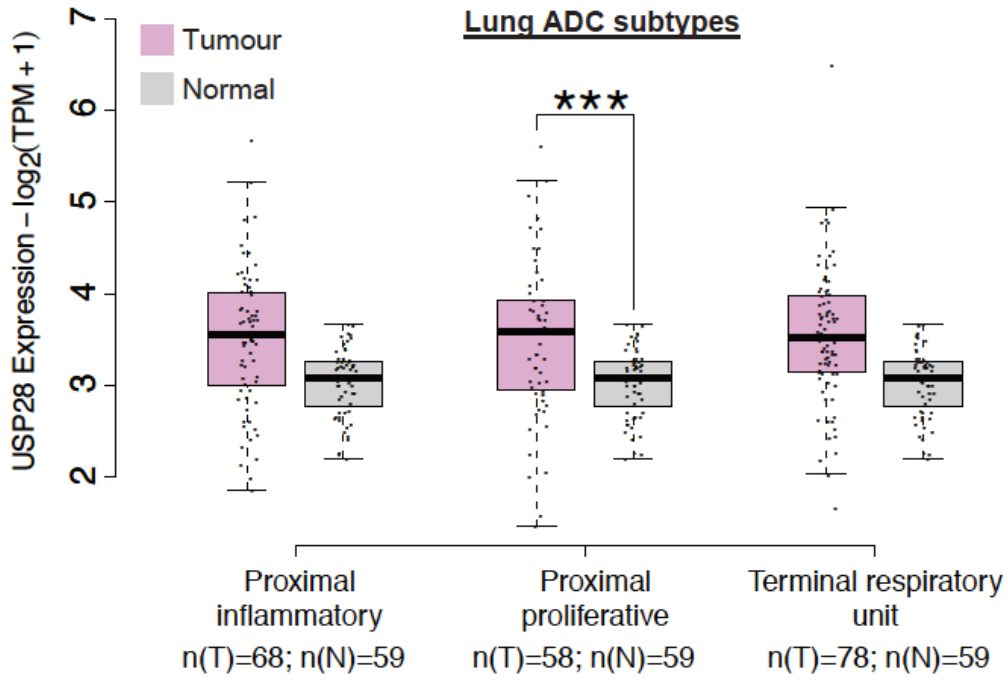
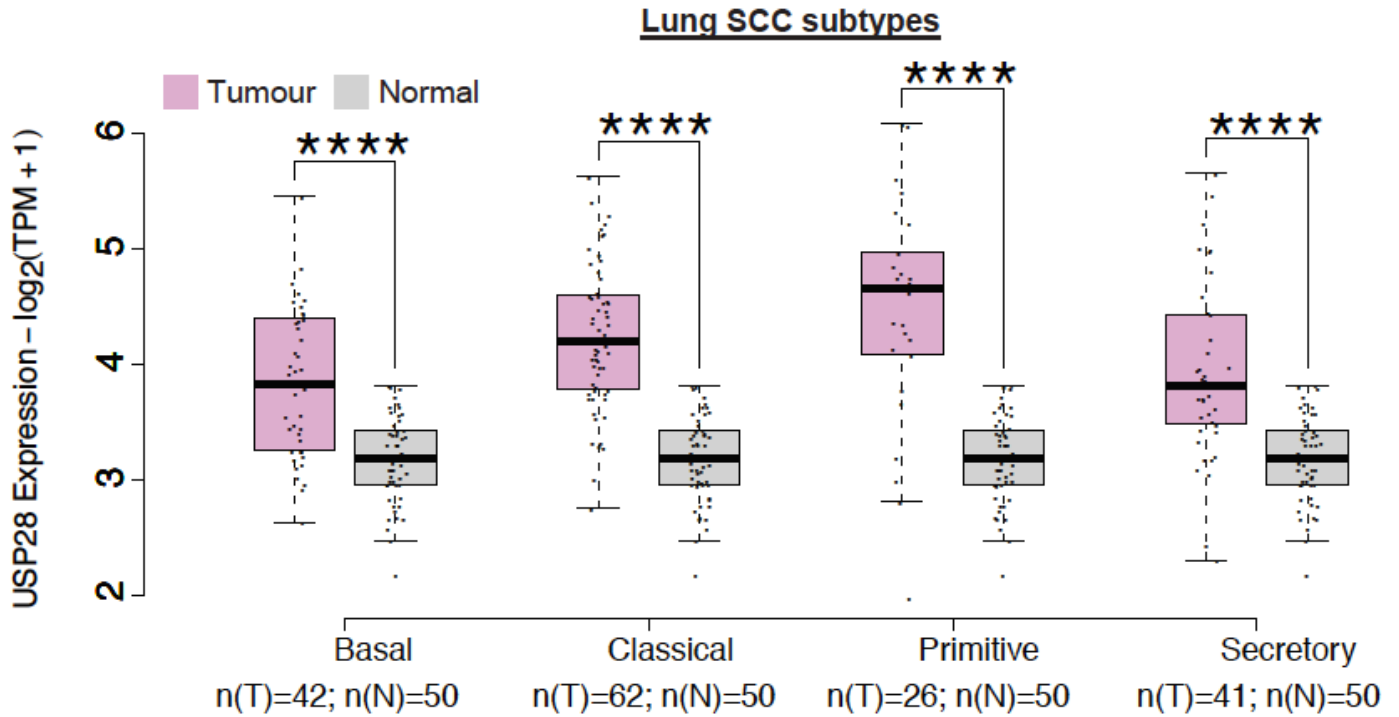


A



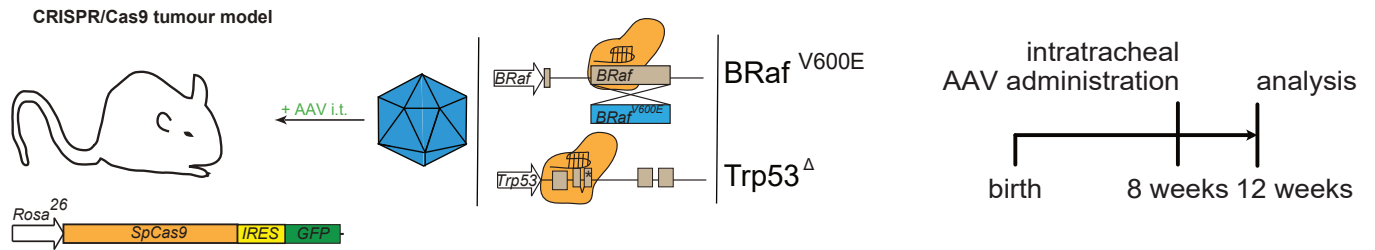
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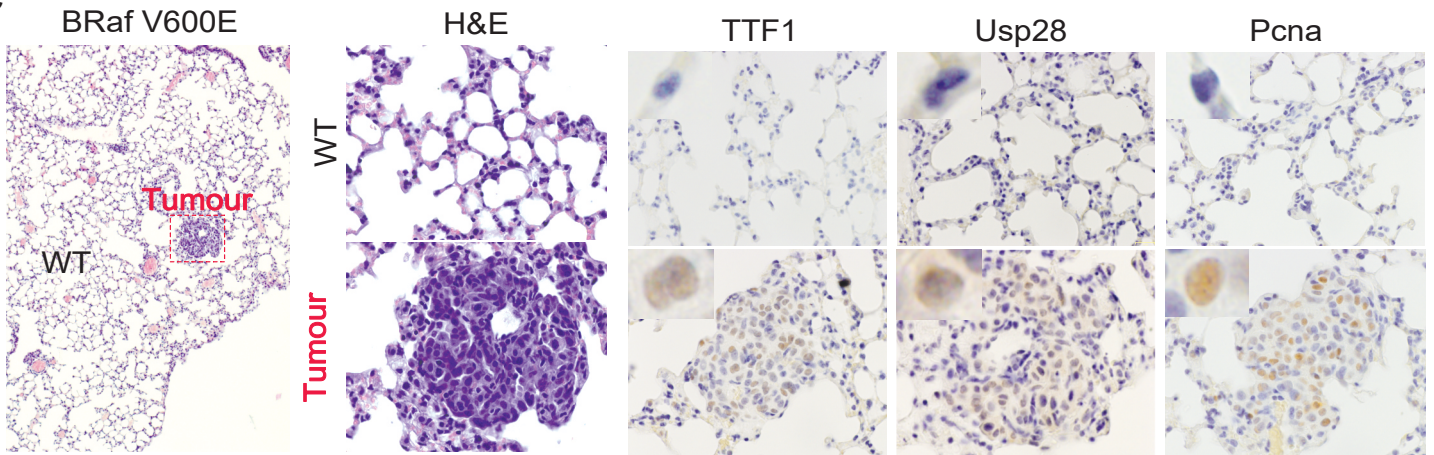
A

	ErbB Family	RAS Family	PIK3 class1 Family	RAF Family
N=501	<u>SCC (43% altered)</u>	<u>SCC (45% altered)</u>	<u>SCC (85% altered)</u>	<u>SCC (63% altered)</u>
	EGFR 13%	HRAS 8%	PIK3CA 77%	A-RAF 19%
	HER1 17%	KRAS 25%	PIK3CB 35%	B-RAF 28%
	HER2 13%	NRAS 22%	PIK3CD 3%	C-RAF 39%
	HER3 13%		PIK3CG 11%	
N=515	<u>ADC (59% altered)</u>	<u>ADC (47% altered)</u>	<u>ADC (50% altered)</u>	<u>ADC (51% altered)</u>
	EGFR 28%	HRAS 8%	PIK3CA 29%	A-RAF 14%
	HER1 26%	KRAS 27%	PIK3CB 18%	B-RAF 25%
	HER2 20%	NRAS 22%	PIK3CD 12%	C-RAF 28%
	HER3 9%		PIK3CG 13%	C-RAF= Down-reg.

B



C



A

RAS Family

SCC

HRAS 0.43
KRAS 0.47
NRAS 0.38

ADC

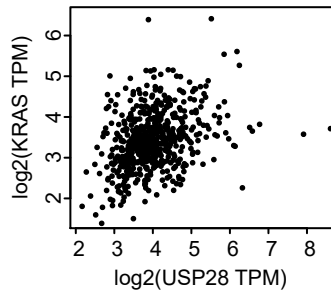
HRAS 0.12
KRAS 0.36
NRAS 0.36

SPEARMAN Correlation with USP28

B

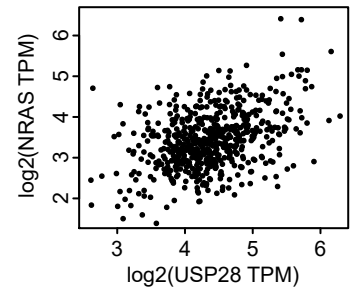
ADC

R=0.36 p=1.1e-19

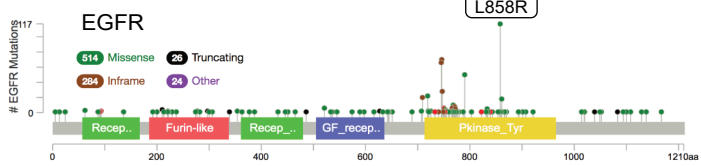


ADC

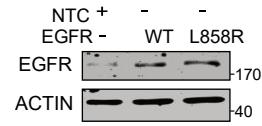
R=0.36 p=4.8e-20



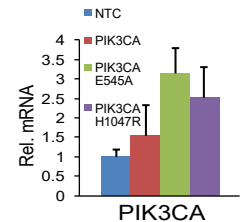
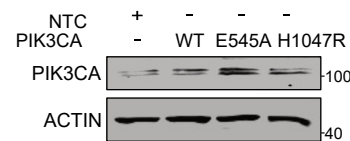
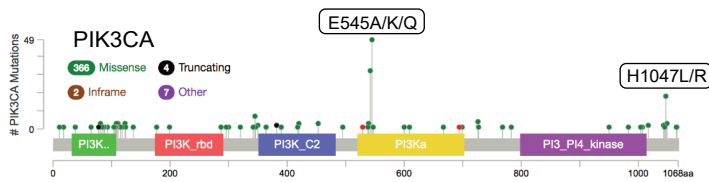
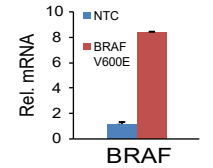
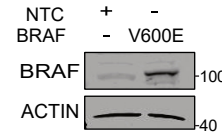
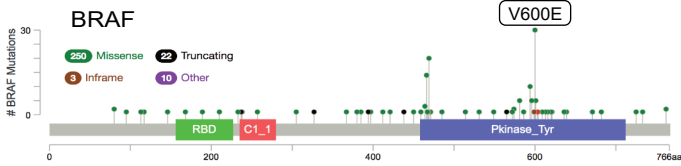
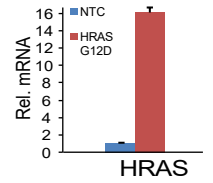
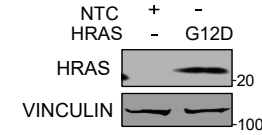
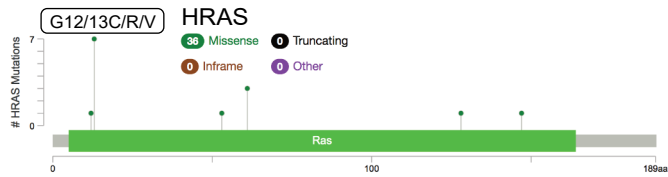
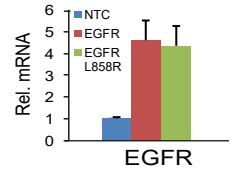
C



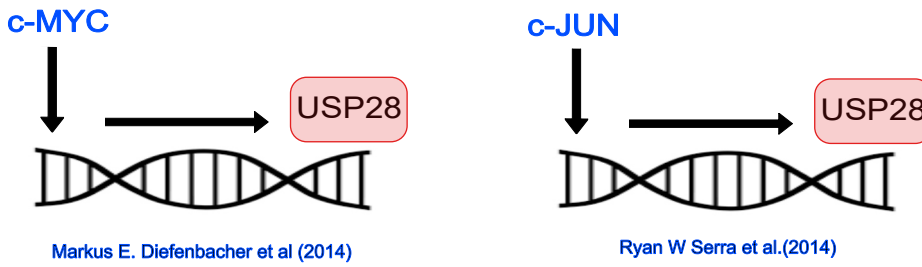
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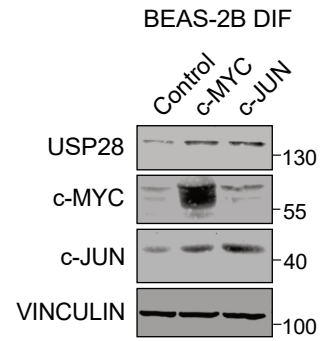
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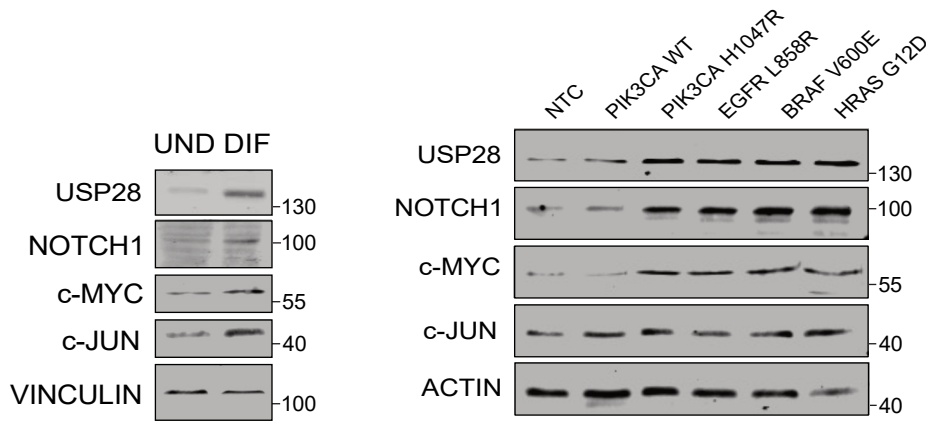
A



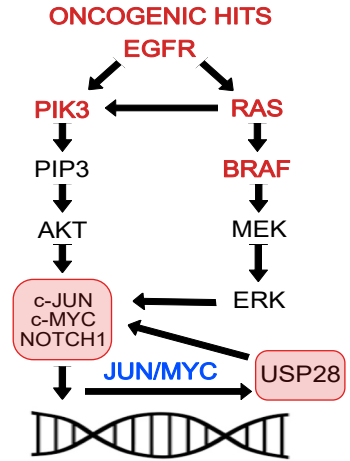
B



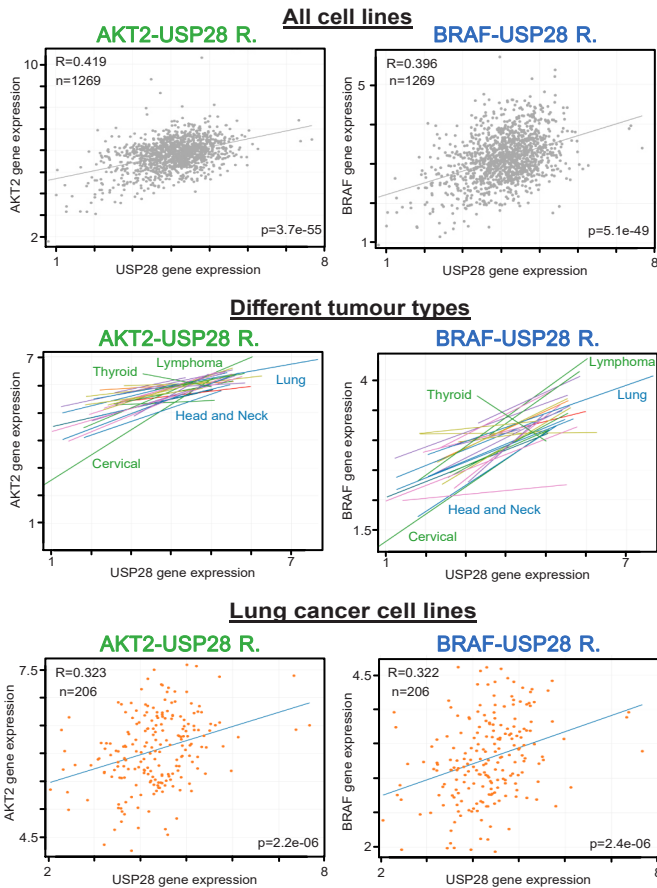
C



D



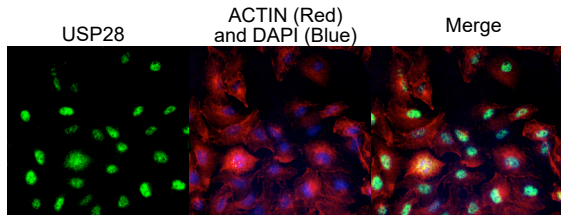
E



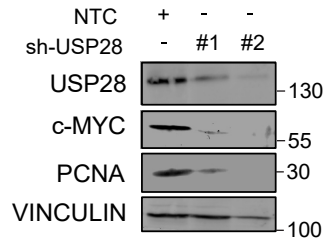
Cell line Tumour type	AKT2-USP28 R.			BRAF-USP28 R.		
	Pearson R	Slope	p-value	Pearson R	Slope	p-value
Thyroid Cancer	-0.253	-2.72E-1	4.28E-1	-0.665	-4.40E-1	1.82E-2
Skin Cancer	0.244	2.04E-1	4.34E-2	0.090	7.03E-2	4.62E-1
Sarcoma	0.579	4.16E-1	2.72E-4	0.386	2.60E-1	2.22E-2
Rhabdoid	0.569	8.10E-1	8.78E-3	0.467	6.02E-1	3.78E-2
Prostate Cancer	0.300	2.59E-1	5.13E-1	0.580	4.75E-1	1.72E-1
Pancreatic Cancer	0.427	5.44E-1	1.99E-3	0.422	2.68E-1	2.29E-3
Ovarian Cancer	0.321	3.50E-1	1.50E-2	0.569	4.00E-1	3.91E-6
Neuroblastoma	0.550	4.60E-1	3.59E-3	0.342	3.42E-1	8.74E-2
Myeloma	0.112	8.42E-2	5.56E-1	0.270	3.09E-1	1.48E-1
Lymphoma	0.685	6.06E-1	9.21E-12	0.602	4.84E-1	8.67E-9
Lung Cancer	0.323	2.54E-1	2.24E-6	0.322	2.34E-1	2.38E-6
Liver Cancer	0.068	4.60E-2	7.51E-1	0.110	8.65E-2	6.10E-1
Liposarcoma	0.818	5.94E-1	7.00E-3	0.218	6.46E-2	5.73E-1
Leukemia	0.436	3.09E-1	1.14E-5	0.378	2.45E-1	1.72E-4
Kidney Cancer	0.418	2.79E-1	1.55E-2	0.481	3.59E-1	4.61E-3
Head and Neck Cancer	0.580	4.91E-1	8.86E-5	0.573	4.40E-1	1.11E-4
Gastric Cancer	0.364	4.66E-1	1.95E-2	0.334	3.28E-1	3.30E-2
Gallbladder Cancer	0.834	4.60E-1	7.89E-2	0.480	1.71E-1	4.13E-1
Fibroblast	0.428	3.06E-1	6.60E-3	0.269	1.63E-1	9.75E-2
Eye Cancer	0.120	6.63E-2	7.98E-1	0.502	2.90E-1	2.51E-1
Esophageal Cancer	0.385	3.43E-1	2.98E-2	0.409	2.79E-1	2.02E-2
Endometrial/Uterine Cancer	0.303	3.99E-1	9.19E-2	0.672	5.28E-1	2.51E-5
Colon/Colorectal Cancer	0.575	4.52E-1	4.41E-7	0.521	3.37E-1	7.38E-6
Cervical Cancer	0.935	9.08E-1	8.25E-6	0.760	4.59E-1	4.12E-3
Breast Cancer	0.336	3.53E-1	1.15E-2	0.338	2.70E-1	1.08E-2
Brain Cancer	0.244	1.69E-1	3.12E-2	0.009	5.47E-3	9.35E-1
Bone Cancer	0.107	9.25E-2	5.36E-1	0.342	3.08E-1	4.09E-2
Bladder Cancer	0.191	1.72E-1	2.63E-1	0.212	1.66E-1	2.15E-1
Bile Duct Cancer	0.416	3.31E-1	1.78E-2	0.449	2.65E-1	9.92E-3

A

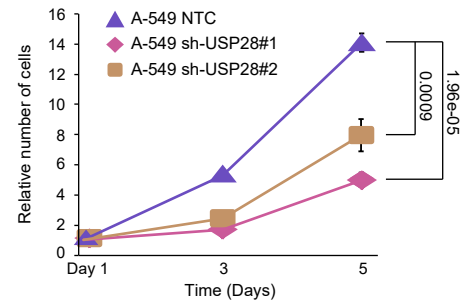
A-549: KRAS G12S mutant NSCLC cell line



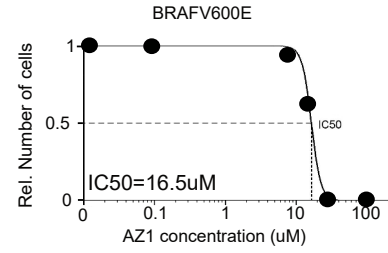
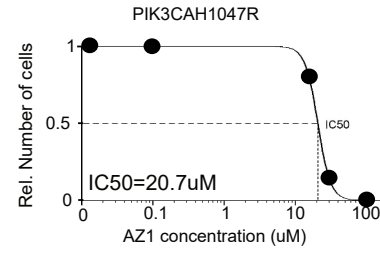
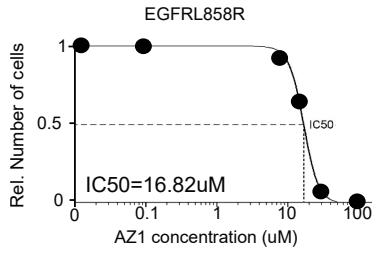
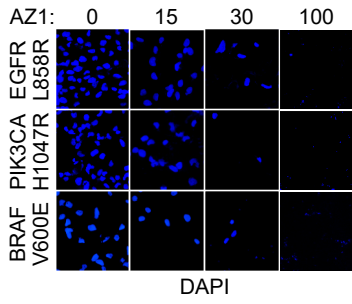
B



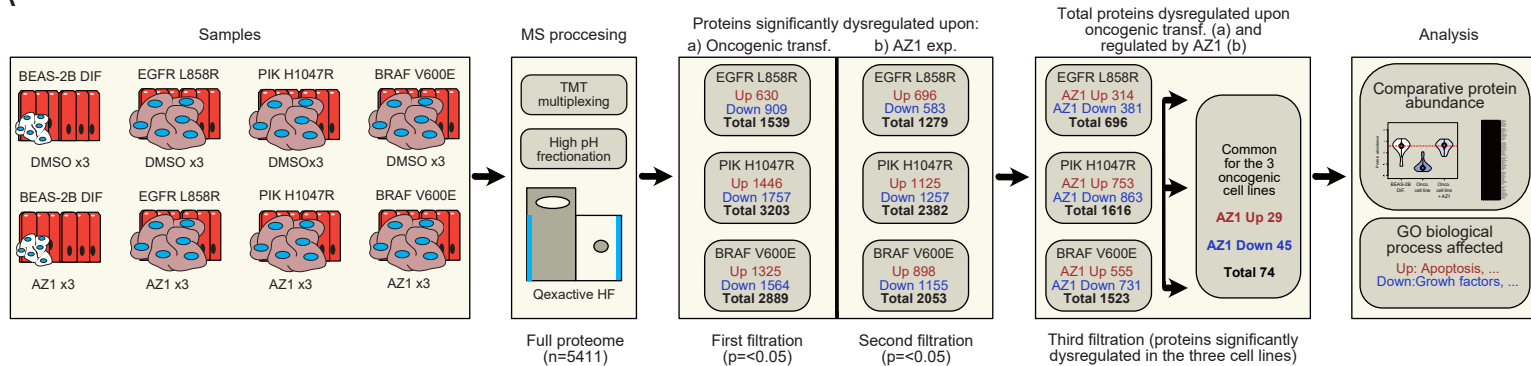
C



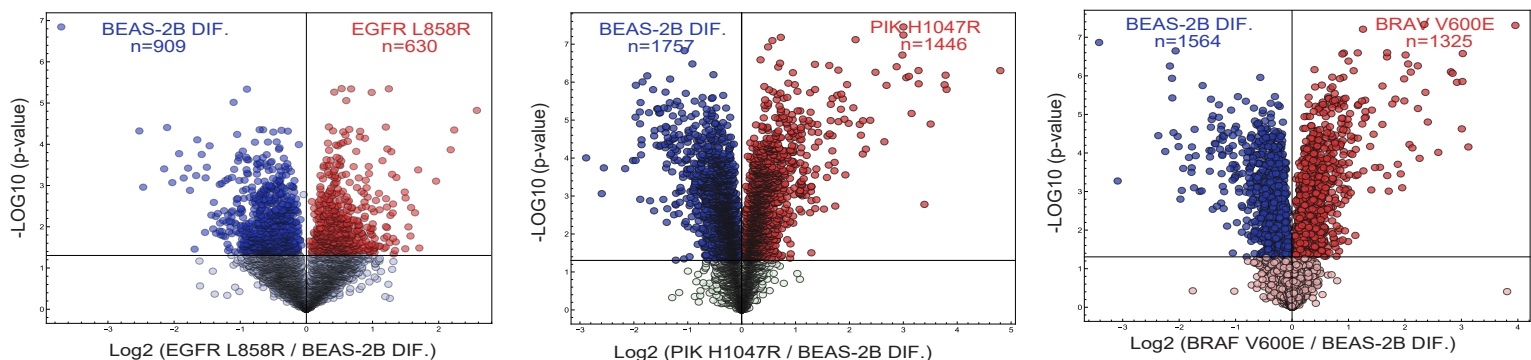
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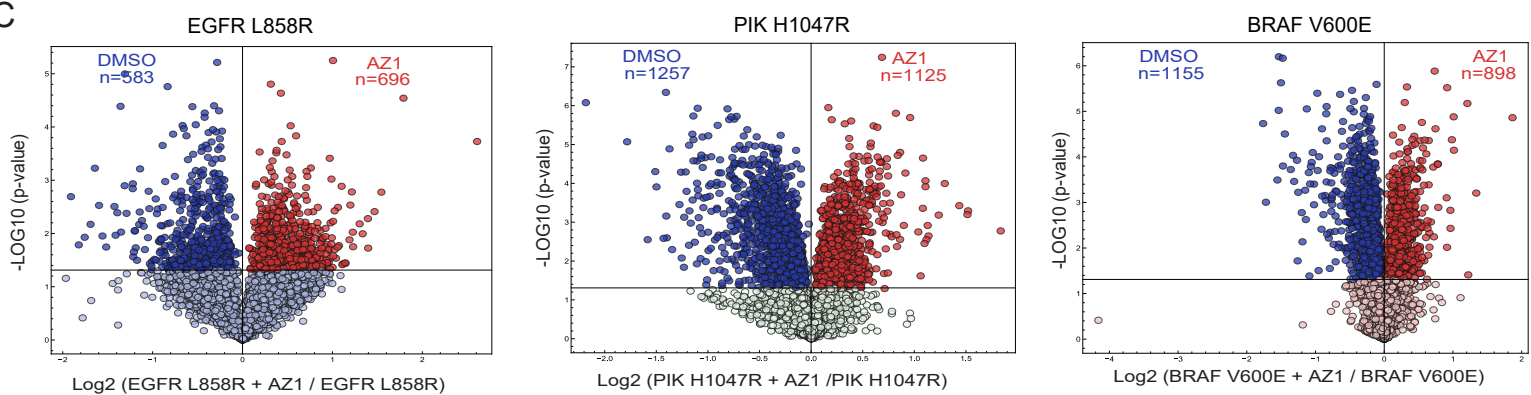
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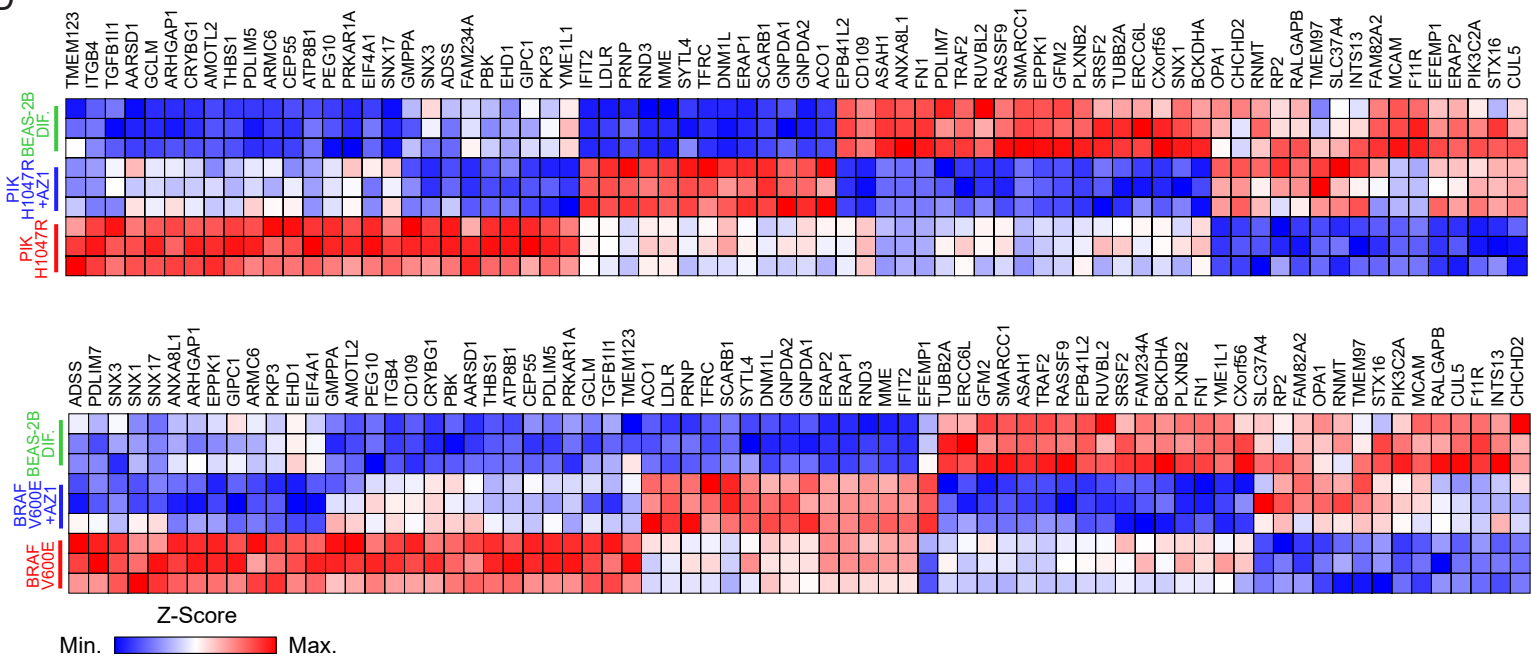
B



C

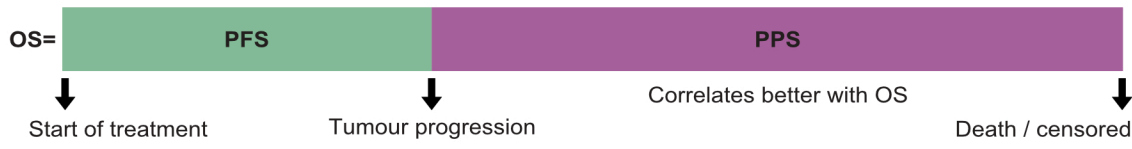
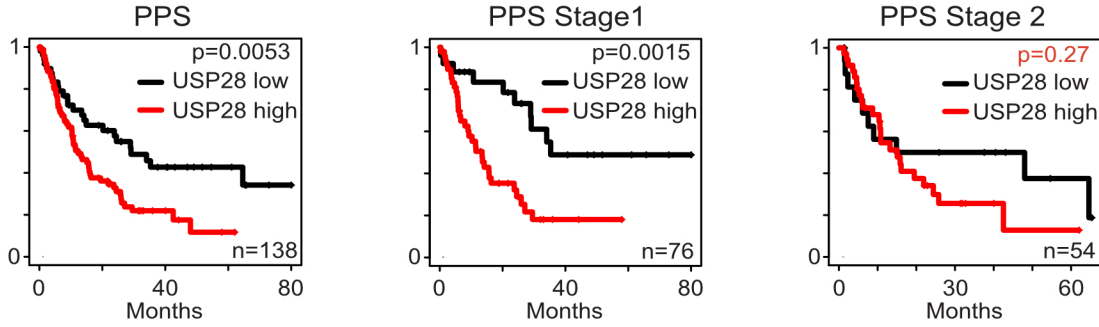
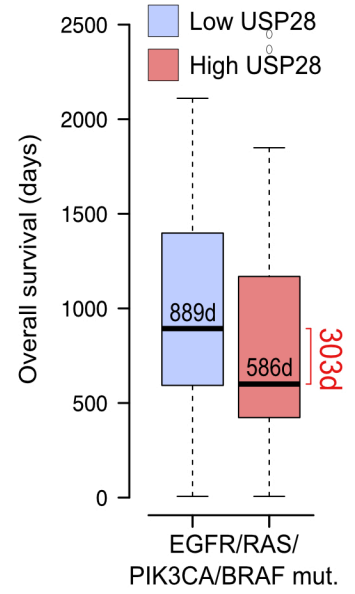
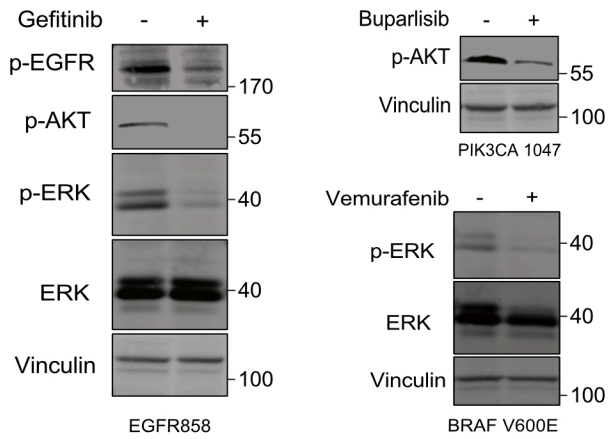


D



A

Overall Survival (OS) = Progression free disease (PFS) + Post progression survival (PPS)

**B****C****D****E**