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Supplemental Information

A Spontaneous Aggressive ERα+ Mammary Tumor Model Is Driven by Kras Activation

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Supplemental Figures

Figure S1. Somatic discovery in the Discovery and Extension Sets. Related to Figure 3.

A. Representative screenshot from the Integrated Genome Viewer (IGV) displaying a *Kras* G12 mutation in the Discovery Set, present in tumor whole genome, whole exome, and RNA sequencing reads (WGS, WES, RNA), but not in the normal WGS and WES, nor RNA from matched aged mammary glands (AMGs). **B.** Representative Sanger traces from the Extension Set, including mutations detected in *Kras* at either G12, G13, or Q61. **C.** Copy number landscape of the Discovery Set. Fill color represents the relative copy number of the genomic region.

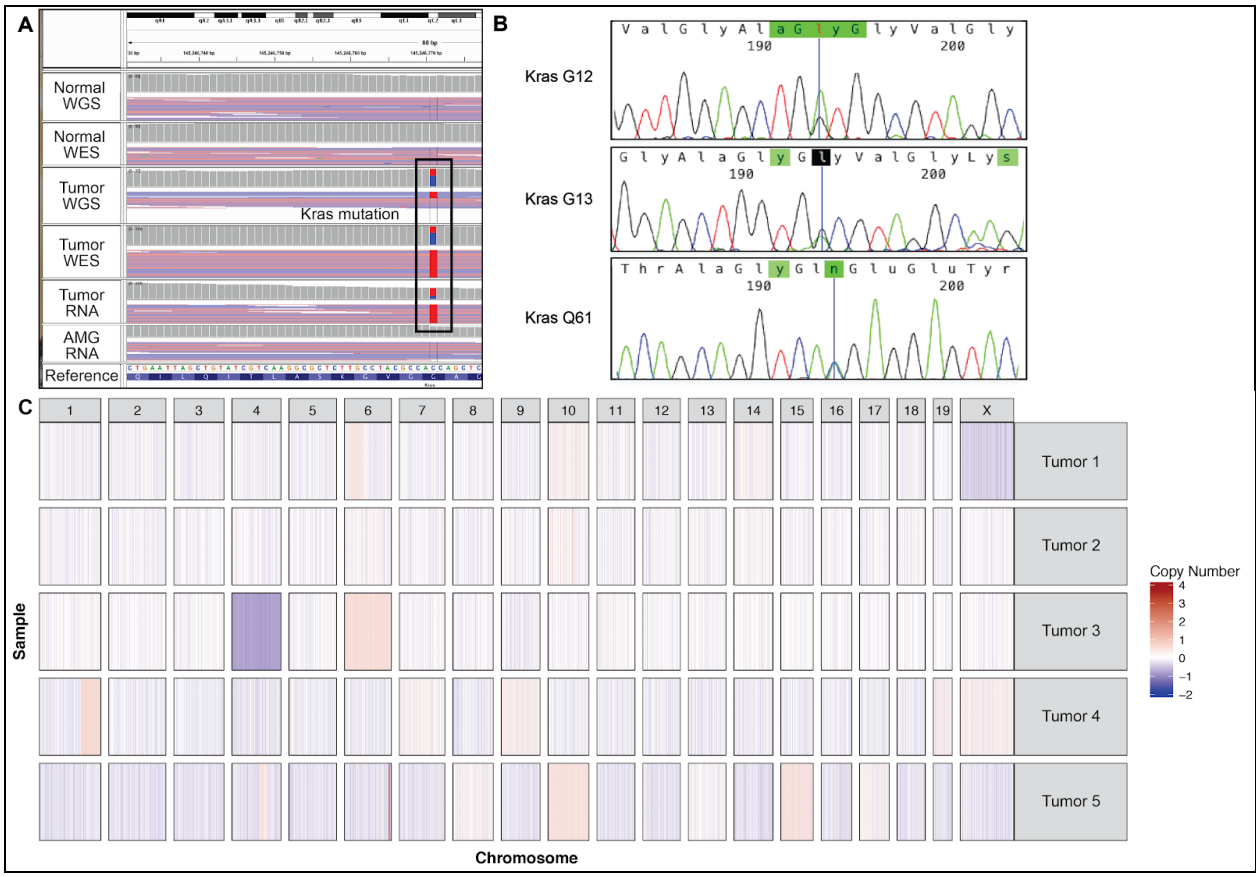
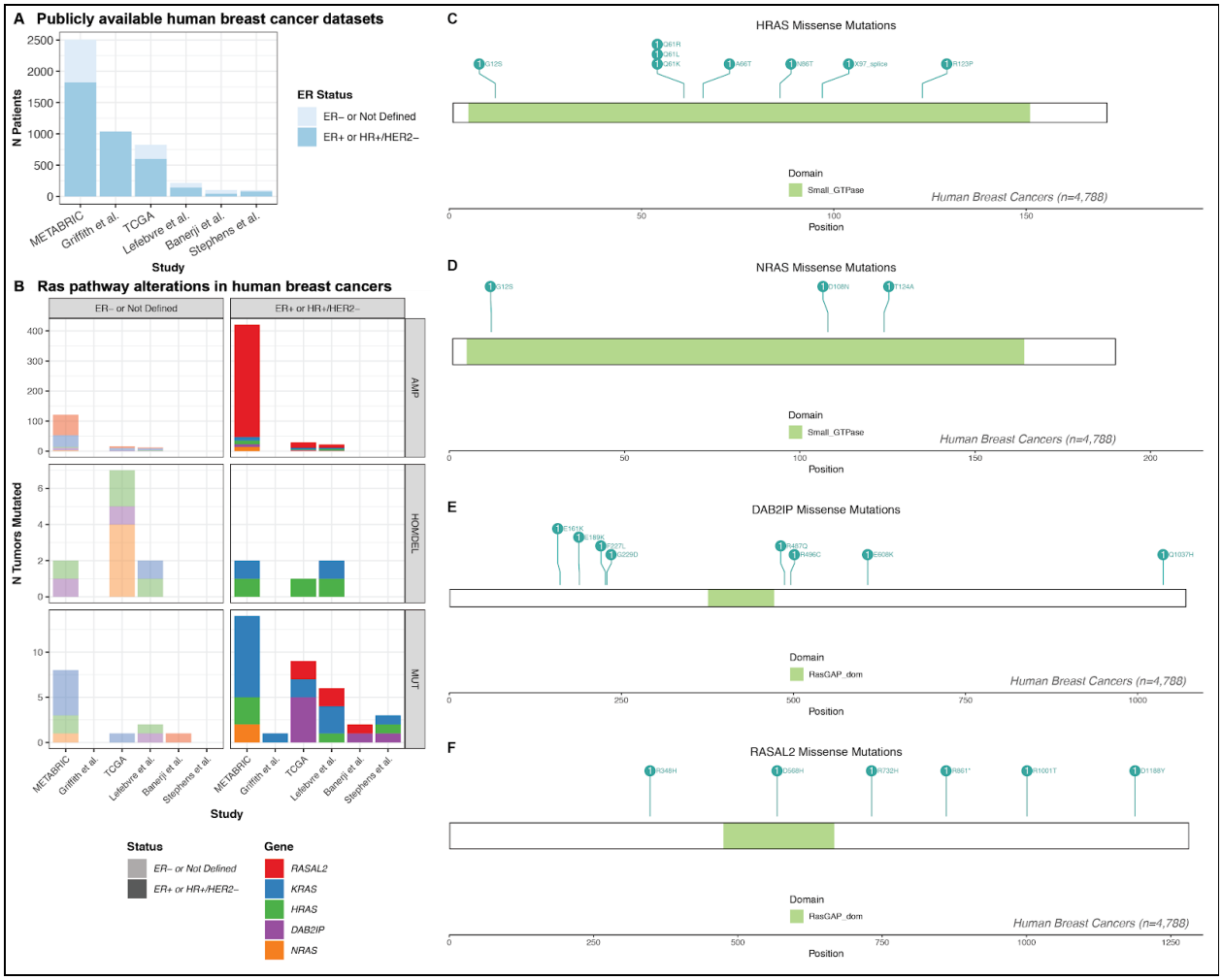


Figure S2. Ras pathway alterations in human breast cancer datasets. Related to Figure 3 and Table S3.

A. Summary of samples assessed from publicly available human breast cancer datasets. Samples are differentiated as either 'ER+ or HR+/HER2-' or 'ER- or Not Defined' (indicated by color), as described in cBioPortal (Banerji et al., 2012; Cancer Genome Atlas Network, 2012; Curtis et al., 2012; Griffith et al., 2018; Lefebvre et al., 2016; Stephens et al., 2012). **B.** Somatic alterations detected in samples from A, categorized by gene (color) and ER status. Alterations are summarized as copy number amplifications (AMP), homozygous deletion (HOMDEL), or point mutations (MUT). **C-F.** Schematics Lolliplots depicting specific point mutations identified in samples from A across Ras pathway genes (*HRAS, NRAS, DAB2IP,* and *RASAL2*).



Supplemental Tables

Table S3. Ras pathway alterations in human breast cancer datasets. Related to Figures 3 and S2.

The number of somatic alterations - including mutations, amplifications, and deletions - detected across public datasets. Values indicate the number of patients with alterations in each corresponding gene (row), or the total number of patients with mutations in any gene (bottom row; percent is calculated as the number of patients with alterations within the associated subtype). “NA” indicates that the gene was not evaluated in the corresponding gene (The Griffith et al. dataset did not evaluate mutations in genes other than *KRAS*). * Patients may have alterations in more than one gene.

	METABRIC (n=2,506)		Griffith et al. (n=1,038)	TCGA (n=825)		Lefebvre et al. (n=216)		Banerji et al. (n=103)		Stephens et al. (n=100)	
	ER+ (n=1,824)	ER- (n=682)	ER+ (n=1,038)	ER+ (n=601)	ER- (n=224)	ER+ (n=143)	ER- (n=73)	ER+ (n=44)	ER- (n=59)	ER+ (n=79)	ER- (n=21)
KRAS	22	44	1	7	9	8	7	0	0	1	0
HRAS	16	6	NA	3	2	7	4	0	0	1	0
NRAS	15	4	NA	2	4	1	0	0	0	0	0
DAB2IP	9	9	NA	7	3	1	2	1	0	1	0
RASAL2	374	68	NA	19	6	12	3	1	1	0	0
Total Patients with Alterations* (% of subtype)	417 (22.9%)	121 (17.7%)	1 (0.1%)	37 (6.2%)	24 (10.7%)	26 (18.2%)	14 (19.2%)	2 (4.5%)	1 (1.7%)	3 (3.8%)	0 (0%)