

Figure S1. Examples of tumors exhibiting different grades of staining. (A) Grade 0 cytoplasmic staining with grade 2 nuclear staining (RAB6C+) and (B) grade 1 cytoplasmic staining with grade 0 nuclear staining (RAB6C-). Scale bar, 200 μ m. RAB6C, Ras-related protein Rab-6C.

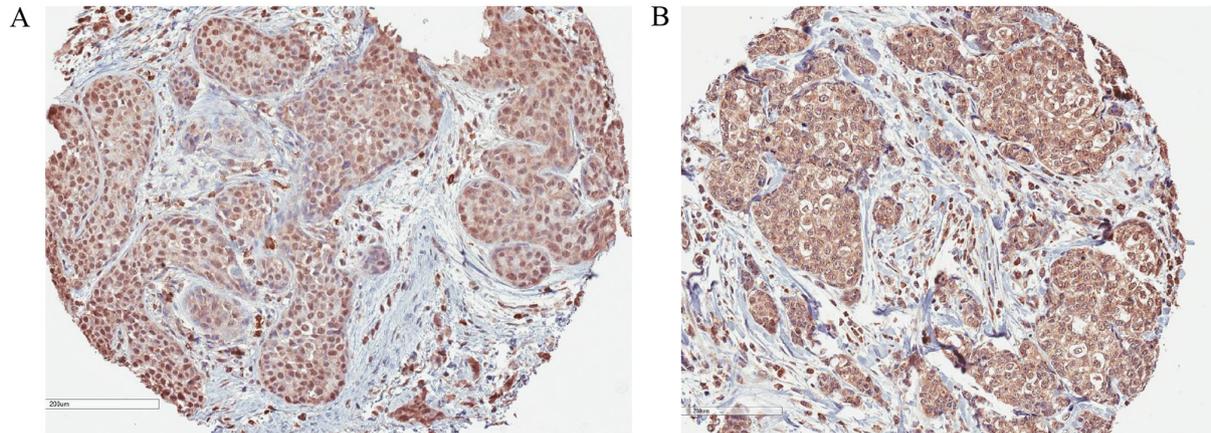


Figure S2. Cumulative distant recurrence risk in relation to the protein expression of RAB6C in ‘low-risk’ patients of the independent cohort. (A) Patients with ER+/PR- tumors (HR, 0.22; 95% CI, 0.06-0.79; P=0.02). (B) Patients with ER+/PR+ tumors (HR, 1.56; 95% CI, 0.72-3.41; P=0.26). The cumulative distant recurrence risk was also determined in ‘high-risk’ patients of the independent cohort with (C) ER+/PR- tumors (HR, 0.21; 95% CI, 0.041-1.10; P=0.07) and (D) ER+/PR+ tumors (HR, 1.21; 95% CI, 0.44-3.31; P=0.72). ER, estrogen receptor; PR, progesterone receptor; HR, hazard ratio; RAB6C, Ras-related protein Rab-6C.

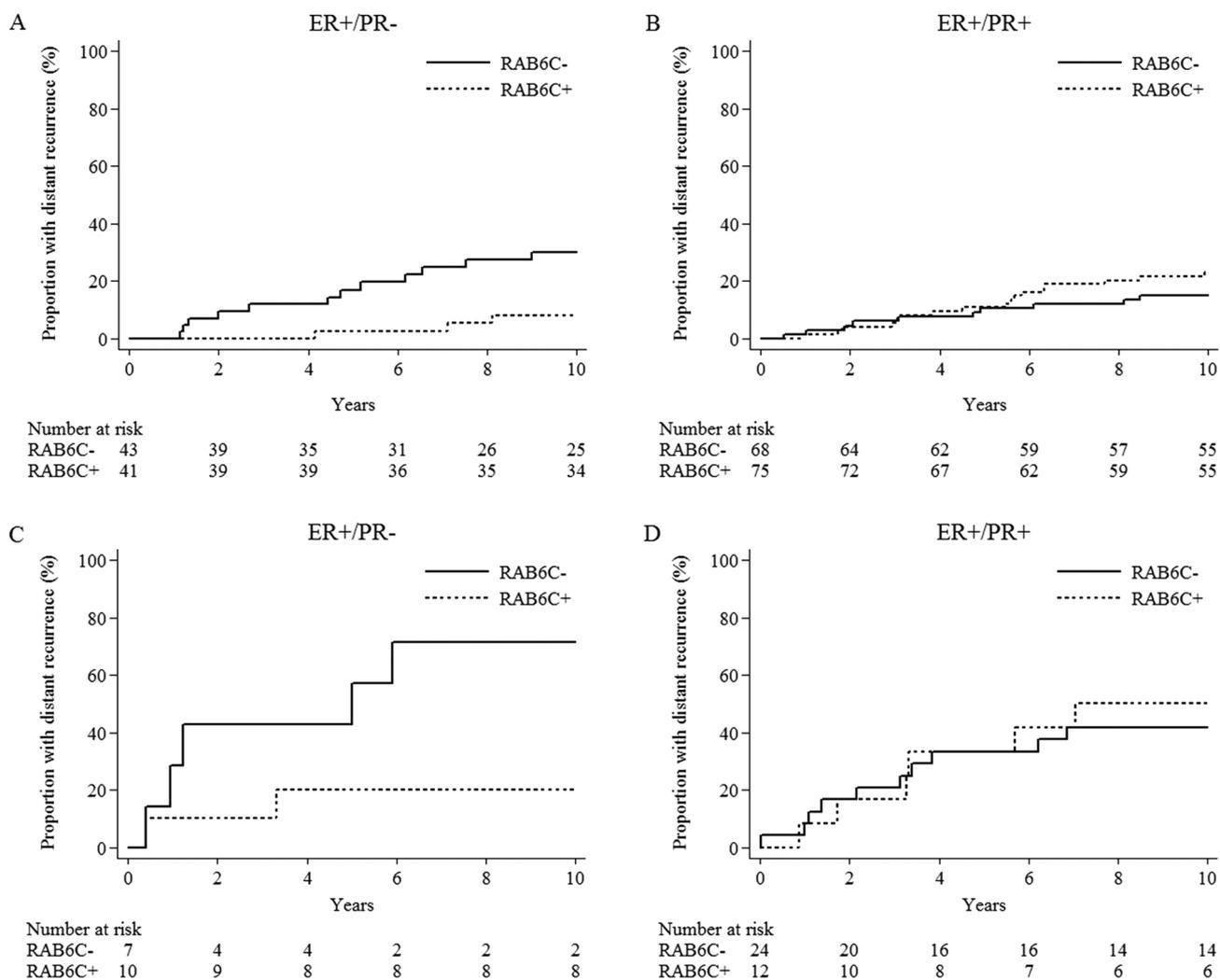


Table SI. Top 20 most varying single nucleotide polymorphisms.

Chromosome	Cytoband	Gene	Physical position ^a	IQR	Min	Max	Median	P-value
19	p13.11	<i>Homo sapiens</i> mucoepidermoid carcinoma translocated 1 (MECT1), mRNA.	18643376	1.60	0.42	11.45	3.06	0.61
16	p13.3	<i>Homo sapiens</i> ubinuclein 1 (UBN1), mRNA.	4859254	1.33	2.27	10.77	5.83	0.33
16	p13.3	<i>Homo sapiens</i> ubinuclein 1 (UBN1), mRNA.	4858366	1.33	2.27	10.77	5.83	0.33
16	p13.3	<i>Homo sapiens</i> ubinuclein 1 (UBN1), mRNA.	4858327	1.33	2.27	10.77	5.83	0.33
1	p36.33	<i>Homo sapiens</i> v-ski sarcoma viral oncogene homolog (avian) (SKI), mRNA.	2266413	1.19	1.04	5.57	2.94	0.25
12	q24.33	<i>Homo sapiens</i> UDP-N-acetyl-alpha-D-galactosamine: polypeptide N-acetylglactosami	131618920	1.18	0.55	5.93	2.38	0.37
4	p16.3	<i>Homo sapiens</i> hypothetical protein FLJ35424 (FLJ35424), mRNA.	3788967	1.18	1.41	5.97	3.40	0.76
1	q21.1	<i>Homo sapiens</i> Fc fragment of IgG, high affinity Ia, receptor for (CD64) (FCGR1A)	145940032	1.14	0.13	4.75	2.74	0.88
3	q26.32	<i>Homo sapiens</i> p53 target zinc finger protein (WIG1), transcript variant 2, mRNA.	180154400	1.14	1.76	21.75	4.15	0.31
2	q21.1	<i>Homo sapiens</i> RAB6C, member RAS oncogene family (RAB6C), mRNA.	130399760	1.13	2.02	6.29	3.57	0.001
X	q22.3	<i>Homo sapiens</i> melanoma associated antigen (mutated) 1-like 1 (MUM1L1), mRNA.	105365400	1.10	1.32	6.30	3.59	0.01
7	p22.3	---	1307029	1.09	1.24	4.52	2.22	0.58
8	q24.21	<i>Homo sapiens</i> POU 5 domain protein (POU5FLC20) mRNA, complete cds.	128759808	1.06	2.17	13.25	3.35	0.30
11	p15.4	<i>Homo sapiens</i> zinc finger protein 195 (ZNF195), mRNA.	3359636	1.04	0.30	3.77	1.99	0.65
1	q21.1	<i>Homo sapiens</i> hypothetical protein LOC200030 (LOC200030), mRNA.	143536496	0.99	0.82	4.90	2.35	0.85
14	q32.33	<i>Homo sapiens</i> hypothetical protein BC015003 (LOC122618), mRNA.	104475432	0.98	1.41	6.35	2.69	0.58
8	q22.3	<i>Homo sapiens</i> outer dense fiber of sperm tails 1 (ODF1), mRNA.	103723248	0.98	2.26	10.11	3.12	0.43
8	q22.2	<i>Homo sapiens</i> odd-skipped-related 2A protein (OSR2), mRNA.	100014624	0.98	1.80	8.68	2.99	0.22
8	q22.2	<i>Homo sapiens</i> odd-skipped-related 2A protein (OSR2), mRNA.	99975800	0.98	1.80	8.66	2.99	0.22
8	q22.2	<i>Homo sapiens</i> odd-skipped-related 2A protein (OSR2), mRNA.	99975432	0.98	1.80	8.66	2.99	0.22

^aGenome version: hg17, NCBI Build 35, May 2004. Chromosomal location and copy number variation over the 199 ER+ tumors. P-values shown here are achieved from Cox regression and are unadjusted for multiple comparisons. IQR, interquartile range; Min, minimum; Max, maximum.

Table SII. Multivariable analysis for the data set GSE10099 of estrogen receptor-positive tumors.

Variables	HR (95% CI)	P-value
Age, years		
>50 vs. ≤50	0.82 (0.51-1.30)	0.39
Tumor stage		
T2-T4 vs. T1	1.32 (0.84-2.07)	0.23
PR		
Positive vs. negative	0.70 (0.42-1.17)	0.17
Grade		
III vs. I-II	2.12 (0.99-4.54)	0.05
Unknown vs. I-II	2.29 (1.04-5.08)	0.04
<i>RAB6C</i>		
Positive vs. negative	0.45 (0.28-0.72)	0.001

HR, hazard ratio; PR, progesterone receptor; *RAB6C*, Ras-related protein Rab-6C.

Table SIII. Multivariable analysis for the data set GSE10099 stratified by hormone receptor status.

Variables	ER ⁺ /PR ⁺		ER ⁺ /PR ⁻	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, years >50 vs. ≤50	0.91 (0.53-1.57)	0.73	0.71 (0.29-1.73)	0.46
Tumor stage T2-T4 vs. T1	1.48 (0.85-2.55)	0.16	1.23 (0.51-2.92)	0.65
Grade III vs. I-II	4.30 (1.30-14.25)	0.017	0.63 (0.21-1.96)	0.43
Unknown vs. I-II	3.94 (1.18-13.19)	0.026	1.75 (0.44-6.96)	0.43
<i>RAB6C</i> Positive vs. negative	0.55 (0.32-0.95)	0.033	0.15 (0.05-0.46)	0.001

ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor; RAB6C, Ras-related protein Rab-6C.

Table SIV. Multivariable analysis for the ER⁺ tumors in the independent cohort.

Variables	HR (95% CI)	P-value
Study group ^a		
2 vs. 1	1.11 (0.15-8.36)	0.92
3 vs. 1	2.70 (1.25-5.82)	0.01
4 vs. 1	7.36 (3.68-14.72)	<0.001
HER2		
Positive vs. negative	0.84 (0.31-2.27)	0.72
Grade		
II vs. I	1.76 (0.81-3.81)	0.15
III vs. I	2.31 (0.91-5.85)	0.08
PR		
Positive vs. negative	0.46 (0.22-0.95)	0.04
RAB6C		
Positive vs. negative	0.17 (0.05-0.60)	<0.01
Interaction		
PRxRAB6C	7.66 (1.86-31.51)	<0.01

^aStudy group indicates the patient groups as follows: i) Study group 1, postmenopausal, tumor size <30 mm, lymph node negative; ii) study group 2, premenopausal, tumor size ≥30 mm, lymph node negative; iii) study group 3, premenopausal, tumor size <30 mm, lymph node positive; and iv) study group 4, premenopausal, tumor size ≥30 mm, lymph node positive. N=246 with 58 events. ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor; RAB6C, Ras-related protein Rab-6C.