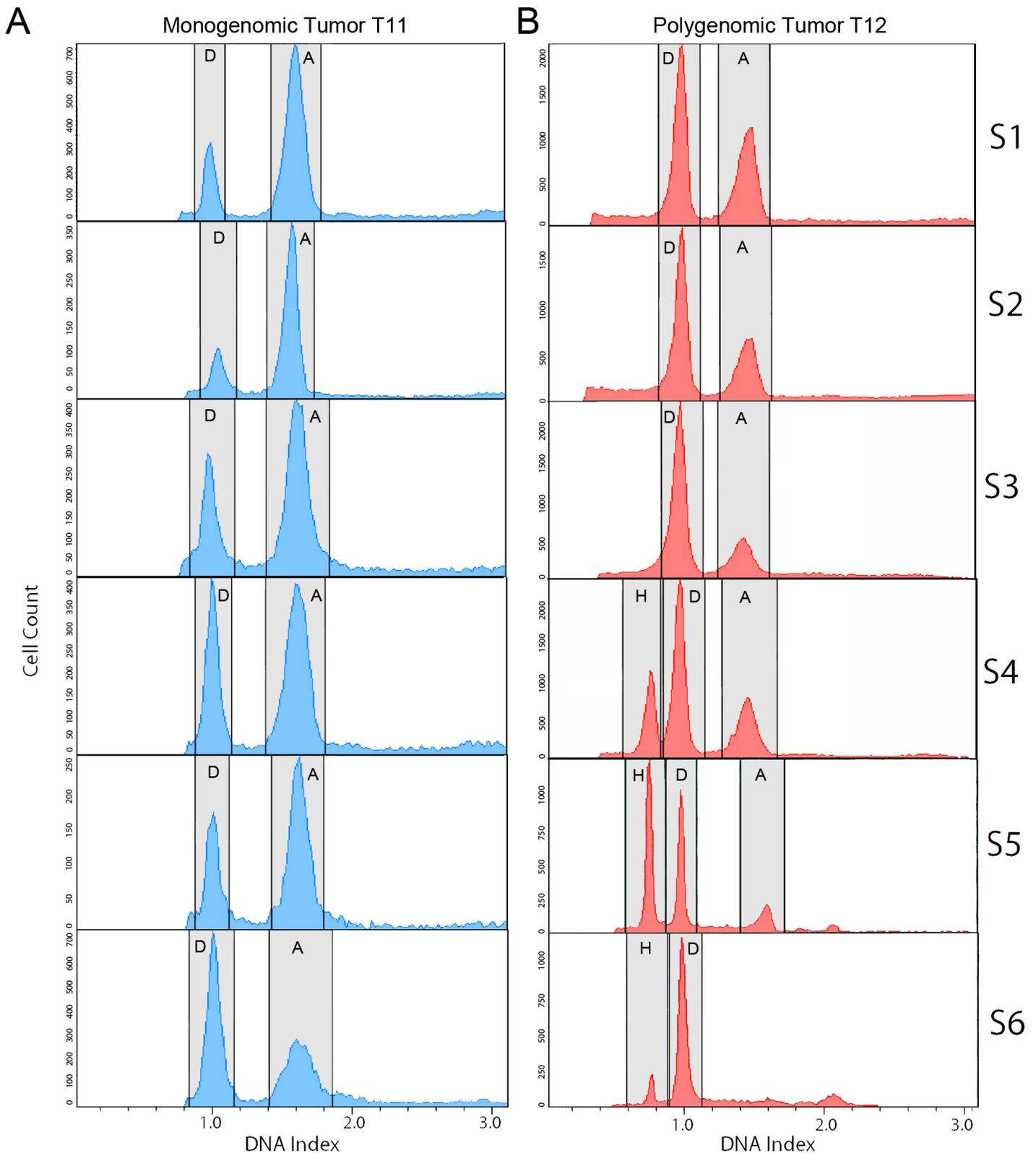


**Figure S1.** Sector-ROMA Analysis of Tumor Quadrants. Tumors were macro-dissected into four sectors and each quadrant was analyzed by ROMA for genomic copy number variation. **(A)** Tumor T1 displays a highly similar copy number profile in all four sectors (S1-S4) suggesting that it consists of a single tumor subpopulation and may be classified as monogenomic. **(B)** Tumor T4 displays a near diploid copy number profile in sectors S1-S2, but progresses to a highly aneuploid copy number profile in sectors (S3-S4), suggesting that it consist of at least two tumor subpopulations and may be classified as polygenomic.



**Figure S2.** FACS Histograms of DNA Content in Tumor Sectors. Nuclei were isolated from tumor sectors and sorted by total genomic DNA content (ploidy). **(A)** The monogenic tumor T11 contains two cellular distributions: diploid (D) and aneuploid (A) which were gated and sorted. The DNA index of the diploid distribution was identical (1.0) in all six tumor sectors (S1-S6). The DNA index of the aneuploid distribution was also identical (1.62) in all six sectors. **(B)** The polygenomic tumor T12 contained three cellular distributions: hypodiploid (H), diploid (D) and aneuploid (A). The diploid distribution was present in all six sectors with an identical DNA index of 1.00. The DNA index of the hypodiploid distribution was present in only three sectors (S4-S6) with a mean index of 0.79. The aneuploid distribution was only present in five sectors (S1-S5) with a mean index of 1.48.

ID	Sectors	FACS	n	c	Sub	Co-oc	Class	Grade	Size (cm)	ER	PR	Her2
T1	4	no	8	-	-	-	mono	2	2.0 x 1.0 x 0.5	na	na	-
T2	4	no	8	-	-	-	mono	3	0.5 x 0.4 x 0.3	na	na	na
T3	4	no	4	-	-	-	poly	3	0.2 x 3.0 x 1.2	+	+	na
T4	4	no	4	-	-	-	poly	3	1.0 x 1.0 x 1.0	+	+	na
T5	4	yes	10	0.81	2	yes	poly	3	2.8 x 0.5 x 0.5	na	na	na
T6	4	yes	8	0.95	1	no	mono	3	2.0 x 0.8 x 0.4	na	na	na
T7	4	yes	8	0.99	1	no	mono	2	1.5 x 1.5 x 1.5	+	+	-
T8	5	yes	10	0.94	2	no	poly	3	2.8 x 2.8 x 2.8	na	na	na
T9	6	yes	12	0.92	1	no	mono	3	2.0 x 1.3 x 0.4	+	-	-
T10	6	yes	14	0.47	3	yes	poly	3	2.7 x 1.4 x 1.1	-	-	na
T11	6	yes	12	0.90	1	no	mono	3	2.0 x 1.0 x 1.0	na	na	na
T12	6	yes	16	0.64	3	yes	poly	3	6.0 x 6.0 x 5.0	na	na	na
T13	6	yes	12	0.76	2	yes	poly	3	2.0 x 2.0 x 1.0	-	-	na
T14	6	yes	15	0.68	1	no	poly	3	2.0 x 0.8 x 0.5	na	na	-
T15	4	yes	8	0.92	1	no	mono	3	0.5 x 0.5 x 0.3	na	na	na
T16	4	yes	8	0.99	1	no	mono	3	1.5 x 1.0 x 0.5	-	-	-
T17	4	yes	8	0.53	3	yes	poly	3	2.6 x 1.0 x 1.0	na	na	na
T18	4	yes	8	0.84	3	no	poly	3	2.2 x 1.0 x 0.8	-	-	-
T19	6	yes	12	0.77	1	no	poly	3	2.0 x 1.3 x 0.8	+	+	+
T20	5	yes	10	0.94	1	no	mono	3	5.0 x 3.0 x 2.0	-	-	-

**Table S1.** Summary of Solid Breast Tumors Analyzed. Twenty primary ductal carcinomas were analyzed by SPP to identify tumor subpopulations. Nine tumors were classified as monogenomic and eleven tumors as polygenomic. T1-T4 were macro-dissected and analyzed by ROMA. T5-T20 were analyzed by SPP. The column descriptions are:

<b>ID</b>	Tumor identification number
<b>Sectors</b>	Number of tumor sectors that were macro-dissected
<b>FACS</b>	Samples from which tumor nuclei were stained with DAPI and flow-sorted by ploidy
<b>n</b>	Total number of copy number profiles analyzed from a single tumor
<b>cc</b>	is the the minimum Pearson's correlation calculated using the autosomes of all aneuploid copy number profiles
<b>Sub</b>	Number of subpopulations identified
<b>Co-oc</b>	Two or more tumor subpopulations co-occupied a single sector in the FACS histogram
<b>Class</b>	Tumor was classified as monogenomic (mono) or polygenomic (poly).
<b>Grade</b>	Histological tumor grade scored using the modified Bloom-Richardson system
<b>Size</b>	Dimension of the frozen solid tumor in centimeters
<b>ER</b>	Estrogen receptor status of the tumor determined by immunohistochemistry
<b>PR</b>	Progesterone receptor status of the tumor determined by immunohistochemistry
<b>Her2</b>	Herceptin receptor status of the tumor determined by FISH or Immunohistochemistry

#	Tumor	Present	Absent	Loc	Exc	Event	Ratio	Size (kb)	Chr	Cytoband	Start HG18	Stop HG18	Cancer Genes	Known Genes
1	T5	A2	A1	S3-S4	S1-S2	del	1:2	1,148	1	q32.2	207859891	209007930	-	LAMB3, GOS2, HSD11B1, IRF6, SYT14, HHAT, KCNH1
2	T5	A1	A2	S1-S2	S3-S4	del	1:2	97	12	p13.33	2060341	2157396	-	CACNA1C
3	T5	A1	A2	S1-S2	S3-S4	del	1:2	37	16	q12.1	47582130	47619657	-	NT_010498.59
4	T5	A1	A2	S1-S2	S3-S4	amp	3:2	287	16	q22.2	69470004	69757528	-	HYDIN
5	T8	A2	A1	S4-S5	S1-S3	amp	4:2	864	12	q21.1	72269679	73134226	-	BC061638, BC094833
6	T8	A2	A1	S4-S5	S1-S3	amp	6:2	373	12	q21.2-21.31	78696935	79069950	PPP1R12A	-
7	T8	A2	A1	S4-S5	S1-S3	amp	4:2	206	12	q21.31	83688476	83895005	-	SLC6A15
8	T10	A1,A2	H	S5,S6	S1-S4	del	1:2	149	3	q21.3	127728953	127878837	-	CHST13, TR2IT1
9	T10	A1,A2	H	S5-S6	S1-S4	amp	4:2	5	4	q31.3	151282090	151287122	-	DCLK2
10	T10	A2	H,A1	S5,S6	S1-S4	del	1:2	7978	5	q21.1-22.1	101814799	109793050	EFNA5, FER	PAM, FBXL17, SLC06A1, PJA2, MAN2A1
11	T10	A2	H,A1	S5,S6	S1-S4	amp	10:2	3652	12	p12.1	22083693	25736050	KRAS	SOX5, ETNK1, CMAS, BCAT1, LRMP, CASC1
12	T12	A1	H	S1-S4	S5-S6	del	1:2	128	5	q33.2	153282447	153410942	-	MFAP3, FAM114A2
13	T12	A1	H	S1-S4	S5-S6	del	0:2	153	11	q22.3	108696368	108849416	-	c11orf87
14	T12	A1	H	S1-S4	S5-S6	amp	3:2	215	17	q21.1-q21.2	35505295	35720207	CDC6, RARA	NR1D1, CASC3, RAPGEFL1, WIRE, WIPF2
15	T12	A1	H	S1-S4	S5-S6	amp	4:2	419	20	q13.13	48157873	48577190	PTPN1	UBE2V1, CEBPB, TMEM189
16	T14	A2	A1	S2-S4	S1,S5-6	del	1:2	371	2	q36.3	229951523	230322758	-	DNER
17	T14	A2	A1	S2-S4	S1,S5-6	del	0:2	220	11	q12.1	58007425	58227622	LPXN	ZFP91, CNTF
18	T14	A2	A1	S2-S4	S1,S5-6	del	0:2	639	22	q13.31	46146803	46786015	-	FLJ46257
19	T17	A1	A2	S1-S3	S4	amp	3:2	1247	1	q44	242836931	244084235	SMYD3	FAM36A, HNRNPU, EFCAB2, KIF26B
20	T17	A1	A2	S1-S3	S4	amp	3:2	671	22	q11.21	17671011	18342500	SEPT5, CDC45L	HIRA, UFD1L, CDC45L, CLDN5, TBX1, TXNRD2, COMT
21	T18	A1	A2	S1-S2	S3-S4	del	1:2	97	7	q21.13	89450127	89547319	CREB3L2	-
22	T18	A1	A2	S1-S2	S3-S4	del	1:2	422	X	p11.4	41494040	41916836	CASK	-
23	T19	A1	A2	S1-S3	S4-S6	amp	3:2	6652	10	p14-p12.33	11137382	17789776	MCM10	32 known genes
24	T19	A2	A1	S4-S6	S1-S3	amp	3:2	1790	18	p11.21	12150130	13940735	PTPN2	CIDEA, TUBB6, SPIRE1, SEH1L, CEP192, RNMT, MCSR

**Table S2.** Subpopulation-specific focal lesions. Focal lesions that differ between tumor subpopulations were annotated for cancer genes and known genes. Twelve amplifications and twelve deletions were mapped to the UCSC human genome 18 (March, 2006). Cancer genes were annotated using the NCI Cancer gene index by Sophic Alliance ([www.sophicalliance.com](http://www.sophicalliance.com)) and the Sanger Cancer Gene Census ([www.sanger.ac.uk/genetics/CGP/Census](http://www.sanger.ac.uk/genetics/CGP/Census)). Known genes were annotated using the UCSC known gene index ([genome.ucsc.edu](http://genome.ucsc.edu)). The highlighted regions in grey appear in Figure 4. The columns are:

**#** identification number of the focal lesion  
**Tumor** tumor identification number  
**Present** indicates the tumor subpopulation that contains the lesion  
**Absent** indicates the tumor subpopulation that does not contain the lesion  
**Loc** the anatomical sector(s) that contains the lesion  
**Exc** the anatomical sector(s) from which the lesion is excluded  
**Event** describes if the focal lesion is an amplification (amp) or deletion (del)  
**Ratio** log ratio of the focal lesion from the segmented coalesced copy number profile  
**Size** genomic interval of the focal lesion in kilobases (kb)  
**Chr** chromosome to which the lesion has been mapped  
**Cytoband** cytogenetic band in which the lesion has been mapped  
**Start HG18** start coordinate of the focal lesion  
**Stop HG18** stop coordinate of the focal lesion