	SNP calls (%) in Tissue / Sample Group						
	Leucocyte [all]	**Control P**	**On follow-up P1**	**On follow-up P2**	**Pre-surgical P**	**On follow-up T**	**Pre-surgical T**
n	73	8	50	50	15	40	15
Mean	96.89	83.06	91.37	88.62	86.80	88.52	93.61
Median	98.64	89.45	90.39	86.96	86.64	88.63	96.60
Range	70.14-99.32	69.62-92.33	85.04-98.51	85.21-98.33	85.85-88.36	86.65-89.52	87.06-98.70

Supplementary Table 1. Summary of SNP call-rates for patients and controls by sample type. SNP call-rate is the percent of SNP probes hybridised to template DNA during experimentation and is used as an indicator of sample quality. The highest call-rate was seen in leucocyte DNA, but with similar high values obtained from blood plasma and FFPE tumor DNA. Control P, control plasma, P1, first plasma, P2, second plasma, pre-surgical P, pre-surgery plasma, T, tumor DNA.

	SNP concordance (%) in Tissue / Sample Group					
	Control P	**On follow-up P1**	**On follow-up P2**	**Pre-surgical P**	**On follow-up T**	**Pre-surgical T**
Mean	89.00	68.95	54.42	44.88	33.84	35.92
Median	90.34	69.46	48.20	43.17	33.80	36.15
Range	81.10 -94.08	33.17-99.44	33.31-97.96	36.00-68.27	32.90-40.1	34.45-37.57

Supplementary Table 2. Concordance of SNP genotype calls for tumor and plasma DNA with matched normal leucocyte DNA.

Chromosomal Interval		**CNV size (kb) and number of markers in group by sample type [mean]**						
		Healthy controls		**Pre-Surgical Breast Cancer**		**Breast Cancer on Follow up**		
		L	**P**	**P**	**T**	**P1**	**P2**	**T**
		n=8	**n=8**	**n=15**	**n=15**	**n=50**	**n=50**	**n=40**
1p36.33	Size Range	84-762 [343]	106-482 [294]	151-274 [212]	207-624 [335]	72-531 [270]	84-500 [266]	146-298 [244]
	No. of markers	51-193 [81]	50-126 [77]	59-62 [61]	51-174 [94]	50-147 [75]	51-147 [72]	50-71 [58]
1p36.21	Size Range	49-711 [116]	39-928 [149]	45-636 [109]	42-634 [220]	40-1022 [172]	37-952 [113]	42-861 [178]
	No. of markers	50-176 [77]	50-129 [77]	50-124 [65]	60-108 [77]	50-248 [76]	50-212 [68]	51-77 [60]
1q21.1	Size Range	47-543 [156]	50-454 [115]	57-701 [133]	86-621 [338]	48-1054 [200]	46-679 [164]	88-607 [175]

	No. of markers	51-167 [79]	50-84 [57]	50-74 [61]	53-195 [116]	50-128 [66]	50-133 [65]	50-86 [57]
2p11.2	Size Range	62-1438 [254]	58-1202 [170]	45-1218 [153]	69-451 [187]	49-1317 [220]	32-1207 [167]	55-1327 [232]
	No. of markers	51-147 [85]	50-161 [74]	50-146 [72]	50-166 [96]	50-149 [76]	50-180 [74]	50-131 [90]
4q13.2	Size Range	43-543 [166]	50-745 [163]	45-555 [157]	63-835 [400]	49-652 [163]	37-626 [163]	61-595 [386]
	No. of markers	50-165 [76]	52-220 [74]	50-123 [64]	54-363 [127]	50-175 [70]	50-150 [67]	52-86 [65]
5p11	Size Range	3352-3645 [3454]	142-3379 [2276]		216-3475 [2348]	196-3646 [2785]	103-3675 [2215]	268-320 [291]
	No. of markers	58-106 [75]	51-72 [61]		51-100 [69]	53-106 [70]	50-115 [67]	60-65 [63]
5q13.2	Size Range	42-1660 [314]	42-212 [101]	63-191 [106]	44-301 [141]	45-600 [108]	34-1936 [121]	52-145 [103]
	No. of markers	51-78 [59]	50-114 [65]	50-122 [69]	50-118 [75]	50-117 [66]	50-117 [64]	51-72 [57]
7p11.2	Size Range	40-113 [87]	38-98 [72]	27-172 [77]	26-129 [90]	24-543 [99]	23-438 [87]	26-128 [73]
	No. of markers	51-137 [82]	60-96 [82]	50-90 [61]	55-110 [79]	50-189 [71]	50-188 [68]	51-107 [67]
7q11.21	Size Range	57-520 [241]	75-417 [180]	31-180 [88]	108-597 [262]	61-513 [194]	48-634 [180]	55-292 [150]
	No. of markers	51-212 [77]	50-137 [78]	50-134 [67]	55-133 [98]	51-160 [70]	50-128 [63]	50-74 [58]
7q11.23	Size Range	69-366 [182]	68-186 [122]	59-215 [114]	68-222 [157]	35-1085 [171]	36-1226 [142]	44-1232 [261]
	No. of markers	57-174 [90]	50-95 [66]	51-78 [63]	50-148 [92]	50-226 [71]	50-147 [67]	50-69 [56]
8p23.1	Size Range	25-475 [87]	25-356 [88]	22-365 [82]	30-464 [123]	21-714 [103]	22-949 [100]	22-361 [86]
	No. of markers	50-93 [63]	50-190 [68]	50-122 [63]	50-196 88]	50-146 [66]	50-205 [66]	50-70 [57]
9p11.2	Size Range		1522	663-21784 [4018]	1503	835-21570 [7978]	983-22860 [13125]	641-1503 [976]
	No. of markers		63	58-108 [75]	52	65-86 [75]	56-136 [82]	51-63 [55]
9q12	Size Range		1363	654-1142 [970]	1099	76-2416 [1230]	508-1358 [969]	445-573 [509]
	No. of markers		70	54-80 [63]	65	51-71 [59]	50-81 [59]	56-60 [58]
10q11.22	Size Range	27-543 [105]	33-826 [97]	32-332 [80]	55-1073 [210]	27-865 [110]	26-832 [115]	31-801 [146]
	No. of markers	50-190 [79]	50-120 [72]	50-144 [68]	51-265 [108]	50-170 [74]	50-157 [70]	50-75 [60]
10q11.23	Size Range	51-133 [84]	42-265 [80]	27-115 [71]	41-131 [84]	21-272 [84]	19-469 [89]	25-281 [98]
	No. of markers	50-77 [60]	51-109 [69]	51-124 [63]	50-85 [60]	50-118 [67]	50-134 [65]	52-84 [61]
14q11.1	Size Range	314-1087 [808]	811-1321 [1081]	1004-1005 [1029]	630-970 [800]	563-1238 [1013]	563-1248 [960]	
	No. of markers	52-142 [84]	52-130 [84]	64-82 [73]	64-136 [100]	50-143 [76]	51-83 [65]	
14q11.2	Size Range	39-231 [101]	26-222 [94]	41-139 [74]	40-215 [102]	23-366 [94]	23-313 [91]	45-150 [82]
	No. of markers	50-146 [78]	50-149 [68]	50-110 [61]	50-148 [79]	50-321 [72]	50-286 [71]	50-80 [60]
14q32.33	Size Range	55-478 [208]	62-460 [200]	61-315 [189]	74-441 [224]	56-572 [200]	55-695 [188]	52-447 [216]
	No. of markers	51-174 [76]	51-171 [80]	51-144 [71]	50-164 [83]	50-240 [74]	50-268 [72]	50-149 [77]
15q11.2	Size Range	46-399 [123]	49-579 [135]	51-474 [147]	56-446 [158]	41-545 [144]	39-942 [144]	45-257 [144]

	No. of markers	50-194 [74]	50-139 [73]	50-96 [65]	50-133 [68]	50-212 [76]	50-174 [73]	50-98 [64]
15q25.2	Size Range	57-778 [191]	47-596 [141]	66-324 [119]	92-796 [229]	35-715 [145]	37-695 [136]	83-133 [110]
	No. of markers	50-139 [79]	50-91 [63]	50-98 [64]	53-107 [80]	50-141 [67]	50-161 [64]	50-69 [57]
16p12.3	Size Range	48-686 [118]	45-674 [120]	52-215 [87]	45-731 [215]	43-908 [126]	49-705 [102]	54-144 [86]
	No. of markers	50-125 [71]	53-128 [75]	50-194 [64]	53-246 [127]	50-262 [75]	50-230 [71]	50-95 [60]
16p11.2	Size Range	71-326 [149]	68-716 [210]	61-557 [179]	68-518 [218]	51-816 [217]	39-698 [200]	75-272 [189]
	No. of markers	50-84 [59]	50-86 [60]	50-92 [62]	51-138 [76]	50-142 [64]	50-115 [64]	50-69 [60]
19p13.3	Size Range	95-748 [333]	100-502 [232]	61-371 [175]	99-582 [299]	52-1158 [240]	52-903 [230]	63-297 [163]
	No. of markers	50-183 [99]	51-137 [71]	50-93 [64]	53-148 [85]	50-274 [80]	50-202 [74]	50-121 [63]

Supplementary Table 3. CNV size and number of markers for chromosomal intervals showing common amplification in plasma and tumor. Size of CNV (Kb) and number of markers showing range and mean by group and sample type, defined by applying a Gaussian smoothed signal threshold of > 6·0. Intervals highlighted in bold showed amplification in >90% of tumor DNA samples of patients on follow-up and > 25% of matched plasma samples applying a lower smoothed signal threshold of > 4·0 (see Supplementary Table 4).

Interval	**Overlapping genes**		**Group**								
			Healthy controls		**Pre-surgical breast cancer**			**Breast cancer on follow-up**			
			L n=8	P n=8	L n=15	P n=15	T n=15	L n=50	P1 n=50	P2 n=50	T n=40
4q13.2	***TMPRSS11BNL*, *TMPRSS11B*, *UGT2B 15 17*, *YTHDC1***	**Frequency**	0%	12.5%	33.3%	26.6%	40%	28%	30%	42%	100%
		CN Range	2	1-6	1-4	2-7	1-8	2-4	2-9	2-10	6-10
5q13.2	***SERF1A*, *SERF1B*, *NAIP*, SMA5*, *SMN1 2***	**Frequency**	12.5%	12.5%	46.6%	93.3%	40%	50%	68%	79%	100%
		CN Range	0-3	2-9	2-4	2-13	2-15	2-6	2-10	2-10	6-10
7q11.23	***CLIP2*, *GATSL1*, *GTF2IRD1 2*, *LOC100093631*, *NCF1*, *NCF1C*, *PMS2P5 6*, *SPDYE8P*, *STAG3L2*,**	**Frequency**	12.5%	62.50%	33.3%	93.3%	60%	24%	62%	82%	100%
		CN Range	2-4	0-9	2-4	2-10	2-10	2-8	2-10	2-10	9-10

	WBSCR16										
8p23.1	***DEFB130*, *DUB3*, *FAM66A*, *FAM66D*, *FAM85A*, *FAM86B1*, *LOC392196**, *ZNF705D***	**Frequency**	0%	25%	20%	46.6%	33.3%	22%	32%	34%	95%
		CN Range	2	2-4	2-3	2-6	2-7	2-4	2-10	2-8	2-10
10q11.22 and 10q11.23	***AGAP 7 8*, *BMS1P5*, *C10orf53*, *CHAT*, *FRMPD2P1*, *GDF2 10*, *OGDHL*, *PARG*, *PTPN20B*, *RBP3*, *ZNF488***	**Frequency**	87.50%	100%	80%	100%	40%	86%	92%	86%	100%
		CN Range	2-10	4-10	2-10	6-10	2-10	2-24	2-13	2-30	6-28
15q25.2	***GOLGA6L4 5 9*, *LOC440297* 727849* 80154**, *RPS17***	**Frequency**	37.50%	0%	46.666%	73.333%	40%	22%	54%	96%	100%
		CN Range	2-6	2	2-5	2-9	2-9	2-5	2-10	2-10	4-20
16p12.3	***ABCC6P1*, *NOMO2***	**Frequency**	62.50%	75%	66.666%	100%	80%	54%	66%	90%	100%
		CN Range	2-6	2-7	2-6	5-11	2-9	2-6	2-10	2-15	5-12

Supplementary Table 4. Most common amplified intervals in plasma and tumor DNA. Showing frequency of amplification (%) and copy number range by group and sample type, defined by applying a smoothed signal threshold ratio > 4.0. Gene nomenclature (alphabetically for each interval) taken from HGNC (http://www.genenames.org/). Genes with an asterisk only appear in the RefSeq (http://www.ncbi.nlm.nih.gov/gene/) gene database. L, normal leucocytes, P, plasma, T, tumor DNA.

Chromosome	Start bp	End bp	Cytoband	Length (bp)	Affected genes
On follow-up P1					
1	21047616	21114833	1p36.12	67217	*HP1BP3* (-) Overlaps with 17.14% of *SH2D5* (-)
1	47055993	47068677	1p33	12684	Contained within *MKNK1* (-)
1	182542082	183804609	1q25.3	1262527	*APOBEC4* (-), *ARPC5* (-), *DHX9* (+), *LAMC1* (+), *LAMC2* (+), *LOC284648**(+), *NCF2* (-), *NMNAT2* (-), *NPL* (+), *RGS16* (-), *RGS8* (-), *RNASEL* (-), *SMG7* (+), *SHCBP1L* (-) Overlaps with 15.79% of *RGL1* (+)

2	96787899	97172125	2q11.1-2q11.2	384226	*ASTL* (-), *CIAO1* (+), *DUSP2* (-), *ITPRIPL1* (+), *LOC285033** (+), *NCAPH* (+), *SNRNP200* (-), *STARD7* (-), *TMEM127* (-) Overlaps with 2.28% of *NEURL3* (-)
4	138229548	139308745	4q28.3	1079197	*PCDH18* (-), *SLC7A11* (-)
5	37604905	37616554	5p13.2	11649	Contained within *WDR70* (+)
6	71556566	71565478	6q13	8912	Contained within *SMAP1* (+)
7	52095655	53331026	7p12.1	1235371	*POM121L12* (+)
7	137005809	137059416	7q33	53607	Overlaps with 42.42% of *PTN* (-)
8	79028009	84510629	8q21.12-8q21.13	5482620	*CHMP4C* (+), *FABP12* (-), *FABP4* (-), *FABP5* (+), *FABP9* (-), *FAM164A* (+), *HEY1* (-), *IL7* (-), *IMPA1* (-), *MRPS28* (-), *PAG1* (-), *PKIA* (+), *PMP2* (-), *SLC10A5* (-), *SNX16* (-), *STMN2* (+), *TPD52* (-), *ZBTB10* (+), *ZFAND1* (-), *ZNF704* (-)
8	120825226	120883743	8q24.12	58517	*DSCC1* (-) Overlaps with 33.92% of *TAF2* (-)
9	30995741	32798727	9p21.1	1802986	*ACO1* (+), *DDX58* (-), *LOC100129250** (+), *NDUFB6* (-), *TAF1L* (-), *TMEM215* (+), *TOPORS* (-)
9	32798728	33473893	9p21.1-9p13.3	675165	*APTX* (-), *AQP3* (-), *AQP7* (-), *B4GALT1* (-), *BAG1* (-), *CHMP5* (+), *DNAJA1* (+), *NFX1* (+), *SMU1* (-), *SPINK4* (+) Overlaps with 1.86% of *NOL6* (-)
9	137610423	137666414	9q34.3	55991	Contained within *COL5A1* (+)
9	137807802	137834125	9q34.3	26323	Overlaps with 7.62% of *FCN1* (-)
10	16905500	17520442	10p13-10p12.33	614942	*LOC100128098** (+), *ST8SIA6* (-), *TRDMT1* (-), *VIM* (+) Overlaps with 43.31% of *CUBN* (-)
11	44283722	44302311	11p11.2	18589	Contained within *ALX4* (-)
12	58010163	58010164	12q13.3	1	Contained within *ARHGEF25* (+)
13	49559791	50791372	13q14.2	1231581	*ARL11* (+), *C13orf1* (-), *CAB39L* (-), *CDADC1* (+), *CTAGE10P* (+), *DLEU1* (+), *DLEU2* (-), *EBPL* (-), *FNDC3A* (+), *KCNRG* (+), *KPNA3* (-), *MIR15A* (-), *MIR16*-1 (-), *MIR3613* (-), *MLNR* (+), *PHF11* (+), *RCBTB1* (-), *SETDB2* (+), *ST13P4* (+), *TRIM13* (+)
13	50791373	52422211	13q14.2-13q14.3	1630838	*DHRS12* (-), *DLEU7* (-), *FAM124A* (+), *GUCY1B2* (-), *INTS6* (-), *NCRNA00282* (-), *RNASEH2B* (+), *SERPINE3* (+), *WDFY2* (+)
16	49821501	49825482	16q12.1	3981	Contained within *ZNF423* (-)
16	84925626	85139173	16q24.1	213547	*KIAA0513* (+), *ZDHHC7* (-) Overlaps with 3.38% of *FAM92B* (-) Overlaps with 8.19% of *CRISPLD2* (+)
21	39235347	39367443	21q22.13	132096	Overlaps with 40.39% of *KCNJ6* (-)
On follow-up P2					
2	50034686	50977979	2p16.3	943293	*NRXN1* (-)
3	123019763	123435754	3q21.1	415991	*MYLK* (-), *PTPLB* (-) Overlaps with 27.75% of *ADCY5* (-)
5	95084131	95084132	5q15	1	Contained within *RHOBTB3* (+)
6	38140658	38140659	6p21.2	1	Contained within *BTBD9* (-)
6	78066685	78366842	6q14.1	300157	*HTR1B* (-)
9	134612965	135042885	9q34.13	429920	*MED27* (-) Overlaps with 1.29% of *NTNG2* (+)
11	103792043	103808152	11q22.3	16109	Contained within *PDGFD* (-)
13	56872356	59648355	13q21.1-13q21.2	2775999	*PCDH17* (+), *PRR20A* (+), *PRR20B* (+), *PRR20C* (+), *PRR20D* (+), *PRR20E* (+)

17	30114328	31319764	17q11.2	1205436	*ARGFXP2* (-), *C17orf75* (-), *C17orf79* (-), *CDK5R1* (+), *LRRC37B* (+), *MIR632* (+), *MYO1D* (-), *PSMD11* (+), *RHBDL3* (+), *RHOT1* (+), *SH3GL1P1* (+), *SUZ12* (+), *TMEM98* (+), *UTP6* (-), *ZNF207* (+) Overlaps with 0.07% of *SPACA3* (+)
22	19643245	19775287	22q11.21	132042	*GP1BB* (+), *SEPT5* (+), *GP1BB* (+), *TBX1* (+)
22	38594668	38678564	22q13.1	83896	*MAFF* (+), *TMEM184B* (-)
Pre-surgical P					
1	19698026	19707302	1p36.13	9276	*CAPZB* (-)
1	39355371	39360730	1p34.3	5359	*RHBDL2* (-)
1	79024688	79126050	1p31.1	101362	*IFI44L* (+)
1	89472197	89558103	1p22.2	85906	*GBP1* (-), *GBP3* (-)
1	237978001	237997087	1q43	19086	*RYR2* (+)
2	38281096	38298139	2p22.2	17043	Overlaps with 19.91% of *CYP1B1* (-) Overlaps with 77.39% of *FAM82A1* (+)
2	38298139	38306935	2p22.2	8796	Overlaps with 58.95% of *CYP1B1* (-)
2	62413989	62495209	2p15	81220	*B3GNT2* (+)
2	127446853	127464384	2q14.3	17531	Overlaps with 42.18% of *GYPC* (+)
3	38350519	38350543	3p22.2	24	*SLC22A14* (+)
3	65530707	65641243	3p14.1	110536	*MAGI1* (-)
3	132533091	132548645	3q22.1	15554	*NCRNA00119* (+)
3	132548646	132594820	□q22.1	46174	Overlaps with 96.17% of *NCRNA00119* (+)
4	10528226	10559817	4p16.1	31591	*CLNK* (-)
4	79347625	79443850	4q21.21	96225	*FRAS1* (+)
5	177977679	178084843	5q35.3	107164	*CLK4* (-) Overlaps with 37.21% of *COL23A1* (-)
5	178084843	178179234	5q35.3	94391	*ZNF354A* (-)
6	12654540	13005284	6p24.1	350744	Overlaps with 81.95% of *PHACTR1* (+)
6	13025819	13063824	6p24.1	38005	*PHACTR1* (+)
6	37595546	37609305	6p21.2	13759	Overlaps with 65.57% of *MDGA1* (-)
6	152521244	152826222	6q25.2	304978	*SYNE1* (-)
8	17532573	17535058	8p22	2485	*MTUS1* (-)
8	87221488	87241319	8q21.3	19831	Overlaps with 75.80% of *SLC7A13* (-)
10	14519892	14638939	10p13	119047	Overlaps with 65.84% of *FAM107B* (-)
10	70502288	70502289	10q21.3	1	*CCAR1* (+)
11	19351515	19401124	11p15.1	49609	Overlaps with 58.16% of *NAV2* (+)
11	47969152	55683985	11p11.2-11q11	7714833	*FOLH1* (-), *LOC440040** (+), *LOC441601** (-), *LOC646813** (+), *OR4A15* (+), *OR4A16* (+), *OR4A47* (+), *OR4A5* (-), *OR4B1* (+), *OR4C11* (-), *OR4C12* (-), *OR4C13* (+), *OR4C15* (+), *OR4C16* (+), *OR4C3* (+), *OR4C45* (-), *OR4C46* (+), *OR4C6* (+), *OR4P4* (+), *OR4S1* (+), *OR4S2* (+), *OR4X1* (+), *OR4X2* (+), *OR5D13* (+), *OR5D14* (+), *OR5D16* (+), *OR5D18* (+), *OR5L1* (+), *OR5L2* (+), *OR5W2* (-), *PTPRJ* (+), *SPRYD5* (+), *TRIM48* (+)
13	74054816	74327204	13q22.1	272388	Overlaps with 24.62% of *KLF12* (-)
13	74327205	74474851	13q22.1	147646	*KLF12* (-)
14	31895975	32247665	14q12	351690	*C14orf126* (-), *GPR33* (-) Overlaps with 61.72% of *NUBPL* (+)

16	2330169	2336394	16p13.3	6225	*ABCA3* (-)
16	19646235	19691514	16p12.3	45279	*C16orf62* (+)
16	31102589	31102590	16p11.2	1	*VKORC1* (-)
16	81223646	81237214	16q23.2	13568	*PKD1L2* (-)
16	81237214	81242637	16q23.2	5423	*PKD1L2* (-)
22	30450660	30486826	22q12.2	36166	Overlaps with 28.68% of *HORMAD2* (+)

Supplementary Table 5. LOH detected in plasma of breast cancer patients.

For each patient, plasma samples were compared to the matched leucocytes in paired LOH analysis using a HMM and using 0.98 as maximal probability, genomic decay of 1Mbp, and no more than 2% genotype error. We also pre-filtered the data using Hardy-Weinberg Equilibrium (HWE) p-values of <0.001 or <0.0001. Additionally, only LOH reported in gene exons were analysed. The DNA strand (+, coding; -, non-coding) for each affected gene is indicated in parentheses. Gene nomenclature (alphabetically for each interval) taken from HGNC (http://www.genenames.org/). Genes with an asterisk only appear in the RefSeq (http://www.ncbi.nlm.nih.gov/gene/) gene database. P1, first plasma, P2, second plasma, pre-surgical P, pre-surgery plasma.