

Supplementary Table I. Cell lines

<i>Breast</i>	<i>Source</i>	<i>Reference</i> ^a
VP229, VP267, VP185, VP303	M. McCallum, Glasgow, UK	[1]
MDA-MB-157 ^c , MDA-MB-175, MDA-MB-435s ^c , MDA-MB-361 ^c , MCF-7 ^c , DU4475 ^c , Hs578T ^c , MDA-MB-468, MDA-MB-231 ^c , MDA-MB-436, BT549 ^c , ZR-75-1	M. Stratton, Sutton, UK	
MDA-MB-134, SK-BR-7, SK-BR-3 ^c	M. O'Hare, UK	[2]
OCUB-F, OCUB-M	Riken cell bank	[3]
SUM159 ^c , SUM149 ^c , SUM102, SUM1315 ^c , SUM52, SUM185 ^c , SUM190, SUM225 ^c , SUM44, SUM229	S. Ethier, Michigan, USA	[4-6]
CAL51 ^c	B. Dutrillaux, France	[7]
MT-3	M. Bibby, Bradford, UK	[8]
KPL1	Kurebayashi, Japan	[9]
<i>Ovarian</i>		
OC314, OC315, OC316	A. Alama, Genova, Italy	[10]
OVI-P, OAW41M, 59M, A2780, CH1, Hx62, LK1, LK2, OAW42/83, PA-1 ^c , Pxn94	M. Stratton, Sutton, UK	
UCI-101, UCI-107	Carpenter, UC, USA	[11,12]
EC, KEN-3, MN-1, SHIN-3	Kiyozuka, Kansai, Japan	[13-15]
KK	Kikuchi, Japan	[16]
OVISE, OVKATE, OVMANA, OVSAHO, OVSAYO, OVTOKO	Gorai, Yokohama, Japan	[17,18]
<i>Other</i>		
MT-1, MaTu ^b	M. Bibby, Bradford, UK	[8,19]
HCT116 ^c , LoVo ^c , DLD-1 ^c , CACO-2 ^c , COLO205	ATCC	

^aReferences are given to lines not in the ATCC catalogue

^bSubsequent to carrying out our analysis, we realised that these cell lines are HeLa derivatives (McLeod et al., 1999), however this fact does not substantially alter our conclusions.

^cScreened for BUB1 mutation – no mutation found [20-22]

Supplementary Table II. Mutations in target genes

<i>Cell line</i>	<i>BAX^a</i>	<i>BRCA1</i>	<i>hMSH3</i>	<i>hMSH6</i>	<i>IGFIIR</i>	<i>TGFβRII</i>	<i>NSEP</i>	<i>NGFR</i>	<i>BRCA2</i>
<u>Ovarian</u>									
A2780									
OC314						0, -1			-T, +A
OVI-P	0, +1	0, -1	0, -2	-1					
UCI-101									
UCI-107									
<u>Breast</u>									
CAL51					0, -1	-1			
MT-3	-1		-1	0, -1	0, -1	-1		0, +1	-A
OCUB-F									
OCUB-M									
Total ^b	2/8	1/8	3/8	2/8	2/8	3/8	0/8	1/8	2/8

^ablank, normal; -1, -2, one and two bp deletions; 0, normal; +1, +2, one and two bp insertions; -T, homozygous 1 bp deletion at (T)₁₀ in intron 2; +A, heterozygous 1 bp insertion at (A)₇ in exon 11; -A, heterozygous 1 bp deletion at (A)₈ in exon 23.

^bTotal excludes OC314, OC315 and OCUB-F.

Supplementary Table III. Centromeric FISH data

Chromosome modal number

<i>Cell line</i>	<i>MSI Status</i>	3	7	8	9	12	15	17	18
Lymphocytes	-	2	2	2	2	2	2	2	2
A2780	+	2	2	2	2	2	2	2	2
CAL51	+	2	2	2	nd	2	2	2	nd
UCI-101	+	2	2	2	2	nd	nd	2	2
UCI-107	+	2	2	2	2	nd	nd	2	2
SUM159	-	2	2	2	2	2	2	2	2
LK-1	-	2	2	2	2	3	2	2	2
MT-3	+	2	3	2	nd	2	2	2	nd
MDA-MB-157	-	3	3	4	2	nd	nd	2	3
MDA-MB-468	-	4	nd	2	3	nd	nd	2	4
OC314 ^a	+	3	4	3	3	3	2	4	2
MaTu	-	3	4	4	3	4	3	3	2
KPL1	-	4	4	3	3	4	3	4	3
OCUB-F	+	4	4	2	4	nd	nd	4	4
OCUB-M	+	4	4	4	5	nd	nd	4	3
OVI-P	+	4	5	4	3	4	4	4	4
MT-1	-	6	3	6	4	5	3	4	4

^aThe same chromosome modal numbers and similar variability were found in OC315 and OC316

SUPPLEMENTARY Table IV. Summary of molecular cytogenetic findings

MSS cell lines				MSI cell lines			
	<i>Break index</i>	<i>Modal number</i>	<i>CGH - arms with alterations</i>		<i>Break index</i>	<i>Modal number</i>	<i>CGH - arms with alterations</i>
MaTu	25	69	14	CAL51	0	46	3
MCF-7	99	65	25	MT-3	2	46	5
MDA-MB-134	9	44/66	22	OCUB-F	64	77	17
MDA-MB-157	43	62/116	25	OVI-P	18	92	n.d.
MDA-MB-175	10	48	27				
MDA-MB-435	38	57	21				
MDA-MB-361	57	51	12				
MT-1	71	103	27				
SK-BR-3	77	79	26				
SK-BR-7	8	43	8				
SUM159	8	47	5				
VP229	92	62	22				
VP267	98	59	24				
ZR-75-1	26	72	15				
Average	47.2		19.5		21		8.3

SUPPLEMENTARY TABLE V Details of parental cell lines

<i>Cell line</i>	<i>MT-1(MSS)</i>	<i>MT-3(MSI)</i>	<i>SUM159(MSS)</i>	<i>Normal lymphocytes</i>
Modal number	103	46	47	46
SKY break index	71	2	8	n.d.
<u>Centromeric FISH</u>				
Chromosome 3 mode (% variation)	6 (20)	2 (5)	2 (9.1)	2 (3.6)
Chromosome 8 mode (% variation)	6 (24)	2 (5.1)	2 (24)	2 (5.4)
Chromosome 15 mode (% variation)	3 (18)	2 (10)	2 (11)	2 (4.4)
Chromosome 17 mode (% variation)	4 (13)	2 (7.6)	2 (26)	2 (4.2)
<u>6-colour FISH</u> ^{a, b}				
Chromosome 4	3N	2N	2N	2N
Chromosome 5	2N, der(5)t(5;3), der(17)t(5;17), del(5), 2x der(5)t(5;10), der(5)t(5;15)	2N	2N, del(5)	2N
Chromosome 7	2N, i(7q), del(7), der(2)t(X;2;7), der(7)t(7;15)	3N	2N, der(17)t(7;17)	2N
Chromosome 8	4N, der(8)t(9;8;17), der(8)t(6;8;17), der(22)t(8;22)	2N	2N, der(13)t(8;13), der(?)t(8;13;14)	2N
Chromosome 15	3N, der(2)t(2;11;15), 2x der(?)t(?;15;?)	2N	2N	2N
Chromosome 18	3N, del(18), der(2)t(2;18)	2N	2N	2N

^aN, normal chromosome

^bTranslocation partners based on SKY data (Davidson et al 2000). One novel aberration, an insertion of chromosome 15 material in MT-1, was not identified in the SKY analysis due to the low resolution in detecting this type of alteration and thus the translocation partner(s) are unknown.

^cFor SUM159 the most commonly observed karyotype is given (60% of metaphases), however there were additional variant karyotypes within the parental cell line observed in more than two metaphases. These were always alternative translocations involving chromosomes 7 and 8.

Supplemental methods:

1. Chromosome number was taken into account for the clonal centromeric FISH data in the following manner. Firstly, the total number of chromosomes analysed was calculated by multiplying the number of nuclei by the modal number of signals for each chromosome (e.g. for MT-1, chromosome eight was analysed 6618 times). Secondly, the number of chromosomes that were gained/lost was calculated for each chromosome by the number of signals above/below the mode multiplied by the number of nuclei with that signal number (e.g. for MT-1 chromosome eight, there were 338 chromosome losses and 51 chromosome gains). Finally, for each cell line the values for the four chromosomes were then summed and used for chi-squared comparisons with the other cell lines.

2. Unstable alterations included chromosome breaks, chromatid breaks, acentric fragments, double minutes and dicentric chromosomes. These alterations were considered unstable as they a) would have occurred in the last division (breaks), b) would be unlikely to remain in the same form from one mitosis to the next (dicentrics), or c) would swiftly vary in number by cell division (acentrics, double minutes). Stable aberrations included new translocations, deletions, duplications and isochromosomes. If an aberration was observed in two different metaphases within the same clone, it was counted twice, however this only occurred once, in SUM159.

3. In order to compensate for the different amounts of chromosome material present in each cell line for the clonal analysis of structural aberrations, a consensus of the chromosomes was taken from the parental cell line data for centromeric FISH, comparative genomic hybridisation and SKY. For example, of the chromosomes included in the 6-colour analysis, MT-3 had two copies of chromosomes 4, 5, 8, 15 and 18, and three copies of 7, giving a total of 13 chromosomes. SUM159, with extra chromosome 5 and 8 materials, also had approximately 13 chromosomes per metaphase, while the best estimate for MT-1 including all translocations was 26 chromosomes. All statistical comparisons were done using the proportion of aberrations per total number of chromosomes analysed, i.e. for SUM159, 13 chromosomes were analysed in ten clones with a total of 303 metaphases for a grand total of 3939 chromosomes analysed. This meant that in MT-1, proportions of chromosome aberrations were lower than the raw numbers suggested; MT-1 was analysed at 7748 chromosomes.

References to Supplementary Information

1. McCallum, H.M. and Lowther, G.W. (1996) Long-term culture of primary breast cancer in defined medium. *Breast Cancer Res Treat*, **39**, 247-59.
2. Davidson, J.M., Gorringer, K.L., Chin, S.F., Orsetti, B., Besret, C., Courtay-Cahen, C., Roberts, I., Theillet, C., Caldas, C. and Edwards, P.A. (2000) Molecular cytogenetic analysis of breast cancer cell lines. *Br J Cancer*, **83**, 1309-17.
3. Sawada, T., Chung, Y.S., Nakata, B., Kubo, T., Kondo, Y., Sogabe, T., Onoda, N., Ogawa, Y., Yamada, N. and Sowa, M. (1994) [Establishment and characterization of a human breast cancer cell line, OCUB-1]. *Hum Cell*, **7**, 138-44.
4. Forozan, F., Mahlamaki, E.H., Monni, O., Chen, Y., Veldman, R., Jiang, Y., Gooden, G.C., Ethier, S.P., Kallioniemi, A. and Kallioniemi, O.P. (2000) Comparative genomic hybridization analysis of 38 breast cancer cell lines: a basis for interpreting complementary DNA microarray data. *Cancer Res*, **60**, 4519-25.
5. Ethier, S.P., Kokeny, K.E., Ridings, J.W. and Dilts, C.A. (1996) erbB family receptor expression and growth regulation in a newly isolated human breast cancer cell line. *Cancer Res*, **56**, 899-907.
6. Flanagan, L., Van Weelden, K., Ammerman, C., Ethier, S.P. and Welsh, J. (1999) SUM-159PT cells: a novel estrogen independent human breast cancer model system. *Breast Cancer Res Treat*, **58**, 193-204.
7. Gioanni, J., Francois, D.L., Zhanghellini, E., Mazeau, C., Ettore, F., Lambert, J.-C., Schneider, M. and Dutrillaux, B. (1990) Establishment and characterisation of a new tumourigenic cell line with a normal karyotype from a human breast adenocarcinoma. *British Journal of Cancer*, **62**, 8-13.
8. Hambly, R., Double, J., Thompson, M. and Bibby, M. (1997) Establishment and characterisation of new cell lines from human breast tumours initially established as tumour xenografts in NMRI nude mice. *Breast Cancer Research and Treatment*, **43**, 247-258.
9. Kurebayashi, J., Kurosumi, M. and Sonoo, H. (1995) A new human breast cancer cell line, KPL-1 secretes tumour-associated antigens and grows rapidly in female athymic nude mice. *Br J Cancer*, **71**, 845-53.
10. Alama, A., Barbieri, F., Favre, A., Cagnoli, M., Noviello, E., Pedulla, F., Viale, M., Foglia, G. and Ragni, N. (1996) Establishment and characterization of three new cell lines derived from the ascites of human ovarian carcinomas. *Gynecol Oncol*, **62**, 82-8.
11. Fuchtner, C., Emma, D.A., Manetta, A., Gamboa, G., Bernstein, R. and Liao, S.Y. (1993) Characterization of a human ovarian carcinoma cell line: UCI 101. *Gynecol Oncol*, **48**, 203-9.
12. Gamboa, G., Carpenter, P.M., Podnos, Y.D., Dorion, G., Irvani, L., Bolton, D., Mascarello, J.T. and Manetta, A. (1995) Characterization and development of UCI 107, a primary human ovarian carcinoma cell line. *Gynecol Oncol*, **58**, 336-43.
13. Imamura, K., Kiyozuka, Y., Nishimura, H. and Yakushijim, M. (1995) Novel germ cell tumour cell line established from testicular feminization syndrome. *Oncol Rep*, **2**, 17-25.
14. Kiyozuka, Y., Nishimura, H., Iwanaga, S., Yakushiji, M., Ito, K., Nakano, S., Tamori, N., Adachi, S., Noda, T. and Imai, S. (1992) [Establishment and characterization of human ovarian fibrosarcoma cell line and its sensitivity to anticancer agents]. *Nippon Sanka Fujinka Gakkai Zasshi*, **44**, 461-8.
15. Imai, S., Maeda, H., Kiyozuka, Y., Noda, T., Moriyama, I. and Ichijo, M. (1989) Characterization of the CA125 antigen secreted from a newly established human ovarian cancer cell line (SHIN-3). *Acta Pathol Jpn*, **39**, 43-9.
16. Kikuchi, Y., Hirata, J., Kita, T., Imaizumi, E., Tode, T. and Nagata, I. (1993) Enhancement of antiproliferative effect of cis-diamminedichloroplatinum(II) by clomiphene and tamoxifen in human ovarian cancer cells. *Gynecol Oncol*, **49**, 365-72.
17. Gorai, I., Nakazawa, T., Miyagi, E., Hirahara, F., Nagashima, Y. and Minaguchi, H. (1995) Establishment and characterization of two human ovarian clear cell adenocarcinoma lines from metastatic lesions with different properties. *Gynecol Oncol*, **57**, 33-46.
18. Yanagibashi, T., Gorai, I., Nakazawa, T., Miyagi, E., Hirahara, F., Kitamura, H. and Minaguchi, H. (1997) Complexity of expression of the intermediate filaments of six new human ovarian carcinoma cell lines: new expression of cytokeratin 20. *Br J Cancer*, **76**, 829-35.
19. Widmaier, R., Wildner, G., Papsdorf, G. and Graffi, I. (1974) Ueber einer neue, in vitro unbegrenzt wachsende Zelllinie, MaTu, von Mamma-Tumorzellen des Menschen. *Archiv fuer Geschwulstforschung*, **44**, 1-10.
20. Myrie, K.A., Percy, M.J., Azim, J.N., Neeley, C.K., Petty, E.M. (2000) Mutation and expression analysis of human BUB1 and BUB1B in aneuploid breast cancer cell lines. *Cancer Lett*, **152**, 193-9.

- 21 Cahill, D.P., Lengauer, C., Yu, J., Riggins, G.J., Willson, J.K., Markowitz, S.D., Kinzler, K.W., Vogelstein, B. (1998) Mutations of mitotic checkpoint genes in human cancers. *Nature*, **392**, 300-3.
- 22 Mimori, K., Inoue, H., Alder, H., Ueo, H., Tanaka, Y., Mori, M. (2001) Mutation analysis of hBUB1, human mitotic checkpoint gene in multiple carcinomas. *Oncol Rep* **8**, 39-42.