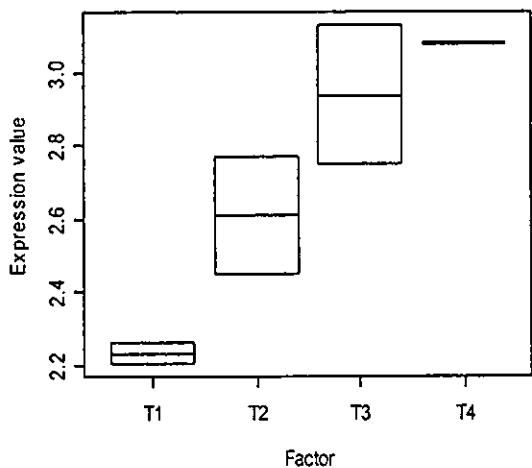
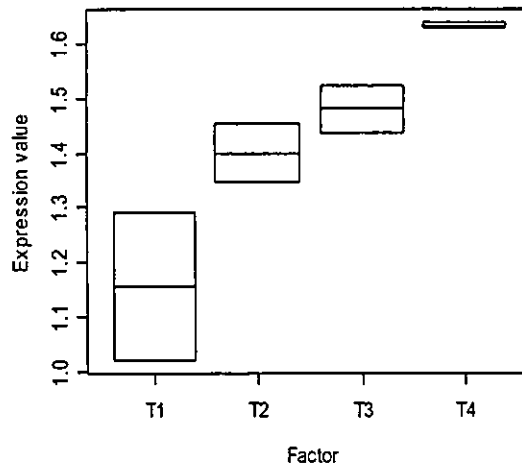




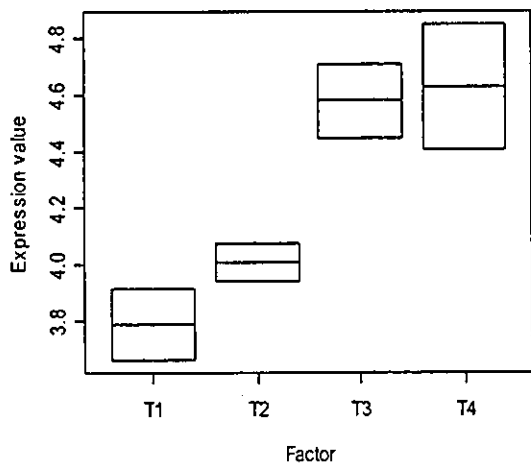
1: VEGFC; VRP; FLT4 ligand



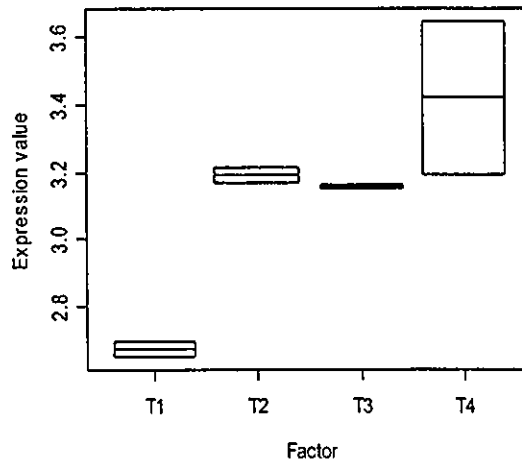
21: COL6A3



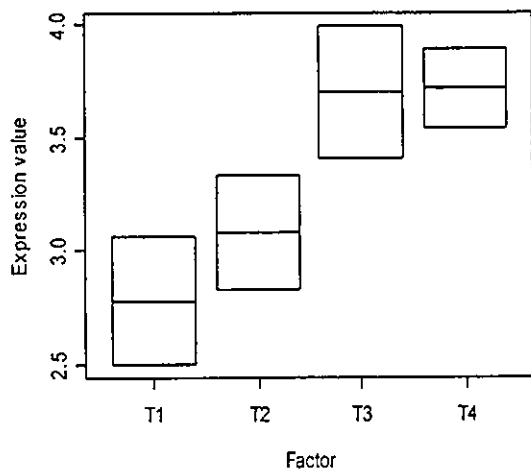
122: FAST



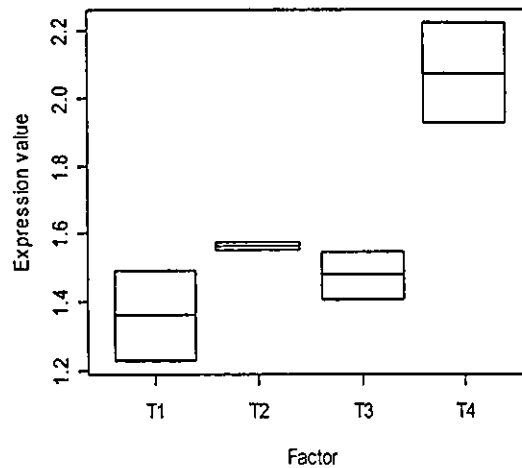
367: CGR19



17: ILK



376: IGF1A; IGFBP1; IGF1



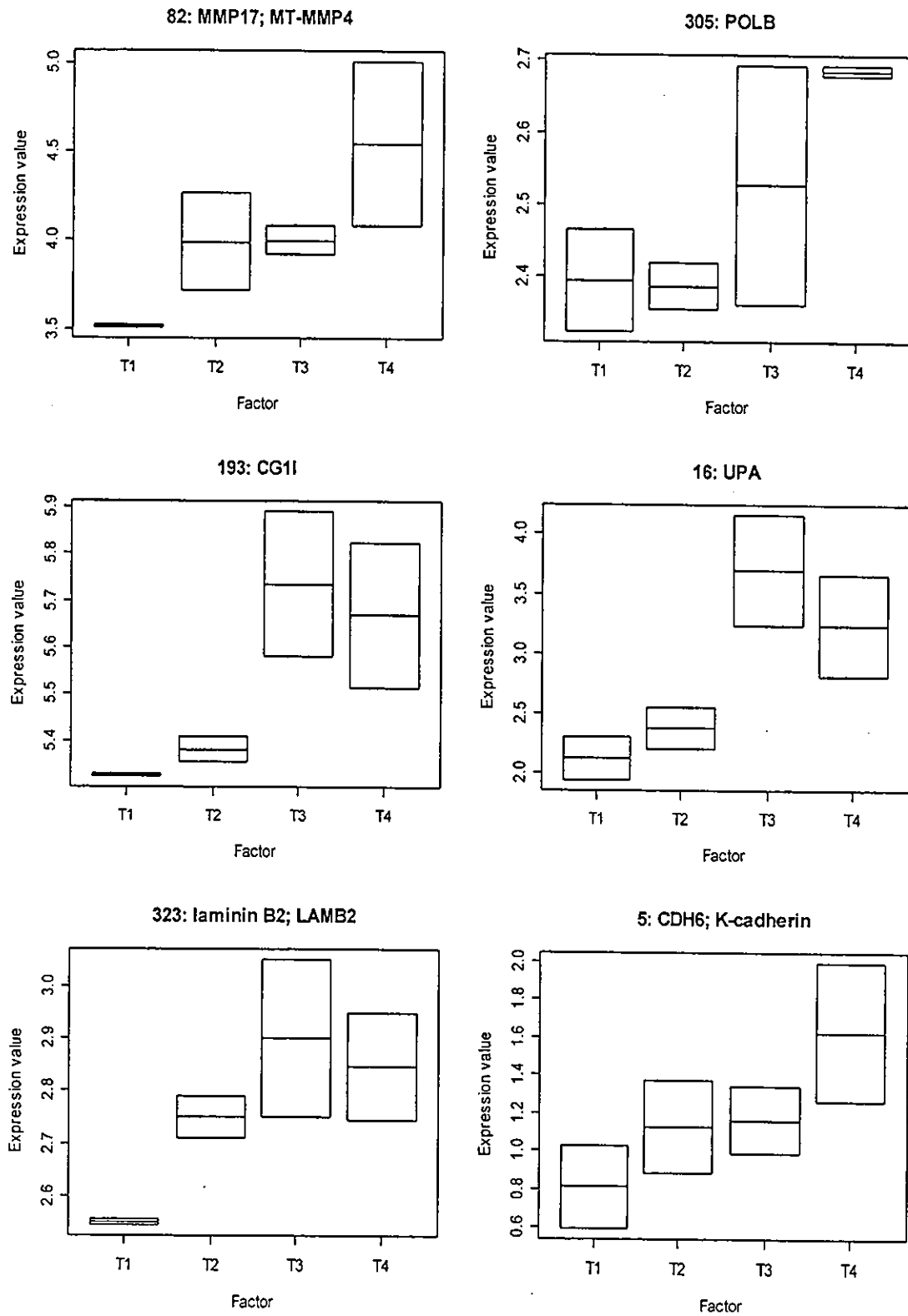
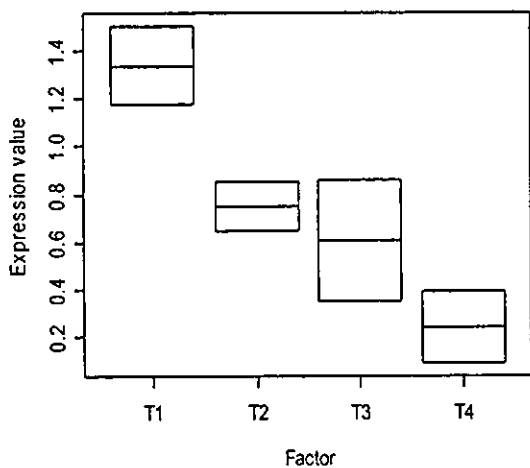
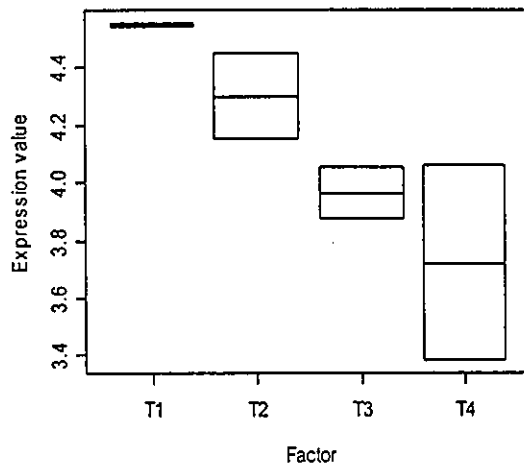


図 16 MDA-MB-231 細胞株における増加傾向遺伝子のプロット  
(箱の上下はデータ点、中線は平均値)

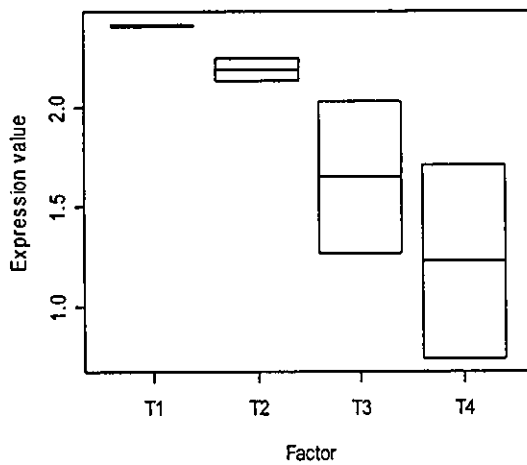
239: IL4; BSF-1



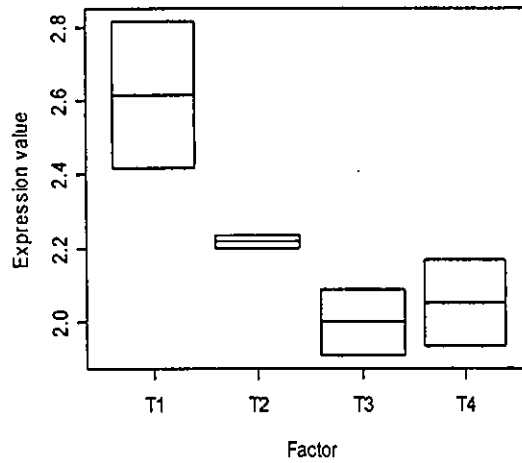
627: DNAJ2; hDJ2; HSJ2



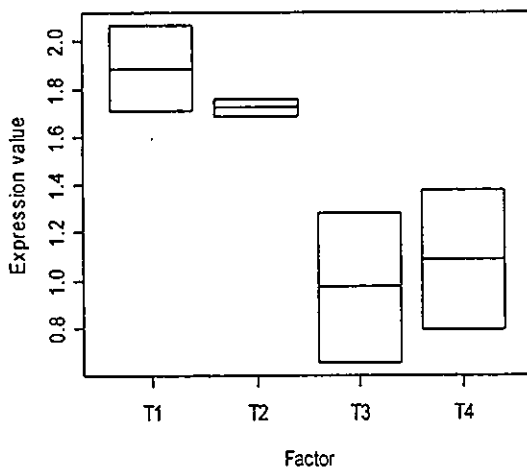
141: TRAIL; APO2L



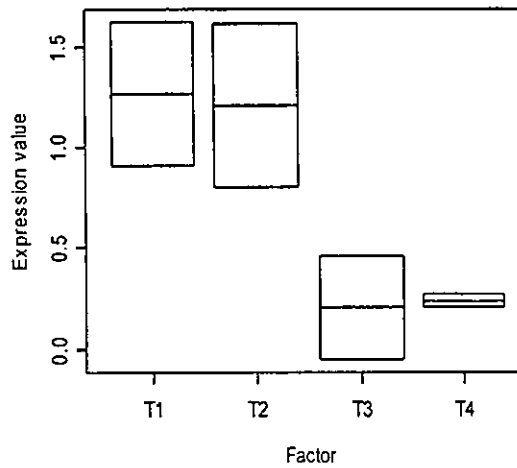
689: DNA polymerase iota (POLI); RAD30B



523: ras-related protein RAB3B



459: MAPKKK; MAP3K; MTK1



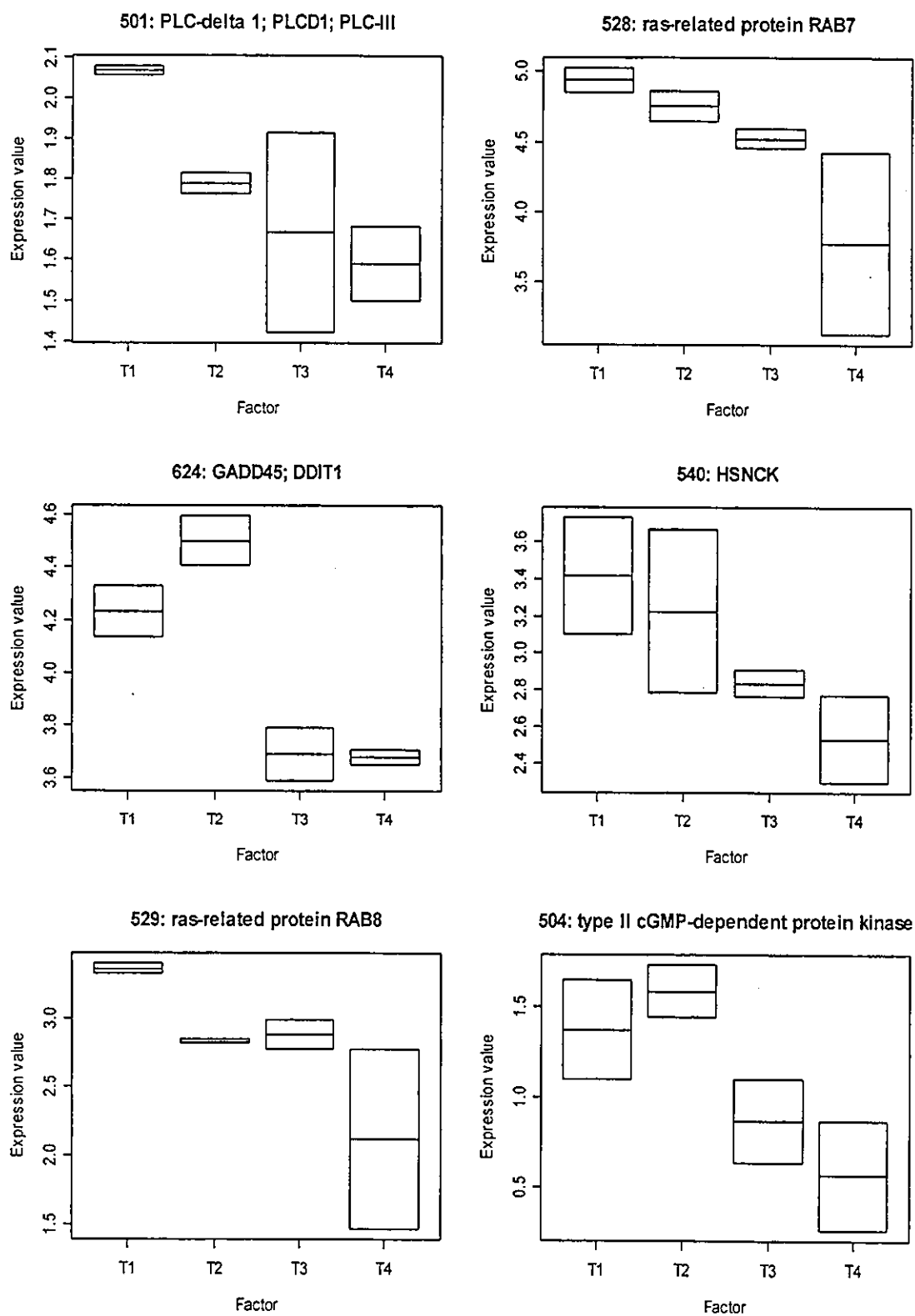


図 17 MDA-MB-231 細胞株における減少傾向遺伝子のプロット  
(箱の上下はデータ点、中線は平均値)

	Estrogen Only	E+Tamoxifen L	E+Tamoxifen H	Estrogen Free
BT474	BTT1	BTT2	BTT3	BTT4
MCF7	MCT1	MCT2	MCT3	MCT4
MDA-MB-231	MDT1	MDT2	MDT3	MDT4
SK-BR-3	SKT1	SKT2	SKT3	SKT4

表 1 細胞株と処理の組み合わせ

各セルはデータ解析における変数名、上記組み合わせの反復は R1、R2 と記載

	Estrogen Only	E+Tamoxifen L	E+Tamoxifen H	Estrogen Free
BT474	0.8664495	0.8566374	0.8401288	0.851142
MCF7	0.8700674	0.8393638	0.8230427	0.8538145
MDA-MB-231	0.8616289	0.8359358	0.8971913	0.8512897
SK-BR-3	0.8786277	0.817145	0.9019523	0.8640634

表 2 同一条件の実験間における発現強度のピアソン相関係数

Index	Function	Raw p
652	recA-like protein HsRad51; DNA repair protein RAD51 homolog	0.0048
415	B-raf proto-oncogene (RAFB1)	0.0050
498	phospholipase C beta 2 (PLC-beta 2; PLCB2); 1-phosphatidylinositol 4、5-bisphosphate phosphodiesterase beta 2	0.0074
201	p21-activated kinase alpha (PAK-alpha; PAK1)	0.0076
667	RAD50	0.0088
719	cytosolic superoxide dismutase 1 (SOD1)	0.0090

表 3 処理に関連する遺伝子

(未調整 p 値が 0.01 未満のものを抽出)

Index	Function	Raw p
415	B-raf proto-oncogene (RAF1)	0.0025
652	recA-like protein HsRad51; DNA repair protein RAD51 homolog	0.0028
498	phospholipase C beta 2 (PLC-beta 2; PLCB2); 1-phosphatidylinositol 4、5-bisphosphate phosphodiesterase beta 2	0.0035
719	cytosolic superoxide dismutase 1 (SOD1)	0.0043
402	serine/threonine-protein kinase NEK2; NIMA-related protein kinase 2; NIMA-like protein kinase 1; HSPK 21	0.0047
625	growth arrest & DNA damage-inducible protein 45 beta (GADD45 beta)	0.0054
19	laminin alpha 4 subunit precursor (laminin A4; LAMA4)	0.0070
3	Vascular endothelial growth factor receptor 2 precursor (VEGFR2); kinase insert domain receptor (KDR); FLK1	0.0085
201	p21-activated kinase alpha (PAK-alpha; PAK1)	0.0096

表 4 細胞と処理の交互作用に関連する遺伝子  
(未調整 p 値が 0.01 未満のものを抽出)

Index	Function
424	cAMP-dependent 3', 5'-cyclic phosphodiesterase 4B (DPDE4); PDE32
55	endoglin precursor (ENG; END); CD105 antigen
766	type I cytoskeletal 16 keratin (KRT16); cytokeratin 16 (CK16); pseudo-keratin K16 type I
537	retinoic acid receptor beta (RXR-beta; RXRB)
486	ribosomal protein kinase B (RSKB)
125	BCL2 & p53 binding protein Bbp/53BP2 (BBP/53BP2)

表 5 MCF7 において遺伝子発現に増加傾向が示唆された遺伝子

Index	Function
749	multidrug resistance-associated protein 3 (MRP3); MLP2; ABCC3
760	GTP-binding nuclear protein RAN (TC4)
737	thioredoxin reductase
315	farnesyltransferase beta
721	glutathione peroxidase (GSHPX1; GPX1)
712	adducin gamma subunit
773	type I cytoskeletal 9 keratin (KRT9); cytokeratin 9 (CK 9)
748	ATP-binding cassette subfamily B (MDR/TAP) member 1 (ABCB1); multiple drug resistance 1 protein (MDR1); P glycoprotein 1 (PGY1)

表 6 MCF7 において遺伝子発現に減少傾向が示唆された遺伝子

Index	Function
441	FOS-related antigen 1 (FRA1); FOS-like antigen 1 (FOSL1)
401	serine/threonine-protein kinase NEK3; NIMA-related protein kinase 3; HSPK 36
705	UV excision repair protein RAD23 homolog A (RAD23A; hHR23A)
38	female organ- & adipocyte-specific extracellular matrix protein 2 (ECM2)
507	ras-related protein RAP-1A; C21KG; KREV-1 protein; GTP-binding protein SMG-p21A; G-22K
600	cbl-associated protein SH3P12
72	laminin gamma 2 subunit precursor (LAMC2)
261	CC chemokine receptor type 4 (CMKBR4; CCCKR4; CCR4)
352	insulin precursor (INS)
81	matrix metalloproteinase 16 precursor (MMP16); membrane-type matrix metalloproteinase 3 (MT-MMP3); MMP-X2
497	phospholipase C (PLCL)

表 7 BT474 において遺伝子発現に増加傾向が示唆された遺伝子



Index	Function
102	tissue inhibitor of metalloproteinase 2 precursor (TIMP2)
18	40S ribosomal protein SA (RPSA); 34/67-kDa laminin receptor; laminin receptor 1 (LAMR1); colon carcinoma laminin-binding protein; NEM/1CHD4
340	mitochondrial brown fat uncoupling protein 1 (UCP1)
109	vascular endothelial growth factor B precursor (VEGFB) + VEGF-related factor 186 (VRF186)
433	mitogen-activated protein kinase P38 beta (MAP kinase P38 beta); stress-activated protein kinase 2 (SAPK2)
79	matrix metalloproteinase 15 (MMP15); membrane-type matrix metalloproteinase 2 (MT-MMP2)

表 8 BT474 において遺伝子発現に減少傾向が示唆された遺伝子

Index	Function
512	ras-related protein RAB1A; YPT1-related protein
707	guanine nucleotide release/exchange factor (GNRP); ras-GRF; sos
501	phospholipase C beta 4 (PLC-beta 4; PLCB4)
10	cadherin 8 (CDH8)
6	cadherin 11 precursor (CDH11); osteoblast-cadherin (OB-cadherin); OSF4
9	cadherin 4 (CDH4); retinal cadherin precursor (R-cadherin; RCAD)
459	mitogen-activated protein kinase kinase kinase (MAPKKK; MAP3K); MTK1
67	integrin beta 5 precursor (ITGB5)
387	ras homolog gene family member C (RHOC; ARHC); ARH9; H9
281	adenine phosphoribosyltransferase (APRT)
35	wingless-related MMTV integration site 8b protein (WNT8B)

表 9 SK-BR-3 において遺伝子発現に増加傾向が示唆された遺伝子

厚生労働科学研究費補助金（平成 15 年度萌芽の先端医療技術推進 研究事業）  
分担研究報告書

Index	Function
379	erythropoietin receptor (EPOR)
525	ras-related protein RAB5B
278	microsomal UDP-glucuronosyltransferase 2B15 precursor (UDPGT); UDPGTH-3; UGT2B15 + microsomal 2B10 precursor (UDPGT); UGT2B10 + 2microsomal B8 precursor
182	cyclin-dependent kinase inhibitor 1C (CDKN1C); p57-KIP2
404	c-src kinase (CSK); protein-tyrosine kinase cyl
345	Lymphopain
747	canalicular multispecific organic anion transporter; multidrug resistance-associated protein 2 (MRP2); canalicular multidrug resistance protein
669	BRCA1-associated ring domain protein
423	allograft inflammatory factor 1 (AIF1); ionized calcium-binding adapter molecule 1
708	telomerase reverse transcriptase (hTERT)
646	thioredoxin peroxidase 2 (TDPX2); thioredoxin-dependent peroxide reductase 2; proliferation-associated gene (PAG); natural killer cell enhancing factor A (NKEFA)
274	microsomal UDP-glucuronosyltransferase 1-2 precursor (UDPGT; UGT1. 2; UGT1B; GNT1); HLUGP4

表 10 SK-BR-3 において遺伝子発現に減少傾向が示唆された遺伝子

Index	Function
1	vascular endothelial growth factor C precursor (VEGFC); vascular endothelial growth factor related protein (VRP); FLT4 ligand
21	collagen VI alpha 3 subunit (COL6A3)
122	fas-activated serine/threonine kinase (FAST)
367	p53-dependent cell growth regulator CGR19
17	integrin-linked kinase (ILK)
376	insulin-like growth factor IA precursor (IGF1A); IGFBP1; somatomedin C + insulin-like growth factor I (IGF1)
82	matrix metalloproteinase 17 (MMP17); membrane-type matrix metalloproteinase 4 (MT-MMP4)
305	DNA polymerase beta (POLB)
193	putative cyclin G1-interacting protein (CG1I)
16	urokinase-type plasminogen activator precursor (U-plasminogen activator; UPA)
323	laminin beta 2 subunit precursor (laminin B2; LAMB2); S-laminin
5	cadherin 6 precursor (CDH6); kidney cadherin (K-cadherin)

表 11 MDA-MB-231 において遺伝子発現に増加傾向が示唆された遺伝子

厚生労働科学研究費補助金（平成 15 年度萌芽の先端医療技術推進 研究事業）  
分担研究報告書

Index	Function
239	interleukin 4 precursor (IL4); B-cell stimulatory factor 1 (BSF-1)
627	DNAJ protein homolog 2 (DNAJ2; hDJ2; HSJ2)
141	TNF-related apoptosis inducing ligand (TRAIL); APO-2 ligand (APO2L)
689	DNA polymerase iota (POLI); RAD30B
523	ras-related protein RAB3B
459	mitogen-activated protein kinase kinase kinase (MAPKKK; MAP3K); MTK1
501	phospholipase C delta-1 (PLC-delta 1; PLCD1); PLC-III
528	ras-related protein RAB7
624	growth arrest & DNA damage-inducible protein (GADD45); DNA damage-inducible transcript 1 (DDIT1)
540	NCK melanoma cytoplasmic src homolog (HSNCK)
529	ras-related protein RAB8; MEL oncogene
504	type II cGMP-dependent protein kinase

表 12 MDA-MB-231 において遺伝子発現に減少傾向が示唆された遺伝子

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Tominaga, R., Koyama, H., Toge, T., Miura, S., Sugimachi, K., Ymaguchi, S., Hirata, K., <u>Ohashi, Y.</u> , Abe, O.	Randomized controlled trial comparing oral doxifluridine plus oral cyclophosphamide with doxifluridine alone in women with node-positive breast cancer after primary surgery.	J. Clin. Oncol.	21	991-998	2003
Yanaka, N., Kinoshita, T., Asada, T., <u>Ohashi, Y.</u>	Long-linear models for assessing gene-ageinteraction and their application to case-control studies of the apolipoprotein E (apoE) gene in Alzheimer's disease.	J. Human Genet.	48	520-524	2003
Kawado, M., Hinotsu, S., Matsuyama, Y., Yamaguchi, T., Hashimoto, S., <u>Ohashi, Y.</u>	A comparison of error detection rates between the reading aloud method and the double date entry method.	Controlled Clinical Trials	24	560-569	2003
Taguchi, F., Kusaba, H., Asai, A., Iwamoto, Y., Yano, K., Nakano, H., Mizukami, T., <u>Saijo, N.</u> , Kato, H., <u>Nishio, K.</u>	hnRNP L enhances sensitivity of the cells to KW-2189.	Int. J. Cancer	108	679-685	2004
Koizumi, F., Kanzawa, F., Ueda, Y., Koh, Y., Tsukiyama, S., Taguchi, F., <u>Tamura, T.</u> , <u>Saijo, N.</u> , <u>Nishio, K.</u>	Synergistic interaction between the EGFR tyrosine kinase inhibitor gefitinib ('Iressa') and the DNA topoisomerase I inhibitor CPT-11 (Irinotecan) in human colorectal cancer cells.	Int. J. Cancer	108	464-472	2004
Nishiyama, N., Okazaki, S., Cabral, H., Miyamoto, M., Kato, Y., Sugiyama, Y., <u>Nishio, K.</u> , Matsumura, Y., Kataoka, K.	Novel cisplatin-incorporated polymeric micelles can eradicate solid tumors in mice.	Cancer Res.	63	8977-8983	2003
Suzuki, T., Agui, M., Togawa, T., Naganuma, A., <u>Nishio, K.</u> , Tanabe, S.	MRP5b/SMRP mRNA is highly expressed in metallothionein- deficient mouse liver.	J. Health Sci.	49	524-526	2003
Tsunoda, T., Koh, Y., Koizumi, F., Tsukiyama, S., Ueda, H., Taguchi, F., <u>Saijo, N.</u> , <u>Nishio, K.</u>	Differential gene expression profiles and identification of the genes relevant to clinicopathologic factors in colorectal cancer selected by cDNA array method in combination with principal component analysis.	Int. J. Oncol.	23	49-59	2003
Usuda, J., Inomata, M., Fukumoto, H., Iwamoto, Y., Suzuki, T., Kuh, HJ., Fukuoka, K., Kato, H., <u>Saijo, N.</u> , <u>Nishio, K.</u>	Restoration of p53 gene function in 12-O-tetradecanoylphorbol 13-acetate-resistant human leukemia K562/TPA cells.	Int. J. Oncol.	22	81-86	2003
<u>Saijo, N.</u> , <u>Nishio, K.</u> , <u>Tamura, T.</u>	Translational and clinical studies of target-based cancer therapy.	Int. J. Clin. Oncol.	8	187-192	2003
Kanzawa, F., Akiyama, Y., <u>Saijo, N.</u> , <u>Nishio, K.</u>	In vitro effects of combinations of cis-amminedichloro (2-methylpyridine) platinum (II) (ZD0473) with other novel anticancer drugs on the growth of SBC-3, a human small cell lung cancer cell line.	Lung Cancer	40	325-332	2003

Nishiyama, N., Koizumi, F., Okazaki, S., Matsumura, Y., <u>Nishio, K.</u> , Kataoka, K.	Differential gene expression profile between PC-14 cells treated with free cisplatin and cisplatin-incorporated polymeric micelles.	Bioconjug. Chem.	14	449-457	2003
Hirama, M., Takahashi, F., Takahashi, K., Akutagawa, S., Shimizu, K., Soma, S., Shimanuki, Y., <u>Nishio, K.</u> , Fukuchi, Y.	Osteopontin overproduced by tumor cells acts as a potent angiogenic factor contributing to tumor growth.	Cancer Lett.	198	107-117	2003
Natsume, T., Watanabe, J., Koh, Y., Fujio, N., Ohe, Y., Horiuchi, T., <u>Saijo, N.</u> , <u>Nishio, K.</u> , Kobayashi, M.	Antitumor activity of TZT-1027 (Soblidotin) against VEGF-secreting human lung cancer <i>in vivo</i> .	Cancer Sci.	94	826-833	2003
<u>Saijo, N.</u> , <u>Tamura, T.</u> , <u>Nishio, K.</u>	Strategy for the development of novel anticancer drugs.	Cancer Chemother. Pharmacol.	52	S97-S101	2003
Yamanaka, R., Akutagawa, S., Taguchi, F., Yajima, N., Tsuchiya, N., Uzuka, T., Morii, K., Takahashi, H., Tanaka, R., <u>Saijo, N.</u> , <u>Nishio, K.</u>	Selection of surrogate marker genes in primary central nervous system lymphomas for radio-chemotherapy by DNA array analysis of gene expression profiles.	Int. J. Oncol.	23	913-923	2003