

Fig. 11. 脳特異的発現変動遺伝子

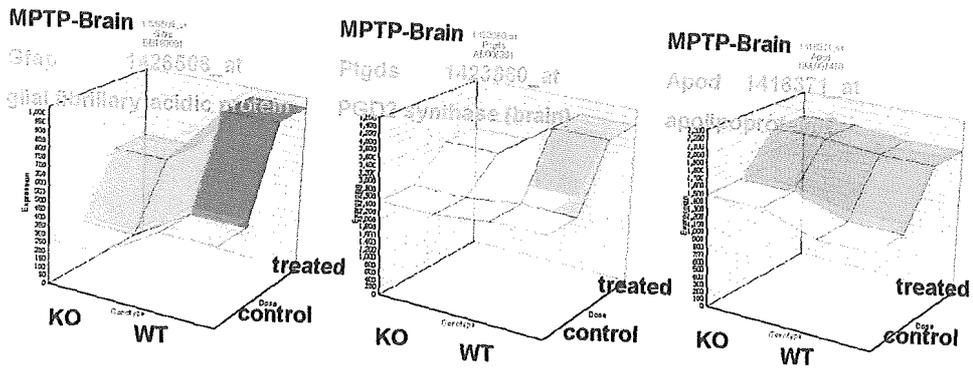


Fig. 12. 酸化ストレス関連 遺伝子—肝臓

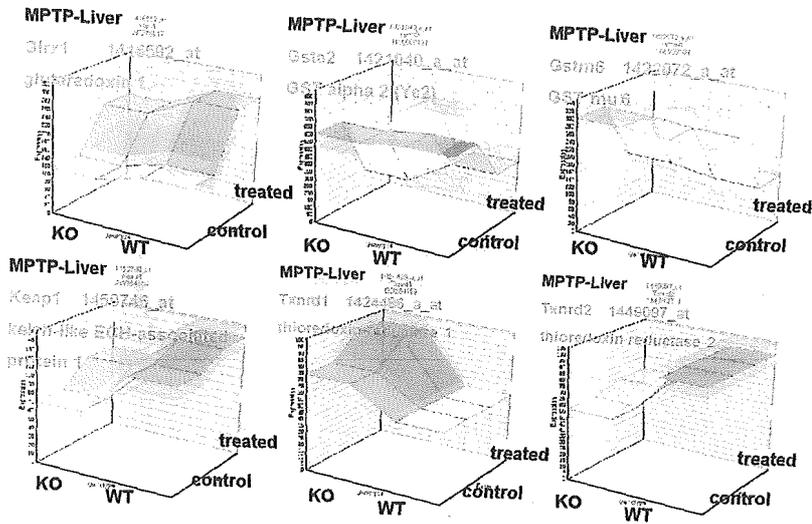


Fig. 13. 酸化ストレス関連 遺伝子—脳

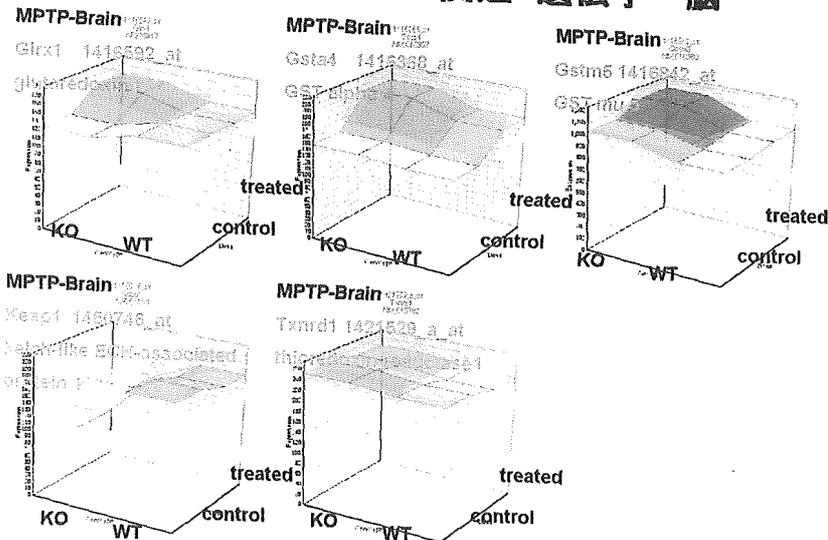


Fig. 14. KOで発現に差のみられた遺伝子

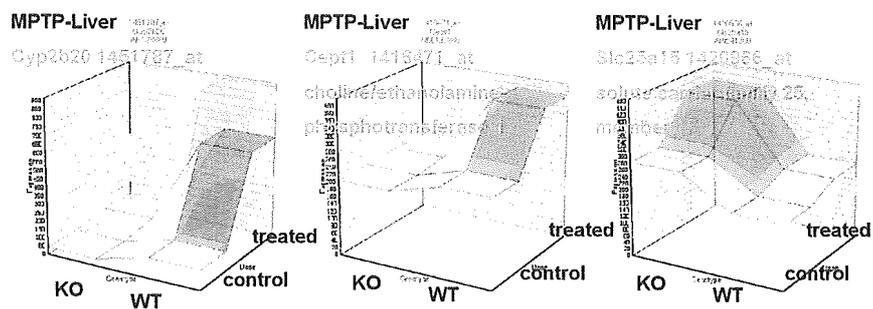


Fig. 15

Mouse primary cultured hepatocytes (24 hr)

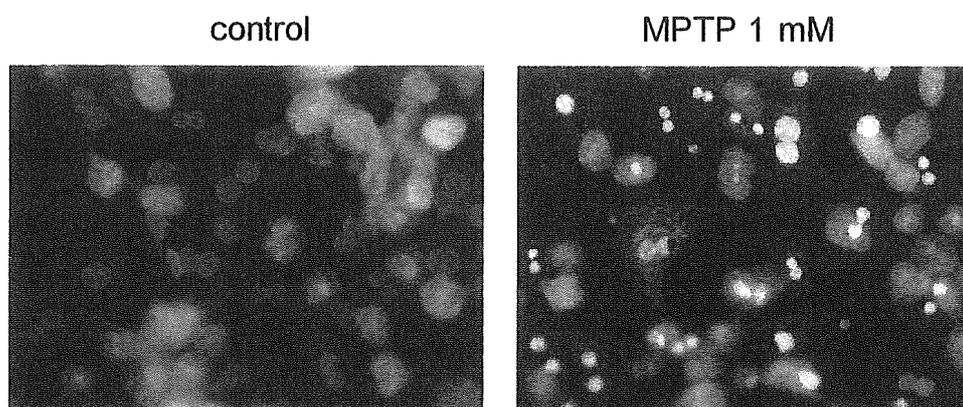


Fig. 16

24hr
MPTP
0.3mM

WT

KO

Nucleus

Free 3'OH DNA Terminal

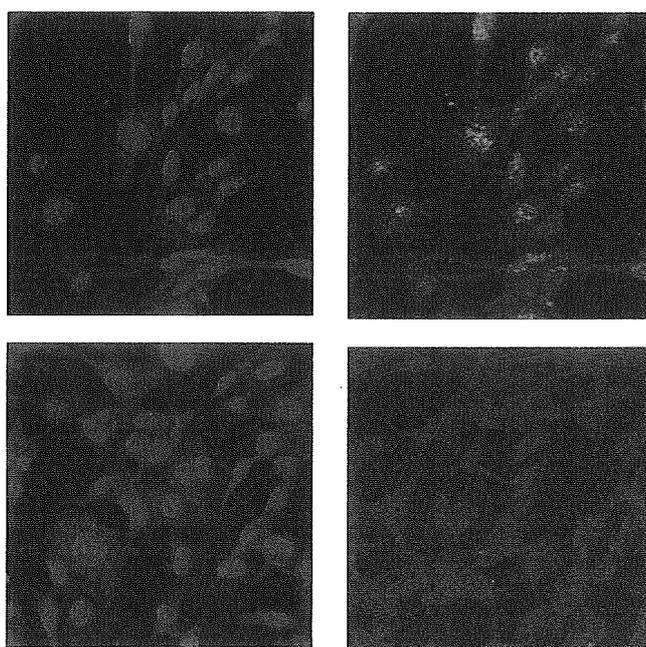


Fig. 17

Expressed genes (SCal value >50, 14,300)

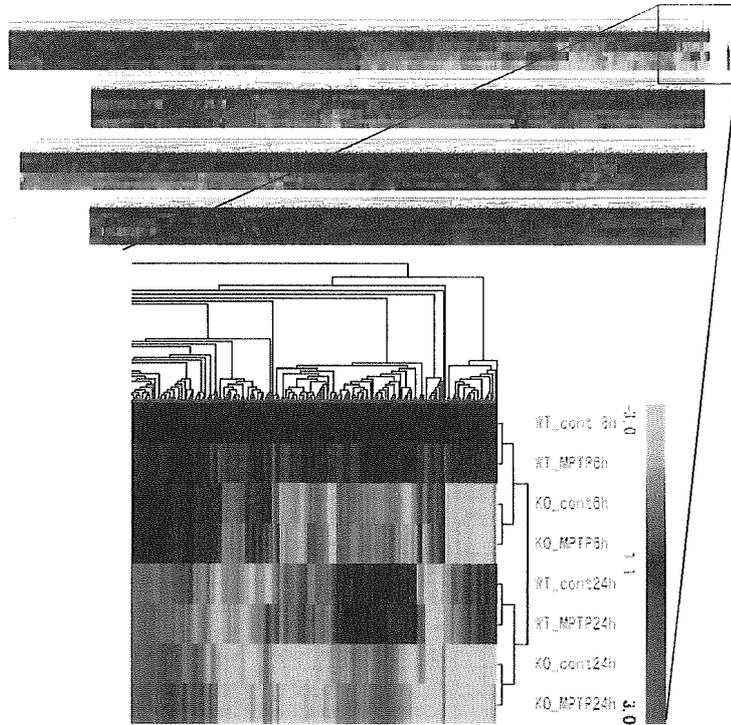


Fig. 18

K-mean clustering using differentially expressed genes(4,300)

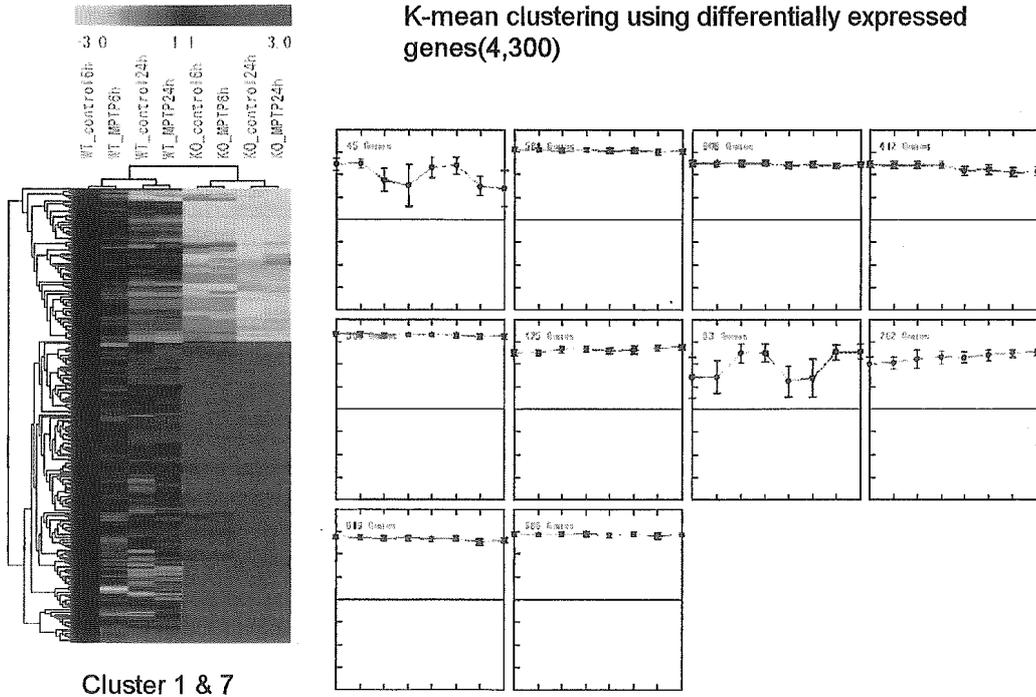


Table 2.

x1.5 Up in WT & KO

GO ID	GO Term	Total Probe Sets	Probe Sets in List	hit_fold vs total	Chi2
30844	chloride ion homeostasis	3	2	31.114	58.295
30920	monovalent inorganic anion homeostasis	5	3	28.002	78.128
46246	terpene biosynthesis	5	2	18.668	33.447
9241	polyisoprenoid biosynthesis	5	2	18.668	33.447
30002	anion homeostasis	9	3	15.557	40.671
8299	isoprenoid biosynthesis	26	7	12.565	74.556
16096	polyisoprenoid metabolism	10	2	9.334	14.886
5721	terpenoid metabolism	10	2	9.334	14.886
6720	isoprenoid metabolism	37	7	8.630	48.64
51130	positive regulation of cell organization and biogenesis	11	2	5.486	13.21
7520	myoblast fusion	11	2	8.486	13.21
50850	positive regulation of calcium-mediated signaling	17	3	5.236	19.079
50848	regulation of calcium-mediated signaling	19	3	7.369	15.521
6668	glycosphingolipid biosynthesis	13	2	7.190	10.642
45453	bone resorption	15	2	5.223	6.7695
50852	T cell receptor signaling pathway	16	2	5.834	8.0133
48562	embryonic organ morphogenesis	16	2	5.834	8.0133
6687	glycosphingolipid metabolism	18	2	5.186	6.7696
9247	glycolipid biosynthesis	21	2	4.445	5.3421
7271	synaptic transmission, cholinergic	22	2	4.243	4.9594
43064	flagellum organization and biogenesis	22	2	4.243	4.9594
1759	induction of an organ	24	2	3.889	4.2949
10092	specification of organ identity	24	2	3.889	4.2949
42102	positive regulation of T cell proliferation	39	3	3.590	5.6106
7568	aging	45	3	3.044	4.121
6095	glycolysis	106	6	2.642	6.136
7605	sensory perception of sound	89	5	2.622	5.0266
6084	acetyl-CoA metabolism	91	5	2.564	4.7811

x 1.5 Down in WT & KO

GO ID	GO Term	Total Probe Sets	Probe Sets in List	hit_fold vs total	Chi2
6707	cholesterol catabolism	2	2	49.329	34.702
16127	sterol catabolism	2	2	49.329	34.702
16684	nucleosome spacing	6	3	24.664	58.124
16054	organic acid catabolism	6	2	16.443	29.011
46395	carboxylic acid catabolism	6	2	16.443	29.011
6706	steroid catabolism	6	2	16.443	29.011
43123	positive regulation of I-kappaB kinase/NF-kappaB cascade	8	2	12.332	20.630
50992	intestinal absorption	15	4	12.332	41.668
31295	T cell costimulation	9	1	10.962	18.110
31294	lymphocyte costimulation	9	2	10.962	18.110
44241	lipid digestion	11	2	8.369	14.154
43122	regulation of I-kappaB kinase/NF-kappaB cascade	11	2	8.369	14.154
31032	actomyosin structure organization and biogenesis	12	2	8.221	12.690
18298	protein-chromophore linkage	12	2	8.221	12.690
16074	DNA integration	12	2	8.221	12.690
6924	cobalt ion transport	12	2	8.221	12.690
9048	dosage compensation, by inactivation of X chromosome	16	2	7.569	11.445
7549	dosage compensation	17	2	5.803	7.954
7886	digestion	44	5	5.605	18.938
45086	positive regulation of Interleukin-2 biosynthesis	18	2	5.461	7.330
7257	activation of JNK activity	19	2	5.192	6.773
42116	macrophage activation	19	2	5.192	6.773
7002	plasma membrane organization and biogenesis	19	2	5.192	6.773
43507	positive regulation of JNK activity	19	2	5.192	6.773
45577	regulation of B cell differentiation	19	2	5.192	6.773
5635	fatty acid beta-oxidation	20	2	4.933	5.274
16993	drug transport	20	2	4.933	5.274
19886	antigen processing, exogenous antigen via MHC class II	21	2	4.698	5.824
43506	regulation of JNK activity	21	2	4.698	5.824

Table 3.

x1.5 Up in WT only

GO ID	GO Term	Total Probe Sets	Probe Sets in List	hit_fold vs total	Chi2
46314	phosphocreatine biosynthesis	3	2	12.116	20.399
45581	negative regulation of T cell differentiation	5	2	7.270	10.816
35110	leg morphogenesis	6	2	6.058	8.448
8356	asymmetric cell division	6	2	6.058	8.448
48170	positive regulation of long-term neuronal synaptic plasticity	6	2	6.058	8.448
48133	male germ-line stem cell division	6	2	6.058	8.448
7288	sperm axoneme assembly	13	4	5.592	15.089
30301	cholesterol transport	12	3	4.544	8.294
15918	sterol transport	12	3	4.544	8.294
6548	histidine catabolism	17	4	4.276	10.045
6547	histidine metabolism	17	4	4.276	10.045
43064	flagellum organization and biogenesis	22	5	4.131	11.869
46339	diacylglycerol metabolism	15	3	3.635	5.732
36136	forelimb morphogenesis	17	3	3.207	4.559
6826	iron ion transport	42	7	3.029	9.524
6857	oligopeptide transport	18	3	3.029	4.079
7886	digestion	44	7	2.891	9.669
7595	lactation	26	4	2.796	4.618
7523	circadian rhythm	45	6	2.423	5.021
16358	dendrite morphogenesis	55	7	2.313	5.225
8869	lipid transport	122	13	1.937	5.905
45596	negative regulation of cell differentiation	35	10	1.913	4.368
16043	cell organization and biogenesis	3897	182	0.862	4.390
7242	intracellular signaling cascade	2192	96	0.796	5.277
46907	intracellular transport	1564	60	0.697	9.172
16070	RNA metabolism	939	36	0.697	4.851
16071	mRNA metabolism	584	13	0.591	5.438
42264	ribosome biogenesis and assembly	249	6	0.438	4.352

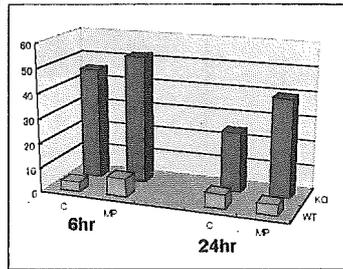
x 1.5 Up in KO only

GO ID	GO Term	Total Probe Sets	Probe Sets in List	hit_fold vs total	Chi2
48165	fused antrum stage oogenesis	3	2	18.824	33.757
6703	estrogen biosynthesis	4	2	14.118	24.360
48157	oogenesis (sensu Mammalia)	5	2	11.295	18.768
15840	urea transport	5	2	11.295	18.768
18208	peptidyl-proline modification	6	2	9.412	15.039
48636	spleen development	6	2	7.059	10.403
7527	adult somatic muscle development	9	2	8.275	8.870
30879	mammary gland development	9	2	6.275	8.870
51227	mitotic spindle assembly	10	2	5.647	7.650
51225	spindle assembly	10	2	5.647	7.650
7525	somatic muscle development	10	2	5.647	7.650
7588	excretion	16	3	5.294	10.453
6432	phenylalanyl-tRNA aminoacylation	11	2	5.134	5.659
46330	positive regulation of JNK cascade	12	2	4.706	5.839
18298	protein-chromophore linkage	12	2	4.706	5.839
10033	response to organic substance	12	2	4.706	5.839
45885	positive regulation of survival gene product activity	13	2	4.344	5.150
17156	calcium ion-dependent exocytosis	20	3	4.235	7.418
7223	frizzled-2 signaling pathway	34	5	4.152	11.375
46328	regulation of JNK cascade	35	5	4.034	11.417
7216	metabotropic glutamate receptor signaling pathway	14	2	4.034	4.565
42591	antigen presentation, exogenous antigen via MHC class II	29	4	3.695	3.611
46339	diacylglycerol metabolism	15	2	3.755	4.062
7613	memory	28	3	3.683	5.667
7215	glutamate signaling pathway	31	4	3.423	7.677
1657	uroterio bud development	33	4	3.423	6.864
48477	oogenesis	25	3	3.322	5.053
E171	cAMP biosynthesis	26	3	3.252	4.696

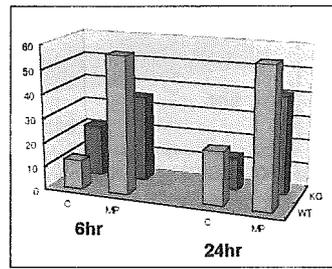
Table 4.

x1/1.5 Down in WT only					x 1/1.5 Down in KO only						
GO ID	GO Term	Total Probe Sets	Probe Sets in	Hit/fold vs total	Ch2	GO ID	GO Term	Total Probe Sets	Probe Sets in	Hit/fold vs total	Ch2
9535	cysteine biosynthesis from serine	2	2	17.322	90.76	43030	regulation of macrophage activation	3	2	16.561	29.244
18943	cysteine biosynthesis via cystathione	2	2	17.322	90.76	7217	tachykinin signaling pathway	4	2	12.421	21.004
9446	gamma-aminobutyric acid metabolism	2	2	17.322	90.76	30259	lipid glycosylation	8	2	9.315	22.272
45568	positive regulation of gamma-delta T cell differentiation	3	2	11.548	19.27	45536	spleen development	9	2	6.210	9.7442
45566	regulation of gamma-delta T cell differentiation	3	2	11.548	19.27	19229	regulation of vasoconstriction	9	2	6.210	9.7442
46645	positive regulation of gamma-delta T cell activation	3	2	11.548	19.27	45630	positive regulation of isotype switching	12	3	6.210	13.117
46643	regulation of gamma-delta T cell activation	3	2	11.548	19.27	45191	regulation of isotype switching	13	3	5.733	11.724
19944	cysteine biosynthesis	3	2	11.548	19.27	45190	isotype switching	19	4	5.230	13.688
19605	butyrate metabolism	3	2	11.648	19.27	55115	embryonic forelimb morphogenesis	11	2	4.517	5.4773
46629	gamma-delta T cell activation	5	3	10.395	25.47	7656	digestion	44	7	3.952	15.48
42223	interleukin-3 biosynthesis	4	2	8.661	13.55	1859	ureteric bud branching	19	3	3.922	8.5345
43306	positive regulation of mast cell degranulation	4	2	8.651	13.55	6546	glycine catabolism	13	2	3.822	4.168
43304	regulation of mast cell degranulation	4	2	8.661	13.55	6182	cGMP biosynthesis	13	2	3.822	4.168
43303	mast cell degranulation	4	2	8.661	13.55	6171	cAMP biosynthesis	26	4	3.822	8.3383
43302	positive regulation of immune cell degranulation	4	2	8.661	13.55	9190	cyclic nucleotide biosynthesis	40	6	3.726	11.978
43300	regulation of immune cell degranulation	4	2	8.661	13.55	7228	finized-2 signaling pathway	34	6	3.659	5.6415
6534	cysteine metabolism	5	2	6.929	10.15	19915	sequestering of lipid	21	3	3.549	5.4941
42253	granulocyte macrophage colony-stimulating factor biosynthesis	5	2	6.929	10.15	9187	cyclic nucleotide metabolism	55	7	3.162	10.358
6890	retrograde transport, Golgi to ER	6	3	5.496	13.95	6749	glutathione metabolism	82	4	3.105	5.7129
46641	positive regulation of alpha-beta T cell proliferation	6	2	5.774	7.90	1657	ureteric bud development	33	4	3.011	5.3766
46640	regulation of alpha-beta T cell proliferation	6	2	5.774	7.90	6825	copper ion transport	25	3	2.981	3.9514
45579	positive regulation of B cell differentiation	13	4	5.330	14.07	7556	blood coagulation	81	9	2.760	10.12
46324	regulation of glucose import	17	5	5.095	16.46	7599	hemostasis	64	3	2.662	9.3629
46323	glucose import	17	5	5.095	16.46	6015	circulation	84	8	2.366	6.9199
46633	alpha-beta T cell proliferation	7	2	4.949	6.30	30298	lipid modification	59	5	2.344	3.6556
40036	regulation of fibroblast growth factor receptor signaling pathway	7	2	4.949	6.30	51251	positive regulation of lymphocyte activation (two component signal transduction system)	36	9	2.329	6.8369
3840	determination of adult life span	7	2	4.949	6.30	160	inception of neuronal defense mechanism (Cereu Vertebrata)	107	10	2.322	7.5413
46325	negative regulation of glucose import	11	3	4.724	8.81	16064		124	11	2.204	7.2518

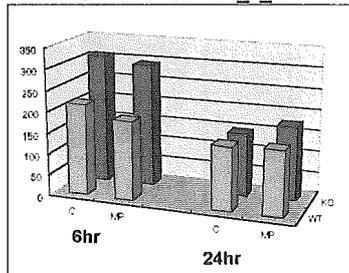
Fig. 19 MAPKKK5(ASK-1) 1439830_at



MAPKK7 1425513_at



MAPKKK5 1427083_a_at



MAPKK7 1449693_at

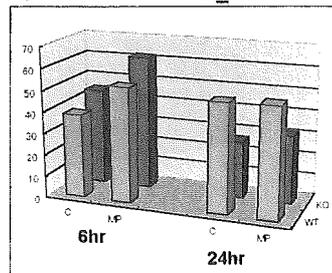
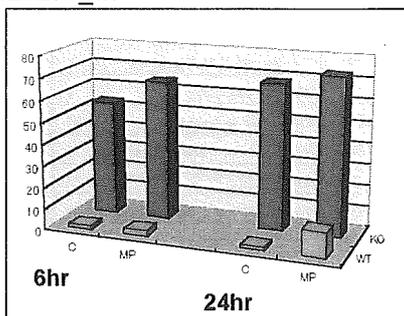
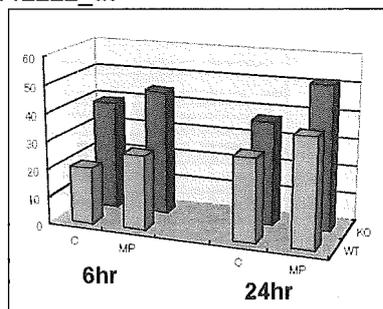


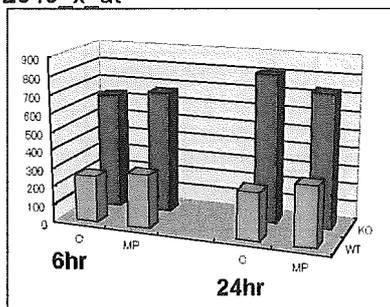
Fig. 20 interferon, alpha-inducible protein 27
1426278_at



interferon (alpha and beta) receptor 1
1442222_at



interferon activated gene 205
1452349_x_at



interferon-induced protein with
tetratricopeptide repeats 31449025_at

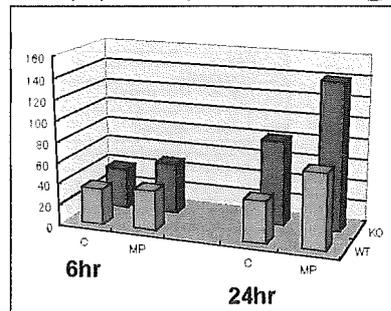
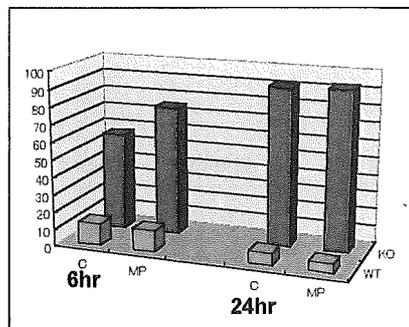
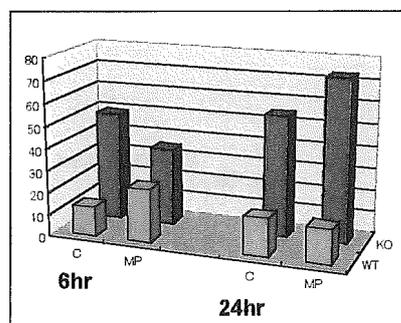


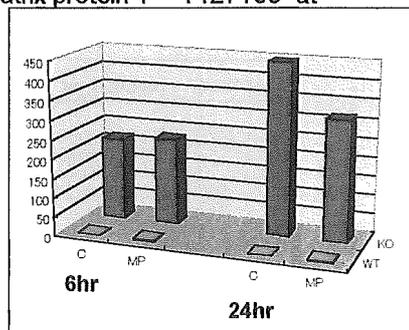
Fig. 21 PDGF receptor-like 1428896_at



HGF 1425379_at



EGF-containing fibulin-like extracellular
matrix protein 1 1427183_at



growth factor receptor bound
protein 10 1430164_a_at

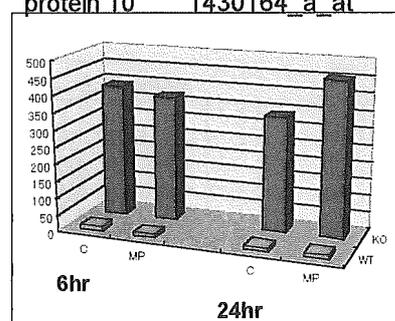
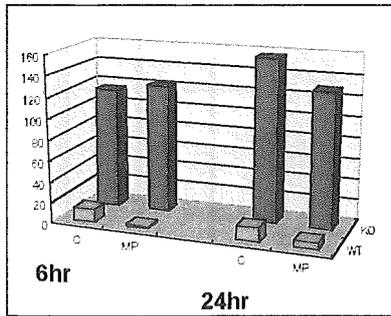
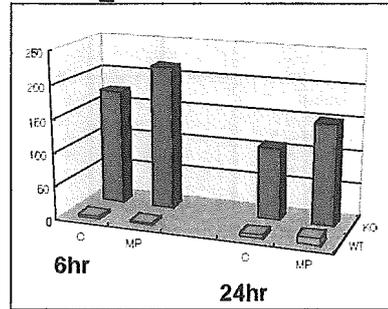


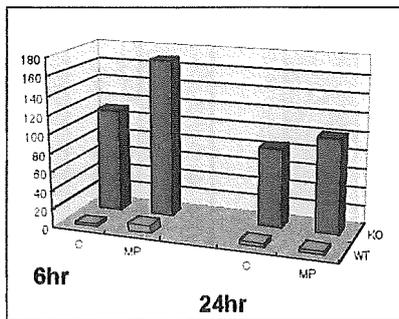
Fig. 22 kelch-like 13 1448269_a_at



keratin complex 1, acidic, gene 19 1417156_at



Rho GTPase activating protein 2 1435108_at



RhoGEF and PH domain containing 6 1435467_at

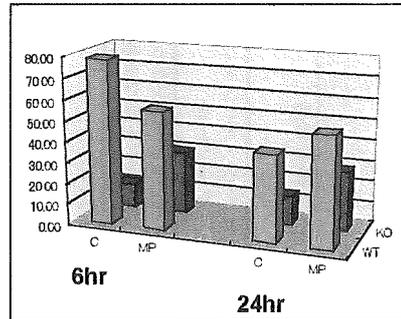
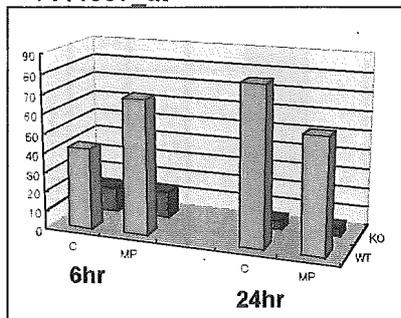
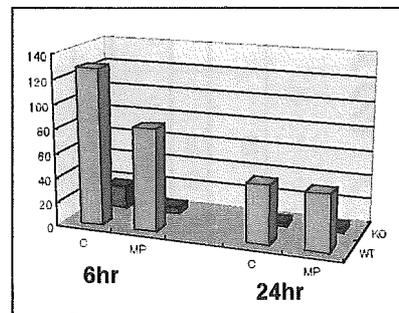


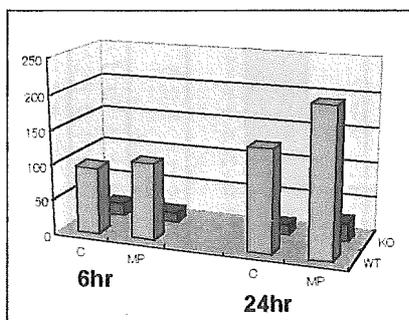
Fig. 23 Lectin, mannose-binding, 1 1444037_at



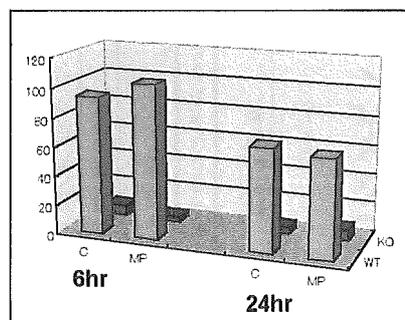
netrin 4 1450512_at



olfactomedin 1 1425784_a_at



Zic 1 1439627_at



化学物質の選択

黒物質(指定化学物質)

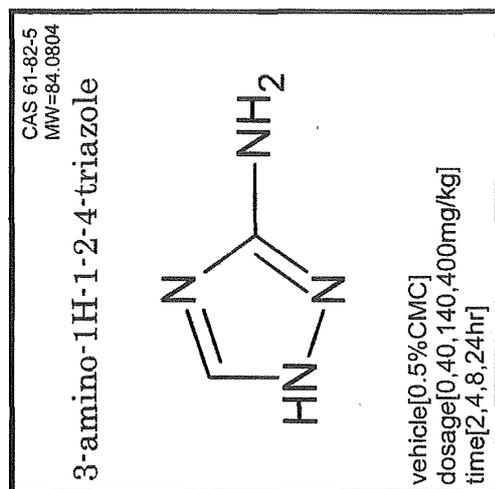
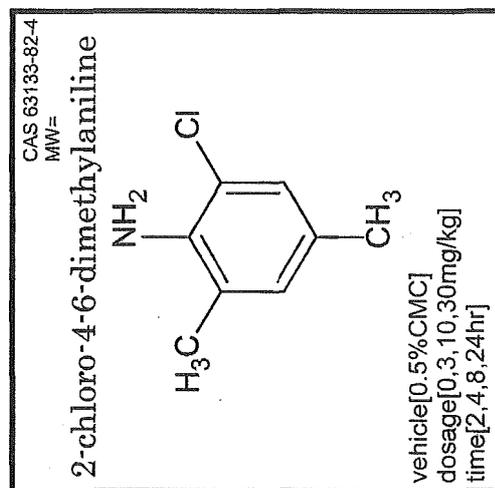
白物質

	官報告示名	官報告示整理番号	CAS	#
1	ペンタクロロフェノール	3-2850	87-86-5	
1	2, 4-ジクロロ-3-メチルフェノール	3-4066	17788-00-0	肝毒性不明
2	2-ピニルピリジン	5-716	100-69-6	
2	3-シアノピリジン	5-742	100-54-9	(注意) 既存化学物質
3	N-メチルアニリン	3-106	100-61-8	
3	3, 4-ジメチルアニリン	3-129	95-64-7	(注意) 既存化学物質
4	3-アミノ-1H-1, 2, 4-トリアゾール (別名アミトロール)	5-602	61-82-5	
4	1, 2, 3-トリアゾール	5-6196	288-36-8	肝毒性不明
5	1, 2-ジクロロ-3-ニトロベンゼン	3-455	3209-22-1	
5	1, 4-ジクロロ-2-ニトロベンゼン	3-455	89-61-2	肝毒性不明
6	2, 4, 6-トリクロロ-1, 3, 5-トリアジン	5-1045	108-77-0	
6	2-クロロ-4, 6-ビス(エチルアミノ)-1, 3, 5-トリアジン	5-3846	122-34-9	肝毒性不明
7	1, 4, 5, 6, 7, 7-ヘキサクロロピシクロ [2.2.1] -5-ヘブテン-2, 3-ジカルボン酸 (別名クロロレンド酸)	4-619	115-28-6	

	官報告示名	官報告示整理番号	CAS	白物質通し番号
1	4-アミノ-2, 6-ジクロロフェノール	3-3818	--	1744
1	4-ブromo-2, 5-ジクロロフェノールナトリウム塩	3-3455	--	80
2	4-ジメチルアニロピリジン	5-5479	--	805
2	2- (アミノメチル) ピリジン	5-5596	--	1199
2	2-アミノ-6-クロロピリジン	5-5826	--	2009
3	2-クロロ-4, 6-ジメチルアニリン	3-3551		494
3	4-クロロ-N-エチルアニリン	3-4009		2723
4	1, 2, 4-トリアゾール	5-5776		1785
4	1, 2, 4-トリアゾール-3-カルボキサミド	5-5651		1417
5	4-エチルニトロベンゼン	3-4058		3014
5	1, 3-ジアミノ-2, 4, 6-トリニトロベンゼン	3-3438		15

発現変動遺伝子の重なり

45000 probe sets



変動probe set数

929 probe sets
(2.06%)

1008 probe sets
(2.24%)

共通probe set数 53 probe sets (5.71% 53/929)

表 1 共同研究参加機関

代表者	所 属
降旗 千恵	青山学院大学理工学部 生物学
浜田 修一	エスエス製薬(株) 中央研究所 薬理研究安全性グループ
兵庫 淳志	三共(株) 安全性研究所 細胞毒性研究グループ
中嶋 圓	(財)安評センター 環境遺伝毒性試験グループ
大内田昭信	大鵬薬品(株) 安全性研究所 第3研究グループ
斎藤 優子	日研化学(株) 大宮研究所 安全性研究室
祖父尼俊雄	株式会社ノバスジーン
鈴木 孝昌	国立医薬品食品衛生研究所 変異遺伝部 (遺伝子細胞医薬部)
馬場 博	三菱ウエルファーマ(株) 安全性研究所
若田 明裕	山之内製薬(株) 安全性研究所
山影 康次	食品薬品安全センター 秦野研究所・細胞生物
山本 康人	ライオン(株) 研究開発本部 安全性評価センター
浅野 哲秀	日東電工(株) 安全性試験センター

表 2 今回検討した化合物と投与量

アルキル化剤		
Dimethylnitrosamine	(DMN)	5 mg/kg
Ethyl nitrosourea	(ENU)	150 mg/kg
Dipropylnitrosamine	(DPN)	250 mg/kg
多環芳香族化合物		
o-Aminoazotoluene	(AAT)	300 mg/kg
Dibenzo[a, l]pyrene	(DBP)	6 mg/kg
7,12-Dimethylbenz[a]anthracene	(DMBA)	20 mg/kg
非遺伝子傷害性物質		
Ethanol	(EtOH)	1000 mg/kg
Phenobarbital sodium	(PB)	30 mg/kg
Carbon Tetrachloride	(CCl ₄)	1000 mg/kg
Diethylhexyl phthalate	(DEHP)	2000 mg/kg
Trichloro ethylene	(C ₂ HCl ₃)	1000 mg/kg

表 3 使用したマイクロアレイの種類

GeneChip (Affymetrix)	
Mouse U74Av2 (Sankyo)	約12000個のマウス遺伝子に対し、遺伝子あたり16個のPerfect Match, Miss Match25merをデザイン基盤上に光リソグラフィにより直接合成、単色ラベルで専用の装置にてハイブリ、洗浄、スキャンを行う
Mouse 430A (NIHS)	プローブの設計を変更した新しいバージョンで、遺伝子あたりのプローブセット数は11、解析アルゴリズムも変更ゲノム情報の進化に伴い、新たな遺伝子も追加し約17000遺伝子を搭載
Atlas Glass Array (Clontech)	
Mouse 1.0 (NIHS)	クロンテック社から市販されたマウス1080遺伝子搭載のガラスアレイ 80merのオリゴをスポットしたもので、各遺伝子特異的なプライマーにてcDNA合成を行う
Mouse Basic Array (NovusGene)	
Ver. 0 (NIHS, Anpyo)	本共同研究にて選んだ遺伝子関連の96遺伝子を搭載したアレイ 1遺伝子に対して2カ所の46merオリゴプローブをダブル法にて設計し、それぞれduplicateにてスポット
Ver. 1 (配布)	Ver. 0に遺伝子を追加し、352遺伝子(1遺伝子1 probe, duplicate)にし、製法にも改良を加える
Toxicogenomics Array (Aoyama)	
Ver.2 (Aoyama)	本共同研究で選んだ遺伝子関連100遺伝子(132 probe)を搭載 CARBOSTATION-U アレイにオリゴ(40-45 mer)をスポット
Ver.3 (作成中)	さらに遺伝子を追加し、197遺伝子(200 probe)に
千葉大アレイ	
	千葉大が旭テクノグラスに依頼して作成した1000遺伝子のアレイに、本共同研究で選んだ遺伝子200種を加えたもの 市販のcDNAクローンを増やしたものをスポット

表 4 Atlas Glass Microarray による DEN 処理 4 時間後の肝臓での遺伝子発現変化

Up-regulated genes (>2.0)				Down-regulated genes (<0.5)			
Gene Name	Ratio	cont.	DEN	Gene Name	Ratio	cont.	DEN
myeloid cell leukemia sequence 1	13.56	100	1288	GATA-binding protein 4	0.15	40647	5724
wingless-related MMTV integration site 3	7.61	139	1000	T-cell leukemia, homeobox 1	0.16	59399	9154
Bcl-associated death promoter	5.34	66	334	related to Drosophila groucho gene	0.17	61512	9826
activating transcription factor 2	4.94	128	599	wingless-related MMTV integration site 3A	0.17	1904	308
desmocollin 2	4.28	100	405	interleukin 1 receptor antagonist	0.18	2313	383
src homology 2 domain-containing transforming protein C3	4.15	172	675	uracil-DNA glycosylase	0.18	1522	255
talin	4.10	137	531	E2F transcription factor 1	0.18	598	104
procollagen, type VI, alpha 1	3.79	4488	16066	insulin-like growth factor 2 receptor (IGF2R)	0.19	1988	354
mitogen activated protein kinase 10	3.01	142	403	guanine nucleotide binding protein, beta 2	0.20	7638	1474
purinergic receptor P2Y, G-protein coupled 1	2.85	1774	4938	interferon regulatory factor 1	0.21	1443	283
MAD homolog 1 (Drosophila)	2.91	311	855	fibronectin 1	0.22	2745	575
protein tyrosine phosphatase, non-receptor type 13	2.91	298	818	dentin sialophosphoprotein	0.24	17201	3899
frizzled homolog 6 (Drosophila)	2.76	244	635	androgen receptor	0.24	1284	297
Kit ligand	2.65	885	2212	plasminogen	0.24	8197	1898
eyes absent 3 homolog (Drosophila)	2.65	1028	2568	serine protease inhibitor 3	0.25	533	128
suppression of tumorigenicity 14 (colon carcinoma)	2.47	785	1832	Parkinson cell protein 4	0.27	950	239
coagulation factor II (thrombin) receptor	2.47	637	1489	Fas antigen	0.27	504	127
growth hormone releasing hormone receptor	2.43	833	1916	ELK1, member of ETS oncogene family	0.27	890	225
beaded filament structural protein in lens-GP94	2.42	8857	15693	caspase 7	0.30	739	209
lysosomal-associated protein transmembrane 5	2.33	1670	3682	low density lipoprotein receptor	0.31	1374	401
wingless-related MMTV integration site 4	2.31	642	1398	sema domain, immunoglobulin domain (Ig)	0.31	790	232
eyes absent 2 homolog (Drosophila)	2.29	5684	12277	hepsin	0.33	1991	617
zinc finger protein, subfamily 1A, 1 (Ikaros)	2.25	1382	2898	phenylalanine hydroxylase	0.33	506	159
dystroglycan 1	2.20	2069	4312	dipeptidylpeptidase 4	0.35	583	191
interleukin 1 beta	2.20	504	1045	radical fringe gene homolog (Drosophila)	0.35	21620	7097
mitogen activated protein kinase kinase kinase 8	2.15	481	976	GATA-binding protein 2	0.35	1300	428
NK2 transcription factor related, locus 6 (Drosophila)	2.12	3722	7481	wingless-related MMTV integration site 7A	0.35	816	203
SWI/SNF related, actin dependent regulator of chromatin	2.11	527	1050	heme oxygenase (decycling) 2	0.36	484	156
laminin, alpha 2	2.11	3490	6947	hemoex box A1	0.38	684	243
laminin, beta 2	2.08	855	1286	achaeate-scute complex homolog-like (Drosophila)	0.38	1133	405
cyclin G	2.07	260	510	ATP-binding cassette, sub-family B (MDR/TAP), member 1	0.38	615	221
zinc finger protein 60	2.06	446	870	solute carrier family 8 (noradrenalin)	0.39	654	239
matrix metalloproteinase 2	2.03	349	671	angiogenin	0.39	3052	1135
integrin beta 2 (Cd18)	2.03	1317	2529	glial cell line derived neurotrophic factor	0.40	1554	582
Bcl2-like 2	2.02	834	1593	heat shock protein, 60 kDa	0.40	4366	1651
Jun oncogene	2.00	7302	13832	transferrin	0.43	17041	6887
epidermal growth factor	2.00	459	867	P40-8, functional	0.43	2031	834
protein tyrosine phosphatase, receptor type	2.00	1933	3644	nuclear receptor subfamily 2, group F, member 6	0.44	616	254
				ribosomal protein S29	0.48	8146	3685
				kallikrein 3, plasma	0.48	982	450
				apolipoprotein E	0.49	12098	5558
				RAD23b homolog (S. cerevisiae)	0.49	782	355

* 328/1080 genes are available

表 5 NovusGene Microarray による DEN 処理 4 時間後の肝臓での遺伝子発現変化

Up-regulated genes (>1.5)		66/192 spots, 47/96 genes are available						
Category	Gene	Av. Ratio	Ratio-1	cont-1	DEN-1	Ratio-2	cont-2	DEN-2
Transcription factor	E2f1	3.96	3.76	50	283	4.19	44	277
Tumor suppressor	APC	3.40	2.72	26	106	4.53	15	102
Tumor development, Growth factor	TGF-beta R	2.52	2.10	712	2244	3.16	522	2478
Xenobiotic metabolism	GST p1	2.25	1.92	1767	5106	2.70	1708	6920
Xenobiotic metabolism	mGSTpiA	2.19	1.94	1412	4102	2.52	2386	9031
Oncogene	c-mos	2.17	1.92	147	425	2.48	169	628
Transcription factor	Ddit3	2.04	1.93	41	119	2.16	30	97
Transcription factor	c-jun	1.94	2.07	17	53	1.82	15	41
Xenobiotic metabolism	Eph1	1.79	1.73	145	377	1.84	79	219
Stress protein	Osi	1.78	1.71	97	249	1.86	51	142
Transcription factor	Pax-5	1.67	1.43	323	693	2.01	229	692
Stress protein	Stip1	1.63	1.51	49	111	1.78	46	123
Tumor suppressor	Brca2	1.61	1.81	21	57	1.45	23	50
Transcription factor	Tcf3	1.53	1.56	686	1606	1.51	573	1298

Down-regulated genes (<1/1.5)								
Category	Gene	Av. Ratio	Ratio-1	cont-1	DEN-1	Ratio-2	cont-2	DEN-2
Stress protein	Cu-Zn SOD	0.60	0.55	524	429	0.66	646	644
Apoptosis	Bcl-2	0.60	0.52	59	46	0.71	51	54
Transcription factor	Tcf3	0.52	0.50	1980	1494	0.53	1066	847
Xenobiotic metabolism	Cyp2a5	0.52	0.47	159	113	0.57	159	135
Tumor suppressor	p14	0.51	0.46	59	41	0.58	52	45
Xenobiotic metabolism	GST1-i	0.49	0.41	145	90	0.59	299	265
Xenobiotic metabolism	Cyp1b1	0.48	0.51	46	35	0.45	53	36
Xenobiotic metabolism	GST mu1	0.48	0.56	135	113	0.41	172	107
Stress protein	Herpud1	0.46	0.41	106	66	0.53	52	41
Xenobiotic metabolism	Cyp2a5	0.43	0.45	318	215	0.42	287	179
Xenobiotic metabolism	Cyp2e1	0.38	0.45	4932	3320	0.33	3216	1593
Tumor suppressor	Men1	0.25	0.26	74	29	0.23	71	25
Apoptosis	p53	0.24	0.19	25751	7462	0.32	16431	7997
Apoptosis	Fas ligand	0.15	0.12	37140	6879	0.19	14380	4110

表 6 Affymetrix GeneChip (Mouse 430A)を用いた個体ごとの解析結果

Description	4 h						28 d					
	Mouse-1			Mouse-2			Mouse-1			Mouse-2		
	Ratio	Call*	Value									
cyclin-dependent kinase inhibitor 1A (P21)	119.79	P	2654	125.09	P	2867	13.21	P	784	13.68	P	1075
cyclin G1	24.50	P	2079	26.35	P	2313	6.46	P	349	8.63	P	618
cyclin G1	7.22	P	773	8.63	P	956	2.83	P	271	3.28	P	416
pleckstrin homology-like domain, family A, member 3	7.79	P	964	8.23	P	1054	3.14	P	466	2.80	P	551
stress induced protein	7.32	P	2606	4.84	P	1783	3.39	P	943	3.19	P	1173
B-cell translocation gene 1, anti-proliferative	3.15	P	537	4.01	P	709	2.01	P	410	2.60	P	676
lipin 1	3.08	P	2002	3.92	P	2636	3.63	P	618	3.34	P	752
RKEN cDNA 1110025L05 gene	3.10	P	327	3.66	P	399	6.85	P	179	5.95	P	207
lipin 1	2.62	P	1789	3.51	P	2482	3.96	P	615	5.05	P	1039
MAP kinase-interacting serine/threonine kinase 2	2.96	P	2822	3.47	P	3419	3.21	P	935	3.16	P	1219
tumor necrosis factor receptor superfamily, member 12a	154.60	P	842	163.62	P	922	0.82	A	5	1.00	A	8
tumor necrosis factor receptor superfamily, member 12a	36.55	P	928	50.24	P	1320	0.78	A	24	0.84	A	33
RKEN cDNA 2310057H16 gene	26.29	P	337	27.00	P	359	2.85	A	32	0.98	A	15
cyclin-dependent kinase inhibitor 1A (P21)	25.58	P	748	16.38	P	496	3.82	A	139	3.74	P	180
activating transcription factor 3	23.82	P	600	35.94	P	937	0.67	A	25	0.51	A	25
Jun oncogene	13.26	P	899	18.52	P	1300	0.55	A	49	0.48	A	55
serum-inducible kinase	12.57	P	818	15.45	P	1041	3.31	A	189	3.23	A	244
core promoter element binding protein	10.01	P	229	21.58	P	511	1.70	P	50	1.44	P	56
Down syndrome critical region homolog 1 (human)	9.94	P	1785	10.06	P	1869	1.10	P	134	1.05	P	169
Highly similar to promyelocyte leukemia Zn finger protein	9.68	P	103	6.87	P	75	2.04	P	53	1.38	M	48
odd Oz/ten-m homolog 3 (Drosophila)	0.22	A	21	0.16	A	16	0.95	P	75	1.05	P	109
insulin degrading enzyme	0.29	A	21	0.15	A	11	1.09	P	171	1.28	P	264
amyloid beta (A4) precursor-like protein 2	0.20	P	41	0.15	A	31	1.45	P	448	0.88	P	358
Tnfr1-induced adipose-related protein	0.26	P	237	0.13	A	128	1.30	P	336	1.24	P	423
solute carrier family 21 (organic anion transporter), member 10	0.13	P	41	0.12	P	40	1.05	P	803	1.57	P	1584
RKEN cDNA B130055L10 gene	0.33	P	77	0.11	P	26	0.92	P	301	1.21	P	526
ATP-binding cassette, sub-family A (ABC1), member 1	0.14	A	19	0.09	A	13	1.15	P	176	1.49	P	302
glial cell line derived neurotrophic factor family receptor alpha 1	0.44	P	173	0.06	A	23	1.08	P	428	1.01	P	527
RKEN cDNA 9030401P18 gene	0.27	A	38	0.04	A	6	0.86	P	151	0.86	P	198
serum amyloid A 2	0.37	P	1960	0.25	P	1399	0.96	P	417	0.81	P	466
one cut domain, family member 1	0.36	M	32	0.31	A	28	0.45	P	54	0.45	P	71
suppressor of cytokine signaling 2	0.48	P	66	0.24	A	35	0.40	M	49	0.33	P	54

* P: presence, M: marginal, A: absence

Up-regulation

Down-regulation

表7 9種の化合物に共通して変化の見られた遺伝子

Genes Commonly Up-regulated among All Chemicals

UP
 Down

芳香族			遺伝毒性がない						アルキル化剤						Gene name									
AAT			DMBA		DBP		EtOH		PB		DMN		ENU			DPN								
4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h	28d		4h	20h	28d						
repeat 10 times																								
2.77	1.68	3.00	0.79	1.52	2.78	2.17	2.05	1.53	2.28	2.53	1.44	0.93	1.05	1.09	3.91	2.42	3.29	12.2	21.2	14.43	20.7	10.6	6.98	cyclin-dependent kinase inhibitor 1A (P21)
repeat 9 times																								
0.94	1.76	2.76	0.98	2.65	3.44	0.95	2.77	2.37	1.17	1.05	8.60	0.92	0.71	2.78	1.24	1.68	1.19	3.35	0.85	1.26	2.66	1.04	0.67	tp53
0.84	1.79	3.14	0.95	2.48	4.09	0.91	2.99	2.64	1.09	0.71	10.1	0.93	0.73	2.60	1.23	1.42	1.17	3.13	0.97	1.44	3.36	1.11	0.60	tp53
0.92	3.33	2.49	1.05	3.62	4.29	0.99	4.33	3.81	1.37	0.21	6.40	1.11	1.03	2.00	1.28	1.05	1.10	2.39	1.09	0.83	2.34	1.24	0.87	sialyltransferase 9
1.06	9.34	1.65	0.93	1.85	1.34	0.57	1.32	1.39	0.97	2.54	1.10	1.02	1.37	1.13	2.98	7.75	1.07	5.18	6.17	0.97	10.7	8.09	2.47	cyclin G1
repeat 8 times																								
1.41	3.19	2.90	1.08	4.73	3.95	1.33	3.94	4.04	1.56	1.09	5.40	1.00	0.33	1.31	1.43	0.92	1.47	4.26	1.20	0.42	2.13	0.56	0.44	Hermansky-Pudlak syndrome 4 homolog (human)
0.93	4.28	2.62	1.40	1.04	1.43	0.83	0.85	1.29	0.82	1.05	1.45	2.29	1.10	0.82	1.09	3.46	2.64	5.00	18.4	8.40	14.8	7.53	5.55	clone IMAGE3493956, mRNA, partial cds
2.29	2.24	1.25	1.25	1.13	1.02	1.08	0.78	0.85	1.07	1.10	1.14	0.97	0.89	0.77	2.87	3.10	0.96	4.21	2.63	0.90	3.33	3.10	1.30	stress induced protein
0.91	2.65	3.53	1.12	1.14	2.10	1.04	1.09	1.38	1.04	1.41	0.95	1.14	1.35	1.58	0.90	2.64	4.73	0.84	2.35	2.66	0.77	1.53	6.56	lymphocyte antigen 6 complex, locus A
repeat 7 times																								
1.32	0.40	1.15	2.62	1.04	8.10	2.90	1.27	0.88	0.93	0.31	2.91	0.79	7.29	1.00	0.20	6.48	0.29	1.10	14.6	0.82	0.03	0.09	2.53	neuronal PAS domain protein 2
0.51	1.16	3.27	0.37	4.95	5.15	0.76	2.44	3.47	1.06	2.02	6.96	0.44	0.67	1.11	1.22	0.69	2.42	3.31	0.50	2.07	2.07	3.98	1.21	gamma-aminobutyric acid (GABA-B) receptor, 1
11.2	4.01	4.47	0.30	13.5	3.46	6.54	0.79	3.31	1.64	8.73	0.45	0.48	1.94	0.76	1.14	14.7	2.05	3.67	11.8	7.16	4.19	8.80	9.88	clone IMAGE3493956, mRNA, partial cds
1.36	3.28	1.86	0.87	0.85	1.96	0.99	0.74	1.15	0.83	1.16	0.76	0.90	0.94	0.89	1.75	8.97	1.44	2.56	2.95	1.06	3.84	9.49	3.07	pleckstrin homology-like domain, family A, member 3
1.28	4.85	1.17	0.84	1.44	1.08	0.85	1.19	0.92	0.99	0.59	1.47	1.21	0.98	0.99	2.55	6.64	1.86	4.17	3.75	1.30	5.31	7.53	1.92	cyclin G1

Genes Commonly Down-regulated among All Chemicals

芳香族			遺伝毒性がない						アルキル化剤						Gene name									
AAT			DMBA		DBP		EtOH		PB		DMN		ENU			DPN								
4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h	28d		4h	20h	28d						
repeat 7 times																								
1.05	0.77	1.15	1.22	1.09	8.95	1.23	1.07	1.00	0.30	0.22	3.74	0.16	5.64	1.21	0.55	1.04	0.09	1.57	12.4	0.97	0.07	0.06	0.71	serum amyloid A 2
repeat 6 times																								
1.41	0.15	0.63	1.40	0.26	0.60	1.11	0.16	0.06	0.64	1.44	0.32	0.58	1.10	0.51	0.12	0.11	0.47	1.62	3.75	1.64	0.49	1.21	0.13	growth arrest and DNA-damage-inducible 45 gamma
0.80	0.47	0.86	0.83	0.65	0.57	0.55	0.76	0.43	0.40	4.26	0.46	0.55	1.65	0.64	0.39	0.38	0.76	0.76	0.97	0.69	0.79	0.35	0.43	pleckstrin homology-like domain, family A, member 1
1.32	0.40	1.15	2.62	1.04	8.10	2.90	1.27	0.88	0.93	0.31	2.91	0.79	7.29	1.00	0.20	6.48	0.29	1.10	14.6	0.82	0.03	0.09	2.53	lipocalin 2
repeat 5 times																								
0.34	0.13	1.00	1.15	0.83	4.10	0.83	0.28	0.91	0.54	0.94	1.31	0.44	1.05	0.51	0.28	0.66	1.31	0.56	1.46	0.74	0.05	1.29	1.08	chemokine (C-X-C motif) ligand 1
5.12	0.12	0.77	3.06	0.56	1.36	2.19	0.36	0.50	1.10	0.86	1.83	2.16	0.99	0.95	0.28	0.22	0.26	2.95	0.73	1.37	0.87	0.90	1.60	insulin-like growth factor binding protein 5
0.93	0.77	0.97	1.19	1.00	5.91	1.40	1.14	1.32	0.59	0.63	2.52	0.37	3.47	0.98	10.45	1.04	0.16	2.74	4.70	0.78	0.16	0.12	0.77	serum amyloid A 2
1.68	0.60	0.86	1.43	1.04	0.84	1.39	1.09	0.73	0.54	0.38	1.26	1.00	1.65	1.24	0.82	0.47	0.86	0.92	0.23	1.01	0.74	0.25	0.89	stearyl-Coenzyme A desaturase 1

表8 遺伝子傷害性物質に特異的に変化の見られた遺伝子(ver1)

Genes Commonly Changed only by Genotoxic Chemicals

AAT			DMBA		DBP		DMN		ENU		DPN		EtOH		PB		Gene name							
4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h	28d	4h	20h		28d						
2.77	1.68	3.00	0.79	1.52	2.78	2.17	2.05	1.53	3.91	2.42	3.29	12.2	21.2	14.43	20.7	10.6		6.98	cyclin-dependent kinase inhibitor 1A (P21)					
5.12	0.12	0.77	3.06	0.56	1.36	2.19	0.36	0.50	3.32	3.69	0.93	2.22	2.19	0.84	4.51	3.15	1.89	1.11	0.47	0.80	1.02	0.69	1.08	transferrin receptor 3
0.93	4.28	2.82	1.40	1.04	1.43	0.83	0.85	1.29	1.09	3.46	2.64	5.00	18.4	8.40	14.83	7.53	5.55	0.82	1.06	1.45	2.29	1.10	0.82	clone IMAGE3493956, mRNA, partial cds
2.29	2.24	1.26	1.25	1.13	1.02	1.08	0.78	0.85	2.87	3.10	0.96	4.21	2.63	0.80	3.80	5.10	1.90	1.07	1.10	1.14	0.87	0.89	0.77	stress induced protein
1.12	2.03	4.47	0.30	13.54	3.46	6.54	0.79	3.31	1.14	14.73	2.05	3.67	11.85	7.16	4.19	8.80	9.88	1.64	9.73	0.45	0.46	1.34	0.76	clone IMAGE3493956, mRNA, partial cds
1.36	3.28	1.86	0.87	0.85	1.96	0.98	0.74	1.15	1.75	8.97	1.44	2.80	2.35	1.05	3.84	9.49	3.07	0.83	1.16	0.76	0.90	0.94	0.89	pleckstrin homology-like domain, family A, member 3
1.28	4.85	1.17	0.84	1.44	1.08	0.85	1.19	0.92	2.55	6.64	1.86	4.17	3.75	1.30	5.31	7.53	1.92	0.98	0.69	1.47	1.21	0.98	0.89	cyclin G1
3.50	0.31	0.88	1.61	0.65	0.84	1.64	0.54	0.82	1.03	0.95	0.59	1.78	0.41	0.97	2.46	0.86	1.25	1.37	1.00	0.86	1.45	1.26	1.32	glucosyl-6-phosphatase, catalytic
1.11	0.27	1.41	1.18	1.13	2.37	1.41	1.43	2.84	0.69	0.43	0.44	1.73	1.54	1.59	0.39	0.49	0.74	1.15	0.71	2.01	0.39	0.63	1.62	metallothionein 1
0.96	2.38	1.93	1.05	1.01	1.23	0.94	0.91	1.06	2.23	5.25	1.08	2.30	3.44	1.04	3.31	5.97	2.22	1.00	0.79	1.27	1.03	1.26	1.17	cyclin G1
1.05	3.82	1.43	1.07	0.84	1.57	1.39	0.82	1.70	1.79	3.58	1.48	4.11	4.50	1.16	5.76	4.95	1.51	1.80	0.16	1.06	1.01	1.13	0.88	RIKEN cDNA 2700083E06 gene
0.92	2.77	1.01	1.13	0.94	1.16	1.08	0.87	0.83	1.62	2.56	1.77	2.33	2.53	1.16	3.33	3.05	1.43	1.13	1.26	1.01	1.04	0.78	0.87	RIKEN cDNA 2700083E06 gene
0.34	0.13	1.00	1.15	0.83	4.10	0.83	0.28	0.91	0.28	0.66	1.31	0.56	1.46	0.74	0.05	1.29	1.08	0.54	0.94	1.31	0.44	1.05	0.51	chemokine (C-X-C motif) ligand 1
2.46	2.12	3.04	2.28	0.53	3.40	1.43	0.23	2.44	1.88	1.42	0.86	2.83	0.87	0.67	7.20	3.64	2.14	2.43	0.41	0.44	2.49	3.55	0.68	Jun oncogene
1.63	6.82	1.43	1.36	1.29	0.94	0.94	1.05	1.05	3.32	3.69	0.93	2.22	2.19	0.84	4.51	3.15	1.89	1.11	0.47	0.80	1.02	0.69	1.08	transferrin receptor 3
0.70	3.25	1.35	1.16	1.41	0.87	0.69	1.24	1.31	1.24	1.12	0.88	2.54	7.15	0.81	4.41	15.49	1.16	0.93	2.17	0.83	0.63	0.97	0.63	cytosolic acyl-CoA thioesterase 1
0.91	3.10	1.14	0.82	0.89	1.02	0.81	0.71	0.95	1.64	3.05	0.92	2.88	1.82	1.09	3.93	4.79	1.08	1.13	0.73	0.84	1.07	1.22	1.20	RIKEN cDNA 4930542G03 gene
1.57	3.59	1.97	1.13	1.44	0.85	1.16	1.38	1.62	1.65	1.90	1.37	1.43	1.09	1.00	2.01	0.88	0.50	1.05	0.64	1.04	1.43	0.87	1.54	aminolevulinic acid synthase 1
0.91	0.22	1.82	0.95	1.00	2.99	1.22	1.28	2.71	1.16	1.11	0.78	3.05	1.00	0.85	0.84	1.59	1.81	1.07	0.91	1.14	0.67	0.76	1.31	RIKEN cDNA 4933425F03 gene
2.42	1.26	0.80	1.42	0.97	0.77	2.07	1.01	0.88	1.72	0.83	1.03	2.51	0.88	1.09	5.44	1.13	1.26	1.45	1.63	0.79	1.13	0.97	1.10	protein phosphatase 1, regulatory (inhibitor) subunit 3
1.47	2.05	0.97	1.45	1.06	0.89	1.61	0.87	0.79	1.93	1.03	0.79	2.41	1.16	0.97	4.21	3.00	1.26	2.00	1.99	0.81	1.25	1.22	1.07	tubulin, beta 2
0.42	0.25	1.24	1.10	1.10	1.28	1.28	0.91	1.31	0.79	0.39	1.03	0.44	0.61	1.07	0.16	0.44	0.95	1.10	1.32	1.04	1.00	0.84	1.56	epidermal growth factor receptor
1.52	1.20	1.62	1.43	1.60	3																			

表 9 GeneChip 解析より選択した遺伝子(ver.1)

1 acetyl-Coenzyme A carboxylase beta	23 heat shock protein 1
2 B-cell translocation gene 2, anti-proliferative	24 insulin-like growth factor binding protein 1
3 Bcl2-associated X protein	25 Jun oncogene
4 CCR4 carbon catabolite repression 4-like (S. cerevisiae)	26 low density lipoprotein receptor-related protein 1
5 cerebellum postnatal development associated protein 2	27 lymphocyte antigen 6 complex, locus A
6 cyclin G1	28 Mus musculus, clone IMAGE:3493956, mRNA, partial c
7 cyclin-dependent kinase inhibitor 1A (P21)	29 phosphomannomutase 1
8 cytochrome P450, 1a1, aromatic compound inducible	30 pleckstrin homology-like domain, family A, member 3
9 cytochrome P450, 1a2, aromatic compound inducible	31 protein phosphatase 1, regulatory (inhibitor) subunit 3
10 cytochrome P450, 2b10, phenobarbital inducible, type b	32 protein tyrosine phosphatase, receptor type, D
11 cytochrome P450, 2b20	33 RIKEN cDNA 1300007C21 gene
12 cytochrome P450, 4a10	34 RIKEN cDNA 1700037B15 gene
13 cytosolic acyl-CoA thioesterase 1	35 RIKEN cDNA 1810073K19 gene
14 Down syndrome critical region homolog 1 (human)	36 RIKEN cDNA 2700083B06 gene
15 epidermal growth factor receptor	37 RIKEN cDNA 4930542G03 gene
16 epoxide hydrolase 1, microsomal	38 RIKEN cDNA 4933425F03 gene
17 fatty acid binding protein 5, epidermal	39 RIKEN cDNA B130055L10 gene
18 glutamate-ammonia ligase (glutamine synthase)	40 serum/glucocorticoid regulated kinase
19 glutathione S-transferase, mu 3	41 stress induced protein
20 growth arrest and DNA-damage-inducible 45 beta	42 transformed mouse 3T3 cell double minute 2
21 growth arrest and DNA-damage-inducible 45 gamma	43 tubulin, beta 2
22 growth differentiation factor 15	

表 10 3種の非遺伝子傷害性物質を加えた再解析の結果共通して変化の見たれた遺伝子

Genotoxic															Non-genotoxic																																																																																				
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

表 11 重み付け採点により高スコアを示した遺伝子

	Score	Gene	Description	
UP	32	BC005512	similar to BC005512 protein /// hypothetical LOC432650	
	32	Ly6a	lymphocyte antigen 6 complex, locus A	
	29	Ppp1r3c	protein phosphatase 1, regulatory (inhibitor) subunit 3C	
	28	Phlda3	pleckstrin homology-like domain, family A, member 3	
	27	Gsta2	glutathione S-transferase, alpha 2 (Yc2)	
	27	Cdkn1a	cyclin-dependent kinase inhibitor 1A (P21)	
	27	Ccng	cyclin G1	
	27	Ccng	cyclin G1	
	26	Ccng	cyclin G1	
	26	Rbx1	ring-box 1	
	25	Sds	serine dehydratase	
	25	Ppp1r3c	protein phosphatase 1, regulatory (inhibitor) subunit 3C	
	25	Fkbp5	FK506 binding protein 5	
	25	A1467657	zinc finger and BTB domain containing 16	
	25	BM122014	Mus musculus, clone IMAGE:5050186, mRNA, partial cds	
	25	A1467657	zinc finger and BTB domain containing 16	
	24	Stinp	transformation related protein 53 inducible nuclear protein 1	
	24	Eva	epithelial V-like antigen 1	
	24	BB794742	---	
	24	Mbl2	mannose binding lectin (C)	
	24	AW763751	similar to BC005512 protein /// hypothetical LOC432650	
	24	Siat9	ST3 beta-galactoside alpha-2,3-sialyltransferase 5	
	23	2700083B06Rik	interferon stimulated exonuclease gene 20-like 1	
	23	1700037B15Rik	DNA-damage-inducible transcript 4-like	
	23	Sultn	sulfotransferase family 1D, member 1	
	23	2700083B06Rik	interferon stimulated exonuclease gene 20-like 1	
	22	Lpin1	lipin 1	
	22	Sphk2	D site albumin promoter binding protein	
	22	Bhlhb2	basic helix-loop-helix domain containing, class B2	
	22	MGC28623	RIKEN cDNA 4930542G03 gene	
	22	Hbb-bh1	metastasis suppressor 1	
	22	Herpud1	homocysteine-inducible, ubiquitin-like domain member 1	
	21	Bax	Bcl2-associated X protein	
	21	Serpina3n	serine (or cysteine) proteinase inhibitor, clade A, member 3N	
	21	Ephx1	epoxide hydrolase 1, microsomal	
	21	3300001H21 Rik	RIKEN cDNA 3300001H21 gene /// UbiE-YGHL1 fusion protein	
	21	Nfe2l2	nuclear factor, erythroid derived 2, like 2	
	21	Mknk2	MAP kinase-interacting serine/threonine kinase 2	
	21	1300007C21Rik	similar to Retrovirus-related POL polyprotein (Endonuclease)	
	21	Rps8	ribosomal protein S8	
	21	CD151	CD151 antigen	
	20	Lpin1	lipin 1	
	20	Lcn2	lipocalin 2	
	20	A1467657	---	
	20	5830413E08Rik	DNA-damage-inducible transcript 4	
	20	Ppp2r1a	protein phosphatase 2 (formerly 2A), regulatory subunit A (PR 65)	
	Down	31	Igfbp1	insulin-like growth factor binding protein 1
		30	Htr1b	5-hydroxytryptamine (serotonin) receptor 1B
		30	Nono	non-POU-domain-containing, octamer binding protein
		27	Gadd45g	growth arrest and DNA-damage-inducible 45 gamma
		26	Nrp	neuropilin 1
		25	Lpl	lipoprotein lipase
		24	Nrp	neuropilin 1
		24	Phlda1	pleckstrin homology-like domain, family A, member 1
		24	Fabp5	fatty acid binding protein 5, epidermal
		24	F5	coagulation factor V
		23	Dio1	deiodinase, iodothyronine, type I
		23	Egfr	epidermal growth factor receptor
		23	2810439F02Rik	RIKEN cDNA 2810439F02 gene
		22	Cyp4a14	cytochrome P450, family 4, subfamily a, polypeptide 14
21		Acacb	acetyl-Coenzyme A carboxylase beta	
21		Tgfb14	transforming growth factor beta 1 induced transcript 4	
21		Hamp	hepcidin antimicrobial peptide 2	
21		Rps24	ribosomal protein S24	
21		2210408B16Rik	acetoacetyl-CoA synthetase	
20		Hhex	hematopoietically expressed homeobox	
20	Srebff1	sterol regulatory element binding factor 1		
20	MGC36662	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1		
20	Cp	ceruloplasmin		
20	Glns	glutamate-ammonia ligase (glutamine synthase)		

図1 発現強度のスクタープロットと発現強度に応じた段階的遺伝子選択法

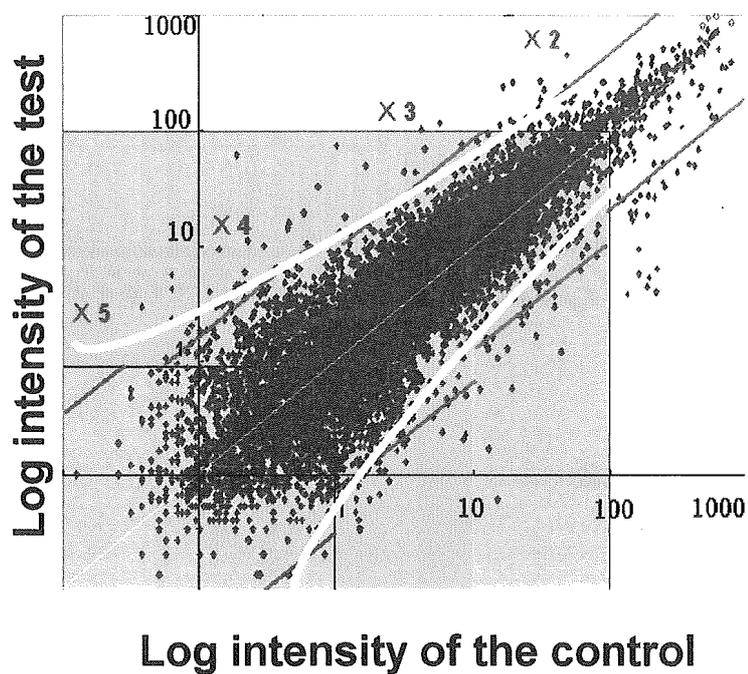


図2 全遺伝子および変化の見られた遺伝子を用いたクラスタリング解析

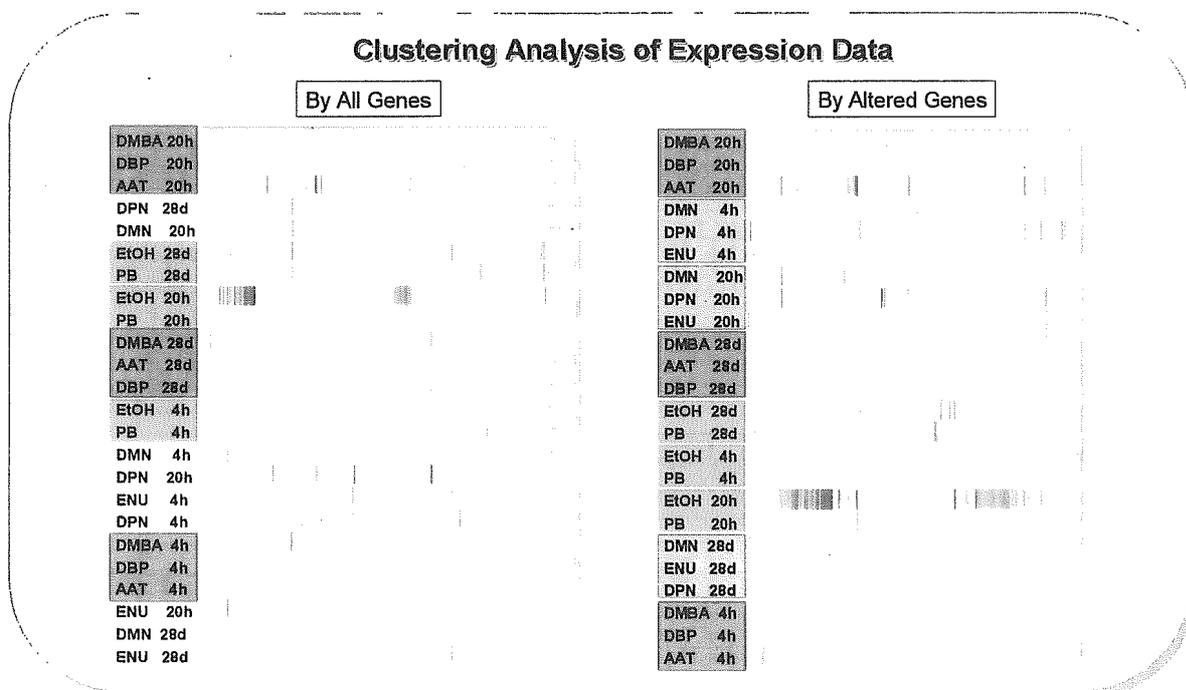


図3 GAPDH 遺伝子の GeneChip 解析結果

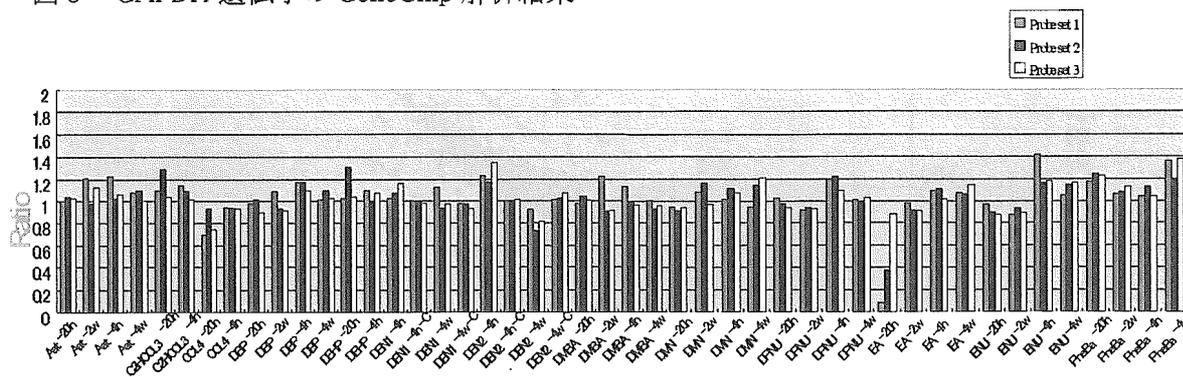


図4 RT-PCR と GeneChip データの比較

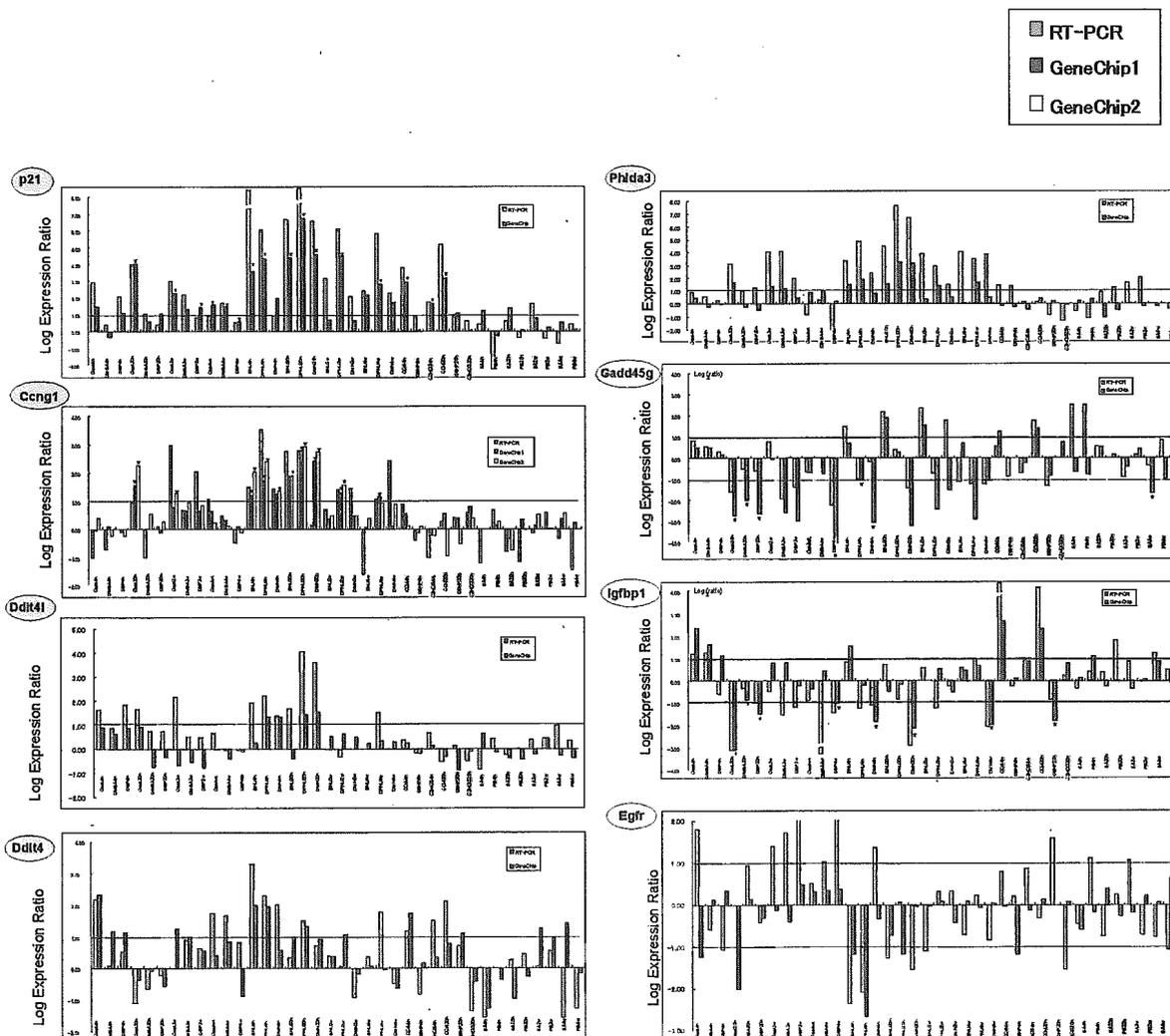


図5 RT-PCR 法による DEN および ENU の用量反応性の解析

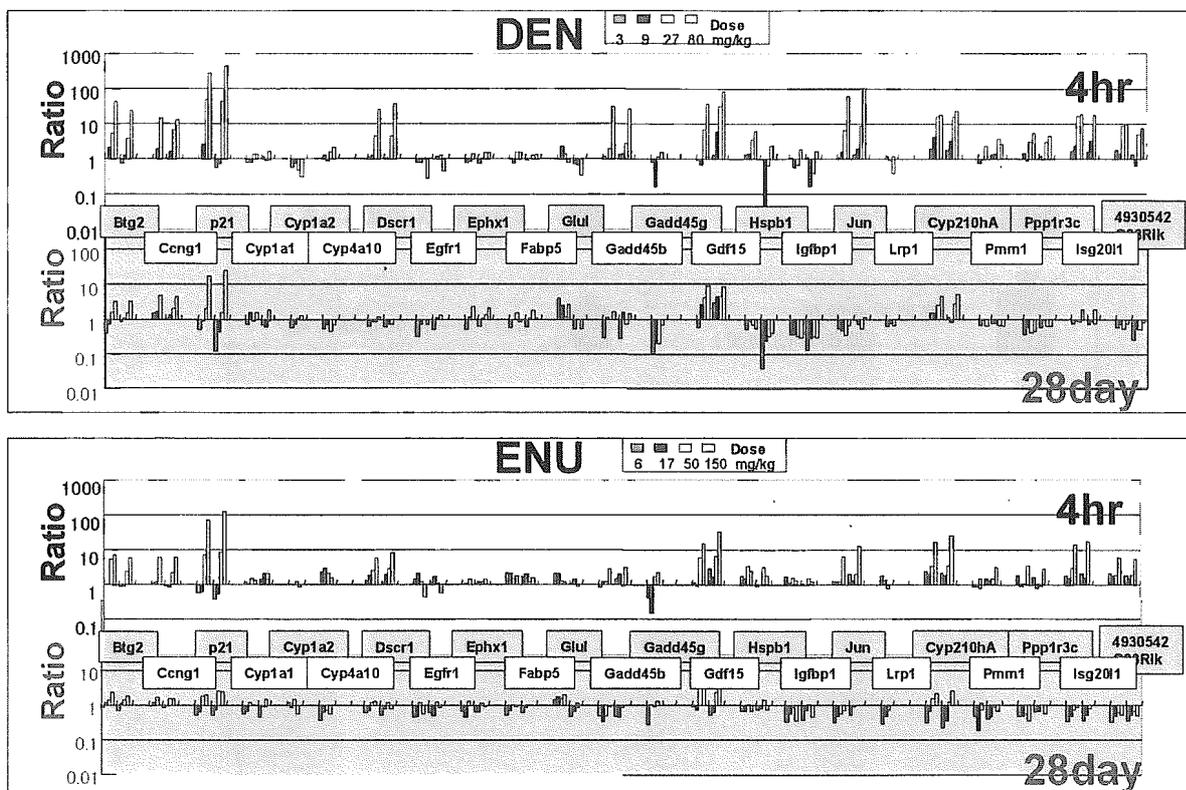


図7 再解析後に変化の見られた遺伝子数

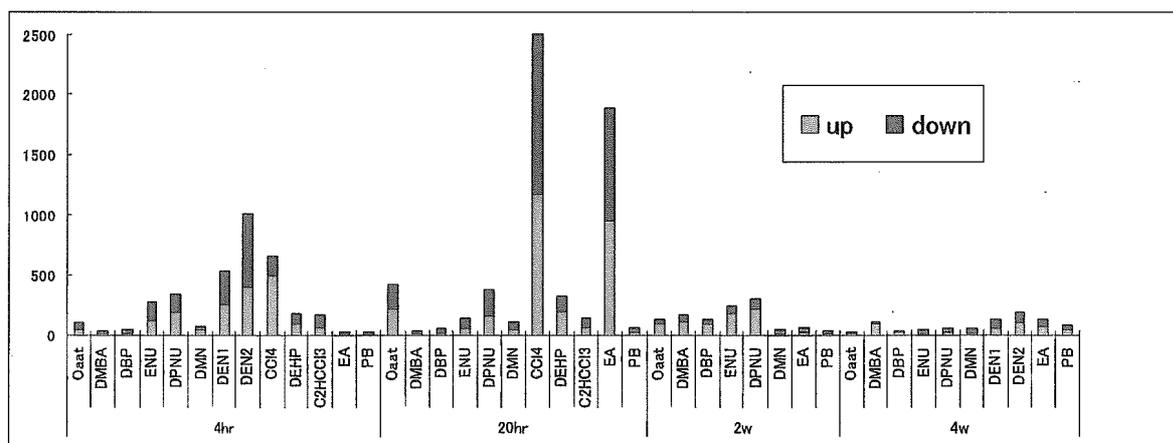


図8 候補遺伝子選択における評価項目と重み付け

