Identification of Differentially Expressed Genes Between Preadipocytes and Adipocytes Using Affymetrix Bovine Genome Array

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ABSTRACT

Adipocytes are differentiated from preadipocytes and have large capacity for storing fats inside cells. In cattle, intramuscular fat (IMF) content is one of the major determinants for meat quality and also highly affects market prices, especially in Japan and Korea. In order to profiling differentially expressed genes between intramuscular fibroblast-like cells (preadipocytes) and their differentiated adipocytes, we have established intramuscular fibroblast-like cells from *M. longissimus thoracis* in Korean cattle (Hanwoo). The differentially expressed genes were selected by comparing these two types of cells ug thecommercially available 23kese two types of cells ug theco. The results indan ced that 206 arecomelements were differentially expressed. Of these, 67 and 94 ks wn genes were up and d wn regulaced, respectively, in adipocytes ug ng both 2-fold difference and Welch's t-test as the cut-off points. The differentially expressed genes identified in this study can be used as good markers for improving meat quality traits with further verification of their biological functions, especially IMF contents in cattle.

(Key words : Adipocytes, Bovine genome array, Differentially expressed genes, Intramuscular fat, Korean cattle)

INTRODUCTION

Adipogenesis is the differentiation processes from the primitive mesoderm stem cells to preadipocytes and ultimately become adipocytes. This process occurs at both prenatal and postnatal states. The adipose tissues are very important because they can store fats as energy sources. Recently, researches on these cells have been growing because the basic mechanisms of the adipose tissue development can give the solutions for obesity, type II diabetes, hypertension and coronary heart diseases (Zalesin et al., 2008). The basis of these researches was started by making immortal preadipocyte cell lines (Green and Kehinde, 1975). Later on, molecular regulation of adipocyte differentiation has been investigated using immortalized cell lines such as 3T3-L1, Ob1771, and 3T3-F442A. The results were confirmed by in vivo studies including knock out mice and/or transgenic mice (Rosen and Spiegelman, 2000). These results indicated that adipocyte differentiation was controlled by a number of adipogenic transcription factors, including CCAAT-enhancer binding protein (C/EBP), peroxisome proliferator activated receptor- γ (PPARr) families, and adipocyte determination and differentiation dependent factor 1 (ADD1) (Rosen and Spiegelman, 2000; Rangwala and Lazar, 2000). Also, adipocyte differentiation was regulated by differentiation-inducing agents including insulin, dexamethasone and methyl-isobutylxanthine (MIX; a phosphodiesterase inhibitor) (Girard et al., 1994; Wu et al., 1999; Reusch et al., 2000).

In case of cattle, many researches already have been carried out for identifying underline mechanisms for intramuscular fat deposition. The fat deposition inside muscles is called marbling and this trait is one of the important factors for determining meat quality in cattle (Wood et al., 1999). However, meat quality is very complex trait because it includes all meat related factors containing tenderness, flavor, and juiciness. Aso et al. (1995) firstly established intramuscular preadipocyte (BIP) cell line in cattle and they suggested that adipose tissue metabolism in ruminants was different from that of non-ruminants. In addition, they found that extracellular matrix (ECM) of adipose tissue

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during adipogenesis was newly organized and alternations of this extracellular matrix were associated with ECM proteins (collagen, laminin and fibronectin) as well as caveolin-1 and cytoskeletal proteins (actin and vimentin), which play important roles in intracellular accumulation of lipid droplets (Aso et al., 1995; Nakajima et al., 1998; Inoue-Murayama et al., 2000; Nakajima et al., 2002; Tahara et al., 2004; Takenouchi et al., 2004). However, these results have limitations for only investigation of extracellular matrix. Recently, Taniguchi et al. (2007) profiled differentially expressed genes during early adipogenic differentiation of bovine perimuscular fat (PMF) preadipocytes.

In this study, we investigated differentially expressed genes between intramuscular fibroblast-like cells and their differentiated adipocytes using 23k bovine genome array (Affymetrix, USA) in order to identify important genes for adipogenesis and ultimately give the basic information for identification of genes for the IMF contents in cattle.

MATERIALS AND METHODS

1. Preparation and Differentiation of intramuscular fibroblast-like cells

The primary intramuscular fibroblast like cells were prepared and differentiated using the method described by Jeong et al. (2008). In order to confirm the cell differentiation, the cells were stained with Oil Red O. The triglycerides (TG) in the differentiated cells were quantified using Triglyceride G Test Kit (Wako, USA). All experiments were performed in triplicate.

2. Total RNA preparation

In order to isolate total RNA from intramuscular fibroblast-like cells and their differentiated adipoctyes, 0.8 ml Tri Reagent (Molecular Research Center, USA) was added to the cultured cells in 60 mm dish and the cells were lysed by repetitive pipettings. The homogenates were stored at room temperature for 5 min for the complete dissociation of nucleoprotein complexes. Then it was vigorously mixed with 0.2 volume of chloroform and centrifuged at 12,000 rpm for 15 min at 4°C. The aqueous phase was transferred to a fresh tube and 0.5 volume of isopropanol was added. Then, the samples were left at room temperature for 10 min, and centrifuged at 12,000 rpm for 8 min at 4°C. In order to obtain the RNA pellet, supernatant was removed and RNA pellet

was washed with 1 volume of 75% ethanol and briefly air-dried. Total RNA was subjected to RNA clean up by RNeasyTM kit (QIAGEN, Germany). Total RNA integrity was monitored by denaturing 1% agarose gel electrophoresis. RNA concentrations and purities were measured by spectrophotometer (Amersham Pharmacia Biotech, UK).

3. GeneChip array analysis and data analysis

Microarray analyses were performed in two replicates according to the Affymetrix GeneChip Expression Analysis Technical Manual (Affymetrix, USA). First strand cDNA was synthesized from reaction containing 10 µg total RNA, 50 µM T7-Oligomer, 1× first-strand reaction buffer, 100 mM DTT, 500 µM dNTP, and 200 U/µl Superscript II RTase (Gibco BRL, USA) at 42°C for 1 hour. To synthesis second strand of DNA, the first strand DNA was added in the solution containing 5× second-strand reaction buffer, 200 µM dNTP, 10 unit E. coli DNA ligase, 40 unit E. coli DNA polymerase I, and E. coli RNase H and reaction was carried out at 16°C for 2 hour. Double-stranded cDNA was purified using Sample Cleanup Module (Affymetrix, USA) and labeled Biotin by in vitro transcription using Enzo Bioarray (Affymetrix, USA). The cDNA was hybridized with the solution containing 50 pM Oligo B2 (3 nM), 0.1 mg/ml herring sperm DNA, 0.5 mg/ml acetylated BSA, 1× hybridization buffer, and 10% DMSO at 45°C for 16 hours. After hybridization, the arrays were washed in a GeneChip Fluidics station and stained with a streptavidin-phycoerythrin complex. The intensities of chip elements were determined with a GeneChip scanner. After scanning, data acquisition and image processing were carried out with the GeneChip Operating Software (GCOS) and normalization of the data was done with MA-plot. Finally, significant test was performed using Welch's t-test and Volcano Plot. In order to identify differentially expressed genes in duplicate experiments, multiple test correction was also performed. The classification of gene ontology was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID; http://david. abcc.ncifcrf.gov/).

4. Quantitative real-time PCR

Single-stranded cDNA was synthesized from $1 \mu g$ total RNA of intramuscular fibroblast-like cells and their differentiated adipoctyes. Initially, RNA was denatured at 70°C

for 10 min and reverse transcription was performed in reactions containing 5 mM MgCl₂, 10 mM Tris-HCl (pH 9.0), 50 mM KCl, 0.1% Triton[®] X-100, 1 mM each dNTP, 0.5 unit Recombinant RNasin[®] Ribonuclease Inhibitor, 15 unit AMV Reverse Transcriptase (Promega, USA) and 500 ng Oligo (dT)¹⁵ primer at 42°C for 1 hour.

Quantitative real-time PCR was performed using Rotor Gene 2000 PCR machine and analyzed using Rotor Gene 2000 program (Corbett Research, Australia) on five selected bovine genes showing differential expression in two samples examined: matrix metalloproteinase 1 (MMP1), caveolin 1 (CAV1), caveolin 2 (CAV2), transthyretin (TTR), dual specificity phosphatase 10 (DUSP10). Two expression control genes, namely, bovine β -actin and glyceraldehyde-3-phosphate dehydrogenase (GAPDH), were used for the RT-PCR reaction. The thermal profiles included 25 cycles of denaturation at 94 °C for 30 sec, annealing at 56 °C for 30 sec and extension at 72 °C for 3 min.

RESULTS AND DISCUSSION

1. Preparation and differentiation of intramuscular fibroblast-like cells

In order to profile differentially expressed genes between intramuscular fibroblast-like cells and their differentiated adipocytes, intramuscular fibroblast-like cells were prepared from sirloin tissues of 12-month-old Korean cattle (Hanwoo) and differentiated adipocytes were obtained by inducing for 18 days with differential medium contained insulin, dexamethasone, 1-methy-3-isobutylxanthine and acetic acid. In order to confirm the adipocytes differentiation, Oil red O staining and triglyceride assays were performed. As the results, differentiated adipocytes gave strong Oil red O positive and significantly increased the amount of triglycerides in induced cells for 18 days of differentiation (Jeong et al., 2008). Asakura et al. (2001) suggested that muscle satellite cells for postnatal growth and regeneration have multipotential stem cell activity. Therefore, these cells also have the ability for adipocyte formation. Recently, Kook et al. (2006) reported that bovine primary satellite cells in skeletal muscle can differentiate into adipocytes in adult cattle. Based on the evidence in the previous publications and the increase of triglycerides, we can conclude that the preadipocytes in the bovine skeletal muscle were successfully differentiated into adipocytes in this study.

2. Identification of differentially expressed genes

The differentially expressed genes between intramuscular fibroblast-like cells and their differentiated adipocytes were investigated using 23k Bovine Genome array (Affymetrix, USA). In order to identify differentially expressed genes between the two samples, both 2-fold expression differences and p-value 0.05 in Welch's t-test were applied. As the results, 2,747 chip elements were identified as significantly differentially expressed genes. Of these, 1,484 elements were up-regulated and 1,263 were down-regulated in the adipogenesis. However, large number of chip elements are currently unknown ESTs (Expressed Sequence Tags) and hard to estimate their functions, even though the bovine genome sequence has been released. Therefore excluding the functionally unknown transcripts, we found 927 elements were up-regulated and 1.028 were down-regulated in the development of adipocytes based on the BLAST search results. Also, we found that only 652 elements were significantly differentially expressed genes based on Welch's t-test (P<0.05). Of these, 476 chip elements are known genes. Based on the two statistical methods, 206 chip elements were identified as differentially expressed, which includes 67 up-regulated and 94 down-regulated chip elements, respectively, in differentiated adipocytes (Table 1 and 2). In order to find more statistically differentially expressed genes, multiple test correction was also performed. However, we could not identify any significant genes using the multiple test correction, indicating high variability of the duplicate chip experiments. This also indicates the differentially expressed genes in this study need to be confirmed using other methods including quantitative real time PCR.

The 161 differentially expressed chip elements were subjected to three main functional classifications, namely, biological process, molecular function and cellular component, using the web-based DAVID program (Table 3). The results indicated that 38 up-regulated and 39 down-regulated genes were the known genes for their functions. The up-regulated chip elements belong to ion binding in molecular function (26.3%), proteinaceous extracellular matrix (7.9%) and organelle membrane in cellular function (10.5%). The down-regulated chip elements were related with extracellular space in cell component (7.7%), protein binding in molecular function (33.3%) and nitrogen compound metabolic process in biological process (7.7%). Especially, 23 differentially expressed genes (29.9%) were related with ion and protein binding. Therefore, these results suggested that the cell properties

UniGene ID	Gene name	Symbol	Fold change
Bt.19813	Similar to delta/notch-like EGF-related receptor	LOC540552	654.4
Bt.22693	Transcribed locus	—	138
Bt.5401	Transglutaminase 2	TGM2	92.1
Bt.594	Uterine milk protein precursor	LOC286871	79.5
Bt.96035	Fibroblast growth factor receptor 2	FGFR2	74.8
Bt.1171	Smoothelin-like2	SMTNL2	60.5
Bt.24823	Transcribed locus	—	58.1
Bt.8088	Fibroblast growth factor receptor 2	FGFR2	53.6
Bt.16059	Distal-less homeobox 5	DLX5	48.3
Bt.64947	phosphoglucomutase 5	PGM5	42
Bt.25236	Matrix-remodelling associated 5	MXRA5	41.9
Bt.91101	Metallothionein 1E	MT1E	39.1
Bt.29868	Cytochrome c oxidase subunit VIb testes-specific isoform	COX6B2	34.2
Bt.11436	Transcribed locus	—	33.5
Bt.13670	Alkaline phosphatase, liver/bone/kidney	ALPL	28.1
Bt.15658	Transcribed locus	—	27.3
Bt.3595	Matrix Gla protein	MGP	23.3
Bt.23505	Pyruvate dehydrogenase kinase, isozyme 4	PDK4	22.2
Bt.5530	Dehydrogenase/reductase (SDR family) member 3	DHRS3	17.5
Bt.74139	T-cell lymphoma invasion and metastasis 1	TIAM1	17.1
Bt.36109	ATPase, aminophospholipid transporter (APLT), Class I, type 8A, member 1	ATP8A1	15
Bt.13108	ADAM metallopeptidase with thrombospondin type 1 motif, 5	ADAMTS5	13.2
Bt.87249	S100 calcium binding protein A9	S100A9	11.3
Bt.24413	Similar to transmembrane and tetratricopeptide repeat containing 2	LOC781126	11
Bt.53247	Sushi domain containing 2	SUSD2	10.3
Bt.46188	Similar to cAMP-dependent protein kinase inhibitor beta	LOC781283	9.8
Bt.3946	Similar to Coiled-coil domain-containing protein 3	LOC509875	9.2
Bt.96928	Transcribed locus	—	8.62
Bt.92589	Roundabout, axon guidance receptor, homolog 1 (Drosophila)	ROBO1	8.48
Bt.8644	Potassium voltage-gated channel, Shal-related subfamily, member 1	KCND1	8.35
Bt.13057	Calcium channel, voltage-dependent, T type, alpha 1H subunit	CACNA1H	6.45
Bt.16951	Frizzled homolog 2 (Drosophila)	FZD2	6.33
Bt.12314	6-phosphofructo-2-kinase/fructose-2, 6-biphosphatase 3	PFKFB3	6.2
Bt.14241	Transcribed locus	_	6.12
Bt.21766	Myeloid leukemia factor 1	MLF1	6.12
Bt.92908	Transcribed locus	—	6.02
Bt.11489	Similar to histone cluster 1, H3f	LOC523214	5.77
Bt.16951	Matrix metalloproteinase 1	MMP1	5.72
Bt.27611	Similar to Zinc finger protein ZIC 2	LOC514433	5.71
Bt.96693	Transcribed locus	—	5.69
Bt.42710	Rho guanine nucleotide exchange factor (GEF) 11	ARHGEF11	5.47
Bt.64960	Teashirt zinc finger homeobox 1	TSHZ1	5.4
Bt.3138	Transcribed locus	_	5.33

Table 1. List of up-regulated genes in differentiated adipocytes

Table	1. (Conti	nued
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UniGene ID	Gene name	Symbol	Fold change
Bt.11850	Phosphatidic acid phosphatase type 2A	PPAP2A	5.32
Bt.5523	Golgi membrane protein 1	GOLM1	4.94
Bt.4067	Myristoylated alanine-rich protein kinase C substrate	MARCKS	4.41
Bt.19745	Elongation factor, RNA polymerase II, 2	ELL2	4.41
Bt.89975	Transcribed locus	—	4.29
Bt.51574	Caveolin 1, caveolae protein, 22kDa	CAV1	4.18
Bt.16628	Transcribed locus	—	4.03
Bt.11856	Transcribed locus	—	3.63
Bt.23265	Sprouty-related, EVH1 domain containing 1	SPRED1	3.56
Bt.26635	Frizzled homolog 1 (Drosophila)	FZD1	3.54
Bt.13989	Caveolin 2	CAV2	3.51
Bt.43663	Similar to Transcription factor COE4 (Early B-cell factor 4)	LOC506470	3.48
Bt.96693	Transcribed locus	—	3.45
Bt.16738	Iroquois homeobox 3	IRX	3.4
Bt.16087	Nidogen 2 (osteonidogen)	NID2	3.4
Bt.26682	Transcribed locus	_	3.32
Bt.5292	Period homolog 1 (Drosophila)	PER1	3.24
Bt.16125	Ring finger protein, transmembrane 1	RNFT1	3.23
Bt.14853	RAB3A interacting protein (rabin3)	RAB3IP	3.21
Bt.19081	Laminin, gamma 1 (formerly LAMB2)	LAMC1	3.09
Bt.100290	Transcribed locus	_	3.01
Bt.10146	Similar to E3 ubiquitin-protein ligase MARCH5	LOC788125	3
Bt.18938	Similar to BCL-6 interacting corepressor	LOC541088	2.87
Bt.10882	Tissue inhibitor of metalloproteinase 3	TIMP3	2.84
Bt.40036	Transmembrane protein 135	TMEM135	2.75
Bt.21959	transmembrane protein 64	TMEM64	2.64
Bt.96928	Transcribed locus	_	2.48
Bt.25998	Similar to Glioma tumor suppressor candidate region gene 1 protein	LOC531868	2.48
Bt.12578	Origin recognition complex, subunit 5-like (yeast)	ORC5L	2.46
Bt.19382	Transcribed locus	_	2.43
Bt.29527	STARD3 N-terminal like	STARD3NL	2.43
Bt.52756	Prostaglandin F2 receptor negative regulator	PTGFRN	2.38
Bt.18938	Similar to BCL-6 interacting corepressor	LOC541088	2.38
Bt.10147	Pyruvate carboxylase	PC	2.38
Bt.24324	Amyloid beta (A4) precursor protein-binding, family B, member 2 (Fe65-like)	APBB2	2.29
Bt.24150	Hepatitis A virus cellular receptor 1 N-terminal domain containing protein	MGC137099	2.28
Bt.20496	Oxysterol binding protein-like 2	OSBPL2	2.19
Bt.92182	Transcribed locus	_	2.17
Bt.55266	Similar to procollagen alpha 2(V)	LOC782818	2.15
Bt.26139	Transcribed locus	_	2.14
Bt.6993	Non-metastatic cells 7, protein expressed in (nucleoside-diphosphate kinase)	NME7	2.12
Bt.64611	Hypothetical LOC513716	MGC143285	2.1
Bt.21079	Similar to solute carrier family 35, member F2	LOC533008	2.1
Bt.11304	Paroxysmal nonkinesigenic dyskinesia	PNKD	2.04

Table	2.	List	of	down-regulated	genes	in	differentiated	adipocytes

UniGene ID	Gene name	Symbol	Fold change
Bt.69254	Transcribed locus	_	0.01
Bt.57510	Adhesion molecule with Ig-like domain 2	AMIGO2	0.01
Bt.207	Transthyretin	TTR	0.01
Bt.62498	Similar to subtilisin-like proprotein convertase PACE4 precursor, splice form A	LOC524684	0.02
Bt.26772	Calcium homeostasis modulator 2	CALHM2	0.02
Bt.34795	Fas apoptotic inhibitory molecule 2	FAIM2	0.04
Bt.42349	Transcribed locus	_	0.05
Bt.89962	Ankyrin repeat domain 29	ANKRD29	0.05
Bt.33139	Selenium binding protein 1	SELENBP1	0.05
Bt.44938	La ribonucleoprotein domain family, member 6	LARP6	0.06
Bt.64516	Renin binding protein	RENBP	0.07
Bt.47512	Platelet-derived growth factor receptor-like	PDGFRL	0.07
Bt.28164	Transcribed locus	_	0.07
Bt.15886	acyl-CoA synthetase long-chain family member 5	ACSL5	0.07
Bt.3686	Interleukin 6 (interferon, beta 2)	IL6	0.07
Bt.11576	Spermidine/spermine N1-acetyltransferase family member 2	SAT2	0.08
Bt.17884	Pirin (iron-binding nuclear protein)	PIR	0.10
Bt.21071	Transcribed locus	_	0.11
Bt.29580	Transcribed locus	_	0.11
Bt.2070	Dual specificity phosphatase 10	DUSP10	0.11
Bt.24813	Receptor transporter protein 4	RTP4	0.11
Bt.7724	Septin 11	SEP11	0.12
Bt.28110	Transcribed locus	_	0.12
Bt.4040	Platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit (29kD)	PAFAH1B3	0.13
Bt.57742	Transmembrane protein 140	TMEM140	0.13
Bt.59240	SP140 nuclear body protein	SP140	0.15
Bt.16118	Similar to C-type lectin domain family 2, member h	LOC504309	0.15
Bt.2408	Chemokine (C-C motif) ligand 2	CCL2	0.15
Bt.49579	Solute carrier family 29 (nucleoside transporters), member 1	SLC29A1	0.17
Bt.28855	Transcribed locus	_	0.17
Bt.20267	Glutamate-cysteine ligase, modifier subunit	GCLM	0.18
Bt.14163	Chloride intracellular channel 2	CLIC2	0.19
Bt.16053	Similar to plexin D1	LOC781625	0.20
Bt.4204	Alpha-N-acetylglucosaminidase	NAGLU	0.20
Bt.57860	Membrane bound O-acyltransferase domain containing 1	MBOAT1	0.21
Bt.49270	Receptor accessory protein 4	REEP4	0.21
Bt.64813	Rho GTPase activating protein 22	ARHGAP22	0.22
Bt.7142	Similar to Absent in melanoma 1 protein	LOC526200	0.22
Bt.46096	Acyl-CoA synthetase long-chain family member 1	ACSL1	0.23
Bt.53697	Proteasome subunit, beta type 8	PSMB8	0.23
Bt.63482	Mesenchyme homeobox 2	MEOX2	0.23
Bt.59240	SP140 nuclear body protein	SP140	0.24
Bt.20910	Microspherule protein 1	MCRS1	0.24
Bt.3913	Vascular endothelial growth factor C	VEGFC	0.24
Bt 101334	choline phosphotransferase 1	CHPT1	0.24
Bt.996	Transcribed locus	_	0.24
Bt.32841	HECT domain containing 3	HECTD3	0.25
Bt.52452	Proteasome (prosome, macropain) activator subunit 1 (PA28 alpha)	PSME1	0.25
Bt.9728	ATPase Na^+/K^+ transporting beta 3 polypeptide	ATP1B3	0.26
Bt.24736	Similar to sperm associated antigen 1	LOC530104	0.27
Bt.26919	Netrin 4	NTN4	0.27
Bt 3726	Development and differentiation enhancing factor 2	DDEF?	0.27
Bt.54952	Elongation of very long chain fatty acids (FEN1/Elo2 SUR4/Elo3 veast)-like 4	ELOVI 4	0.27
Bt.22036	Transcribed locus	_	0.28

Table	2.	Contir	nued
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B1.53493 Gelsolin (amyloidosis, Finnish type) GN 0.29 B1.4770 Glycogenin 2 OPTN 0.29 B1.2833 Endoplasmic reticulum aminopeptidase 1 ERAPI 0.3 B1.2833 Endoplasmic reticulum aminopeptidase 1 ERAPI 0.3 B1.2655 GTF21 repet domin containing 2 GTF21RD2 0.31 B1.26547 Transcribed locus - 0.31 B1.21731 Drebrin 1 DBN1 0.32 B1.20432 Serpin peptidase inhibitor, clade B (ovalburnin), member 8 SERPINB8 0.32 B1.20433 Extodermal-neural cortex (with BTB-like domain) ENC1 0.33 B1.6339 Interleakin TD L17D 0.35 B1.0004 Branched chain aminotransferase 2, mitochondrial PLCA12 0.36 B1.1418 RYK receptor-like tyrosine kinase RXM 0.36 B1.35943 Chromsome 1 opan reading firms 21 ortholog H16C10R721 0.38 B1.8587 Transmerberd BAx inhibitor rooff containing 1 TNBIM1 0.37 B1.45843 Transcribed Iocus	UniGene ID	Gene name	Symbol	Fold change
Bt.49466 Optimutin OPTN 0.29 Bt.17770 GYo2ge in 3 GYG2 0.3 Bt.28555 GTF21 regred nomin containing 2 ERAP1 0.3 Bt.26555 GTF21 regred nomin containing 2 - 0.31 Bt.64755 Transcribed locus - 0.31 Bt.21731 Drebrin 1 0.32 DRNI 0.32 Bt.20432 Serpin peridase inhibitor, clade B (ovalburnin), member 8 SERPINB8 0.32 Bt.30530 Interleukin 17D 0.33 Bt.63539 Interleukin 17D 0.35 Bt.9366 Inser-clated tyrosine kinase 3 ligand FL13L 0.36 0.37 Bt.63052 RYK receptor-like tyrosine kinase 2, mitchondrial RCA12 0.36 Bt.9368 Transmenbrane BAX inhibitor motif containing 1 TMBHM1 0.37 Bt.63692 RNA binding motif protein 19 REM1418 RCM16 0.38 Bt.76883 Transcribed locus - 0.38 Bt.76883 Transcribed locus - 0.38 Bt.268564 Transcribed locus <td>Bt.53493</td> <td>Gelsolin (amyloidosis, Finnish type)</td> <td>GSN</td> <td>0.29</td>	Bt.53493	Gelsolin (amyloidosis, Finnish type)	GSN	0.29
Bt 1770Giveogenin 2GYG20.3BL28338Endoplasmic reticulum aninopeptidase 1ERAP10.3Bt26255GTF21 repeat domain containing 2	Bt.49466	Optineurin	OPTN	0.29
B122838 Endoplasmic reticulum aminopsptidase 1 ERAPI 0.3 B122657 GTT21 repeat domain containing 2 0.31 B1261731 Derbrin 1 DBN1 0.32 B121731 Derbrin 1 DBN1 0.32 B1201731 Derbrin 1 DBN1 0.32 B1201731 Cytochrome bit reductase 3 SERPINB8 0.33 B14373 Cytochrome bit reductase 3 CYTBS8 0.34 B146303 Interleakun 17D 0.35 B1	Bt.17770	Glycogenin 2	GYG2	0.3
Bt.26475GT121 repeat domain containing 2GT121RU20.31Bt.56475Transcribed locus-0.31Bt.20472Prebrin 1DRN10.32Bt.20432Serpin peptidase inhibitor, clade B (ovalburnin), member 8SERPINB80.32Bt.20432Ectodarmal-neural cortex (with BTB-like domain)ENCL0.33Bt.4733Cytochrome b5 reductase 3CYBSR30.34Bt.66339Interleukin 17DLL17D0.35Bt.9064Branched chain aminotransferase 2, mitochondrialBCA120.36Bt.1118RYK receptor-like trosine kinase 3Branched chain aminotransferase 2, mitochondrialBCA120.36Bt.11418RYK receptor-like trosine kinase 3RNA binding motif protein 19RBM190.37Bt.63579RNA binding motif protein 19RBM190.37Bt.63587TRNA methyltransferase 6 homolog (S. cerevisiae)TRMT60.38Bt.7088Transcribed locus-0.38Bt.7088Transcribed locus-0.39Bt.7088Transcribed locus-0.39Bt.64949Transcribed locus-0.39Bt.28056Myotubularin related protein 2MTME20.39Bt.28075Myotubularin related protein 2MTME20.39Bt.24728Gladcosidase, beta 1-likeGBB110.39Bt.24708Transcribed locus-0.39Bt.24709Pioly(ADP-ribose) polymerase family, member 8PARP80.39Bt.24728Gladcosidase, beta 1-like<	Bt.28338	Endoplasmic reticulum aminopeptidase 1	ERAP1	0.3
Bt.56475 Transcribed locus - 0.31 Bt.21731 Derbrin 1 DBN1 0.32 Bt.3943 Serpin paptidase inhibitor, clade B (ovallumin), member 8 SERPINB8 0.32 Bt.3943 Ectodermal-normal cortex (with BT-like domain) ENCI 0.33 Bt.4873 Cytochrome b5 reductase 3 CYH5R3 0.34 Bt.6303 Interleaktin 17D 0.35 Bt.4373 Cytochrome kinase 3 ligand HL17D 0.35 Bt.9306 fins-related tyrosine kinase 3 ligand HL17D 0.35 Bt.537 RNA binding motif protein 19 RBM19 0.37 Bt.63052 RNA binding motif protein 19 RBM110 0.37 Bt.63857 TRNA nuchyltransferase 6 homolog (S. cerevisiae) TRNT6 0.38 Bt.7688 Transcribed locus - 0.39 Bt.84243 0.594 3.39 Bt.01068 Oxysterol binding protein-like (Lorsophila) ASH1L 0.39 Bt.64249 Transcribed locus - 0.39 Bt.42428 Cranscribed locus - 0.39 Bt.64449 Transcribed loc	Bt.22655	GTF2I repeat domain containing 2	GTF2IRD2	0.31
Bt21731 Drebrin 1 DRNI 0.32 Bt20423 Serpin peptidase inhibitor, clade B (ovalhumin), member 8 SERPINB8 0.33 Bt373 Cytochrome b5 roductise 3 CYB5R3 0.34 Bt4673 Cytochrome b5 roductise 3 CYB5R3 0.34 Bt4673 Cytochrome b5 roductise 3 CYB5R3 0.34 Bt4673 Dytosine kinase 3 ligand FL17D 0.35 Bt3789 Aconitase 1, soluble RX 0.36 Bt11418 RYK receptor-like tytosine kinase Branket chain aminotransferase 2, mitochondrial BCAT2 0.36 Bt3789 Aconitase 1, soluble ACO1 0.37 Bt35378 Aconitase 1, soluble ACO1 0.37 Bt56387 Transmerbeane BAX inhibitor motif containing 1 TMBIM1 0.37 Bt3538 FRNA methyltransferase 6 homolog (S. crevisiae) - 0.38 Bt76883 Transcribed locus - 0.38 Bt 70585 Transcribed locus - 0.39 Bt164949 - 0.39 Bt 80566 Oxystotiolinding protein-like 1A OSBP1.1	Bt.56475	Transcribed locus	—	0.31
B1.20432 Serpin peptidase inhibitor, clade B (ovalbumin), member 8 SFRPINB8 0.32 B1.53943 Extodermal-neural cortex (with BTB-like domain) ENC1 0.33 B1.63039 Intercluckin 17D L17D 0.35 B1.5986 Intercluckin 17D B1.77D 0.36 B1.9980 Branched chain aminotransferase 2, mitochondrial BCA12 0.36 B1.01418 RYK receptor-like tyrosine kinase RYK 0.36 B1.63052 RNA binding motif protein 19 RBM19 0.37 B1.63052 RNA binding motif protein 19 RBM19 0.37 B1.6383 Transernhed locus - 0.38 B1.7883 Transcribed locus - 0.38 B1.7883 Transcribed locus - 0.38 B1.8857 TRNA methyltransferase 6 homolog (S. cerevisiae) TRM16 0.38 B1.7883 Transcribed locus - 0.39 B1.89864 Transcribed locus - 0.39 B1.49125 Transcribed locus - 0.39 B1.49264 Transcribed locus - 0.39 B1.49276 Myoubularin related protein 2 MTMR2 0.39 B1.492705 Myoubularin related protein 2 GIB11 0.39 </td <td>Bt.21731</td> <td>Drebrin 1</td> <td>DBN1</td> <td>0.32</td>	Bt.21731	Drebrin 1	DBN1	0.32
Bt.53943 Ectodermal-neural cortex (with BTB-like domain) ENCI 0.33 Bt.4873 Cytoshrome br seductase 3 IL17D 0.35 Bt.66339 Interleukin 17D 0.35 Bt.9004 Branched chain aminotransferase 2, micochondrial BCAT2 0.36 Bt.11418 RYK receptor-like tyrosine kinase BKW 0.36 Bt.11418 RYK receptor-like tyrosine kinase RWK 0.36 Bt.03578 Aconitase 1, soluble ACOI 0.37 Bt.6358 Chronesome 1 open reading frame 21 ortholog H16C10RF21 0.38 Bt.7688 Transcribed locus - 0.38 Bt.7688 Transcribed locus - 0.39 Bt.0768 Transcribed locus - 0.39 Bt.0768 Ash1 (absent, small, or homeotic)-like (Drosophila) ASHII. 0.39 Bt.26375 Mytotubalarin related protein 2 MIMR2 0.39 Bt.26376 Mytotubalarin related protein 2 MIMR2 0.39 Bt.27957 Mytotubalarin related protein 2 G1B11. 0.39 <t< td=""><td>Bt.20432</td><td>Serpin peptidase inhibitor, clade B (ovalbumin), member 8</td><td>SERPINB8</td><td>0.32</td></t<>	Bt.20432	Serpin peptidase inhibitor, clade B (ovalbumin), member 8	SERPINB8	0.32
Bt.4873Cytochrome b5 reductase 3CYtoSR30.34Bt.66339Intercukin TD0.15Bt.9986fms-related tyrosine kinase 3 ligandFLT3LG0.36Bt.9904Branched chain aminotransferase 2, mitochondrialBCAT20.36Bt.11418RYK receptor-like tyrosine kinaseRYK0.35Bt.3579Aconitase 1, solubleACO10.37Bt.63052RNA binding motif protein 19RBM190.37Bt.6358Transmembrane BAX inhibitor notif containing 1TIMBIM10.37Bt.63587TRNA methyltransferase 6 homolog (S. cerevisiae)TRMT60.38Bt.7058Transcribed locus-0.38Bt.7058Transcribed locus-0.39Bt.85853Asht1 (absent, small, or homeotic)-like (Drosophila)ASHL0.39Bt.80664Transcribed locus-0.39Bt.80585Collactoridizes, beat 1-likeGLBIL0.39Bt.42705Myotubularin related protein 2MTMR20.39Bt.42705Myotubularin related protein 2TRMN760.4Bt.44212Transcribed locus-0.391.44728Bt.24470Transcribed locus0.39Bt.44212Transcribed locus-0.391.44728Bt.44212Transcribed locus-0.39Bt.44212Transcribed locus-0.39Bt.44212Transcribed locus-0.40Bt.6484Transcribed locus-0.39Bt.44212 <t< td=""><td>Bt.53943</td><td>Ectodermal-neural cortex (with BTB-like domain)</td><td>ENC1</td><td>0.33</td></t<>	Bt.53943	Ectodermal-neural cortex (with BTB-like domain)	ENC1	0.33
Bit 66339 Interleakin 17D 0.35 Bit 5986 fms-related tryonine kinase 3 ligand ELT31G 0.36 Bit 9004 Branched chain aminotransferase 2, mitochondrial BCAT2 0.36 Bit 11418 RYK receptor-like tryosine kinase RYK 0.36 Bit 3538 Aconitase 1, soluble ACO1 0.37 Bit 3538 Transcriben ocus TMBIMI 0.37 Bit 3538 Transcribed locus - 0.38 Bit 76883 Transcribed locus - 0.39 Bit 80664 Transcribed locus - 0.39 Bit 6949 Transcribed locus - 0.39 Bit 28705 Myotubularin related protein-like 1A 0.39 39 Bit 24212 Transcribed locus - 0.39 Bit 24212 Transcribed locus - 0.39 <td>Bt.4873</td> <td>Cytochrome b5 reductase 3</td> <td>CYB5R3</td> <td>0.34</td>	Bt.4873	Cytochrome b5 reductase 3	CYB5R3	0.34
Bt.9866 fms-related tyrosine kinase 3 ligand BCA12 0.36 Bt.9004 Branched chain aminotransferase 2, mitochondrial BCA12 0.36 Bt.11418 RYK receptor-like tyrosine kinase RYK 0.36 Bt.63502 RNA binding motif protein 19 RBM19 0.37 Bt.6989 Transmembrane BAX inhibitor motif containing 1 HIGC10RF21 0.38 Bt.85857 TRNA methyltransferase 6 homolog (S. crevisiae) TRM16 0.38 Bt.70883 Transcribed locus - 0.38 Bt.8664 Transcribed locus - 0.39 Bt.80644 Transcribed locus - 0.39 Bt.01068 Oxysterol binding protein-like (Drosophila) ASH1L 0.39 Bt.28705 Myotubularin related protein 2 MTMR2 0.39 Bt.44212 Galactosidase, beta 1-like GLBL 0.39 Bt.44278 Galactosidase, beta 1-like GLBL 0.39 Bt.297957 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.39 Bt.204700 Transcribed locus - <td>Bt.66339</td> <td>Interleukin 17D</td> <td>IL17D</td> <td>0.35</td>	Bt.66339	Interleukin 17D	IL17D	0.35
BE9004 Branched chain aminotransferase 2, mitochondrial BCAT2 0.36 Bt.11418 RYK receptor-like tyrosine kinase ACO1 0.37 Bt.63578 Aconitase 1, soluble ACO1 0.37 Bt.63582 RNA binding motif protein 19 TMBIM1 0.37 Bt.65857 Transnerbare BAX inhibitor motif containing 1 TMBIM1 0.37 Bt.15378 Chromesome 1 open reading frame 21 ortholog H16C10RF21 0.38 Bt.75883 Transcribed locus - 0.38 Bt.70888 Transcribed locus - 0.39 Bt.89664 Transcribed locus - 0.39 Bt.101066 Oxysterol binding protein-like (Drosophila) ASH1L 0.39 Bt.101066 Oxysterol binding protein-like 1A OSBPL1A 0.39 Bt.44212 Transcribed locus - 0.39 Bt.44212 <td>Bt.5986</td> <td>fms-related tyrosine kinase 3 ligand</td> <td>FLT3LG</td> <td>0.36</td>	Bt.5986	fms-related tyrosine kinase 3 ligand	FLT3LG	0.36
Bit 11418 RYK receptor-like tyrosine kinase RYK 0.36 Bit 33789 Acconitase 1, soluble ACO1 0.37 Bit 68022 RNA binding motif protein 19 RBM19 0.37 Bit 08089 Transmembrane BAX inhibitor motif containing 1 HIGC10RF21 0.38 Bit 3543 Chromosome 1 open reading frame 21 ortholog HIGC10RF21 0.38 Bit 76883 Transcribed locus - 0.38 Bit 7058 Transcribed locus - 0.39 Bit 80583 Ash1 (dissent, small, or homeotic)-like (Drosophila) ASH1L 0.39 Bit 101608 Crysterol binding protein-like 1A OSBPL1A 0.39 Bit 4212 Galactosidase, beta 1-like - 0.39 Bit 42212 Transcribed locus - 0.39 Bit 42761 <td>Bt.9004</td> <td>Branched chain aminotransferase 2, mitochondrial</td> <td>BCAT2</td> <td>0.36</td>	Bt.9004	Branched chain aminotransferase 2, mitochondrial	BCAT2	0.36
Bit 53789 Aconitase ¹ , soluble ⁷ AcOl 0.37 Bit 63052 RNA binding motif protein 19 RBM19 0.37 Bit 63052 Transmembrane BAX inhibitor motif containing 1 TMBIMI 0.37 Bit 5357 Transmembrane BAX inhibitor motif containing 1 TMBIMI 0.37 Bit 5357 TRNN methyltransferase 6 homolog (S. cerevisiae) TRNT6 0.38 Bit 7058 Transcribed locus - 0.38 Bit 89664 Transcribed locus - 0.39 Bit 63493 Transcribed locus - 0.39 Bit 64949 Transcribed locus - 0.39 Bit 64940 Transcribed locus - 0.39 Bit 101068 Oxysterol binding protein-like 1A OSBPL1A 0.39 Bit 44278 Galactosidase, beta 1-lake GIB1L 0.39 Bit 44272 Transcribed locus - 0.39 Bit 24707 Tripartite motif-containing 37 TRIM37 0.4 Bit 9711 THAP 0.42 1.14AP7 Bit 0348 <	Bt.11418	RYK receptor-like tyrosine kinase	RYK	0.36
Bit 63052 RNA binding motif protein 19 RBM19 0.37 Bit 6989 Transmembrane BAX inhibitor motif containing 1 TMBIM1 0.37 Bit 13543 Chromosome 1 open reading frame 21 ortholog H16C10RF21 0.38 Bit 3585 TRNA methyltransferase 6 homolog (S. cerevisiae) TRNT6 0.38 Bit 7058 Transcribed locus - 0.38 Bit 89664 Transcribed locus - 0.39 Bit 89664 Transcribed locus - 0.39 Bit 101068 Oxysterol binding protein-like (Drosophila) ASHIL 0.39 Bit 28705 Myotubularin related protein 2 MTMR2 0.39 Bit 24212 Galactosidase, beta 1-like OSBPL1A 0.39 Bit 24212 Transcribed locus - 0.39 Bit 24217 Galactosidase, beta 1-like - 0.39 Bit 24217 Transcribed locus - 0.39 Bit 24217 Transcribed locus - 0.39 Bit 24217 Transcribed locus - 0.49 Bit 6	Bt.53789	Aconitase 1, soluble	ACO1	0.37
Bit 6989 Transmembrane BAX inhibitor motif containing 1 TMBIM1 0.37 Bt.13543 Chromosome 1 open reading frame 21 ortholog TRN16 0.38 Bt.5857 TRNA methyltransferase 6 homolog (S. cerevisiae) TRNT6 0.38 Bt.7058 Transcribed locus - 0.38 Bt.7058 Transcribed locus - 0.39 Bt.85853 Ash1 (absent, small, or homeotic)-like (Drosophila) ASHIL 0.39 Bt.85853 Ash1 (absent, small, or homeotic)-like (Drosophila) - 0.39 Bt.128705 Myotubularin related protein 12 MTMR2 0.39 Bt.24212 Transcribed locus - 0.39 Bt.424278 Galactosidase, beta 1-like GLB1L 0.39 Bt.44212 Transcribed locus - 0.39 Bt.27957 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.39 Bt.24212 Transcribed locus - 0.42 Bt.991711 THAP domain containing 7 TRIM37 0.4 Bt.9111 THAP 0.4 0.42 </td <td>Bt.63052</td> <td>RNA binding motif protein 19</td> <td>RBM19</td> <td>0.37</td>	Bt.63052	RNA binding motif protein 19	RBM19	0.37
Bt.13543 Chromosome 1 open reading frame 21 ortholog H16C10RF21 0.38 Bt.5857 TRNA methyltransferase 6 homolog (S. cerevisiae) TRMT6 0.38 Bt.76883 Transcribed locus - 0.39 Bt.70585 Transcribed locus - 0.39 Bt.89664 Transcribed locus - 0.39 Bt.85553 Ash1 (absent, small, or homeotic)-like (Drosophila) ASHIL 0.39 Bt.101066 Oxysterol binding protein-like 1A 0.59 0.39 Bt.1210106 Oxysterol binding protein-like 1A 0.39 0.39 Bt.4212 Transcribed locus - 0.39 Bt.44212 Transcribed locus - 0.39 Bt.44212 Transcribed locus - 0.39 Bt.24470 Galactosidase, beta 1-like 0.39 - Bt.24477 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.39 Bt.24470 Tripartite motif-containing 37 TRIM37 0.4 Bt.60919 Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 NFKB1 0.4 Bt.61548 HERPUD family member 2 <td< td=""><td>Bt.6989</td><td>Transmembrane BAX inhibitor motif containing 1</td><td>TMBIM1</td><td>0.37</td></td<>	Bt.6989	Transmembrane BAX inhibitor motif containing 1	TMBIM1	0.37
B: 5857TRNA methyltransferase 6 homolog (S. cerevisiae)TRMT60.38Bt.76883Transcribed locus-0.38Bt.7058Transcribed locus-0.39Bt.85853Ashl (absent, small, or homeotic)-like (Drosophila)ASHIL0.39Bt.64944Transcribed locus-0.39Bt.64944Transcribed locus-0.39Bt.64944Transcribed locus-0.39Bt.100068Oxysterol binding protein-like IAOSBPLIA0.39Bt.24705Myotubularin related protein 2MITMR20.39Bt.44278Galactosidase, beta 1-likeGLBIL0.39Bt.44212Transcribed locus-0.39Bt.24707Tripartite motif-containing 37TRIM370.4Bt.09111THAP ondain containing 7THAP70.4Bt.0911Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKBI0.42Bt.16384HERPUD family member 2HERPUD20.420.42Bt.26817Arginyl aminopeptidase (aninopeptidase B)-like 1RNPEPL10.42Bt.6685Methylenetertahydrofolate chydrogenase (NADP+ dependent) 2, methonyltetrahydrofolate cyclohydrolase-0.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.20233Hypothetical LOC513740-0.45Bt.20323Hypothetical LOC513740 <td< td=""><td>Bt.13543</td><td>Chromosome 1 open reading frame 21 ortholog</td><td>H16C10RF21</td><td>0.38</td></td<>	Bt.13543	Chromosome 1 open reading frame 21 ortholog	H16C10RF21	0.38
BT 76883 Bt 7058 Bt 7058 Transcribed locus-0.38 -Bt 7058 Bt 7058 Bt 7058 Transcribed locus-0.39 -Bt 89664 Bt 89664 Transcribed locus-0.39 -Bt 69499 Bt 64949 Transcribed locus-0.39 -Bt 64949 Bt 101068 Bt 64949Transcribed locus-0.39 -Bt 101068 Bt 28705 Bt 42778 Calactosidase, beta 1-like Galactosidase, beta 1-likeOSBPL1A0.39 -Bt 44278 Bt 4272 Calactosidase, beta 1-like-0.39 -Bt 44273 Bt 27957 Bt 2917 Bt 24770Franscribed locus 0.39 Bt 24470 Bt 24777 Bt 24777 Bt 24777 Bt 24777 Bt 24777 Bt 24777 Bt 24777-0.39 Bt 24470 Bt 24777 Bt 247777 Bt 247877 Bt 247777 Bt 247877 Bt 247777 Bt 247877 Bt 247777 Bt 247877 Bt 247777 Bt 247877 Bt 247777 Bt 247877 Bt 247777 Bt 2478777 Bt 247777 Bt 247877 Bt 247777 Bt 247877 Bt 247777 Bt 2478777 Bt 2478777 Bt 2478777 Bt 2478777 Bt 24787777 Bt 247877777777777777777777777777777777777	Bt.5857	TRNA methyltransferase 6 homolog (S. cerevisiae)	TRMT6	0.38
Bt.7058 Transcribed locus - 0.38 Bt.89664 Transcribed locus - 0.39 Bt.58583 Ash1 (absent, small, or homeotic)-like (Drosophila) ASH1L 0.39 Bt.64949 Transcribed locus - 0.39 Bt.101068 Oxysterol binding protein-like 1A OSBPL1A 0.39 Bt.28705 Myotubularin related protein 2 MTMR2 0.39 Bt.44212 Transcribed locus - 0.39 Bt.27957 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.39 Bt.27957 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.39 Bt.27957 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.39 Bt.27957 Poly (ADP-ribose) polymerase family, member 8 PARP8 0.42 Bt.060919 Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 NFKB1 0.4 Bt.97111 THAP domain containing 7 THAP7 0.4 Bt.91611 Transcribed locus - 0.42 Bt.63818 HERPUD1D family member 2 MTHFD2 0.42 Bt.64884 Transcribed lo	Bt.76883	Transcribed locus	_	0.38
Bt.89664 Transcribed locus - 0.39 Bt.58583 Ash1 (absent, small, or homeotic)-like (Drosophila) ASH1L 0.39 Bt.64949 Transcribed locus - 0.39 Bt.101068 Oxysterol binding protein-like 1A OSBPL1A 0.39 Bt.28705 Myotubularin related protein 2 MTMR2 0.39 Bt.44212 Transcribed locus - 0.39 Bt.44217 Transcribed locus - 0.39 Bt.24470 Tripartite motif-containing 37 TRIM37 0.4 Bt.60919 Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 NFKB1 0.4 Bt.163823 Vacular protein sorting 41 homolog (S. cerevisiae) VPS41 0.42 Bt.16348 HERPUD family member 2 HERPUD2 0.42 Bt.6685 Methylenetetrahydrofolate celohydrogenase (NADP+ dependent) 2, metheryliterahydrofolate celohydro	Bt.7058	Transcribed locus	_	0.38
Bt.58583Ash1 (absent, small, or homeotic)-like (Drosophila)ASH1L 0.39 Bt.64049Transcribed locus- 0.39 Bt.101068Oxysterol binding protein-like 1AOSBPL1A 0.39 Bt.28705Myotubularin related protein 2MTMR2 0.39 Bt.44278Galactosidase, beta 1-likeGLBIL 0.39 Bt.44212Transcribed locus- 0.39 Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP8 0.39 Bt.24270Tripartite motif-containing 37TRIM37 0.4 Bt.660919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB1 0.42 Bt.135232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS41 0.42 Bt.16348HERPUD family member 2HERPUD2 0.42 Bt.265917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL1 0.42 Bt.2684Transcribed locus- $ 0.42$ Bt.6484Transcribed locus-0.42methenylterahydrofolate eyclohydrolaseBt.21055MAP kinase interacting serinc/thrconine kinase 1MKNK1 0.43 Bt.43257Transcribed locus- $ 0.45$ Bt.42764ProsaposinPSAP 0.45 Bt.42754Transcribed locus- $ 0.45$ Bt.42764ProsaposinPSAP 0.45 Bt.42764ProsaposinPSAP 0.45 Bt.3233Hypothetical LOCS13740 0.46 Bt.43257Transcribed loc	Bt.89664	Transcribed locus	_	0.39
Bt.64949Transcribed locus-0.39Bt.101068Oxysterol binding protein-like 1AOSBPL1A0.39Bt.28705Myotubularin related protein 2MTINR20.39Bt.44278Galactosidase, beta 1-likeGLB1L0.39Bt.44212Transcribed locus-0.39Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP80.39Bt.24470Tripartite motif-containing 37TRIM370.4Bt.05919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB10.4Bt.91711THAP domain containing 7THAP70.4Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS410.42Bt.16348HERPUD family member 2HERPUD20.42Bt.2685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenylterahydrofolate cyclohydrolase-0.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.42764Prosaposin-0.45Bt.42764ProsaposinPSAP0.45Bt.642764ProsaposinPSAP0.45Bt.642764ProsaposinPSAP0.45Bt.64884Transcribed locus-0.42Bt.64884Transcribed locus-0.45Bt.42764ProsaposinPSAP0.45Bt.42764ProsaposinPSAP0.45Bt.63024V-mar musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.65044v	Bt.58583	Ash1 (absent, small, or homeotic)-like (Drosophila)	ASH1L	0.39
Bt.101068Oxysterol binding protein-like 1AOSBPL1A0.39Bt.28705Myotubularin related protein 2MTMR20.39Bt.44212Galactosidase, beta 1-likeGLB1L0.39Bt.4212Transcribed locus $-$ 0.39Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP80.39Bt.24470Tripartite motif-containing 37TRIM370.4Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB10.4Bt.91711THAP domain containing 7THAP70.4Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS410.42Bt.264917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL10.42Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase-0.42Bt.26484Transcribed locus-0.440.43Bt.97014TBCI domain family, member 24TBCID240.44Bt.43257Transcribed locus-0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.63484Transcribed locus-0.45Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.97014TBCI domain family, member 24TBCID240.44Bt.43257Transcribed locus-0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.5044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)M	Bt.64949	Transcribed locus	_	0.39
Bt.28705Myotubularin related protein 2MTMR2 0.39 Bt.44278Galactosidase, beta 1-likeGLBIL 0.39 Bt.44217Transcribed locus- 0.39 Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP8 0.39 Bt.24470Tripartite motif-containing 37TRIM37 0.4 Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB1 0.4 Bt.91711THAP domain containing 7THAP7 0.4 Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS41 0.42 Bt.16348HERPUD family member 2HERPUD2 0.42 Bt.2685Methylenetetrahydrofolate (antinopeptidase B)-like 1RNPEPL1 0.42 Bt.98161Transcribed locus- 0.42 Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK1 0.43 Bt.45844Transcribed locus- 0.44 Bt.45257Transcribed locus- 0.44 Bt.45257Transcribed locus- 0.44 Bt.45257Transcribed locus- 0.45 Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK1 0.43 Bt.45257Transcribed locus- 0.45 Bt.21055MAP kinase interacting serine/threonine kinase 1MCNST1 0.46 Bt.45264Transcribed locus- 0.45 Bt.42764ProsaposinPSAP 0.45 Bt.20323Hypothetical LOC513740LOC513740LOC513740 <td>Bt.101068</td> <td>Oxysterol binding protein-like 1A</td> <td>OSBPL1A</td> <td>0.39</td>	Bt.101068	Oxysterol binding protein-like 1A	OSBPL1A	0.39
Bt.44278Galactosidase, beta 1-likeGLBIL 0.39 Bt.44212Transcribed locus- 0.39 Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP8 0.39 Bt.24470Tripartite motif-containing 37TRIM37 0.4 Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB1 0.4 Bt.91711THAP domain containing 7THAP7 0.4 Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS41 0.42 Bt.16348HERPUD family member 2HERPUD2 0.42 Bt.98161Transcribed locus- 0.42 Bt.6685Methylenetterahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase- 0.44 Bt.9105MAP kinase interacting serine/threonine kinase 1MKNK1 0.43 Bt.6484Transcribed locus- 0.44 Bt.9214TBC1 domain family, member 24TBC1D24 0.44 Bt.43257Transcribed locus- 0.45 Bt.442764ProsaposinPSAP 0.45 Bt.20323Hypothetical LOC513740LOC513740 0.46 Bt.6689Chromosome 10 open reading frame 35 orthologC28H100RF35 0.46 Bt.9125Transcribed locus- 0.47 Bt.9125Transcribed locus- 0.47 Bt.9125Transcribed locus- 0.47 Bt.9125Transcribed locus- 0.47 Bt.92323Hypothetical LOC513740LOC513740 </td <td>Bt.28705</td> <td>Myotubularin related protein 2</td> <td>MTMR2</td> <td>0.39</td>	Bt.28705	Myotubularin related protein 2	MTMR2	0.39
Bt.44212Transcribed locus-0.39Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP80.39Bt.24470Tripartite motif-containing 37TRIM370.4Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB10.4Bt.91711THAP domain containing 7THAP70.4Bt.5232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS410.42Bt.16348HERPUD family member 2HERPUD20.42Bt.26917Arginyl aminopeptidase (aninopeptidase B)-like 1RNPEPL10.42Bt.98161Transcribed locus-0.42Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase-0.42Bt.1055MAP kinase interacting serinc/threonine kinase 1MKNK10.43-Bt.4844Transcribed locus-0.45-Bt.47074ProsaposinPSAP0.45-Bt.20323Hypothetical LOC513740LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.47Bt.91525Transcribed locus-0.47Bt.91525Transcribed locus-0.47Bt.91525Transcribed locus-0.47Bt.91525Transcribed locus-0.47Bt.91525Transcribed locus-0.47Bt.91525Transcribed locus-0.47Bt.77226K(lysine) ace	Bt.44278	Galactosidase, beta 1-like	GLB1L	0.39
Bt.27957Poly (ADP-ribose) polymerase family, member 8PARP8 0.39 Bt.24470Tripartite motif-containing 37TRIM370.4Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB10.4Bt.91711THAP domain containing 7THAP70.4Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS410.42Bt.16348HERPUD family member 2HERPUD20.42Bt.26917Arginyl aminopeptidase (aninopeptidase B)-like 1RNPEPL10.42Bt.6685Methylenettrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase-0.42Bt.1685MAP kinase interacting serine/threonine kinase 1MKNK10.430.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.42764Prosaposin-0.450.45Bt.20323Hypothetical LOC513740LOC5137400.460.46Bt.3032Hypothetical LOC513740JAG62NF750.47Bt.31525Transcribed locus0.47Bt.31525Transcribed locus-0.470.46Bt.3253Hypothetical LOC513740JAG60.460.46Bt.3032Hypothetical LOC5137400.460.460.46Bt.31525Transcribed locus-0.470.46Bt.31525Transcribed locus-0.470.46Bt.31525Transcribed locus-0.470.46Bt.3233Hypothe	Bt.44212	Transcribed locus	_	0.39
Bt.24470Tripartite motif-containing 37TRIM37 0.4 Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB1 0.4 Bt.91711THAP domain containing 7THAP7 0.4 Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS41 0.42 Bt.16348HERPUD family member 2HERPUD2 0.42 Bt.26917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL1 0.42 Bt.685Methylenettrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase $ 0.42$ Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK1 0.43 $-$ Bt.9105MAP kinase interacting serine/threonine kinase 1MKNK1 0.44 $-$ Bt.917TBC1 domain family, member 24TBC1D24 0.44 $-$ Bt.42764ProsaposinPSAP 0.45 0.45 Bt.42764ProsaposinPSAP 0.46 0.45 Bt.64884Tanscribed locus $ 0.46$ Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF 0.46 Bt.6389Chromosome 10 open reading frame 35 orthologC28H100RF35 0.46 Bt.91525Transcribed locus $ 0.47$ Bt.77226K(lysine) acetyltransferase 5KAT5 0.48 Bt.7226K(lysine) acetyltransferase 5KAT5 0.48 Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF6 0.49 Bt.7226 <td>Bt.27957</td> <td>Poly (ADP-ribose) polymerase family, member 8</td> <td>PARP8</td> <td>0.39</td>	Bt.27957	Poly (ADP-ribose) polymerase family, member 8	PARP8	0.39
Bt.60919Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1NFKB1 0.4 Bt.91711THAP domain containing 7THAP7 0.4 Bt.5232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS41 0.42 Bt.16348HERPUD family member 2HERPUD2 0.42 Bt.26917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL1 0.42 Bt.98161Transcribed locus $ 0.42$ Bt.6685Methylenetterlahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase $ 0.42$ Bt.16484Transcribed locus $ 0.44$ Bt.97014TBC1 domain family, member 24TBC1D24 0.44 Bt.477014TBC1 domain family, member 24TBC1D24 0.44 Bt.42764ProsaposinPSAP 0.45 Bt.42764ProsaposinPSAP 0.45 Bt.42764ProsaposinLOCS13740 0.46 Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF 0.46 Bt.3689Chromosome 10 open reading frame 35 orthologC28H100RF35 0.46 Bt.91525Transcribed locus $ 0.47$ Bt.77226K(lysine) acetyltransferase 5KAT5 0.48 Bt.77226K(lysine) acetyltransferase 5KAT5 0.48 Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF6 0.49 Bt.1523Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF6 0.49 Bt.7726K(Bt.24470	Tripartite motif-containing 37	TRIM37	0.4
Bt.91711THAP domain containing 7THAPTHAP70.4Bt.35232Vacuolar protein sorting 41 homolog (S. crevisiae)VPS410.42Bt.16348HERPUD family member 2HERPUD20.42Bt.26917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL10.42Bt.98161Transcribed locus-0.42Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase-0.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.4884Transcribed locus-0.44Bt.477014TBC1 domain family, member 24TBC1D240.44Bt.43257Transcribed locus-0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.6689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.91525Transcribed locus-0.47Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransfe	Bt.60919	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	NFKB1	0.4
Bt.35232Vacuolar protein sorting 41 homolog (S. cerevisiae)VPS410.42Bt.16348HERPUD family member 2HERPUD20.42Bt.26917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL10.42Bt.98161Transcribed locus-0.42Bt.6685Methylenettrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolaseMTHFD20.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.64884Transcribed locus-0.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.4257Transcribed locus-0.45Bt.24254ProsaposinPSAP0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.47Bt.9187Zinc finger protein 75 (D8C6)ZNF750.47Bt.1525Transcribed locus-0.47Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.7726K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.4264Transcribed locus-0.49Bt.7636Transcribed locus-0.49	Bt.91711	THAP domain containing 7	THAP7	0.4
Bt.16348HERPUD family member 2HERPUD family member 2HERPUD 20.42Bt.26917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL10.42Bt.98161Transcribed locus-0.42Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolaseMTHFD20.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43-Bt.64884Transcribed locus-0.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.43257Transcribed locus-0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.689Chromosome 10 open reading frame 35 orthologC28H100RF350.46Bt.94187Zinc finger protein 75 (D8C6)ZNF750.47Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.1726TBC1 domain family, member 17TBC110170.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49 <td>Bt.35232</td> <td>Vacuolar protein sorting 41 homolog (S. cerevisiae)</td> <td>VPS41</td> <td>0.42</td>	Bt.35232	Vacuolar protein sorting 41 homolog (S. cerevisiae)	VPS41	0.42
Bt.26917Arginyl aminopeptidase (aminopeptidase B)-like 1RNPEPL10.42Bt.98161Transcribed locus-0.42Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolaseMTHFD20.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.64884Transcribed locus-0.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.43257Transcribed locus-0.45Bt.42764ProsaposinPSAP0.45Bt.6389Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.7226K(lysine) acetyltransferase 5KAT50.48Bt.17226TBC1 domain family, member 17TBC1D170.49Bt.1726SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.47Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.16348	HERPUD family member 2	HERPUD2	0.42
Bt.98161Transcribed locus-0.42Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolaseMTHFD20.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.64884Transcribed locus-0.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.43257Transcribed locus-0.45Bt.42764ProsaposinPSAP0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.91525Transcribed locus-0.47Bt.7722EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.42756SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.26917	Arginyl aminopeptidase (aminopeptidase B)-like 1	RNPEPL1	0.42
Bt.6685Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolaseMTHFD20.42Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK10.43Bt.64884Transcribed locus-0.44Bt.97014TBC1 domain family, member 24TBC1D240.44Bt.43257Transcribed locus-0.45Bt.42764ProsaposinPSAP0.45Bt.2023Hypothetical LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.3689Chromosome 10 open reading frame 35 orthologC28H100RF350.46Bt.91525Transcribed locus-0.47Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.75231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC508120.5	Bt.98161	Transcribed locus	—	0.42
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Bt.21055MAP kinase interacting serine/threonine kinase 1MKNK1 0.43 Bt.64884Transcribed locus $ 0.44$ Bt.97014TBC1 domain family, member 24TBC1D24 0.44 Bt.43257Transcribed locus $ 0.45$ Bt.42764ProsaposinPSAP 0.45 Bt.20323Hypothetical LOC513740LOC513740 0.46 Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF 0.46 Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF35 0.46 Bt.91525Transcribed locus $ 0.47$ Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP2 0.48 Bt.77226K(lysine) acetyltransferase 5KAT5 0.48 Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF6 0.49 Bt.1726TBC1 domain family, member 17TBC1D17 0.49 Bt.7636Transcribed locus $ 0.49$ Bt.7636Transcribed locus $ 0.49$ Bt.9289Similar to carnitine O-palmitoyltransferaseLOC506812 0.5		methenyltetrahydrofolate cyclohydrolase		
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Bt.97014TBC1 domain family, member 24TBC1D24 0.44 Bt.43257Transcribed locus- 0.45 Bt.42764ProsaposinPSAP 0.45 Bt.20323Hypothetical LOC513740LOC513740 0.46 Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF 0.46 Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF35 0.46 Bt.91525Transcribed locus- 0.47 Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP2 0.48 Bt.77226K(lysine) acetyltransferase 5KAT5 0.49 Bt.1726TBC1 domain family, member 17TBC1D17 0.49 Bt.7636Transcribed locus- 0.49 Bt.7636Transcribed locus- 0.49 Bt.7636Transcribed locus- 0.49 Bt.9289Similar to carnitine O-palmitoyltransferaseLOC506812 0.5	Bt.64884	Transcribed locus	_	0.44
Bt.43257Transcribed locus $ 0.45$ Bt.42764ProsaposinPSAP 0.45 Bt.20323Hypothetical LOC513740LOC513740 0.46 Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF 0.46 Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF35 0.46 Bt.94187Zinc finger protein 75 (D8C6)ZNF75 0.47 Bt.91525Transcribed locus $ 0.47$ Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP2 0.48 Bt.77226K(lysine) acetyltransferase 5KAT5 0.48 Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF6 0.49 Bt.1726TBC1 domain family, member 17TBC1D17 0.49 Bt.7636Transcribed locus $ 0.49$ Bt.7636Transcribed locus $ 0.49$ Bt.7636SERTA domain containing 1SERTAD1 0.49 Bt.9289Similar to carnitine O-palmitoyltransferase $ 0.49$	Bt.97014	TBC1 domain family, member 24	TBC1D24	0.44
Bt.42764ProsaposinPSAP0.45Bt.20323Hypothetical LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.94187Zinc finger protein 75 (D8C6)ZNF750.47Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.7636Transcribed locus-0.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.43257	Transcribed locus	_	0.45
Bt.20323Hypothetical LOC513740LOC5137400.46Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.94187Zinc finger protein 75 (D8C6)ZNF750.47Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.42764	Prosaposin	PSAP	0.45
Bt.65044v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)MAFF0.46Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.94187Zinc finger protein 75 (D8C6)ZNF750.47Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.20323	Hypothetical LOC513740	LOC513740	0.46
Bt.3689Chromosome 10 open reading frame 35 orthologC28H10ORF350.46Bt.94187Zinc finger protein 75 (D8C6)ZNF750.47Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.65044	v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)	MAFF	0.46
Bt.94187Zinc finger protein 75 (D8C6)ZNF750.47Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.3689	Chromosome 10 open reading frame 35 ortholog	C28H10ORF35	0.46
Bt.91525Transcribed locus-0.47Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.94187	Zinc finger protein 75 (D8C6)	ZNF75	0.47
Bt.7572EGF-containing fibulin-like extracellular matrix protein 2EFEMP20.48Bt.77226K(lysine) acetyltransferase 5KAT50.48Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.91525	Transcribed locus	_	0.47
Bt. 77226K(lysine) acetyltransferase 5KAT50.48Bt. 15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt. 1726TBC1 domain family, member 17TBC1D170.49Bt. 49556SERTA domain containing 1SERTAD10.49Bt. 7636Transcribed locus-0.49Bt. 9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.7572	EGF-containing fibulin-like extracellular matrix protein 2	EFEMP2	0.48
Bt.15231Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6ARHGEF60.49Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.77226	K(lysine) acetyltransferase 5	KAT5	0.48
Bt.1726TBC1 domain family, member 17TBC1D170.49Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.15231	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	ARHGEF6	0.49
Bt.49556SERTA domain containing 1SERTAD10.49Bt.7636Transcribed locus-0.49Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.1726	TBC1 domain family, member 17	TBC1D17	0.49
Bt. 7636Transcribed locus-0.49Bt. 9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.49556	SERTA domain containing 1	SERTAD1	0.49
Bt.9289Similar to carnitine O-palmitoyltransferaseLOC5068120.5	Bt.7636	Transcribed locus	_	0.49
	Bt.9289	Similar to carnitine O-palmitoyltransferase	LOC506812	0.5

	Category	Term	Genes	Count	%	P-value
Up rogulated	Molecular function	Ion binding	LOC540552, ATP8A1, PC, NME7, ALPL, ADAMTS5, MGP, TGM2, MMP1, KCND1	10	26.3	3.5E-2
genes	Cellular component	Cellular Organelle membrane PC, CAV1, COX6B2, CAV2		4	10.5	9.7E-2
	Cellular component	Proteinaceous extracellular matrix	ADAMTS5, MMP1, TIMP3	3	7.9	3.6E-2
Down-regulated - genes	Molecular function	Protein binding	TTR, CCL2, PAFAH1B3, MAFF, IL6, NFKB1, VEGFC, GCLM, DBN1, AMIGO2, FLT3LG, ATP1B3, PSME1	13	33.3	1.9E-2
	Cellular component	Extracellular space	CCL2, FLT3LG, IL6	3	7.7	4.0E-2
	Biological component	Nitrogen compound metabolic process	GCLM, TTR, BCAT2	3	7.7	8.1E-2

Table 3. Functional Annotation of differentially expressed genes between preadipocyte and its differentiated adipocyte cells using DAVID program

have been changed during the process of differentiation. Particularly, we found that hypothetical protein, LOC540552, was the most highly expressed chip element for adipocyte differentiation, which is unknown gene in cattle. Further investigation of this chip element indicated that the nucleotide sequence of LOC540552 has similarity to Delta/Notch-like EGF-related receptor (DNER) gene based on the BLAST search result (http://www.ncbi.nlm.nih.gov/BLAST/). DNER was known to bind Notch1 gene at cell-to-cell contact and it has a function as an activator in Notch1 signaling. Garces et al. (1997) suggested that expression of Notch1 plays a key role in adipocyte differentiation of 3T3-L1 cells in mouse. Moreover, DNER was located on BTA3, where the quantitative trait loci (QTL) for marbling score was located (Casas et al. 2001; 2004). In monkey and human cell lines, Transglutaminase 2 (TGM2) was expressed dependently by binding all-trans-retinoic acid (RA) into retinoic acid receptor-retinoid X receptor (RAR · RXR) heterodimeric complexes (Nagy et al., 1996; Ma et al., 2003). Therefore, we can expect that RA can increase the TGM2 expression in relation to the differentiation of adipocytes. However, until now, no known relationship was identified between TGM2 expression and adipogenesis.

Validation of expression by semi-quantitative realtime PCR

To validate differentially expressed genes from the bovine genome array data, five genes were selected, namely matrix metalloproteinase 1 (MMP1), Calveolin 1 (CAV1), Calveolin 2

(CAV2), Transthyretin (TTR) and Dual specificity phosphatase 10 (DUSP10) and confirmed with semi-quantitative real-time PCR assays. Based on bovine genome array results, MMP1, CAV1 and CAV2 genes were up-regulated and TTR and DUSP10 genes were down-regulated in differentiated adipocytes (Fig. 1). The mRNA expression patterns of selected five genes were highly consistent with the bovine genome array results. MMPs block cholesterol efflux in macrophage foam cells (Lindstedt et al., 1999) and have a function as modulator of adipogenesis (Chavey et al., 2003). Therefore, we assumed that MMP1 of the fibroblast type collagenase, which associated with alteration of cell membrane according to adipogenesis of intramuscular fibroblast-like cells. Upregulated CAV1 and CAV2 genes play an important role in cholesterol homeostasis as major structural component of caveolae in vivo (Martin and Parton, 2005). CAV1 gene induced adipogenesis in 3T3-L1 cells (Scherer et al., 1994) as well as increased during adipocyte differentiation of bovine intramuscular preadipocyte (BIP) cells (Takenouchi et al., 2004). Moreover, CAV2 protein increased expression in 3T3-L1 adipocytes (Scherer et al., 1997). Therefore, we can conclude that CAV1 and CAV2 genes are highly related with adipogenesis. Down-regulated TTR gene was reported that it can bind to plasma membrane and related to change of membrane fluidity (Hou et al., 2005). DUSP10 gene was included as a subclass of protein tyrosine phosphatase (PTP) gene superfamily, which has important roles for control of Mitogen-activated protein (MAP) kinase functions (Camps et al., 2000). Therefore, we assumed that expression changes of these genes can ultimately give the different cell properties



Fig. 1. The mRNA expression patterns based on the semi-quantitative real time PCR for the five selected genes among differentially expressed genes in bovine genome array. Black bars indicate intramuscular fibroblast-like cells and gray bars are their differentiated adipocytes. The numbers in vertical line indicate fold differences. The gene expression levels of each gene were normalized to the expression level of beta-actin (A, B) and GAPDH (C, D).

between fibroblast-like cells and differentiated adipocytes.

Based on this experiment, we found that the large number of differentially expressed chip elements was currently unknown functions and enormous efforts were needed for the further verification of the differentially expressed genes.

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