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Requirement for ERK MAP kinase in mouse preimplantation development

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Preimplantation development is a crucial step for successful implantation and pregnancy. Although both compaction and blastocyst formation have been extensively studied, mechanisms regulating the early cell division stages before compaction have remained unclear. Here, we show that extracellular signal regulated kinase (ERK) mitogen-activated protein (MAP) kinase function is required for early embryonic cell division before compaction. Our analysis demonstrates that inhibition of ERK activation in late two-cell-stage embryos leads to a reversible arrest in the G2 phase at the four-cell stage. The G2-arrested four-cell-stage embryos showed weakened cell-cell adhesion as compared with control embryos. Remarkably, microarray analyses showed that most of the programmed changes of upregulated and downregulated gene expression during the four- to eight-cell stages proceeded normally in four-cell-stage-arrested embryos that were subsequently released to resume development; however, the expression profiles of a proportion of genes in these embryos closely paralleled the stages of embryonic rather than normal development. These parallel genes included the genes encoding intercellular adhesion molecules, whose expression appeared to be positively regulated by the ERK pathway. We also show that, whereas ERK inactivation in eight-cell-stage embryos did not lead to cell division arrest, it did cause this arrest when cadherin-mediated cell-cell adhesion was disrupted. These results demonstrate an essential role of ERK function in two-cell to eight-cell-stage embryos, and suggest a loose parallelism between the gene expression programs and the developmental stages before compaction.

KEY WORDS: Preimplantation development, MAP kinase, Adhesion, Mouse

INTRODUCTION

Preimplantation development is a mammalian-specific occurrence and involves a number of important events. Both compaction and blastocyst formation are the best-studied, represent morphologically dynamic changes and are important for successful implantation (Wang and Dey, 2006). Although these conspicuous events have been extensively studied, genes or mechanisms regulating early cell division stages before compaction have remained unclear. Recently, global gene expression profiles during preimplantation development have been examined, and two principal transient waves of de novo transcription have been identified (Hamatani et al., 2004; Wang et al., 2004a). However, the possible link between global gene expression profiles and developmental stages has not been addressed.

The mitogen-activated protein kinase (MAPK) cascades are highly conserved and have central roles in diverse cellular functions (Sturgill and Wu, 1991; Nishida and Gotoh, 1993; Robinson and Cobb, 1997; Lewis et al., 1998; Pearson et al., 2001; Pouyssegur and Lenormand, 2003; Chang and Karin, 2001). In mammals, MAPK members include extracellular signal-regulated kinases 1 and 2 (ERK1/2; MAPK3 and MAPK1, respectively), cJun N-terminal kinase (JNK), p38 and ERK5 (MAPK7). Each member of the MAPK family is activated in response to various extracellular stimuli and regulates various biological processes, mainly through regulating gene expression. Recent studies have shown that JNK and p38 are involved in cavity formation during preimplantation development (Natale et al., 2004; Maekawa et al., 2005). However, the ERK pathway inhibitor U0126 (Favata et al., 1998) has no apparent effect on cavity formation when added at the eight-cell stage (Maekawa et al., 2005), suggesting that ERK might not have a role in mouse preimplantation development. We, however, considered the possibility that ERK function is required for the early cell division stages before compaction. In this study, we describe an essential role of ERK function in two-cell to eight-cell-stage embryos, and suggest a loose parallelism between the gene expression programs and the developmental stages before compaction.

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MATERIALS AND METHODS

Embryo collection and culture

Two-cell-stage embryos were flushed from oviducts of ICR mice (Japan SLC) using M2 medium (Nagy et al., 2003). In the experiments shown in Fig. 4, females were superovulated with pregnant mare serum gonadotropin (PMSG) and human chorionic gonadotropin (hCG). Embryos were cultured in KSOM culture media (Chemicon) at 37°C in 5% CO_2. U0124 was purchased from Calbiochem, U0126 was from Promega and actinomycin D was from Sigma. In some experiments, the zona pellucida was removed by the method using acid tyrode. Embryos were transferred in acid tyrode (Sigma) at room temperature and observed continuously under the stereomicroscope. As soon as the zona was dissolved, embryos were collected and transferred back to in KSOM culture media.

Immunohistochemistry

Prior to fixation, the zona pellucida was removed. Embryos were fixed overnight in 4% paraformaldehyde in PBS at 4°C and washed in 2% BSA in PBS. The fixed embryos were permeabilized and blocked by incubation overnight in 2% BSA in PBS plus 0.2% Triton X-100 at 4°C. The embryos were then washed and incubated with anti-phospho-p44/42 MAPK (Thr202/Tyr204) E10 monoclonal antibody (Cell Signaling) (×100), anti-phospho-ELK1 (Ser383) antibody (Cell Signaling; ×400), anti-cyclin B1 (Santa Cruz; ×50), or anti-phospho-histone H3 antibody (Upstate; ×500)

in 2% BSA in PBS for 16 hours at 4°C. Embryos were washed and incubated with anti-rabbit or anti-mouse IgG secondary antibodies and Hoechst (10 μg/ml) in 2% BSA in PBS for 16 hours at 4°C. To detect BrdU-positive embryos, embryos were incubated for 1 hour at 37°C with anti-BrdU monoclonal antibody (Becton Dickinson) and DNase I followed by incubation with anti-mouse IgG secondary antibody and Hoechst. Fluorescence images were viewed with a Bio-Rad confocal microscope (Radiance 2000) or a DeltaVision Image Restoration Microscope (Applied Precision Instruments, Olympus and Seki Technotron) with softWoRx software. In the images of Fig. 3B (Hoechst and p-Histone H3), deconvolving images were performed by using softWoRx.

Microarray experiments

For microarray analysis, we performed two independent experiments. For each microarray experiment, we collected two sets of 40 embryos from six kinds of pools: control embryos at day 1.5 (cont. 1.5), day 2.5 (cont. 2.5) and day 3.5 (cont. 3.5); U0126-treated embryos at day 2.5 (U2.5); and embryos released from the U0126-induced arrest, collected at day 3.5 (U3.5) and at day 4.5 (U4.5), as shown in Fig. 5B. Each stage embryos were collected and stored at –80°C. Total RNA was isolated by following the manual of ISOGEN (Nippon Gene). A total of 80 embryos were used for each array. Synthesis of cDNA, in vitro transcription and biotin labeling of cRNA, and hybridization to the Mouse Genome 430 2.0 array (Affymetrix) were performed according to Affymetrix protocols (Two-Cycle Target Labeling Assays). Hybridized arrays were scanned using an Affymetrix GeneChip Scanner. Scanned chip images were analyzed with GeneChip Operating Software v. 1.2 (GCOS).

Microarray data analysis

The Affymetrix output (CEL files) was imported into GeneSpring 7.3 (Agilent Technologies) microarray analysis software for statistical analysis and presentation of the condition tree, the expression profiles and the average expression profiles. Probe intensities were normalized, and expression signals of all genes (probe sets) were calculated using GCRMA (GC robust multi-array analysis, as implemented in GeneSpring software). Differentially expressed genes and ERK-regulated genes were identified by fold-changes and statistical analysis. Statistical analysis was performed by one-way ANOVA with a Benjamini and Hochberg False Discovery Rate (BH-FDR=0.05) for multiple testing correction followed by Tukey's post-hoc tests (GeneSpring). The microarray data have been submitted to the Gene Expression Omnibus (GEO) public database at NCBI, and the accession number is GSE7309.

RESULTS

To examine the effect of ERK pathway inhibition on early cell division cycles, we added U0126 at the late two-cell stage. Rather surprisingly, the inhibition of the ERK pathway resulted in the arrest of cell division at the four-cell stage (Fig. 1A, U0126). At 2 days after U0126 addition, when control embryos entered the morula or blastocyst stage, U0126-treated embryos remained at the four-cell stage (Fig. 1A). An inactive analog of U0126, U0124, had no effect (Fig. 1A, U0124). Moreover, another MEK inhibitor, PD98059, also had the same effect as U0126, and the effects of PD98059 and U0126 were dose-dependent (data not shown). U0126 and PD98059 are known to inhibit not only the ERK1/2 pathway but also the ERK5 pathway (Kamakura et al., 1999; Mody et al., 2001). To see which pathway is important for progression passed the four-cell stage, we used PD184352, which selectively inhibits the ERK1/2 pathway (Mody et al., 2001; Squires et al., 2002; Tanimura et al., 2003). PD184352, like U0126, induced cell division arrest at the four-cell stage. The effect of PD184352 was also dose-dependent; the drug at 5 μM, which does not inhibit the ERK5 pathway (Mody et al., 2001; Squires et al., 2002), significantly induced cell division arrest (Fig. 1A). Therefore, we conclude that the ERK1/2 pathway is required for progression of early cell division cycles. In addition, we found that the ERK1/2-pathway-inhibited embryos showed a weakened adhesion between blastomeres, especially at later time points, as clearly seen in the photographs shown in Fig. 1B. To confirm this, we investigated the ability of one embryo to adhere to another embryo. When two-cell-stage embryos were placed very close to one another, control four- or eight-cell-stage embryos often aggregated into large aggregates within a day, but the ERK1/2-inhibited embryos (four-cell stage) remained unaggregated (data not shown), confirming the weakened adhesiveness in ERK1/2-inhibited blastomeres.

We then examined whether the inhibitor-induced developmental arrest was reversible or not. Late two-cell-stage embryos were treated with U0126 for 24 hours, and then U0126 was washed out and embryos were cultured in a drug-free medium. After the drug washout, embryos started to develop again and, 24 and 48 hours after the washout, they became morphologically normal eight-cell embryos and morula or blastocyst embryos, respectively (Fig. 1B). These results indicate that treatment with ERK pathway inhibitor induces a reversible developmental arrest during early cell division cycles.

To examine whether the ERK1/2 pathway is activated during mouse preimplantation development, embryos were stained with anti-phospho-ERK antibody and anti-phospho-ELK1 antibody. ELK1 is a well-known substrate of ERK1/2. The obtained immunofluorescence images showed that both phospho-ERK and phospho-ELK1 began to appear between the two-cell and four-cell stages, and remained until blastocyst stages (Fig. 2A). This result is in good agreement with previously reported data on embryonic day (E)2.5 and E3.5 embryos (Wang et al., 2004b). Treatment with U0126 for 1 hour markedly decreased the staining intensities of phospho-ERK1/2 and phospho-ELK1 (Fig. 2B). Furthermore, our kinase assay showed that the ability of the lysates obtained from four-cell-stage embryos to phosphorylate ELK1 in vitro was significantly reduced by U0126 treatment of the embryos. These results show that the ERK1/2 pathway is activated in mouse preimplantation development, and that U0126 is able to inhibit the ERK pathway in this system.

We then determined a cell cycle phase in which the ERK-inhibited, four-cell-stage embryos were arrested. First, BrdU incorporation into the nucleus was investigated to determine whether embryos entered the S phase. BrdU and U0126 were added at the late two-cell stage after S phase, and embryos were cultured until untreated control embryos reached the eight-cell stage. Neither U0126-untreated (DMSO, control) nor U0126-treated embryos at the early four-cell stage incorporated BrdU, but both did incorporate BrdU at later time points (Fig. 3A), indicating that the U0126-treated, four-cell-stage-arrested embryos were in G2 or M phase. Then, expression of cyclin B1 protein was examined. At the early four-cell stage, neither control nor U0126-treated embryos showed cyclin B1 accumulation. When these two groups of embryos developed to the late four-cell stage, cyclin B1 was accumulated in the nucleus. When control embryos reached the eight-cell stage, U0126-treated four-cell-arrested embryos still showed cyclin B1 accumulation (Fig. 3B), indicating that they did not enter late M phase and were in late G2 or early M phase. Next, embryos were stained with anti-phospho-histone H3 antibody. At the early four-cell stage, two out of four blastomeres exhibited strong nuclear staining for phospho-histone H3, and the other two blastomeres showed weak staining, suggesting that the former two blastomeres were still in late M phase and the latter had already entered G1 phase. In late four-cell-stage embryos, the phosphorylated form of histone H3 was detected in dots in the nucleus in both control and U0126-treated embryos. Thereafter, the U0126-treated, four-cell-

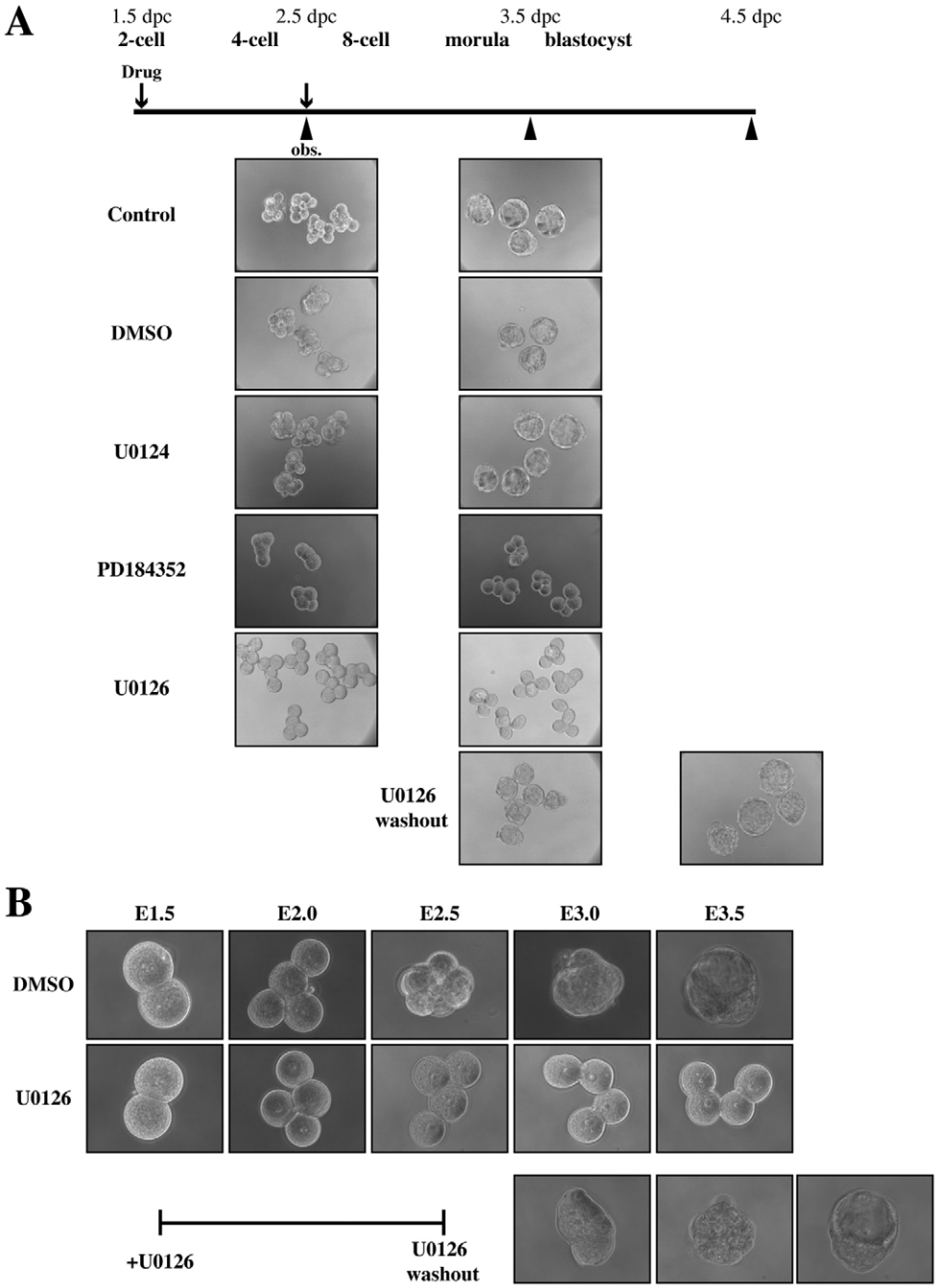

Fig. 1. Effect of U0126 and PD184352 on preimplantation development. (**A**) Schedule of mouse preimplantation development (top). At the time points indicated, embryos were treated with inhibitors (Drug, arrows) and observed (obs., arrowheads). The inhibitor was added at the late two-cell stage, and embryos were examined 1 day (2.5 dpc) and 2 days (3.5 dpc) later. The zona pellucida was removed before inhibitor treatment. (Below) Embryos treated with 20 μM U0126 or 5 μM PD184352 were compared with control embryos (control, DMSO and 20 μM U0124). Typical images of embryos are shown. The bottom row shows the results when U0126 treatment was allowed to continue for 24 hours but the drug was then washed out. Observation of these embryos took place at 2 and 3 days after initial treatment. (**B**) Reversibility of the inhibitor-induced developmental arrest. (Bottom right) Late two-cell-stage embryos shown in the bottom row were treated with 20 μM U0126 for 24 hours before the U0126 was washed out. The embryos were cultured in a drug-free medium and then observed until E4.5. The top two rows show control embryos, which were treated with DMSO (vehicle, top) or U0126 that was not washed out (middle). dpc, days post-coitum.

arrested embryos showed the same, dotted phospho-histone H3 staining pattern (Fig. 3B), suggesting that they did not enter M phase. Next, we performed Hoechst staining. In early four-cell or eight-cell-stage embryos, some blastomeres showed chromosome condensation (Fig. 3B, and data not shown). However, in U0126-treated, four-cell-arrested embryos, chromosome condensation was not observed (Fig. 3B). Taken together, these results demonstrate that U0126-induced developmental arrest at the four-cell-stage occurs at G2 arrest, just before M phase.

Next, we added U0126 to early two-cell-stage embryos to determine whether it induces arrest at the two-cell stage or the four-cell stage. As a result, the embryos did not proceed to the four-cell stage, and were arrested in the two-cell stage (Fig. 4A). Then, we performed the same experiments as above to determine a cell cycle phase in which the U0126-treated, two-cell-stage embryos were arrested. The results from BrdU incorporation (Fig. 4B), and cyclin B1 and phospho-histone H3 staining (Fig. 4C), experiments demonstrate that the U0126-induced developmental arrest at the two-cell stage also occurs at the G2 phase, just before M phase. Therefore, it is likely that ERK activity is essential for cells to enter M phase in very early embryonic cell cycles before compaction during mouse preimplantation development.

Because the ERK pathway is known to regulate gene expression, we examined the effect of inhibition of transcription on the early cell cycles. In agreement with a previous study with another inhibitor, α-amanitin (Clarke et al., 1992), treatment of late two-cell-stage embryos with the transcription inhibitor actinomycin D completely blocked development between the two-cell and four-cell

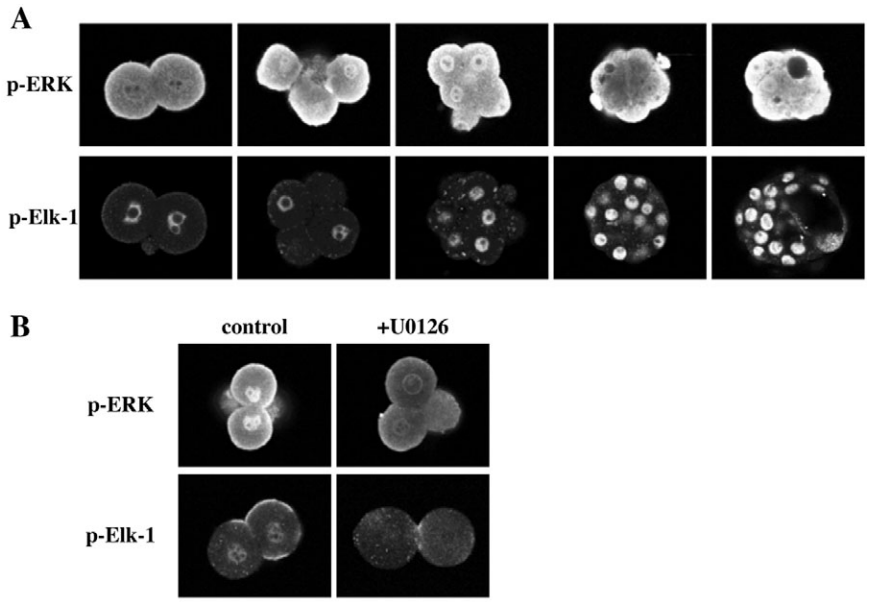

Fig. 2. ERK and ELK1 are phosphorylated during mouse preimplantation development. (**A**) Phosphorylated ERK (p-ERK, upper) and phosphorylated ELK1 (p-Elk-1, lower) were detected using anti-phospho-ERK antibody and anti-phospho-ELK1 antibody, respectively. Embryos (from left to right) at the two-cell, four-cell, eight-cell, morula or blastocyst stages were fixed and stained. Fluorescence was viewed with a confocal microscope. (**B**) Phosphorylation of ERK or ELK1 with or without U0126. Four-cell (top) and two-cell (bottom) stage embryos were treated with U0126 for 1 hour, and then the embryos were fixed and stained with either anti-phospho-ERK antibody (four cell) or anti-phospho-ELK1 antibody (two cell). Fluorescence was viewed with a confocal microscope.

stages (Fig. 5A). Therefore, normal cell division to the eight-cell stage requires de novo synthesis of mRNAs. To identify those genes whose expression levels are regulated by the ERK pathway during the early cell division stages, we performed the genome-wide analysis by using Affymetrix GeneChip oligonucleotide microarrays, which contain about 30,000 genes (about 45,000 probe sets). For this analysis, we collected embryos at six points, as follows: control embryos at day 1.5 (cont. 1.5, two-cell stage), day 2.5 (cont. 2.5, four- to eight-cell) and day 3.5 (cont. 3.5, morula to blastocyst); U0126-treated embryos at day 2.5 (U2.5, four-cell

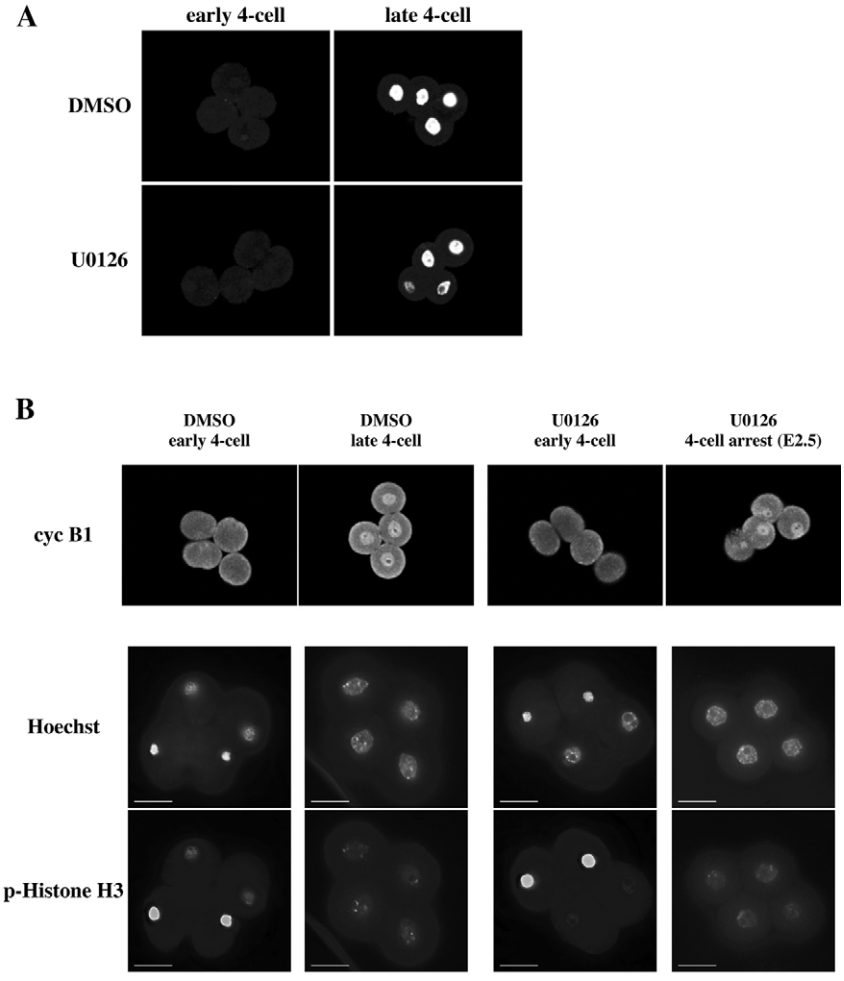

Fig. 3. ERK inactivation in late two-cell-stage embryos induces developmental arrest in the G2 phase, just before M phase in the four-cell stage. (**A**) BrdU incorporation into the nucleus was investigated. Late two-cell-stage embryos were cultured in the presence of BrdU and U0126 or BrdU and DMSO (control), fixed, and stained with anti-BrdU antibody. Fluorescence was viewed with a confocal microscope at the early and late four-cell stages. (**B**) Cyclin B1 (cyc B1) accumulation in the nucleus and phosphorylation of histone H3 (p-Histone H3) were examined. Late two-cell-stage embryos were cultured in the presence of U0126 or DMSO (control). Embryos were fixed and stained with anti-cyclin B1, Hoechst or anti-phospho-histone H3 antibody. Fluorescence was viewed with a confocal microscope (cyc B1) or a DeltaVision Image Restoration Microscope (Hoechst and p-Histone H3). Scale bars: 20 μm.

arrested); and embryos released from the U0126-induced arrest were collected at day 3.5 (U3.5, eight-cell) and at day 4.5 (U4.5, morula to blastocyst), as shown in Fig. 5B. We identified 6863 probe sets whose expression levels in cont. 2.5 or cont. 3.5 were increased or decreased by more than threefold as compared to those in cont. 1.5 with statistical significance in replicate experiments (see Fig. 5C). These probe sets included genes encoding NANOG and CDX2, which are known to be crucial for cell-lineage segregation during preimplantation development (Wang and Dey, 2006). Then, to analyze the gene expression program in the U0126-treated and released embryos, samples at six points were clustered according to their relative distances by using the above-mentioned 6863 probe sets (Fig. 5D). The obtained hierarchical clustering data showed that the gene expression profile in U3.5 embryos is most similar to

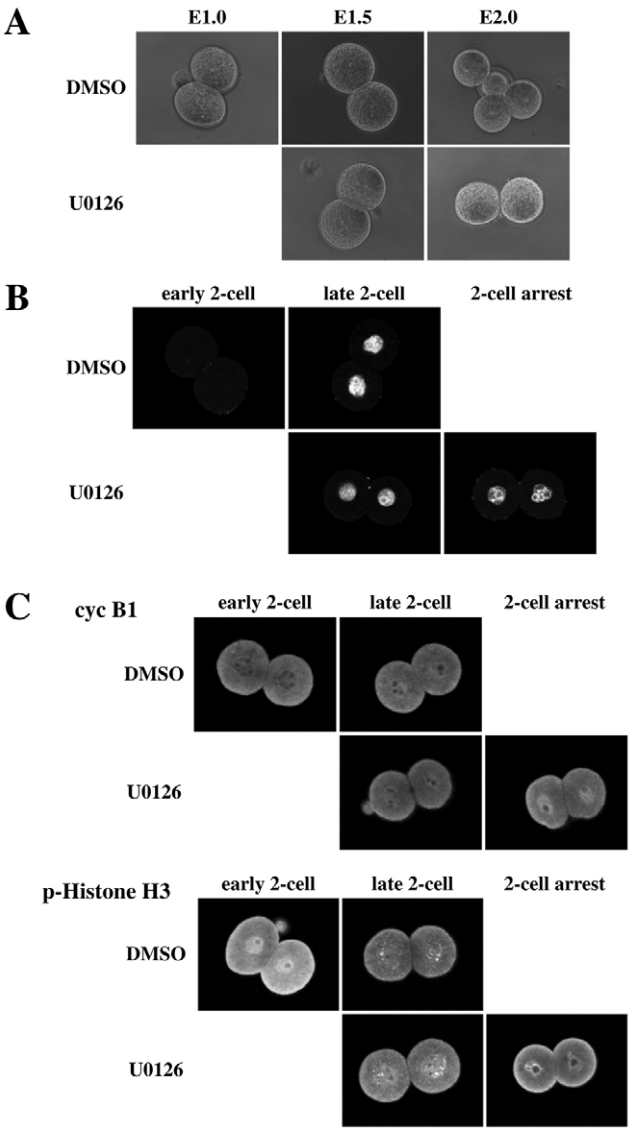

Fig. 4. ERK inactivation in early two-cell-stage embryos induces developmental arrest in the G2 phase, just before M phase in the two-cell stage. (**A**) Early two-cell-stage embryos were treated with 20 μM U0126 or DMSO, and embryos were observed from E1.0 to E2.0. The zona pellucida was removed before inhibitor treatment. (**B**) BrdU incorporation into the nucleus was investigated. Early two-cell-stage embryos were cultured in the presence of BrdU and U0126 or BrdU and DMSO (control), fixed, and stained with anti-BrdU antibody. Fluorescence was viewed at the stages indicated with a confocal microscope. (**C**) Cyclin B1 accumulation in the nucleus and phosphorylation of histone H3 were examined. Early two-cell-stage embryos were cultured in the presence of U0126 or DMSO. Embryos were fixed and stained with anti-cyclin B1 or anti-phospho-histone H3 antibody. Fluorescence was viewed with a confocal microscope at the stages indicated.

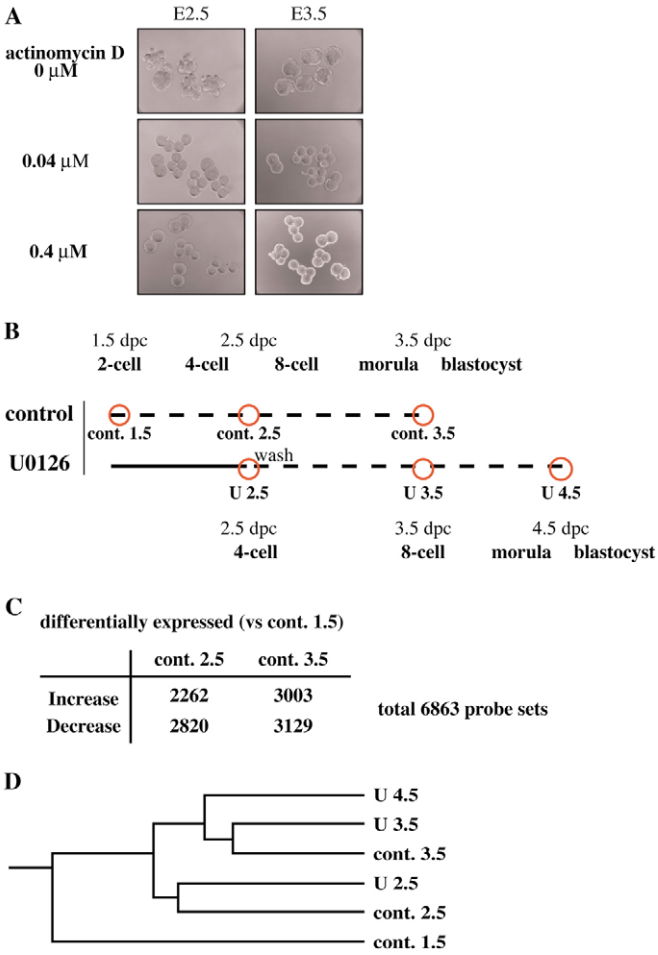

Fig. 5. The transcriptional program during mouse preimplantation development. (**A**) Actinomycin D completely blocked development. Two-cell-stage embryos were treated with actinomycin D (0.04 μM or 0.4 μM), and compared with control embryos (0 μM) at 24 (E2.5) and 48 (E3.5) hours after treatment. (**B**) Schedule of inhibitor treatment and of the microarray experiment. Solid and broken lines indicate the duration of U0126 and DMSO (vehicle) treatment, respectively. The inhibitor was added at the late two-cell stage, and embryos were collected for microarray experiments at the time points shown with red circles. (**C**) The numbers of genes whose expression levels in cont. 2.5 or cont. 3.5 were increased or decreased with statistical significance by more than threefold as compared with those in cont. 1.5 are shown. Because overlapping genes exist, in total, 6863 probe sets were differentially expressed. (**D**) Hierarchical clustering analysis showed the similarity in transcription profiles among the samples tested. This was performed by GeneSpring 7.3. dpc, days post-coitum; cont. 1.5/cont. 2.5/cont. 3.5, control embryos collected at day 1.5/2.5/3.5, respectively; U2.5, U0126-treated embryos collected at day 2.5; U3.5/U4.5, embryos released from the U0126-induced arrest, collected at day 3.5/4.5, respectively.

that in cont. 3.5, although U3.5 embryos (at the eight-cell stage) and cont. 3.5 embryos (morula or blastocyst) are in different stages of development. Similarly, the gene expression profile in U2.5 embryos is most similar to that in cont. 2.5. These results show that most of the programmed changes of upregulated and downregulated gene expression during the four- to eight-cell stages proceeded normally in the four-cell stage-arrested embryos, and therefore suggest that the gene expression program does not necessarily parallel the stages of embryonic development during the early cell division stages. Moreover, the results show that the ERK pathway regulates only a portion of gene expression programs, and suggest that the ERK-regulated genes might be involved in the cell cycle arrest.

To identify genes whose expression is regulated by the ERK pathway, we first defined ERK-dependent genes as genes whose change in expression level was reduced by more than half after the 24 hours of U0126 treatment. In those genes whose expression level in cont. 2.5 was increased or decreased by more than threefold as compared to that in cont. 1.5, we identified 420 and 109 probe sets as ERK-dependent, upregulated and downregulated genes, respectively. In addition, there were a number of genes whose expression level was not significantly changed from cont. 1.5 to cont. 2.5, but was changed by ERK inactivation; 173 and 64 probe sets were increased and decreased, respectively, more than threefold by U0126 treatment. These 237 probe sets were the second type of ERK-dependent genes. Both the first and second types of ERK-dependent genes were analyzed with respect to their gene ontology (GO-annotation) as given in NetAffyx (http://www.affymetrix.com/analysis/index.affx). The ERK-dependent genes were assigned to GO biological process categories, and 30 genes were found to belong to the 'cell cycle' category (Table 1), of which ten genes belonged to the 'M phase' category (Table 1). Six out of ten genes were in the first type of ERK-dependent genes (downregulated). The concentration of the 'M phase' category genes to the ERK-dependent genes (downregulated) was statistically significant (P=0.00569). Although the concentration of the 'M phase' category genes in the ERK-dependent genes might result from ERK-inhibition-induced G2 arrest, it is also possible that ERK regulation of these 'M phase' genes would be important for progression to M phase in the early embryonic cell division stages.

To identify genes whose expression profiles closely parallel the stages of embryonic development when arrested in the four-cell G2 phase and released to resume development, we further analyzed the ERK-dependent genes. Thus, genes whose expression levels in cont. 1.5, cont. 2.5 and cont. 3.5 (Fig. 6A, gray) were similar to those in U2.5, U3.5 and U4.5, respectively (Fig. 6A, yellow), were classified into eight groups (Fig. 6A). In Fig. 6B, the number of genes in each group, the expression pattern of each gene (left) and the average expression profiles for genes (right) in groups 1-8 are shown (see Table S1 in the supplementary material for a complete list of genes in groups 1-8). GenMAPP/MAPPFinder was used to examine the biological context (Doniger et al., 2003) and, for each group, pathways with the permute p-value less than 0.01 were searched for. As a result, two pathways were found to have a significant coherence

Table 1. ERK-dependent genes that belong to the 'cell cycle' category

	Entrez gene ID	Gene symbol	Description	GO:279: M phase
Upregulated I	12487	*CD28*	CD28 antigen	+
	15481	*HSPA8*	Heat shock protein 8	
	17869	*MYC*	Myelocytomatosis oncogene	
	19243	*PTP4A1*	Protein tyrosine phosphatase 4a1	
	20362	*SEPT8*	Septin 8	
	20843	*STAG2*	Stromal antigen 2	+
	50523	*LATS2*	Large tumor suppressor 2	+
	81004	*TBL1XR1*	Transducin (beta)-like 1X-linked receptor 1	+
	214498	*CDC73*	Vcell division cycle 73, PAF1/RNA polymerase II complex component, homolog (*S. cerevisiae*)	
Upregulated II	13000	*CSNK2A2*	Casein kinase II, alpha 2, polypeptide	
	15258	*HIPK2*	Homeodomain interacting protein kinase 2	
	26413	*MAPK1*	Mitogen activated protein kinase 1	
	98828	G431001I09Rik	RIKEN cDNA G431001I09 gene	
Downregulated I	14175	*FGF4*	Fibroblast growth factor 4	
	18861	*PMS2*	Postmeiotic segregation increased 2 (*S. cerevisiae*)	+
	23872	*ETS2*	E26 avian leukemia oncogene 2, 3′ domain	
	23955	*NEK4*	NIMA (never in mitosis gene a)-related expressed kinase 4	+
	30939	*PTTG1*	Pituitary tumor-transforming 1	+
	53892	*PPM1D*	Protein phosphatase 1D magnesium-dependent, delta isoform	
	72415	*SGOL1*	Shugoshin-like 1 (*S. pombe*)	+
	213389	*PRDM9*	VPR domain containing 9	+
	269582	*CLSPN*	Claspin homolog (*Xenopus laevis*)	
Downregulated II	12443	*CCND1*	Cyclin D1	
	14281	*FOS*	FBJ osteosarcoma oncogene	
	14853	*GSPT2*	G1 to S phase transition 2	
	17873	*GADD45B*	Growth arrest and DNA-damage-inducible 45 beta	
	23882	*GADD45G*	Growth arrest and DNA-damage-inducible 45 gamma	
	74213	*RBM26*	RNA binding motif protein 26	
	76499	*CLASP2*	CLIP associating protein 2	+
	83456	*MOV10L1*	Moloney leukemia virus 10-like 1	

The ERK-dependent genes were assigned to gene ontology (GO) biological process categories, and 30 genes were found to belong to the 'cell cycle' category, of which ten genes (denoted as +) belong to the 'M phase' category. I and II denote the first and second type of ERK-dependent genes, respectively.

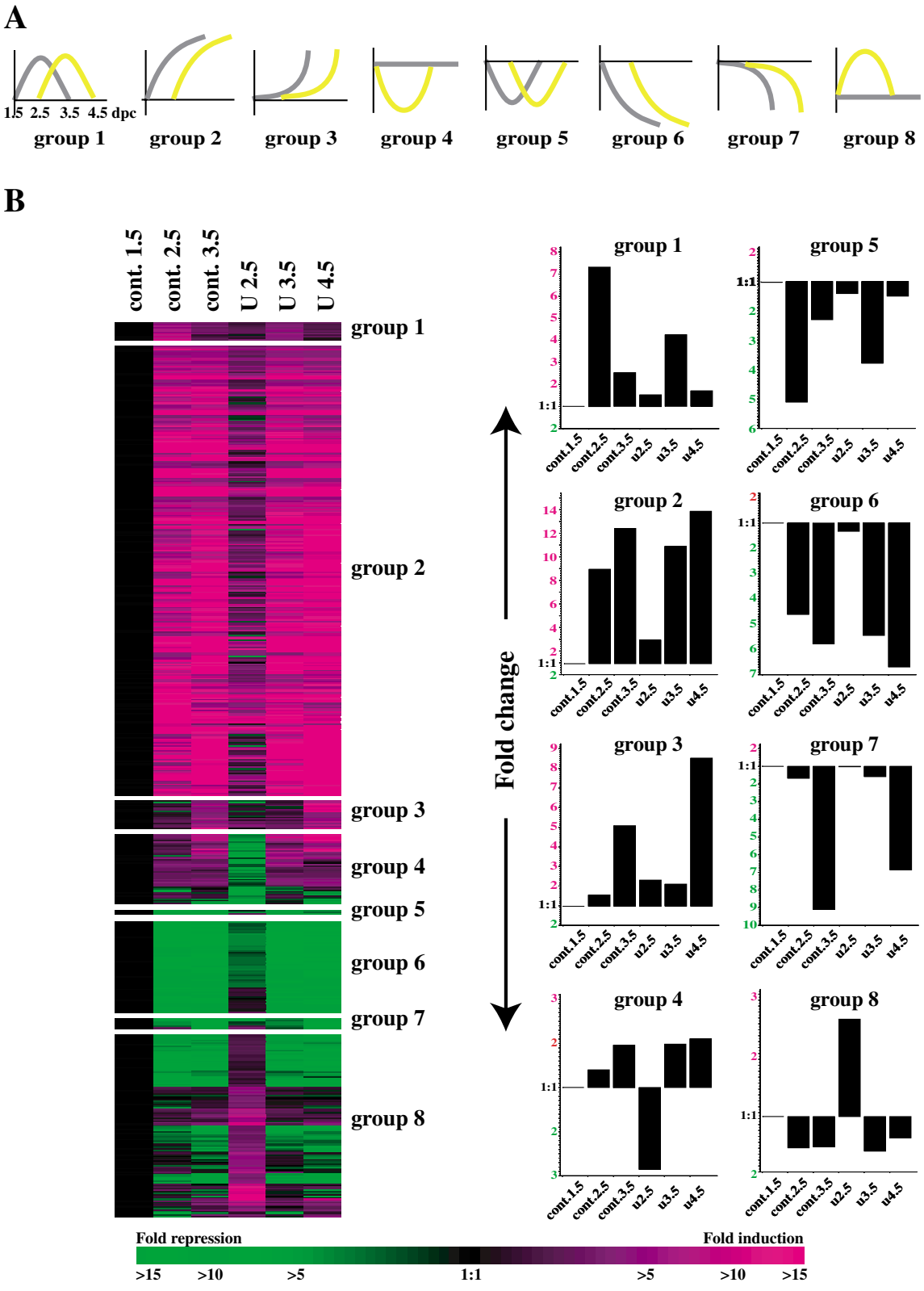

Fig. 6. Genes whose expression profiles closely parallel the stages of embryonic development. (**A**) ERK-dependent genes were classified into eight groups by their differing expression patterns. Gray and yellow lines show patterns of control and U0126-treated gene expression profiles, respectively. (**B**, left) The expression pattern of each gene in each of the eight groups is displayed as a horizontal strip. Each of the treatment groups in represented vertically. For each gene, the ratio of mRNA level in the indicated sample to its level in control embryos at day 1.5 (cont. 1.5) is represented by a color, according to the color scale at the bottom. (Right) The bar graphs show the average expression profiles for the genes in the corresponding groups (1-8). cont. 1.5/cont. 2.5/cont. 3.5, control embryos collected at day 1.5/2.5/3.5, respectively; U2.5, U0126-treated embryos collected at day 2.5; U3.5/U4.5, embryos released from the U0126-induced arrest, collected at day 3.5/4.5, respectively.

indicator in group 2: one is Mm_mRNA_processing_binding_Reactome (permute p-value=0.003) and the other is cell junction (permute p-value=0.006). The 'cell junction' pathway is intriguing, because our present result has shown that cell-cell adhesion is weakened in ERK-pathway-inhibited embryos, as described before. Then, we searched for genes that belong to the 'cell junction' category in all eight groups, and identified five genes, as shown in Fig. 7A. Because these five genes belong to group 2 or group 3, their expression is positively regulated by the ERK pathway. These genes encode products that participate in (i) tight junctions, which contribute to the epithelial barrier function by regulating the free diffusion of solutes between adjacent cells (CLDN4, OCLN) (Furuse and Tsukita, 2006); (ii) adherens junctions [ECAD (also known as CDH1 – Mouse Genome Informatics)], which mediate cell-cell adhesion, connect actin filaments to the cell surface and produce cytoskeleton-regulated cell communication (Takeichi, 1988); (iii) gap junctions [CX43 (also known as GJA1 – Mouse Genome Informatics)], which provide an intercellular communication pathway directly connecting adjacent cell cytoplasms (Evans et al., 2006); and (iv) desmosomes (DSG2), which connect intermediate filaments to the cell surface and mediate strong cell-cell adhesion (Kottke et al., 2006). The ERK-pathway-dependent upregulation of these genes might contribute to integrity and to strengthened cell-cell adhesion in four-cell to eight-cell-stage embryos. It is also possible that enhanced cell-cell adhesion could facilitate progression to the M phase during early cell division cycles (see below). Our analyses thus strongly suggest the importance of cell adhesion in the early cell division stages before compaction, in addition to the established role of cadherin in compaction (Takeichi, 1988).

These analyses suggested the possibility that inhibition of cell-cell adhesion, similar to inhibition of the ERK pathway, might induce cell cycle arrest in four-cell-stage embryos. To test this possibility, we added ECCD-1, the monoclonal antibody that inhibits Ca^{2+}-dependent cell-cell adhesion (Yoshida-Noro et al., 1984), to late two-cell-stage embryos. However, developmental arrest at the four-cell stage did not take place (data not shown). It is possible that inhibition of other types of cell-cell adhesion would also be needed to induce cell cycle arrest. However, we have found that ECCD-1 treatment potentiates the sensitivity of embryos to U0126 treatment. Thus, consistent with our previous results (Maekawa et al., 2005), U0126 addition in eight-cell-stage embryos did not significantly affect subsequent developmental processes (Fig. 7B). Similarly, ECCD-1 alone did not inhibit cell division or blastocyst formation when added to eight-cell stage embryos (Fig. 7B), although it did induce defects in compaction (data not shown). These observations are consistent with the previous report that embryos cultured in the presence of ECCD-1 remained uncompacted at the morula stage, but the morphology of the embryos became undistinguishable from that of control embryos at the blastocyst stage (Shirayoshi et al., 1983). However, when both U0126 and ECCD-1 were added, cell division arrest between the eight-cell to the 16-cell stages occurred (Fig. 7B). These results suggest that cadherin-mediated cell-cell adhesion should facilitate cell cycle progression.

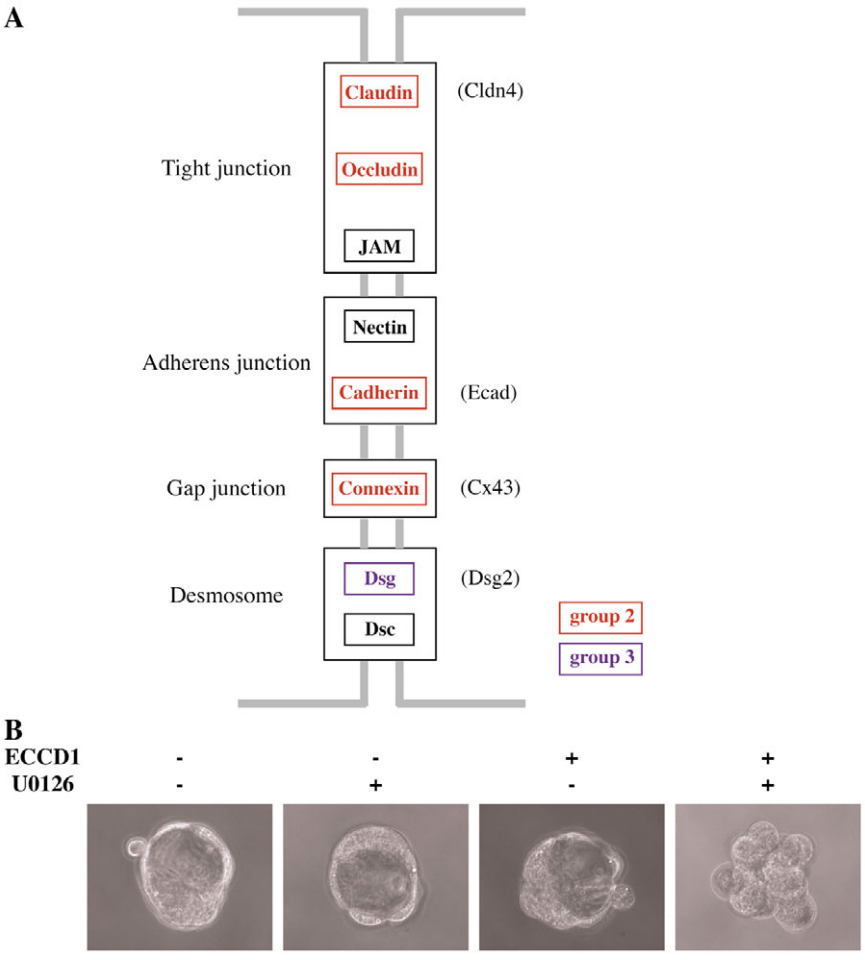

Fig. 7. Cell adhesion is important for early cell division cycles. (**A**) Genes that belong to the 'cell junction' category in all of the eight groups of ERK-dependent genes were searched for by using GenMAPP/MAPPFinder software, and five genes were identified (red and purple). In the diagram, genes were color coded by the expression patterns that we assigned to each group. The figure is based on the Kyoto Encyclopedia of Genes and Genomes pathway database (http://www.genome.ad.jp/kegg/), with slight modification. (**B**) ECCD-1 treatment potentiates the sensitivity of embryos to U0126 treatment. Eight-cell-stage embryos were cultured for 24 hours in the presence of either 20 μM U0126 or ECCD-1 or both, and were then observed. The concentration of ECCD-1 used in the experiment was 1:500.

DISCUSSION

Preimplantation development involves a number of biologically significant events, such as compaction and blastocyst formation, which represent morphologically dynamic changes. Although both compaction and blastocyst formation have been well examined, molecular mechanisms regulating the early cell division stages following these events remain unclear. In this study, we have shown that the ERK pathway is activated in the early cell division stages during mouse preimplantation development, and has an essential role in the G2/M transition during the cell cycle progression of 2-cell to 8-cell-stage embryos. This role of ERK MAPK is different from the one in mammalian cultured cells, in which ERK activity is involved in the cell cycle progression from G0/G1 to S phase (Lewis et al., 1998; Pearson et al., 2001; Pouyssegur and Lenormand, 2003). In addition, because it is also known that the ERK pathway plays an important role in producing M phase arrest in unfertilized vertebrate eggs (Gotoh and Nishida, 1995; Brunet and Maro, 2005), our present finding suggests that the role of the ERK pathway might alter after fertilization. Elucidating a molecular basis for the different roles of ERK MAPK in cell cycle progression in different situations should be performed in future studies.

Our microarray experiments have identified a set of cell cycle-related genes whose expression levels are increased or decreased by the inhibition of the ERK pathway (Table 1). These genes would be good candidates for transcriptional targets of the ERK pathway, which could regulate the G2/M transition during early cell division cycles. Moreover, our microarray analysis has demonstrated that the expression programs of most genes do not parallel the developmental stages before compaction, and that the expression programs of a subset of genes, particularly adhesion-related genes, correlate well with the cell cycle progression and/or the developmental stages. Clarifying the biological significance of the loose parallelism between the gene expression programs and the developmental stages, and the regulatory mechanisms of the expression of adhesion molecules, will provide new insights into preimplantation development.

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Supplementary material

Supplementary material for this article is available at
http://dev.biologists.org/cgi/content/full/134/15/2751/DC1

References

Brunet, S. and Maro, B. (2005). Cytoskeleton and cell cycle control during meiotic maturation of the mouse oocyte: integrating time and space. *Reproduction* **130**, 801-811.

Chang, L. and Karin, M. (2001). Mammalian MAP kinase signalling cascades. *Nature* **410**, 37-40.

Clarke, H. J., Oblin, C. and Bustin, M. (1992). Developmental regulation of chromatin composition during mouse embryogenesis: somatic histone H1 is first detectable at the 4-cell stage. *Development* **115**, 791-799.

Doniger, S. W., Salomonis, N., Dahlquist, K. D., Vranizan, K., Lawlor, S. C. and Conklin, B. R. (2003). MAPPFinder: using Gene Ontology and GenMAPP to create a global gene-expression profile from microarray data. *Genome Biol.* **4**, R7.

Evans, W. H., De Vuyst, E. and Leybaert, L. (2006). The gap junction cellular internet: connexin hemichannels enter the signalling limelight. *Biochem. J.* **397**, 1-14.

Favata, M. F., Horiuchi, K. Y., Manos, E. J., Daulerio, A. J., Stradley, D. A., Feeser, W. S., Van Dyk, D. E., Pitts, W. J., Earl, R. A., Hobbs, F. et al. (1998). Identification of a novel inhibitor of mitogen-activated protein kinase kinase. *J. Biol. Chem.* **273**, 18623-18632.

Furuse, M. and Tsukita, S. (2006). Claudins in occluding junctions of humans and flies. *Trends Cell Biol.* **16**, 181-188.

Gotoh, Y. and Nishida, E. (1995). The MAP kinase cascade: its role in *Xenopus* oocytes, eggs and embryos. *Prog. Cell Cycle Res.* **1**, 287-297.

Hamatani, T., Carter, M. G., Sharov, A. A. and Ko, M. S. (2004). Dynamics of global gene expression changes during mouse preimplantation development. *Dev. Cell* **6**, 117-131.

Kamakura, S., Moriguchi, T. and Nishida, E. (1999). Activation of the protein kinase ERK5/BMK1 by receptor tyrosine kinases. Identification and characterization of a signaling pathway to the nucleus. *J. Biol. Chem.* **274**, 26563-26571.

Kottke, M. D., Delva, E. and Kowalczyk, A. P. (2006). The desmosome: cell science lessons from human diseases. *J. Cell Sci.* **119**, 797-806.

Lewis, T. S., Shapiro, P. S. and Ahn, N. G. (1998). Signal transduction through MAP kinase cascades. *Adv. Cancer Res.* **74**, 49-139.

Maekawa, M., Yamamoto, T., Tanoue, T., Yuasa, Y., Chisaka, O. and Nishida, E. (2005). Requirement of the MAP kinase signaling pathways for mouse preimplantation development. *Development* **132**, 1773-1783.

Mody, N., Leitch, J., Armstrong, C., Dixon, J. and Cohen, P. (2001). Effects of MAP kinase cascade inhibitors on the MKK5/ERK5 pathway. *FEBS Lett.* **502**, 21-24.

Nagy, A., Gertsentein, M., Vintersten, K. and Behringer, R. (2003). *Manipulating the Mouse Embryo*. New York: Cold Spring Harbor Laboratory Press.

Natale, D. R., Paliga, A. J. M., Beier, F., D'Souza, S. L. A. and Watson, A. J. (2004). P38 MAPK signaling during murine preimplantation development. *Dev. Biol.* **268**, 76-88.

Nishida, E. and Gotoh, Y. (1993). The MAP kinase cascade is essential for diverse signal transduction pathways. *Trends Biochem. Sci.* **18**, 128-131.

Pearson, G., Robinson, F., Beers Gibson, T., Xu, B. E., Karandikar, M., Berman, K. and Cobb, M. H. (2001). Mitogen-activated protein (MAP) kinase pathways: regulation and physiological functions. *Endocr. Rev.* **22**, 153-183.

Pouyssegur, J. and Lenormand, P. (2003). Fidelity and spatio-temporal control in MAP kinase (ERKs) signalling. *Eur. J. Biochem.* **270**, 3291-3299.

Robinson, M. J. and Cobb, M. H. (1997). Mitogen-activated protein kinase pathways. *Curr. Opin. Cell Biol.* **9**, 180-186.

Shirayoshi, Y., Okada, T. S. and Takeichi, M. (1983). The calcium-dependent cell-cell adhesion system regulates inner cell mass formation and cell surface polarization in early mouse development. *Cell* **35**, 631-638.

Squires, M. S., Nixon, P. M. and Cook, S. J. (2002). Cell-cycle arrest by PD184352 requires inhibition of extracellular signal-regulated kinases (ERK) 1/2 but not ERK5/BMK1. *Biochem. J.* **366**, 673-680.

Sturgill, T. W. and Wu, J. (1991). Recent progress in characterization of protein kinase cascades for phosphorylation of ribosomal protein S6. *Biochim. Biophys. Acta* **1092**, 350-357.

Takeichi, M. (1988). The cadherins: cell-cell adhesion molecules controlling animal morphogenesis. *Development* **102**, 639-655.

Tanimura, S., Asato, K., Fujishiro, S. H. and Kohno, M. (2003). Specific blockade of the ERK pathway inhibits the invasiveness of tumor cells: down-regulation of matrix metalloproteinase-3/-9/-14 and CD44. *Biochem. Biophys. Res. Commun.* **304**, 801-806.

Wang, H. and Dey, S. K. (2006). Roadmap to embryo implantation: clues from mouse models. *Nat. Rev. Genet.* **7**, 185-199.

Wang, Q. T., Piotrowska, K., Ciemerych, M. A., Milenkovic, L., Scott, M. P., Davis, R. W. and Zernicka-Goetz, M. (2004a). A genome-wide study of gene activity reveals developmental signaling pathways in the preimplantation mouse embryo. *Dev. Cell* **6**, 133-144.

Wang, Y., Wang, F., Sun, T., Trostinskaia, A., Wygle, D., Puscheck, E. and Rappolee, D. A. (2004b). Entire mitogen activated protein kinase (MAPK) pathway is present in preimplantation mouse embryos. *Dev. Dyn.* **231**, 72-87.

Yoshida-Noro, C., Suzuki, N. and Takeichi, M. (1984). Molecular nature of the calcium-dependent cell-cell adhesion system in mouse teratocarcinoma and embryonic cells studied with a monoclonal antibody. *Dev. Biol.* **101**, 19-27.

Table S1. Array data for genes in groups 1 to 8

Group 1 **11 genes (12 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1418747_at	20375	Sfpi1	13.9±1.8	50.3±5.7	39±9.6	19.7±0.3	42±14.1	32±5.6
1455699_at			20.7±1.4	100.3±20.7	54.3±3.2	27.4±8.3	63.6±14.8	32±6.6
1437694_at			73.4±10.1	363.9±77.2	165.5±5	125.1±16.8	224.8±28.7	134.7±53.4
1435070_at			91.7±5.9	466.6±70.6	222±45.4	218.5±64.5	292.6±41.4	155.9±18.9
1420688_a_at	20392	Sgce	17.5±7.8	108.8±16.6	48.7±2	36.5±12.5	74±2.3	29.2±5
1436585_at			102.4±4.7	672.4±175.6	317.3±67	161.5±96.5	419±49.5	175.7±18.1
1417342_at	66849	Ppp1r2	16.7±0.1	113.8±43.8	49.4±6.2	40.2±6.9	78.6±28.6	36.8±5.3
1437502_x_at	12484	Cd24a	28.4±1.6	213.5±28.8	34.2±16.5	26.1±6.7	121.7±45.7	40.5±3.3
1433789_at			352±40	2727.1±634.7	671.5±115.3	429.9±82.7	1428.6±304	358.4±55.2
1448182_a_at	12484	Cd24a	39.1±5.9	336.8±34.8	55.2±23.9	54.1±19.4	175.2±42.8	88.4±13.5
1428583_at	68564	1110001M19Rik	125.8±26.4	1256.2±134.7	575.5±211.1	187.3±137.7	827.7±163.7	427.9±105
1441298_at			11.9±0.2	126.5±39.7	25.4±3.3	41.7±9.3	44±9.9	13.4±0.6

Group 2 **248 genes (293 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1450937_at	22343	Lin7c	265.2±7.6	1183.4±139.7	1246.6±115.3	685.4±57.1	819.8±111.3	819.6±164.8
1437658_a_at			51.4±0.8	193.3±41.7	196.3±27.2	52.4±14.6	159.1±10.9	271.6±24.7
1438230_at	225467	Pggt1b	17±3.9	82.8±21	61.8±1.9	17.1±1.9	53.9±14.7	98.2±28.5
1435139_at	74838	Narg1	17±5.6	66.5±0.7	136.8±5.1	63.9±12.7	55±0.4	138.8±3.5
1447171_at			7.8±0.2	63.1±1	35±15.8	14.3±6.3	27±4.8	40.6±11
1436067_at	229055	Zbtb10	83.2±1.7	577.6±67.4	296.2±0.6	233.7±87	295.7±10.1	466.9±5.2
1447122_at			25.1±8.6	90.2±6.4	168.3±44.3	28.1±2.1	90.6±6	101.3±10.5
1452864_at	329650	Med12l	84.6±27.8	293.6±19.2	577.5±29.3	108±27.1	306.6±30.6	909.8±55.2
1420879_a_at	54401	Ywhab	512.4±171.1	2214.3±191	1742.2±179.9	833.1±174.2	1863.3±434.5	2068.9±437.6
1452712_at	229279	Hnrpa3	251.9±4.3	838.9±55.8	805.9±28.7	479±20.1	919.7±175.3	1078.5±103.6
1435881_at	18521	Pcbp2	57.7±13.7	253.2±28.2	174.8±15.4	72.2±13.1	216.3±58.8	363.2±94
1457079_at			5.2±0.1	21.7±0.4	25.2±2.4	7.5±2.9	19.7±2.1	21.8±2.6
1437593_x_at	11800	Api5	2060.4±467.8	8827.8±502	9320±309	4520.2±94.8	7975.3±987.3	7051.6±18.2
1428362_at	77989	E130105L11Rik	229±79.9	1107±125.5	786.7±38	163.4±54.5	889.4±25	1003.2±145.3
1437714_x_at	59025	Usp14	152.1±17.3	639.2±114.8	819.2±14.5	287.3±36.7	602.7±83.2	522.7±94.5
1448526_at	16211	Kpnb1	315.4±156.6	2002.5±1.2	1142.2±129.3	703.7±127.4	1249.9±56.3	1512.4±383
1420478_at	53605	Nap1l1	597.4±87.7	3005.7±317.3	3042.9±275.6	1698.7±40.9	2380.3±430	2402.9±212
1438671_at			11.6±1.8	82.3±5.6	64.3±3.2	18.5±1.5	46.8±11.1	39.4±13.1
1440085_at			9.8±4	33.5±9.7	33.5±5.4	12.5±1.4	39.9±2.2	48.7±0.3
1435235_at	53382	Txnl1	58.8±6	226.3±11.9	408.4±65.7	104.5±8.4	244±49	540.8±25.7
1418515_at	17765	Mtf2	546.6±193.9	2293.1±315.9	3301.2±771.8	953.8±180.5	2295.1±91.1	2788.4±33.6
1424723_s_at	228410	Cstf3	155.7±46.5	639.8±136.5	772.3±139.4	221.9±44.4	655.5±43	583.8±110.8
1438650_x_at	14609	Gja1	1303.9±348	6327.2±351.8	6508.1±20.8	3163.3±600.4	5760.7±272.9	4533.2±174.3
1422045_a_at	19248	Ptpn12	700.3±53.3	3183.9±206.5	3849±184.8	1556.3±373.1	3094.1±245.1	2885.8±12.1
1432418_a_at	12716	Ckmt1	7.9±0.4	36.7±15.9	29.9±8.6	10.1±0.3	35.6±4.1	54.2±11.5
1437533_at	11798	Birc4	115.7±49	644.6±21.3	478.9±37.4	227.6±55.7	522±26	483.6±62.1

1417404_at	170439	Elovl6	572.3±155.6	2588.1±278.5	2542.7±417.1	1025±5.6	2585.9±49.7	4209.4±24.5
1435335_a_at	432486		256.8±21.2	1463.3±11.5	1202.1±21.9	547.5±89.3	1176.9±21.4	846.4±17.3
1458303_at	225743	Gm96	17.7±5.1	93.2±29.1	84.5±5.7	40±4.1	81.5±17.5	55.3±3.9
1429581_at	229211	Acad9	12.6±0	44.9±10.8	111.2±11.5	41.4±5.7	58.3±7.2	80.8±18
1441709_at			12.2±0.6	146.5±61.7	39.7±0.8	40.8±2.6	57.1±11.9	41.2±8.7
1415972_at	17118	Marcks	7.1±0.7	23±2.9	58.4±13.6	7.5±0.5	33.6±0.9	65.5±1.3
1434691_at	72193	Sfrs2ip	11.5±0.1	45±15	101.9±18	10.2±1.3	54.8±4.5	103.3±12.9
1448880_at	22195	Ube2l3	55.7±1	269.5±7.7	229±42.2	110.8±35.5	264.8±18.3	355.4±50.7
1429771_at	73201	3110073H01Rik	67.2±18.4	395.7±77	398.1±33.2	144.7±30.4	322.1±44.2	272.7±20.4
1444726_at			17.8±6	77.5±24.3	84.9±6.7	28.4±8.8	87.9±8.1	72.7±0.2
1455789_x_at			5436.9±2083.9	26759.9±1113.6	30644.5±2254.3	9926.7±4024.9	27496.2±677.3	25353.8±765.6
1442062_at	319898	7120426M23Rik	6.5±0.5	33.8±2	50.5±6.1	14.4±6.1	32.8±0.4	62.9±9.6
1426527_at	68276	Toe1	120.5±12.2	595.5±10	844.4±114.2	226.2±61.7	663.7±246.5	721.2±147.6
1416505_at	15370	Nr4a1	21.5±5.5	70.2±8.4	101.3±8.9	28.5±1.1	119±32.3	84.5±2.1
1437215_at	214254	Nudt15	11.7±2.5	122.1±17.4	61±14.2	49.1±10.9	65.7±8	64.5±8.3
1451228_a_at	68416	Sycn	10.8±0.7	112±26.4	74.3±13.2	40±13.5	60.6±4.8	188.2±21.6
1451046_at	22761	Zfpm1	15.9±1.3	50.6±8.5	62±8.1	13.7±2.4	90.1±22	49.3±10
1453016_at	72938	2900042B11Rik	28±4.5	152.5±15	196.9±58.6	65.9±22.3	159.1±7.3	296.2±50.9
1420504_at	56774	Slc6a14	20.2±1.2	74.3±34.2	161.2±11.9	16.1±2.3	115.4±9.1	350.5±112.6
1437181_at			7.2±0.3	41.6±16.4	64.7±9.5	12.3±6.9	41.2±0	57.6±9.7
1451626_x_at			261.1±33	1657.4±111.5	1952.3±533.1	464.7±140.9	1502.3±112.2	834.9±62.9
1426548_a_at	66632	Atpbd4	18.6±5.5	73.5±11.4	118.4±43	14.8±6.4	107±37.8	110.7±4.8
1448270_at	56200	Ddx21	149.6±42.5	1258.8±20.1	1073.7±287.5	568.4±96.1	864.9±53.6	606.8±4.5
1454816_at	19889	Rp2h	18.8±2.4	81.4±10.8	177.2±43.3	20.5±3.6	109.7±8.1	131.8±39.9
1420907_at	12488	Cd2ap	139.4±15.6	534.6±24.6	1337.9±408.9	206±59.5	815±2.8	1651.7±21.4
1417914_at	74012	Rap2b	45.9±3.2	138.6±39.2	250.2±14.9	55.8±7.9	269.7±69.4	317.5±66.9
1457026_at	239759	Liph	7.6±0.8	37.5±2.2	38.8±2.3	18.6±5.3	45±5.5	53.4±14
1434513_at	224088	Atp13a3	354.5±87.3	1967±162.1	2821.9±359.6	947.7±112.5	2122.4±291.8	2067.9±60
1438695_at			12.3±1	38±13.2	148.7±10.1	11.1±2.9	74.1±4.2	126±36.4
1433521_at	433667	Ankrd13c	123.2±29.8	1300.8±2.4	889.2±82.4	706±79.1	743.4±29.6	873.4±185.5
1448829_at	67241	Smc6l1	16.9±7.1	160.7±41.3	104.6±2.8	23.8±13.8	102.3±37.6	135.7±19.9
1452654_at			8±3.5	117.9±4.6	70.5±10.1	24.2±4.4	48.3±1.4	71.4±25.6
1429940_at	214498	Cdc73	10.9±4.2	65±36.3	81.6±6.4	9.3±0.3	66.1±9.6	64.2±24
1438945_x_at	14609	Gja1	1118.8±313.6	7193.6±693.5	7896.6±515.8	2873.3±982.2	6862.9±295.8	4710.5±615.4
1433503_at			13.1±3.1	63.7±3.3	159±73.9	14.2±3.9	82±44.2	318.3±0.5
1456012_x_at			982.5±39	4432.4±952.6	6378.9±124.5	2230.1±415.6	6146.6±45.2	4075.2±176.6
1416288_at	15502	Dnaja1	2315.2±462.5	12871±795	13749.1±76.5	6919.5±293.3	14651.9±2390.7	8735.1±1453.3
1422071_at	16857	Lgals6	224.7±21.3	817±166.3	1702.1±795.1	136.7±11.5	1425.2±268.6	2643.1±1016.2
1438971_x_at			85.4±9.9	299.5±1.9	412.6±98.1	136.4±30.6	546.8±4.6	1014.7±53.7
1452199_at	72649	2700094F01Rik	26.1±2.8	161.3±76.8	149.3±9.9	44±2.8	167.4±18.9	128.9±22.1
1424438_a_at	230514	Leprot	25.3±6.7	83.4±14	268.8±100.9	32.8±0.3	162.9±18	441.9±81.4
1417818_at	97064	Wwtr1	72.6±30.7	564.4±67.4	545.1±86.4	168±6.7	470.8±53.9	619.9±129.3
1417386_at	19155	Npepps	13±1.3	47.8±11.3	88.5±0.5	14.9±0	86.8±9.4	162.4±36.7
1455173_at			11.7±6.2	91.8±7.1	118.9±14.9	24.5±2.6	80.6±7.6	113.8±26
1449108_at	14148	Fdx1	667.7±53.8	2996.2±147	4699.2±923.6	1230.4±257.1	4617±148.1	2024.3±304.1

1428585_at	109711	Actn1	139.5±21.2	670.2±55.1	807.5±64.4	336.5±14.5	991.6±48.5	926±19.5
1437290_at	242291	Impad1	8.8±2.6	45.2±0.1	91.9±24.9	14.5±5.5	63.5±14.6	94.8±18.7
1437885_at	99324	D030029J20Rik	8.2±0.8	31.8±14.3	57.6±17.7	9.6±1.2	58.9±0.3	74.6±28
1422698_s_at	16468	Jarid2	677.6±152.7	4557.6±825.8	5571±386.3	1823.8±397.7	4985.9±259.7	7574.7±612.9
1434170_at	245404	Wdr40b	18.9±8.9	259.1±96.7	87.4±7.2	64.8±2	139.7±16.6	63.2±2.8
1424448_at	633467	Trim6	33.1±7.6	453.9±36.2	249.3±47.9	166.5±16.1	244.6±38.9	323.1±60.4
1456028_x_at			30.1±8.3	173.3±50.4	304.6±33.8	53.9±14	223.4±55.4	324.4±116.8
1448252_a_at	55949	Eef1b2	2089.7±309.6	14760.3±249.9	19616.4±1971.9	6363.4±176.7	15584.1±976.3	16074±1887.8
1458675_at			9.3±0.1	140.5±35	112.2±51.9	19.6±11.7	70.1±37.8	114.6±5.3
1449625_at			12.5±1.3	177.9±37.7	60.4±21.8	44.4±5.2	94.9±14.6	146.9±12
1443816_s_at			11.8±2.3	83.9±26.8	119.6±26.1	13.3±5.2	91.3±0.9	77.3±10.1
1456830_at			6.5±0.1	65.4±1.7	19.5±5.2	6.8±0.4	50.2±13.4	23.2±11.3
1427541_x_at	15366	Hmmr	11.7±0.2	41.2±2.9	115.9±33.1	24.5±1.4	90.8±4.4	152.6±9
1434039_at			39.3±7	381±36.9	389.1±107.5	71.4±9.1	304.8±6.6	404±23.8
1426750_at	286940	Flnb	76.8±28.5	395.3±59.9	492.4±67.9	124.1±36.2	608.7±254	733.9±154.4
1455002_at	19243	Ptp4a1	88.6±20.2	566.3±74	572.2±12.8	201.2±47.6	704.4±137.8	648.2±65.2
1427893_a_at	68603	Pmvk	54.1±6	230.4±16.3	721.3±203.3	90.1±8.4	432.5±114.6	818.9±69.2
1435627_x_at	17357	Marcksl1	50.2±27.2	347.6±0	370.5±47.8	120.9±13.3	402.6±37.6	465.2±41.3
1434716_at	171283	Havcr1	64.2±2.8	540±138.1	566.3±27.8	124.9±89.9	517.6±44.7	4168.2±737.2
1424200_s_at	72124	Seh1l	110.2±8.4	942.5±137.1	900.3±56.8	471.4±101.5	890.6±7.5	794.6±210.4
1417443_at	230579	BC026682	32.1±3.9	221.9±45.1	278.3±52.2	57.4±7.2	259.9±103.1	218.8±43.2
1438922_x_at	433326; 630624	Slc25a5	343.7±47.3	2280.3±162.4	4017.8±250.1	714.8±36	2793.7±499.3	3119.3±620.8
1433831_at	75763	4833418A01Rik	9.5±1.1	74.9±13.9	82.5±0.4	39.5±11.2	77.7±5.4	75.8±8
1441376_at	93739	Gabarapl2	16.2±5.8	150.5±69.8	155.7±40.1	27.1±16.8	134.5±22.5	136.5±6.6
1434418_at			33.3±8.8	135±25.8	250.7±26.3	23.4±5.7	276.3±27.9	288.7±15.3
1420622_a_at	15481	Hspa8	1409.2±1093.9	10564.6±2140.9	13369.2±4193.2	1706.3±69.8	11750.4±1766.7	9828.7±1982.5
1428136_at	20377	Sfrp1	15.1±4.2	319.2±49.8	102.5±20.6	75.8±14.1	126.1±2.6	48.9±3.7
1438021_at			32±2.7	234.6±94.8	305.3±52.2	90.6±0	275.1±12.6	257.9±77.6
1433624_at	227723	5830434P21Rik	14.9±4.1	65.6±22.5	142.3±33.1	23.7±4.6	128.2±15.1	243.7±14.3
1426649_at	230157	Tmeff1	10.7±1.4	63.9±17	102.2±29.8	21.8±3.1	91.8±21.4	61.7±0.8
1431012_a_at	23986	Peci	21.6±5.2	138.7±5.1	246.4±87.5	34.3±10.1	187.4±30.6	387.9±68.5
1428323_at	14571	Gpd2	57.7±21.2	884.1±17.1	615.3±131.1	289.1±100.3	503.6±1.3	721.4±2.1
1438546_x_at	433326; 433923; 623402; 630624; 633283	Slc25a5	85.4±9.3	592.8±115.2	1060.9±170.6	165.1±20.9	758.5±114.5	1038.5±89.2
1438360_x_at	433326; 630624	Slc25a5	583.6±47.4	3920.2±552.5	7235.1±736.5	1042.1±127.3	5207.7±922.9	6023.9±1353.5
1448469_at	630776	Nid1	9.8±1.7	137.8±3.5	75.8±20.2	34.6±13	87.8±30.3	72.4±0.3
1415800_at	14609	Gja1	671±183.6	5919.9±485.3	7425.5±52.2	2218.9±1036	6032.3±195.8	3885.3±369.6
1419571_at	114304	Slc28a3	9.8±3.1	54.8±3.9	115.4±7.4	20±5.6	88.5±23.3	376.2±91.4
1423723_s_at	230908	Tardbp	344.4±6.8	4728.1±453.2	3831.5±1389.2	1902.5±177	3135.9±802.9	3060.5±162.4
1443624_at			7.3±0.1	65.1±4	90±45.7	14.9±2.6	66.7±5.6	140.2±23
1428752_at	233836	Slc5a11	22.5±2.6	138.6±92.1	195.2±13.6	20±3.5	205.8±79.7	116.8±10.5

1426682_at	104625	Cnot6	79.5±24.7	841.9±158.1	856.8±116	345.2±33	736.6±35.4	574.8±2.8
1452123_s_at	232288	Frmd4b	31.4±7.5	166±82.4	953.2±352	27.5±11.7	294.5±103.6	1284.4±145.2
1435777_at			8±1.6	28.8±4.9	164.5±8.8	34.9±9.7	75.5±2.4	218.6±29.8
1455134_at			8.2±0.6	85±4.7	120.9±11.3	29.2±3.7	77.8±5.2	169.3±32.3
1428823_at	69692	Hddc2	13.1±0.4	78.7±0.9	138.6±12.4	35.5±4.8	125±32.4	202±36.1
1426441_at	18174	Slc11a2	14.3±1.1	285.8±19.2	76.6±17.6	56.8±11.9	137.2±29.1	84.5±15.1
1455223_at	140486	Igf2bp1	17.6±5.9	98.1±27.8	203.4±43.6	25.6±10.6	171.1±46.9	316.7±5.7
1449288_at	14562	Gdf3	17±3.2	118.1±57.5	153±28.7	10.7±1.5	166±90.7	114±16.7
1418479_at	245944	Vps54	58.9±7.2	356.5±38.1	891.2±122.4	109.2±20.1	574.5±60.6	949.5±119.6
1440220_at			14.3±0.2	132.6±16.3	101.7±42.1	48.8±11.7	140.8±15.2	136.9±4.9
1450989_at	21667	Tdgf1	29±18.8	873.8±64.2	383.6±80.3	177±94.5	287.9±40.4	1135.7±332.4
1427564_at	54004	Diap2	8±2.5	169.4±82.6	112.8±31.4	8.3±2.9	79.4±3.7	74.1±25.1
1451468_s_at	72322	Xpo5	9.6±1.7	69.4±2.8	111.7±10.1	31.8±2.9	96.6±7.2	66.5±0.6
1416041_at	20393	Sgk	406.9±66	6795±32.7	4486.7±1255.3	2872±893.8	4089.2±590.2	5194.8±880.3
1435450_at	70568	Cpne3	24±5.7	351.7±50.1	335±23.5	123.5±32.6	242.4±7.7	774.2±194.7
1416630_at	15903	Id3	10.5±2.7	312.4±152.8	51.8±1.1	35.5±2	105.8±51.7	75±9.8
1435415_x_at	17357	Marcksl1	34.4±7.2	224.3±7.4	293.4±7.4	90.2±7.2	347.3±9.9	365.7±90.9
1449052_a_at	13436	Dnmt3b	204.6±48.9	1533±126.9	2015.5±137.8	456.6±32.3	2088.1±405.9	3277.5±216.1
1452740_at	77579	Myh10	514.6±32.1	2159.1±528.8	6725.2±2071.6	740.7±1.9	5286.8±219.9	14976.7±1076.8
1435104_at	100255	D130004H04Rik	6.6±0.6	45.5±15.6	80.9±17.5	9.9±5.3	68±1.8	131.2±4.2
1436971_x_at	22631	Ywhaz	381.6±135.8	2284.9±209.7	5320.3±891.6	935.3±69.9	3946.5±336.2	5022.8±74.1
1448299_at	20510	Slc1a1	76.8±14	721.3±55.9	710.2±37.1	284.3±0.8	807.5±5.4	534.5±88.5
1425332_at	20402	Zfp106	85.1±29	1165.3±163.9	1260.8±164	483.1±125.2	897.9±51.6	1592.7±182.3
1450853_at	21888	Tle4	194.2±31.2	3634±84.6	2059.8±19.3	1670±148.8	2050.8±214.8	1957.9±83.1
1418417_at	17681	Msc	9.5±0.8	76.1±36.3	157±10.2	21.5±1.1	100.9±34.5	92.3±16.1
1444456_at			6.9±0.7	66.7±17.5	57.4±4.7	22±6	72.9±8.9	83.7±0.2
1435374_at			8.1±3	87.6±70.9	229±12.4	9.2±0.2	86.4±23.9	214.9±90.1
1422851_at	15364	Hmga2	182.2±42	2449±145.4	2525.8±473.2	490.6±108.6	1976.3±47.2	1872.7±113.9
1437338_x_at	74195	Elp3	8±0.6	76.2±17.6	95±16.4	32.1±9.6	87.3±9.2	70.1±13
1421849_at	20843	Stag2	204.2±3.5	3494.7±183.7	2394±643.7	1343.4±151.1	2224.2±50.6	1514.8±20.1
1419351_a_at	67669	0610007P06Rik	149.8±4	934.8±121.8	2046.7±154.7	477.7±70.5	1665.6±384.8	1699.7±271
1450780_s_at	15364	Hmga2	79.7±0.7	1219.7±54.7	1191.8±208.1	284±87.7	886.5±136.6	817.2±0.2
1429488_at	68268	Zdhhc21	7.5±0.6	41.7±4.6	140.9±3.7	8.3±0.3	84.2±2.4	204.9±19.2
1448573_a_at	26366	Ceacam10	24±2	96.1±14.4	371.8±61.8	11.3±3.2	269.2±21.9	263.2±64.9
1418351_a_at	13436	Dnmt3b	32±7.6	294.5±45	391.6±56.7	64.4±6.9	361.7±46.7	552.3±79.9
1429556_at	269987	2610024B07Rik	17.5±9	273.2±10.7	264.1±10.4	100.1±18.7	200.4±8.1	303±36.3
1418703_at	56878	Rbms1	5.7±3	60±5.7	121.7±2.2	10.6±1.3	65.1±21.4	299.8±16.1
1441751_at			7.1±0.7	86±22.6	97±21.8	5.9±1	81.2±18.3	81.2±2.8
1420623_x_at	15481	Hspa8	1168.3±636.7	12108.9±2110	13921.6±1994.7	2294.9±133	13729.5±3146	11623.7±2468.3
1455819_at			58.6±19.4	455.5±115.5	683±53.5	141±41.2	694.5±192.3	1286±164.1
1437185_s_at	19240	Tmsb10	1286.2±509.5	7714.5±406.4	14272.6±189	2504.8±788.1	15326.8±931	23782.1±593.5
1428670_at	72520	2610305J24Rik	20±2.1	192.4±13	192.5±38.3	39.4±15.7	244.4±44.8	226.6±64.4
1438545_at	433326; 433923; 623402;	Slc25a5	32.7±1	350±83.1	613.1±65.9	62.7±30.2	407.5±114.3	554.6±64.6

	630624; 633283							
1419821_s_at	15926	Idh1	18.1±1.3	211.8±28.9	308.2±21.2	44.1±21.8	227.3±13.8	397.9±108.3
1448261_at	12550	Cdh1	172.7±65	1701.6±147.4	2614.1±395.4	588.7±129.1	2179.1±195.2	3433.6±488.5
1435223_at	244373	Spfh2	13.8±2.3	124.4±6.1	271.2±11.4	66.4±21.6	174.5±0.1	245.3±27
1454899_at	210126	Lpp	6.9±0	24.1±9.4	118.8±8.4	8.9±0.2	87.2±9.4	187.7±16.3
AFFX-b-ActinMur/M12481_3_at			1230.1±238.4	9088.9±230.5	18019.7±2693.3	4214.3±880.9	15707.3±1592.3	25026.1±1407.4
1433683_at	77411	Rbm35b	46.6±17.3	1050.6±128.5	585.9±88.9	365.7±45.2	600±46.2	616.4±82.7
1434548_at	26943	Serinc3	24±1	262.3±0.9	195.9±13.5	81.2±18.7	312.2±100.1	193.9±19
1422697_s_at	16468	Jarid2	288.4±177.7	3562.2±37.5	4564.8±61	1134.3±128.6	3757.1±142.9	6173.4±484.2
1418538_at	105785	Kdelr3	11±0.7	104.1±25.7	119.1±17.4	23.7±2.4	144.2±82.8	106.7±42.8
1426566_s_at	57890	Il17re	16.3±2.9	94.6±23.6	148.8±24	21.7±9.7	214.2±61.4	383.7±116.4
1434803_a_at	68416	Sycn	17.8±6.7	483.7±38.5	285.3±19.2	148±72.8	235.7±56.5	609.6±121.9
1426402_at	56403	Syncrip	62.6±30.5	1299.4±69.9	898.9±185	420.9±148.2	855.6±74.4	557.9±44.8
1455294_at			79.8±13.9	1216.4±23.7	1365.7±205.3	565.7±2.2	1092.7±195.3	578.4±96.1
1420913_at	24059	Slco2a1	24±7.1	168.9±94.8	319.9±64.1	24±2.3	329.5±43.7	256.1±38
1428339_at	68219	Nudt21	11.3±5.4	99.9±29.9	122.4±20	16.6±7.7	156.1±12.1	185.7±49.2
1450781_at	15364	Hmga2	187.7±18.6	4008.5±322.7	3289.2±684.2	869.8±19.8	2617.8±184.8	2096.1±32.1
1424650_at	72599	Pdia5	103.7±21.3	1056±98.3	1575.6±5.9	267±32.6	1451.5±56.5	1329.8±101.2
1436194_at	77619	C330008K14Rik	86.1±10.2	613.1±174.1	1530.4±292.5	216.7±55.1	1210.1±267.5	298±15.2
1449576_at	66235	Eif1ay	7.1±1.4	175.5±17.4	101.8±17.2	73.3±27.9	99.4±26.8	69.9±1.6
1417143_at	14745	Edg2	6.7±1.3	205.9±49.1	84.7±14.6	54±23	95.5±22.3	91.8±9.5
1445007_at			22.2±1.6	842.1±33.7	322.7±28.3	188.3±52.3	315.9±22.2	181.8±48.1
1417227_at	72039	Mccc1	20.7±3.8	190.8±34	284.9±56.2	91.1±10.5	295.1±62.3	474.7±21.9
1455314_at	210126	Lpp	10.6±3.9	58.7±5.2	281.2±49.3	9.4±1.3	152.9±5.1	577.2±43.6
1422567_at	63913	Niban	28±3.6	155.2±36.7	793.2±58.3	16.1±13.1	412.2±79.6	1450±340.7
1422433_s_at	15926	Idh1	79.3±28	1143.4±80.7	1362.8±15.2	232.8±154	1170.5±27.6	2478±468
1423796_at	71514	Sfpq	90.9±14.7	1281.6±480.1	1004.6±178	240±94.1	1348.1±365.2	780.7±363.2
1435397_at			54.8±2.7	1209.4±18.1	1037.3±117.2	265.5±24.8	812.4±150.5	857.7±82.9
1456319_at			106.9±22.6	1320.7±4.7	1544.7±243.9	177.3±70.7	1599.4±97	1806.7±950.9
1423596_at	59126	Nek6	7.2±0.2	31.1±0.8	226.8±62.1	10.3±4.4	107.7±10.1	218.2±26.5
1456795_at	399584	D330027G24Rik	11.9±2.6	168.4±5.8	284.4±81.6	51±19.8	181.2±53.5	883.2±217.6
1421840_at	11303	Abca1	10.5±4.2	112.8±23.6	176±69.7	27.4±9.9	162.1±48	148.2±21.4
1423960_at	14792	Grcc3f	74.2±9.2	748.7±169.5	1323.8±194.9	230.3±37.9	1164±59.6	1183.3±102
1426802_at	20362	Sept8	9.6±3	59.8±11.4	130.1±1.4	20.7±5.6	154.8±38.7	93.1±27.6
1460541_at	330836	Slc7a6	11.9±5	159±22.5	271±9.8	38.7±8.6	192.7±78.4	492.8±67.4
1433519_at	98415	Nucks1	321.2±57.5	4970±263.9	7690±889.2	2185±502.8	5208.1±343.2	7991.1±1255.9
1436762_x_at	74195	Elp3	33.4±2.9	410.5±31.1	656.4±55.6	184.2±41	561.6±70.7	420.4±15.7
1418635_at	27049	Etv3	4.4±0.1	123.5±11.6	119.5±42.9	38.2±16.8	74.8±3.7	175.5±10.6
1436181_at	16413	Itgb1bp1	4.8±0.5	61.4±6.5	96.5±1.7	26.4±3.2	82.7±27.1	107.4±16.8
1452387_a_at	56332	Amotl2	17.8±0.3	462.8±73.9	239.9±21.8	156.4±72.8	308.5±94	460.2±118
1418637_at	27049	Etv3	13.6±1.7	285.7±25.4	370.5±7.7	99.9±2	236.5±27.7	441.8±45.1
1436902_x_at	19240	Tmsb10	188.8±83.3	1307±111.5	2964.2±484.4	305.6±48.5	3332.2±725.1	8375.4±1684.9

1441682_s_at	73192	Xpot	175.8±50.4	3082.9±508.1	3148.2±667.3	1019.8±430.3	3171±90.3	2447.5±342.3
1460330_at	11745	Anxa3	7.4±1.8	85.5±8.1	139.6±46.7	23.8±7.6	135.6±26.3	929.9±318.9
1423829_at	223601	0910001A06Rik	31.5±5	389.7±27.2	997±33	132.4±17.8	576±139.4	790.4±101.3
1417673_at	50915	Grb14	10.1±1	146.5±53.6	189±50.9	57.5±3.4	186.1±6.3	150.5±31.6
1417769_at	67089	Psmc6	8.4±0.1	136.7±22.9	219.6±26.2	50.3±6.2	156.7±54.8	152.9±13.1
1456700_x_at			12.9±8	141.4±50.8	483.9±120.3	17.7±1.2	244.7±60.2	1044.5±463.5
1435787_at	242083	Ppm1l	18.1±1.4	525±28.3	204.4±74.6	200.3±4.7	348.1±23.6	177.8±17.2
1434642_at	114664	Dhrs8	7±0.1	116.8±9.7	104±9.3	33.4±23	135.7±22.4	226.2±16.8
1437226_x_at	17357	Marcksl1	149.4±33.3	2095.9±888.3	2695.7±252	433.2±65.9	2924.9±455.7	3659±497
1442003_at			7.4±0.5	214.4±0.5	156.7±2.6	11.3±9.5	145.8±57.7	143.1±24.1
1456309_x_at			28.5±14.7	523.2±0.3	374.9±0.3	56.5±23.6	575.9±88.4	699.1±103
1455680_at	319878	9630025H16Rik	13.6±11.7	219.3±6.3	503.7±40.6	33.2±4.9	275.4±26.4	497.2±122.3
1438169_a_at	232288	Frmd4b	48.9±18.4	489.8±163.1	1979±507.5	38.3±34.5	1013.6±322.2	2618.7±264.7
1424246_a_at	21753	Tes	5.4±2.3	86.1±18.8	249±71.4	10.3±4.8	112.4±13	495.5±77.6
1436519_a_at	68832	1110057K04Rik	18±4.6	374.9±34.3	601.8±19.1	147.4±9.3	376.9±81.8	354.9±31.3
1434839_s_at	81004	Tbl1xr1	39.4±7.7	539.4±79.1	877.6±86.1	145±9.7	827.5±176.7	1139.5±41.4
1433754_at	105559	Mbnl2	9.3±0.3	105±10.4	251.6±36.7	18.1±14.8	195.8±8.9	341.6±33.6
1455437_at	109199	9030204A07Rik	10.6±4.4	373.5±38.9	287.3±33.9	85.8±18.9	225.9±31.9	252.1±63.6
1449095_at	245944	Vps54	12.6±0.4	244.2±23.4	441±52.3	90.9±19.5	273.4±31.8	832.4±138.2
1449210_at	140486	Igf2bp1	21.8±0.4	379.4±69.6	480.7±49.7	173.4±52.6	490.5±33.3	284.2±21
1455011_at	170459	Stard4	6.9±0.5	174.5±2.9	146.7±1.5	18.5±0.1	164.9±4.6	322.8±65.6
1428772_at	73192	Xpot	55.6±18.5	1394.3±115.1	1465.7±294.4	390.4±176.7	1329.5±68	1078.6±226.2
1421830_at	11639	Ak3l1	83.9±16.4	1454.5±216.6	2811.3±520.3	489.4±105.5	2021.5±191.4	2385±222.6
1449128_at	52715	Ccdc43	15.1±0.9	341.1±27	534.9±76.6	95.4±0.3	368.5±83.7	156.3±30.6
1449011_at	20499	Slc12a7	6.3±0.6	49.3±15.9	103.3±32.3	17.3±0.2	156.9±8.3	59.8±11.4
1450387_s_at	11639	Ak3l1	174.2±26.6	3184.7±148.1	5193.5±105.3	1551.4±155.9	4361.5±360.2	4489.5±6.3
1426195_a_at	13010	Cst3	32.7±9.6	492±136.2	756.6±24.5	233.4±6.1	820.1±32.8	1014.2±106
1455300_at			13.5±4.9	132.1±8.3	335.1±91.6	37.4±8.4	342.6±132.1	345.4±127.7
1416675_s_at	18799	Plcd1	12.7±0.9	538.3±54.3	341.4±11.1	163±12.6	331.8±9.5	805.8±52.5
1434897_a_at			216.7±33.7	5186.8±304.5	7744.8±433.8	2012.4±45.8	5715.1±670.5	6021.3±850.3
1450700_at	260409	Cdc42ep3	11±0.6	156.1±1.6	299.2±105.5	41±26.5	294.3±20	212.1±1.1
1428829_at	75743	6820401H01Rik	13.1±5.1	206.8±14	419.9±58.8	10.2±2	351.9±27.1	482.9±103.7
1440167_s_at			11.7±0.9	90.4±3.8	392.3±19.9	21±6.5	329±44.5	717.4±56.1
1451493_at	65113	Ndfip1	35.8±3.4	334.6±71.4	1353.8±272.4	154.7±12	1023.8±55.2	1746.8±420.4
1434162_at			21±2.2	614.9±47.7	545.7±63.2	226.1±19.7	613.4±92.9	510.3±17.9
1417957_a_at	66805	Tspan1	10.5±4.1	697.6±190.1	312.8±118	35.4±33.2	319.4±122.8	159±0.9
1455827_at	105559	Mbnl2	6.9±0.7	77.6±16.8	263.4±169.3	7.7±0.1	220.8±36.9	420±15.3
1426248_at	223255	Stk24	22.2±8.2	517.6±37.4	1087.5±315.4	147.7±62.4	730.3±30.8	1499.9±133.2
1426697_a_at	16976	Lrpap1	72.2±23.7	3197±423.8	1354.5±139.9	809.1±24.3	2434.6±23.2	2045.6±328.1
1448432_at	18799	Plcd1	3.6±0.2	201.8±95.8	118.5±38.4	60.2±8.6	122.5±27.3	317.7±49.5
1460173_at	16796	Lasp1	13.9±0.6	431.7±144.3	312.7±75.6	22.6±2.6	473±199.8	611.8±277.4
1451594_s_at	97848	Serpinb6c	12±4	61.3±14.8	674.1±154.7	17.7±6.1	416±62.7	1330.3±178.9
1449888_at	13819	Epas1	36.3±7.6	515±102.3	897.7±10.8	169.3±48.5	1295.8±155.8	324.3±56.6
1437289_at	242291	Impad1	8±0.9	122±57.1	399.1±56.3	31±4.6	288±25.1	390.7±26
1429240_at	170459	Stard4	8.7±3	302.7±21.3	266.5±50.4	36±8.6	318.8±6.6	576.5±153.7

1436340_at	100223	9630041G16Rik	6.5±0.8	151.5±46.9	294.5±17.9	49.9±14.9	239.6±15.1	277.4±68.7
1438512_at			10.7±3.5	146.4±47.2	313.4±32	34.6±13.4	404.6±79.7	280.3±74
1436609_a_at	16976	Lrpap1	363.3±1	9472.6±415	15171.7±894.8	3397.6±669.3	13762.4±2.8	16668.3±806.8
1439264_x_at	16796	Lasp1	116.3±68.2	5170.8±673	4526.2±325.2	923.5±95.9	4540±29.3	5377.5±282.2
1436317_at	241062	D230012E17Rik	7.9±0.3	39.3±3.8	426.5±126	13.5±1.1	314.2±0.9	301.7±20.2
1427133_s_at	14725	Lrp2	10.4±0.5	35.3±0.9	812.6±399	12.9±2.1	418.6±57.9	2384.1±26.5
1417089_a_at	12716	Ckmt1	11.3±2.3	609.4±293.7	421.9±109.4	69.2±17.6	474.7±104.6	764.2±220.1
1438633_x_at	16796	Lasp1	95.8±68.4	4759.2±277.6	4448.7±474.6	657.8±117	4301.7±105.5	5525.1±534.6
1438223_at	245944	Vps54	42.7±7.2	1891.3±141.8	2860±273.8	404.3±241.8	1974.3±146.5	2557±39
1454709_at	100201	Tmem64	36±13.2	2529.4±53	1628.8±451.2	731.1±228.7	1730.2±201.7	1002.9±104.5
1452973_at	243382	Ppm1k	4.4±1.4	261.6±8.3	224.4±84.5	46.8±18.2	210.8±49.4	148.1±3.1
1456036_x_at			100.2±7.6	4451.3±34.8	5314.5±464	920.5±532.2	4827.8±596	4645.1±582.5
1417125_at	269378	Ahcy	19.9±9.1	405.9±46	1592.4±247.3	137.9±16	999.8±84.4	1519.4±118.3
1439407_x_at	21346	Tagln2	22.4±2.3	371.4±127.7	895.6±188.5	137.4±6.9	1126.9±112	2175±59.6
1452840_at	69784	1500009L16Rik	12±0.7	342.9±110	823±3.3	41.6±33.5	650.3±153.9	418.8±26
1438634_x_at	16796	Lasp1	114.7±90	6544.5±281.3	6197±333.9	657.9±203.6	6264.5±329.7	7760.5±521.8
1452148_at	16976	Lrpap1	26.8±13.7	2258.5±144.2	924.4±49	501.5±13.8	1538±167.1	1223.3±117.5
1448265_x_at	14012	Eva1	7.9±3.6	342.7±9.4	774±142.7	67.8±14	457±45	854.2±183.5
1415971_at	17118	Marcks	5.2±1.1	180.5±5.1	561.1±48.5	22.7±9.7	303.7±57.7	858.1±433
1455470_x_at			20.5±9.9	1354.9±4	1193.5±46.4	111.1±43.9	1232.5±8.8	1605.3±160.6
1428579_at	71409	Fmnl2	13.4±0.1	153.3±5.3	1721.8±449.7	35.3±18.2	812.8±14.8	3629.3±251.1
1416953_at	14219	Ctgf	10.4±5.8	1026.9±118.8	551±47.7	322.2±62.9	642±10.2	204.1±38.9
1417311_at	68337	Crip2	37.1±11.2	878.9±233.3	1904.3±524.5	154.6±117.3	2292.8±785.8	2679.4±1038.8
1417185_at	110454	Ly6a	30.8±10.3	1524.2±145.5	3993.8±61.5	308.6±93.5	1951.4±192.8	3132.2±414.1
1416808_at	18073	Nid1	14.3±5.8	1110.4±191	834.9±94.2	231.5±32.7	904.1±49.1	755.1±72.2
1434307_at	100201	Tmem64	14.2±5.3	1734.8±358.1	796.9±281.8	556.4±85.1	924.8±184.2	355.7±25.1
1418091_at	81879	Tcfcp2l1	21.8±12.3	765.7±223.7	1807.2±331.7	82.5±5.9	1462.4±61.8	1749±256.7
1453351_at	57246	Tbx20	6.3±0.4	396.2±23.4	703.9±337	74.4±9.8	422.6±92.9	462.9±90.7
1428283_at	74134	Cyp2s1	57.7±11.4	2854.1±300.3	3181.1±502	617.3±171.9	3913.2±446.1	4360.3±886.3
1456642_x_at			20.1±9.6	384.3±88.6	1244.3±240.4	96.5±25.1	1382.6±418.7	4048.7±399.4
1426696_at	16976	Lrpap1	90.6±33	3688.7±1374.5	7394.4±1908.8	665.4±83.6	6252.3±1369.7	8833.8±2493.7
1448022_at			34.3±6.1	2460.8±647.6	4764.7±126.2	344.1±205.4	2465.7±182.6	2900.3±81.1
1448967_at	66536	Nipsnap3a	8.4±0.6	405.4±9.7	694.6±55.6	96.2±65.1	643.1±200.4	914.3±148.3
1418283_at	12740	Cldn4	9±0.2	350.3±194.3	653.5±202.9	42±22.9	699.9±401.6	1479±628.9
1422075_at	12591	Cdx2	6.5±3.3	172.1±46.2	810.5±121	20.5±1.8	591±158.8	1143.7±84
1429388_at	71950	Nanog	16.5±2	337.8±55.5	2194.4±344.7	122.8±44	1613.2±426.5	1063.5±80.4
1434909_at	52187	Rragd	38.9±2.6	3295.1±67.8	4072.2±596.4	794.8±262.7	3999.9±2.7	3434.6±145.3
1448987_at	11363	Acadl	24.6±7.8	3890.3±468.8	3356.9±238.9	1604.8±289	2749.6±527.7	4082.1±489.6
1434369_a_at	12955	Cryab	11.1±4.6	106±61	702.7±78.6	12.9±2	1273.9±352.5	1978.2±183.2
1460351_at	20195	S100a11	11.8±7.7	388.2±51.9	1706±312.8	68.1±10.3	1445.9±64.6	4376.5±14.2
1423933_a_at	76509	1600029D21Rik	9.6±4.3	188.4±73.7	1103.5±460.4	14.8±0.9	1218.6±570.4	1053.1±700.1
1429377_at	66991	2410004A20Rik	37.8±3	1998.1±811.4	5574.2±372.4	491.8±214.2	5057.4±770.9	6162.5±1252.7
1416236_a_at	14012	Eva1	11.3±0.5	1338.8±281.3	2283.8±291.1	354.4±32.8	1843.4±38.9	3134.2±578
1416531_at	14873	Gsto1	26.9±1.9	4185.5±865	4966.8±40.5	1011.1±161.5	5992.7±181.8	5867.7±376.8
1419091_a_at	12306	Anxa2	9.4±1	360.7±10.6	1928.1±78.4	113.9±66	2315.1±199	5245.4±181

1416635_at	57319	Smpdl3a	7.1±1.6	1515.3±207.1	2000.5±93.2	383.1±207.5	1841.4±161.7	2687.2±144.3
1435436_at			10.9±5.5	2031.9±132	3177.2±112.2	343.9±110.6	2880.3±266.9	2920.8±193.8
1448894_at	14187	Akr1b8	8.7±5	297.4±56	3605.5±1744.4	13.6±2	2518.6±199	7769.5±871.1
1448649_at	13809	Enpep	7.7±0.5	555.3±320.5	4590.9±1128.8	63.4±43.4	2348.9±1155.9	9907.4±1632.9
1435989_x_at			10.5±0.3	518.7±198.7	5732.6±1940.3	55.1±13.7	4818.3±74.4	10300.6±1681.3
1420647_a_at	16691	Krt2-8	11.6±4.3	532.7±98.9	6803±1912.8	61±14.1	6460.9±71	13413.1±1241.4
1452320_at	14725	Lrp2	7.3±0.6	417.8±270.7	4968.3±1419.8	57.1±11.5	4114.3±756.5	6091.8±1454.4
1423691_x_at	16691	Krt2-8	13±1.6	797.5±301.7	11355.6±4647.7	89.7±46.1	9248.9±55	22021.2±3423.7

Group 3 **19 genes (19 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1460222_at	20401	Sh3bp1	22.9±0.2	23.2±0.1	69.8±22.9	17.7±0.1	29.3±6.4	159.5±7.8
1430774_at			6.7±1.9	8±3.1	21±1.3	8±1.1	8.2±0.4	24.4±5.5
1434511_at	102093	Phkb	32.2±6.6	18.5±2.6	101.6±27.4	10.6±3.4	38.1±0.7	229.2±53.3
1446094_at			8.7±0.9	17.6±2.9	28±2	9.9±0.2	12.3±2.3	42.6±6
1453377_at	72281	Sh2d4a	11.6±0.4	12.7±0	39.3±12.8	10.3±2.9	10.2±2.5	115.5±44.9
1424025_at	215751	BC013529	20.7±0.2	25.1±0	72.1±9.9	45.6±0.9	39.2±8.4	86.2±1.7
1452404_at			8.9±2.1	9.1±2	31.7±8.6	10.6±0.1	11.2±1.7	35.6±2.3
1447060_at			21.3±0.6	25.6±2.9	84.2±6.7	17.7±0.5	47.9±8.9	86.3±13.3
1436107_at	76522	Lsm8	7.3±1.6	11.1±3	29±13.1	7.2±0.1	8.1±1.1	23.9±5.5
1449559_at	17702	Msx2	4.8±0.1	10.1±1.2	21.4±4.8	5.9±0	12.8±1.3	52.3±0.6
1448160_at	18826	Lcp1	11±1.4	8.1±0.9	49.5±18.7	8.5±1.9	15.8±0	523.2±4.3
1416617_at	68738	Acss1	8.9±0.6	19.2±3.2	44.1±21.4	11.1±1	7.9±0.6	142.6±23.8
1434889_at	233765	Plekha7	6.7±0.1	8.5±2.3	37.3±10.6	10±1.7	9.9±4.4	89.1±15.1
1455403_at			7.7±2	17.6±1.5	43.1±4	23.3±0.8	17.8±5.5	64.2±18.1
1448406_at	58521	Cri1	25.8±2.3	59±1.2	154.1±4.9	86.9±14.3	75.2±0.6	111.4±11.9
1416187_s_at	52830	Pnrc2	100.9±22.7	214.1±14.7	631.4±66.4	454.2±13.5	297±48.2	768.6±166.2
1445281_a_at			10±0.8	16.1±5.2	72.7±2	19.7±3.3	25.4±9.7	54.7±4.2
1426153_a_at	13511	Dsg2	6.2±1.1	8.5±0.6	54.9±20.9	6.8±0.2	18±2.8	129.6±14.7
1436473_at	72720	Zfp248	8.1±0.3	8.5±0.1	101.4±12.2	7.9±0.2	16.5±10	88.9±18.3

Group 4 **43 genes (47 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1426936_at	630153; 631386; 637482; 630525		95.1±26.6	371.9±75.8	554.6±20.2	83.1±57.4	749.8±27.1	517.5±198.8
1440555_at			4.2±0.4	13.6±6.8	18.8±4.8	3.9±0	18.8±0.7	19.4±6.4
1429239_a_at	170459	Stard4	113.6±31.5	465.7±65.3	461.5±231.1	92±56.2	810.5±180.1	354.1±119.7
1455241_at			13±8.1	36.7±6.8	102.8±24.2	8±2.1	145.2±60.6	211.7±21.7
1429116_at			40.1±16.7	115.8±15.5	123.9±28.8	35.6±0.5	144.6±13.8	168±33.9
1459900_at			20.1±5.4	57.5±3.2	138.1±0.1	13.7±0	128.2±60.6	233.3±15.1
1419832_s_at	56318	Acpp	26.1±9.4	79.8±4.5	119.8±9.5	21.1±5.1	102.7±11.8	33.2±18.7
1444479_at			20.9±0.1	71.4±31	84.3±43.9	17±1.3	76.8±24.4	104.8±4.1
1420498_a_at	13132	Dab2	345.8±222.7	1237.5±292.7	3161.4±503.7	132.8±83.7	3323.8±675.5	5090.5±565

1428357_at	72148	2610019F03Rik	424.2±43.8	986.9±89.6	3328.2±274.2	240.6±53.3	2933.5±559.3	7128.3±525.4
1454942_at			17.9±8.4	28.3±4.1	203±40.9	7.6±2	141.4±25.1	769.8±157.3
1430604_a_at	13132	Dab2	36.5±3.3	76.8±0.3	245.8±3.8	16.8±3	226.7±20.2	222.4±22.8
1428822_a_at	69226	Snx24	11.4±7.7	40±8.1	39.1±11.1	7.9±1.5	39±5.1	98.4±1.9
1416763_at	98828	G431001I09Rik	77.5±10.3	92.3±27.8	616.3±160.2	24.2±1.1	487.9±15.8	1082.3±44.6
1428935_at	12330	Canx	88.2±7.6	228.9±35.9	242.4±20.5	53.9±4.3	350.4±60.5	341.8±151
1419106_at	72381	2210409E12Rik	186.2±23.6	333.1±188.5	1649.8±687.9	37.5±23.9	1311.1±549.4	643.5±226.1
1416354_at	19655	Rbmx	76.7±22.2	227.7±26.4	190.3±24.3	35.2±23.8	362.5±22.1	76.2±2.7
1449344_s_at	72381	2210409E12Rik	351.4±64.8	497.3±158.5	2191.5±197.6	106.6±68.2	1945.5±302.9	972.9±6.9
1435081_at	19027	Sypl	29.8±9.5	76.3±18.1	89.6±12.5	20.4±1.2	86.2±9.6	70.2±16
1445062_at			65.2±19.8	186.7±58.8	165.5±21.5	52.9±9.5	138.3±22.8	261.2±10.9
1426981_at	18553; 631913	Pcsk6	31.8±14.7	74.2±15	152±24.9	21.4±3.4	87.5±13.6	385.1±99.1
1434773_a_at	20525	Slc2a1	386.1±16.4	260.1±22.5	1355.3±27.3	55.5±48.7	1891.6±678.2	1442.8±99.2
1443579_s_at			17.6±1.6	40.3±2.7	37.1±3.5	13.3±1.2	36.6±11.8	40.8±5.2
1435140_at	15925	Ide	255.8±74.4	477.2±119	878.6±48.6	136.1±38.8	775.1±261.8	1581.8±153.8
1447260_at	69717	2410017I17Rik	22±5.7	33±5.7	45.1±3.3	9.8±0.1	70.1±24	42.2±1.6
1422619_at	19012	Ppap2a	103.7±68.6	223.5±42.5	302.1±14.6	41.9±24.7	341.6±25.4	334.5±30.7
1428622_at	97998	Depdc6	60.9±5.8	139.7±19.8	130.2±1.8	41±16.6	132.9±24.8	132.5±31.2
1438468_at	347710; 347709	Pramel5; Pramel4	490.7±288.3	1197.6±279.9	1160.1±106.5	160.9±18	1491.4±520.2	587.8±150.3
1426358_at	216965	Taok1	105.1±12	258.5±52	155±9.1	69.5±4.9	195.9±26.2	120.2±28.2
1434599_a_at	21873	Tjp2	453.5±86.9	601.1±104.6	1670.1±271	157.6±85.6	1171.2±280.8	2469.4±220.4
1447898_s_at			284.5±40.7	754.3±87.4	613.6±102.7	132.6±73.6	499.8±119	563.9±77.2
1416721_s_at	67996	Sfrs6	258.8±3	783.4±40.5	561±163.5	97.1±46	480±130.3	720.4±197.9
1424652_at	232146	BC014699	305.5±3.7	744.3±83	406.3±76.8	184±78.2	457.5±11.4	572.4±50.8
1454973_at	54343	Atf7ip	36.6±2	66±13.9	78.9±10.7	19.1±2	53.3±17.5	155±3.9
1453104_at	26413	Mapk1	392.7±20.2	528.4±95	1029.1±151.2	128.3±39.3	640.6±197.6	1315.3±322.1
1436979_x_at	56275	Rbm14	2544.2±2.8	4526.8±529.2	3222.1±388.8	1471.5±179.9	3465.6±103.3	2193.7±8.2
1451318_a_at	17096	Lyn	112.3±40.8	171.4±36.8	203.9±49.2	28.9±6.5	165.1±9.2	214.9±43.1
1452094_at	18451	P4ha1	95±13.4	133.5±38.9	127.7±22.5	32.2±4.1	117.9±25.3	48.9±17.6
1444991_at			39.4±13.4	53.4±0.4	20.4±6.8	13.9±4.5	44.3±3.6	15.2±5.8
1437361_at	217122	A430060F13Rik	6777.4±1408.1	6414±335.7	6386.2±872.4	1930.3±701.4	7138.4±1439.7	3658.1±1088.1
1427347_s_at	22151; 73710	Tubb2a; Tubb2b	849.6±6.1	373.7±133.5	996.2±79.3	83.9±10	902.9±16.9	371.2±93.3
1418966_a_at	66686	Dcbld1	265.1±91.9	214.6±45.2	134.9±43.3	61.1±16.6	249.4±28.8	107.9±5.8
1460646_at	13000	Csnk2a2	518.9±38.9	410.6±39.3	348.5±10.2	100.2±36.7	423.1±26.3	247.4±10.6
1420477_at	53605	Nap1l1	901.3±27.3	674±43.6	880.1±151.4	212±92.1	732.8±107.4	1581.9±21.2
1436531_at			352±63.6	574.4±47.6	299.6±58.6	129.7±34	286.6±16.6	203.7±8.7
1428433_at	15258	Hipk2	40.3±14	35.9±0.1	44.8±17.5	9.6±0.4	29.1±7.7	51.1±9.5
1455991_at	229905	Ccbl2	162.1±10.1	62.5±16.8	202.7±2.3	20.7±2.5	101.1±22.8	153.9±45.9

Group 5 **3 genes (3 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1427983_at	208968	Suhw3	162.5±43.7	13.9±1.6	76.6±12.3	148.1±25.5	41.5±0.7	94.2±3.9
1436048_at	102058	Exoc8	615.3±175.5	136.7±11.6	262.2±7.1	376.9±13.2	164.2±15.3	441.8±114.2

1451053_a_at	17245	Mdm1	21.5±3.5	6.7±0.4	9.3±2.8	42.9±7.1	6.5±0.3	9.6±4.9

Group 6 **58 genes (60 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1423286_at	12404	Cbln1	704.1±28.6	32.6±14.1	16.1±5.6	372.2±176	33.1±4.3	12.8±3.5
1435092_at	11861	Arl4a	325.7±13.2	29.2±13.3	16.2±0.4	254.2±67	20.7±0.6	17.9±8
1454867_at	433938; 634779	Mn1	209.9±42.5	18.9±8.1	13.3±0.3	231.6±197	14.1±3.2	8.8±0.2
1429671_at	71970	2410018M08Rik	245±16.3	35.8±5.9	19.4±0.1	206.6±4.7	19.8±12.6	14.5±4.5
1441098_at	240023	Pnldc1	603.6±93.2	60.2±22.9	65.3±12.6	343.3±195.2	53.3±7.6	59.5±14.7
1425280_at	69757	Leng1	421.4±207.2	58.9±16.6	26.1±1.5	279.1±79.7	37.4±20.2	30.2±2
1423809_at	106795	Tcf19	311.8±12.8	56.5±23.4	45.7±10.2	226.6±13.4	27.8±0.5	93.5±7.2
1457279_at			491.2±35.6	48.6±14.5	55.2±0.5	391.4±141.3	44.1±8.9	18.1±0.1
1416490_at	66269	Tmed6	330.1±79.6	68.7±3.9	16.5±5.6	210.6±0	30.8±3.2	7.2±0.2
1437924_at	20658	Son	855.1±343.5	122.5±6.3	96.1±20.2	509.1±49.2	81.9±19.9	106.1±29.5
1425197_at	19255	Ptpn2	1386.2±129.6	410.1±131.4	95.1±13.5	1027.4±176.7	145.3±11.3	42.8±4.1
1424237_at	67778	Zfp639	1120.1±115.4	161.7±14.7	114.9±19.6	670±1.4	118.3±4	133.7±14.6
1458130_at			224.9±10.3	27.1±4.8	28±7.8	134±92	24.7±7.6	14.7±2.1
1437693_at	110957	D1Pas1	517.5±42.3	87.7±16.8	51.2±10.6	315.8±145.9	61.8±5.9	34.8±5.7
1433623_at			1254.2±26.7	306.6±112.6	226.5±36.1	791±22.6	152.1±60.8	93.8±14.4
1431429_a_at	11861	Arl4a	658.2±64	127.7±29.4	81.1±4.3	403±54.1	84.6±1.9	81.1±18.9
1421273_at	67296	Socs4	116.6±14.7	19.8±3.4	14.7±2.7	69.7±2.6	15.3±0.6	9.4±2.3
1421340_at	26408	Map3k5	107.6±10.3	16.8±6.1	15.7±5.7	64.8±19.9	14.5±6.3	11.2±0.6
1435556_at			391.3±251.7	58.7±18.3	71.5±1	280.9±43	53.2±11.1	63.9±20.1
1457672_at	109151	Chd9	132.4±18.2	11.1±1.8	25.4±0.6	95.3±72.3	18.4±3.8	17.6±0
1429667_at			533.3±206	74.2±5.4	40.1±2	392.1±55.9	78.4±48.9	45.6±13.2
1426832_at	236790	6330505F04Rik	174.9±9.2	37.8±6.5	45.4±7.3	244.4±37.2	26±1.4	53.5±6.7
1428742_at	268882	Fbxo45	285.6±89	44.8±18.7	26.3±5.1	223.2±23.9	43.9±16.3	32.6±1.1
1450026_a_at	53625	B3gnt1	198.5±9.6	25.1±6.9	41.3±7	181.7±40.3	31.1±1.8	32.5±4
1442099_at	76179	Usp31	60.1±33.1	10.8±0.4	12.6±1.1	128.8±13.2	9.4±5.6	9.4±2.4
1449668_s_at			1147±276.9	287.7±13.2	286.3±83.7	854.5±248.8	184.2±40.9	346.4±24.7
1456914_at			168±37.8	20.9±11.1	33±10.1	119.2±28	27±4.2	38.3±5.4
1451439_at	212547	BC027231	2040.2±60.4	677.8±11.8	278.8±49.4	1642.8±511.4	330.1±99.8	242.7±53.5
1425114_at	19647	Rbbp6	566.1±80.6	110.1±14.1	22.8±2.1	421.7±145.4	93.9±26.4	26.2±8.2
1426107_at	213389	Prdm9	49.2±8.9	8.9±2.5	9.5±0.3	34.9±14.9	8.7±1.5	9.1±1.1
1423475_at	94219	Cnnm2	749±33.3	202±71.4	50.2±12.5	680.1±211.4	136.4±8.6	49±7
1423249_at	18087	Nktr	773.3±188.7	246.3±6.3	145.9±0.5	818.2±143.6	140.9±23.8	134.6±14.3
1435156_at	230967	BC046331	303.5±52.8	80.1±2.4	51.1±12	236.5±116.8	56.9±6.1	49.1±7.7
1417527_at	64933	Ap3m2	69.9±2	9.5±0.3	9.2±0.2	51.1±1.3	13.5±5.5	8.7±0.2
1426625_at	78834	Zfp623	794.4±23.5	120.7±33.8	191.3±32	530.3±88.6	153.3±28.9	137.4±4.7
1452330_a_at	74761	Mxra8	181.7±32.8	28.2±2	24.9±3.5	119.5±5.3	35.1±10.2	35.5±12.6
1454975_at			598.9±203.2	124.7±16.5	120.4±33.4	678.9±1.4	118.5±44.1	166±23.7
1417773_at	94181	Nans	920.2±214.1	209.5±23.8	138.7±26.9	565.8±1.4	186.9±70.6	200.7±57.3
1419301_at	14366	Fzd4	86.2±49.8	15.3±0.9	12.8±0.1	123.9±30	18±7.4	19.1±2.7
1449813_at	22693	Zfp30	46.8±16.7	9.2±1.4	8.8±0.9	35.3±14.6	10.2±1.2	8.3±0.8

1423539_at	18861	Pms2	358.2±32.1	86.5±12.8	83.6±11	245.7±44.7	81.6±27.2	98.9±7.5
1441045_at			182.1±2.3	34.1±7.8	28.5±14.8	177.3±48.7	42.2±12	46.2±12.8
1435366_at	233865	D430042O09Rik	38±2.9	11.4±4.3	12±1.2	25.9±4.2	9.2±0.6	12.4±2.4
1427879_at	69171	1810031K17Rik	2741.3±823.5	697.5±23.7	504.4±33.2	1950.6±796	666.3±114.3	395±90.2
1460673_at	14287	Fpgs	299.4±6.5	92.3±1.9	70.7±4	212.9±41.9	73.1±11	55.7±0.2
1435430_at	216131	Tmem1	1990.5±136.7	413.2±85.2	534.5±18.8	1369.2±179.8	501.1±51.3	625±12.5
1424175_at	21685	Tef	151.6±34.8	43.8±6.3	26.9±1.1	204.6±45.1	38.4±17.2	37.8±3.2
1424611_x_at	227682	Trub2	5223.2±258.2	1168.7±321.5	1308.3±471	4213.2±18.1	1343.3±501.2	768.7±271.6
1434405_at	216742	A730024A03Rik	289.4±36.1	88.7±44.2	80.9±28.9	323.5±11.2	74.6±16.7	76.4±1.6
1451553_at	11875	Art5	40.7±12.6	12.6±0.9	10.4±1.3	46.3±2.6	10.5±0.8	11.3±2
1445274_at			42.7±15.4	14.1±6.4	9.8±0.5	40.4±6.2	11±0.5	10.5±0.9
1456280_at	269582	Clspn	757.9±27.1	197.5±25.9	227.9±17.8	523.2±42.5	197±16.6	157.4±0.3
1451408_at	227682	Trub2	225.3±16	45.7±22.7	51±12.3	158.9±44	59.2±0.2	32.6±2.5
1420617_at	67579	Cpeb4	800.1±28.5	183.2±5.7	139.2±14.9	561.4±215.6	216.8±52.7	90.9±0.4
1455877_a_at			113.1±42.6	32.4±9.7	25.2±4.3	134.1±39.7	31.3±3.7	17.8±1.2
1423233_at	12609	Cebpd	55.6±25.5	11±2	6.7±0	53.9±14	15.6±5	9±1.1
1450292_a_at	67981	Hormad1	179.3±45.2	49.6±11.2	47.7±25.5	173.1±11.2	50.9±10.4	36.9±6.9
1417464_at	21925	Tnnc2	53±0.4	14.2±1.2	15.4±4.2	69.5±34.9	15.3±3.1	14.8±5.7
1444628_at	110751	Adam33	21.4±10.7	6.8±0	5.9±0.5	24.4±5.6	6.6±0.1	6.4±0.1
1455353_at	330401	Tmcc1	107.8±28.4	25.4±5.1	19±4.4	87±5	34.7±5.8	29.4±10.7

Group 7 **6 genes (6 probe sets)**

Probe set ID	Entrez Gene ID	Gene Symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1416316_at	26458	Slc27a2	768.4±98.8	218.3±99.1	32±8.6	372±142.3	459.6±216.6	82.4±60.6
1428776_at	75750	Slc10a6	378±2.3	210.1±50.1	39.8±31.2	328.4±33.8	225.4±0.2	71.2±35.5
1417649_at	12577	Cdkn1c	152.4±88.7	41.4±1.1	21.8±6	64.4±12.5	109.8±31.8	34.7±2
1455498_at	14765	Gpr50	84±20.9	48±1.8	12.6±5	68±32.3	50.5±14.5	11.6±1.4
1416590_a_at	19376	Rab34	109.7±0.8	78±5.4	20.6±1.9	183.6±48.5	77.3±27.8	17.5±6
1418355_at	53322	Nucb2	212.4±56.7	422.9±21.7	70.1±9.9	645.5±81.3	170.2±20.1	51.7±0.4

Group 8 **115 genes (119 probe sets)**

Probe set ID	Entrez gene ID	Gene symbol	cont.1.5 (*n*=2)	cont.2.5 (*n*=2)	cont.3.5 (*n*=2)	u2.5 (*n*=2)	u3.5 (*n*=2)	u4.5 (*n*=2)
1434881_s_at	239217	Kctd12	30.8±5.5	10.3±0.2	7.1±1.7	32.9±13.8	6.6±0.1	7.1±0.9
1450071_at	192195	Ash1l	343.4±1.7	121.4±15.7	122.1±6.5	374±194.1	89.6±12	118±29.8
1455999_at	105594	C330003B14Rik	857±102.1	303.6±55.1	93.8±46.5	1013.8±71.2	163.6±50.4	15.3±0
1441753_at			24.6±5.4	8.4±0.4	16.1±0.6	28.4±1.2	9.2±4.6	28.3±5.6
1435742_at	68734	1110034C04Rik	224.1±34.6	89.8±1	38.9±0.8	272.3±12.7	56.1±13.6	41.4±1.7
1419234_at	117599	Helb	47.7±9.1	17.5±3.4	19.5±5.4	57.4±21.6	17.2±1.1	13.7±2.3
1439979_at			35.4±14.1	12.2±0.3	13.5±3	41.9±5.7	15.3±1.1	14.4±1.8
1419165_at	26466; 635007	Zfp260	197.1±82.6	70.8±11.4	79.3±5	237.3±27.9	83.5±2	47.7±7.5
1436495_s_at	26466	Zfp260	187.5±69.4	75.4±19.6	82.7±19.6	227.8±38.9	91±3.2	67.2±0.4
1428731_at	78787	Usp54	332.8±67.8	145.4±18.1	48.6±8.2	455.2±80.3	57.8±0	36.9±7.5
1460453_at	72536	Tagap1	244.3±40.4	97±4.1	84.5±3.3	316.5±82.4	107.4±16.2	86.2±31.3

1424446_at	276905	Armc7	163.1±53.1	61.9±6.6	44.7±5.3	226.1±2.1	53.2±7.7	39.8±10.9
1460722_at	223920	Soat2	19.1±10.4	7.4±0.4	6.4±0.6	28.2±4.6	6.9±0.1	6±0.7
1431031_at	94246	Arid4b	15.1±2.2	7.2±0.2	6.6±1.1	22.4±12.5	6.4±0	6.2±0.1
1430318_at	69215	Sat2	245.4±49.7	90.1±33.6	36.3±1.8	435.2±198.5	41±7.3	29.4±8.7
1456904_at			17±4.1	6.4±0.9	10.2±0.3	23.2±4.7	10.5±0	9.9±0.6
1454798_at			48.1±10.6	24±1.5	24.3±9.5	72.1±16.4	24.6±4.8	19.4±0.2
1419569_a_at	57444	Isg20	25.8±6	10.4±0	8.8±0.2	40.9±1.4	11.1±2.3	9.4±0.3
1423083_at	19338	Rab33b	306.7±12.6	119.8±33.5	163.6±35.4	485.9±59.9	140.1±41.6	164±20.7
1417190_at	59027	Pbef1	365.6±130	186.5±16.2	179±39.6	633.6±272.8	123.6±19.6	162.3±18.4
1429125_at	474156	Zbtb9	257.7±86.8	105.4±0.8	156.3±0.3	355.3±44.3	173.3±12.6	126.7±16.4
1417316_at	66834	Them2	252.4±16.1	97.5±8.6	88.8±16.4	393.6±74.6	137.1±57.4	229.5±53.8
1420061_s_at	100552	AA675344	27±0.2	14±1.8	11.4±0.9	44.8±2.7	13±3.7	12.1±1.7
1424570_at	212880	Ddx46	79.2±6.2	33.4±10.5	29.9±3.1	129.2±16.4	42.5±19.2	19.6±5.7
1449050_at	19687	Recc1	624.6±302	344.1±36.3	367.7±50.2	1054.6±14.8	328.2±30.7	241.1±3.3
1439189_at	329679	D630023B12Rik	132.4±32.2	56.3±17	55.3±9.2	247.7±6.3	57.7±18.7	58.1±29.7
1440914_s_at			646.9±74.2	351.5±17.8	77.8±7	1579.5±293.8	64±5.2	39.4±5.4
1456915_at			45.8±22.9	28.8±2.8	17.7±2.5	89.3±0.4	19.1±4.9	21.7±0.7
1418170_a_at	142682	Zcchc14	49.9±24.3	17.9±1.7	16.4±0.8	90.1±34.4	27±6.8	21.9±1.4
1430222_at			20.9±2.6	11±4	11.6±1.9	39.3±7.4	10.6±0.1	7.6±0.5
1447432_s_at			516.8±74.7	275.9±31.2	309.4±26.8	962.9±288.2	273.7±47.1	329.8±52.4
1450184_s_at	21685	Tef	18.8±0.3	10.1±1.8	10.3±0.3	35.1±2.7	10.3±0	10.4±0.5
1455567_at			71.8±15.3	45.1±6.7	21.8±2.3	175.6±52.6	22.8±10.6	27.4±0.5
1429795_at	69291	1700001L05Rik	50.3±12.2	28±10	14.4±1.2	115.5±62.6	23.1±4	21.7±2.7
1434724_at	76179	Usp31	72.1±22.7	54.7±3.2	31.1±7	173.1±26.2	31.1±6	21.1±1.4
1418109_at	14853	Gspt2	131.5±22.3	69±4.4	97.5±18.7	227.5±27.9	93.1±16.4	62.8±7.8
1438944_at			33.2±13.9	13.7±1	12.4±2	82.2±19.7	14.5±2.4	10.5±3
1453195_at	68112	Sdccag3	28.6±1.8	20±6.4	18.7±1	64.6±13.8	16.3±1.5	16.3±2.5
1426979_at	208104	Mlxip	95.8±19.7	79±21.4	24.2±1.3	267±43.2	41.2±4	65±1.5
1457302_at			120.2±10.1	69±12.2	65.3±6.7	250.9±36.5	79.4±17.3	47.2±16.4
1438575_a_at	72997	2900056M20Rik	22.2±4.5	15.2±0.8	11±1.3	51.1±17.9	13.7±4.2	11.8±1.2
1448706_at	56196	Ttrap	791.1±98.9	448±100	369.6±67.4	1934.8±227.9	457.8±26.1	616.3±304.9
1446737_a_at			34.5±0.9	22.1±4.4	38±6.8	68.1±16.8	24.9±0.8	57.1±5.4
1422787_at	56299	Fkbpl	91.4±30	52.8±7.3	31.2±7.6	293±123.4	35.9±3	18.6±2.1
1454835_at	77781	Epm2aip1	52.4±6.5	17.7±4.2	22.4±1.3	175.2±13	20±11.9	20.3±0.1
1449773_s_at	17873	Gadd45b	194.4±61.4	69.9±9.7	44.1±15.5	574.9±61.6	97.7±15.3	44±14.5
1452919_a_at	67078	1700012G19Rik	925.8±21.7	692.5±28.3	669.9±26	2255.2±86.6	604.2±114.9	462.8±22
1448257_at	13340	Slc29a2	17.4±2.3	14.8±5.6	8.3±0.8	51.5±28.2	9.4±0.8	6.9±0.2
1418868_at	13799	En2	22.9±12.4	14.7±0.1	10±1.9	72.1±8.3	11.8±0.2	15.5±4.9
1447336_at			16.7±6.9	11.4±2.2	8.7±0.3	41.5±9.5	11±0.9	10.4±1.1
1427344_s_at	75141	Rasd2	20.6±6	7.1±2.1	6.8±1.9	84.4±2.7	7±2.1	6.3±1.6
1418100_at	80515	A030009H04Rik	42±8.4	24.7±5.2	14.5±0	129.2±72.2	24±11.6	15.5±0.7
1438740_at	18108	Nmt2	181.5±44.2	106.4±17.9	120.9±26.8	359.3±69.9	146.6±25.7	123.1±26.3
1416598_at	83396	Glis2	92.9±1.8	118.6±9.4	18.3±0.2	396.7±162.7	33.7±10	16±4
1438256_at			94.2±60.3	61.9±7.3	32.7±21.8	422.1±32.1	46±0.6	18.4±2
1443842_at	99371	Arfgef2	9.2±0.5	7.2±0.2	6.6±0.6	27.7±10.2	6.6±0.4	7.1±0

1445368_at			51.4±1	54.5±3.3	29.3±12.2	196.2±47	34.8±2.7	25±6.8
1443691_at			7.3±0.2	6.2±0.2	5.9±0.3	19.2±4.4	6±0.2	5.9±0.1
1428970_at	72117	Mak3	1112.6±68.8	1019.9±237.7	824.5±118.8	3669.3±672.5	828.9±52.5	513.8±250.2
1423835_at	218820	Zfp503	26.4±4.5	29.5±7.6	15.9±3.4	94.1±13.3	21.9±2.9	17.8±4.8
1455638_at	79233	Zfp319	34.8±21.2	26.9±1.9	14.7±2.8	110.4±32.1	30.2±4.9	10.7±1.2
1419639_at	13642	Efnb2	539.7±98.8	287.7±70.8	673.5±172	1206.3±243.5	501.1±65.1	2381.1±189.9
1425163_at	224833	AI661453	229.8±27	299±60	152.6±5.8	1064.5±97.6	182.2±12	193.8±62.4
1440074_at			12.7±1.2	20.9±9.6	7.7±0.3	70.2±21.8	10.2±0	7.4±1.1
1429800_at	77124	9130221H12Rik	18.1±4.4	23.9±3.2	24.1±10.4	96.7±14.1	15.9±5.8	40.9±1.9
1425779_a_at	21380	Tbx1	7.2±1.7	6.9±1.4	5.3±0.3	31.5±18.3	6.6±1	5.1±0.8
1424419_at	223664	Lrrc14	41.8±9.5	36.5±5.5	49.9±2.3	115.9±30.1	40±9.3	52.3±0.8
1435768_at	94246	Arid4b	109.2±19.3	137.7±28.6	124.3±37.7	440.8±89.2	104.8±6.6	98.6±4.4
1416149_at	50914	Olig1	5.6±0.2	5.6±0.1	5.4±0	18.8±0.5	5.5±0	5.7±0.3
1438211_s_at	13170	Dbp	56.9±10.6	42.1±37	39.3±6.2	573.7±88	52.9±25.2	39.2±13.7
1427683_at	13654	Egr2	9.4±0.8	9.1±0.3	8±0.5	101.4±58.5	8.7±0.8	8±0.8
1417363_at	22719	Zfp61	21±2	18.6±4.7	28.9±3.1	63.1±8.6	20.7±1.8	42.1±10.5
1445361_at			13.7±1.3	10.1±1.1	9±0.7	46.9±3.7	13.6±3.8	10.4±3.6
1419135_at	16994	Ltb	19.5±3.4	24.5±2.1	10.3±1.3	298.5±284.1	19±0.3	9.2±2.5
1453125_at	20666	Sox11	6.3±0.1	9.5±4.3	6±0.2	35.5±3.3	6.3±0.1	6±0
1440256_at			9±0.3	10.9±1	10.2±0	430.8±244.3	10.3±2	8.7±0.2
1418290_a_at	14055	Ezh1	10.5±1	8.2±0.1	12.9±2.7	36.5±5.3	10.7±2.6	11.1±0.1
1456901_at			7.2±0.2	8.9±1.7	6.5±0	56.9±21	7.6±0.7	7.1±0.2
1434569_at	231151	AA474455	64.9±16.1	61.9±18.1	87.1±30.6	201±0.3	66.5±4.2	87.6±4.8
1447933_at	238403	Kif26a	12.1±1	12.7±2.4	18.6±3.6	180.8±135.5	14.3±1.2	13.2±0
1420585_a_at	83454	Nxf2	20.6±8.9	56.2±6.7	13±0.3	345.1±67.2	25.2±6.7	9.5±2.6
1419340_at	83456	Mov10l1	56.2±8.7	53.6±3.6	103.5±17	280.9±5.9	60.4±16.7	61±17.5
1455626_at			7.1±0.6	6.9±0.1	5.8±0	29.7±10.4	7.5±1.8	5.8±0.1
1429976_at	76499	Clasp2	10.6±0.6	17.3±6.4	10.6±0.7	97.9±1.8	12.7±6.5	13.4±5.9
1418174_at	13170	Dbp	9.6±1.2	9.1±0.2	10.3±2	43.1±19.4	10.4±2.7	8.5±0.3
1426470_at	21374	Tbp	6.2±0.4	6.2±0.1	5.7±0.1	19.9±1.3	6.5±2.7	5.8±0.2
1439381_x_at	277010	Marveld1	29.3±3.8	28.1±0.1	17.8±4	146.2±23	32.4±10	17.9±4.2
1456140_at	624168		11.8±4.4	18.1±5.1	18.2±1.4	143.7±6.9	16.1±4.2	23.8±7.1
1426420_at	74213	1700009P03Rik	30±6.2	17.2±1.7	34±5.8	74.2±5.3	31.6±4	21.9±8.1
1453851_a_at	23882	Gadd45g	14.8±1.8	10.5±0.4	42.3±18.2	355±309.7	27.4±2.4	136±9.4
1418517_at	16373	Irx3	6.1±0.4	8.5±1.4	8±0	28.1±14	7±2.1	18±2.1
1437305_at	228491	6430601A21Rik	58±11.2	65.9±6.1	49.2±10.5	249.1±76.1	66.6±0.7	24.4±13
1435117_a_at	217378	C330021A05Rik	6.4±0.7	10.2±2.7	8.3±0.1	35.3±11.1	7.7±0.5	11.7±2.3
1448877_at	13392	Dlx2	8.1±0.3	8.7±0.4	7.9±0.7	37.3±12.9	9.5±2.7	6.2±0.8
1448698_at	12443	Ccnd1	9.7±0.3	9.8±2.6	6.8±0.1	46.9±2.7	11.5±6.4	6.2±0.9
1425736_at	12493	Cd37	7.1±0.2	7.5±0.2	7.7±0.7	23.3±9.7	8.2±1.4	9±0.8
1460624_at	109045	6330564D18Rik	18.3±7.2	35.1±0.4	56.2±15.2	194±88.5	30.1±17.7	67±3.9
1434335_at	239667	AI317237	227.1±96.1	153±21.7	333.7±15.3	783.9±93.5	265.1±45.6	441.6±75.9
1442035_at			7.9±0.3	9.1±0.8	8±0.3	35.6±14.6	9.8±3.1	8.2±0
1437884_at			75.5±6.3	115.6±25.8	101.2±16.7	363.5±199	98±0.8	86.8±0
1433946_at	22775	Zik1	7.4±0.2	10.9±0.6	23.9±12.6	56.5±4.2	12.2±5	11.9±4

1434866_x_at	12894	Cpt1a	156.3±31.3	130.1±18.9	487.4±155.3	503.6±163	192.4±24.7	459.1±28.5
1431265_at			10.7±1.2	15.2±1.8	10.1±0.7	65.9±16.3	17±7.8	11.5±2.8
1447788_s_at			4.9±0.1	5.5±0.3	6.3±2.1	48.6±21.1	10.1±7.2	9.8±2.2
1438719_at			12.9±0.7	22.2±0.5	16±0.3	67.6±35.7	19.8±4	16.3±0.4
1435880_at	99696	Ankrd50	34.7±13.2	31.6±2.9	53.5±4.4	156.6±21.6	50.4±12.2	68.5±9.8
1460073_at			6.4±0.7	6.5±0	6.5±0.3	24.9±3.4	8.9±2.4	6±0.6
1428334_at	14628	Ostm1	295.4±28	312±15.9	501.2±64.1	1766.9±414.4	494.5±144.7	334.9±8.9
1427114_at	72795	Ttc19	113.1±13.5	151.9±18.3	169.6±5.4	525.8±105.5	169.6±22.5	130.6±47.4
1426421_s_at	74213	1700009P03Rik	120.3±7	101.7±20.1	153.9±1.4	379.2±6.4	156.4±14.9	99.7±3
1460483_at			7.7±0.2	14.6±3.3	31.7±1.7	84.4±1.1	18.8±7.2	18.8±6.4
1427074_at	245867	Pcmtd2	13.4±5.3	19±2.7	35.7±5.9	77.2±33.4	23.5±6.7	45±1.4
1444177_at			11.8±4.2	14.7±0.6	20.3±4.6	72±4.8	22.6±2.9	11±1.1
1435227_at			6.9±0.2	12.5±0.8	18.1±3.7	46.3±15.5	14±6.1	9.5±3.6
1425576_at	229709	Ahcyl1	38.6±2.7	109.1±4.3	117.8±8.3	364.3±79.3	105.1±19.7	54.5±0.4
1437287_at	68646	1110020G09Rik	7.7±3.5	28.6±4.9	35.4±2.2	116.3±28.3	31.3±18.2	36.9±5
1422092_at	18640	Pfkfb2	6.9±0.1	15.2±7.1	7.3±1.4	52.7±3.1	17.7±3.4	6.4±1.2
1427918_a_at	104215	Rhoq	13.7±2.1	17.1±4.9	51.1±3.7	112.5±30.8	38.6±1.9	49.4±1.9
1435538_at	68364	0610030E20Rik	101.8±5.6	239.1±58.2	314.8±55.1	736.9±155.2	295.2±47.7	358.1±71.6

The values represent the mean of signal log ratio (log2-fold change)±s.d.