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Transcriptome analysis and *in vivo* activiy of Fluvastatin versus Zoledronic acid in a murine breast cancer metastasis model

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List of abbreviation:

Zol: zoledronate

Fluva: fluvastatin

BP: bisphosphonate

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ABSTRACT

Statins and bisphosphonates (BPs) are two distinct classes of isoprenoid pathway inhibitors targeting downstream enzyme of HMG-CoA reductase (upstream enzyme) and Farnesyl-pyrophosphate synthase, respectively. Here, we studied Fluvastatin (Fluva) and Zoledronate (Zol), representative molecules of each class, respectively. *In vivo* metastatic potentials of both molecules were assessed. For the first time, we observed a significant reduction of established metastasis progression under Fluva treatment. Treatment with Zol at 100 µg/kg and Fluva at 15 mg/kg both inhibited 80% of metastasis bioluminescence signal and increased mice survival. The Zol and Fluva transcriptomic profiles of MDA-MB-231 treated cells, revealed analogous patterns of affected genes but each of them reached with different kinetics. The observable changes in gene expression started after 24 h for Fluva IC₅₀_{72h} and only after 48 h for Zol IC₅₀_{72h}. To obtain early changes in gene expression of Zol treated cells, three times higher dose of Zol IC₅₀_{72h} had to be applied. Combining Fluva and Zol *in vivo* showed no synergy but a several days benefit in mice survival. This study demonstrated that Zol or Fluva are of potential clinical use for the treatment of established metastasis.

INTRODUCTION

Breast cancers are frequently characterized by overexpression of Rho family GTPases and constitutive activation of Ras or other small GTP-binding proteins that are mutated in a variety of tumors, thereby regulating cancer cell migration and invasion (Fritz et al., 1999). To be functional, these proteins require prenylation, a lipid post-translational modification that assures their translocation and attachment to the plasma membrane crucial for their ultimate involvement in signal transduction. In human cells, isoprenoids (farnesyl-pyrophosphate, FPP, and geranylgeranyl-pyrophosphate, GGPP) are derived from the mevalonate pathway that starts from the reaction of conversion of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) to mevalonic acid catalyzed by the HMG-CoA reductase (the rate-limiting reaction in cholesterol biosynthesis). Recent evidence has accumulated on the direct inhibiting effects of bisphosphonates (BPs) and statins, initially known as potent inhibitors of osteoclast-mediated bone resorption and cholesterol lowering drugs respectively, on cancer progression and metastasis (Fig. 1).

Use of bisphosphonates (Russell, 2011) in solid tumours to prevent or treat bone metastases is supported by numerous clinical studies and is recommended by international consensus conferences (Aapro et al., 2008). Effects of bisphosphonates on soft tissue metastases are less clear (Fournier et al., 2010) Moreover, recent studies show that (Zometa), Zoledronic acid (Zol) could induce adverse cytotoxic effects as osteonecrosis of the jaw. This effect could be bypassed using Zol in combination with other chemotherapeutic molecules. (Zol), the more potent drug among aminobisphosphonates (NBPs), is described to suppress prenylation of several intracellular small GTPases essential for many cellular functions important in carcinogenesis (Caraglia et al., 2006). However, the inhibition of breast cancer cell proliferation by NBPs, including zoledronic acid (Zol), appears to involve other mechanisms besides the inhibition of the mevalonate pathway as none of the mevalonate pathway intermediates completely reversed the effect of NBPs on MDA-MB-231 proliferation (Reinholz et al., 2002). On the other hand, novel non-nitrogen containing BP (BP7033) has been shown to prevent post-translational Ras processing similarly to NBPs (Hamma-Kourbali et al., 2003). In addition, Zol, has been found to induce formation of a novel ANT-inhibiting cytotoxic ATP analogue, ApppI. Thus, Zol could act on cell apoptosis both via inhibition of the mevalonate pathway and by the blockage of mitochondrial ANT (Monkkonen et al., 2006). Zol has been demonstrated to inhibit proliferation and induce apoptosis (Jagdev et al., 2001; Senaratne et al., 2002), inhibit cell invasion (Denoyelle et al., 2003), and potently

diminishes bone, but also visceral metastasis *in vivo* (Duivenvoorden et al., 2007; Green et al., 2000; Hiraga et al., 2004; Peyruchaud et al., 2001). In addition, accumulating evidences indicate that bisphosphonates antitumor effects could be potentiated by other chemotherapeutic drugs (Yano et al., 2003). Several cases of possible synergy between bisphosphonates and statins or other mevalonate pathway inhibitors *in vitro* (Budman and Calabro, 2006; Dudakovic et al., 2008; Issat et al., 2007) and *in vivo* (Issat et al., 2007) have been reported showing potentiated effects.

Lescol, Fluvastatin (Fluva) represents lipophilic statins able to directly cross cell membranes in contrast to hydrophilic statins, like pravastatin, unable to penetrate membrane lipid bilayers (Istvan, 2003). Interestingly, recent results from epidemiological studies conclude in the protective effects of lipophilic statins on breast cancer risk (Ahern et al., 2011; Cauley et al., 2006). In breast cancer cells, Fluva is shown to exert significant growth inhibitory activity (Campbell et al., 2006), and reduce transendothelial migration of MDA-MB-231 cells in correlation with the inhibition of the membrane localization of RhoA and RhoC, but not with Ras (Kusama et al., 2006).

Fluva and Zol are used to treat and prevent atherosclerosis and osteoporosis respectively, mainly in elderly at an age where the prevalence of cancers increases sharply. Both drugs are therefore often co-prescribed in cancerous patients and they might influence the progression of the disease (Jadhav et al., 2006). Since *in vivo* potential effects of Fluva have not been described yet on breast cancer established metastases and since statins and bisphosphonates are frequently co-administrated, we proposed to investigate effects of these drugs using *in vivo* imaging system with a highly invasive bioluminescent MDA-MB-231 breast cancer subpopulation characterized by oncogenic KRAS mutation (Kozma et al., 1987) and constitutive activation of Ras as well as overexpression of RhoA (Fritz et al., 1999). Furthermore, as BPs induced apoptosis by forming ATP analogues (AppI) that could be complementary to Fluvastatin inhibition effect involving small G protein, we also evaluated the combination of these two drugs on established MDA-MB-231 metastases (fig 1).

MATERIALS AND METHODS

Cell culture and Drugs

The human breast adenocarcinoma MDA-MB-231 cells, obtained from the American Type Culture Collection (Manassas, VA, USA), were maintained in Dulbecco's minimal essential medium supplemented with 10% fetal bovine serum (FBS), 1% sodium pyruvate and antibiotics (1% penicillin sodium and 1% streptomycin) at 37°C in a humidified atmosphere containing 5% carbon dioxide. D3H2LN cell line isolated from MDA-MB-231 lymph node metastasis was purchased from Caliper Life Sciences (Alameda, CA, USA). D3H2LN cell line was a clone selected from a MDA-MB-231 stable clone expressing luciferase. MDA-MB-231 cells expressing luciferase were injected into the mammary fad pad of nude mice and after 12 weeks of growth *in vivo*, they were harvested and re-propagated *in vitro*. This subclone was injected once more into the mammary fad pad of mice to yield a second cell line D3H2LN, harvested from a lymph node metastasis (Jenkins et al., 2005). D3H2LN cells were cultured in Minimum Essential Medium with Earl's Balanced Salts Solution MEM/EBSS medium supplemented with 10% fetal bovine serum, 1% nonessential amino acids, 1% L-glutamine, and 1% sodium pyruvate and antibiotics (all from Hyclone, Logan, UT, USA) at 37°C in a humidified atmosphere containing 5% carbon dioxide.

Fluvastatin was purchased from (Axxora, Coger S.A.R.L., Paris), Zoledronic Acid (Zol), was synthesized as described earlier (Lecouvey et al., 2001; Monteil et al., 2005).

In vitro viability inhibition assay

MDA-MB-231 and D3H2LN cell viability was assessed using the MTT-microculture tetrazolium assay (Mosmann, 1983). The cells (5000 cells per well in 96 well plate) were then incubated with different concentrations of Zol or Fluva, for 24h, 48h, and 72h at 37°C in a 5% CO₂-incubator. Optical density was measured at 570 nm using a Labsystems Multiskan MS microplate reader.

Intracardiac experimental metastasis model

Fluva and Zol effects were evaluated on already established metastasis. Zol administration of 100 µg/kg, corresponding to 2.5 µg/mouse, was chosen to be inferior to the effective dose described earlier in 4T1/luc mouse breast cancer model (5 µg/mouse, i.e. 150-200 µg/kg) (Hiraga et al., 2004). The highest Fluva dose (15 mg/kg/d), equivalent to a human dose of 80mg/d, was chosen according to previous publication (Campbell et al., 2006). Drug Curative effects were evaluated on the progression of established metastases as following: Female nude

mice 8-10 weeks old (Janvier) were anesthetized intraperitoneally with 120 mg/kg ketamine and 6 mg/kg xylazine and were injected with D3H2LN (1×10^5 cells) in 100 μ l sterile PBS into the left ventricle of the heart by non surgical means. A successful intracardiac injection (IC) was immediately confirmed by systemic bioluminescence signal distributed throughout the animal. Only mice with satisfactory injection continued the experiment. Once metastatic colonisation had been confirmed 7-10 days after cells IC injection (the baseline of metastasis bioluminescent signal was set to 300 photon counts/sec maintained for 2-3 days, i.e. seen at two subsequent acquisitions), treatments were administered by intraperitoneal injection with 100 μ l of PBS solutions of Zol (100 μ g/kg three times a week) or Fluva (1 or 15 mg/kg daily) or PBS alone (daily for control group). The first drug administration was denoted as Day 0, and the treatments lasted for 3 weeks (Day 21).

Bioluminescent Imaging

Anesthetized mice by exposure to 1-3% Isoflurane, were placed in the IVIS™ Imaging System (Xenogen) and imaged from both dorsal and ventral views approximately 5 min after intraperitoneal injection of 150 μ l D-luciferin (Caliper Life Science) at 30 mg/ml per mice. Assessment of established metastasis was evaluated by imaging during the treatment period (3 weeks). Acquisition time was 5 min at the beginning of the time course and was progressively reduced afterwards in accordance with signal strength to avoid saturation. Analysis was performed using Living Image software (Xenogen) by measurement of photon flux (photon/s/cm²) with a region of interest (ROI) drawn around the whole animal bioluminescence signal. Signals of both dorsal and ventral views at early stages, and from 4 views (dorsal, ventral, left and right) at later stages were averaged for each animal in order to avoid the discrepancy related to the depth of metastases location.

Gene Expression Profiling

MDA-MB-321 cells were lysed after 12h and 24h treatment with 2 μ M Fluvastatine, or 30 μ M Zoledronate (concentrations corresponding to IC₅₀ at 72h treatment), or treated with Zoledronate for longer time (48h at 30 μ M) or with its higher concentration (24h at 100 μ M of Zoledronate). Control were treated with equivalent volume of PBS 1X added to each drug solution. Total RNA from these treated or control cell cultures (four independent replicates for each condition) were isolated using RNeasy mini kit (Qiagen, Valencia, CA, Germany) by direct lyses on the 10 cm culture dish with 600 μ l RLT Buffer following manufacturer's instructions. Purified RNA was quantified with the Nanodrop ND-1000 spectrophotometer

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(Thermo Fisher Scientific, Hudson, NH, USA) and its quality was checked by running the Eukaryotic Total RNA Nano Assay in the Bioanalyser 2100 (Agilent Technologies, Chandler AZ, USA) using Agilent RNA 6000 Nano Kit. Samples were prepared for hybridization to Affymetrix GeneChip® Human Gene 1.0 ST arrays according to manufacturer's instructions starting from 300 ng of total RNAs. Quality Control of cRNA synthesis, hybridization and data acquisition was performed according to the manufacturer's protocol completed with personal QC and data visualization.

Data Analysis

Raw data were processed with the apt-probeset-summarize program from the Affymetrix Power Tools (v1.10.2) for background correction and normalization. RMA (Robust Multichip Analysis) algorithm (Irizarry et al., 2003) with full quantile normalization was applied using the array design library files V1 release 4 and normalised values expressed on a log base 2 scale. Transcripts and genes were annotated with the Affymetrix release 29 annotation files based on the human genome version 18 assemblies. Data analysis was performed with the R Bioconductor LIMMA package. The microarray data have been deposited in NCBI's Gene Expression Omnibus (Edgar et al., 2002) and are accessible through GEO Series accession number GSE33552 (<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE33552>). Probe sets corresponding to control genes or having a low intensity signal (median log2 of intensity <4) or having low variability (trimmed range excluding the min-max values <0.5) were not considered for further analyses, yielding a total of 22289 probe sets. Only genes with a false discovery rate<0.05 and fold change \geq 1.5 in paired comparison between treatments and their corresponding controls were considered as differentially regulated. Analysis of genes associated with cell functions was carried out using Ingenuity Pathways Analysis (IPA) software (Ingenuity Systems Inc.) to identify biological processes and pathways which may be associated with modulated gene expression.

Quantitative real-time RT-PCR analysis

Total RNA (20 μ g) was reverse-transcribed using MMLV RT (Invitrogen, Carlsbad, CA, USA) and Random primers from Roche Applied Science (Roche, Indianapolis, IN, USA); 40 ng of reverse transcribed RNA was used as template for each reaction. qRCR assays were designed using Universal Probe Library site <https://www.roche-applied-science.com/sis/rtpcr/upl/index.jsp> (Roche Applied Science). Real-time PCR was carried out

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on LightCycler® 1.5 Real-Time PCR System (Roche, Indianapolis, IN, USA) either using LightCycler® FastStart DNA Master^{PLUS} SYBR Green I Kit with primers purchased from Tib Molbiol Syntheselabor GmbH (Germany), or LightCycler TaqMan Master Kit and Universal ProbeLibrary probes (Roche Applied Science) with primers from Tib Molbiol. The reactions were cycled 45 times (95°C, 10 sec; 60°C, 30 sec) after initial 10 min incubation at 95°C for TaqMan procedure or 95°C for 10 min, followed by 45 cycles of 95°C for 10 sec, 60°C for 10 sec and 72°C for 10 sec for SYBR Green procedure. Results were normalised to the expression of the *PPia* or *beta2M*, two genes that exhibit little variation in this data set out of five tested house-keeping genes. Similar results were obtained for both genes of reference. The mRNA transcript level for target genes was calculated as outlined in previously (Pfaffl et al., 2002)

$$\text{Ratio} = (\text{Eff target})^{\Delta\text{Cp insulin(MEANcontrol - MEANsample)}} / (\text{Eff reference})^{\Delta\text{Cp 18S(MEANcontrol-MEANsample)}}$$

Statistical Analysis

Analysis of *in vitro* and *in vivo* metastasis progression (bioluminescent signal or number of metastatic sites) was performed using the ANOVA Tukey-Kramer Multiple Comparisons Test for and Student's t-test. P<0.05 was considered significant. Kaplan-Meyer survival curves were generated using Graph Pad Prism software.

RESULTS

***In vivo* anti-metastatic potential of Zol and Fluva**

Drug effect was evaluated on the progression of established metastases (Fig. 2 and 3). Mice with successful intracardiac injection (Fig. 2A) developed metastases within 2 weeks. Once metastasis detected (Bioluminescent signal > 3 00 photon counts), mice were randomly divided in four groups and received intra-peritoneal injections three times a week with Zol at 100 µg/kg (n=8), or daily with Fluva at 1 mg/kg (n=8) or 15 mg/kg (n=7) or treated daily with PBS for control group (n=8) during 3 weeks. While no significant effect on metastasis bioluminescence was observed with Fluva at 1mg/kg (supplemental Figure S1), treatment with Fluva at 15 mg/kg or Zol 100 µg/kg induced about 80 % inhibition of luminescence signalling at the end of treatment ($p=0.01$ and 0.02, respectively, Fig. 2B,C). During last (third) week of treatment, 3 out of 7 Fluva-treated (15 mg/kg) mice manifested a decrease of established metastatic sites, and 5 out of 7 mice showed visible reduced/stabilized bioluminescent signal (Fig. 3A and Supplementary Table 1); this decrease of metastasis luminescence was not observed with Zol.

In order to visualize the organs affected by metastases, we performed *ex vivo* analysis. *Ex vivo* imaging of the different tissues after the final imaging *in vivo*, showed bone lesions (legs, scull, spine) as well as ovary, brain, lung, kidney, or lymph node ones (Fig 3B).

Mice survival curves were generated from the first drug administration followed by 3-week-treatment and until they died (Fig. 3C). Fluva (15 mg/kg) or Zol (100µg/kg) treatment significantly reduced the death of mice as compared to control with median survival of 21 days for control, 33 for Zol and 28 for Fluva ($P=0.0245$, Fig.3C).

Transcriptomic profiling of Zol or Fluva

In order to evaluate the different genes regulated by Zol and Fluva, we performed a transcriptomic analysis. To find a comparable treatment condition for each drug, their effects on MDA-MB-231 breast cancer cells survival/proliferation were first tested using a standard MTT assay at 12h, 24h, 48h, and 72h (supplemental Figure S2). Initially, we chose the concentration as the half maximal inhibitory concentration detected after 72 h treatment ($IC_{50,72h}$), corresponding to 2 µM for Fluvastatin and 30 µM for Zoledronate. Early treatment was chosen (12h and 24h). RNAs extracted from four replicates (four independent treatments

and respective controls for each condition) at each time point were subjected to hybridization on HuGene 1.0ST Affymetrix arrays (Fig.4). Analysis of genes functions common to Zol and Fluva (540 probesets: 373 up- and 167 down-regulated annotated genes, Supplementary Table 4A,B) showed that the majority of them were involved in functions critical for metastatic steps such as cellular proliferation, migration, invasion and apoptosis (Fig 4 A , B). In addition, only 9 genes (DKK1, FGF1, FST, G0S2, HIF1A, LGALS3, PVR, TNFRSF12, UAP1) dependenting on Ras activation were modified as compared to previous work (Loboda et al., 2010). In addition, by compiling genes whose expression is dependent on MAPK/PI3K pathways as described in a previous data (Bild et al., 2006) only 9% of the concerning genes whose expression depends on prenylation of Ras protein or Rho activation were modified. Transcriptomic data were validated by qPCR on 13 differentially regulated by Zol or Fluva genes (5 Zol-specific and 8 common Zol/Fluva genes asterisked in supplemental Tables 3-4).

The analysis of significant differentially expressed genes between treated and control cells (FDR<0.05, fold change>1.5) revealed 29 probe sets (18+11 on the diagram) for Fluva at 12h, additional 526 probe sets for Fluva at 24h (16+365+145 on the diagram) (supplemental Figure S3A) and no significant genes for Zol at 12h nor at 24h (supplemental Figure S3B) Analysis of genes specifically regulated by each drug, revealed 16 probe sets for Fluva corresponding to 12 annotated genes (supplemental Figure S3A, C, Supplementary Table 2) and a more important number (1032 probe sets corresponding to 951 annotated genes) for Zol treatments (supplemental Figure. S3A, D, Supplementary Table 3). The majority of genes regulated by Fluva at 12h or 24h (100% and 97%, respectively), were common to Zol100 24h gene profile (supplemental Figure S3A). Clustering of common Fluva and Zol genes (supplemental Figure S3B) reveals that for Zol treatment the pattern starts to appear at 24h with the shortest distance found between Zol at 48h (ZOLCONT48) and Fluva at 12h (FLUVACONT12) indicating early changes. It might indicate retarded Zol kinetics as changes induced by Zol at 48h were most similar to those induced by Fluva at 12h.

In vivo anti-metastatic potential of Zol and Fluva combination

Since Zol can inhibited apoptosis differently from Fluva by inducing cytotoxic analog AppI (Fig 1) and since the combination of these two drugs was also described synergistic *in vitro* (Budman and Calabro, 2006) we tested the combination treatment *in vivo* using the same concentrations as described above for these drugs alone. Mice were treated with Zol (100 µg/kg, three times a week) combined with Fluva at 1 mg/kg or 15 mg/kg administered daily (Supplemental Fig. S1, and Fig 5). The combination of Zol with the highest Fluva concentration (15mg/kg) did not change significantly the level of bioluminescence metastasis signal (Fig. 5A) nor metastatic site number (data not shown) as compared to Zol or Fluva alone. Survival analysis showed no significant differences between Zol, Fluva (at 15mg/kg) or their combination (Fig. 5B), with median survival of 33, 38, and 34 days respectively. Moreover, combinatorial treatment did not result in any improvement of the effect seen with Fluva when administered at a non-efficient 1 mg/Kg concentration (supplemental Figure S1).

DISCUSSION

For the first time, we demonstrate the curative effect of Fluva on breast cancer metastases *in vivo* using MDA-MB-231 population (D3H2LN) metastasis model. Indeed, Fluva induces a strong inhibition of the progression of established metastases (80%) when administered at 15 mg/kg. As compared to Zol, Fluva alone delayed the growth of established metastases as soon as the first week of the treatment. It is to note that we observed a partial metastasis regression in three out of seven mice characterized by decay of bioluminescent signal. However this effect was not observed in all mice since we only detected 40% of inhibition in the mean number of metastasis sites (data not shown). Concerning organs affected by metastases both Zol and Fluva affected bone as well as visceral metastases localisation.

Transcriptomic analyses of MDA-MB-231 cells treated with Fluva or Zol demonstrate common regulation of genes implicated in metastatic capacities of tumor cells. The majority of differentially expressed genes under 12h and 24h Fluva (2 μ M for IC 50_{72h} concentration) treatment were regulated in the same manner by Zol when incubated at its IC 50_{72h} (30 μ M) for a longer time (48h), or with higher concentration (100 μ M) for the same time treatment (24h). This kinetic difference between proliferation and transcriptomic activity could be explained by the higher lipophilicity of Fluva versus Zol (LogP 3.69 versus -0.93, respectively) that allowed a better penetration of Fluva into the cells. In addition, proliferation might involve protein post translational changes that cannot be directly evaluated in transcriptome analysis. Genes implicated in cellular movement, cellular growth and proliferation, development as well as apoptosis are regulated in the same manner and provide target metastatic genes for both molecules. For instance gene expression is consistent with the pro-apoptotic activity of both drugs : the expression of 14 pro-apoptotic genes (TP53INP1, BTG1, TNS4, PGEP1, TP53I3, MAP3K5, BINP3L, IFIH1, IER3, PTPRH, TMEM173, SLK, CD14, TNFRSF1A) is increased while only 6 pro-apoptotic genes are down-regulated (TGM2, ERCC2, PAWR, AEN, TNFRSF12A, FAM176A).

To note that some genes modified by both drugs are also involved in immune and inflammatory responses. Genes modulating the immune response are up regulated when they stimulate the immune system (CMKLR1, APOBE3CF, TLR6, REG, IFIH1, ANXA11, TMEM173, CD14) and down regulated when they are immuno-suppressive (PTGER4, PDCD1LG2, CD174), attributing globally to both drugs an immuno-stimulant profiles. This effect of Fluva on cancer cells is notably different of what is observed in immune cells, in

which statins inhibit the immune system (Greenwood et al., 2006). This point is important since it demonstrates that these molecules could interact in concert with the immune system to induce suppression of cancer cells. To verify this finding, it would be interesting to further study drug effects on metastases processes in immuno-competent mice model.

Only one *in vivo* study of statins combined with bisphosphonates showed a delay in pancreatic tumor growth and an increase in mouse survival when combining lovastatin and pamidronate (Issat et al., 2007). Also, Fluva alone or in association has been described to inhibit tumor growth and metastases formation of hepatocarcinoma cell lines (Issat et al., 2007; Paragh et al., 2003). In addition, Fluva is effective on other cancers such as pancreatic and head and neck carcinomas (Bocci et al., 2005; Fujiwara et al., 2008). For breast cancer cells, the use of Fluva in combination with other chemotherapeutic molecules was also described *in vitro* (Budman et al., 2007) lacking for *in vivo* data. In our *in vivo* study of Fluva combination, we observed no differences in metastatic growth in combination treatments. Association of Fluva and Zol at their efficient concentrations (15 mg/kg and 100 µg/kg, respectively) resulted in no significant differences compared to the effects of these drugs alone, as well as combination treatment with Fluva at non-efficient 1mg/kg concentration. Observation of common transcriptomic profiles between Zol and Fluva supported this finding of the absence of synergy *in vivo*. The differences observed between our work on metastasis and other ones on tumor xenograft can also be explained by these molecule activities since they both target Rho/Ras proteins. However, concerning genes whose expression depends on prenylation of Ras protein or Rho activation (Bild et al., 2006), only 9% of the total number of these genes was modified by Zol or Fluva. This finding suggested that other mechanisms are involved in the inhibition of metastasis formation by the two drugs. Furthermore the specific capacity of Zol to inhibit DNA synthesis could complete the Fluva one in primary tumor rather than in metastatic cell growth. In conclusion, this study demonstrates the potential benefit of the use of Fluva associated or not with bisphosphonates in the context of established breast cancer metastases. It also suggests that the frequent association of statins and bisphosphonates in old patients could influence the course of breast metastasis

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AUTHORSHIP CONTRIBUTIONS

Participated in research design: Vintonenko, Crepin, Perret, and Di Benedetto

Conducted experiments: Vintonenko, Kassis, and Abdelkarim

Contributed new reagents or analytic tools: Lecouvey

Performed data analysis: Di Benedetto, Vintonenko and Jais.

Wrote or contributed to the writing of the manuscript: Vintonenko, Jais, Perret, and Di Benedetto

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FOOTNOTES

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LEGENDS OF FIGURES

Figure 1. Mevalonate pathway inhibition scheme. Prenylation of small G-proteins can be inhibited either by statins acting on upstream enzyme HMG-CoA reductase, or by Bisphosphonates targeting downstream enzyme Farnesyl-pyrophosphate synthase which could lead to cytotoxic ATP analog AppI accumulation.

Figure 2. Fluvastatin or Zoledronate alone reduce metastatic burden in breast cancer metastasis mice model. A, Bioluminescent MDA-MB-231 (D3H2LN) cells (10^5) were injected into the left ventricle of nude mice. Only mice with successful intracardiac cells injection, witnessed by overall luminescent signal, continued the experiment. B, Plot of bioluminescent signal for control group treated (daily with PBS 1x) and treated with Zol (at 100 μ g/kg three times a week) and Fluva (at 15mg/kg daily) mice; each point represents a mean (\pm SEM) signal of eight (Control or Zol) or seven (Fluva) mice** p<0.01 vs Control (ANOVA Tukey-Kramer Multiple Comparisons Test for j21 Control, Zol, Fluva) C, Treatment by Zol, Fluva, or PBS for control group was started upon confirmation of detectable established metastasis within two weeks after injections (denoted as Day 0 for treatment); representative bioluminescent images for indicated days of treatment are rendered at the same photon scale for control group, and mice treated with Zol (100 μ g/kg) and Fluva (15mg/kg).

Figure 3. Effects of Fluva on number of metastatic sites and mice survival.

A. The number of detected metastatic sites in treated Fluva at 15mg/kg and control mice. The duration of treatment was 21 days. B, Ex vivo representative images of metastatic sites in mice treated with Fluva (15mg/kg). C, Kaplan-Meyer survival curves for control, Zol (100 μ g/kg), and Fluva (15mg/kg) treated mice (median survival of 21, 33, and 38 days respectively) generated for 3-weeks treatment period and followed up until they died.

Figure 4. Functional analysis of genes commonly regulated by Fluva or Zol.

Ingenuity Pathways Analysis for 540 probe sets common between Fluva (either at 12h or 24h) and Zol (either at 30 μ M at 48h or 100 μ M at 24h) treatments. A, 373 up-regulated probe sets corresponding to 370 annotated genes. B, 167 down-regulated probe sets corresponding to 166 annotated genes.

Figure 5. Effect of Fluva and Zol combination *in vivo*.

Bioluminescent MDA-MB-231 (D3H2LN) cells (10^5) were injected into the left ventricle of nude mice. Only mice with successful intracardiac cells injection, witnessed by overall luminescent signal, continued the experiment. As described in Fig. 2, mice were treated upon detection of established metastasis (referred as Day 0) with Zol (at 100 μ g/kg three times a week), Fluva (at 15mg/kg daily), their combination (100 μ g/kg Zol twice a week + 15mg/kg Fluva daily), or PBS (daily for control group) during 3 weeks. A, Plot of bioluminescent signal; each point represents a mean (\pm SEM) signal of eight (Control, Zol, Fluva or Zol with Fluva combination) or seven (Fluva) mice. ** p<0,01 vs Control (ANOVA Tukey-Kramer Multiple Comparisons Test for Day 21 Control, Zol, Fluva15, Zol+Fluva15). B, Kaplan-Meyer survival curves for control and treated mice (median survival of 21 days for Control, and 33, 38, and 34 days for Zol, Fluva, or Zol with Fluva combination respectively) generated for 3-weeks treatment period and followed up until they died.

Figure 1.

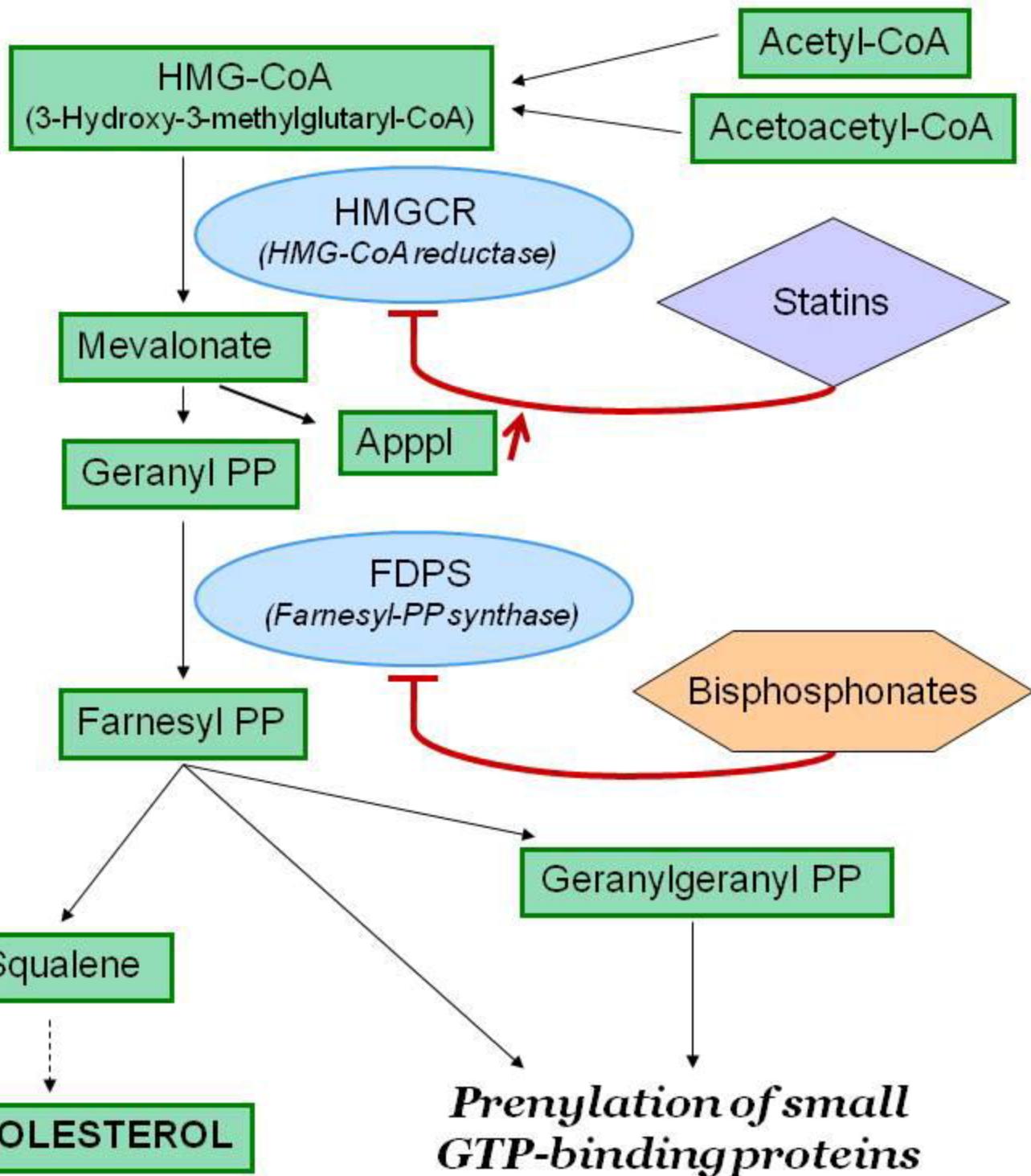


Figure 2.

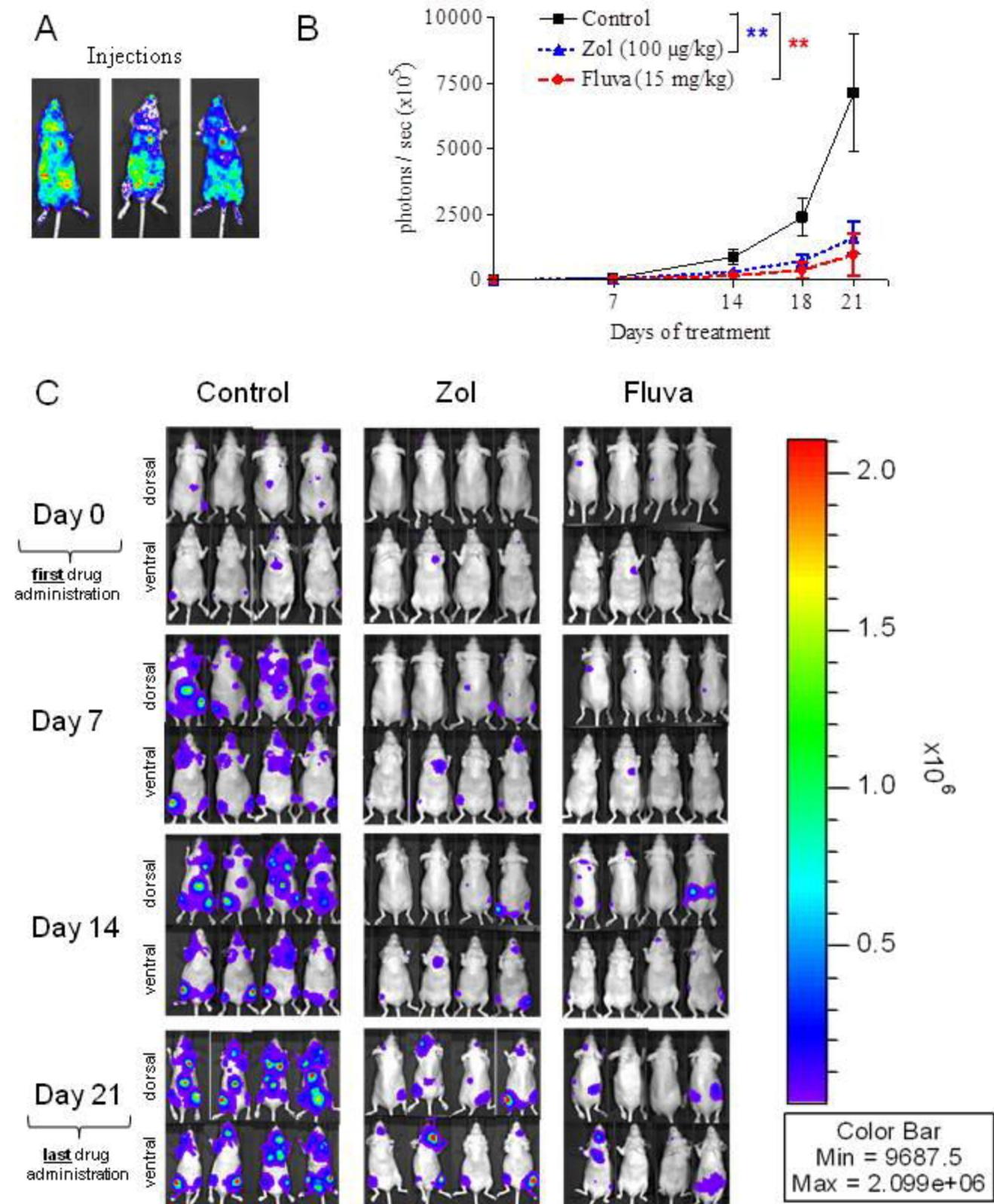
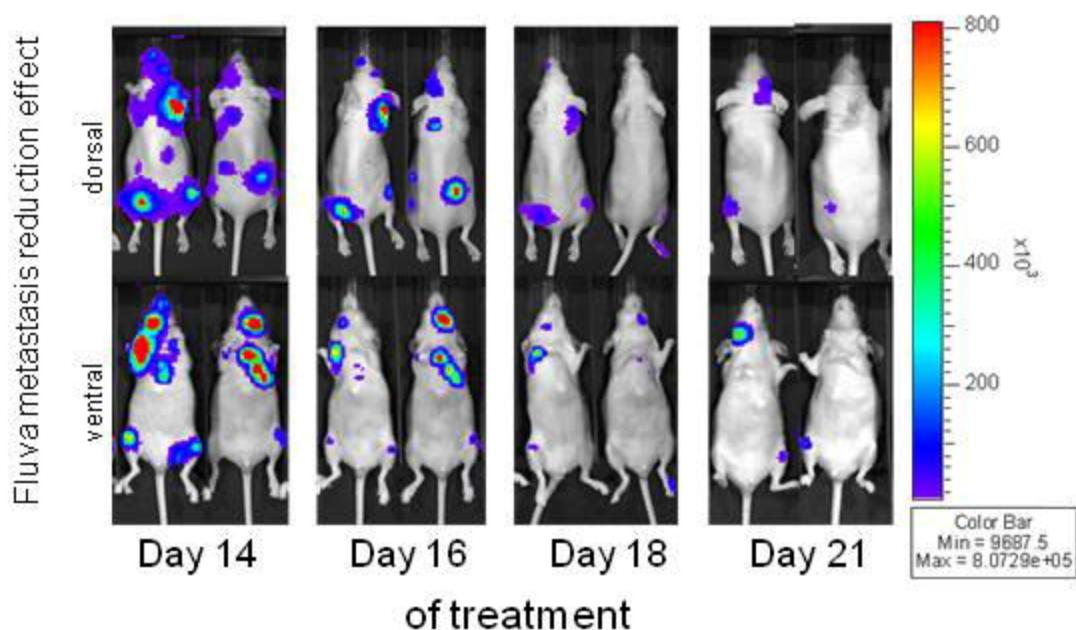
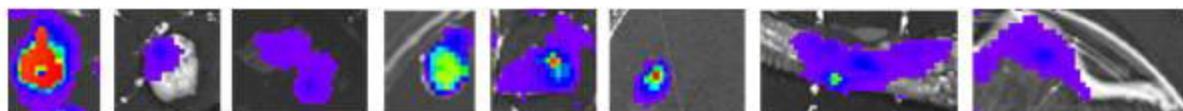


Figure 3.

A



B



C

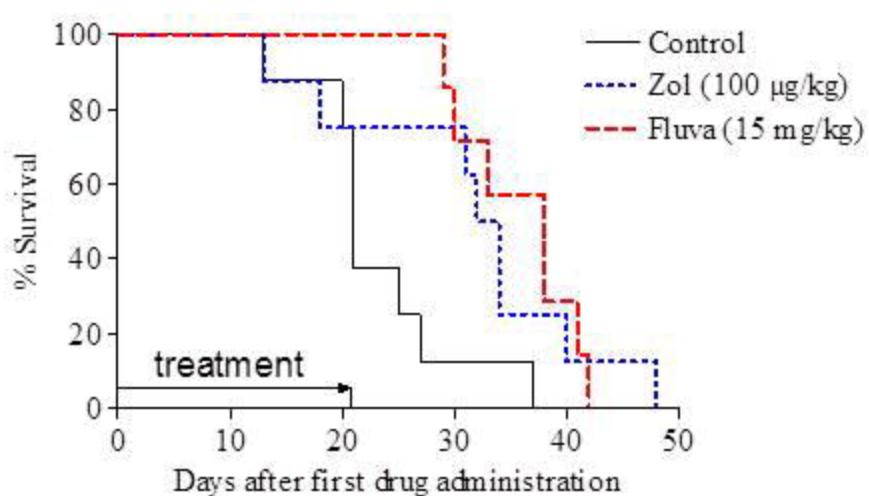
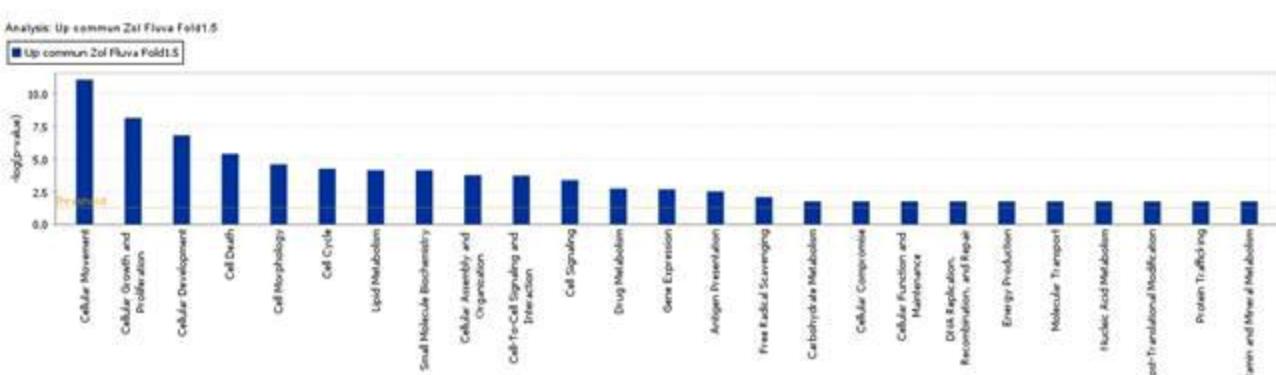


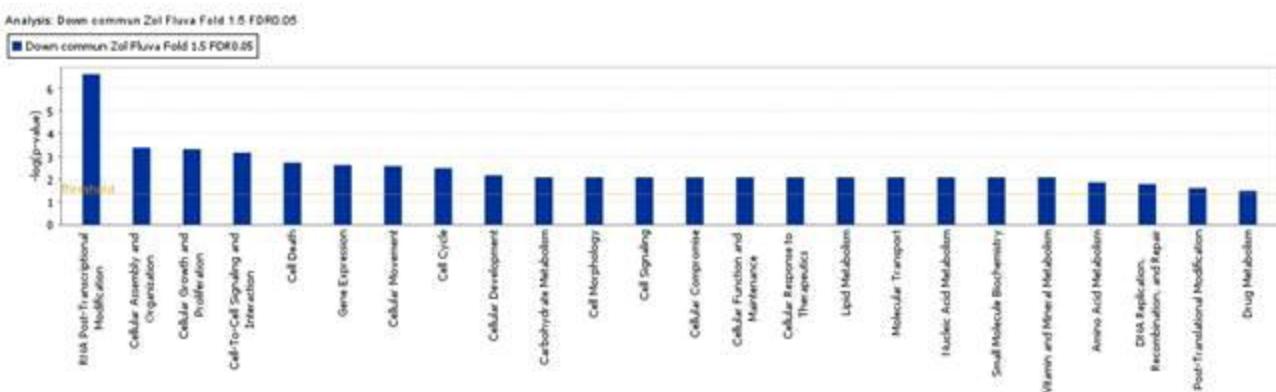
Figure 4.

A



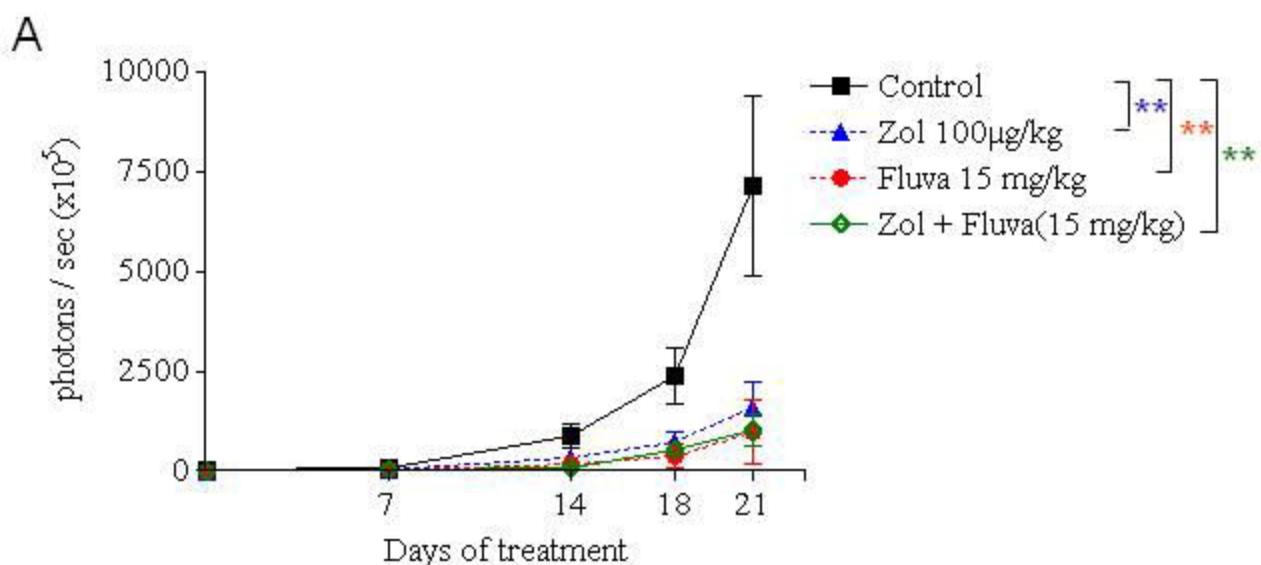
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B

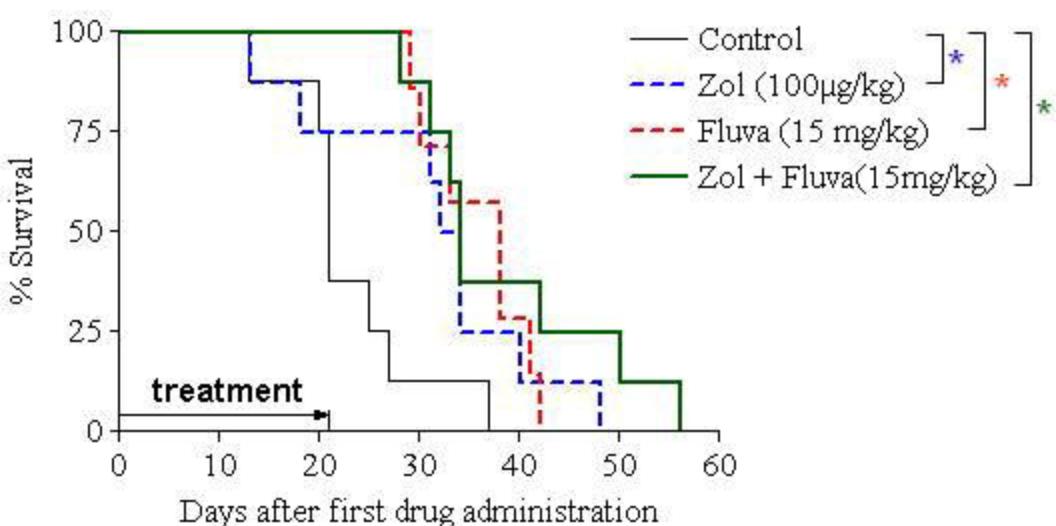


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Figure 5.



B



Supplementary Table 1. Frequency of decreased metastasis in Zol and/or Fluva treated mice.

Condition	# of mice with:	
	decreased # of metastatic sites	Decreased or stabilized bioluminescent signal
Control	0/8	0/8
Zol (100 ug/kg)	0/8	1/8
Fluva (1 mg/kg)	0/8	2/8
Zol (100 ug/kg) + Fluva (1 mg/kg)	0/8	2/8
Fluva (15 mg/kg)	3/7	5/7
Zol (100 ug/kg) + Fluva (15 mg/kg)	1/8	2/8

Supplementary Table 2. Genes specifically regulated by Fluva (non-significant for Zol).

Gene ProbeSet ID	Gene symbol	Gene title	Fold change (log2) Fluva 24h vs Control
7921031			1,317
8119423	LOC221442	adenylate cyclase 10 pseudogene	1,27
8031646	MGC9913	hypothetical protein MGC9913	0,962
8156253	FAM75A7	family with sequence similarity 75, member A7	0,823
8059955	RAB17	RAB17, member RAS oncogene family	0,747
		aldo-keto reductase family 1, member B1 (aldo-	
8143054	AKR1B1	reductase)	0,737
8019643	DOC2B	double C2-like domains, beta	0,69
8098195	SC4MOL	sterol-C4-methyl oxidase-like	0,688
		cytochrome P450, family 1, subfamily A,	
7990391	CYP1A1	polypeptide 1	0,651
		anterior pharynx defective 1 homolog B (<i>C. elegans</i>)	
7984124	APH1B		0,642
	ANKRD20		
7970381	B	ankyrin repeat domain 20B	0,593
8065541	C20orf191	chromosome 20 open reading frame 191	-0,601
8073511			-0,643
7952810	IGSF9B	immunoglobulin superfamily, member 9B	-0,752
8066391			-0,78
8013987			-1,282

Supplementary Table 3. Genes specifically regulated by Zol (non-significant for Fluva).

Genes Probe Set ID	Genes Symbol	Genes Title	log2	
			Zol100 vs Control (24h)	Zol vs Control (48h)
8065412	CST1	cystatin SN	2,168	1,772
7928308	DDIT4	DNA-damage-inducible transcript 4	2,066	0,349
8154100	VLDLR	very low density lipoprotein receptor	1,99	0,413
8149749	TNFRSF10D	tumor necrosis factor receptor superfamily, member 10d, decoy with truncated death domain	1,973	0,659
8006531	SLFN5	schlafen family member 5	1,692	0,183
8147145	ATP6V0D2	ATPase, H ⁺ transporting, lysosomal 38kDa, V0 subunit d2	1,689	0,71
8013660	ALDOC	aldolase C, fructose-bisphosphate	1,649	0,871
8140967	SAMD9	sterile alpha motif domain containing 9	1,611	0,66
8113709	LOX	lysyl oxidase	1,566	0,524
7934278	P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	1,527	0,428
8027002	GDF15	growth differentiation factor 15	1,415	0,201
7961175	KLRC3	killer cell lectin-like receptor subfamily C, member 3	1,403	1,038
8081288	TMEM45A	transmembrane protein 45A	1,342	0,401
8012126	CLDN7	claudin 7	1,339	0,415
7993588	TMC7	transmembrane channel-like 7	1,318	0,3
8073088	APOBEC3G	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G	1,302	0,174
8046408	PDK1	pyruvate dehydrogenase kinase, isozyme 1	1,287	0,382
8161174	GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase	1,283	0,562
7937079	BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3	1,278	0,5
8043283	KDM3A	lysine (K)-specific demethylase 3A	1,274	0,453
7923991	PLXNA2	plexin A2	1,252	0,481
8163618	TNFSF15	tumor necrosis factor (ligand) superfamily, member 15	1,249	1,254
8115490	ADAM19	ADAM metallopeptidase domain 19 (meltrin beta)	1,231	0,517
8041383	LTBP1	latent transforming growth factor beta binding protein 1	1,228	0,75
7920877	ARHGEF2	rho/rac guanine nucleotide exchange factor (GEF) 2	1,194	0,219
8065416	CST2	cystatin SA	1,177	1,153
8139656	GRB10	growth factor receptor-bound protein 10	1,173	0,141
7899955			1,165	0,453

8156571	C9orf3	chromosome 9 open reading frame 3	1,116	0,541
8058765	FN1 *	fibronectin 1	1,151	0,649
8105077	CARD6	caspase recruitment domain family, member 6	1,127	0,415
7908879	PPFIA4	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	1,125	0,455
8021301	RAB27B	RAB27B, member RAS oncogene family	1,113	0,272
7999642	KIAA0430	KIAA0430	1,112	0,195
8143341	JHDM1D	jumonji C domain containing histone demethylase 1 homolog D (<i>S. cerevisiae</i>)	1,097	0,072
8032410	MOBKL2A	MOB1, Mps One Binder kinase activator-like 2A (yeast)	1,075	0,433
7949719	PC	pyruvate carboxylase	1,07	0,344
8048489	ANKZF1	ankyrin repeat and zinc finger domain containing 1	1,07	0,281
7973743			1,063	0,313
8164810	RALGDS	ral guanine nucleotide dissociation stimulator	1,052	0,405
7908072	LAMC2	laminin, gamma 2	1,051	0,747
8171105	CRLF2	cytokine receptor-like factor 2	1,048	0,37
8110032	C5orf41	chromosome 5 open reading frame 41	1,033	-0,135
8012949	CDRT1	CMT1A duplicated region transcript 1	1,029	0,468
8152703	FBXO32	F-box protein 32	1,013	0,315
8148304	TRIB1	tribbles homolog 1 (<i>Drosophila</i>)	1,01	0,483
8062190	SPAG4	sperm associated antigen 4	1,008	0,42
7964927	TSPAN8	tetraspanin 8	1,003	0,665
8093258	IQCQ	IQ motif containing G	1,001	0,252
7923974			0,997	0,438
7963774	ZNF385A	zinc finger protein 385A	0,984	0,399
8001818	TK2	thymidine kinase 2, mitochondrial	0,98	0,304
8040430	VSNL1	visinin-like 1	0,969	0,462
8098604	ANKRD37	ankyrin repeat domain 37	0,969	0,08
7955441	METTL7A	methyltransferase like 7A	0,954	0,595
7934297			0,953	0,4
8113369	SLCO4C1	solute carrier organic anion transporter family, member 4C1	0,946	0,445
8022711	DSC2	desmocollin 2	0,94	0,382
8151457	HEY1	hairy/enhancer-of-split related with YRPW motif 1	0,939	0,418
7960654	ING4	inhibitor of growth family, member 4	0,932	0,12
8102532	PDE5A	phosphodiesterase 5A, cGMP-specific	0,932	0,246
7967486	CCDC92	coiled-coil domain containing 92	0,93	0,153
8085716	SATB1	SATB homeobox 1	0,929	0,304

8131719	DNAH11	dynein, axonemal, heavy chain 11	0,928	0,277
8017675	PLEKHM1P	pleckstrin homology domain containing, family M (with RUN domain) member 1 pseudogene	0,924	0,259
8061564	ID1	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	0,918	0,219
8064904	FERMT1	fermitin family homolog 1 (Drosophila)	0,918	0,175
7945377	SIGIRR	single immunoglobulin and toll-interleukin 1 receptor (TIR) domain	0,912	0,26
8044766	INSIG2	insulin induced gene 2	0,912	0,163
8088436	C3orf67	chromosome 3 open reading frame 67	0,909	0,325
7953943	GABARAPL1	GABA(A) receptor-associated protein like 1	0,907	0,059
8095356			0,906	0,066
8084589	MAP3K13	mitogen-activated protein kinase kinase kinase 13	0,903	0,245
7921434	AIM2	absent in melanoma 2	0,902	0,26
8167185	TIMP1 *	TIMP metallopeptidase inhibitor 1	0,901	0,558
8088247	ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3	0,9	0,208
8143279	ZC3HAV1	zinc finger CCCH-type, antiviral 1	0,898	0,347
8095736	AREG	amphiregulin	0,897	0,53
8160637	B4GALT1	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1	0,894	0,34
7937612	MUC5B	mucin 5B, oligomeric mucus/gel-forming	0,892	0,494
8015914	HDAC5	histone deacetylase 5	0,89	0,303
8111101	ANKH	ankylosis, progressive homolog (mouse)	0,89	0,36
7955694	IGFBP6	insulin-like growth factor binding protein 6	0,888	0,437
7928491	MYST4	MYST histone acetyltransferase (monocytic leukemia) 4	0,886	0,28
7993624	SYT17	synaptotagmin XVII	0,886	0,376
7910379	DUSP5P	dual specificity phosphatase 5 pseudogene	0,884	0,095
8001800	CDH11	cadherin 11, type 2, OB-cadherin (osteoblast)	0,883	0,713
8047577	ALS2CR8	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 8	0,88	0,31
7963206			0,877	-0,421
7989277	MYO1E	myosin IE	0,874	0,338
8162276	NFIL3	nuclear factor, interleukin 3 regulated	0,872	0,182
7942007	LRP5	low density lipoprotein receptor-related protein 5	0,871	0,523
7957759	APAF1	apoptotic peptidase activating factor 1	0,871	0,418

8003875	SPNS2	spinster homolog 2 (Drosophila)	0,871	0,272
8171624	GPR64	G protein-coupled receptor 64	0,87	0,154
8012464	LOC100128288	hypothetical protein LOC100128288	0,866	0,186
7973336	MMP14	matrix metallopeptidase 14 (membrane-inserted)	0,865	0,497
7997332	NUDT7	nudix (nucleoside diphosphate linked moiety X)-type motif 7	0,861	-0,01
8032392	MKNK2	MAP kinase interacting serine/threonine kinase 2	0,861	0,354
7917052	SLC44A5	solute carrier family 44, member 5	0,859	0,408
8008885	MIR21	microRNA 21	0,859	0,611
7927876	TET1	tet oncogene 1	0,856	0,321
8016239	PLEKHM1	pleckstrin homology domain containing, family M (with RUN domain) member 1	0,855	0,095
8102518	C4orf3	chromosome 4 open reading frame 3	0,855	0,183
7903404	RNPC3	RNA-binding region (RNP1, RRM) containing 3	0,848	0,138
8151512	PAG1	phosphoprotein associated with glycosphingolipid microdomains 1	0,845	0,256
7978932	SOS2	son of sevenless homolog 2 (Drosophila)	0,844	0,087
8014189	RFFL	ring finger and FYVE-like domain containing 1	0,844	0,224
8093304	CCRL2	chemokine (C-C motif) receptor-like 2	0,844	0,346
8145470	DPYSL2	dihydropyrimidinase-like 2	0,838	0,477
7956088	RAB5B	RAB5B, member RAS oncogene family	0,837	0,235
7908993	SOX13	SRY (sex determining region Y)-box 13	0,831	0,351
8095826	STBD1	starch binding domain 1	0,83	0,195
7984475	CORO2B	coronin, actin binding protein, 2B	0,829	0,249
8153021	ST3GAL1	ST3 beta-galactoside alpha-2,3-sialyltransferase 1	0,829	0,563
7921713	F11R	F11 receptor	0,828	0,266
7958913	OAS2	2'-5'-oligoadenylate synthetase 2, 69/71kDa	0,828	0,342
8169145	MUM1L1	melanoma associated antigen (mutated) 1-like 1	0,821	0,219
7897441	H6PD	hexose-6-phosphate dehydrogenase (glucose 1-dehydrogenase)	0,813	0,179
8012906			0,812	0,23
7928395	FUT11	fucosyltransferase 11 (alpha (1,3)fucosyltransferase)	0,81	0,432
8015412	JUP	junction plakoglobin	0,808	0,283
8115210	TNIP1	TNFAIP3 interacting protein 1	0,805	0,265
7898957	RCAN3	RCAN family member 3	0,803	0,463
8035445	JUND	jun D proto-oncogene	0,799	0,34

7926037	PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	0,796	0,294
7938100	SMPD1	sphingomyelin phosphodiesterase 1, acid lysosomal	0,794	0,404
7970441	GJB2	gap junction protein, beta 2, 26kDa	0,793	0,29
8012896	PMP22	peripheral myelin protein 22	0,793	0,281
8111941	HMGCS1	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1 (soluble)	0,792	0,596
8129880	PERP	PERP, TP53 apoptosis effector	0,792	0,341
7963786	ITGA5	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	0,79	0,292
8049317	DGKD	diacylglycerol kinase, delta 130kDa	0,786	0,303
7904726	TXNIP	thioredoxin interacting protein	0,782	0,158
8145490	PTK2B	PTK2B protein tyrosine kinase 2 beta	0,779	0,244
7973306	ABHD4	abhydrolase domain containing 4	0,775	0,297
8035793	ZNF737	zinc finger protein 737	0,775	0,497
8088958	GBE1	glucan (1,4-alpha-), branching enzyme 1	0,774	0,226
8116534	TRIM52	tripartite motif-containing 52	0,774	0,137
8136954	FAM115C	family with sequence similarity 115, member C	0,773	0,25
7985934	SEMA4B	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4B	0,772	0,382
8029950	EHD2	EH-domain containing 2	0,772	0,282
8081069	ZNF654	zinc finger protein 654	0,771	0,17
7964872	PTPRB	protein tyrosine phosphatase, receptor type, B	0,77	0,268
8131550	SCIN	scinderin	0,77	0,421
7936115	SH3PXD2A	SH3 and PX domains 2A	0,769	0,287
8055952	NR4A2	nuclear receptor subfamily 4, group A, member 2	0,768	0,286
7899289	WDTC1	WD and tetratricopeptide repeats 1	0,767	0,22
8086125	LBA1	lupus brain antigen 1	0,767	0,265
7990545	CSPG4	chondroitin sulfate proteoglycan 4	0,766	0,021
7974117	C14orf28	chromosome 14 open reading frame 28	0,762	0,014
7912157	ERRFI1	ERBB receptor feedback inhibitor 1	0,76	0,17
8089261	CBLB	Cas-Br-M (murine) ecotropic retroviral transforming sequence b	0,76	0,235
8169186	TBC1D8B	TBC1 domain family, member 8B (with GRAM domain)	0,758	0,28
7912145	TNFRSF9	tumor necrosis factor receptor superfamily, member 9	0,757	0,473
7906978	MGST3	microsomal glutathione S-transferase 3	0,756	0,236
8175393	ARHGEF6	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	0,756	0,206

7954469	RASSF8	Ras association (RalGDS/AF-6) domain family (N-terminal) member 8	0,752	0,101
8070097	DNAJC28	DnaJ (Hsp40) homolog, subfamily C, member 28	0,751	0,274
7949410	MALAT1	metastasis associated lung adenocarcinoma transcript 1 (non-protein coding)	0,749	0,501
7914603	RNF19B	ring finger protein 19B	0,745	0,339
8008933	BCAS3	breast carcinoma amplified sequence 3	0,745	-0,05
8079407	CCRL2	chemokine (C-C motif) receptor-like 2	0,744	0,317
7930413	DUSP5	dual specificity phosphatase 5	0,741	0,478
7983940	FAM63B	family with sequence similarity 63, member B	0,741	0,113
7930927	INPP5F	inositol polyphosphate-5-phosphatase F	0,74	0,205
8138202	ICA1	islet cell autoantigen 1, 69kDa	0,74	0,181
8057599	TFPI	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)	0,738	0,222
8130528	RSPH3	radial spoke 3 homolog (Chlamydomonas)	0,738	0,288
8103986	LRP2BP	LRP2 binding protein	0,735	0,141
8026047	JUNB	jun B proto-oncogene	0,734	0,441
7994981	ORAI3	ORAI calcium release-activated calcium modulator 3	0,733	0,437
7957386	ACSS3	acyl-CoA synthetase short-chain family member 3	0,732	0,052
8020508	RIOK3	RIO kinase 3 (yeast)	0,732	0,046
8037005	TGFB1 *	transforming growth factor, beta 1	0,731	0,641
8136940	FAM115C	family with sequence similarity 115, member C	0,731	0,219
8042402	APLF	aprataxin and PNKP like factor	0,73	0,135
7898663	PINK1	PTEN induced putative kinase 1	0,729	0,278
8154135	SLC1A1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system X ^{ag}), member 1	0,729	0,346
7956819	RASSF3	Ras association (RalGDS/AF-6) domain family member 3	0,728	0,134
7997139	CALB2	calbindin 2	0,728	0,141
7935572	PYROXD2	pyridine nucleotide-disulphide oxidoreductase domain 2	0,726	0,223
8040340	LPIN1	lipin 1	0,726	0,176
8063028	DNTTIP1	deoxynucleotidyltransferase, terminal, interacting protein 1	0,726	0,074
8120992	ZNF292	zinc finger protein 292	0,725	0,125
8047606	NBEAL1	neurobeachin-like 1	0,722	0,35

8032926	PTPRS	protein tyrosine phosphatase, receptor type, S	0,721	0,385
7931353	PTPRE	protein tyrosine phosphatase, receptor type, E	0,72	0,236
8066574	WFDC10B	WAP four-disulfide core domain 10B	0,72	0,285
8072710	APOL6	apolipoprotein L, 6	0,72	0,322
7927186	RASSF4	Ras association (RalGDS/AF-6) domain family member 4	0,719	0,119
8120176	C6orf141	chromosome 6 open reading frame 141	0,719	0,315
7977507	RPPH1	ribonuclease P RNA component H1	0,718	0,108
8030049	CYTH2	cytohesin 2	0,718	0,269
8130739	RPS6KA2	ribosomal protein S6 kinase, 90kDa, polypeptide 2	0,718	-0,19
8141206	BAIAP2L1	BAI1-associated protein 2-like 1	0,718	0,003
8111772	DAB2	disabled homolog 2, mitogen-responsive phosphoprotein (<i>Drosophila</i>)	0,716	0,401
7908178	C1orf26	chromosome 1 open reading frame 26	0,713	0,086
7998835			0,711	0,203
7908694	NAV1	neuron navigator 1	0,708	0,197
7925257	LYST	lysosomal trafficking regulator	0,708	0,284
8072876	LGALS1	lectin, galactoside-binding, soluble, 1	0,708	0,274
7921088	NES	nestin	0,706	0,449
8146921	RDH10	retinol dehydrogenase 10 (all-trans)	0,706	0,458
7934997	PPP1R3C	protein phosphatase 1, regulatory (inhibitor) subunit 3C	0,706	0,179
7964579	CTDSP2	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 2	0,706	0,263
7993281	SNX29	sorting nexin 29	0,705	0,116
8140113	STX1A	syntaxin 1A (brain)	0,705	0,291
7922773	NCF2	neutrophil cytosolic factor 2	0,703	0,625
7968789	C13orf15	chromosome 13 open reading frame 15	0,702	0,489
7992463	SLC9A3R2	solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 2	0,702	0,485
8098204	CPE	carboxypeptidase E	0,702	0,578
8154531	DENND4C	DENN/MADD domain containing 4C	0,702	0,284
7959500	HIP1R	huntingtin interacting protein 1 related	0,701	0,306
8041061	PLB1	phospholipase B1	0,7	0,244
8155540	CNTNAP3	contactin associated protein-like 3	0,697	0,611
8161460	CNTNAP3	contactin associated protein-like 3	0,697	0,611
7987454	BMF	Bcl2 modifying factor	0,696	0,203
8044417	TMEM87B	transmembrane protein 87B	0,696	0,435

7942520			0,694	0,052
8026915	ARRDC2	arrestin domain containing 2	0,693	0,408
7986250	CHD2	chromodomain helicase DNA binding protein 2	0,693	0,221
8021169	LIPG	lipase, endothelial	0,693	0,264
8076734	WNT7B	wingless-type MMTV integration site family, member 7B	0,693	0,196
8013860	MYO18A	myosin XVIIIA	0,691	0,394
8133549	GTF2IRD2B	GTF2I repeat domain containing 2B	0,691	0,443
7912496	MTHFR	5,10-methylenetetrahydrofolate reductase (NADPH)	0,689	0,292
8127872	SNAP91	synaptosomal-associated protein, 91kDa homolog (mouse)	0,689	-0,12
7897803	PLOD1	procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 1	0,688	0,384
7983173	CCNDBP1	cyclin D-type binding-protein 1	0,688	0,101
7987192	SLC12A6	solute carrier family 12 (potassium/chloride transporters), member 6	0,688	0,264
8159850	VLDLR	very low density lipoprotein receptor	0,688	0,292
7923394	ARL8A	ADP-ribosylation factor-like 8A	0,687	0,259
8175871	L1CAM	L1 cell adhesion molecule	0,687	0,232
8141843	RASA4	RAS p21 protein activator 4	0,686	0,424
7922756	NMNAT2	nicotinamide nucleotide adenyllyltransferase 2	0,685	0,353
8059580	DNER	delta/notch-like EGF repeat containing	0,682	0,368
8053406	RETSAT	retinol saturase (all-trans-retinol 13,14-reductase)	0,681	0,222
8141328	CYP3A5	cytochrome P450, family 3, subfamily A, polypeptide 5	0,68	0,481
7964089	PAN2	PAN2 poly(A) specific ribonuclease subunit homolog (<i>S. cerevisiae</i>)	0,679	0,191
8017346	TBC1D3P2	TBC1 domain family, member 3 pseudogene 2	0,678	0,308
8103563	DDX60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60	0,678	0,116
8145291	SLC25A37	solute carrier family 25, member 37	0,678	0,528
8120335	FAM83B	family with sequence similarity 83, member B	0,677	0,184
7910383			0,674	-0,01
8022022	LPIN2	lipin 2	0,674	0,226
7977046	TNFAIP2	tumor necrosis factor, alpha-induced protein 2	0,672	0,41
8016215	ARHGAP27	Rho GTPase activating protein 27	0,672	0,318
7913824	C1orf63	chromosome 1 open reading frame 63	0,671	0,303
7958884	OAS1	2',5'-oligoadenylate synthetase 1, 40/46kDa	0,671	0,276
8078380	ZNF860	zinc finger protein 860	0,671	0,048

8154333	KDM4C	lysine (K)-specific demethylase 4C	0,671	0,197
7993622	ITPRIPL2	inositol 1,4,5-triphosphate receptor interacting protein-like 2	0,67	0,241
8035278	ANO8	anoctamin 8	0,669	0,407
8092691	BCL6	B-cell CLL/lymphoma 6	0,666	0,227
8001564	DOK4	docking protein 4	0,665	0,29
8010983	ABR	active BCR-related gene	0,663	0,274
8023377	MEX3C	mex-3 homolog C (<i>C. elegans</i>)	0,663	0,175
8048523	DNAJB2	DnaJ (Hsp40) homolog, subfamily B, member 2	0,663	0,134
8057821	DNAH7	dynein, axonemal, heavy chain 7	0,663	0,007
7930139	TRIM8	tripartite motif-containing 8	0,662	0,396
8007931	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	0,661	0,809
8146285	HGSNAT	heparan-alpha-glucosaminide N-acetyltransferase	0,661	0,266
7964834	CPM	carboxypeptidase M	0,659	0,446
8089930	GOLGB1	golgin B1, golgi integral membrane protein	0,659	0,298
8140170	GTF2IRD2	GTF2I repeat domain containing 2	0,659	0,363
7983867	CGNL1	cingulin-like 1	0,658	0,001
8047401			0,658	0,294
8080714	FLNB	filamin B, beta (actin binding protein 278)	0,658	0,294
8116831	TFAP2A	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)	0,657	0,326
8045736	FMNL2	formin-like 2	0,656	0,228
8056999	TTC30A	tetratricopeptide repeat domain 30A	0,656	-0,085
7970844	KATNAL1	katanin p60 subunit A-like 1	0,655	0,479
8058127	CLK1	CDC-like kinase 1	0,654	0,229
8034217	EPOR	erythropoietin receptor	0,653	0,086
8087433	NICN1	nicolin 1	0,653	0,366
8116070	PDLM7	PDZ and LIM domain 7 (enigma)	0,653	0,259
8064978	JAG1	jagged 1 (Alagille syndrome)	0,652	0,413
8094476	TBC1D19	TBC1 domain family, member 19	0,652	-0,095
7913682	HMGCL	3-hydroxymethyl-3-methylglutaryl-Coenzyme A lyase	0,651	0,061
8129666	SLC2A12	solute carrier family 2 (facilitated glucose transporter), member 12	0,651	0,149
8075705			0,65	0,214
7916926			0,649	-0,105
8009353	PITPNC1	phosphatidylinositol transfer protein, cytoplasmic 1	0,649	0,216
8048304	CTDSP1	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 1	0,649	0,272
8036304	ZFP14	zinc finger protein 14 homolog (mouse)	0,648	-0,08
8077612	TTLL3	tubulin tyrosine ligase-like family, member 3	0,648	0,455

8079966	SEMA3B	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B	0,648	0,297
8162586	SLC35D2	solute carrier family 35, member D2	0,647	0,113
8057990	ANKRD44	ankyrin repeat domain 44	0,646	0,284
8086981	UCN2	urocortin 2	0,646	0,474
8155359	CNTNAP3	contactin associated protein-like 3	0,644	0,569
8053648	KRCC1	lysine-rich coiled-coil 1	0,643	-0,029
8164105	GOLGA1	golgi autoantigen, golgin subfamily a, 1	0,643	0,147
7907893	MR1	major histocompatibility complex, class I-related	0,642	0,225
8070961	LSS	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	0,642	0,208
8095626			0,642	0,146
8009746	SLC16A5	solute carrier family 16, member 5 (monocarboxylic acid transporter 6)	0,641	0,3
7926679	KIAA1217	KIAA1217	0,64	0,071
8114593	APBB3	amyloid beta (A4) precursor protein-binding, family B, member 3	0,64	0,157
8080184	ALAS1	aminolevulinate, delta-, synthase 1	0,639	0,24
8083166	TRPC1	transient receptor potential cation channel, subfamily C, member 1	0,639	0,368
8168472	ATP7A	ATPase, Cu++ transporting, alpha polypeptide	0,639	0,231
8087485	UBA7	ubiquitin-like modifier activating enzyme 7	0,638	0,494
8037444	ZNF235	zinc finger protein 235	0,638	0,12
8160297	ADFP	adipose differentiation-related protein	0,638	0,238
8165866	STS	steroid sulfatase (microsomal), isozyme S	0,638	0,425
7922707	RNASEL	ribonuclease L (2',5'-oligoisoadenylate synthetase-dependent)	0,637	0,172
7987840	VPS39	vacuolar protein sorting 39 homolog (S. cerevisiae)	0,636	0,143
8029065	BCKDHA	branched chain keto acid dehydrogenase E1, alpha polypeptide	0,636	-0,035
8039340	TNNT1	troponin T type 1 (skeletal, slow)	0,636	0,23
8143038			0,635	0,23
7932985	NRP1	neuropilin 1	0,633	0,209
7937772	IGF2	insulin-like growth factor 2 (somatomedin A)	0,633	0,166
8046020	SCN2A	sodium channel, voltage-gated, type II, alpha subunit	0,633	0,127
8086517	CDCP1	CUB domain containing protein 1	0,633	0,347
8117343	HFE	hemochromatosis	0,633	0,218

8058118	KCTD18	potassium channel tetramerisation domain containing 18	0,632	-0,241
8091283	PLOD2	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2	0,63	0,193
7930380	ADD3	adducin 3 (gamma)	0,629	0,134
8020551	LAMA3	laminin, alpha 3	0,627	0,399
8090162	ITGB5	integrin, beta 5	0,627	0,244
8067055	ATP9A	ATPase, class II, type 9A	0,626	0,298
8122317	HEBP2	heme binding protein 2	0,626	0,188
8125818	C6orf1	chromosome 6 open reading frame 1	0,625	0,073
8164464	ZER1	zer-1 homolog (<i>C. elegans</i>)	0,625	0,184
8031659	ZFP28	zinc finger protein 28 homolog (mouse)	0,624	0,174
7965510	TMCC3	transmembrane and coiled-coil domain family 3	0,623	0,325
8099721	KIAA0746	KIAA0746 protein	0,623	0,49
7899486	TRNAU1AP	tRNA selenocysteine 1 associated protein 1	0,622	0,217
7962112	CAPRIN2	caprin family member 2	0,622	0,352
7976084	SPATA7	spermatogenesis associated 7	0,622	0,094
8119473	PRICKLE4	prickle homolog 4 (<i>Drosophila</i>)	0,622	0,187
8120880	TPBG	trophoblast glycoprotein	0,622	0,356
8003410	GALNS	galactosamine (N-acetyl)-6-sulfate sulfatase	0,621	0,206
8037071	RABAC1	Rab acceptor 1 (prenylated)	0,62	0,288
8178676	NEU1	sialidase 1 (lysosomal sialidase)	0,62	0,263
8179595	GABBR1	gamma-aminobutyric acid (GABA) B receptor, 1	0,62	0,407
8075720	APOL2	apolipoprotein L, 2	0,619	0,245
8007976	NPEPPS	aminopeptidase puromycin sensitive	0,618	0,257
8038126	CA11	carbonic anhydrase XI	0,618	0,387
8007620	GRN	granulin	0,617	0,305
7948829	ZBTB3	zinc finger and BTB domain containing 3	0,615	0,028
8041676	DYNC2LI1	dynein, cytoplasmic 2, light intermediate chain 1	0,615	0,149
8026763	SLC27A1	solute carrier family 27 (fatty acid transporter), member 1	0,614	0,25
8087419	AMT	aminomethyltransferase	0,613	0,256
8119926	TMEM63B	transmembrane protein 63B	0,612	0,223
7899753	LCK	lymphocyte-specific protein tyrosine kinase	0,611	0,195
7978544	EGLN3	egl nine homolog 3 (<i>C. elegans</i>)	0,611	0,283
7984922	MPI	mannose phosphate isomerase	0,61	0,043
8013159	TOM1L2	target of myb1-like 2 (chicken)	0,609	0,177
7951429	KBTBD3	kelch repeat and BTB (POZ) domain containing 3	0,608	0,255
8152280	LRP12	low density lipoprotein-related protein 12	0,608	0,272

8017671	PLEKHM1P	pleckstrin homology domain containing, family M (with RUN domain) member 1 pseudogene	0,606	0,236
8176133	G6PD	glucose-6-phosphate dehydrogenase	0,606	0,21
7940079	CTNND1	catenin (cadherin-associated protein), delta 1	0,605	0,331
8013135	SREBF1	sterol regulatory element binding transcription factor 1	0,605	0,079
8072360	TCN2	transcobalamin II; macrocytic anemia	0,605	0,195
8087547	MST1R	macrophage stimulating 1 receptor (c-met-related tyrosine kinase)	0,604	0,304
8107133	PAM	peptidylglycine alpha-amidating monooxygenase	0,604	0,259
7954090	EMP1	epithelial membrane protein 1	0,603	0,155
7984771	LOXL1	lysyl oxidase-like 1	0,603	0,2
8109093	ABLIM3	actin binding LIM protein family, member 3	0,603	0,115
7923119	ZBTB41	zinc finger and BTB domain containing 41	0,601	0,107
8156569	C9orf3	chromosome 9 open reading frame 3	0,601	0,455
8103755	FBXO8	F-box protein 8	0,6	-0,087
8137526	INSIG1	insulin induced gene 1	0,6	0,316
8106722	ATP6AP1L	ATPase, H ⁺ transporting, lysosomal accessory protein 1-like	0,599	-0,074
7930074	NFKB2	nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100)	0,598	0,337
8041048	FOSL2	FOS-like antigen 2	0,598	0,177
8073470	CTA-216E10.6	hypothetical FLJ23584	0,598	0,171
8099965	ACOT7	acyl-CoA thioesterase 7	0,598	-0,018
8163825	TRAF1	TNF receptor-associated factor 1	0,596	0,534
8113512	EPB41L4A	erythrocyte membrane protein band 4.1 like 4A	0,596	0,12
7961891	BHLHE41	basic helix-loop-helix family, member e41	0,595	0,265
8112596	ANKRA2	ankyrin repeat, family A (RFXANK-like), 2	0,595	0,134
8132980	TNRC18	trinucleotide repeat containing 18	0,595	0,021
7928354	FAM149B1	family with sequence similarity 149, member B1	0,594	0,096
8121312	C6orf203	chromosome 6 open reading frame 203	0,594	0,073
7919326	ACP6	acid phosphatase 6, lysophosphatidic	0,592	-0,012
7953442	GPR162	G protein-coupled receptor 162	0,592	0,314
8026163	IER2	immediate early response 2	0,592	0,27
8113413	NUDT12	nudix (nucleoside diphosphate linked moiety X)-type motif 12	0,592	-0,132

8068697	MX2	myxovirus (influenza virus) resistance 2 (mouse)	0,588	0,201
8101284	PRKG2	protein kinase, cGMP-dependent, type II	0,588	-0,153
8019778	PCYT2	phosphate cytidylyltransferase 2, ethanolamine	0,587	0,264
8082314	PLXNA1	plexin A1	0,587	0,287
8108475	C5orf53	chromosome 5 open reading frame 53	0,587	0,331
8146859			0,587	0,108
7953409	PTMS	parathymosin	0,586	0,062
8002992	C16orf46	chromosome 16 open reading frame 46	0,586	0,13
7914094	WASF2	WAS protein family, member 2	0,585	-0,009
7941111	SNX15	sorting nexin 15	0,585	0,141
7950671	GAB2	GRB2-associated binding protein 2	0,585	0,23
8076547	TTLL1	tubulin tyrosine ligase-like family, member 1	0,585	0,025
8008627	NOG *	noggin	0,536	0,614
8065410	CST4	cystatin S	0,461	0,979
8131581			0,457	-0,919
8095680	IL8	interleukin 8	0,304	0,6
7977270	LOC388022	hypothetical gene supported by AK131040	0,071	0,731
8173671			0,061	0,626
8165656			-0,214	-0,643
8120838	TTK	TTK protein kinase	-0,228	-0,613
7969374	C13orf34	chromosome 13 open reading frame 34	-0,254	-0,608
8049542	LRRFIP1	leucine rich repeat (in FLII) interacting protein 1	-0,272	-0,679
7916898	DEPDC1	DEP domain containing 1	-0,275	-0,761
7909271	IL24	interleukin 24	-0,276	-0,989
7979307	DLGAP5	discs, large (Drosophila) homolog-associated protein 5	-0,302	-0,62
8105842	CENPH	centromere protein H	-0,309	-0,604
8124406	HIST1H2BC	histone cluster 1, H2bc	-0,312	-0,731
8109712	HMMR	hyaluronan-mediated motility receptor (RHAMM)	-0,313	-0,875
7972225			-0,318	-0,587
7947248	KIF18A	kinesin family member 18A	-0,331	-0,785
8102076	CENPE	centromere protein E, 312kDa	-0,355	-0,779
7904465	HIST2H2BA	histone cluster 2, H2ba	-0,368	-0,641
7923189	KIF14	kinesin family member 14	-0,377	-0,615
7896746			-0,38	-0,635
7906930	NUF2	NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae)	-0,442	-0,603
8124397	HIST1H1C	histone cluster 1, H1c	-0,475	-0,605
8117372	HIST1H2AC	histone cluster 1, H2ac	-0,478	-0,683
8124448	HIST1H4H	histone cluster 1, H4h	-0,496	-0,653

8117368	HIST1H4C	histone cluster 1, H4c	-0,5	-0,65
7905079	HIST2H2AA3	histone cluster 2, H2aa3	-0,503	-0,585
7919619	HIST2H2AA3	histone cluster 2, H2aa3	-0,503	-0,585
7994109	PLK1	polo-like kinase 1 (Drosophila)	-0,519	-0,777
8133976	DBF4	DBF4 homolog (<i>S. cerevisiae</i>)	-0,525	-0,631
8022612	ZNF521	zinc finger protein 521	-0,54	-0,64
8117583	HIST1H2AI	histone cluster 1, H2ai	-0,542	-0,802
8068898	HIST1H2BK	histone cluster 1, H2bk	-0,544	-0,733
8117334	HIST1H4A	histone cluster 1, H4a	-0,549	-0,771
8030128	PPP1R15A	protein phosphatase 1, regulatory (inhibitor) subunit 15A	-0,574	-0,793
8179055	ZNRD1	zinc ribbon domain containing 1	-0,578	-0,585
8117535	HIST1H2AG	histone cluster 1, H2ag	-0,585	-0,568
7927681	BICC1	bicaudal C homolog 1 (Drosophila)	-0,585	-0,244
8050869			-0,585	0,175
8019316	PYCR1	pyrroline-5-carboxylate reductase 1	-0,586	-0,253
8066256	SNORA71B	small nucleolar RNA, H/ACA box 71B	-0,586	-0,102
8166723	XK	X-linked Kx blood group (McLeod syndrome)	-0,586	-0,333
8124540	HIST1H2AM	histone cluster 1, H2am	-0,587	-0,698
7942527	POLD3	polymerase (DNA-directed), delta 3, accessory subunit	-0,587	-0,131
8001776			-0,587	0,107
8003621	RNMTL1	RNA methyltransferase like 1	-0,587	-0,309
8144281	ARHGEF10	Rho guanine nucleotide exchange factor (GEF) 10	-0,587	-0,098
8161242	EXOSC3	exosome component 3	-0,587	-0,18
8124388	HIST1H3B	histone cluster 1, H3b	-0,588	-0,858
8081135	CDV3	CDV3 homolog (mouse)	-0,588	-0,319
7935425	RRP12	ribosomal RNA processing 12 homolog (<i>S. cerevisiae</i>)	-0,589	-0,311
7948037			-0,589	-0,214
8020411	SNRPD1	small nuclear ribonucleoprotein D1 polypeptide 16kDa	-0,589	-0,433
8069943	URB1	URB1 ribosome biogenesis 1 homolog (<i>S. cerevisiae</i>)	-0,589	-0,167
8138489	CDCA7L	cell division cycle associated 7-like	-0,589	0,002
7951032	SNORA1	small nucleolar RNA, H/ACA box 1	-0,59	0,013
8027330	PCGF6	polycomb group ring finger 6	-0,59	-0,147
7919642	HIST2H2AB	histone cluster 2, H2ab	-0,591	-1,07
7983306	WDR76	WD repeat domain 76	-0,591	-0,185
8017262	BRIP1	BRCA1 interacting protein C-terminal helicase 1	-0,591	-0,204
8166230	CXorf15	chromosome X open reading frame 15	-0,591	-0,257
8147548	POP1	processing of precursor 1, ribonuclease P/MRP subunit (<i>S. cerevisiae</i>)	-0,592	-0,238

8158544	METTL11A	methyltransferase like 11A	-0,592	-0,207
7999304	FAM86A	family with sequence similarity 86, member A	-0,594	-0,18
8013616	SLC46A1	solute carrier family 46 (folate transporter), member 1	-0,594	0,155
8152255	SLC25A32	solute carrier family 25, member 32	-0,594	-0,217
7979281	WDHD1	WD repeat and HMG-box DNA binding protein 1	-0,595	0,006
8097335	HSPA4L	heat shock 70kDa protein 4-like	-0,595	-0,081
7936637	SNORA19	small nucleolar RNA, H/ACA box 19	-0,596	0,025
8099051	NOP14	NOP14 nucleolar protein homolog (yeast)	-0,596	-0,225
8164742	DDX31	DEAD (Asp-Glu-Ala-Asp) box polypeptide 31	-0,597	-0,198
7974198	PPI5	peptidylprolyl isomerase (cyclophilin)-like 5	-0,598	-0,27
8020254	SEH1L	SEH1-like (S. cerevisiae)	-0,598	-0,184
8022514	C18orf45	chromosome 18 open reading frame 45	-0,598	-0,195
8140151	RFC2	replication factor C (activator 1) 2, 40kDa	-0,598	-0,293
7940479	TMEM216	transmembrane protein 216	-0,599	-0,227
7997152	CHST4	carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 4	-0,599	-0,12
8014755	SNORA21	small nucleolar RNA, H/ACA box 21	-0,599	0,084
7914851	CLSPN	claspin homolog (Xenopus laevis)	-0,6	0,077
7959354	BCL7A	B-cell CLL/lymphoma 7A	-0,6	-0,168
8101143	NUP54	nucleoporin 54kDa	-0,6	-0,297
8116910	HIVEP1	human immunodeficiency virus type I enhancer binding protein 1	-0,6	-0,247
8089040	MINA	MYC induced nuclear antigen	-0,602	-0,358
8095585	SLC4A4	solute carrier family 4, sodium bicarbonate cotransporter, member 4	-0,602	-0,263
8104568	UNQ1870	GALI1870	-0,602	0,056
8161829	C9orf41	chromosome 9 open reading frame 41	-0,602	0,021
8045697	RIF1	RAP1 interacting factor homolog (yeast)	-0,603	-0,242
8085531	MRPS25	mitochondrial ribosomal protein S25	-0,603	0,013
7951038	SNORA40	small nucleolar RNA, H/ACA box 40	-0,604	-0,109
8008754	RAD51C	RAD51 homolog C (S. cerevisiae)	-0,604	-0,151
8125919	FKBP5	FK506 binding protein 5	-0,604	-0,234
8142019	ORC5L	origin recognition complex, subunit 5-like (yeast)	-0,605	-0,344
7960771	CD163L1	CD163 molecule-like 1	-0,605	-0,263
8047780	SNORA41	small nucleolar RNA, H/ACA box 41	-0,605	-0,078

7904452	FAM72D	family with sequence similarity 72, member D	-0,606	-0,707
7989647	KIAA0101	KIAA0101	-0,606	-0,306
8097867	KIAA0922	KIAA0922	-0,606	-0,164
7939376	LDLRAD3	low density lipoprotein receptor class A domain containing 3	-0,607	-0,254
8099760	ARAP2	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 2	-0,607	-0,324
7996891	CIRH1A	cirrhosis, autosomal recessive 1A (cirhin)	-0,609	-0,287
7909146	FAM72D	family with sequence similarity 72, member D	-0,61	-0,711
8036351	ZNF850P	zinc finger protein 850 pseudogene	-0,61	-0,373
8104825	BXDC2	brix domain containing 2	-0,61	-0,301
7932160	FAM107B	family with sequence similarity 107, member B	-0,612	-0,18
8150204			-0,612	-0,204
7970329	GAS6	growth arrest-specific 6	-0,613	-0,088
7979416	TIMM9	translocase of inner mitochondrial membrane 9 homolog (yeast)	-0,613	-0,394
8152668	ATAD2	ATPase family, AAA domain containing 2	-0,613	-0,189
8051746	THUMPD2	THUMP domain containing 2	-0,614	-0,144
7920687	GBAP	glucosidase, beta; acid, pseudogene	-0,615	-0,136
8121489	AMD1	adenosylmethionine decarboxylase 1	-0,615	-0,063
8122365	GPR126	G protein-coupled receptor 126	-0,615	-0,206
7926299	HSPA14	heat shock 70kDa protein 14	-0,616	-0,198
8050255	NOL10	nucleolar protein 10	-0,616	-0,262
8149296	PINX1	PIN2-interacting protein 1	-0,616	-0,185
8170418	LOC643015	hypothetical LOC643015	-0,616	-0,283
8039109	VSTM1	V-set and transmembrane domain containing 1	-0,618	-0,478
8064844	PCNA	proliferating cell nuclear antigen	-0,619	-0,048
8146357	MCM4	minichromosome maintenance complex component 4	-0,619	-0,08
8092726	CLDN1	claudin 1	-0,621	-0,382
8039928	FAM72D	family with sequence similarity 72, member D	-0,622	-0,699
7929078	KIF20B	kinesin family member 20B	-0,623	-0,475
8062571	FAM83D	family with sequence similarity 83, member D	-0,623	-0,524
8146130	GINS4	GINS complex subunit 4 (Sld5 homolog)	-0,623	-0,23
7981447	XRCC3	X-ray repair complementing defective repair in Chinese hamster cells 3	-0,624	-0,144
7996211	GINS3	GINS complex subunit 3 (Psf3 homolog)	-0,625	-0,144
8138640	CYCS	cytochrome c, somatic	-0,625	-0,183
8090448	RUVBL1	RuvB-like 1 (E. coli)	-0,626	-0,395

8065510	NANP	N-acetylneuraminic acid phosphatase	-0,626	-0,136
7931268	BCCIP	BRCA2 and CDKN1A interacting protein	-0,627	-0,269
7952601	ETS1	v-ets erythroblastosis virus E26 oncogene homolog 1 (avian)	-0,627	-0,257
8002762	RFWD3	ring finger and WD repeat domain 3	-0,627	-0,126
8100347	SCFD2	sec1 family domain containing 2	-0,627	-0,221
8112582			-0,627	-0,118
7912659	AGMAT	agmatine ureohydrolase (agmatinase)	-0,628	-0,285
7943577	RAB39	RAB39, member RAS oncogene family	-0,629	-0,15
7995797	MT1E	metallothionein 1E	-0,629	-0,225
8085145	RAD18	RAD18 homolog (S. cerevisiae)	-0,629	-0,172
8157216	UGCG	UDP-glucose ceramide glucosyltransferase	-0,629	-0,157
8169868	UTP14A	UTP14, U3 small nucleolar ribonucleoprotein, homolog A (yeast)	-0,629	-0,192
8174047	TIMM8A	translocase of inner mitochondrial membrane 8 homolog A (yeast)	-0,629	-0,087
7915529	HYI	hydroxypyruvate isomerase homolog (E. coli)	-0,63	-0,204
7989975	CLN6	ceroid-lipofuscinosis, neuronal 6, late infantile, variant	-0,63	-0,27
8105577			-0,63	-0,032
8121087	PM20D2	peptidase M20 domain containing 2	-0,63	-0,162
8080938	MITF	microphthalmia-associated transcription factor	-0,631	-0,385
8020814	RNF138	ring finger protein 138	-0,632	-0,25
7900167	CDCA8	cell division cycle associated 8	-0,633	-0,655
8012403	AURKB	aurora kinase B	-0,633	-0,384
8039491	UBE2S	ubiquitin-conjugating enzyme E2S	-0,635	-0,54
8041360	TTC27	tetratricopeptide repeat domain 27	-0,636	-0,415
8050689	C2orf44	chromosome 2 open reading frame 44	-0,636	-0,121
7959986	PUS1	pseudouridylate synthase 1	-0,637	-0,212
7982620	EIF2AK4	eukaryotic translation initiation factor 2 alpha kinase 4	-0,637	-0,221
8151824	RAD54B	RAD54 homolog B (S. cerevisiae)	-0,637	-0,251
8112312	DIMT1L	DIM1 dimethyladenosine transferase 1-like (S. cerevisiae)	-0,639	-0,311
7977018	TRAF3	TNF receptor-associated factor 3	-0,639	-0,166
8113790	MARCH3	membrane-associated ring finger (C3HC4) 3	-0,64	-0,045
8124510	HIST1H2BL	histone cluster 1, H2bl	-0,64	-0,563
7948229	SLC43A3	solute carrier family 43, member 3	-0,641	-0,21
8169240	PRPS1	phosphoribosyl pyrophosphate synthetase 1	-0,641	-0,181
7976621	VRK1	vaccinia related kinase 1	-0,642	-0,284

8138888	PDE1C	phosphodiesterase 1C, calmodulin-dependent 70kDa	-0,643	-0,339
8148325			-0,643	-0,194
7957649	SNRPF	small nuclear ribonucleoprotein polypeptide F	-0,644	-0,43
8059538	SLC19A3	solute carrier family 19, member 3	-0,644	-0,316
8097262	SPATA5	spermatogenesis associated 5	-0,644	-0,207
8117580	HIST1H2AI	histone cluster 1, H2ai	-0,645	-0,982
7926807	PDSS1	prenyl (decaprenyl) diphosphate synthase, subunit 1	-0,645	-0,291
8076463	RRP7B	ribosomal RNA processing 7 homolog B (<i>S. cerevisiae</i>)	-0,645	-0,018
8128977	TUBE1	tubulin, epsilon 1	-0,645	-0,417
8117598	HIST1H4J	histone cluster 1, H4j	-0,646	-0,623
8061471	GINS1	GINS complex subunit 1 (<i>Psf1</i> homolog)	-0,646	-0,143
8089835	FSTL1	follistatin-like 1	-0,646	-0,218
8045171	IMP4	IMP4, U3 small nucleolar ribonucleoprotein, homolog (<i>yeast</i>)	-0,647	-0,283
7962811	C12orf41	chromosome 12 open reading frame 41	-0,647	-0,122
7914216	SNORA16A	small nucleolar RNA, H/ACA box 16A	-0,648	0,113
7981346	RAGE	renal tumor antigen	-0,648	-0,354
7996934	NIP7	nuclear import 7 homolog (<i>S. cerevisiae</i>)	-0,648	-0,233
8076449	RRP7B	ribosomal RNA processing 7 homolog B (<i>S. cerevisiae</i>)	-0,648	-0,111
8102440	ARSJ	arylsulfatase family, member J	-0,649	-0,195
8118721	ZBTB9	zinc finger and BTB domain containing 9	-0,649	-0,08
7912374	SRM	spermidine synthase	-0,65	-0,188
7955613	KRT7	keratin 7	-0,65	-0,248
8067040	NFATC2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	-0,651	-0,364
8077914	TSEN2	tRNA splicing endonuclease 2 homolog (<i>S. cerevisiae</i>)	-0,651	-0,24
8027642	PDCD2L	programmed cell death 2-like	-0,653	-0,331
7914878			-0,654	-0,011
7951654	FDXACB1	ferredoxin-fold anticodon binding domain containing 1	-0,655	-0,354
8003068	MPHOSPH6	M-phase phosphoprotein 6	-0,657	-0,128
8071332	RANBP1	RAN binding protein 1	-0,657	-0,296
8157092	TMEM38B	transmembrane protein 38B	-0,657	-0,219
8012958	UBE2S	ubiquitin-conjugating enzyme E2S	-0,658	-0,552
7953594	EMG1	EMG1 nucleolar protein homolog (<i>S. cerevisiae</i>)	-0,658	-0,4
8070330	PSMG1	proteasome (prosome, macropain) assembly chaperone 1	-0,658	-0,209
7928429	PLAU	plasminogen activator, urokinase	-0,659	-0,139

7953100	FKBP4	FK506 binding protein 4, 59kDa	-0,659	-0,079
8147447	PTDSS1	phosphatidylserine synthase 1	-0,659	-0,125
7907702	SOAT1	sterol O-acyltransferase 1	-0,66	-0,274
7941707	RBM14	RNA binding motif protein 14	-0,66	0,106
8069565	BTG3	BTG family, member 3	-0,66	-0,214
8081786	QTRTD1	queuine tRNA-ribosyltransferase domain containing 1	-0,66	-0,236
7906021	MSTO1	misato homolog 1 (<i>Drosophila</i>)	-0,661	-0,193
8116530	SNORD96A	small nucleolar RNA, C/D box 96A	-0,661	-0,255
7904967			-0,662	-0,015
7953218	RAD51AP1	RAD51 associated protein 1	-0,662	-0,337
8110147	C5orf25	chromosome 5 open reading frame 25	-0,662	-0,22
8145782	MAK16	MAK16 homolog (<i>S. cerevisiae</i>)	-0,663	-0,35
7982287	ARHGAP11B	Rho GTPase activating protein 11B	-0,663	-0,593
7927669	TFAM	transcription factor A, mitochondrial	-0,664	-0,343
8154733	ACO1	aconitase 1, soluble	-0,664	-0,406
8072113	SRRD	SRR1 domain containing	-0,665	-0,306
8102950	INPP4B	inositol polyphosphate-4-phosphatase, type II, 105kDa	-0,665	-0,426
7948267	TIMM10	translocase of inner mitochondrial membrane 10 homolog (<i>yeast</i>)	-0,665	-0,321
7960702	CDCA3	cell division cycle associated 3	-0,665	-0,397
7901091	TOE1	target of EGR1, member 1 (nuclear)	-0,666	-0,217
7966462	C12orf30	chromosome 12 open reading frame 30	-0,666	-0,251
7997940	SNORD68	small nucleolar RNA, C/D box 68	-0,666	-0,003
7971866	DIAPH3	diaphanous homolog 3 (<i>Drosophila</i>)	-0,667	-0,675
8117614	HIST1H2BO	histone cluster 1, H2bo	-0,667	-0,598
8152582	DSCC1	defective in sister chromatid cohesion 1 homolog (<i>S. cerevisiae</i>)	-0,667	-0,148
8000236	CDR2	cerebellar degeneration-related protein 2, 62kDa	-0,668	-0,159
8104746	NPR3	natriuretic peptide receptor C/guanylate cyclase C (atrionatriuretic peptide receptor C)	-0,668	-0,14
7983350	EIF3J	eukaryotic translation initiation factor 3, subunit J	-0,669	-0,415
7965918	NT5DC3	5'-nucleotidase domain containing 3	-0,67	-0,227
7979269	GCH1	GTP cyclohydrolase 1	-0,671	-0,057
7973182	LOC554207	hypothetical LOC554207	-0,672	-0,15
7896961	ATAD3B	ATPase family, AAA domain containing 3B	-0,673	-0,175
7919160			-0,674	-0,231
7919166			-0,674	-0,231
8149438	SGCZ	sarcoglycan zeta	-0,674	-0,231
8157843	RABEPK	Rab9 effector protein with kelch motifs	-0,674	-0,213
7924071	KCNH1	potassium voltage-gated channel, subfamily H (eag-related), member	-0,677	-0,208

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8028563	MRPS12	mitochondrial ribosomal protein S12	-0,678	-0,107
8097288	FAT4	FAT tumor suppressor homolog 4 (Drosophila)	-0,678	-0,163
8104930	SLC1A3	solute carrier family 1 (glial high affinity glutamate transporter), member 3	-0,678	0,247
8122202	MYB	v-myb myeloblastosis viral oncogene homolog (avian)	-0,678	-0,113
7901123	NASP	nuclear autoantigenic sperm protein (histone-binding)	-0,679	-0,146
7900699	CDC20	cell division cycle 20 homolog (S. cerevisiae)	-0,68	-0,493
7941702	RBM14	RNA binding motif protein 14	-0,68	0,051
8024900	UHRF1	ubiquitin-like with PHD and ring finger domains 1	-0,681	-0,142
8097679	LSM6	LSM6 homolog, U6 small nuclear RNA associated (S. cerevisiae)	-0,681	-0,305
8005753			-0,682	-0,129
8065537	CTD-2514C3.1	hypothetical LOC100134868	-0,682	-0,537
7918657	PTPN22	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	-0,684	-0,341
7972180	RNF219	ring finger protein 219	-0,685	-0,147
8040843	CAD	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase	-0,685	-0,211
8005097	HS3ST3B1	heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1	-0,686	-0,159
8043349	ANAPC1	anaphase promoting complex subunit 1	-0,687	-0,31
8117106	RNF144B	ring finger protein 144B	-0,687	-0,3
8165622	ZMYND19	zinc finger, MYND-type containing 19	-0,687	-0,091
8127109	ICK	intestinal cell (MAK-like) kinase	-0,688	-0,353
7935146	NOC3L	nucleolar complex associated 3 homolog (S. cerevisiae)	-0,689	-0,261
8051622	SFRS7	splicing factor, arginine-serine-rich 7, 35kDa	-0,689	-0,121
8142424	GPR85	G protein-coupled receptor 85	-0,689	-0,254
7915045	C1orf109	chromosome 1 open reading frame 109	-0,69	-0,217
7917322	SYDE2	synapse defective 1, Rho GTPase, homolog 2 (C. elegans)	-0,691	-0,085
7940147	FAM111B	family with sequence similarity 111, member B	-0,691	-0,015
8043322	ANAPC1	anaphase promoting complex subunit 1	-0,691	-0,306
8092177	AADACL1	arylacetamide deacetylase-like 1	-0,691	-0,188
8097480	NARG1	NMDA receptor regulated 1	-0,691	-0,302

7905054			-0,692	-0,181
8107578	SRFBP1	serum response factor binding protein 1	-0,692	-0,252
8081241	C3orf26	chromosome 3 open reading frame 26	-0,693	-0,401
8027448	DPY19L3	dpy-19-like 3 (<i>C. elegans</i>)	-0,694	-0,291
7901046	SNORD55	small nucleolar RNA, C/D box 55	-0,696	-0,034
8003503	FANCA	Fanconi anemia, complementation group A	-0,696	-0,033
8122440	LTV1	LTV1 homolog (<i>S. cerevisiae</i>)	-0,696	-0,288
7919591	FAM72D	family with sequence similarity 72, member D	-0,697	-0,731
7927964	SRGN	serglycin	-0,698	-0,312
7916219	C1orf163	chromosome 1 open reading frame 163	-0,7	-0,054
8009241	SNORD104	small nucleolar RNA, C/D box 104	-0,7	-0,172
8024843	CHAF1A	chromatin assembly factor 1, subunit A (p150)	-0,7	-0,177
8107594	SNCAIP	synuclein, alpha interacting protein	-0,7	-0,326
8103706	AADAT	aminoacidate aminotransferase	-0,702	-0,19
8027429			-0,704	0,059
7912303	DFFA	DNA fragmentation factor, 45kDa, alpha polypeptide	-0,705	-0,225
8159803	FAM138A	family with sequence similarity 138, member A	-0,705	-0,181
7989069	PYGO1	pygopus homolog 1 (<i>Drosophila</i>)	-0,708	-0,148
8076339	PHF5A	PHD finger protein 5A	-0,708	-0,263
7925978	C10orf18	chromosome 10 open reading frame 18	-0,709	-0,119
7989657	UNQ353	GKGM353	-0,709	0,308
7990345	SEMA7A	semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group)	-0,709	-0,197
7988687	GABPB1	GA binding protein transcription factor, beta subunit 1	-0,71	-0,468
7921076	GPATCH4	G patch domain containing 4	-0,71	-0,226
7989146	MNS1	meiosis-specific nuclear structural 1	-0,712	-0,534
8178090	C6orf48	chromosome 6 open reading frame 48	-0,712	-0,188
8179326	C6orf48	chromosome 6 open reading frame 48	-0,712	-0,188
8069676	ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif, 1	-0,713	0,029
7916167	ORC1L	origin recognition complex, subunit 1-like (yeast)	-0,717	0,029
8141421			-0,717	0,028
8128316	GPR63	G protein-coupled receptor 63	-0,718	-0,3
8117389	HIST1H2BE	histone cluster 1, H2be	-0,72	-0,942
7983123	HAUS2	HAUS augmin-like complex, subunit 2	-0,72	-0,199
7984540	KIF23	kinesin family member 23	-0,72	-0,548

8005839	TMEM97	transmembrane protein 97	-0,721	-0,172
8105348	GPX8	glutathione peroxidase 8 (putative)	-0,721	-0,265
8117589	HIST1H3H	histone cluster 1, H3h	-0,723	-0,642
7986068	BLM	Bloom syndrome, RecQ helicase-like	-0,723	-0,294
8082816	SRPRB	signal recognition particle receptor, B subunit	-0,723	-0,01
8014066	EVI2A	ecotropic viral integration site 2A	-0,724	-0,758
8112045	ESM1	endothelial cell-specific molecule 1	-0,724	-0,277
7950042	SHANK2	SH3 and multiple ankyrin repeat domains 2	-0,726	-0,039
7995806	MT1A	metallothionein 1A	-0,726	-0,2
8129458	ARHGAP18	Rho GTPase activating protein 18	-0,727	-0,509
8042705	SMYD5	SMYD family member 5	-0,727	-0,337
7951545	EXPH5	exophilin 5	-0,728	-0,408
7914214	SNORA44	small nucleolar RNA, H/ACA box 44	-0,729	0,071
8097128	EXOSC9	exosome component 9	-0,729	-0,281
7924619	ENAH	enabled homolog (Drosophila)	-0,73	-0,392
8068478	CHAF1B	chromatin assembly factor 1, subunit B (p60)	-0,73	-0,199
8010978	LOC100130876	hypothetical LOC100130876	-0,731	0,094
7919761			-0,734	-0,112
8107307	CAMK4	calcium/calmodulin-dependent protein kinase IV	-0,734	-0,437
7938629	PDE3B	phosphodiesterase 3B, cGMP-inhibited	-0,735	-0,207
8103630	SH3RF1	SH3 domain containing ring finger 1	-0,736	-0,186
8153457	EEF1D	eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)	-0,736	0,19
8165705	ND6	NADH dehydrogenase, subunit 6 (complex I)	-0,736	-0,215
7910997	EXO1	exonuclease 1	-0,737	-0,217
8047518	NOP58	NOP58 ribonucleoprotein homolog (yeast)	-0,737	-0,259
8054437	ANAPC1	anaphase promoting complex subunit 1	-0,737	-0,345
8098150	C4orf43	chromosome 4 open reading frame 43	-0,738	-0,194
8117054	CAP2	CAP, adenylate cyclase-associated protein, 2 (yeast)	-0,738	-0,207
8006634	PIGW	phosphatidylinositol glycan anchor biosynthesis, class W	-0,739	-0,222
7915563	LOC100129492	hypothetical protein LOC100129492	-0,74	-0,468
8117426	HIST1H2BH	histone cluster 1, H2bh	-0,741	-1,089
8089038			-0,741	-0,294
8112914	DHFR	dihydrofolate reductase	-0,741	-0,294

8086222	SCN5A	sodium channel, voltage-gated, type V, alpha subunit	-0,742	-0,29
8128138	MDN1	MDN1, midasin homolog (yeast)	-0,742	-0,246
8096081	ENOPH1	enolase-phosphatase 1	-0,744	-0,19
7968563	RFC3	replication factor C (activator 1) 3, 38kDa	-0,745	-0,237
7909730	KCNK2	potassium channel, subfamily K, member 2	-0,747	-0,229
8016194	MAP3K14	mitogen-activated protein kinase kinase kinase 14	-0,747	-0,026
8105681	ERBB2IP	erbb2 interacting protein	-0,747	-0,351
8016476	HOXB9	homeobox B9	-0,749	-0,204
8081590	PHLDB2	pleckstrin homology-like domain, family B, member 2	-0,752	-0,301
7917359	ZNHIT6	zinc finger, HIT type 6	-0,754	-0,353
7933180	ZNF239	zinc finger protein 239	-0,756	-0,306
8122803			-0,757	-0,315
8051030	SLC5A6	solute carrier family 5 (sodium-dependent vitamin transporter), member 6	-0,758	-0,152
8089544	CCDC80	coiled-coil domain containing 80	-0,758	-0,307
7911038	ZNF238	zinc finger protein 238	-0,759	-0,13
8004804	PFAS	phosphoribosylformylglycinamidine synthase	-0,759	-0,362
8080419	GNL3	guanine nucleotide binding protein-like 3 (nucleolar)	-0,759	-0,123
7960438	ANO2	anoctamin 2	-0,761	-0,895
8052331	PNPT1	polyribonucleotide nucleotidyltransferase 1	-0,761	-0,252
8180034	TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	-0,761	-0,22
7907611	RASAL2	RAS protein activator like 2	-0,762	-0,305
8070615	WDR4	WD repeat domain 4	-0,762	-0,094
8020468	RBBP8	retinoblastoma binding protein 8	-0,763	-0,263
8159900	GLIS3	GLIS family zinc finger 3	-0,763	-0,157
8069003	PWP2	PWP2 periodic tryptophan protein homolog (yeast)	-0,764	-0,185
7943690	DDX10	DEAD (Asp-Glu-Ala-Asp) box polypeptide 10	-0,765	-0,422
8124484	HIST1H2BJ	histone cluster 1, H2bj	-0,765	-0,755
8163525	POLE3	polymerase (DNA directed), epsilon 3 (p17 subunit)	-0,765	-0,264
8127544	EEF1A1	eukaryotic translation elongation factor 1 alpha 1	-0,766	-0,045
8165911	TBL1X	transducin (beta)-like 1X-linked	-0,766	-0,397
8110450	HNRNPAB	heterogeneous nuclear ribonucleoprotein A/B	-0,769	-0,307
7977075	SNORA28	small nucleolar RNA, H/ACA box 28	-0,77	-0,121
8152340	NUDCD1	NudC domain containing 1	-0,77	-0,344
7902398	SNORD45A	small nucleolar RNA, C/D box 45A	-0,771	-0,122

8113010	CCNH	cyclin H	-0,771	-0,335
7982290			-0,772	-0,347
7995354	ORC6L	origin recognition complex, subunit 6 like (yeast)	-0,772	-0,384
8056890	CHN1	chimerin (chimaerin) 1	-0,773	-0,121
8046461	ZAK	sterile alpha motif and leucine zipper containing kinase AZK	-0,774	-0,453
7937483	SNORA52	small nucleolar RNA, H/ACA box 52	-0,774	-0,057
8035838	ZNF724P	zinc finger protein 724 pseudogene	-0,775	-0,471
8134904	POP7	processing of precursor 7, ribonuclease P/MRP subunit (<i>S. cerevisiae</i>)	-0,775	-0,204
8108422			-0,776	-0,13
8047243	MARS2	methionyl-tRNA synthetase 2, mitochondrial	-0,777	-0,178
8110920	FASTKD3	FAST kinase domains 3	-0,778	-0,568
7957260	GLIPR1	GLI pathogenesis-related 1	-0,779	-0,486
7940473	TMEM138	transmembrane protein 138	-0,782	-0,232
8041961	CHAC2	ChaC, cation transport regulator homolog 2 (<i>E. coli</i>)	-0,782	-0,371
8035628	NR2C2AP	nuclear receptor 2C2-associated protein	-0,783	-0,194
8041888	MSH6	mutS homolog 6 (<i>E. coli</i>)	-0,784	-0,158
7904364	WDR3	WD repeat domain 3	-0,785	-0,249
7981273	CCDC85C	coiled-coil domain containing 85C	-0,785	-0,241
7970473	XPO4	exportin 4	-0,786	-0,303
7946567			-0,787	-0,368
8152828	GSDMC	gasdermin C	-0,788	-0,316
8094938	NIPAL1	NIPA-like domain containing 1	-0,79	-0,171
7918517	WDR77	WD repeat domain 77	-0,791	-0,066
8124521	HIST1H4K	histone cluster 1, H4k	-0,795	-0,713
7914334	SNRNP40	small nuclear ribonucleoprotein 40kDa (U5)	-0,795	-0,19
7968915	GTF2F2	general transcription factor IIF, polypeptide 2, 30kDa	-0,796	-0,53
8121510	BXDC1	brix domain containing 1	-0,798	-0,348
8104758	C5orf23	chromosome 5 open reading frame 23	-0,801	-0,157
7974771	C14orf135	chromosome 14 open reading frame 135	-0,802	-0,362
8023727	DSEL	dermatan sulfate epimerase-like	-0,802	-0,143
7962427	PUS7L	pseudouridylate synthase 7 homolog (<i>S. cerevisiae</i>)-like	-0,803	-0,282
8044278	CCDC138	coiled-coil domain containing 138	-0,803	-0,262
7958211	C12orf45	chromosome 12 open reading frame 45	-0,808	-0,239
8009366	NOL11	nucleolar protein 11	-0,808	-0,284
7909568	DTL	denticleless homolog (<i>Drosophila</i>)	-0,809	-0,087
7974337			-0,809	-0,683

8055426	MCM6	minichromosome maintenance complex component 6	-0,812	-0,442
8138454	TWISTNB	TWIST neighbor	-0,813	-0,328
8138857	GGCT	gamma-glutamyl cyclotransferase	-0,814	-0,193
8000884	DCTPP1	dCTP pyrophosphatase 1	-0,816	-0,065
8052231			-0,816	-0,096
8153678	BOP1	block of proliferation 1	-0,816	-0,304
7968234	SNORA27	small nucleolar RNA, H/ACA box 27	-0,817	0,01
8104422	MTRR	5-methyltetrahydrofolate-homocysteine methyltransferase reductase	-0,817	-0,258
8166278	SCML1	sex comb on midleg-like 1 (<i>Drosophila</i>)	-0,819	-0,3
8171561	SCML2	sex comb on midleg-like 2 (<i>Drosophila</i>)	-0,819	-0,299
7897460	SLC25A33	solute carrier family 25, member 33	-0,82	-0,4
7991777	C4orf46	chromosome 4 open reading frame 46	-0,822	-0,228
8072242	NF2	neurofibromin 2 (merlin)	-0,822	-0,283
8117330	HIST1H3A	histone cluster 1, H3a	-0,822	-0,689
7985213	CHRNA5	cholinergic receptor, nicotinic, alpha 5	-0,823	-0,216
8041170			-0,825	-0,305
8135514	IFRD1	interferon-related developmental regulator 1	-0,827	-0,447
8025584	SNORD105	small nucleolar RNA, C/D box 105	-0,831	-0,207
8015796			-0,832	-0,186
8011861	DHX33	DEAH (Asp-Glu-Ala-His) box polypeptide 33	-0,834	-0,28
7970569	SACS	spastic ataxia of Charlevoix-Saguenay (sacsin)	-0,835	-0,21
8097792	SNORD73A	small nucleolar RNA, C/D box 73A	-0,836	-0,007
7948088	SLC25A33	solute carrier family 25, member 33	-0,838	-0,47
8017098			-0,838	0,033
8109830	CCDC99	coiled-coil domain containing 99	-0,838	-0,455
7959777	BRI3BP	BRI3 binding protein	-0,84	-0,172
8089954	IQCB1	IQ motif containing B1	-0,841	-0,219
7907847			-0,842	-0,116
8171879	LOC389842	similar to RanBP1	-0,844	-0,532
8155327	ALDH1B1	aldehyde dehydrogenase 1 family, member B1	-0,845	-0,134
8059319	FARSB	phenylalanyl-tRNA synthetase, beta subunit	-0,846	-0,403
8174975			-0,85	-0,35
8066254	LOC388796	hypothetical LOC388796	-0,853	-0,193
8132960			-0,853	-0,336
7926319	SUV39H2	suppressor of variegation 3-9 homolog 2 (<i>Drosophila</i>)	-0,854	-0,25
7930148	SFXN2	sideroflexin 2	-0,855	-0,534
8022996	KIAA1632	KIAA1632	-0,856	-0,569

8043413	RPIA	ribose 5-phosphate isomerase A	-0,858	-0,312
7922610	ABL2	v-abl Abelson murine leukemia viral oncogene homolog 2 (arg, Abelson-related gene)	-0,861	-0,407
8103485	NAF1	nuclear assembly factor 1 homolog (S. cerevisiae)	-0,864	-0,212
7944765			-0,866	-0,422
8117225	GMNN	geminin, DNA replication inhibitor	-0,867	-0,164
7978846	POLE2	polymerase (DNA directed), epsilon 2 (p59 subunit)	-0,868	-0,296
8115907	NOP16	NOP16 nucleolar protein homolog (yeast)	-0,868	-0,304
8018352	SLC25A19	solute carrier family 25 (mitochondrial thiamine pyrophosphate carrier), member 19	-0,869	-0,182
8080676	PDE12	phosphodiesterase 12	-0,871	-0,25
8039484	IL11	interleukin 11	-0,874	-0,201
7922414	SNORD76	small nucleolar RNA, C/D box 76	-0,875	0,023
8159854	KIAA0020	KIAA0020	-0,879	-0,368
7974164			-0,881	-0,232
8158998	RPL7A	ribosomal protein L7a	-0,881	-0,158
8120402	BAG2	BCL2-associated athanogene 2	-0,882	-0,23
8107204			-0,883	-0,408
8107563	PRR16	proline rich 16	-0,884	-0,35
8047161	OBFC2A	oligonucleotide/oligosaccharide-binding fold containing 2A	-0,885	-0,21
8171876	METTL1	methyltransferase like 1	-0,889	-0,191
7963333	KRT80	keratin 80	-0,89	-0,141
7965322	KITLG	KIT ligand	-0,89	0,022
8066247	LOC388796	hypothetical LOC388796	-0,891	-0,284
7938890	PRMT3	protein arginine methyltransferase 3	-0,893	-0,427
8165709			-0,893	-0,296
7929438	HELLS	helicase, lymphoid-specific	-0,894	-0,096
7962146	FAM60A	family with sequence similarity 60, member A	-0,896	-0,406
8100495	PPAT	phosphoribosyl pyrophosphate amidotransferase	-0,899	-0,293
7938291	SNORA3	small nucleolar RNA, H/ACA box 3	-0,9	0,168
8128322	NDUFAF4	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, assembly factor 4	-0,901	-0,225
8104912	SKP2	S-phase kinase-associated protein 2 (p45)	-0,902	-0,209
8115164			-0,903	0,056
8142061	PUS7	pseudouridylate synthase 7 homolog (S. cerevisiae)	-0,905	-0,142
8020825			-0,907	-0,192
8023259	SNORD58A	small nucleolar RNA, C/D box 58A	-0,913	-0,177
8156043	PSAT1	phosphoserine aminotransferase 1	-0,913	-0,332
8017096			-0,914	-0,155
8060501	SNORA51	small nucleolar RNA, H/ACA box	-0,916	0,109

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8133114	VKORC1L1	vitamin K epoxide reductase complex, subunit 1-like 1	-0,918	-0,187
7998129	POLR3K	polymerase (RNA) III (DNA directed) polypeptide K, 12.3 kDa	-0,924	-0,215
8097647	ABCE1	ATP-binding cassette, sub-family E (OABP), member 1	-0,925	-0,295
7900365	MFSD2	major facilitator superfamily domain containing 2	-0,927	-0,141
8120602	OGFRL1	opioid growth factor receptor-like 1	-0,927	-0,386
7925182	SNORA14B	small nucleolar RNA, H/ACA box 14B	-0,929	-0,14
8089247			-0,93	0,273
8083594	PTX3	pentraxin-related gene, rapidly induced by IL-1 beta	-0,932	-0,071
8124524	HIST1H2AK	histone cluster 1, H2ak	-0,94	-1,34
7926259	MCM10	minichromosome maintenance complex component 10	-0,94	-0,164
7998666	SNORA64	small nucleolar RNA, H/ACA box 64	-0,94	0,154
7998664	SNORA10	small nucleolar RNA, H/ACA box 10	-0,944	-0,1
8041204	SNORA10	small nucleolar RNA, H/ACA box 10	-0,944	-0,1
7940717	SLC3A2	solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	-0,952	-0,383
8129677	SGK1	serum/glucocorticoid regulated kinase 1	-0,955	-0,366
8130580	SNORA29	small nucleolar RNA, H/ACA box 29	-0,956	0,048
8014241	SLFN12	schlafen family member 12	-0,965	-0,514
8151101	MYBL1	v-myb myeloblastosis viral oncogene homolog (avian)-like 1	-0,965	-0,438
8104625			-0,968	-0,235
8124391	HIST1H2AB	histone cluster 1, H2ab	-0,972	-1,357
7900510	CTPS	CTP synthase	-0,972	-0,264
7901050	SNORD38A	small nucleolar RNA, C/D box 38A	-0,972	-0,034
8150877	SNORD54	small nucleolar RNA, C/D box 54	-0,973	-0,003
7968232	SNORD102	small nucleolar RNA, C/D box 102	-0,976	-0,068
8055688	RND3	Rho family GTPase 3	-0,98	-0,508
7970513	C13orf3	chromosome 13 open reading frame 3	-0,98	-0,537
8003204	GINS2	GINS complex subunit 2 (Psf2 homolog)	-0,98	-0,494
8076219	SNORD83B	small nucleolar RNA, C/D box 83B	-0,98	0,076
7904572			-0,983	-0,447
8085407	RPL32	ribosomal protein L32	-0,984	-0,062
7952339	LOC85389	RNA, small nucleolar	-0,986	-0,067
8007071	CDC6	cell division cycle 6 homolog (S. cerevisiae)	-0,987	-0,103

8113120	TOB2	transducer of ERBB2, 2	-0,988	-0,447
8165707	TOB2	transducer of ERBB2, 2	-0,988	-0,447
7913852	C1orf135	chromosome 1 open reading frame 135	-0,989	-0,327
8005202	SNORD49A	small nucleolar RNA, C/D box 49A	-0,989	-0,17
8042381	PNO1	partner of NOB1 homolog (S. cerevisiae)	-0,989	-0,353
7970810	SLC7A1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1	-0,992	-0,441
8091648	SSR3	signal sequence receptor, gamma (translocon-associated protein gamma)	-0,996	-0,338
8041168	SNORD53	small nucleolar RNA, C/D box 53	-0,997	-0,47
7929383	TMEM20	transmembrane protein 20	-0,999	-0,158
7914202	SNHG12	small nucleolar RNA host gene 12 (non-protein coding)	-1	0,09
8169115	NRK	Nik related kinase	-1,002	-0,524
8117543	HIST1H2AH	histone cluster 1, H2ah	-1,005	-0,872
7909782	RRP15	ribosomal RNA processing 15 homolog (S. cerevisiae)	-1,009	-0,533
8060484	NOP56	NOP56 ribonucleoprotein homolog (yeast)	-1,01	-0,101
8106193	UTP15	UTP15, U3 small nucleolar ribonucleoprotein, homolog (S. cerevisiae)	-1,011	-0,393
8030366	SNORD35A	small nucleolar RNA, C/D box 35A	-1,014	0,019
8152867	ASAP1	ArfGAP with SH3 domain, ankyrin repeat and PH domain 1	-1,026	-0,532
8101429	PLAC8	placenta-specific 8	-1,027	-0,277
8146685	RRS1	RRS1 ribosome biogenesis regulator homolog (S. cerevisiae)	-1,027	-0,243
7924476	TAF1A	TATA box binding protein (TBP)-associated factor, RNA polymerase I, A, 48kDa	-1,03	-0,411
8116848	PAK1IP1	PAK1 interacting protein 1	-1,033	-0,385
7947230	BDNF	brain-derived neurotrophic factor	-1,035	-0,483
8090565	SNORA7B	small nucleolar RNA, H/ACA box 7B	-1,035	0,191
7957890	UTP20	UTP20, small subunit (SSU) processome component, homolog (yeast)	-1,036	-0,38
8165974	CLCN4	chloride channel 4	-1,036	-0,394
8124385	HIST1H4B	histone cluster 1, H4b	-1,042	-0,919
7957298	NAV3	neuron navigator 3	-1,046	-0,339
8144036	XRCC2	X-ray repair complementing defective repair in Chinese hamster cells 2	-1,047	-0,215
7914212	SNORA61	small nucleolar RNA, H/ACA box 61	-1,055	0,164

8115410	GEMIN5	gem (nuclear organelle) associated protein 5	-1,058	-0,284
7950983	CHORDC1	cysteine and histidine-rich domain (CHORD)-containing 1	-1,06	-0,417
8096050	FGF5	fibroblast growth factor 5	-1,068	-0,211
7942592	SNORD15A	small nucleolar RNA, C/D box 15A	-1,074	0,141
8107326	SNORA13	small nucleolar RNA, H/ACA box 13	-1,075	-0,042
8124394	HIST1H2BB	histone cluster 1, H2bb	-1,077	-1,402
7916018			-1,085	0,056
7942832	C11orf82	chromosome 11 open reading frame 82	-1,087	-0,511
8084064	MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	-1,09	-0,507
8084708	SNORA4	small nucleolar RNA, H/ACA box 4	-1,09	-0,06
7906919	RGS4	regulator of G-protein signaling 4	-1,091	-0,227
7902396	SNORD45C	small nucleolar RNA, C/D box 45C	-1,093	-0,039
7989915	TIPIN	TIMELESS interacting protein	-1,093	-0,398
7938293	SNORA45	small nucleolar RNA, H/ACA box 45	-1,096	-0,047
8147049	FABP5	fatty acid binding protein 5 (psoriasis-associated)	-1,098	-0,478
8108180			-1,099	-0,397
8042830	MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	-1,1	-0,501
8046488	CDCA7	cell division cycle associated 7	-1,103	-0,454
7948420	FABP5	fatty acid binding protein 5 (psoriasis-associated)	-1,11	-0,502
7958375			-1,119	0,133
7957551	SOCS2	suppressor of cytokine signaling 2	-1,148	-0,489
8174715	SNORA69	small nucleolar RNA, H/ACA box 69	-1,155	-0,105
7969576	MIRHG1	microRNA host gene 1 (non-protein coding)	-1,16	-0,229
8023575	CCBE1	collagen and calcium binding EGF domains 1	-1,166	-0,451
8015210	KRTAP2-4	keratin associated protein 2-4	-1,17	-0,478
8019576	KRTAP2-4	keratin associated protein 2-4	-1,17	-0,478
8106820	POLR3G	polymerase (RNA) III (DNA directed) polypeptide G (32kD)	-1,174	-0,502
8005955	SNORD42A	small nucleolar RNA, C/D box 42A	-1,177	-0,176
8139456	SNORA9	small nucleolar RNA, H/ACA box 9	-1,178	0,036
8092067	RPL22L1	ribosomal protein L22-like 1	-1,179	-0,504
7997491	HSD17B2	hydroxysteroid (17-beta) dehydrogenase 2	-1,196	-0,381
8048870	WDR69	WD repeat domain 69	-1,198	-0,694
8092765	C3orf59	chromosome 3 open reading frame	-1,199	-0,441

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7974335			-1,209	-0,756
8053646			-1,211	-0,239
8136347	CALD1	caldesmon 1	-1,218	-0,743
8078916	SNORA6	small nucleolar RNA, H/ACA box 6	-1,228	0,037
7902400	SNORD45B	small nucleolar RNA, C/D box 45B	-1,23	-0,235
7903022	SNORD21	small nucleolar RNA, C/D box 21	-1,234	-0,056
7948902	SNORD29	small nucleolar RNA, C/D box 29	-1,245	-0,135
7922402	SNORD47	small nucleolar RNA, C/D box 47	-1,253	-0,179
8124537	HIST1H3J	histone cluster 1, H3j	-1,258	-1,157
8039025	ZNF702P	zinc finger protein 702 pseudogene	-1,259	-0,443
8052355	EFEMP1	EGF-containing fibulin-like extracellular matrix protein 1	-1,274	-0,637
8159004	RPL7A	ribosomal protein L7a	-1,275	-0,206
8023598	RNF152	ring finger protein 152	-1,28	-0,053
8032749	SNORD37	small nucleolar RNA, C/D box 37	-1,295	-0,308
8003298	SLC7A5	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5	-1,309	-0,329
8084704	EIF4A2	eukaryotic translation initiation factor 4A, isoform 2	-1,309	-0,131
8078918	SNORA62	small nucleolar RNA, H/ACA box 62	-1,331	-0,101
8076221	SNORD83A	small nucleolar RNA, C/D box 83A	-1,338	-0,204
8086880	CDC25A	cell division cycle 25 homolog A (S. pombe)	-1,345	-0,246
8118322	SNORD52	small nucleolar RNA, C/D box 52	-1,354	0,061
8081235	COL8A1	collagen, type VIII, alpha 1	-1,362	-0,474
8083690	IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	-1,367	-0,524
7956269			-1,368	-0,193
7922406	SNORD79	small nucleolar RNA, C/D box 79	-1,404	-0,184
8010080	SNORD1B	small nucleolar RNA, C/D box 1B	-1,408	0,087
8005953	SNORD4A	small nucleolar RNA, C/D box 4A	-1,419	-0,298
8030364	SNORD34	small nucleolar RNA, C/D box 34	-1,425	0,07
8164215	SNORA65	small nucleolar RNA, H/ACA box 65	-1,437	0,124
7922410	SNORD44	small nucleolar RNA, C/D box 44	-1,465	-0,246
8159006	RPL7A	ribosomal protein L7a	-1,466	-0,093
7956759	SRGAP1	SLIT-ROBO Rho GTPase activating protein 1	-1,486	-0,672
8136200	CPA4	carboxypeptidase A4	-1,496	-0,361
8115732	UNQ9374	VCEW9374	-1,5	-0,538
8150698	SNAI2	snail homolog 2 (Drosophila)	-1,508	-0,354
8005957	SNORD4B	small nucleolar RNA, C/D box 4B	-1,516	-0,093
8067140	CYP24A1	cytochrome P450, family 24, subfamily A, polypeptide 1	-1,536	-0,882
7922404	SNORD80	small nucleolar RNA, C/D box 80	-1,551	-0,297
8010082	SNORD1A	small nucleolar RNA, C/D box 1A	-1,556	-0,207

8127989	SNORD50B	small nucleolar RNA, C/D box 50B	-1,561	-0,209
8117594	HIST1H2BM	histone cluster 1, H2bm	-1,563	-1,877
8005951	SNORD42B	small nucleolar RNA, C/D box 42B	-1,591	-0,175
8047778	SNORD51	small nucleolar RNA, C/D box 51	-1,601	0,108
7901052	SNORD38B	small nucleolar RNA, C/D box 38B	-1,613	-0,425
8175432	SNORD61	small nucleolar RNA, C/D box 61	-1,618	0,126
8122142	SNORD101	small nucleolar RNA, C/D box 101	-1,626	-0,252
8059708	SNORA75	small nucleolar RNA, H/ACA box 75	-1,671	-0,124
7922418	SNORD74	small nucleolar RNA, C/D box 74	-1,672	-0,153
7922400			-1,687	-0,114
7982597	THBS1	thrombospondin 1	-1,741	-0,4
7922408	SNORD78	small nucleolar RNA, C/D box 78	-1,745	-0,127
8076223	SNORD43	small nucleolar RNA, C/D box 43	-1,765	-0,147
8112202	PLK2	polo-like kinase 2 (<i>Drosophila</i>)	-1,772	-0,331
8122144	SNORA33	small nucleolar RNA, H/ACA box 33	-1,805	-0,037
7948900	SNORD30	small nucleolar RNA, C/D box 30	-1,834	-0,032
7948898	SNORD31	small nucleolar RNA, C/D box 31	-1,867	-0,049
8116921	EDN1 *	endothelin 1	-1,874	-0,785
7952335	LOC85391	RNA, small nucleolar	-1,884	0,112
7948896	SNORD22	small nucleolar RNA, C/D box 22	-1,905	-0,088
8108420	SNORA74A	small nucleolar RNA, H/ACA box 74A	-1,928	-0,135
7948908	SNORD26	small nucleolar RNA, C/D box 26	-1,972	-0,036
8063345	SNORD12C	small nucleolar RNA, C/D box 12C	-1,992	-0,009
7922416	SNORD75	small nucleolar RNA, C/D box 75	-1,998	-0,099
8059710	SNORD20	small nucleolar RNA, C/D box 20	-2,025	-0,402
7922412	SNORD77	small nucleolar RNA, C/D box 77	-2,036	-0,261
7902495	NEXN	nexilin (F actin binding protein)	-2,076	-0,534
7948910	SNORD25	small nucleolar RNA, C/D box 25	-2,099	-0,176
7948906	SNORD27	small nucleolar RNA, C/D box 27	-2,14	-0,07
7909789	TGFB2	transforming growth factor, beta 2	-2,149	-0,552
8059712	SNORD82	small nucleolar RNA, C/D box 82	-2,15	-0,056
8104901	IL7R	interleukin 7 receptor	-2,174	-0,872

Supplementary Table 4. Common to Zol and Fluva differentially regulated genes.**A. Up-regulated genes (compared to corresponding control)**

Genes Probe Set ID	Genes Symbol	Genes Title	log2 vs control			
			Fluva 12h	Fluva 24h	Zol100 24h	Zol 48h
7915543	SLC6A9	solute carrier family 6 (neurotransmitter transporter, glycine), member 9	0,309	0,79	0,937	0,167
7917530			0,313	1,19	1,54	0,746
7917532	GBP2	guanylate binding protein 2, interferon-inducible	0,177	1,266	1,539	0,753
7919872	FAM63A	family with sequence similarity 63, member A	0,105	0,608	0,795	0,157
7920271	S100A4	S100 calcium binding protein A4	0,448	0,907	0,845	0,678
7920278	S100A3	S100 calcium binding protein A3	0,548	1,041	1,14	0,589
7920285	S100A2	S100 calcium binding protein A2	0,292	0,799	0,712	0,295
7920664	THBS3	thrombospondin 3	0,302	0,635	1,185	0,343
7923662	PIK3C2B	phosphoinositide-3-kinase, class 2, beta polypeptide	0,303	0,924	1,27	0,443
7925918	AKR1C1	aldo-keto reductase family 1, member C1 (dihydrodiol dehydrogenase 1; 20-alpha (3-alpha)-hydroxysteroid dehydrogenase)	0,623	0,754	1,048	0,489
7926596	COMM3	COMM domain containing 3	0,245	0,605	1,107	0,426
7926677	OTUD1	OTU domain containing 1	0,318	0,62	0,698	0,244
7928558	ZMIZ1	zinc finger, MIZ-type containing 1	0,426	0,616	1,074	0,381
7930276	SLK	STE20-like kinase (yeast)	0,313	0,716	0,95	0,339
7931832	AKR1C2	aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogenase 2; bile acid binding protein; 3-alpha hydroxysteroid dehydrogenase, type III)	0,864	1,518	1,374	0,322
7934690	ZCCHC24	zinc finger, CCHC domain containing 24	0,481	0,605	0,833	0,392
7934898	ANKRD22	ankyrin repeat domain 22	1,004	1,542	1,292	0,634
7935553	LOXL4	lysyl oxidase-like 4	0,089	0,728	0,609	0,307
7936111	CALHM3	calcium homeostasis modulator 3	0,539	0,896	0,756	0,201
7936134	OBFC1	oligonucleotide/oligosaccharide-binding fold containing 1	0,284	0,663	1,045	0,389
7939839	PTPRJ	protein tyrosine phosphatase, receptor type, J	0,316	0,8	1,181	0,459
7941272	MALAT1	metastasis associated lung adenocarcinoma transcript 1 (non-protein coding)	0,243	0,728	0,626	0,617
7944931	SLC37A2	solute carrier family 37 (glycerol-3-phosphate transporter), member 2	0,358	0,848	1,274	0,498

	ADAMTS 15	ADAM metallopeptidase with thrombospondin type 1 motif, 15	0,55	0,766	0,711	0,254
7945232	CTSD	cathepsin D	0,35	0,658	0,999	0,324
7945666	MUC15	mucin 15, cell surface associated	0,312	0,712	0,681	0,447
7947199	LGR4	leucine-rich repeat-containing G protein-coupled receptor 4	0,47	0,826	1,254	0,547
7949746	POLD4	polymerase (DNA-directed), delta 4	0,208	0,675	1,032	0,269
7950391	PGM2L1	phosphoglucomutase 2-like 1	0,394	0,642	1,213	0,533
7951077	SESN3	sestrin 3	0,49	0,721	1,13	0,525
7957608	KRT19P2	keratin 19 pseudogene 2	0,07	0,659	1,048	0,208
7958262	TCP11L2	t-complex 11 (mouse)-like 2	0,759	1,713	3,204	0,705
7965846	CCDC53	coiled-coil domain containing 53	0,129	0,642	0,866	0,18
7966089	CMKLR1	chemokine-like receptor 1	0,604	0,662	0,876	0,281
7968883	C13orf31	chromosome 13 open reading frame 31	0,002	0,636	0,634	0,322
7973084	ANG	angiogenin, ribonuclease, RNase A family, 5	0,379	0,623	1,286	0,278
7974270	ATL1	atlastin GTPase 1	0,349	0,677	0,68	0,343
7985560	LOC727963	similar to elongation factor Tu GTP binding domain containing 1	- 0,078	0,747	0,66	0,3
7988970	KIAA1370	KIAA1370	0,278	0,598	1,334	0,439
7996081	GPR56	G protein-coupled receptor 56	0,783	0,979	1,285	0,397
8004360	KCTD11	potassium channel tetramerisation domain containing 11	0,015	0,651	0,714	0,261
8009243	C17orf60	chromosome 17 open reading frame 60	0,304	0,916	1,868	0,477
8009666	RAB37	RAB37, member RAS oncogene family	0,154	0,789	1,073	0,423
8012416	C17orf44	chromosome 17 open reading frame 44	0,144	0,679	0,99	0,252
8015349	KRT19	keratin 19	0,46	0,737	1,533	0,496
8019954	FLJ35776	hypothetical LOC649446	0,416	0,651	1,146	0,288
8041781	EPAS1	endothelial PAS domain protein 1	0,365	1,072	1,459	0,489
8042503	MXD1	MAX dimerization protein 1	0,356	0,678	0,82	0,108
8045539	KYNU	kynureninase (L-kynurenone hydrolase)	0,483	0,916	1,185	0,325
8046824	FSIP2	fibrous sheath interacting protein 2	0,456	0,813	1,471	0,304
8046833	FLJ44048	FLJ44048 protein	0,543	0,913	1,307	0,06
8048350	PLCD4	phospholipase C, delta 4	0,244	0,95	1,12	0,336
8051583	CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	0,747	0,811	0,899	0,149
8052872	TGFA	transforming growth factor, alpha	0,371	0,797	1,039	0,44
8072626	TIMP3	TIMP metallopeptidase inhibitor 3	0,34	0,612	0,912	0,406
8073068	APOBEC 3C	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3C	0,268	0,704	1,201	0,352
8073072	APOBEC 3D	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3D	0,272	0,603	0,963	0,319
8073081	APOBEC 3F	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F	0,468	0,754	1,343	0,168
8075635	TIMP3	TIMP metallopeptidase inhibitor 3	0,319	0,734	1,225	0,446

8084219	KLHL24	kelch-like 24 (Drosophila)	0,399	0,657	1,421	0,397
8088550	PRICKLE 2	prickle homolog 2 (Drosophila)	0,405	0,593	0,618	0,178
8092134	PLD1	phospholipase D1, phosphatidylcholine-specific	0,17	0,89	1,307	0,527
8092541	LIPH	lipase, member H	0,439	0,89	1,202	0,452
8094609	FAM114 A1	family with sequence similarity 114, member A1	0,29	0,617	1,105	0,494
8095744	AREG	amphiregulin	0,299	0,674	1,001	0,588
8099841	TLR6	toll-like receptor 6	0,095	0,666	1,197	0,498
8099912	C4orf34	chromosome 4 open reading frame 34	0,578	1,16	1,708	0,486
8103769	HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	0,139	1,027	0,995	0,638
8105300			0,314	0,688	0,947	0,643
8112940	SSBP2	single-stranded DNA binding protein 2	0,353	0,686	1,151	0,359
8113073	ARRDC3	arrestin domain containing 3	0,478	0,812	1,916	0,539
8115261	CCDC69	coiled-coil domain containing 69	0,324	0,729	1,004	0,386
8116980	RNF182	ring finger protein 182	0,298	0,699	0,971	0,432
8119898	VEGFA	vascular endothelial growth factor A	0,583	0,958	0,956	0,342
8123598	SERPINB 1	serpin peptidase inhibitor, clade B (ovalbumin), member 1	0,178	0,801	1,171	0,423
8124040	ATXN1	ataxin 1	0,487	0,933	1,341	0,51
8125048	DDAH2	dimethylarginine dimethylaminohydrolase 2	0,599	0,82	1,089	0,374
8131143	LFNG	LFNG O-fucosylpeptide 3-beta-N- acetylglucosaminyltransferase	0,27	0,776	1,209	0,418
8133770	CCDC146	coiled-coil domain containing 146	0,035	0,679	0,798	0,131
8135392	HBP1	HMG-box transcription factor 1	0,598	0,839	1,582	0,371
8138289	ETV1	ets variant 1	0,39	0,715	1,011	0,232
8140709	KIAA132 4L	KIAA1324-like	0,215	0,617	0,859	0,105
8140971	SAMD9L	sterile alpha motif domain containing 9-like	0,347	0,674	1,259	0,269
8149551	PSD3	pleckstrin and Sec7 domain containing 3	0,256	0,592	0,925	0,13
8151890	TP53INP 1	tumor protein p53 inducible nuclear protein 1	0,488	1,186	1,67	0,596
8154381	C9orf150	chromosome 9 open reading frame 150	0,679	0,889	1,003	0,242
8156573	C9orf3	chromosome 9 open reading frame 3	0,126	0,764	0,786	0,452
8156826	TGFBR1	transforming growth factor, beta receptor 1	0,456	0,625	0,759	0,412
8164580	PTGES	prostaglandin E synthase	0,681	1,073	1,154	0,412
8166469	SAT1	spermidine/spermine N1- acetyltransferase 1	0,23	0,701	0,693	0,579
8178590	DDAH2	dimethylarginine dimethylaminohydrolase 2	0,627	0,886	1,092	0,37
8179819	DDAH2	dimethylarginine dimethylaminohydrolase 2	0,627	0,886	1,092	0,37

		eukaryotic translation initiation factor 2C, 4	0,131	0,545	0,741	0,187
7900009	EIF2C4	tetraspanin 1	0,126	0,565	0,824	0,455
7901175	TSPAN1	phosphoglucomutase 1	0,108	0,302	0,707	0,234
	KIAA1107	KIAA1107	0,384	0,498	1,013	0,083
7902977	STXBP3	syntaxin binding protein 3	0,205	0,418	0,63	0,187
7903541	LMNA	lamin A/C	0,39	0,485	0,979	0,313
		inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase epsilon	-0,07	0,364	0,748	0,31
7909188	IKBKE	cornichon homolog 3 (Drosophila)	0,343	0,576	0,75	0,338
7910022	ZNF436	zinc finger protein 436	0,138	0,429	0,673	0,241
	TTLL7	tubulin tyrosine ligase-like family, member 7	0,228	0,538	0,903	0,199
7918911			0,189	0,478	0,77	0,152
7920258	S100A6	S100 calcium binding protein A6	0,335	0,565	0,989	0,417
		pre-B-cell leukemia homeobox interacting protein 1	0,211	0,375	0,646	0,207
7920575	PBXIP1	kinesin-associated protein 3	0,214	0,44	0,81	0,24
7922268	KIFAP3	lysine (K)-specific demethylase 5B	0,234	0,551	0,964	0,255
7923453	NET1	neuroepithelial cell transforming 1	0,247	0,391	1,239	0,302
7925954	OPTN	optineurin	0,282	0,519	1,223	0,455
7930162	C10orf26	chromosome 10 open reading frame 26	0,284	0,284	0,795	0,269
7931852	TUBAL3	tubulin, alpha-like 3	0,271	0,581	0,933	0,369
7932796	SVIL	supervillin	0,161	0,508	0,948	0,356
7937150	ADAM8	ADAM metallopeptidase domain 8	0,425	0,552	1,116	0,427
7938396	AMPD3	adenosine monophosphate deaminase (isoform E)	0,149	0,403	0,62	0,249
7939751	NR1H3	nuclear receptor subfamily 1, group H, member 3	0,097	0,443	0,651	0,351
7941087	PPP2R5B	protein phosphatase 2, regulatory subunit B', beta isoform	0,076	0,341	0,859	0,296
7941148	TM7SF2	transmembrane 7 superfamily member 2	0,221	0,535	0,883	0,301
7943314	JRKI	jerky homolog-like (mouse)	-0,01	0,41	0,683	0,168
7944803	VWA5A	von Willebrand factor A domain containing 5A	0,356	0,468	0,629	0,261
7946142	PRKCDBP	protein kinase C, delta binding protein	0,357	0,485	0,866	0,314
7947624	PHF21A	PHD finger protein 21A	0,003	0,561	1,006	0,297
7948667	AHNAK	AHNAK nucleoprotein	0,235	0,551	0,741	0,328
7953626	CLSTN3	calsyntenin 3	0,177	0,484	0,618	0,342
7956038	MMP19	matrix metallopeptidase 19	0,015	0,411	0,634	0,336
7956046	DGKA	diacylglycerol kinase, alpha 80kDa	0,327	0,571	0,887	0,192
7956166	FAM62A	family with sequence similarity 62 (C2 domain containing), member A	0,119	0,321	0,606	0,268

7956301	LRP1	low density lipoprotein-related protein 1 (alpha-2-macroglobulin receptor)	0,222	0,373	0,72	0,333	
7956613	TSPAN31	tetraspanin 31	0,123	0,454	0,773	0,081	
		transmembrane and tetratricopeptide repeat containing 2	0,139	0,575	1,211	0,522	
7957417	TMTC2	host cell factor C2	0,168	0,4	0,672	0,104	
		host cell factor C2	0,168	0,4	0,672	0,104	
7958158	HCFC2	tumor necrosis factor receptor superfamily, member 1A	0,233	0,399	0,655	0,197	
		tumor necrosis factor receptor superfamily, member 1A	0,233	0,399	0,655	0,197	
7960518	SLC2A14	solute carrier family 2 (facilitated glucose transporter), member 14	0,442	0,455	0,865	0,256	
		solute carrier family 2 (facilitated glucose transporter), member 14	0,442	0,455	0,865	0,256	
7961865	KRAS	v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog	0,262	0,425	0,624	0,036	-
		v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog	0,262	0,425	0,624	0,036	-
7963721	CALCOC O1	calcium binding and coiled-coil domain 1	0,165	0,577	1,376	0,316	
		calcium binding and coiled-coil domain 1	0,165	0,577	1,376	0,316	
7965423	BTG1	B-cell translocation gene 1, anti-proliferative	0,257	0,409	0,9	0,132	
		B-cell translocation gene 1, anti-proliferative	0,257	0,409	0,9	0,132	
7973352	LRP10	low density lipoprotein receptor-related protein 10	0,17	0,418	0,752	0,407	
		low density lipoprotein receptor-related protein 10	0,17	0,418	0,752	0,407	
7973618	IRF9	interferon regulatory factor 9	0,246	0,528	0,836	0,392	
		interferon regulatory factor 9	0,246	0,528	0,836	0,392	
7973840	ARHGAP 5	Rho GTPase activating protein 5	0,303	0,586	0,796	0,361	
		Rho GTPase activating protein 5	0,303	0,586	0,796	0,361	
7974461	LGALS3	lectin, galactoside-binding, soluble, 3	0,261	0,353	0,822	0,263	
		lectin, galactoside-binding, soluble, 3	0,261	0,353	0,822	0,263	
7978739	TRAPPC 6B	trafficking protein particle complex 6B	0,119	0,472	0,675	0,133	
		trafficking protein particle complex 6B	0,119	0,472	0,675	0,133	
7979710	PLEK2	pleckstrin 2	0,408	0,509	1,047	0,403	
		pleckstrin 2	0,408	0,509	1,047	0,403	
7979984	ZFYVE1	zinc finger, FYVE domain containing 1	0,343	0,44	0,883	0,131	
		zinc finger, FYVE domain containing 1	0,343	0,44	0,883	0,131	
7980005	NUMB	numb homolog (<i>Drosophila</i>)	0,26	0,495	0,715	0,291	
		numb homolog (<i>Drosophila</i>)	0,26	0,495	0,715	0,291	
7982564	SPRED1	sprouty-related, EVH1 domain containing 1	0,117	0,528	0,654	0,319	
		sprouty-related, EVH1 domain containing 1	0,117	0,528	0,654	0,319	
7985777	ISG20	interferon stimulated exonuclease gene 20kDa	0,344	0,358	0,815	0,303	
		interferon stimulated exonuclease gene 20kDa	0,344	0,358	0,815	0,303	
7986411	MEF2A	myocyte enhancer factor 2A	0,193	0,379	0,847	0,204	
		myocyte enhancer factor 2A	0,193	0,379	0,847	0,204	
7990054	UACA	uveal autoantigen with coiled-coil domains and ankyrin repeats	0,164	0,426	0,687	0,162	
		uveal autoantigen with coiled-coil domains and ankyrin repeats	0,164	0,426	0,687	0,162	
7998136	RHBDF1	rhomboid 5 homolog 1 (<i>Drosophila</i>)	0,103	0,41	0,867	0,317	
		rhomboid 5 homolog 1 (<i>Drosophila</i>)	0,103	0,41	0,867	0,317	
8001211	ITFG1	integrin alpha FG-GAP repeat containing 1	0,163	0,557	0,657	0,258	
		integrin alpha FG-GAP repeat containing 1	0,163	0,557	0,657	0,258	
8001507	BBS2	Bardet-Biedl syndrome 2	0,13	0,47	0,874	0,255	
		Bardet-Biedl syndrome 2	0,13	0,47	0,874	0,255	
8004266	SLC16A1 3	solute carrier family 16, member 13 (monocarboxylic acid transporter 13)	0,191	0,555	0,622	0,266	
		solute carrier family 16, member 13 (monocarboxylic acid transporter 13)	0,191	0,555	0,622	0,266	
8005475	TRIM16L	tripartite motif-containing 16-like	0,278	0,472	0,612	0,33	
		tripartite motif-containing 16-like	0,278	0,472	0,612	0,33	
8005765	WSB1	WD repeat and SOCS box-containing 1	0,156	0,432	0,836	0,105	
		WD repeat and SOCS box-containing 1	0,156	0,432	0,836	0,105	
8006746	TBC1D3	TBC1 domain family, member 3	0,199	0,481	0,943	0,398	
		TBC1 domain family, member 3	0,199	0,481	0,943	0,398	
8012953	TRIM16	tripartite motif-containing 16	0,432	0,504	0,908	0,286	
		tripartite motif-containing 16	0,432	0,504	0,908	0,286	
8014603	TBC1D3 D	TBC1 domain family, member 3D	0,207	0,483	0,956	0,394	
		TBC1 domain family, member 3D	0,207	0,483	0,956	0,394	
8014650	NPEPPS	aminopeptidase puromycin sensitive	0,146	0,383	0,592	0,208	
		aminopeptidase puromycin sensitive	0,146	0,383	0,592	0,208	
8014825	FBXL20	F-box and leucine-rich repeat protein 20	0,047	0,449	0,709	0,05	
		F-box and leucine-rich repeat protein 20	0,047	0,449	0,709	0,05	
8015016	TNS4	tensin 4	0,201	0,539	0,676	0,531	

8015759	VAT1	vesicle amine transport protein 1 homolog (<i>T. californica</i>)	0,214	0,408	0,686	0,264
8017173	TBC1D3P2	TBC1 domain family, member 3 pseudogene 2	0,172	0,388	0,72	0,294
8018264	C17orf28	chromosome 17 open reading frame 28	0,107	0,465	0,64	0,357
8018922	CYTH1	cytohesin 1	0,17	0,443	0,698	0,241
8020068	ANKRD12	ankyrin repeat domain 12	0,084	0,412	0,595	0,034
8021275	POLI	polymerase (DNA directed) iota	0,146	0,511	0,693	0,128
8024572	GNA15	guanine nucleotide binding protein (G protein), alpha 15 (Gq class)	0,32	0,42	0,63	0,253
8025421	MARCH2	membrane-associated ring finger (C3HC4) 2	0,304	0,459	0,616	0,118
8026861	B3GNT3	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 3	0,288	0,338	0,667	0,233
8026991	PGPEP1	pyroglutamyl-peptidase I	0,258	0,503	0,831	0,254
8028206	ZNF345	zinc finger protein 345	0,159	0,513	0,87	0,147
8028311	SPINT2	serine peptidase inhibitor, Kunitz type, 2	0,181	0,434	0,675	0,302
8030007	EMP3	epithelial membrane protein 3	0,307	0,33	0,659	0,279
8031047	MYADM	myeloid-associated differentiation marker	0,242	0,468	0,791	0,273
8037594	RTN2	reticulon 2	0,246	0,418	0,708	0,233
8038407	RRAS	related RAS viral (r-ras) oncogene homolog	0,127	0,48	1,06	0,264
8039034	ZNF160	zinc finger protein 160	0,196	0,419	0,806	0,124
8040238	HPCAL1	hippocalcin-like 1	0,288	0,522	0,767	0,409
8041197	YPEL5	yippee-like 5 (<i>Drosophila</i>)	0,339	0,529	1,005	0,326
8041913	KLRAQ1	KLRAQ motif containing 1	0,261	0,48	0,813	0,168
8042867	WBP1	WW domain binding protein 1	0,112	0,365	0,783	0,279
8043377	WBP1	WW domain binding protein 1	0,121	0,449	0,841	0,286
8047086	NAB1	NGFI-A binding protein 1 (EGR1 binding protein 1)	0,022	0,402	0,75	0,334
8050702	TP53I3	tumor protein p53 inducible protein 3	0,133	0,494	0,942	0,27
8053417	CAPG	capping protein (actin filament), gelsolin-like	0,155	0,388	0,636	0,224
8053576	RNF103	ring finger protein 103	0,25	0,403	0,772	0,246
8053599	WBP1	WW domain binding protein 1	0,15	0,448	0,822	0,286
8055350	TMEM163	transmembrane protein 163	0,047	0,46	0,646	0,229
8060745	SMOX	spermine oxidase	0,331	0,468	0,607	0,072
8063536	TFAP2C	transcription factor AP-2 gamma (activating enhancer binding protein 2 gamma)	0,284	0,549	0,642	0,371
8064637	C20orf194	chromosome 20 open reading frame 194	0,12	0,472	0,711	0,23
8065444	ACSS1	acyl-CoA synthetase short-chain family member 1	0,209	0,373	0,822	0,213
8067248	PPP4R1L	protein phosphatase 4, regulatory subunit 1-like	0,269	0,555	0,859	0,328

8068612	WRB	tryptophan rich basic protein	0,296	0,373	0,683	0,036
8070489	RIPK4	receptor-interacting serine-threonine kinase 4	0,321	0,415	0,643	0,312
8071420	SERPIND1	serpin peptidase inhibitor, clade D (heparin cofactor), member 1	0,011	0,583	0,787	0,223
8071981	CTA-221G9.4	KIAA1671 protein	0,357	0,458	0,854	0,241
8075423	DUSP18	dual specificity phosphatase 18	0,337	0,582	0,714	0,04
8079746	TCTA	T-cell leukemia translocation altered gene	0,182	0,586	0,995	0,121
8080144	PARP3	poly (ADP-ribose) polymerase family, member 3	0,003	0,353	0,636	0,179
8080926	ARL6IP5	ADP-ribosylation-like factor 6 interacting protein 5	0,277	0,562	0,816	0,261
8082380	ABTB1	ankyrin repeat and BTB (POZ) domain containing 1	0,229	0,382	0,723	0,124
8090018	PARP9	poly (ADP-ribose) polymerase family, member 9	0,136	0,543	0,613	0,325
8091422	WWTR1	WW domain containing transcription regulator 1	0,259	0,537	0,761	0,308
8092095	TNIK	TRAF2 and NCK interacting kinase	0,259	0,529	0,754	0,271
8095728	EREG	epiregulin	0,51	0,585	0,805	0,313
8098995	MXD4	MAX dimerization protein 4	0,213	0,428	0,696	0,195
8106784	RASA1	RAS p21 protein activator (GTPase activating protein) 1	0,285	0,563	0,768	0,209
8109612	ADRA1B	adrenergic, alpha-1B-, receptor	0,176	0,44	0,598	0,328
8113358	ST8SIA4	ST8 alpha-N-acetyl-neuraminate alpha-2,8-sialyltransferase 4	0,25	0,488	0,66	0,278
8113469	PJA2	praja ring finger 2	0,315	0,477	0,741	0,236
8119670	KLC4	kinesin light chain 4	0,13	0,322	0,652	0,075
8121277	AIM1	absent in melanoma 1	0,194	0,512	0,676	0,242
8122986	SNX9	sorting nexin 9	0,21	0,465	0,77	0,258
8126486	CUL7	cullin 7	0,031	0,387	0,621	0,327
8127425	LMBRD1	LMBR1 domain containing 1	0,252	0,473	0,665	0,014
8128737	MICAL1	microtubule associated monooxygenase, calponin and LIM domain containing 1	0,134	0,371	0,659	0,153
8129317	SERINC1	serine incorporator 1	0,249	0,454	0,591	0,089
8129804	MAP3K5	mitogen-activated protein kinase kinase kinase 5	0,22	0,422	0,826	0,377
8129953	HIVEP2	human immunodeficiency virus type I enhancer binding protein 2	0,178	0,442	0,671	0,363
8132218	BBS9	Bardet-Biedl syndrome 9	0,122	0,518	0,819	0,14
8137639	WDR60	WD repeat domain 60	0,192	0,502	1,103	0,425
8137680	ADAP1	ArfGAP with dual PH domains 1	0,188	0,573	0,92	0,174
8138689	SKAP2	src kinase associated phosphoprotein 2	0,118	0,586	0,996	0,276
8140620	PCLO	piccolo (presynaptic cytomatrix protein)	0,184	0,472	0,592	0,383
8142307	PNPLA8	patatin-like phospholipase domain containing 8	0,265	0,435	0,747	0,057

8142415	C7orf60	chromosome 7 open reading frame 60	0,233	0,509	0,841	0,249
8142886	UBE2H	ubiquitin-conjugating enzyme E2H (UBC8 homolog, yeast)	0,185	0,493	0,755	0,099
8144184	FAM62B	family with sequence similarity 62 (C2 domain containing) member B	0,086	0,326	0,926	0,263
8145454	BNIP3L	BCL2/adenovirus E1B 19kDa interacting protein 3-like	0,019	0,358	1,13	0,353
8145977	PLEKHA2	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 2	0,26	0,513	0,862	0,257
8146550	SDCBP	syndecan binding protein (syntenin)	0,183	0,369	0,674	0,244
8149555	PSD3	pleckstrin and Sec7 domain containing 3	0,201	0,466	0,935	0,268
8150076	DUSP4	dual specificity phosphatase 4	0,242	0,486	0,59	0,297
8150714	PCMTD1	protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 1	0,172	0,43	0,682	0,358
8156404	C9orf89	chromosome 9 open reading frame 89	0,29	0,417	0,668	0,362
8157021	NIPSNAP3A	nipsnap homolog 3A (<i>C. elegans</i>)	0,126	0,545	0,637	0,243
8160011	KIAA2026	KIAA2026	0,278	0,506	0,611	0,17
8160981	KIAA1539	KIAA1539	0,307	0,543	0,964	0,283
8161648	KLF9	Kruppel-like factor 9	0,29	0,501	0,953	0,239
8164535	CRAT	carnitine acetyltransferase	0,218	0,363	0,725	0,292
8167815	MAGED2	melanoma antigen family D, 2	0,133	0,53	0,873	0,408
8168179	DLG3	discs, large homolog 3 (<i>Drosophila</i>)	0,398	0,476	0,947	0,341
8168205	FOXO4	forkhead box O4	0,196	0,482	0,644	0,305
8169541	DOCK11	dedicator of cytokinesis 11	0,238	0,52	0,883	0,18
8172858	IQSEC2	IQ motif and Sec7 domain 2	0,178	0,437	0,851	0,361
7957654	AMDHD1	amidohydrolase domain containing 1	0,096	0,671	0,501	0,134
7974851	HIF1A	hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	0,36	0,663	0,412	0,131
8056285	IFIH1	interferon induced with helicase C domain 1	0,014	0,721	0,561	0,223
8081386	NFKBIZ	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta	0,105	0,715	0,551	0,422
8085360	TIMP4	TIMP metallopeptidase inhibitor 4	0,153	0,619	0,468	0,115
7904812	PIAS3	protein inhibitor of activated STAT, 3	0,314	0,677	0,964	0,45
7918902	CD58	CD58 molecule	0,395	0,666	1,19	0,558
7929711	GOLGA7B	golgi autoantigen, golgin subfamily a, 7B	0,21	0,669	0,975	0,403
7961365	MANSC1	MANSC domain containing 1	0,201	0,624	1,161	0,568
7963054	TUBA1A	tubulin, alpha 1a	0,394	0,791	1,166	0,549
7980338	C14orf4	chromosome 14 open reading frame 4	0,435	0,636	1,113	0,491
7994659	MVP	major vault protein	0,255	0,882	1,435	0,569

8009639	GPRC5C	G protein-coupled receptor, family C, group 5, member C	0,46	1,101	1,049	0,569
8017599	PECAM1	platelet/endothelial cell adhesion molecule	0,355	0,917	1,273	0,589
8042468	ANXA4	annexin A4	0,264	0,68	1,228	0,477
8043945	MAP4K4	mitogen-activated protein kinase kinase kinase kinase 4	0,169	0,606	1,033	0,488
8050894	KIF3C	kinesin family member 3C	0,397	0,608	0,835	0,502
	hCG_201					
8067546	8279	hypothetical protein LOC100127888	0,497	0,655	1,269	0,575
8072798	CYTH4	cytohesin 4	0,519	0,864	1,279	0,577
8094599	KLF3	Kruppel-like factor 3 (basic)	0,342	0,711	1,789	0,556
		proline-rich nuclear receptor coactivator 1	0,418	0,601	0,987	0,514
8121076	PNRC1					
8169249	MID2	midline 2	0,174	0,708	0,894	0,427
		colony stimulating factor 1 (macrophage)	0,275	0,808	1,587	0,916
7903786	CSF1					
7904361	FAM46C	family with sequence similarity 46, member C	0,443	0,701	1,02	0,66
7904761	ITGA10	integrin, alpha 10	0,607	1,196	2,425	1,49
		E74-like factor 3 (ets domain transcription factor, epithelial-specific)	0,504	1,078	2,417	0,848
7908940	ATP2B4	ATPase, Ca++ transporting, plasma membrane 4	0,649	0,842	1,492	0,804
		aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)	0,751	1,371	2	0,843
7930299	C10orf78	chromosome 10 open reading frame 78	0,177	0,68	1,263	0,617
7949412	LTBP3	latent transforming growth factor beta binding protein 3	0,132	0,7	1,32	0,778
7950473	ARRB1	arrestin, beta 1	0,271	0,749	0,988	0,594
7957023	LYZ	lysozyme (renal amyloidosis)	0,113	0,751	2,013	0,727
		solute carrier family 2 (facilitated glucose transporter), member 3	0,455	0,766	1,614	0,66
7960865	SLC2A3					
7970676	SHISA2	shisa homolog 2 (Xenopus laevis)	0,332	0,861	1,15	0,635
		chromosome 14 open reading frame 128	0,602	1,155	1,765	0,855
7978538	C14orf12					
	AHNAK2	AHNAK nucleoprotein 2	0,41	1,073	2,004	0,605
8009951	ITGB4	integrin, beta 4	0,343	1,123	2,526	0,909
8016739	TOB1	transducer of ERBB2, 1	0,582	1,083	1,699	0,797
8026564	KLF2	Kruppel-like factor 2 (lung)	0,692	0,664	1,108	0,628
8040365	TRIB2	tribbles homolog 2 (Drosophila)	0,464	0,863	1,194	0,658
		UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 5 (GalNAc-T5)	0,5	1,099	2,192	1,203
8045835	GALNT5					
8054479	MALL	mal, T-cell differentiation protein-like	0,378	0,733	1,386	0,617
8062041	ACSS2	acyl-CoA synthetase short-chain family member 2	0,091	0,72	1,145	0,601

8067409	LAMA5	laminin, alpha 5	0,287	0,618	1,113	0,665
8068353	SLC5A3	solute carrier family 5 (sodium/myo-inositol cotransporter), member 3	0,164	0,602	0,785	0,894
8068361	SLC5A3	solute carrier family 5 (sodium/myo-inositol cotransporter), member 3	0,25	0,858	1,064	1,135
8069269	COL6A1 *	collagen, type VI, alpha 1	0,428	0,686	1,354	0,59
8077441	BHLHE40	basic helix-loop-helix family, member e40	0,663	1,152	2,436	1,034
8094169	CPEB2	cytoplasmic polyadenylation element binding protein 2	0,422	0,767	1,128	0,612
8100026	ATP8A1	ATPase, aminophospholipid transporter (APLT), class I, type 8A, member 1	0,162	0,896	1,168	0,684
8105267	ITGA2 *	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	0,445	0,8	1,093	0,606
8122099	ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	0,316	0,906	1,341	0,892
8123006	SYNJ2	synaptojanin 2	0,452	0,866	1,541	0,725
8124848	IER3	immediate early response 3	0,402	0,643	0,895	0,64
8138381	AGR2	anterior gradient homolog 2 (Xenopus laevis)	0,268	1,89	2,519	1,487
8144078	SHH	sonic hedgehog homolog (Drosophila)	0,481	1,066	0,877	0,64
8149825	STC1	stanniocalcin 1	0,281	0,856	1,44	1,068
8150509	PLAT	plasminogen activator, tissue	0,133	0,915	1,511	0,958
8150889	SDR16C5	short chain dehydrogenase/reductase family 16C, member 5	0,502	0,921	1,681	0,696
8153002	NDRG1 *	N-myc downstream regulated 1	0,705	1,274	3,158	1,515
8157582	GSN	gelsolin (amyloidosis, Finnish type)	0,26	0,954	1,449	0,591
8164200	ANGPTL2	angiopoietin-like 2	0,574	0,829	1,61	0,748
8169263	VSIG1	V-set and immunoglobulin domain containing 1	0,314	1,31	1,88	1,066
8178435	IER3	immediate early response 3	0,406	0,675	0,953	0,663
8179704	IER3	immediate early response 3	0,402	0,643	0,895	0,64
7933204	C10orf10	chromosome 10 open reading frame 10	0,082	0,506	1,358	0,627
8086961	PFKFB4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	0,369	0,586	1,648	0,639
7914270	LAPTM5	lysosomal multispanning membrane protein 5	0,211	0,546	0,809	0,491
7918593	RHOC	ras homolog gene family, member C	0,208	0,332	0,807	0,415
7919669	MTMR11	myotubularin related protein 11	0,239	0,529	1,108	0,363
7922689	GLUL	glutamate-ammonia ligase (glutamine synthetase)	0,138	0,306	0,717	0,444
7924636	TMEM63A	transmembrane protein 63A	0,079	0,415	0,839	0,439
7929919	SFXN3	sideroflexin 3	0,111	0,296	0,778	0,4

7931031	TACC2	transforming, acidic coiled-coil containing protein 2	0,183	0,335	0,717	0,346
7934733	ANXA11	annexin A11	0,114	0,451	0,834	0,345
7941179	CAPN1	calpain 1, (mu/I) large subunit	0,231	0,437	0,829	0,346
7953291	CD9	CD9 molecule	0,198	0,525	1,01	0,448
7953532	ENO2	enolase 2 (gamma, neuronal)	0,25	0,4	1,343	0,572
7970301	TMCO3	transmembrane and coiled-coil domains 3	0,263	0,391	0,705	0,351
7977511	TEP1	telomerase-associated protein 1	0,196	0,345	0,847	0,474
7988467	FBN1	fibrillin 1	0,158	0,507	0,938	0,523
8009685	SLC9A3R1	solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 1	0,328	0,481	0,88	0,394
8014376	TBC1D3B	TBC1 domain family, member 3B	0,225	0,456	0,869	0,399
8014397	TBC1D3C	TBC1 domain family, member 3C	0,2	0,452	0,87	0,413
8014420	TBC1D3H	TBC1 domain family, member 3H	0,202	0,463	0,921	0,424
8014437	TBC1D3G	TBC1 domain family, member 3G	0,198	0,46	0,9	0,436
8014633	TBC1D3D	TBC1 domain family, member 3D	0,195	0,472	0,931	0,396
8019655	TBC1D3B	TBC1 domain family, member 3B	0,221	0,458	0,875	0,401
8019716	TBC1D3G	TBC1 domain family, member 3G	0,205	0,462	0,919	0,435
8030064	CYTH2	cytohesin 2	0,238	0,374	0,782	0,46
8036908	SERTAD3	SERTA domain containing 3	0,245	0,528	0,658	0,462
8039389	PTPRH	protein tyrosine phosphatase, receptor type, H	-	0,444	0,67	0,558
8049487	MLPH	melanophilin	0,229	0,347	0,794	0,532
8061447	PYGB	phosphorylase, glycogen; brain	0,276	0,496	1,092	0,523
8077786	IRAK2	interleukin-1 receptor-associated kinase 2	0,189	0,321	0,676	0,41
8087337	LAMB2	laminin, beta 2 (laminin S)	0,082	0,336	0,692	0,5
8104570	FAM105A	family with sequence similarity 105, member A	0,223	0,473	0,786	0,541
8105229	PELO	pelota homolog (Drosophila)	0,059	0,46	0,613	0,389
8107005	CAST	calpastatin	0,236	0,451	0,986	0,4
8109344	GM2A	GM2 ganglioside activator	0,259	0,523	0,865	0,459
8113981	P4HA2	prolyl 4-hydroxylase, alpha polypeptide II	0,324	0,429	1,198	0,54
8114536	TMEM173	transmembrane protein 173	0,165	0,412	0,916	0,421
8114797	SPRY4	sprouty homolog 4 (Drosophila)	0,359	0,479	0,81	0,494
8127549	SLC17A5	solute carrier family 17 (anion/sugar transporter), member 5	0,318	0,553	0,868	0,449
8131013	UNC84A	unc-84 homolog A (C. elegans)	0,146	0,309	0,632	0,303
8154951	GLUL	glutamate-ammonia ligase (glutamine synthetase)	0,177	0,458	0,739	0,534

8173955	SYTL4	synaptotagmin-like 4	0,355	0,556	0,615	0,427
7936100	CALHM2	calcium homeostasis modulator 2	0,556	0,421	0,842	0,294
8133360	CLDN4	claudin 4	0,674	0,447	0,702	0,337
7931810	KLF6	Kruppel-like factor 6	0,633	0,594	1,2	0,434
7968637	CCNA1	cyclin A1	1,268	1,17	1,227	0,055
8058477	KLF7	Kruppel-like factor 7 (ubiquitous)	0,796	0,766	1,631	0,58
8095870	CCNG2	cyclin G2	0,702	0,673	1,459	0,247
8125843	SPDEF	SAM pointed domain containing ets transcription factor	0,888	1,661	2,252	0,588
8141094	PDK4	pyruvate dehydrogenase kinase, isozyme 4	0,768	1,132	1,357	0,358
7971350	TSC22D1	TSC22 domain family, member 1	0,602	0,883	1,394	0,736
7982326	KLF13	Kruppel-like factor 13	0,709	0,648	1,331	0,632
8040473	RHOB *	ras homolog gene family, member B	1,551	1,815	2,996	1,14
8063923	SLCO4A1	solute carrier organic anion transporter family, member 4A1	0,645	0,734	1,301	0,759
8174361	TSC22D3	TSC22 domain family, member 3	0,883	1,126	2,328	0,826
8037408	KCNN4	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	0,563	0,634	1,168	0,495
8044499	SLC20A1	solute carrier family 20 (phosphate transporter), member 1	0,463	0,713	0,703	0,45
8129071	FRK	fyn-related kinase	0,217	0,624	0,236	0,548
8059783	NGEF	neuronal guanine nucleotide exchange factor	0,283	0,328	0,586	0,04
8068254	IL10RB	interleukin 10 receptor, beta	0,125	0,388	0,588	0,246
8098512	C4orf41	chromosome 4 open reading frame 41	0,003	0,439	0,589	0,066
8116780	DSP	desmoplakin	0,219	0,455	0,588	0,334
8114612	CD14	CD14 molecule	0,23	0,586	0,447	0,342

B. Down-regulated genes (compared to corresponding control)

Genes Probe Set ID	Genes Symbol	Genes Title	log2 vs control			
			Fluva 12h	Fluva 24h	Zol100 24h	Zol 48h
7902687	CYR61	cysteine-rich, angiogenic inducer, 61	-0,947	-1,051	-3,579	-0,577
7909503	SERTAD4	SERTA domain containing 4	-0,394	-0,636	-0,78	-0,036
7917942	FLJ35409	FLJ35409 protein	-0,83	-0,825	-1,802	-0,507
7917944			-0,619	-0,944	-1,626	-0,526
7927631	DKK1	dickkopf homolog 1 (Xenopus laevis)	-0,604	-0,991	-3,219	-0,604
7930341	SORCS3	sortilin-related VPS10 domain containing receptor 3	-0,354	-0,694	-1,221	-0,537
7934145	LRRC20	leucine rich repeat containing 20	-0,281	-0,62	-0,936	-0,282
7934979	ANKRD1	ankyrin repeat domain 1 (cardiac muscle)	-0,575	-0,627	-2,709	-0,396

7939365	FJX1	four jointed box 1 (Drosophila)	-0,449	-0,634	-1,246	-0,273
7956261	RBMS2	RNA binding motif, single stranded interacting protein 2	-0,495	-0,686	-1,028	-0,346
7977854	JUB	jub, ajuba homolog (Xenopus laevis)	-0,49	-0,653	-1,458	-0,315
7997427	CMIP	c-Maf-inducing protein	-0,54	-0,69	-1,554	-0,528
8047300	AOX1	aldehyde oxidase 1	-0,232	-0,83	-1,586	-0,531
8090852	AMOTL2	angiomotin like 2	-0,663	-0,827	-1,588	-0,366
8097628	HHIP	hedgehog interacting protein	-0,637	-0,921	-2,009	-0,59
8103508	MARCH1	membrane-associated ring finger (C3HC4) 1	-0,427	-0,75	-0,797	-0,454
8114805	FGF1	fibroblast growth factor 1 (acidic)	-0,427	-0,728	-0,687	-0,453
8122860	MYCT1	myc target 1	-0,699	-0,74	-0,593	-0,373
8144786	SLC7A2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2	-0,402	-0,596	-1,344	-0,339
8151423	JPH1	junctophilin 1	-0,283	-0,603	-1,378	-0,254
8161513	PGM5P2	phosphoglucomutase 5 pseudogene 2	-0,532	-0,625	-1,092	-0,189
8161520	PGM5P2	phosphoglucomutase 5 pseudogene 2	-0,53	-0,65	-1,145	-0,191
8163257	LPAR1	lysophosphatidic acid receptor 1	-0,594	-0,783	-1,391	-0,367
7897469	TMEM201	transmembrane protein 201	-0,317	-0,443	-0,651	-0,071
7898549	MRT04	mRNA turnover 4 homolog (S. cerevisiae)	-0,366	-0,553	-1,148	-0,452
7899462	RCC1	regulator of chromosome condensation 1	-0,149	-0,425	-0,695	-0,145
7900911	DPH2	DPH2 homolog (S. cerevisiae)	-0,18	-0,323	-0,646	-0,15
7906995	UCK2	uridine-cytidine kinase 2	-0,147	-0,312	-0,716	-0,206
7909441	G0S2	G0/G1switch 2	-0,396	-0,587	-1,507	-0,307
7910416	URB2	URB2 ribosome biogenesis 2 homolog (S. cerevisiae)	-0,306	-0,369	-1,143	-0,112
7917347	DDAH1	dimethylarginine dimethylaminohydrolase 1	-0,393	-0,44	-1,155	-0,27
7917885	CNN3	calponin 3, acidic	-0,197	-0,439	-0,729	-0,293
7922018	ILDR2	immunoglobulin-like domain containing receptor 2	-0,209	-0,444	-0,876	-0,255
7928589	PPIF	peptidylprolyl isomerase F	-0,262	-0,443	-1,05	-0,199
7929990	PPRC1	peroxisome proliferator-activated receptor gamma, coactivator-related 1	-0,44	-0,407	-1,061	-0,167
7930008	NOLC1	nucleolar and coiled-body phosphoprotein 1	-0,182	-0,296	-0,816	-0,227
7932227	NMT2	N-myristoyltransferase 2	-0,191	-0,324	-0,897	-0,285
7936809	FAM24B	family with sequence similarity 24, member B	-0,061	-0,479	-0,712	-0,342
7940349	CCDC86	coiled-coil domain containing 86	-0,289	-0,382	-0,771	-0,037

7946641	GALNTL4	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase-like 4	-0,29	-0,431	-0,591	-0,316
7952205	MCAM	melanoma cell adhesion molecule	-0,175	-0,389	-0,683	-0,165
7955361	LARP4	La ribonucleoprotein domain family, member 4	-0,273	-0,342	-0,786	-0,23
7956826	TBC1D30	TBC1 domain family, member 30	-0,378	-0,492	-0,876	-0,184
7958455	UNG	uracil-DNA glycosylase	-0,09	-0,364	-0,893	-0,165
7959604	DDX55	DEAD (Asp-Glu-Ala-Asp) box polypeptide 55	-0,216	-0,329	-0,738	-0,101
7960575	NOP2	NOP2 nucleolar protein homolog (yeast)	-0,187	-0,304	-0,715	-0,161
7962212	PKP2	plakophilin 2	-0,307	-0,361	-0,697	-0,066
7964271	PRIM1	primase, DNA, polypeptide 1 (49kDa)	-0,146	-0,423	-0,809	-0,363
7966052	CRY1	cryptochrome 1 (photolyase-like)	-0,264	-0,288	-0,668	-0,213
7967544	SCARB1	scavenger receptor class B, member 1	-0,204	-0,322	-0,594	-0,209
7968035	SPATA13	spermatogenesis associated 13	-0,347	-0,456	-0,602	-0,133
7976012	NRXN3	neurexin 3	-0,255	-0,443	-0,689	-0,282
7979505	SIX1	SIX homeobox 1	-0,317	-0,331	-0,618	-0,099
7981525	CDCA4	cell division cycle associated 4	-0,099	-0,347	-0,619	-0,289
7992789	TNFRSF12A	tumor necrosis factor receptor superfamily, member 12A	-0,354	-0,445	-0,985	-0,313
7996772	SLC7A6	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6	-0,272	-0,298	-0,787	-0,024
8007637	FZD2	frizzled homolog 2 (Drosophila)	-0,355	-0,497	-0,689	-0,122
8010946	GEMIN4	gem (nuclear organelle) associated protein 4	-0,303	-0,414	-0,859	-0,245
8011293	KIAA0664	KIAA0664	-0,234	-0,405	-0,686	-0,217
8011640	MYBBP1A	MYB binding protein (P160) 1a	-0,297	-0,378	-0,795	-0,187
8013015	CENPV	centromere protein V	-0,117	-0,305	-0,873	-0,276
8013068	PLD6	phospholipase D family, member 6	-0,356	-0,455	-0,805	-0,206
8014214	NLE1	notchless homolog 1 (Drosophila)	-0,274	-0,536	-0,808	-0,363
8024111	CNN2	calponin 2	-0,264	-0,348	-0,734	-0,184
8026490	UCA1	urothelial cancer associated 1	-0,317	-0,539	-0,743	-0,336
8027117	ARMC6	armadillo repeat containing 6	-0,152	-0,422	-0,797	-0,25
8029006	AXL	AXL receptor tyrosine kinase	-0,183	-0,497	-0,728	-0,315
8029437	PVR	poliovirus receptor	-0,314	-0,327	-0,68	-0,297
8030035	GRWD1	glutamate-rich WD repeat containing 1	-0,207	-0,349	-0,723	-0,133

8032530	SGTA	small glutamine-rich tetratricopeptide repeat (TPR)-containing, alpha	-0,163	-0,309	-0,593	-0,209
8037835	SLC1A5	solute carrier family 1 (neutral amino acid transporter), member 5	-0,285	-0,469	-1,025	-0,282
8038624	C19orf48	chromosome 19 open reading frame 48	-0,396	-0,582	-1,165	-0,375
8044844	TMEM177	transmembrane protein 177	-0,292	-0,436	-0,823	-0,344
8045860	PKP4	plakophilin 4	-0,228	-0,372	-0,645	-0,282
8049582	SCLY	selenocysteine lyase	-0,244	-0,412	-0,672	-0,157
8050766	ADCY3	adenylate cyclase 3	-0,183	-0,361	-0,655	-0,09
8051298	GALNT14	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 14 (GalNAc-T14)	-0,182	-0,482	-0,675	-0,291
8053278	FAM176A	family with sequence similarity 176, member A	-0,268	-0,509	-0,643	-0,185
8066214	TGM2	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	-0,318	-0,544	-0,773	-0,203
8068902	RRP1B	ribosomal RNA processing 1 homolog B (<i>S. cerevisiae</i>)	-0,201	-0,331	-0,937	-0,23
8068938	RRP1	ribosomal RNA processing 1 homolog (<i>S. cerevisiae</i>)	-0,133	-0,373	-0,647	-0,248
8076393	CENPM	centromere protein M	-0,14	-0,463	-0,597	-0,197
8076455	RRP7A	ribosomal RNA processing 7 homolog A (<i>S. cerevisiae</i>)	-0,145	-0,349	-0,803	-0,253
8079153	ABHD5	abhydrolase domain containing 5	-0,209	-0,327	-0,822	-0,169
8088642	LRIG1	leucine-rich repeats and immunoglobulin-like domains 1	-0,004	-0,347	-0,59	-0,097
8095986	ANXA3	annexin A3	-0,304	-0,506	-1,196	-0,392
8102232	LEF1	lymphoid enhancer-binding factor 1	-0,302	-0,475	-0,969	-0,235
8105067	PTGER4	prostaglandin E receptor 4 (subtype EP4)	-0,356	-0,444	-0,712	-0,217
8106210	RGNEF	Rho-guanine nucleotide exchange factor	-0,498	-0,49	-1,156	-0,38
8107100	RGMB	RGM domain family, member B	-0,371	-0,491	-0,755	-0,274
8109752	ODZ2	odz, odd Oz/ten-m homolog 2 (<i>Drosophila</i>)	-0,13	-0,556	-0,605	-0,313
8109773	WWC1	WW and C2 domain containing 1	-0,409	-0,572	-1,145	-0,325
8114572	HBEGF	heparin-binding EGF-like growth factor	-0,566	-0,579	-1,451	-0,44
8119492	BYSL	bystin-like	-0,238	-0,335	-0,861	-0,21
8120654	KCNQ5	potassium voltage-gated channel, KQT-like subfamily, member 5	-0,293	-0,506	-1,074	-0,328

8125483	TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	-0,143	-0,345	-0,71	-0,195
8127031	MCM3	minichromosome maintenance complex component 3	-0,088	-0,317	-0,671	-0,203
8135990	FLNC	filamin C, gamma (actin binding protein 280)	-0,297	-0,545	-1,07	-0,288
8153664	BOP1	block of proliferation 1	-0,241	-0,459	-0,767	-0,324
8154245	PDCD1LG2	programmed cell death 1 ligand 2	-0,504	-0,558	-0,903	-0,419
8155268	POLR1E	polymerase (RNA) I polypeptide E, 53kDa	-0,306	-0,443	-1,026	-0,301
8158714	EXOSC2	exosome component 2	-0,213	-0,413	-0,915	-0,197
8160682	NOL6	nucleolar protein family 6 (RNA-associated)	-0,424	-0,418	-1,07	-0,273
8162502	FBP1	fructose-1,6-bisphosphatase 1	-0,12	-0,393	-0,645	-0,375
8162601	ZNF367	zinc finger protein 367	-0,183	-0,373	-0,67	0,029
8162759	TBC1D2	TBC1 domain family, member 2	-0,461	-0,564	-1,12	-0,163
8169709	GLRX5	glutaredoxin 5	-0,067	-0,348	-0,598	-0,207
8178841	TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	-0,143	-0,368	-0,735	-0,222
8090343	KLF15	Kruppel-like factor 15	-0,251	-0,607	-0,383	-0,172
7902441	ST6GALN AC5	ST6 (alpha-N-acetyl-neuraminy1-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 5	-0,64	-0,838	-1,197	-0,573
7974870	SNAPC1	small nuclear RNA activating complex, polypeptide 1, 43kDa	-0,609	-0,708	-1,556	-0,517
8058849	MARCH4	membrane-associated ring finger (C3HC4) 4	-0,437	-0,809	-1,614	-0,57
8117045	RBM24	RNA binding motif protein 24	-0,5	-0,66	-1,499	-0,477
7917875	F3	coagulation factor III (thromboplastin, tissue factor)	-0,515	-0,659	-1,738	-0,652
8037537	ERCC2	excision repair cross-complementing rodent repair deficiency, complementation group 2	-0,456	-0,693	-1,418	-0,599
8058273	MPP4	membrane protein, palmitoylated 4 (MAGUK p55 subfamily member 4)	-0,457	-1,001	-1,912	-0,797
8083471	SGEF	Src homology 3 domain-containing guanine nucleotide exchange factor	-0,545	-0,626	-1,374	-0,606
8105302	FST	follistatin	-0,777	-0,94	-2,209	-0,794
8112342	ADAMTS6	ADAM metallopeptidase with thrombospondin type 1 motif, 6	-0,606	-0,743	-1,626	-0,859
8135734	C7orf58	chromosome 7 open reading frame 58	-0,41	-0,621	-1,399	-0,595

8140650	SEMA3E *	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3E	-0,487	-0,62	-1,109	-1,118
7916986	NEGR1	neuronal growth regulator 1	-0,183	-0,571	-0,953	-0,763
8063796	CDH4 *	cadherin 4, type 1, R-cadherin (retinal)	-0,129	-0,535	-0,812	-0,613
8078330	RBMS3	RNA binding motif, single stranded interacting protein	-0,5	-0,464	-0,969	-0,733
8092707	LEPREL1	leprecan-like 1	-0,365	-0,533	-1,372	-0,604
8094789	LIMCH1	LIM and calponin homology domains 1	-0,473	-0,564	-1,396	-0,67
7900792	PTPRF	protein tyrosine phosphatase, receptor type, F	-0,186	-0,431	-0,717	-0,397
7906564	PEA15	phosphoprotein enriched in astrocytes 15	-0,239	-0,349	-0,769	-0,326
7906863	UAP1	UDP-N-acetylglucosamine pyrophosphorylase 1	-0,414	-0,503	-1,085	-0,451
7913290	SH2D5	SH2 domain containing 5	-0,271	-0,492	-0,675	-0,32
7915485	EBNA1BP2	EBNA1 binding protein 2	-0,212	-0,341	-0,843	-0,372
7925823	GTPBP4	GTP binding protein 4	-0,204	-0,25	-0,627	-0,265
7936641	SFXN4	sideroflexin 4	-0,249	-0,334	-0,882	-0,336
7963187	LIMA1	LIM domain and actin binding 1	-0,342	-0,336	-0,818	-0,418
7965112	PAWR	PRKC, apoptosis, WT1, regulator	-0,362	-0,502	-1,215	-0,554
7970924	STARD13	StAR-related lipid transfer (START) domain containing 13	-0,438	-0,409	-0,841	-0,433
7972021	TBC1D4	TBC1 domain family, member 4	-0,408	-0,431	-0,853	-0,452
7983393	SORD	sorbitol dehydrogenase	-0,155	-0,302	-0,618	-0,38
7985767	AEN	apoptosis enhancing nuclease	-0,091	-0,362	-0,684	-0,301
8001658	C16orf80	chromosome 16 open reading frame 80	-0,161	-0,276	-0,738	-0,331
8006736	DUSP14	dual specificity phosphatase 14	-0,253	-0,455	-0,988	-0,491
8041149	WDR43	WD repeat domain 43	-0,316	-0,335	-0,932	-0,348
8050240	ODC1	ornithine decarboxylase 1	-0,066	-0,356	-0,684	-0,418
8087576	IFRD2	interferon-related developmental regulator 2	-0,155	-0,373	-0,699	-0,292
8087790	RRP9	ribosomal RNA processing 9, small subunit (SSU) processome component, homolog (yeast)	-0,201	-0,435	-0,805	-0,316
8094556	PGM2	phosphoglucomutase 2	-0,213	-0,384	-0,719	-0,404
8127051	TRAM2	translocation associated membrane protein 2	-0,319	-0,376	-0,704	-0,395
8127563	COL12A1	collagen, type XII, alpha 1	-0,275	-0,518	-1,016	-0,465
8141950	RELN	reelin	-0,263	-0,512	-1,086	-0,496
8163063	CTNNAL1	catenin (cadherin-associated protein), alpha-like 1	-0,091	-0,4	-0,901	-0,435

8170971	DKC1	dyskeratosis congenita 1, dyskerin	-0,228	-0,384	-1,077	-0,37
8175369	MAP7D3	MAP7 domain containing 3	-0,296	-0,324	-0,849	-0,53
7943749	LAYN	layilin	-0,433	-0,521	-1,189	-0,258
8029688	CD3EAP	CD3e molecule, epsilon associated protein	-0,526	-0,551	-0,846	-0,222
8129562	CTGF	connective tissue growth factor	-0,791	-0,806	-2,794	-0,496
8154233	CD274	CD274 molecule	-0,634	-0,763	-1,91	-0,769
8171248	KAL1 *	Kallmann syndrome 1 sequence	-0,573	-0,695	-1,877	-0,748
8023497	ATP8B1	ATPase, class I, type 8B, member 1	-0,667	-0,496	-1,327	-0,809
8021376	NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like	-0,476	-0,529	-1,362	-0,606
8148317	MYC	v-myc myelocytomatisis viral oncogene homolog (avian)	-0,438	-0,697	-1,656	-0,589
8033746	ZNF699	zinc finger protein 699	-0,676	-0,431	-0,842	-0,535
7974316	FRMD6	FERM domain containing 6	-0,511	-0,508	-1,017	-0,456
7984298	DIS3L	DIS3 mitotic control homolog (S. cerevisiae)-like	-0,465	-0,51	-0,862	-0,578
7988260	FRMD5	FERM domain containing 5	-0,39	-0,285	-0,735	-0,361
8041447	CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)	-0,389	-0,478	-1,116	-0,452
8112615	ENC1	ectodermal-neural cortex (with BTB-like domain)	-0,501	-0,533	-1,391	-0,47
8138489	CDCA7L	cell division cycle associated 7-like	-0,222	-0,458	-0,589	0,002

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Supplemental Figure S1.

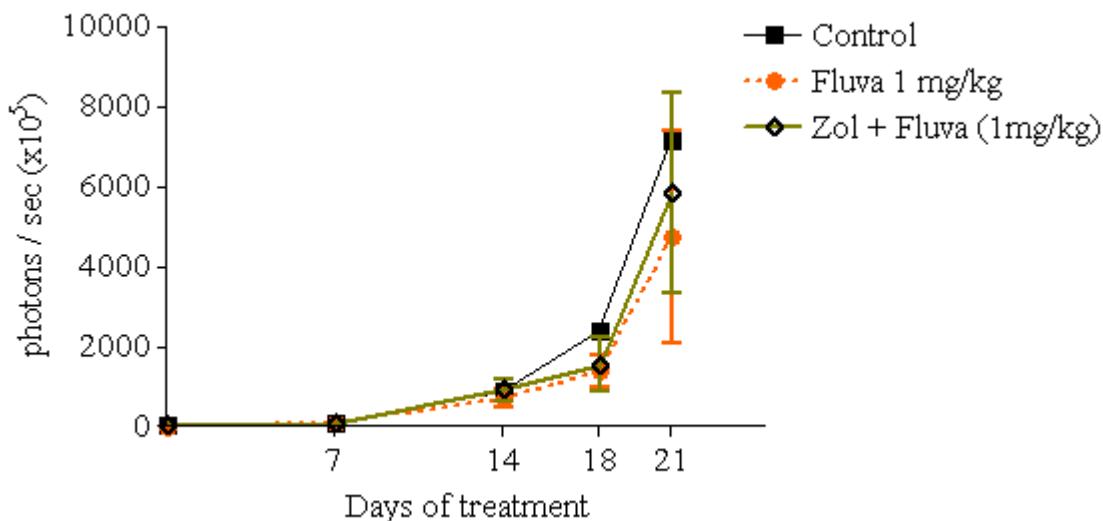


Figure S1. Effect of Fluva (low concentration) and Zol combination *in vivo*.

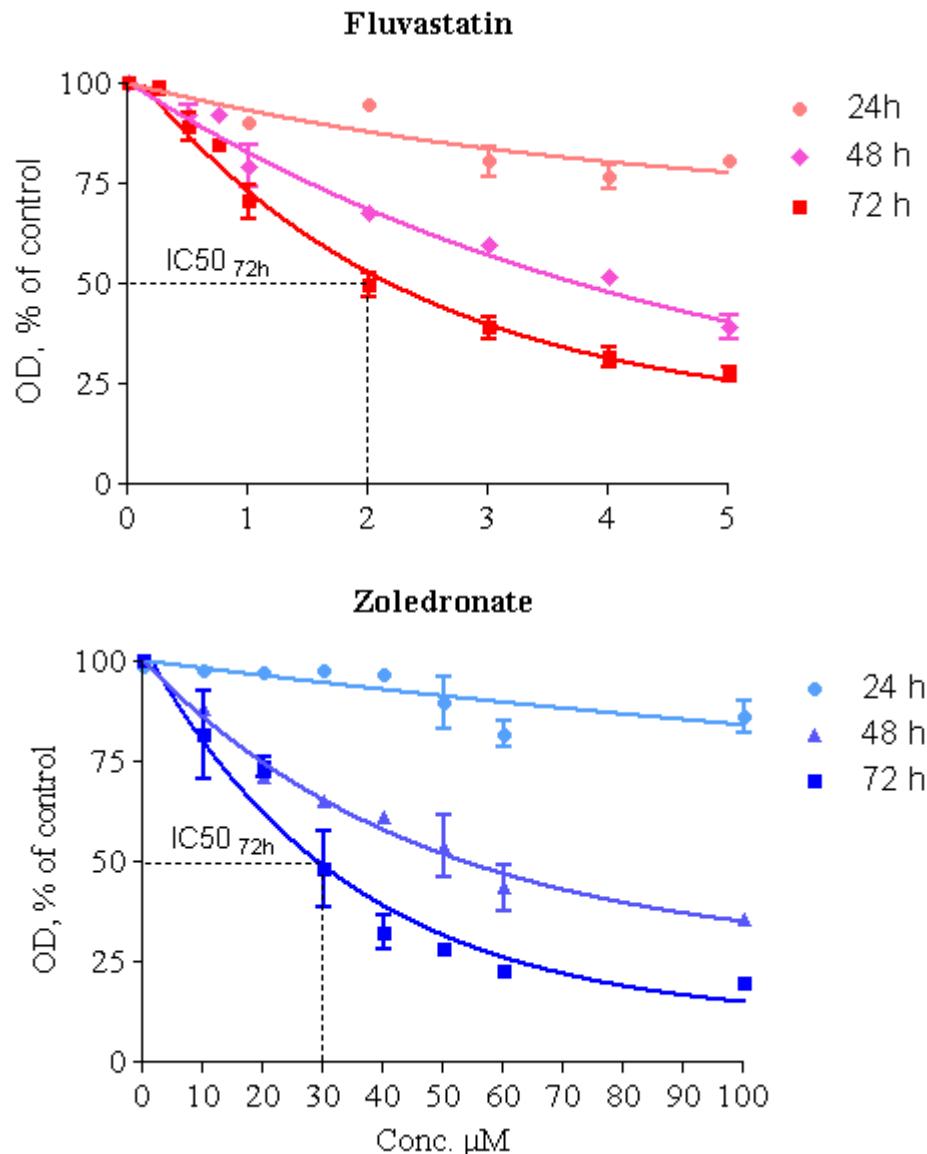
As described in Fig. 2 and 6, mice were treated upon detection of established metastasis (denoted as Day 0) with Zol (at 100 μ g/kg three times a week), Fluva (at 1 mg/kg daily), their combination (100 μ g/kg Zol thrice a week + 1 mg/kg Fluva daily), or PBS (daily for control group) during 3 weeks. A, Plot of bioluminescent signal; each point represents a mean (\pm SEM) signal of eight mice for Control, Fluva 1mg/kg, or combination of 100 μ g/kg Zol with 1mg/kg Fluva . B, Kaplan-Meyer survival curves for Control and treated mice (median survival of 21 days for Control, and 33, 21, and 34.5 days for Zol, Fluva, and Zol/Fluva combination respectively).

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Supplemental Figure S2



Supplemental Fig S2. *In vitro* viability inhibition assay (MTT test)

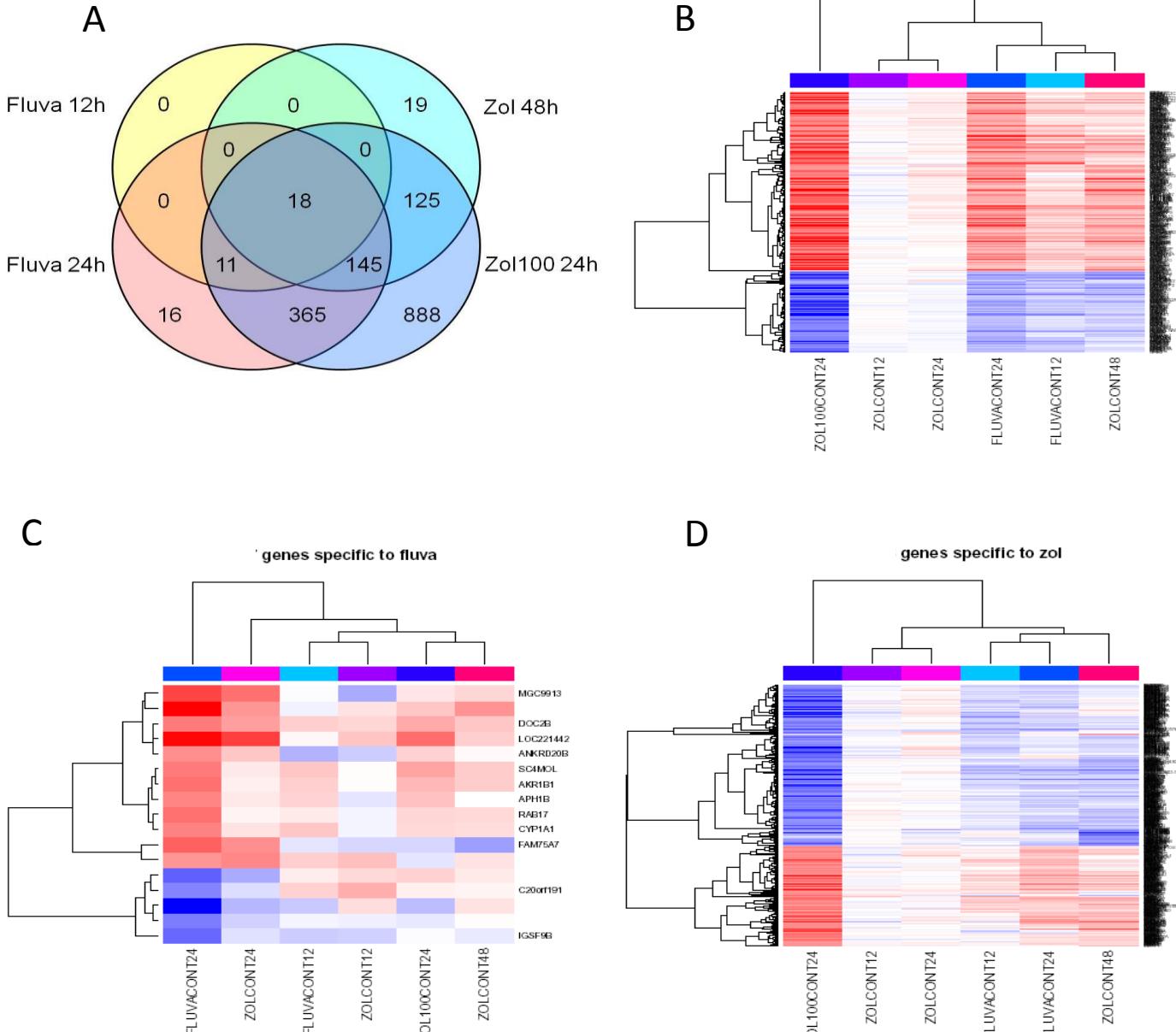
MDA-MB-231 cells (5000 cells per well in 96 well plate) were treated with Fluva or Zol at increasing concentrations for 24h, 48h, and 72 h. Control cells were treated with PBS. Then, the cells were washed and incubated with 0.1 mL of MTT (2 mg/mL) for 4 h. Optical density was measured at 570 nm using a Labsystems Multiskan MS microplate reader. Data represents the mean value ($\pm\text{SEM}$) of three independent experiments.

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Supplemental Figure S3.



Supplemental Figure S3. Transcriptomic analysis of Fluva or Zol effects on breast cancer cells.

Fluva, Zol, or control treatments were performed in four replicates (corresponding to independent treatments) on MDA-MB-231 cells at several early time points before the effect on cell viability was detected. Fluva IC₅₀ concentration determined by MTT test at 72h (2 µM) was applied for 12h treatment (Fluva12h or FLUVACONT12) and 24h treatment (Fluva 24h or FLUVACONT24). Comparable Zol concentration (30 µM for IC₅₀ at 72h in MTT test) was applied for 12h treatment (ZOLCONT12), 24h treatment (ZOLCONT24), or 48h treatment (Zol48h or ZOLCONT48). Also, cells were treated with high Zol concentration (100 µM) for 24h (Zol100 24h or ZOL100CONT24). Paired comparisons were performed to corresponding controls at each time point; only probe sets with FDR<0.05 and fold change≥1.5 were considered as differentially regulated. A, Overlap diagram for differentially