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Mechanistic insight into WEB-2170-induced apoptosis in human acute myelogenous leukemia cells: The crucial role of PTEN

Cristina Cellai^{a,*}, Anna Laurenzana^{a,*}, Elisa Bianchi^b,
Sara Sdelci^a, Rossella Manfredini^b, Alessandro M. Vannucchi^c,
Roberto Caporale^c, Manjola Balliu^a, Francesco Mannelli^c, Sergio Ferrari^b, Alberto Bosi^b,
Debora Miniati^d, Pier L. Cocco^a, Steeve Veronneau^e, Jana Stankova^e, and Francesco Paoletti^a

^aDepartment of Experimental Pathology and Oncology, University of Florence, Florence, Italy;

^bDepartment of Biological Sciences, University of Modena e Reggio Emilia, Modena, Italy; ^cDepartment of Hematology, University of Florence, Florence, Italy; ^dDepartment of Preclinical and Clinical Pharmacology, University of Florence, Florence, Italy; ^eDepartment of Pediatrics, Université de Sherbrooke, Sherbrooke, Québec, Canada

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Objective. This study aimed to investigate the mechanisms of action of WEB-2170, an inverse agonist of platelet-activating factor receptor, capable of inducing apoptosis in human acute myelogenous leukemia (AML) cells.

Material and Methods. Gene expression profiling followed by cytofluorimetric, morphologic, and biologic analyses were used to monitor WEB-2170 effects in AML cell lines (ie, NB4, KG1, NB4-MR4, THP1, and U937) and blasts from patients with different AML (M0–M5) subtypes. PTEN silencing with small interfering RNA was also performed.

Results. We have demonstrated that drug-mediated cytostasis/apoptosis in NB4 cells is characterized by upregulation of cyclin G2, p21/WAF1, NIX, TNF- α , and PTEN expression, and downregulation of cyclin D2 and BCL2 expression. We observed an increase in PTEN protein accompanied by a decrease in phospho-extracellular signal-regulated kinase 2 (ERK2) and phospho-AKT, and by forkhead box O3a (FOXO3a) cytoplasmic-nuclear translocation; the mitochondrial cytochrome C release and PARP cleavage marked the late apoptotic steps. We have found that WEB-2170 triggered apoptosis in NB4, KG1, and NB4-MR4 cells where PTEN was expressed, but not in THP1 and U937 cells where PTEN was absent. Finally, we show that PTEN silencing in NB4 cells by PTEN-specific small interfering RNA resulted in a significant reduction of drug-induced apoptosis.

Conclusion. We demonstrated that WEB-2170 is a powerful antileukemic agent with interesting translational opportunities to treat AML and described mechanisms of drug-induced intrinsic and extrinsic apoptosis both in AML cell lines and blasts from AML patients by addressing PTEN as the master regulator of the whole process. © 2009 ISEH - Society for Hematology and Stem Cells. Published by Elsevier Inc.

Acute promyelocytic leukemia (APL) with t(15;17) chromosomal translocation is a subtype of acute myelogenous leukemia (AML) that can be successfully cured by all-trans-retinoic acid (ATRA) targeted therapy toward the

PML/RAR α fusion protein [1]. ATRA can also be used in combination with other agents to treat elderly AML patients carrying the nucleophosmin-1 mutation [2]. This approach, however, is not effective on ATRA-resistant APL forms and other AML (non-APL) subtypes [3], which are refractory to ATRA-induced differentiation [4]. Therefore, the current treatment for the bulk of the other AML subtypes still consists of high-dose chemotherapy with potential life-threatening toxicity and acquired drug resistance [5].

Inhibitors of histone deacetylases [6] and DNA demethylating agents [7,8] have produced advancements in epigenetic control of chromatin assembling and influenced greatly gene expression

*Drs. Cellai and Laurenzana contributed equally to this work.

Offprint requests to: Francesco Paoletti, Ph.D., Department of Experimental Pathology and Oncology, Viale G. B. Morgagni 50, 50134 Firenze, Italy; E-mail: francesco.paoletti@unifi.it

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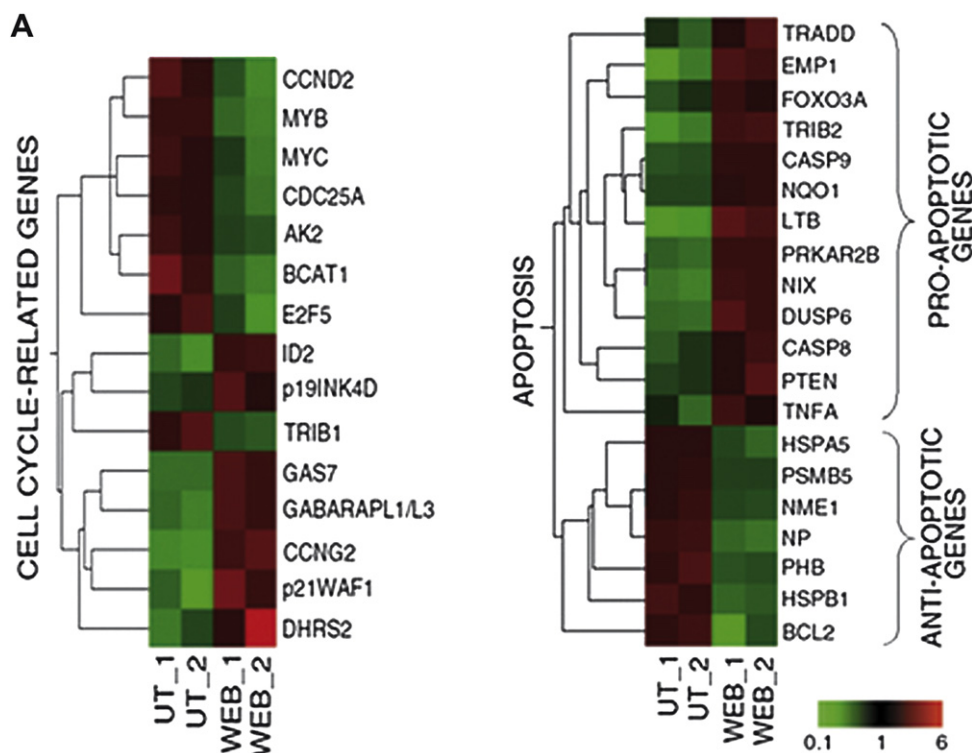


Figure 1. WEB-2170 induces modulation of genes involved in cell cycle progression and apoptosis in NB4 cells. (A) Eisen tree map computed using the GeneSpring gene tree and the Pearson correlation equation on the modulated probe sets belonging to the categories: (i) cell cycle-related genes; (ii) pro- and antiapoptotic genes. The signal-based coloring legend is shown at the bottom of the panel. Microarray analysis was performed in duplicate for both untreated and 0.5 mM WEB-2170–treated NB4 cells. UT_1 = untreated cells, replicate 1; UT_2 = untreated cells, replicate 2; WEB_1 = WEB-2170–treated cells, replicate 1; WEB_2 = WEB-2170–treated cells, replicate 2.

[9], thus providing additional tools for cancer therapy [10]. Indeed, epigenetic modulators are functional to set up an environment permissive for cell differentiation and/or apoptosis, but may not always be sufficient themselves to trigger these processes without the cooperation of other proactive signals. It is of great interest, therefore, to identify and characterize new agents capable of inducing cytostasis, differentiation, and apoptosis in AML cells, and supporting the action of epigenetic modulators and conventional chemotherapy so as to decrease effective therapeutic doses and untoward consequences to the host.

We previously showed that WEB-2170—a ligand of platelet-activating factor receptor (PAF-r) originally synthesized from an anxiolytic triazolobenzodiazepine [11,12]—could also promote murine erythroleukemia cell maturation [13] and trigger apoptosis in ATRA-sensitive and -resistant APL cell lines, and in blasts from patients with APL [14]. The present study aimed to understand mechanisms of WEB-2170-induced cytostasis and apoptosis in the APL cell line NB4, as well as to assess drug efficacy in other AML cell lines and, eventually, *ex vivo* in blasts from patients with different (M0 through M5) AML subtypes. The results reported herein show that WEB-2170 effects were mainly related to the enhanced expression of PTEN (phosphatase and tensin homologue, MMAC/TEP1) [15], the product of a tumor suppressor gene that is lost or

mutated in a number of human solid neoplasms [16,17], while still frequently conserved in myeloid leukemia [18,19]. PTEN is known to counter the activity of the phosphatidylinositol 3-kinase (PI3K)/serine or threonine-specific protein kinase, PI3K/AKT, and extracellular signal-regulated kinase 2 (ERK2) signaling pathways that are implicated in the control of cell-cycle progression and apoptosis, and in leukemogenesis [20]. PTEN-mediated inhibition of PI3K/AKT and ERK pathways allows the translocation of the transcription factor forkhead box O3a (FOXO3a) to the nucleus [21], thus promoting the selective expression of molecules involved in cell growth arrest and activation of apoptosis. Eventually, two facts supported the key role of PTEN in governing WEB-2170–mediated effects: first, apoptosis occurred only in PTEN-positive AML cells and second, PTEN silencing in NB4 cells resulted in a significant reduction of drug efficacy.

Materials and methods

Cell lines, leukemic blasts, culture conditions, and assay for inverse agonist activity of WEB-2170

Different AML cell lines, namely KG1 (M1), NB4 (M3), NB4-MR4 (M3), THP1 (M5), and U937 (M5) have been employed.

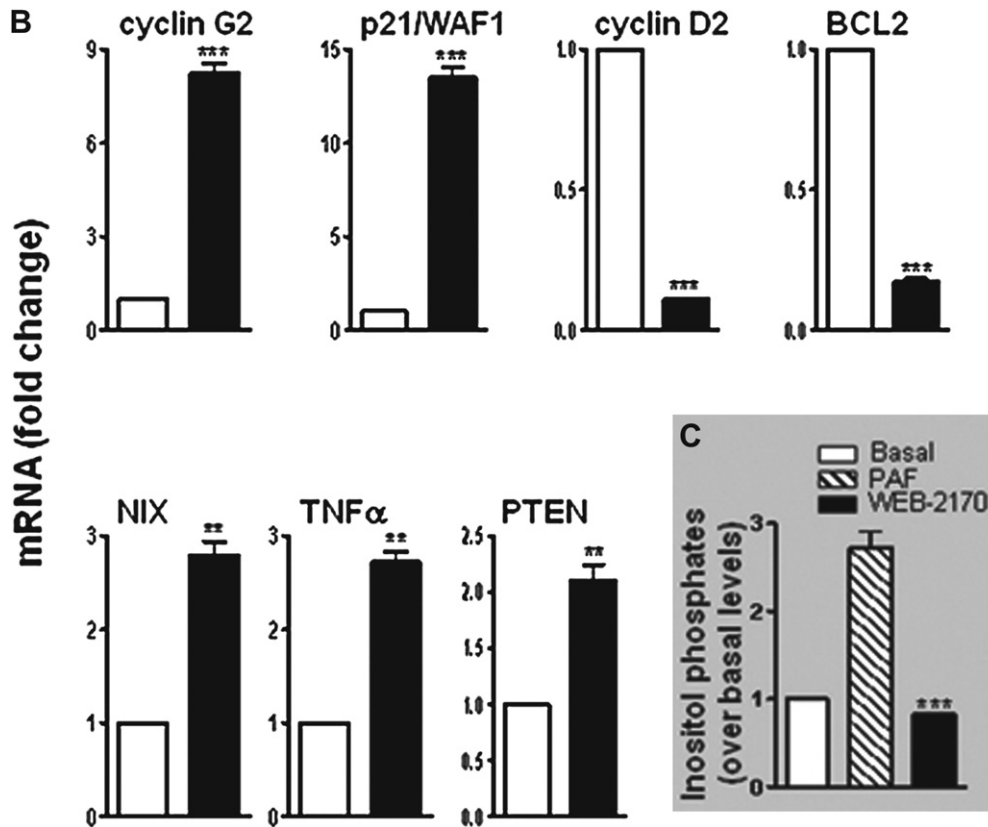


Figure 1. (Continued). (B) Cyclin G2, p21/WAF1, cyclin G2 as well as BCL2, NIX, TNF- α , and PTEN messenger RNA levels from NB4 cells either untreated (open bars) or treated (closed bars) for 24 hours were assayed by quantitative reverse transcriptase polymerase chain reaction. Results were the mean \pm standard deviation of three independent experiments; asterisks indicated significant differences between treated and untreated cells; *** p < 0.001; ** p < 0.01). Inverse agonist activity of WEB-2170. (C; gray box) HEK293 cells, stably transfected with the platelet-activating factor receptor (PAF-r) were incubated for 45 minutes without (open bar) and with either 10 nM PAF (dashed bar) or 10 μ M WEB-2170 (closed bar); then inositol phosphate (IP) accumulation was measured as previously reported [data from 22]. Data were expressed as fold increase or decrease of IP over basal conditions and represented as the means \pm standard error of three independent experiments performed in triplicate.

Culture conditions, cell counting, and viability were as reported previously [14]. Leukemic blasts from bone marrow aspirate and/or peripheral blood of 19 newly diagnosed AML patients with M0 through M5 subtypes were obtained after informed consent and according to the Ethics Hospital Committee guidelines (Helsinki declaration). Blasts and normal peripheral blood mononuclear cells were isolated by centrifugation on lymphocyte separation medium (Eurobio, Les Ulis Cedex, France) and then cultured as described for leukemia cell lines. Human embryonic kidney cells HEK293, stably transfected with PAF-r were also used as the model to assess WEB-2170 inverse agonist activity as described previously [22].

Reagents

WEB-2170 [11] (Boehringer Ingelheim Pharma KG, Biberach, Germany) was dissolved in dimethyl sulfoxide (Sigma-Aldrich, St Louis, MO, USA) and stock solutions (512 mM) were stored at room temperature in the dark. The dimethyl sulfoxide vehicle did not interfere with WEB-2170 activities. All other chemicals employed were reagent grade.

RNA extraction, microarray analysis, and quantitative reverse transcriptase polymerase chain reaction (QRT-PCR) experiments

For details on methodologies and the primers used see Supplementary materials.

Cell lysate preparation, cell fractionation, sodium dodecyl sulfate polyacrylamide gel electrophoresis, and Western blotting

Harvested cells were resuspended in a lysis buffer containing a cocktail of proteinase inhibitors (Calbiochem, Merck KGaA, Darmstadt, Germany), then sonicated and submitted to sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) separation and Western blot as reported elsewhere [14]. Proteins from distinct subcellular compartments have been isolated by using the ProteoExtract Subcellular Proteome Extraction Kit (Calbiochem) as suggested by the manufacturer. Membranes were probed with primary antibodies against phospho-ERK1/2, ERK1/2, p53, PTEN, p21/WAF1, and α -tubulin (Santa Cruz Biotechnology, Santa Cruz, CA, USA); phospho-AKT, AKT, and PARP (Cell

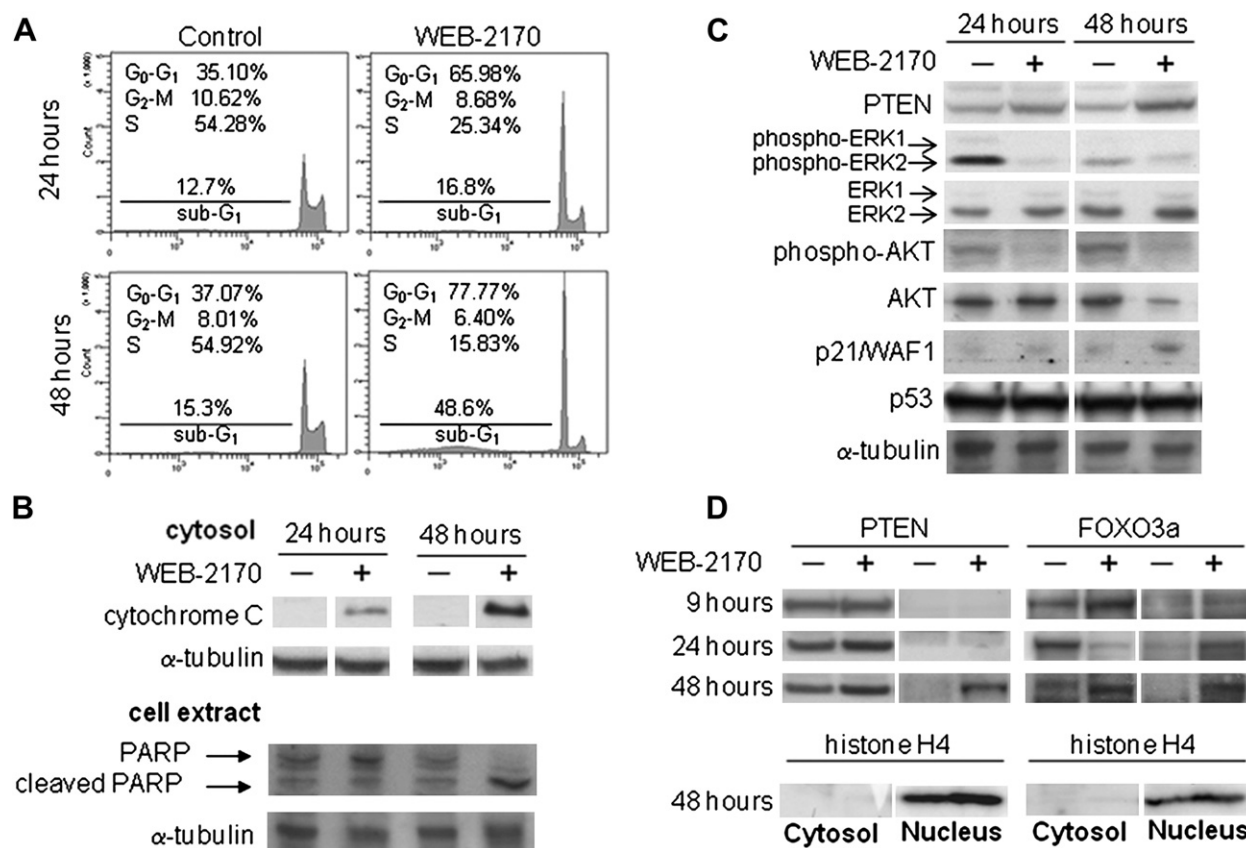


Figure 2. NB4 cells are induced to growth arrest and apoptosis by WEB-2170. Cells have been incubated for 24 and 48 hours with or without 0.5 mM WEB-2170 to assess: (A) the % of propidium iodide (PI)-stained NB4 cells in different phases of the cell cycle as determined by flow cytometry; (PI labeling, X-axis; total events, Y-axis). Cells with a DNA content < 2 N (sub-G₁ fraction) were representative of an apoptotic population; (B) WEB-2170-induced time-dependent release of mitochondrial cytochrome C into the cytosol, and PARP cleavage, by Western blotting; α-tubulin was used to show equal sample loading. WEB-2170 caused an increase in PTEN protein, decrease in phospho-ERK2 and phospho-AKT, and induced nuclear translocation of FOXO3a, in NB4 cells treated as above. (C) Total cell extracts were analyzed by immunoblotting for PTEN, phospho-ERK1/2 and ERK1/2, phospho-AKT, AKT, p21/WAF1 and p53 protein; α-tubulin was used as the reference protein; (D) PTEN and FOXO3a protein partitioning in the cytosolic and nuclear fraction of NB4 cells at different times of incubation with/without the drug (see Materials and Methods). Histone H4 was also immunodetected at 48 hours to assess the purity of the isolated cellular compartments. Results were from a typical experiment out of three.

Signaling Technology, Danvers, MA, USA); and FOXO3a and histone H4 (Upstate Biotechnology, Lake Placid, NY, USA and Millipore, Billerica, MA, USA). Horseradish peroxidase-conjugated IgG preparations were used as secondary antibodies; the electrochemiluminescence (ECL) procedure was employed for development.

Cell cycle analysis and determination of apoptosis

Cell cycle distribution was determined by using the propidium iodide (PI)-hypotonic citrate method with a FACScan flow cytometer (Becton-Dickinson, San Jose, CA, USA) [23]. Apoptosis was assessed either cytofluorimetrically by using the Annexin-V-Fluor/PI detection kit (Roche Molecular Biochemicals, Mannheim, Germany), or morphologically by examining stained cytosmears as reported previously [14]; a microscope (Nikon Eclipse, mod. 50i) equipped with a digital camera (DS-5 M USB2) (Nikon Instruments, Florence, Italy) was employed.

PTEN silencing with small interfering RNA

Exponentially growing NB4 cells were harvested, and approximately 2×10^6 cells were electroporated with 100 μL human Nucleofector solution (Amaxa Biosystems, Gaithersburg, MD, USA) and 100 nM SMARTpool siRNA for PTEN (a mix of four small interfering RNA (siRNA) directed to different parts of human (GenBank accession no. NM_00314) PTEN mRNA (Dharmacon; cat. #M-003023-02), or 100 nM siCONTROL nontargeting siRNA no. 1 (Dharmacon; cat. #D-001206-13-05), by a Nucleofector instrument (Amaxa Biosystems) according to manufacturer's instructions. Transfection efficiency was 90%, as assessed in parallel with Cy3-labeled siGLO RISC-free siRNA. Immediately after electroporation, the cells were suspended in the complete medium and incubated for the indicated time with or without WEB-2170. Mock transfection was performed with the Nucleofector solution alone.

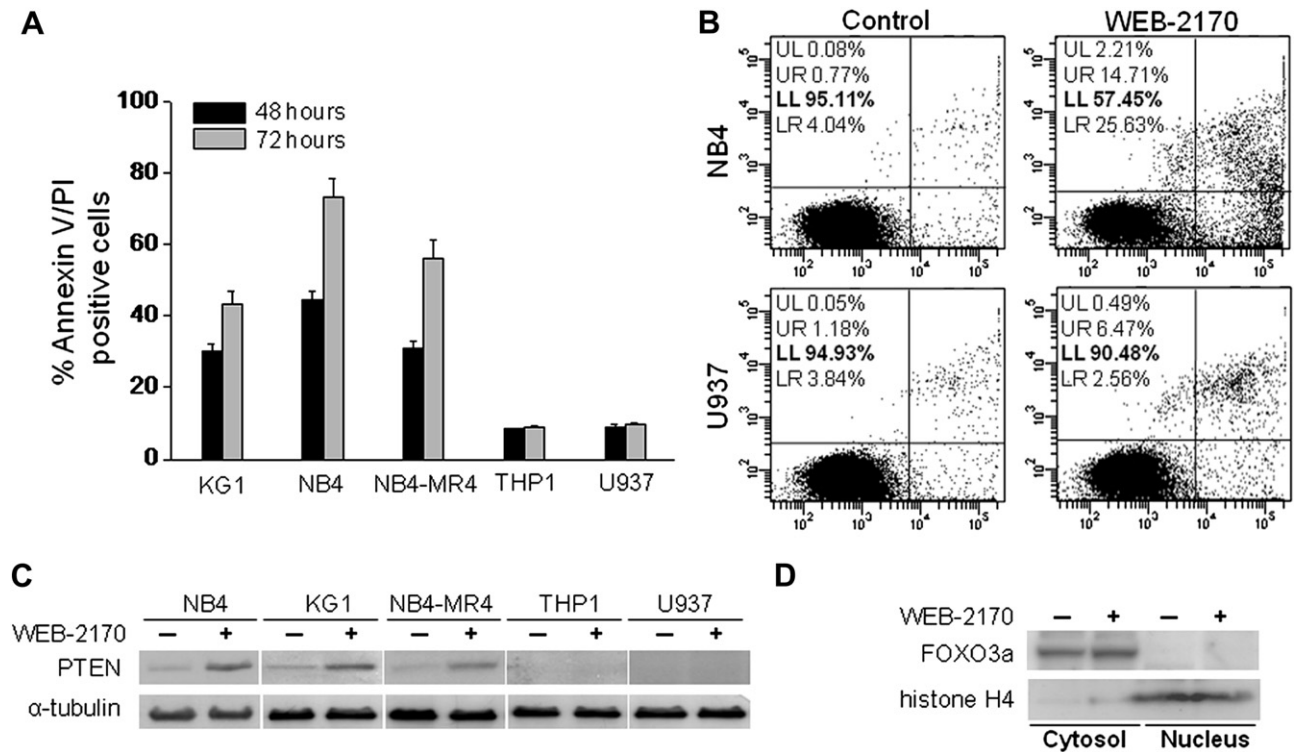


Figure 3. WEB-2170 triggers apoptosis in KG1, NB4, and NB4-MR4 cells but not in THP-1 and U937 cells. (A) Different acute myelogenous leukemia (AML) cell lines were treated with or without 0.5 mM WEB-2170 for 48 and 72 hours and analyzed by flow cytometry using Annexin V – Fluos/PI assay to detect the percentage of apoptotic cells over control rates. Results were the average \pm standard deviation of three independent experiments. (B) A typical Annexin-V–fluorescein isothiocyanate (FITC)/PI dot plot of either NB4 or U937 cells treated with/without WEB-2170 for 48 hours. X-axis, the fluorescent intensity of Annexin-V; Y-axis, the fluorescent intensity of PI. Values reported in each panel indicated the percent of necrotic cells (upper left, UL), late apoptotic cells (upper right, UR), live cells (lower left, LL), and early apoptotic cells (lower right, LR). Similar results were obtained from other two independent experiments. (C) Western blot of PTEN in different AML cell lines either untreated or treated for 48 hours as above; α -tubulin was used as the reference protein. (D) The cytosolic and nuclear fractions of U937 cells were isolated as reported here and probed for FOXO3a by Western blot. Purity of the two subcellular fractions was assessed by the presence of histone H4. Results were from a typical experiment out of three.

Statistical analysis

All data were statistically analyzed by Student's *t*-test. Significance was determined by analysis of variance followed by Newman-Keuls posttests using Prism version 4.0 (GraphPad software, San Diego, CA, USA).

Results

Gene expression profiling and QRT-PCR analysis of either untreated and WEB-2170-treated NB4 cells

In order to define the transcriptome changes induced by WEB-2170 treatment, we assessed the gene-expression profile of NB4 cells incubated with/without 0.5 mM WEB-2170 for 24 hours was assessed using the Affymetrix HG-U133A GeneChip array. These data have been deposited in the Gene Expression Omnibus MIAME compliant public database (Supplementary Table E1, online only, available at www.exphem.org). Using the filtering procedure described in Materials and Methods, we selected a list of 600 probesets as changing genes in all the four pair-wise comparisons between untreated and

WEB-2170–treated NB4 cells (Supplementary Table E2, online only, available at www.exphem.org). This gene list was uploaded onto the Database for Annotation, Visualization and Integrated Discovery tool 2007 (<http://david.abcc.ncifcrf.gov/>) to identify prevalent categories in the gene-ontology–controlled vocabulary family “biological process.” Supplementary Table E3 (Online only, available at www.exphem.org) shows that the prevalent categories that increased in WEB-2170–treated NB4 cells were negative regulation of cell proliferation, positive regulation of cell death, induction of apoptosis, and caspase activation. Conversely, the prevalent categories downregulated by WEB-2170 were negative regulation of apoptosis and positive regulation of cell proliferation. Next, we analyzed expression of genes involved in the regulation of cell growth and apoptosis. Gene-expression profiling data (Fig. 1A) underlined the downregulation of positive regulators of cell-cycle progression, such as CCND2 (cyclin D2), MYB, and MYC, while growth-arrest–related genes, such as the inhibitors of CDK/cyclin complexes CDKN1A (p21/Waf1) and CDKN2D (p19INK4D), GAS7, and CCNG2 (cyclin G2) were upregulated by WEB-2170.

Furthermore, WEB-2170 determined the upregulation of several proapoptotic genes, such as TNF- α , lymphotoxin B, TRADD, CASP9, CASP8, NIX, and PTEN, while some antiapoptotic genes including BCL2 were downregulated.

To validate microarray data, we carried out a quantitative reverse transcriptase polymerase chain reaction analysis on a set of differentially expressed selected genes (Fig. 1B) chosen on the basis of their biological function as master regulators of both proliferation and apoptosis. After a 24-hour treatment with WEB-2170, NB4 cells displayed a marked upregulation of cyclin G2 and p21/WAF1 and downregulation of cyclin D2 and antiapoptotic BCL2; concomitantly, expression of proapoptotic NIX, TNF- α , and PTEN was significantly enhanced. These results were in keeping with those of microarray profiling and, notably, this trend was already evident at 15 hours of treatment (data not shown).

Inverse agonist activity of PAF-r ligand WEB-2170

The changes in gene expression described here led us to verify which might be the real pharmacologic effect of WEB-2170. In fact, the drug did not behave as a pure antagonist of PAF-r, as originally believed but, instead, as an inverse agonist of the receptor as reported for its analogue WEB-2086 [22]. Inverse agonists are described as having the opposite effect of pure agonists (such as PAF in this case) and being capable of sequestering with high affinity the inactive form of PAF-r and shifting the balance of active toward inactive PAF-r pool so as to significantly reduce the PAF-r-mediated signal through G proteins. The assay was carried out by using HEK293 cells stably transfected with the PAF-r as the model according to procedures reported previously [22]; our results showed that WEB-2170 acted as an inverse agonist for PAF-r by decreasing basal levels of inositol phosphate (IP) production (Fig. 1C) due to a significant decrease of the PAF-r-mediated signal.

WEB-2170-treated NB4 cells

undergo growth arrest in G₀-G₁ and apoptosis

Cells were incubated with or without 0.5 mM WEB-2170 and assayed for cell cycle progression. Cytofluorimetric analyses showed that approximately 66% and 77% of cells incubated with WEB-2170 for 24 and 48 hours, respectively, were arrested in G₀-G₁ phase of the cell cycle; this was in line with the drug-mediated increased expression of p21/WAF1 and cyclin G2 observed at 24 hours (see Fig. 1B). Concomitantly, there was a decrease in G₂-M and S cell fraction, and at 48 hours the sub-G₁ fraction accounted for nearly half the treated population (Fig. 2A) to denote the presence of apoptotic cells. This was confirmed by the time-dependent mitochondrial release of cytochrome C into the cytoplasm (Fig. 2B, top), and by the cleavage of PARP after 48 hours of treatment (Fig. 2B, bottom); these

data were in keeping with our previous observations on the cleavage of caspase 9, 8, and 3 [14].

WEB-2170 induces PTEN

increase, dephosphorylation of phospho-ERK2 and phospho-AKT, and nuclear translocation of FOXO3a

Mechanisms of WEB-2170-mediated apoptosis in NB4 cells were further been investigated by analyzing some of the proteins that play a major role in controlling cell growth and survival. Cells treated for 24 and 48 hours showed a time-dependent increase in PTEN accompanied by a rapid decline of phospho-ERK2 and phospho-AKT levels (Fig. 2C). After 48 hours, WEB-2170 also caused a decrease in total AKT levels and an increase in p21/WAF1, while no changes in p53 levels were detected throughout the experiment. To evaluate whether the inhibition of the AKT and ERK pathway affected the intracellular distribution of FOXO3a, which is a substrate for both phospho-AKT [21] and phospho-ERK2 [24], the nuclear and cytoplasmic fractions of NB4 cells at 9, 24, and 48 hours of treatment were isolated and analyzed separately. In treated NB4 cells, there was a progressive translocation of FOXO3a from the cytosol to the nucleus (Fig. 2D), where it can exert its transcriptional activity, and this event associated with an increase in cytosolic PTEN and a decrease in both phospho-AKT and phospho-ERK levels. However, after 48 hours of treatment, PTEN translocated in part to the nucleus, where it may act as a proapoptotic factor [25].

PTEN plays a crucial role in

WEB-2170-mediated apoptosis in AML cell lines

In addition to NB4, other human AML cell lines such as KG1, NB4-MR4, THP-1, and U937 cells were tested at different times for their response to WEB-2170. Cytofluorimetric analysis with Annexin-V/PI confirmed that at 72 hours approximately 60% to 70% of treated NB4 cells were apoptotic. KG1 and NB4-MR4 cells were also sensitive to WEB-2170, yielding about 40% and 55% apoptotic cells, respectively, while THP1 and U937 cells seemed to be virtually unaffected by the drug (Fig. 3A). A comparative cytofluorimetric analysis of NB4 and U937 cells after a 48-hour incubation period with/without WEB-2170 clearly showed the marked drug-induced apoptosis in NB4 cells but not in U937 cells (Fig. 3B). The differential sensitivity of AML cell lines to drug-induced apoptosis was explored further by measuring PTEN after 48 hours of incubation with/without WEB-2170. PTEN was expressed and upregulated by the drug in KG1, NB4, and NB4-MR4 cells, while it was absent in THP1 and U937 cells (Fig. 3C) due to genetic alterations that hampered PTEN translation in U937 [18] and, probably, also in THP1 cells. The close relationship between PTEN expression, nuclear translocation of FOXO3a and apoptosis was confirmed by the fact that in PTEN-negative U937 cells that were resistant to

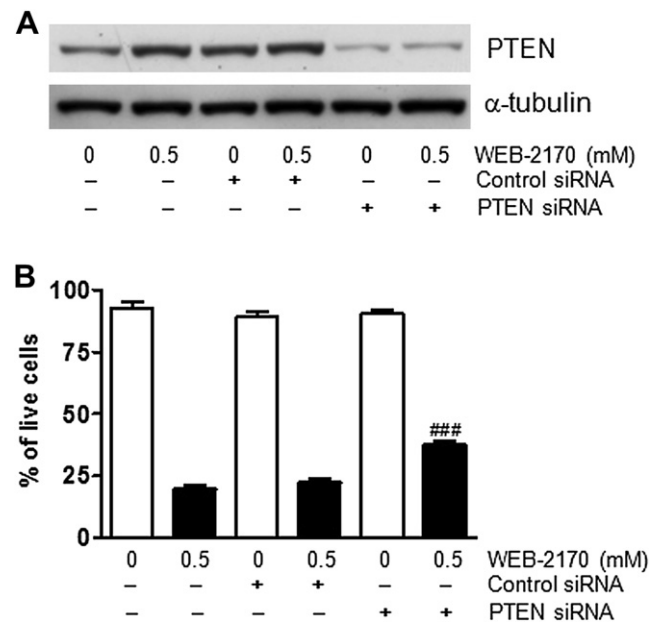


Figure 4. PTEN silencing impairs WEB-2170-induced apoptosis in NB4 cells. (A) Aliquots of cells protein lysates (40 ug/20 uL) were subjected to SDS-PAGE and immunoblotting to detect PTEN or α -tubulin used as loading control. (B) The percentage of apoptotic cells after transfection and 48 hours of treatment with WEB-2170. Number signs indicated the significant difference (### $p < 0.001$) in drug-induced cells in PTEN-specific small interfering RNA (siRNA) transfected cells vs nontargeting siRNA or mock cells.

WEB-2170-induced apoptosis, FOXO3a was always kept within the cytoplasm (Fig. 3D).

PTEN silencing in NB4 cells

by specific siRNA decreases drug-induced apoptosis

To further investigate on the key role of PTEN in WEB-2170-mediated apoptosis, we employed PTEN-specific siRNA to inhibit PTEN expression in either untreated or drug-treated NB4 cells. PTEN silencing was effective in downregulating PTEN mRNA levels by approximately five-fold (Supplementary Fig. E1, online only, available at www.exphem.org), and decreasing PTEN protein levels (Fig. 4A); and, notably, decreased significantly WEB-2170-induced apoptosis as compared to control siRNA-treated cells (Fig. 4B). The mock-transfected cells showed no significant difference of apoptosis with respect to non-targeting siRNA-transfected cells.

WEB-2170 triggers apoptosis in blasts from patients with distinct AML subtypes

Blasts from patients with different AML subtypes (M0 through M5; Fig. 5A) were collected and incubated with or without 0.5 mM WEB-2170 for 48 hours. Blast sensitivity to drug-induced apoptosis, as quantified by the Annexin-V/PI assay (Fig. 5B), was considerably high in all the samples, regardless of the specific AML subtype, and fell within a range of approximately 35% to 60% of cell population. The presence of apoptotic cells was a common morphologic finding in cytosmeareds of all the leukemic specimens following treatment (Fig. 5C), but

not of normal peripheral blood mononuclear cells (PBMC), which were apparently unaffected by the drug. Notably, WEB-2170-treated blasts from patient no.14 with AML (M4 subtype) showed an increase in PTEN protein and the mitochondrial release of cytochrome C (Fig. 5D).

Discussion

This study demonstrated that WEB-2170 is a powerful anti-leukemic agent able to increase levels of PTEN protein, which plays a pivotal role in orchestrating the sequence of events that eventually commit AML cells to growth arrest and apoptosis. Microarray data provided strong molecular support to understand WEB-2170 effects in NB4 cells and traced the way for further investigation in other AML cell lines and blasts from AML patients. Upon addition of WEB-2170 in culture, NB4 cells underwent growth arrest in G₀-G₁ and then a massive apoptosis. These findings were consistent with molecular biology results showing that WEB-2170 caused the downmodulation of several genes linked to cell proliferation and anti-apoptotic pathways, while other genes promoting cell growth arrest, as well as the extrinsic and intrinsic apoptosis, were significantly upregulated. Apparently, the process was independent of p53 [26] and histone acetylation [13]. Moreover, we proved that WEB-2170 acts as an inverse agonist rather than an antagonist of PAF-r; this way, the drug induces the functional inactivation of PAF-r accompanied by a decrease

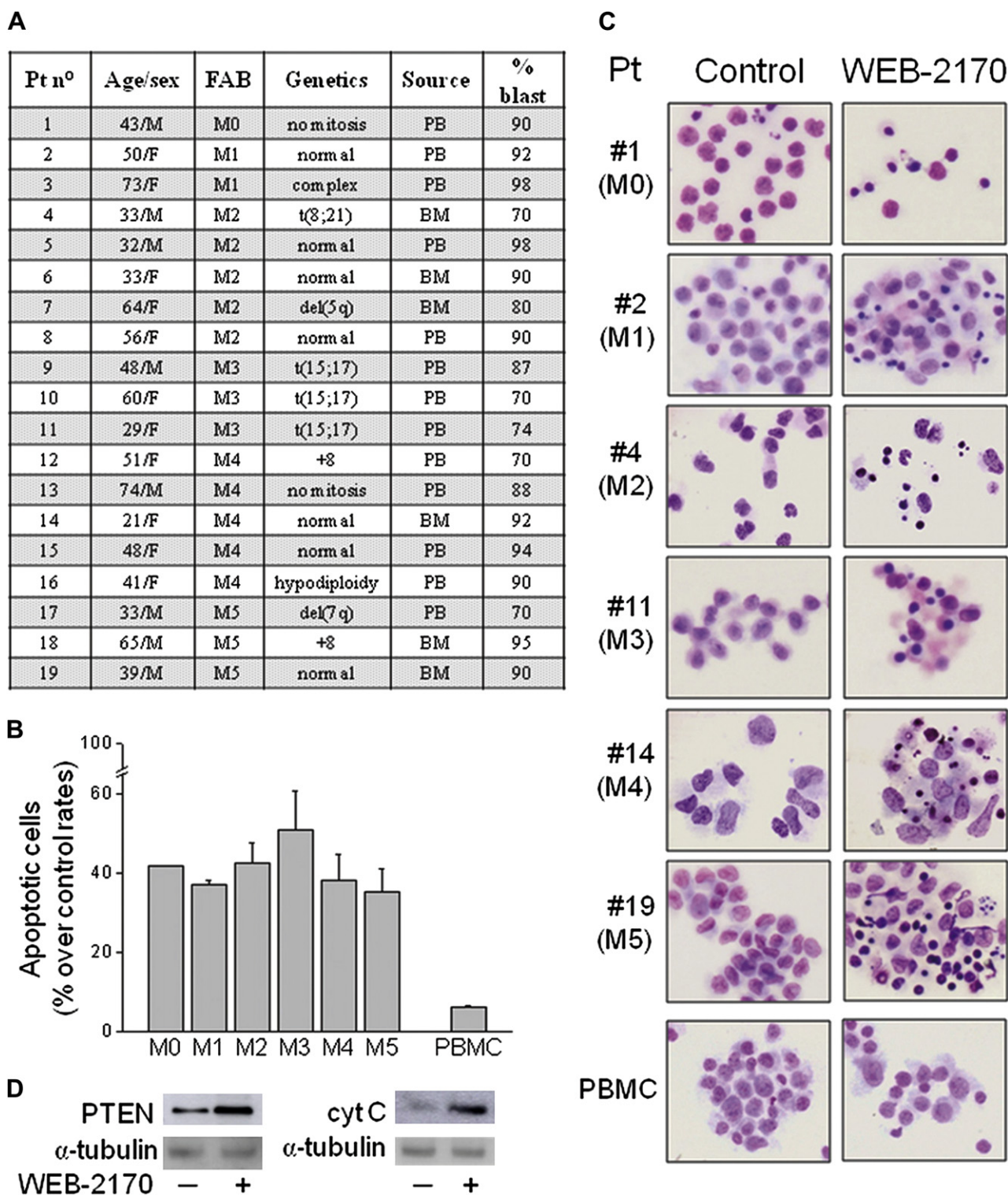


Figure 5. WEB-2170 induces apoptosis in blasts from 19 patients with different acute myelogenous leukemia (AML) subtypes but not in normal peripheral blood mononuclear cells (PBMC). (A) Clinico-biological characteristics of patients. (B) AML blasts from patients and normal PBMC were incubated in culture with or without 0.5 mM WEB-2170 for 48 hours, and then analyzed by flow cytometry to assess the percentage of drug-induced apoptotic cells in treated or untreated cultures. Error bars referred to variations \pm standard deviation of AML cell response to the drug; (C) May-Grünwald/Giemsa-stained cytosmeared cells (magnification: $\times 650$) from patient nos. 1 (M0), 2 (M1), 4 (M2), 11 (M3), 14 (M4), and 19 (M5), and from normal PBMC, after 48 hours of treatment with/without 0.5 mM WEB-2170; (D) a typical Western blot of PTEN and of cytochrome C released in the cytosolic fraction of AML blasts from patient no. 14 (M4 subtype) following a 48-hour treatment with/without the drug; α -tubulin was used as the reference protein.

in IP levels and this might be a critical metabolic event dictating the downstream inhibition of the PI3K/AKT signaling pathway.

However, besides these significant drug-induced modifications, we were interested in understanding the mechanisms whereby WEB-2170 prompted cytostasis/apoptosis in AML cells and, possibly, identifying the key molecules governing these processes. Toward this end, it was crucial to discover that drug-induced apoptosis occurred only in AML cells where PTEN was expressed, but not in AML cells where PTEN was not translated. Based on these results, a possible mechanism of WEB-2170-induced apoptosis in PTEN-expressing AML cells might be as follows. The binding of WEB-2170 to PAF-r prompts the decrease of IP levels due to its inverse agonist activity, and the increase in cytoplasmic PTEN protein that exerts its dual phosphatase activity. The latter leads to indirect dephosphorylation of phospho-ERK2 [27], that is also specifically inactivated by DUSP6 [28], a phosphatase found to be upregulated by WEB-2170; and hydrolysis of the 3'-phosphate of the residual phosphoinositide PIP₃ to PIP₂ that contributes to depressing the PI3K/AKT-mediated signal and, in turn, promotes PTEN allosteric activation [29]. Under these conditions, both PI3K/AKT and ERK signaling pathways are negatively regulated and cannot cooperate to phosphorylate FOXO3a [24] that, once dephosphorylated, translocates from cytoplasm to the nucleus, where activates the transcription of several genes including those involved in cell growth arrest and apoptosis. Conversely, PTEN-lacking AML cells are resistant to WEB-2170-induced apoptosis and remain viable all through the treatment; also, in the absence of PTEN, FOXO3a is phosphorylated by phospho-AKT and phospho-ERK and kept in the cytosol, without translocating to the nucleus [30]. Importantly, results of *in vitro* experiments have been reproduced *ex vivo* in AML blasts, which responded well to WEB-2170-induced apoptosis, while normal PBMC were apparently drug-resistant.

Overall, we demonstrated that WEB-2170 is a potent inhibitor of IP production and a positive regulator of PTEN in opposing the PI3K/AKT- and ERK2-mediated signaling pathways so as to induce growth arrest and apoptosis in AML cells. WEB-2170-mediated upregulation of PTEN function might offer interesting translational opportunities to treat malignant myeloid disorders where the gene is still frequently conserved.

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Conflict of Interest

No financial interest/relationships with financial interest relating to the topic of this article have been declared.

References

- Huang ME, Ye YC, Chen SR, et al. Use of all-trans retinoic acid in the treatment of acute promyelocytic leukemia. *Blood*. 1988;72:567–572.
- Schlenk RF, Dohner K, Kneba M, et al. Gene mutations and response to treatment with all-trans retinoic acid in elderly patients with acute myeloid leukemia. Results from the AMLSG Trial AML HD98B. *Haematologica*. 2009;94:54–60.
- Bennett JM, Catovsky D, Daniel MT, et al. Proposed revised criteria for the classification of acute myeloid leukemia. A report of the French-American-British Cooperative Group. *Ann Intern Med*. 1985;103:620–625.
- Breitman TR, Collins SJ, Keene BR. Terminal differentiation of human promyelocytic leukemic cells in primary culture in response to retinoic acid. *Blood*. 1981;57:1000–1004.
- Tallman MS, Gilliland DG, Rowe JM. Drug therapy for acute myeloid leukemia. *Blood*. 2005;106:1154–1163.
- Mai A, Massa S, Rotili D, et al. Histone deacetylation in epigenetics: an attractive target for anticancer therapy. *Med Res Rev*. 2005;25:261–309.
- Egger G, Liang G, Aparicio A, Jones PA. Epigenetics in human disease and prospects for epigenetic therapy. *Nature*. 2004;429:457–463.
- Moe-Behrens GH, Pandolfi PP. Targeting aberrant transcriptional repression in acute myeloid leukemia. *Rev Clin Exp Hematol*. 2003;7:139–159.
- Yoo CB, Jones PA. Epigenetic therapy of cancer: past, present and future. *Nat Rev Drug Discov*. 2006;5:37–50.
- Maslak P, Chanel S, Camacho LH, et al. Pilot study of combination transcriptional modulation therapy with sodium phenylbutyrate and 5-azacytidine in patients with acute myeloid leukemia or myelodysplastic syndrome. *Leukemia*. 2006;20:212–217.
- Casals-Stenzel J, Heuer HO. Use of WEB 2086 and WEB 2170 as platelet-activating factor antagonists. *Methods Enzymol*. 1990;187:455–465.
- Heuer HO, Casals-Stenzel J, Muacevic G, Weber KH. Pharmacologic activity of bepagant (WEB 2170), a new and selective hexazepinoic antagonist of platelet activating factor. *J Pharmacol Exp Ther*. 1990;255:962–968.
- Cellai C, Laurenzana A, Vannucchi AM, Della Malva N, Bianchi L, Paoletti F. Specific PAF antagonist WEB-2086 induces terminal differentiation of murine and human leukemia cells. *FASEB J*. 2002;16:733–735.
- Laurenzana A, Cellai C, Vannucchi AM, Pancrazzi A, Romanelli MN, Paoletti F. WEB-2086 and WEB-2170 trigger apoptosis in both ATRA-sensitive and -resistant promyelocytic leukemia cells and greatly enhance ATRA differentiation potential. *Leukemia*. 2005;19:390–395.
- Myers MP, Stolarov JP, Eng C, et al. P-TEN, the tumor suppressor from human chromosome 10q23, is a dual-specificity phosphatase. *Proc Natl Acad Sci USA*. 1997;94:9052–9057.
- Steck PA, Pershouse MA, Jasser SA, et al. Identification of a candidate tumour suppressor gene, MMAC1, at chromosome 10q23.3 that is mutated in multiple advanced cancers. *Nat Genet*. 1997;15:356–362.

17. Li J, Yen C, Liaw D, et al. PTEN, a putative protein tyrosine phosphatase gene mutated in human brain, breast, and prostate cancer. *Science*. 1997;275:1943–1947.
18. Aggerholm A, Gronbaek K, Guldborg P, Hokland P. Mutational analysis of the tumour suppressor gene MMAC1/PTEN in malignant myeloid disorders. *Eur J Haematol*. 2000;65:109–113.
19. Liu TC, Lin PM, Chang JG, Lee JP, Chen TP, Lin SF. Mutation analysis of PTEN/MMAC1 in acute myeloid leukemia. *Am J Hematol*. 2000;63:170–175.
20. Salmena L, Carracedo A, Pandolfi PP. Tenets of PTEN tumor suppression. *Cell*. 2008;133:403–414.
21. Brunet A, Bonni A, Zigmond MJ, et al. Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor. *Cell*. 1999;96:857–868.
22. Dupre DJ, Le Gouill C, Rola-Pleszczynski M, Stankova J. Inverse agonist activity of selected ligands of platelet-activating factor receptor. *J Pharmacol Exp Ther*. 2001;299:358–365.
23. Paoletti F, Mocali A, Cellai C, Caporale R, Vannucchi AM. Megakaryocyte-like increase in ploidy of Friend's erythroleukemia cells induced to endoreplication by colcemid. *Exp Hematol*. 1996;24:1441–1448.
24. Yang W, Dolloff NG, El-Deiry WS. ERK and MDM2 prey on FOX-O3a. *Nat Cell Biol*. 2008;10:125–126.
25. Gil A, Andres-Pons A, Pulido R. Nuclear PTEN: a tale of many tails. *Cell Death Differ*. 2007;14:395–399.
26. Cellai C, Laurenzana A, Vannucchi AM, et al. Growth inhibition and differentiation of human breast cancer cells by the PAFR antagonist WEB-2086. *Br J Cancer*. 2006;94:1637–1642.
27. Weng LP, Smith WM, Brown JL, Eng C. PTEN inhibits insulin-stimulated MEK/MAPK activation and cell growth by blocking IRS-1 phosphorylation and IRS-1/Grb-2/Sos complex formation in a breast cancer model. *Human Mol Genet*. 2001;10:605–616.
28. Muda M, Boschert U, Dickinson R, et al. MKP-3, a novel cytosolic protein-tyrosine phosphatase that exemplifies a new class of mitogen-activated protein kinase phosphatase. *J Biol Chem*. 1996;271:4319–4326.
29. Campbell RB, Liu F, Ross AH. Allosteric activation of PTEN phosphatase by phosphatidylinositol 4,5-bisphosphate. *J Biol Chem*. 2003;278:33617–33620.
30. Huang H, Tindall DJ. Dynamic FoxO transcription factors. *J Cell Sci*. 2007;120:2479–2487.

Supplemental material

RNA extraction and microarray analysis

Total RNA samples from two independent experiments for each condition (i.e., NB4 cells untreated and treated with 0.5 mM WEB-2170 for 24 hours) were extracted using RNeasy Mini kit (Qiagen, Valencia, CA, USA). Briefly, biotin-labeled target synthesis was performed, starting from 5 µg total cellular RNA, according to the protocol supplied by the manufacturer (Affymetrix, Santa Clara, CA, USA, <http://www.affymetrix.com>). Labeled cRNA was purified using Affymetrix GeneChip Sample Cleanup Module and fragmented (15 µg) as described in the Affymetrix GeneChip protocol. Disposable RNA chips (Agilent RNA 6000 Nano LabChip kit; Agilent Technologies, Waldbrunn, Germany, <http://www.home.agilent.com>) were used to determine the concentration and purity/integrity of RNA with the Agilent 2100 Bioanalyzer. The biotin-labeled target synthesis reactions, as well as the Affymetrix HG-U133A GeneChip arrays hybridization, staining, and scanning, were performed using Affymetrix standard protocols [1]. The Gene Chip Operating Software absolute analysis algorithm was used to determine the amount of a transcript messenger RNA (Signal), while the Gene Chip Operating Software comparison analysis algorithm was used to compare gene expression levels between two samples. Present genes were selected as the sequences showing the Detection call 'P' and Signal >100 in both the replicates of at least one condition. Differentially expressed genes were selected as the sequences showing a Change call 'I' or 'D' and Signal Log Ratio >1 or <-1 in the pair-wise comparisons between untreated and WEB-2170-treated NB4 cells. The gene list passing this filter was selected as "changing genes." The DAVID (Database for Annotation, Visualization and Integrated Discovery) tool 2007 (<http://david.abcc.ncifcrf.gov/>) was used to examine selected lists of genes to identify over-representation of functional classes accordingly with gene ontology

(GO) classification. All the data have been deposited in the Gene Expression Omnibus MIAME compliant public database, at <http://www.ncbi.nlm.nih.gov/geo> (Supplementary Table E1).

Quantitative real-time polymerase chain reaction analysis

Complementary DNA was prepared from 1 µg total RNA, using Superscript II reverse transcriptase (Invitrogen). The relative quantity of D2, G2, NIX, BCL2, TNF- α and p21/WAF1 mRNA was measured using the Applied Biosystems 7500 Fast Real-Time PCR System, and determined by the comparative CT method using 18S rRNA as normalization gene. Amplification was performed with the default PCR setting: 40 cycles of 95 °C for 15 sec and of 60 °C for 60 sec using a SYBR Green based detection (SYBR Green Master mix; Applied Biosystems) and the following primers: for cyclin D2, forward 5'-CTGCCCCACCTAGATCATA-3' and reverse 5'-TCCCTTATGCTGTA-CTTCAAATAGG-3'; for cyclin G2, forward 5'-AAAAAACATCACCTGTAATCTC-ACC-3' and reverse 5'-AGAGATTATCTTGGATGTTCCAGC-5'; for NIX, forward 5'-CGCCCTGCACAACAAC-3' and reverse 5'-TCATTGCCATTGCTGCTG-3'; for BCL2, forward 5'-GGACAACATCGCCCTGTG-3' and reverse 5'-AGTCTTCAGAGA-CAGCCAGGA-3'; for p21/WAF1 forward 5'-CTGCCCAAGCTCTACCTTCC-3' and reverse 5'-CAGGTCCACATGGTCTTCTT-3'; for TNF α , forward 5'-CACGCTCTT-CTGCCTGCTG-3' and reverse 5'-GATGATCTGACTGCCTGGGC-3'; for PTEN, forward 5'-AAGACAAAGCCAACCGATAC-3' and reverse 5'-GAAGTTGAACTGCTAGCCTC-3'; for 18S rRNA, forward 5'-CGGCTACCACATCCAAGGAA-3' and reverse 5'-GCTGGAATTACC-GCGGCT-3'.

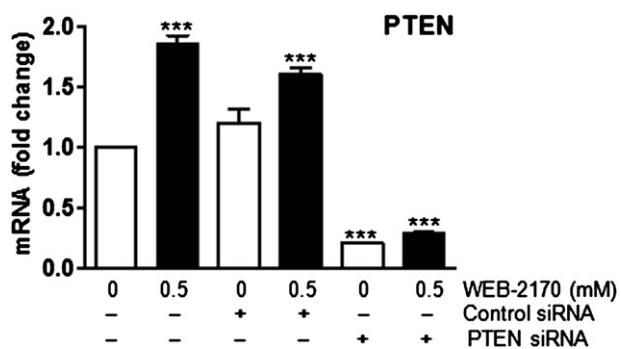
Reference

1. Salati S, Zini R, Bianchi E, et al. Role of CD34 antigen in myeloid differentiation of human hematopoietic progenitor cells. *Stem Cells*. 2008;26:950–959.

Supplementary Table E1. GEO* accession numbers

Title (GEO)	Accession no.
NB4_Untreated_1	GSM317352
NB4_Untreated_2	GSM317353
NB4_WEB2170_0.5 mM_24 hours_1	GSM317354
NB4_WEB2170_0.5 mM_24 hours_2	GSM317355

*Data from <http://www.ncbi.nlm.nih.gov/geo>



Supplementary Figure E1. Quantitative real-time polymerase chain reaction analysis of PTEN expression in NB4 transfected with nontargeting (control small interfering RNA [siRNA]) or PTEN-specific siRNA or with nucleofactor solution alone (mock) and cultured in the presence or absence of 0.5 mM WEB-2170 for 24 hours. Columns, average \pm standard deviation of three independent samples. Asterisk, significant difference (***) $p < 0.001$ from control.

Supplementary Table E2. The list of 975 probesets modulated in WEB-2170 treated vs untreated NB4 cells

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
207156_at	HIST1H2AG	histone cluster 1, H2ag	4.95	NM_021064
221986_s_at	KLHL24	kelch-like 24 (Drosophila)	4.03	AW006750
201325_s_at	EMP1	epithelial membrane protein 1	3.98	NM_001423
210230_at	LOC728965	Hypothetical protein LOC728965	3.93	BC003629
218087_s_at	SORBS1	sorbin and SH3 domain containing 1	3.7	NM_015385
203271_s_at	UNC119	unc-119 homolog (C. elegans)	3.6	NM_005148
213241_at	PLXNC1	plexin C1	3.53	AF035307
201324_at	EMP1	epithelial membrane protein 1	3.48	NM_001423
208791_at	CLU	clusterin	3.3	M25915
202770_s_at	CCNG2	cyclin G2	3.25	NM_004354
210612_s_at	SYNJ2	synaptojanin 2	3.25	AF318616
205352_at	SERPINI1	serpin peptidase inhibitor, clade I (neuroserpin), member 1	3.23	NM_005025
202838_at	FUCA1	fucosidase, alpha-L- 1, tissue	3.15	NM_000147
204174_at	ALOX5AP	arachidonate 5-lipoxygenase-activating protein	3.15	NM_001629
208965_s_at	IFI16	interferon, gamma-inducible protein 16	3.15	BG256677
209684_at	RIN2	Ras and Rab interactor 2	3.13	AL136924
204546_at	KIAA0513	KIAA0513	3.1	NM_014732
205107_s_at	EFNA4	ephrin-A4	3.03	NM_005227
207339_s_at	LTB	lymphotoxin beta (TNF superfamily, member 3)	3.03	NM_002341
212912_at	RPS6KA2	ribosomal protein S6 kinase, 90 kDa, polypeptide 2	3.03	AI992251
204215_at	C7orf23	chromosome 7 open reading frame 23	3	NM_024315
202769_at	CCNG2	cyclin G2	2.95	AW134535
204081_at	NRGN	neurogranin (protein kinase C substrate, RC3)	2.9	NM_006176
204867_at	GCHFR	GTP cyclohydrolase I feedback regulator	2.9	NM_005258
201481_s_at	PYGB	phosphorylase, glycogen; brain	2.88	NM_002862
200762_at	DPYSL2	dihydropyrimidinase-like 2	2.85	NM_001386
206332_s_at	IFI16	interferon, gamma-inducible protein 16	2.85	NM_005531
208966_x_at	IFI16	interferon, gamma-inducible protein 16	2.85	AF208043
202284_s_at	CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	2.8	NM_000389
208792_s_at	CLU	clusterin	2.78	M25915
211559_s_at	CCNG2	cyclin G2	2.73	L49506
204415_at	IFI6	interferon, alpha-inducible protein 6	2.65	NM_022873
209154_at	TAX1BP3	Tax1 (human T-cell leukemia virus type I) binding protein 3	2.65	AF234997
213479_at	NPTX2	neuronal pentraxin II	2.65	U26662
209118_s_at	TUBA3	tubulin, alpha 3	2.6	AF141347
214617_at	PRF1	perforin 1 (pore forming protein)	2.6	AI445650
202478_at	TRIB2	tribbles homolog 2 (Drosophila)	2.58	NM_021643
203827_at	WIP1	WD repeat domain, phosphoinositide interacting 1	2.58	NM_017983
205807_s_at	TUFT1	tuftelin 1	2.5	NM_020127
218303_x_at	KRCC1	lysine-rich coiled-coil 1	2.5	NM_016618
208949_s_at	LGALS3	lectin, galactoside-binding, soluble, 3 (galectin 3)	2.43	BC001120
210130_s_at	TM7SF2	transmembrane 7 superfamily member 2	2.43	AF096304
202479_s_at	TRIB2	tribbles homolog 2 (Drosophila)	2.4	BC002637
215071_s_at	HIST1H2AC	histone cluster 1, H2ac	2.4	AL353759
202996_at	POLD4	polymerase (DNA-directed), delta 4	2.38	NM_021173
220387_s_at	HHLA3	HERV-H LTR-associating 3	2.38	NM_007071
222256_s_at	PLA2G4B	phospholipase A2, group IVB (cytosolic)	2.38	AK000550
205016_at	TGFA	transforming growth factor, alpha	2.35	NM_003236
207761_s_at	METTTL7A	methyltransferase like 7A	2.35	NM_014033
209911_x_at	HIST1H2BD	histone cluster 1, H2bd	2.35	BC002842
204118_at	CD48	CD48 molecule /// CD48 molecule	2.33	NM_001778
206110_at	HIST1H3H	histone cluster 1, H3 h	2.33	NM_003536
212195_at	IL6ST	Interleukin 6 signal transducer (gp130, oncostatin M receptor)	2.33	AL049265
212698_s_at	9/10	septin 10	2.33	BF966021
217979_at	TSPAN13	Tetraspanin 13	2.33	NM_014399
204342_at	SLC25A24	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 24	2.3	NM_013386
222043_at	CLU	clusterin	2.3	AI982754
201739_at	SGK	serum/glucocorticoid regulated kinase	2.28	NM_005627
203845_at	PCAF	p300/CBP-associated factor	2.28	AV727449

(continued)

Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
208893_s_at	DUSP6	dual specificity phosphatase 6	2.28	BC005047
210829_s_at	SSBP2	single-stranded DNA binding protein 2	2.28	AF077048
202820_at	AHR	aryl hydrocarbon receptor	2.25	NM_001621
212886_at	CCDC69	coiled-coil domain containing 69	2.25	AL080169
203787_at	SSBP2	single-stranded DNA binding protein 2	2.23	NM_012446
209686_at	S100B	S100 calcium binding protein B	2.23	BC001766
213836_s_at	WIPI1	WD repeat domain, phosphoinositide interacting 1	2.23	AW052084
201005_at	CD9	CD9 molecule	2.18	NM_001769
202500_at	DNAJB2	DnaJ (Hsp40) homolog, subfamily B, member 2	2.18	NM_006736
209102_s_at	HBP1	HMG-box transcription factor 1	2.18	AF019214
212981_s_at	KIAA0738	KIAA0738 gene product	2.18	BF030508
209683_at	FAM49A	family with sequence similarity 49, member A	2.15	AA243659
207194_s_at	ICAM4	intercellular adhesion molecule 4 (Landsteiner-Wiener blood group)	2.13	NM_001544
208392_x_at	SP110	SP110 nuclear body protein	2.13	NM_004510
214079_at	DHRS2	dehydrogenase/reductase (SDR family) member 2	2.13	AK000345
41577_at	PPP1R16B	protein phosphatase 1, regulatory (inhibitor) subunit 16B	2.13	AB020630
201566_x_at	ID2 /// ID2B	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	2.1	D13891
204446_s_at	ALOX5	arachidonate 5-lipoxygenase	2.1	NM_000698
213238_at	ATP10D	ATPase, Class V, type 10D	2.1	AI478147
218319_at	PELI1	pellino homolog 1 (Drosophila)	2.1	NM_020651
221478_at	BNIP3L	BCL2/adenovirus E1B 19 kDa interacting protein 3-like	2.1	AL132665
201565_s_at	ID2	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	2.08	NM_002166
204675_at	SRD5A1	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)	2.08	NM_001047
209193_at	PIM1	pim-1 oncogene	2.08	M24779
209427_at	SMTN	smoothelin	2.08	AF064238
212364_at	MYO1B	myosin IB	2.08	BF432550
200782_at	ANXA5	annexin A5	2.05	NM_001154
203811_s_at	DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4	2.05	NM_007034
203680_at	PRKAR2B	protein kinase, cAMP-dependent, regulatory, type II, beta	2.03	NM_002736
214211_at	FTH1	ferritin, heavy polypeptide 1	2.03	AA083483
217783_s_at	YPEL5	yippee-like 5 (Drosophila)	2	NM_016061
204224_s_at	GCH1	GTP cyclohydrolase 1 (dopa-responsive dystonia)	1.98	NM_000161
218304_s_at	OSBPL11	oxysterol binding protein-like 11	1.95	NM_022776
201050_at	PLD3	phospholipase D family, member 3	1.93	NM_012268
206471_s_at	PLXNC1	plexin C1	1.93	NM_005761
208961_s_at	KLF6	Kruppel-like factor 6	1.93	AB017493
210959_s_at	SRD5A1	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)	1.93	AF113128
215464_s_at	TAX1BP3	Tax1 (human T-cell leukemia virus type I) binding protein 3	1.93	AK001327
220974_x_at	SFXN3	sideroflexin 3	1.93	NM_030971
202191_s_at	GAS7	growth arrest-specific 7	1.9	BE439987
204859_s_at	APAF1	apoptotic peptidase activating factor 1	1.9	NM_013229
214084_x_at	ABR	Active BCR-related gene	1.9	AW072388
214130_s_at	PDE4DIP /// LOC727942	phosphodiesterase 4D interacting protein (myomegalin)	1.9	AI821791
214720_x_at	9/10	septin 10	1.9	BF981643
217767_at	LOC653879	similar to Complement C3 precursor	1.9	NM_000064
221599_at	C11orf67	chromosome 11 open reading frame 67	1.9	BC002752
202437_s_at	CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	1.88	NM_000104
218854_at	SART2	squamous cell carcinoma antigen recognized by T cells 2	1.88	NM_013352
221618_s_at	TAF9B /// LOC728198	TAF9B RNA polymerase II, TATA box binding protein (TBP)-associated factor, 31 kDa	1.88	AF220509
203946_s_at	ARG2	arginase, type II	1.85	U75667
219489_s_at	NXN	nucleoredoxin	1.85	NM_017821
221664_s_at	F11R	F11 receptor	1.85	AF154005
39582_at	CYLD	cylindromatosis (turban tumor syndrome)	1.85	AL050166
204906_at	RPS6KA2	ribosomal protein S6 kinase, 90 kDa, polypeptide 2	1.83	BC002363
211458_s_at	GABARAPL1 /// GABARAPL3	GABA(A) receptor-associated protein like 1 /// GABA(A) receptors associated protein like 3	1.83	AF180519

(continued)

Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
201467_s_at	NQO1	NAD(P)H dehydrogenase, quinone 1	1.8	AI039874
221479_s_at	BNIP3L	BCL2/adenovirus E1B 19 kDa interacting protein 3-like	1.8	AF060922
201944_at	HEXB	hexosaminidase B (beta polypeptide)	1.78	NM_000521
202435_s_at	CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	1.78	AU154504
203097_s_at	RAPGEF2	Rap guanine nucleotide exchange factor (GEF) 2	1.78	NM_014247
213106_at	—	—	1.78	AI769688
218885_s_at	GALNT12	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12 (GalNAc-T12)	1.78	NM_024642
220603_s_at	MCTP2	multiple C2 domains, transmembrane 2	1.78	NM_018349
221600_s_at	C11orf67	chromosome 11 open reading frame 67	1.78	BC002752
201236_s_at	BTG2	BTG family, member 2	1.75	NM_006763
204451_at	FZD1	frizzled homolog 1 (Drosophila)	1.75	NM_003505
205005_s_at	NMT2	N-myristoyltransferase 2	1.75	AW293531
205441_at	OCEL1	occludin/ELL domain containing 1	1.75	NM_024578
211056_s_at	SRD5A1	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1) /// steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)	1.75	BC006373
213463_s_at	KIAA0974	KIAA0974	1.75	AW300504
201384_s_at	NBR1 /// LOC727732	neighbor of BRCA1 gene 1 /// similar to neighbor of BRCA1 gene 1	1.73	NM_005899
201468_s_at	NQO1	NAD(P)H dehydrogenase, quinone 1	1.73	NM_000903
201613_s_at	APIG2	adaptor-related protein complex 1, gamma 2 subunit	1.73	BC000519
202942_at	ETFB	electron-transfer-flavoprotein, beta polypeptide	1.73	NM_001985
203300_x_at	APIS2	adaptor-related protein complex 1, sigma 2 subunit	1.73	NM_003916
207181_s_at	CASP7	caspase 7, apoptosis-related cysteine peptidase	1.73	NM_001227
208436_s_at	IRF7	interferon regulatory factor 7	1.73	NM_004030
212828_at	SYNJ2	synaptojanin 2	1.73	AA191573
213906_at	MYBL1	v-myb myeloblastosis viral oncogene homolog (avian)-like 1	1.73	AW592266
216041_x_at	GRN	granulin	1.73	AK023348
218217_at	SCPEP1	serine carboxypeptidase 1	1.73	NM_021626
218656_s_at	LHFP	lipoma HMGIC fusion partner	1.73	NM_005780
218802_at	CCDC109B	coiled-coil domain containing 109B	1.73	NM_017918
221589_s_at	ALDH6A1	aldehyde dehydrogenase 6 family, member A1	1.73	AW612403
202917_s_at	S100A8	S100 calcium binding protein A8	1.7	NM_002964
203140_at	BCL6	B-cell CLL/lymphoma 6 (zinc finger protein 51)	1.7	NM_001706
203855_at	WDR47	WD repeat domain 47	1.7	NM_014969
208891_at	DUSP6	dual specificity phosphatase 6	1.7	BC003143
209424_s_at	AMACR	alpha-methylacyl-CoA racemase	1.7	AI796120
210075_at	3/2	membrane-associated ring finger (C3HC4) 2	1.7	AF151074
212074_at	UNC84A	unc-84 homolog A (C. elegans)	1.7	BE972774
212509_s_at	MXRA7	matrix-remodelling associated 7	1.7	BF968134
217226_s_at	SFXN3	sideroflexin 3	1.7	M95929
201348_at	GPX3	glutathione peroxidase 3 (plasma)	1.68	NM_002084
202436_s_at	CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	1.68	AU144855
206542_s_at	SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	1.68	AV725365
212979_s_at	KIAA0738	KIAA0738 gene product	1.68	AW293343
218924_s_at	CTBS	chitinase, di-N-acetyl-	1.68	NM_004388
219736_at	TRIM36	tripartite motif-containing 36	1.68	NM_018700
221985_at	KLHL24	kelch-like 24 (Drosophila)	1.68	AW006750
203227_s_at	TSPAN31	tetraspanin 31	1.65	NM_005981
203409_at	DDB2	damage-specific DNA binding protein 2, 48 kDa	1.65	NM_000107
208892_s_at	DUSP6	dual specificity phosphatase 6	1.65	BC003143
213186_at	DZIP3	zinc finger DAZ interacting protein 3	1.65	BG502305
219889_at	FRAT1	frequently rearranged in advanced T-cell lymphomas	1.65	NM_005479
200678_x_at	GRN	granulin	1.63	NM_002087
201887_at	IL13RA1	interleukin 13 receptor, alpha 1	1.63	NM_001560
203751_x_at	JUND	jun D proto-oncogene	1.63	AI762296
204882_at	ARHGAP25	Rho GTPase activating protein 25	1.63	NM_014882

(continued)

Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
206317_s_at	ABCB8	ATP-binding cassette, sub-family B (MDR/TAP), member 8	1.63	NM_007188
208926_at	NEU1	sialidase 1 (lysosomal sialidase)	1.63	U84246
213552_at	GLCE	UDP-glucuronic acid epimerase	1.63	W87398
218611_at	IER5	immediate early response 5	1.63	NM_016545
202638_s_at	ICAM1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor	1.6	NM_000201
202731_at	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	1.6	NM_014456
208944_at	TGFBR2	transforming growth factor, beta receptor II (70/80 kDa)	1.6	D50683
210705_s_at	TRIM5	tripartite motif-containing 5	1.6	AF220028
211284_s_at	GRN	granulin	1.6	BC000324
212990_at	SYNJ1	synaptojanin 1	1.6	AB020717
215813_s_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	1.6	S36219
218032_at	SNN	stannin	1.6	AF070673
218434_s_at	AACS	acetoacetyl-CoA synthetase	1.6	NM_023928
200904_at	HLA-E	major histocompatibility complex, class I, E	1.58	X56841
202275_at	G6PD	glucose-6-phosphate dehydrogenase	1.58	NM_000402
203411_s_at	LMNA	lamin A/C	1.58	NM_005572
204479_at	OSTF1	osteoclast stimulating factor 1	1.58	NM_012383
211067_s_at	GAS7	growth arrest-specific 7	1.58	BC006454
214259_s_at	AKR7A2	aldo-keto reductase family 7, member A2 (aflatoxin aldehyde reductase)	1.58	AI144075
217707_x_at	SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	1.58	AI535683
221588_x_at	ALDH6A1	aldehyde dehydrogenase 6 family, member A1	1.58	AI640855
56256_at	SIDT2	SID1 transmembrane family, member 2	1.58	AA150165
200765_x_at	CTNNA1	catenin (cadherin-associated protein), alpha 1, 102 kDa	1.55	NM_001903
200866_s_at	PSAP	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	1.55	M32221
201581_at	TXNDC13	thioredoxin domain containing 13	1.55	BF572868
204290_s_at	ALDH6A1	aldehyde dehydrogenase 6 family, member A1	1.55	NM_005589
204912_at	IL10RA	interleukin 10 receptor, alpha	1.55	NM_001558
207467_x_at	CAST	calpastatin	1.55	NM_001750
212588_at	PTPRC	protein tyrosine phosphatase, receptor type, C	1.55	Y00062
212665_at	TIPARP	TCDD-inducible poly(ADP-ribose) polymerase	1.55	AL556438
212762_s_at	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)	1.55	AI375916
215111_s_at	TSC22D1	TSC22 domain family, member 1	1.55	AK027071
202499_s_at	SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	1.53	NM_006931
204044_at	QPRT	quinolate phosphoribosyltransferase (nicotinate-nucleotide pyrophosphorylase (carboxylating))	1.53	NM_014298
205128_x_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	1.53	NM_000962
207704_s_at	GAS7	growth arrest-specific 7	1.53	NM_003644
208908_s_at	CAST	calpastatin	1.53	AF327443
213572_s_at	SERPINB1	serpin peptidase inhibitor, clade B (ovalbumin), member 1	1.53	AI554300
213896_x_at	KIAA0974	KIAA0974	1.53	BE856549
215235_at	SPTAN1	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	1.53	AL110273
218346_s_at	SESN1	sestrin 1	1.53	NM_014454
32502_at	GDPD5	glycerophosphodiester phosphodiesterase domain containing 5	1.53	AL041124
1729_at	TRADD	TNFRSF1A-associated via death domain	1.5	L41690
200899_s_at	MGEA5	meningioma expressed antigen 5 (hyaluronidase)	1.5	NM_012215
202017_at	EPHX1	epoxide hydrolase 1, microsomal (xenobiotic)	1.5	NM_000120
202022_at	ALDOC	aldolase C, fructose-bisphosphate	1.5	NM_005165
202748_at	GBP2	guanylate binding protein 2, interferon-inducible	1.5	NM_004120
202814_s_at	HEXIM1	hexamethylene bis-acetamide inducible 1	1.5	AW193511
204759_at	RCBTB2	regulator of chromosome condensation (RCC1) and BTB (POZ) domain containing protein 2	1.5	NM_001268
205006_s_at	NMT2	N-myristoyltransferase 2	1.5	NM_004808
207390_s_at	SMTN	smoothelin	1.5	NM_006932
218487_at	ALAD	aminolevulinate, delta-, dehydratase	1.5	BC000977
219843_at	IPP	intracisternal A particle-promoted polypeptide	1.5	NM_005897
200701_at	NPC2	Niemann-Pick disease, type C2	1.48	NM_006432

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
202452_at	ZYG11BL	zyg-11 homolog B (C. elegans)-like	1.48	AI991574
203651_at	ZFYVE16	zinc finger, FYVE domain containing 16	1.48	NM_014733
204059_s_at	ME1	malic enzyme 1, NADP(+)-dependent, cytosolic	1.48	NM_002395
209019_s_at	PINK1	PTEN induced putative kinase 1	1.48	AF316873
209531_at	GSTZ1	glutathione transferase zeta 1 (maleylacetoacetate isomerase)	1.48	BC001453
212365_at	MYO1B	myosin IB	1.48	BF215996
218559_s_at	MAFB	v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)	1.48	NM_005461
201760_s_at	WSB2	WD repeat and SOCS box-containing 2	1.45	NM_018639
202388_at	RGS2	regulator of G-protein signalling 2, 24 kDa	1.45	NM_002923
203607_at	INPP5F	inositol polyphosphate-5-phosphatase F	1.45	NM_014937
206544_x_at	SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	1.45	NM_003070
212268_at	SERPINB1	serpin peptidase inhibitor, clade B (ovalbumin), member 1	1.45	NM_030666
212346_s_at	MXD4	MAX dimerization protein 4	1.45	AK026392
212586_at	CAST	calpastatin	1.45	AA195244
200958_s_at	SDCBP	syndecan binding protein (syntenin)	1.43	NM_005625
201888_s_at	IL13RA1	interleukin 13 receptor, alpha 1	1.43	U81379
202743_at	PIK3R3	phosphoinositide-3-kinase, regulatory subunit 3 (p55, gamma)	1.43	BE622627
203186_s_at	S100A4	S100 calcium binding protein A4	1.43	NM_002961
203567_s_at	TRIM38	tripartite motif-containing 38	1.43	AU157590
203688_at	PKD2	polycystic kidney disease 2 (autosomal dominant)	1.43	NM_000297
205047_s_at	ASNS	asparagine synthetase	1.43	NM_001673
209043_at	PAPSS1	3'-phosphoadenosine 5'-phosphosulfate synthase 1	1.43	AF033026
209426_s_at	AMACR	alpha-methylacyl-CoA racemase	1.43	AF047020
210054_at	C4orf15	chromosome 4 open reading frame 15	1.43	BC003648
212870_at	RASSF3	Ras association (RalGDS/AF-6) domain family 3	1.43	AI628605
212989_at	TMEM23	transmembrane protein 23	1.43	AI377497
218923_at	CTBS	chitinase, di-N-acetyl-	1.43	AW304174
218930_s_at	TMEM106B	transmembrane protein 106B	1.43	NM_018374
221718_s_at	AKAP13	A kinase (PRKA) anchor protein 13 /// A kinase (PRKA) anchor protein 13	1.43	M90360
221903_s_at	CYLD	cylindromatosis (turban tumor syndrome)	1.43	BE046443
222088_s_at	SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	1.43	AA778684
205486_at	TESK2	testis-specific kinase 2	1.4	NM_007170
208611_s_at	SPTAN1	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	1.4	U83867
212274_at	LPIN1	lipin 1	1.4	AV705559
212299_at	NEK9	NIMA (never in mitosis gene a)- related kinase 9	1.4	AL117502
38149_at	ARHGAP25	Rho GTPase activating protein 25	1.4	D29642
201648_at	JAK1	Janus kinase 1 (a protein tyrosine kinase)	1.38	AL039831
202338_at	TK1	thymidine kinase 1, soluble	1.38	NM_003258
202880_s_at	PSCD1	pleckstrin homology, Sec7 and coiled-coil domains 1 (cytohesin 1)	1.38	NM_004762
203262_s_at	FAM50A	family with sequence similarity 50, member A	1.38	NM_004699
203538_at	CAMLG /// FAM39DP	calcium modulating ligand /// family with sequence similarity 39, member D pseudogene	1.38	NM_001745
204076_at	ENTPD4	ectonucleoside triphosphate diphosphohydrolase 4	1.38	AB002390
204279_at	PSMB9	proteasome (prosome, macropain) subunit, beta type, 9 (large multifunctional peptidase 2)	1.38	NM_002800
205315_s_at	SNTB2	syntrophin, beta 2 (dystrophin-associated protein A1, 59 kDa, basic component 2)	1.38	NM_006750
206222_at	TNFRSF10C	tumor necrosis factor receptor superfamily, member 10c, decoy without an intracellular domain	1.38	NM_003841
209463_s_at	TAF12	TAF12 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 20 kDa	1.38	D50544
210872_x_at	GAS7	growth arrest-specific 7	1.38	BC001152
213057_at	ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	1.38	AW118608
214121_x_at	PDLIM7	PDZ and LIM domain 7 (enigma)	1.38	AA086229
200905_x_at	HLA-E	major histocompatibility complex, class I, E	1.35	NM_005516
201009_s_at	TXNIP	thioredoxin interacting protein	1.35	AI439556
201015_s_at	JUP	junction plakoglobin	1.35	NM_021991
202139_at	AKR7A2	aldo-keto reductase family 7, member A2 (aflatoxin aldehyde reductase)	1.35	NM_003689

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
203445_s_at	CTDSP2	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 2	1.35	NM_005730
203695_s_at	DFNA5	deafness, autosomal dominant 5	1.35	NM_004403
204340_at	CXorf12	chromosome X open reading frame 12	1.35	NM_003492
205786_s_at	ITGAM	integrin, alpha M (complement component 3 receptor 3 subunit) /// integrin, alpha M (complement component 3 receptor 3 subunit)	1.35	NM_000632
209513_s_at	HSDL2	hydroxysteroid dehydrogenase like 2	1.35	BC004331
218384_at	CARHSP1	calcium regulated heat stable protein 1, 24 kDa	1.35	NM_014316
219147_s_at	C9orf95	chromosome 9 open reading frame 95	1.35	NM_017881
219210_s_at	RAB8B	RAB8B, member RAS oncogene family	1.35	NM_016530
200871_s_at	PSAP	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	1.33	NM_002778
202660_at	ITPR2	inositol 1,4,5-triphosphate receptor, type 2	1.33	AA834576
202801_at	PRKACA	protein kinase, cAMP-dependent, catalytic, alpha	1.33	NM_002730
203741_s_at	ADCY7	adenylate cyclase 7	1.33	NM_001114
204205_at	APOBEC3 G	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3 G	1.33	NM_021822
209006_s_at	C1orf63	chromosome 1 open reading frame 63	1.33	AF247168
209295_at	TNFRSF10B	tumor necrosis factor receptor superfamily, member 10b	1.33	AF016266
209875_s_at	SPP1	secreted phosphoprotein 1 (osteopontin, bone sialoprotein I, early T-lymphocyte activation 1)	1.33	M83248
210778_s_at	MXD4	MAX dimerization protein 4	1.33	BC002713
210844_x_at	CTNNA1	catenin (cadherin-associated protein), alpha 1, 102 kDa	1.33	D14705
211711_s_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	1.33	BC005821
212944_at	SLC5A3	solute carrier family 5 (inositol transporters), member 3	1.33	AK024896
217513_at	C17orf60	chromosome 17 open reading frame 60	1.33	BG334495
219487_at	BBS10	Bardet-Biedl syndrome 10	1.33	NM_024685
219691_at	SAMD9	sterile alpha motif domain containing 9	1.33	NM_017654
220999_s_at	CYFIP2	cytoplasmic FMR1 interacting protein 2	1.33	NM_030778
200748_s_at	FTH1	ferritin, heavy polypeptide 1	1.3	NM_002032
201132_at	HNRPH2	heterogeneous nuclear ribonucleoprotein H2 (H')	1.3	NM_019597
201845_s_at	RYBP	RING1 and YY1 binding protein	1.3	AB029551
203179_at	GALT /// C10orf4	galactose-1-phosphate uridylyltransferase /// chromosome 10 open reading frame 4	1.3	NM_000155
203457_at	STX7	syntaxin 7	1.3	NM_003569
204286_s_at	PMAIP1	phorbol-12-myristate-13-acetate-induced protein 1	1.3	NM_021127
204484_at	PIK3C2B	phosphoinositide-3-kinase, class 2, beta polypeptide	1.3	NM_002646
205804_s_at	TRAF3IP3	TRAF3 interacting protein 3	1.3	NM_025228
207113_s_at	TNF	tumor necrosis factor (TNF superfamily, member 2)	1.3	NM_000594
207238_s_at	PTPRC	protein tyrosine phosphatase, receptor type, C	1.3	NM_002838
209298_s_at	ITSN1	intersectin 1 (SH3 domain protein)	1.3	AF114488
212086_x_at	LMNA	lamin A/C	1.3	AK026584
212594_at	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	1.3	AI185160
212631_at	STX7	Syntaxin 7	1.3	AI566082
217744_s_at	PERP	PERP, TP53 apoptosis effector	1.3	NM_022121
221752_at	SSH1	Slingshot homolog 1 (Drosophila)	1.3	AL041728
200921_s_at	BTG1	B-cell translocation gene 1, anti-proliferative	1.28	NM_001731
202351_at	ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	1.28	AI093579
202501_at	MAPRE2	microtubule-associated protein, RP/EB family, member 2	1.28	NM_014268
202730_s_at	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	1.28	NM_014456
202772_at	HMGCL	3-hydroxymethyl-3-methylglutaryl-Coenzyme A lyase (hydroxymethylglutaricaciduria)	1.28	NM_000191
203778_at	MANBA	mannosidase, beta A, lysosomal	1.28	NM_005908
203912_s_at	DNASE1L1	deoxyribonuclease I-like 1	1.28	NM_006730
204058_at	ME1	malic enzyme 1, NADP(+)-dependent, cytosolic	1.28	AL049699
204805_s_at	H1FX	H1 histone family, member X	1.28	NM_006026
205091_x_at	RECQL	RecQ protein-like (DNA helicase Q1-like)	1.28	NM_002907
209028_s_at	ABII	abl-interactor 1	1.28	AF006516
209585_s_at	MINPP1	multiple inositol polyphosphate histidine phosphatase, 1	1.28	AF084943
210519_s_at	NQO1	NAD(P)H dehydrogenase, quinone 1	1.28	BC000906
210980_s_at	ASAHI	N-acylsphingosine amidohydrolase (acid ceramidase) 1	1.28	U47674

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
212276_at	LPIN1	lipin 1	1.28	D80010
212587_s_at	PTPRC	protein tyrosine phosphatase, receptor type, C	1.28	AI809341
212917_x_at	RECQL	RecQ protein-like (DNA helicase Q1-like)	1.28	AI814728
214091_s_at	GPX3	glutathione peroxidase 3 (plasma)	1.28	AW149846
215017_s_at	FNBP1L	formin binding protein 1-like	1.28	AW270932
218195_at	C6orf211	chromosome 6 open reading frame 211	1.28	NM_024573
218231_at	NAGK	N-acetylglucosamine kinase /// N-acetylglucosamine kinase	1.28	NM_017567
218992_at	C9orf46	chromosome 9 open reading frame 46	1.28	NM_018465
49679_s_at	MMP24	Matrix metalloproteinase 24 (membrane-inserted)	1.28	AA243774
200632_s_at	NDRG1	N-myc downstream regulated gene 1	1.25	NM_006096
200764_s_at	CTNNA1	catenin (cadherin-associated protein), alpha 1, 102 kDa	1.25	AI826881
202192_s_at	GAS7	growth arrest-specific 7	1.25	NM_005890
202887_s_at	DDIT4	DNA-damage-inducible transcript 4	1.25	NM_019058
203085_s_at	TGFB1	transforming growth factor, beta 1 (Camurati-Engelmann disease)	1.25	BC000125
204333_s_at	AGA	aspartylglucosaminidase	1.25	NM_000027
208012_x_at	SP110	SP110 nuclear body protein	1.25	NM_004509
208092_s_at	FAM49A	family with sequence similarity 49, member A	1.25	NM_030797
209379_s_at	KIAA1128	KIAA1128	1.25	AF241785
209425_at	AMACR	alpha-methylacyl-CoA racemase	1.25	AA888589
210240_s_at	CDKN2D	cyclin-dependent kinase inhibitor 2D (p19, inhibits CDK4)	1.25	U20498
212632_at	STX7	Syntaxin 7	1.25	N32035
214326_x_at	JUND	jun D proto-oncogene	1.25	AI339541
214639_s_at	HOXA1	homeobox A1	1.25	S79910
215936_s_at	KIAA1033	KIAA1033	1.25	AK001657
216060_s_at	DAAM1	dishevelled associated activator of morphogenesis 1	1.25	AK021890
216064_s_at	AGA	aspartylglucosaminidase	1.25	W27131
218477_at	TMEM14A	transmembrane protein 14A	1.25	NM_014051
218676_s_at	PCTP	phosphatidylcholine transfer protein	1.25	NM_021213
219099_at	C12orf5	chromosome 12 open reading frame 5	1.25	NM_020375
200761_s_at	ARL6IP5	ADP-ribosylation-like factor 6 interacting protein 5	1.23	NM_006407
202704_at	TOB1	transducer of ERBB2, 1	1.23	AA675892
203132_at	RB1	retinoblastoma 1 (including osteosarcoma)	1.23	NM_000321
204232_at	FCER1 G	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide	1.23	NM_004106
204480_s_at	C9orf16	chromosome 9 open reading frame 16	1.23	NM_024112
209345_s_at	PI4KII	phosphatidylinositol 4-kinase type II	1.23	AL561930
210202_s_at	BIN1	bridging integrator 1	1.23	U87558
210568_s_at	RECQL	RecQ protein-like (DNA helicase Q1-like)	1.23	BC001052
212750_at	PPP1R16B	protein phosphatase 1, regulatory (inhibitor) subunit 16B	1.23	AB020630
218628_at	CCDC53	coiled-coil domain containing 53	1.23	NM_016053
200920_s_at	BTG1	B-cell translocation gene 1, anti-proliferative	1.2	AL535380
201008_s_at	TXNIP	thioredoxin interacting protein	1.2	AA812232
202439_s_at	IDS	iduronate 2-sulfatase (Hunter syndrome)	1.2	NM_000202
202891_at	NIT1	nitrilase 1	1.2	NM_005600
203080_s_at	BAZ2B	bromodomain adjacent to zinc finger domain, 2B	1.2	NM_013450
203568_s_at	TRIM38	tripartite motif-containing 38	1.2	NM_006355
204362_at	SKAP2	src kinase associated phosphoprotein 2	1.2	NM_003930
208786_s_at	MAP1LC3B	microtubule-associated protein 1 light chain 3 beta	1.2	AF183417
209417_s_at	IFI35	interferon-induced protein 35	1.2	BC001356
209575_at	IL10RB	interleukin 10 receptor, beta	1.2	BC001903
209806_at	HIST1H2BK	histone cluster 1, H2bk	1.2	BC000893
212229_s_at	FBXO21	F-box protein 21	1.2	AK001699
212359_s_at	KIAA0913	KIAA0913	1.2	W89120
218218_at	DIP13B	DIP13 beta	1.2	NM_018171
201349_at	SLC9A3R1	solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 1	1.18	NM_004252
201580_s_at	TXNDC13	thioredoxin domain containing 13	1.18	AL544094
201805_at	PRKAG1	protein kinase, AMP-activated, gamma 1 non-catalytic subunit	1.18	NM_002733
202637_s_at	ICAM1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor	1.18	AI608725
204201_s_at	PTPN13	protein tyrosine phosphatase, non-receptor type 13 (APO-1/CD95 (Fas)-associated phosphatase)	1.18	NM_006264
204526_s_at	TBC1D8	TBC1 domain family, member 8 (with GRAM domain)	1.18	NM_007063

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
204873_at	PEX1	peroxisome biogenesis factor 1	1.18	NM_000466
207001_x_at	TSC22D3	TSC22 domain family, member 3	1.18	NM_004089
208763_s_at	TSC22D3	TSC22 domain family, member 3	1.18	AL110191
212530_at	NEK7	NIMA (never in mitosis gene a)-related kinase 7	1.18	AL080111
212675_s_at	—	—	1.18	AB011154
212794_s_at	KIAA1033	KIAA1033	1.18	AK001728
213271_s_at	DOPEY1	dopey family member 1	1.18	AB029040
218248_at	FAM111A	family with sequence similarity 111, member A	1.18	NM_022074
218273_s_at	PPM2C	protein phosphatase 2C, magnesium-dependent, catalytic subunit	1.18	NM_018444
220775_s_at	UEVLD	UEV and lactate/malate dehydrogenase domains	1.18	NM_018314
221059_s_at	COTL1	coactosin-like 1 (Dictyostelium)	1.18	NM_021615
221590_s_at	ALDH6A1	Aldehyde dehydrogenase 6 family, member A1	1.18	AF130089
36553_at	ASMTL	acetylserotonin O-methyltransferase-like	1.18	AA069799
200847_s_at	TMEM66	transmembrane protein 66	1.15	NM_016127
201383_s_at	NBR1 /// LOC727732	neighbor of BRCA1 gene 1 /// similar to neighbor of BRCA1 gene 1	1.15	AL044170
201811_x_at	SH3BP5	SH3-domain binding protein 5 (BTK-associated)	1.15	NM_004844
203984_s_at	CASP9	caspase 9, apoptosis-related cysteine peptidase	1.15	U60521
204068_at	STK3	serine/threonine kinase 3 (STE20 homolog, yeast)	1.15	NM_006281
205263_at	BCL10	B-cell CLL/lymphoma 10	1.15	AF082283
205434_s_at	AAK1 /// LOC647217	AP2 associated kinase 1 /// hypothetical protein LOC647217	1.15	AW451954
209512_at	HSDL2	hydroxysteroid dehydrogenase like 2	1.15	BC004331
210410_s_at	MSH5	mutS homolog 5 (E. coli)	1.15	AF034759
212593_s_at	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	1.15	N92498
212918_at	RECQL	RecQ protein-like (DNA helicase Q1-like)	1.15	AI962943
214439_x_at	BIN1	bridging integrator 1	1.15	AF043899
216080_s_at	FADS3	fatty acid desaturase 3	1.15	AC004770
218208_at	PQLC1	PQ loop repeat containing 1	1.15	NM_025078
218376_s_at	MICAL1	microtubule associated monooxygenase, calponin and LIM domain containing 1	1.15	NM_022765
219681_s_at	RAB11FIP1	RAB11 family interacting protein 1 (class I)	1.15	NM_025151
222217_s_at	SLC27A3	solute carrier family 27 (fatty acid transporter), member 3	1.15	BC003654
41047_at	C9orf16	chromosome 9 open reading frame 16	1.15	AI885170
43427_at	ACACB	acetyl-Coenzyme A carboxylase beta	1.15	AI970898
213373_s_at	CASP8	caspase 8, apoptosis-related cysteine peptidase	1.13	BF439983
200898_s_at	MGEA5	meningioma expressed antigen 5 (hyaluronidase)	1.13	AK002091
201118_at	PGD /// UGDH	phosphogluconate dehydrogenase /// UDP-glucose dehydrogenase	1.13	NM_002631
201847_at	LIPA	lipase A, lysosomal acid, cholesterol esterase (Wolman disease)	1.13	NM_000235
202239_at	PARP4	poly (ADP-ribose) polymerase family, member 4	1.13	NM_006437
202260_s_at	STXBP1	syntaxin binding protein 1	1.13	NM_003165
202498_s_at	SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	1.13	BE550486
202533_s_at	DHFR /// LOC643509	dihydrofolate reductase /// similar to Dihydrofolate reductase	1.13	BC003584
202609_at	EPS8	epidermal growth factor receptor pathway substrate 8	1.13	NM_004447
202677_at	RASA1	RAS p21 protein activator (GTPase activating protein) 1	1.13	NM_002890
202931_x_at	BIN1	bridging integrator 1	1.13	NM_004305
204091_at	PDE6D	phosphodiesterase 6D, cGMP-specific, rod, delta	1.13	NM_002601
204131_s_at	FOXO3A	forkhead box O3A	1.13	N25732
204222_s_at	GLIPR1	GLI pathogenesis-related 1 (glioma)	1.13	NM_006851
204917_s_at	MLLT3	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 3	1.13	AV756536
204918_s_at	MLLT3	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 3	1.13	NM_004529
207677_s_at	NCF4	neutrophil cytosolic factor 4, 40 kDa /// neutrophil cytosolic factor 4, 40 kDa	1.13	NM_013416
209457_at	DUSP5	dual specificity phosphatase 5	1.13	U16996
209761_s_at	SP110	SP110 nuclear body protein	1.13	AA969194
209799_at	PRKAA1	protein kinase, AMP-activated, alpha 1 catalytic subunit	1.13	AF100763
212457_at	TFE3	transcription factor binding to IGHM enhancer 3	1.13	AL161985

(continued)

Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
212872_s_at	TRFP	Trf (TATA binding protein-related factor)-proximal homolog (Drosophila)	1.13	AK023092
216381_x_at	AKR7A3	aldo-keto reductase family 7, member A3 (aflatoxin aldehyde reductase)	1.13	AL035413
218191_s_at	LMBRD1	LMBR1 domain containing 1	1.13	NM_018368
218450_at	HEBP1	heme binding protein 1	1.13	NM_015987
218688_at	DAK	dihydroxyacetone kinase 2 homolog (S. cerevisiae)	1.13	NM_015533
221563_at	DUSP10	dual specificity phosphatase 10	1.13	N36770
40420_at	STK10	serine/threonine kinase 10	1.13	AB015718
200885_at	RHOC	ras homolog gene family, member C	1.1	NM_005167
202693_s_at	STK17A	serine/threonine kinase 17a (apoptosis-inducing)	1.1	AW194730
203810_at	DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4	1.1	BG252490
203814_s_at	NQO2	NAD(P)H dehydrogenase, quinone 2	1.1	NM_000904
207700_s_at	NCOA3	nuclear receptor coactivator 3	1.1	NM_006534
209605_at	TST	thiosulfate sulfurtransferase (rhodanese)	1.1	D87292
209649_at	STAM2	signal transducing adaptor molecule (SH3 domain and ITAM motif) 2	1.1	AL133600
212646_at	RFTN1	raftlin, lipid raft linker 1	1.1	D42043
212795_at	KIAA1033	KIAA1033	1.1	AL137753
213164_at	SLC5A3	solute carrier family 5 (inositol transporters), member 3	1.1	AI867198
213295_at	CYLD	cyldromatosis (turban tumor syndrome)	1.1	AA555096
214683_s_at	CLK1	CDC-like kinase 1	1.1	AI251890
215127_s_at	RBMS1	RNA binding motif, single stranded interacting protein 1	1.1	AL517946
215884_s_at	UBQLN2	ubiquilin 2	1.1	AK001029
216511_s_at	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)	1.1	AJ270770
216860_s_at	GDF11	growth differentiation factor 11	1.1	AF028333
216899_s_at	SKAP2	src kinase associated phosphoprotein 2	1.1	AC003999
217868_s_at	METTL9	methyltransferase like 9	1.1	NM_016025
218342_s_at	KIAA1815	KIAA1815	1.1	NM_024896
218773_s_at	MSRB2	methionine sulfoxide reductase B2	1.1	NM_012228
35254_at	TRAFD1	TRAF-type zinc finger domain containing 1	1.1	AB007447
200931_s_at	VCL	vinculin	1.08	NM_014000
200974_at	ACTA2	actin, alpha 2, smooth muscle, aorta	1.08	NM_001613
201012_at	ANXA1	annexin A1	1.08	NM_000700
202446_s_at	PLSCR1	phospholipid scramblase 1	1.08	AI825926
202625_at	LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	1.08	AI356412
202808_at	—	—	1.08	AK000161
202888_s_at	ANPEP	alanyl (membrane) aminopeptidase (aminopeptidase N, aminopeptidase M, microsomal aminopeptidase, CD13, p150)	1.08	NM_001150
204141_at	TUBB2A	tubulin, beta 2A	1.08	NM_001069
205546_s_at	TYK2	tyrosine kinase 2	1.08	NM_003331
209536_s_at	EHD4	EH-domain containing 4	1.08	AF320070
209715_at	CBX5	chromobox homolog 5 (HP1 alpha homolog, Drosophila)	1.08	L07515
210276_s_at	TRIOBP	TRIO and F-actin binding protein	1.08	AF281030
211552_s_at	ALDH4A1	aldehyde dehydrogenase 4 family, member A1	1.08	U24267
212189_s_at	COG4	component of oligomeric golgi complex 4	1.08	AK022874
212347_x_at	MXD4	MAX dimerization protein 4	1.08	AA831438
212633_at	KIAA0776	KIAA0776	1.08	AL132776
212697_at	LOC162427	hypothetical protein LOC162427	1.08	AL515874
212792_at	DPY19L1	dpy-19-like 1 (C. elegans)	1.08	AB020684
214274_s_at	ACAA1	acetyl-Coenzyme A acyltransferase 1 (peroxisomal 3-oxoacyl-Coenzyme A thiolase)	1.08	AI860341
214703_s_at	MAN2B2	mannosidase, alpha, class 2B, member 2	1.08	AW954107
217996_at	PHLDA1	pleckstrin homology-like domain, family A, member 1	1.08	AA576961
218418_s_at	ANKRD25	ankyrin repeat domain 25	1.08	NM_015493
219297_at	WDR44	WD repeat domain 44	1.08	NM_019045
201010_s_at	TXNIP	thioredoxin interacting protein	1.05	NM_006472
201502_s_at	NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	1.05	AI078167
201719_s_at	EPB41L2	erythrocyte membrane protein band 4.1-like 2	1.05	NM_001431
201972_at	ATP6V1A	ATPase, H+ transporting, lysosomal 70 kDa, V1 subunit A	1.05	AF113129
202561_at	TNKS	tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase	1.05	AF070613

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
203303_at	DYNLT3	dynein, light chain, Tctex-type 3	1.05	NM_006520
203739_at	ZNF217	zinc finger protein 217	1.05	NM_006526
204094_s_at	TSC2D2	TSC22 domain family, member 2	1.05	NM_014779
208785_s_at	MAP1LC3B	microtubule-associated protein 1 light chain 3 beta	1.05	BE893893
208796_s_at	CCNG1	cyclin G1	1.05	BC000196
209027_s_at	ABI1	abl-interactor 1	1.05	BF673013
209113_s_at	HMG20B	high-mobility group 20B	1.05	AF288679
209234_at	KIF1B	kinesin family member 1B	1.05	BF939474
213300_at	KIAA0404	hypothetical protein LOC23130	1.05	AW168132
213471_at	NPHP4	nephronophthisis 4	1.05	AB014573
213485_s_at	ABCC10	ATP-binding cassette, sub-family C (CFTR/MRP), member 10	1.05	AK000002
213578_at	BMPR1A	bone morphogenetic protein receptor, type IA	1.05	AI678679
217967_s_at	FAM129A	family with sequence similarity 129, member A	1.05	AF288391
218456_at	C1QDC1	C1q domain containing 1	1.05	NM_023925
219349_s_at	EXOC2	exocyst complex component 2	1.05	NM_018303
219351_at	TRAPPC2	trafficking protein particle complex 2	1.05	NM_014563
220162_s_at	CARD9	caspase recruitment domain family, member 9	1.05	NM_022352
221561_at	SOAT1	sterol O-acyltransferase (acyl-Coenzyme A: cholesterol acyltransferase) 1	1.05	L21934
221922_at	GPSM2	G-protein signalling modulator 2 (AGS3-like, <i>C. elegans</i>)	1.05	AW195581
78047_s_at	LOC729580 /// LOC730672	hypothetical protein LOC729580 /// hypothetical protein LOC730672	1.05	AW001777
200791_s_at	IQGAP1	IQ motif containing GTPase activating protein 1	1.03	NM_003870
202131_s_at	RIOK3	RIO kinase 3 (yeast) /// RIO kinase 3 (yeast)	1.03	NM_003831
202203_s_at	AMFR	autocrine motility factor receptor	1.03	NM_001144
202213_s_at	CUL4B	cullin 4B	1.03	AI650819
202214_s_at	CUL4B	cullin 4B	1.03	NM_003588
202679_at	NPC1	Niemann-Pick disease, type C1	1.03	NM_000271
202922_at	GCLC	glutamate-cysteine ligase, catalytic subunit	1.03	BF676980
203047_at	STK10	serine/threonine kinase 10	1.03	NM_005990
203474_at	IQGAP2	IQ motif containing GTPase activating protein 2	1.03	NM_006633
203481_at	C10orf6	chromosome 10 open reading frame 6	1.03	AI655902
204054_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	1.03	NM_000314
205147_x_at	NCF4	neutrophil cytosolic factor 4, 40 kDa	1.03	NM_000631
209553_at	VPS8	vacuolar protein sorting 8 homolog (<i>S. cerevisiae</i>)	1.03	BC001001
210201_x_at	BIN1	bridging integrator 1	1.03	AF001383
210312_s_at	IFT20	intraflagellar transport 20 homolog (<i>Chlamydomonas</i>)	1.03	BC002640
212111_at	STX12	syntaxin 12	1.03	AA628051
212126_at	—	CDNA clone IMAGE:4842353	1.03	BG391282
212423_at	C10orf56	chromosome 10 open reading frame 56	1.03	AK024784
212677_s_at	CEP68	centrosomal protein 68 kDa	1.03	BG530481
212877_at	KNS2	kinesin 2	1.03	AA284075
212899_at	CDC2L6	cell division cycle 2-like 6 (CDK8-like)	1.03	AB028951
214266_s_at	PDLIM7	PDZ and LIM domain 7 (enigma)	1.03	AW206786
216033_s_at	FYN	FYN oncogene related to SRC, FGR, YES	1.03	S74774
218124_at	RETSAT	retinol saturase (all-trans-retinol 13,14-reductase)	1.03	NM_017750
218813_s_at	SH3GLB2	SH3-domain GRB2-like endophilin B2	1.03	NM_020145
64486_at	CORO1B	coronin, actin binding protein, 1B	1.03	AI341234
200872_at	S100A10	S100 calcium binding protein A10	1	NM_002966
201482_at	QSCN6	quiescin Q6	1	NM_002826
201734_at	CLCN3	Chloride channel 3	1	AI760629
201753_s_at	ADD3	adducin 3 (gamma)	1	NM_019903
203310_at	STXBP3	syntaxin binding protein 3	1	NM_007269
203752_s_at	JUND	jun D proto-oncogene	1	NM_005354
204703_at	IFT88	intraflagellar transport 88 homolog (<i>Chlamydomonas</i>)	1	NM_006531
205191_at	RP2	retinitis pigmentosa 2 (X-linked recessive)	1	NM_006915
208546_x_at	HIST1H2BH	histone cluster 1, H2bh	1	NM_003524
208671_at	SERINC1	serine incorporator 1	1	AF164794
208723_at	USP11	ubiquitin specific peptidase 11	1	BC000350
209112_at	CDKN1B	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	1	BC001971
211676_s_at	IFNGR1	interferon gamma receptor 1 /// interferon gamma receptor 1	1	AF056979

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
212919_at	DCP2	DCP2 decapping enzyme homolog (<i>S. cerevisiae</i>)	1	AV715578
213000_at	MORC3	MORC family CW-type zinc finger 3	1	AP000693
213275_x_at	CTSB	cathepsin B	1	W47179
214909_s_at	DDAH2	dimethylarginine dimethylaminohydrolase 2	1	AK026191
216250_s_at	LPXN	leupaxin	1	X77598
217731_s_at	ITM2B	integral membrane protein 2B	1	NM_021999
217733_s_at	TMSB10	thymosin, beta 10	1	NM_021103
217973_at	DCXR	dicarbonyl/L-xylulose reductase	1	NM_016286
219201_s_at	TWSG1	twisted gastrulation homolog 1 (<i>Drosophila</i>)	1	NM_020648
221613_s_at	ZFAND6	zinc finger, AN1-type domain 6	1	AL136598
221897_at	TRIM52	tripartite motif-containing 52	1	AA205660
222165_x_at	C9orf16	chromosome 9 open reading frame 16	1	AK022885
37590_g_at	ZNF710 /// DOCK4	Zinc finger protein 710 /// MRNA full length insert cDNA clone EUROIMAGE 375854 /// Deducator of cytokinesis 4	1	AL109698
200670_at	XBP1	X-box binding protein 1	-1	NM_005080
201389_at	ITGA5	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	-1	NM_002205
201420_s_at	WDR77	WD repeat domain 77	-1	BF975273
201675_at	AKAP1	A kinase (PRKA) anchor protein 1	-1	NM_003488
201872_s_at	ABCE1	ATP-binding cassette, sub-family E (OABP), member 1	-1	AI002002
202915_s_at	FAM20B	family with sequence similarity 20, member B	-1	BF115776
202937_x_at	CTA-126B4.3	CGI-96 protein	-1	AL022316
203408_s_at	SATB1	special AT-rich sequence binding protein 1 (binds to nuclear matrix/ scaffold-associating DNA's)	-1	NM_002971
204033_at	TRIP13	thyroid hormone receptor interactor 13	-1	NM_004237
207515_s_at	POLR1C	polymerase (RNA) I polypeptide C, 30 kDa	-1	NM_004875
208910_s_at	C1QBP	complement component 1, q subcomponent binding protein	-1	L04636
209893_s_at	FUT4	fucosyltransferase 4 (alpha (1,3) fucosyltransferase, myeloid-specific)	-1	M58596
210323_at	TEKT2	tektin 2 (testicular)	-1	AB033823
210567_s_at	SKP2	S-phase kinase-associated protein 2 (p45)	-1	BC001441
210787_s_at	CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta	-1	AF140507
212137_at	LARP1	La ribonucleoprotein domain family, member 1	-1	AV746402
213133_s_at	GCSH /// LOC730107	glycine cleavage system protein H (aminomethyl carrier) /// similar to Glycine cleavage system H protein, mitochondrial precursor	-1	AW237404
213416_at	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	-1	BG532690
218238_at	GTPBP4	GTP binding protein 4	-1	NM_012341
218481_at	EXOSC5	exosome component 5	-1	NM_020158
218605_at	TFB2 M	transcription factor B2, mitochondrial	-1	NM_022366
218826_at	SLC35F2	solute carrier family 35, member F2	-1	NM_017515
218877_s_at	TRMT11	tRNA methyltransferase 11 homolog (<i>S. cerevisiae</i>)	-1	NM_021820
221216_s_at	SCMH1	sex comb on midleg homolog 1 (<i>Drosophila</i>)	-1	NM_012236
221235_s_at	LOC644617	Hypothetical LOC644617 /// Hypothetical LOC644617	-1	NM_030825
221845_s_at	CLPB	ClpB caseinolytic peptidase B homolog (<i>E. coli</i>)	-1	AI655698
201459_at	RUVBL2	RuvB-like 2 (<i>E. coli</i>)	-1.03	NM_006666
202349_at	TOR1A	torsin family 1, member A (torsin A)	-1.03	NM_000113
202857_at	TMEM4	transmembrane protein 4	-1.03	NM_014255
204133_at	RRP9	RRP9, small subunit (SSU) processome component, homolog (yeast)	-1.03	NM_004704
204327_s_at	ZNF202	zinc finger protein 202	-1.03	N91520
204905_s_at	EEF1E1	eukaryotic translation elongation factor 1 epsilon 1	-1.03	NM_004280
205429_s_at	MPP6	membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	-1.03	NM_016447
205885_s_at	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	-1.03	L12002
212295_s_at	SLC7A1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1	-1.03	AA148507
212424_at	PDCD11	programmed cell death 11	-1.03	AW026194
218403_at	TRIAP1	TP53 regulated inhibitor of apoptosis 1	-1.03	NM_016399
218460_at	HEATR2	HEAT repeat containing 2	-1.03	NM_017802
200692_s_at	HSPA9	heat shock 70 kDa protein 9 (mortalin)	-1.05	NM_004134
201323_at	EBNA1BP2	EBNA1 binding protein 2	-1.05	NM_006824
206445_s_at	PRMT1	protein arginine methyltransferase 1	-1.05	NM_001536
207348_s_at	LIG3	ligase III, DNA, ATP-dependent	-1.05	NM_002311
207622_s_at	ABCF2	ATP-binding cassette, sub-family F (GCN20), member 2	-1.05	NM_005692

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
208799_at	PSMB5	proteasome (prosome, macropain) subunit, beta type, 5	-1.05	BC004146
208972_s_at	ATP5G1	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C1 (subunit 9)	-1.05	AL080089
209098_s_at	JAG1	jagged 1 (Alagille syndrome)	-1.05	U61276
209262_s_at	NR2F6	nuclear receptor subfamily 2, group F, member 6	-1.05	BC002669
212422_at	PDCD11	programmed cell death 11	-1.05	AL547263
212693_at	MDN1	MDN1, midasin homolog (yeast)	-1.05	BE670928
212739_s_at	NME4	non-metastatic cells 4, protein expressed in	-1.05	AL523860
213838_at	NOL7	nucleolar protein 7, 27 kDa	-1.05	AA191426
217833_at	SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	-1.05	AL520908
218187_s_at	C8orf33	chromosome 8 open reading frame 33	-1.05	NM_023080
219731_at	FLJ34077	weakly similar to zinc finger protein 195	-1.05	NM_024343
219742_at	PRR7	proline rich 7 (synaptic)	-1.05	NM_030567
220416_at	ATP8B4	ATPase, Class I, type 8B, member 4	-1.05	NM_024837
50314_i_at	C20orf27	chromosome 20 open reading frame 27	-1.05	AI761506
201423_s_at	CUL4A	cullin 4A	-1.08	AL037208
202212_at	PES1	pescadillo homolog 1, containing BRCT domain (zebrafish)	-1.08	NM_014303
202246_s_at	CDK4	cyclin-dependent kinase 4	-1.08	NM_000075
202264_s_at	TOMM40	translocase of outer mitochondrial membrane 40 homolog (yeast)	-1.08	NM_006114
203228_at	PAFAH1B3	platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit 29 kDa	-1.08	NM_002573
203857_s_at	PDIA5	protein disulfide isomerase family A, member 5	-1.08	NM_006810
204169_at	IMPDH1	IMP (inosine monophosphate) dehydrogenase 1	-1.08	NM_000883
205241_at	SCO2	SCO cytochrome oxidase deficient homolog 2 (yeast)	-1.08	NM_005138
205761_s_at	DUS4L	dihydrouridine synthase 4-like (<i>S. cerevisiae</i>)	-1.08	AW242981
205768_s_at	SLC27A2	solute carrier family 27 (fatty acid transporter), member 2	-1.08	NM_003645
207824_s_at	MAZ	MYC-associated zinc finger protein (purine-binding transcription factor)	-1.08	NM_002383
210044_s_at	LYL1	lymphoblastic leukemia derived sequence 1	-1.08	BC002796
214173_x_at	C19orf2	chromosome 19 open reading frame 2	-1.08	AW514900
214507_s_at	EXOSC2	exosome component 2	-1.08	NM_014285
215073_s_at	NR2F2	nuclear receptor subfamily 2, group F, member 2	-1.08	AL554245
216952_s_at	LMNB2	lamin B2	-1.08	M94363
217832_at	SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	-1.08	BE672181
218145_at	TRIB3	tribbles homolog 3 (<i>Drosophila</i>)	-1.08	NM_021158
218529_at	CD320	CD320 molecule	-1.08	NM_016579
218767_at	REXO4	REX4, RNA exonuclease 4 homolog (<i>S. cerevisiae</i>)	-1.08	NM_020385
220892_s_at	PSAT1	phosphoserine aminotransferase 1	-1.08	NM_021154
202089_s_at	SLC39A6	solute carrier family 39 (zinc transporter), member 6	-1.1	NM_012319
202159_at	FARSLA	phenylalanine-tRNA synthetase-like, alpha subunit	-1.1	NM_004461
202875_s_at	PBX2	pre-B-cell leukemia transcription factor 2	-1.1	BE397715
203093_s_at	TIMM44	translocase of inner mitochondrial membrane 44 homolog (yeast)	-1.1	NM_006351
204823_at	NAV3	neuron navigator 3	-1.1	NM_014903
205884_at	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	-1.1	NM_000885
209921_at	SLC7A11	solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	-1.1	AB040875
210966_x_at	LARP1	La ribonucleoprotein domain family, member 1	-1.1	BC001460
211162_x_at	SCD	stearoyl-CoA desaturase (delta-9-desaturase)	-1.1	AF116616
211367_s_at	CASP1	caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)	-1.1	U13699
211686_s_at	RBM13	RNA binding motif protein 13 /// RNA binding motif protein 13	-1.1	AF251062
214427_at	NOL1	nucleolar protein 1, 120 kDa	-1.1	NM_006170
214627_at	EPX	eosinophil peroxidase	-1.1	X14346
215152_at	MYB	v-myb myeloblastosis viral oncogene homolog (avian)	-1.1	AI357042
218618_s_at	FNDC3B	fibronectin type III domain containing 3B	-1.1	NM_022763
219869_s_at	SLC39A8	solute carrier family 39 (zinc transporter), member 8	-1.1	NM_022154
200924_s_at	SLC3A2	solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	-1.13	NM_002394
201014_s_at	PAICS	phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase	-1.13	NM_006452
202088_at	SLC39A6	solute carrier family 39 (zinc transporter), member 6	-1.13	AI635449

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
202441_at	SPFH1	SPFH domain family, member 1	-1.13	AL568449
203612_at	BYSL	bystin-like	-1.13	NM_004053
205090_s_at	NAGPA	N-acetylglucosamine-1-phosphodiester alpha-N-acetylglucosaminidase	-1.13	NM_016256
205895_s_at	NOLC1	nucleolar and coiled-body phosphoprotein 1	-1.13	NM_004741
212528_at	—	CDNA clone IMAGE:3878236	-1.13	AI348009
217754_at	DDX56	DEAD (Asp-Glu-Ala-Asp) box polypeptide 56	-1.13	NM_019082
218408_at	TIMM10	translocase of inner mitochondrial membrane 10 homolog (yeast)	-1.13	NM_012456
218969_at	Magmas	mitochondria-associated protein involved in granulocyte-macrophage colony-stimulating factor signal transduction	-1.13	NM_016069
203782_s_at	POLRMT	polymerase (RNA) mitochondrial (DNA directed)	-1.15	NM_005035
203893_at	TAF9	TAF9 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 32 kDa	-1.15	NM_016283
203949_at	MPO	myeloperoxidase	-1.15	NM_000250
205135_s_at	NUFIP1	nuclear fragile X mental retardation protein interacting protein 1	-1.15	AL049842
205748_s_at	RNF126	ring finger protein 126	-1.15	NM_017876
209121_x_at	NR2F2	nuclear receptor subfamily 2, group F, member 2	-1.15	M64497
210627_s_at	GCS1	glucosidase I	-1.15	BC002804
212411_at	IMP4	IMP4, U3 small nucleolar ribonucleoprotein, homolog (yeast)	-1.15	BE747342
213638_at	PHACTR1	phosphatase and actin regulator 1	-1.15	AW054711
218512_at	WDR12	WD repeat domain 12	-1.15	NM_018256
218593_at	RBM28	RNA binding motif protein 28	-1.15	NM_018077
219558_at	ATP13A3	ATPase type 13A3	-1.15	NM_024524
200691_s_at	HSPA9	heat shock 70 kDa protein 9 (mortalin)	-1.18	BC000478
201479_at	DKC1	dyskeratosis congenita 1, dyskerin	-1.18	NM_001363
202016_at	MEST	mesoderm specific transcript homolog (mouse)	-1.18	NM_002402
202475_at	TMEM147	transmembrane protein 147	-1.18	NM_006326
202655_at	ARMET	arginine-rich, mutated in early stage tumors	-1.18	NM_006010
203871_at	SEN3	SUMO1/sentrin/SMT3 specific peptidase 3	-1.18	NM_015670
204999_s_at	ATF5	activating transcription factor 5	-1.18	BC005174
211709_s_at	CLEC11A	C-type lectin domain family 11, member A	-1.18	BC005810
211949_s_at	NOLC1	nucleolar and coiled-body phosphoprotein 1	-1.18	AI355279
213116_at	NEK3	NIMA (never in mitosis gene a)-related kinase 3	-1.18	AI191920
213132_s_at	MCAT	malonyl CoA:ACP acyltransferase (mitochondrial)	-1.18	AL022237
217099_s_at	GEMIN4	gem (nuclear organelle) associated protein 4	-1.18	AF258545
64900_at	FLJ22167	hypothetical protein FLJ22167	-1.18	AA401703
203092_at	TIMM44	translocase of inner mitochondrial membrane 44 homolog (yeast)	-1.2	AF026030
203664_s_at	POLR2D	polymerase (RNA) II (DNA directed) polypeptide D	-1.2	NM_004805
205033_s_at	DEFA1 /// DEFA3 /// LOC728358	defensin, alpha 1 /// defensin, alpha 3, neutrophil-specific /// similar to Neutrophil defensin 1 precursor (HNP-1) (HP-1) (HP1) (Defensin, alpha 1)	-1.2	NM_004084
205769_at	SLC27A2	solute carrier family 27 (fatty acid transporter), member 2	-1.2	NM_003645
207396_s_at	ALG3	asparagine-linked glycosylation 3 homolog (S. cerevisiae, alpha-1,3-mannosyltransferase)	-1.2	NM_005787
207624_s_at	RPGR	retinitis pigmentosa GTPase regulator	-1.2	NM_000328
208676_s_at	DLST /// PA2G4	dihydroliipoamide S-succinyltransferase (E2 component of 2-oxo-glutarate complex) /// proliferation-associated 2G4, 38 kDa	-1.2	U87954
208744_x_at	HSPH1	heat shock 105 kDa/110 kDa protein 1	-1.2	BG403660
209215_at	TETRA	tetracycline transporter-like protein	-1.2	L11669
210830_s_at	PON2	paraoxonase 2	-1.2	AF001602
211150_s_at	DLAT	dihydroliipoamide S-acetyltransferase (E2 component of pyruvate dehydrogenase complex)	-1.2	J03866
215983_s_at	UBXD6	UBX domain containing 6	-1.2	D83768
218774_at	DCPS	decapping enzyme, scavenger	-1.2	NM_014026
200690_at	HSPA9	heat shock 70 kDa protein 9 (mortalin)	-1.23	AA927701
202148_s_at	PYCR1	pyrroline-5-carboxylate reductase 1	-1.23	NM_006907
203010_at	STAT5A	signal transducer and activator of transcription 5A	-1.23	NM_003152
203712_at	KIAA0020	KIAA0020	-1.23	NM_014878
204998_s_at	ATF5	activating transcription factor 5	-1.23	NM_012068
206440_at	LIN7A	lin-7 homolog A (C. elegans)	-1.23	NM_004664

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
206752_s_at	DFFB	DNA fragmentation factor, 40 kDa, beta polypeptide (caspase-activated DNase)	-1.23	NM_004402
212791_at	FLJ38984	hypothetical protein FLJ38984	-1.23	AL042729
213170_at	GPX7	glutathione peroxidase 7	-1.23	AA406605
218027_at	MRPL15	mitochondrial ribosomal protein L15	-1.23	NM_014175
218069_at	XTP3TPA	XTP3-transactivated protein A	-1.23	NM_024096
218112_at	MRPS34	mitochondrial ribosomal protein S34	-1.23	NM_023936
220615_s_at	MLSTD1	male sterility domain containing 1	-1.23	NM_018099
201478_s_at	DKC1	dyskeratosis congenita 1, dyskerin	-1.25	U59151
202453_s_at	GTF2H1	general transcription factor IIH, polypeptide 1, 62 kDa	-1.25	NM_005316
203230_at	DVL1 // LOC642469	dishevelled, dsh homolog 1 (Drosophila) // similar to dishevelled 1 isoform a	-1.25	AF006011
203701_s_at	TRMT1	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae)	-1.25	NM_017722
209120_at	NR2F2	nuclear receptor subfamily 2, group F, member 2	-1.25	AL037401
212174_at	AK2	adenylate kinase 2	-1.25	W02312
213355_at	ST3GAL6	ST3 beta-galactoside alpha-2,3-sialyltransferase 6	-1.25	AI989567
219006_at	C6orf66	chromosome 6 open reading frame 66	-1.25	NM_014165
222206_s_at	NCLN	nicalin homolog (zebrafish)	-1.25	AA781143
204394_at	SLC43A1	solute carrier family 43, member 1	-1.28	NM_003627
205565_s_at	FXN	frataxin	-1.28	NM_000144
210463_x_at	TRMT1	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae)	-1.28	BC002492
211728_s_at	HYAL3	hyaluronoglucosaminidase 3 // hyaluronoglucosaminidase 3	-1.28	BC005896
212173_at	AK2	adenylate kinase 2	-1.28	AU154985
212193_s_at	LARP1	La ribonucleoprotein domain family, member 1	-1.28	BE881529
219031_s_at	NIP7	nuclear import 7 homolog (S. cerevisiae)	-1.28	NM_016101
221987_s_at	TSR1	TSR1, 20S rRNA accumulation, homolog (S. cerevisiae)	-1.28	AI803633
201577_at	NME1	non-metastatic cells 1, protein (NM23A) expressed in	-1.3	NM_000269
202799_at	CLPP	ClpP caseinolytic peptidase, ATP-dependent, proteolytic subunit homolog (E. coli)	-1.3	NM_006012
203685_at	BCL2	B-cell CLL/lymphoma 2	-1.3	NM_000633
205129_at	NPM3	nucleophosmin/nucleoplasm, 3	-1.3	NM_006993
205977_s_at	EPHA1	EPH receptor A1	-1.3	NM_005232
206039_at	RAB33A	RAB33A, member RAS oncogene family	-1.3	NM_004794
211774_s_at	MMACHC	methylmalonic aciduria (cobalamin deficiency) cblC type, with homocystinuria	-1.3	BC006122
211936_at	HSPA5	heat shock 70 kDa protein 5 (glucose-regulated protein, 78 kDa)	-1.3	AF216292
214523_at	CEBPE	CCAAT/enhancer binding protein (C/EBP), epsilon	-1.3	NM_001805
218001_at	MRPS2	mitochondrial ribosomal protein S2	-1.3	NM_016034
218188_s_at	TIMM13	translocase of inner mitochondrial membrane 13 homolog (yeast)	-1.3	NM_012458
218586_at	C20orf20	chromosome 20 open reading frame 20	-1.3	NM_018270
218708_at	NXT1	NTF2-like export factor 1	-1.3	NM_013248
219110_at	NOLA1	nucleolar protein family A, member 1 (H/ACA small nucleolar RNPs)	-1.3	NM_018983
219158_s_at	NARG1	NMDA receptor regulated 1	-1.3	NM_025085
219218_at	BAHCC1	BAH domain and coiled-coil containing 1	-1.3	NM_024696
219420_s_at	C1orf163	chromosome 1 open reading frame 163	-1.3	NM_023077
220587_s_at	GBL	G protein beta subunit-like	-1.3	NM_022372
201797_s_at	VARS	valyl-tRNA synthetase	-1.33	NM_006295
203721_s_at	UTP18	UTP18, small subunit (SSU) processome component, homolog (yeast)	-1.33	NM_016001
203931_s_at	MRPL12	mitochondrial ribosomal protein L12	-1.33	NM_002949
205996_s_at	AK2	adenylate kinase 2	-1.33	NM_013411
207398_at	HOXD13	homeobox D13	-1.33	NM_000523
212627_s_at	EXOSC7	exosome component 7	-1.33	AL581473
214794_at	DLST	dihydrolipoamide S-succinyltransferase (E2 component of 2-oxo-glutarate complex)	-1.33	BF669264
215947_s_at	FLJ14668	hypothetical protein FLJ14668	-1.33	AF090094
218278_at	WDR74	WD repeat domain 74	-1.33	NM_018093
218681_s_at	SDF2L1	stromal cell-derived factor 2-like 1	-1.33	NM_022044
221758_at	ARMC6	armadillo repeat containing 6	-1.33	BC003700
202740_at	ACY1	aminoacylase 1	-1.35	NM_000666
204381_at	LRP3	low density lipoprotein receptor-related protein 3	-1.35	NM_002333

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
209233_at	EMG1	EMG1 nucleolar protein homolog (S. cerevisiae)	-1.35	U72514
212218_s_at	FASN	fatty acid synthase	-1.35	AI954041
218322_s_at	ACSL5	acyl-CoA synthetase long-chain family member 5	-1.35	NM_016234
220417_s_at	THAP4 /// LOC728944	THAP domain containing 4 /// similar to THAP domain-containing protein 4	-1.35	NM_015963
221692_s_at	MRPL34	mitochondrial ribosomal protein L34 /// mitochondrial ribosomal protein L34	-1.35	AB049652
201587_s_at	IRAK1	interleukin-1 receptor-associated kinase 1	-1.38	NM_001569
201819_at	SCARB1	scavenger receptor class B, member 1	-1.38	NM_005505
204175_at	ZNF593	zinc finger protein 593	-1.38	NM_015871
204852_s_at	PTPN7	protein tyrosine phosphatase, non-receptor type 7	-1.38	NM_002832
209409_at	GRB10	growth factor receptor-bound protein 10	-1.38	D86962
209516_at	SMYD5	SMYD family member 5	-1.38	U50383
212432_at	GRPEL1	GrpE-like 1, mitochondrial (E. coli)	-1.38	AL542571
218695_at	EXOSC4	exosome component 4	-1.38	NM_019037
219559_at	C20orf59	chromosome 20 open reading frame 59	-1.38	NM_022082
220234_at	CA8	carbonic anhydrase VIII	-1.38	NM_004056
203622_s_at	PNO1	partner of NOB1 homolog (S. cerevisiae)	-1.4	NM_020143
205527_s_at	GEMIN4	gem (nuclear organelle) associated protein 4	-1.4	NM_015487
209196_at	WDR46	WD repeat domain 46	-1.4	BC000388
214022_s_at	IFITM1	interferon induced transmembrane protein 1 (9-27)	-1.4	AA749101
218710_at	TTC27	tetratricopeptide repeat domain 27	-1.4	NM_017735
200598_s_at	HSP90B1	heat shock protein 90 kDa beta (Grp94), member 1	-1.43	AI582238
201601_x_at	IFITM1	interferon induced transmembrane protein 1 (9-27)	-1.43	NM_003641
201920_at	SLC20A1	solute carrier family 20 (phosphate transporter), member 1	-1.43	NM_005415
203074_at	ANXA8 /// ANXA8L1 /// LOC728113	annexin A8 /// annexin A8-like 1 /// similar to Annexin A8 (Annexin VIII) (Vascular anticoagulant-beta) (VAC-beta)	-1.43	NM_001630
204019_s_at	SH3YL1	SH3 domain containing, Ysc84-like 1 (S. cerevisiae)	-1.43	NM_015677
205883_at	ZBTB16	zinc finger and BTB domain containing 16	-1.43	NM_006006
209567_at	RRS1	RRS1 ribosome biogenesis regulator homolog (S. cerevisiae)	-1.43	BC001811
213302_at	PFAS	phosphoribosylformylglycinamide synthase (FGAR amidotransferase)	-1.43	AL044326
221766_s_at	FAM46A	family with sequence similarity 46, member A	-1.43	AW246673
65588_at	LOC388796	hypothetical LOC388796	-1.43	AA827892
203867_s_at	NLE1	notchless homolog 1 (Drosophila)	-1.45	NM_018096
204548_at	STAR	steroidogenic acute regulator	-1.45	NM_000349
205891_at	ADORA2B	adenosine A2b receptor	-1.45	NM_000676
210999_s_at	GRB10	growth factor receptor-bound protein 10	-1.45	U66065
212512_s_at	CARM1	coactivator-associated arginine methyltransferase 1	-1.45	AA551784
213861_s_at	FAM119B	family with sequence similarity 119, member B	-1.45	N67741
221772_s_at	PPP2R2D	protein phosphatase 2, regulatory subunit B, delta isoform	-1.45	AI138993
201925_s_at	CD55	CD55 molecule, decay accelerating factor for complement (Cromer blood group)	-1.48	NM_000574
208152_s_at	DDX21	DEAD (Asp-Glu-Ala-Asp) box polypeptide 21	-1.48	NM_004728
212680_x_at	PPP1R14B	protein phosphatase 1, regulatory (inhibitor) subunit 14B	-1.48	BE305165
201563_at	SORD	sorbitol dehydrogenase	-1.5	L29008
203973_s_at	CEBPD	CCAAT/enhancer binding protein (C/EBP), delta	-1.5	NM_005195
205774_at	F12	coagulation factor XII (Hageman factor)	-1.5	NM_000505
210783_x_at	CLEC11A	C-type lectin domain family 11, member A	-1.5	D86586
212110_at	SLC39A14	solute carrier family 39 (zinc transporter), member 14	-1.5	D31887
212456_at	KIAA0664	KIAA0664	-1.5	AB014564
213097_s_at	ZRF1	zuotin related factor 1	-1.5	AI338837
219581_at	TSEN2	tRNA splicing endonuclease 2 homolog (S. cerevisiae)	-1.5	NM_025265
201516_at	SRM	spermidine synthase	-1.53	NM_003132
218670_at	PUS1	pseudouridylate synthase 1	-1.53	NM_025215
220446_s_at	CHST4	carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 4	-1.53	NM_005769
203997_at	PTPN3	protein tyrosine phosphatase, non-receptor type 3	-1.55	NM_002829
204521_at	C12orf24	chromosome 12 open reading frame 24	-1.55	NM_013300
204695_at	CDC25A	cell division cycle 25 homolog A (S. cerevisiae)	-1.55	AI343459

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
206397_x_at	GDF1 /// LASS1	growth differentiation factor 1 /// LAG1 homolog, ceramide synthase 1 (S. cerevisiae)	-1.55	NM_001492
208712_at	CCND1	cyclin D1	-1.55	M73554
213113_s_at	SLC43A3	solute carrier family 43, member 3	-1.55	AI630178
213823_at	HOXA11	homeobox A11	-1.55	H94842
216602_s_at	FARSLA	phenylalanine-tRNA synthetase-like, alpha subunit	-1.55	AD000092
203150_at	RABEPK	Rab9 effector protein with kelch motifs	-1.58	NM_005833
204027_s_at	METTL1	methyltransferase like 1	-1.58	NM_005371
205349_at	GNA15	guanine nucleotide binding protein (G protein), alpha 15 (Gq class)	-1.58	NM_002068
205945_at	IL6R	interleukin 6 receptor /// interleukin 6 receptor	-1.58	NM_000565
206613_s_at	TAF1A	TATA box binding protein (TBP)-associated factor, RNA polymerase I, A, 48 kDa	-1.58	NM_005681
218199_s_at	NOL6	nucleolar protein family 6 (RNA-associated)	-1.58	NM_022917
218886_at	PAK1IP1 /// C20orf7	PAK1 interacting protein 1 /// chromosome 20 open reading frame 7	-1.58	NM_017906
202431_s_at	MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	-1.6	NM_002467
202444_s_at	SPFH1	SPFH domain family, member 1	-1.6	NM_006459
203737_s_at	PPRC1	peroxisome proliferator-activated receptor gamma, coactivator-related 1	-1.6	NM_015062
218358_at	CCNK	Cyclin K	-1.6	NM_024324
219837_s_at	CYTL1	cytokine-like 1	-1.6	NM_018659
221712_s_at	WDR74	WD repeat domain 74 /// WD repeat domain 74	-1.6	BC006351
200952_s_at	CCND2	cyclin D2	-1.63	AI635187
216212_s_at	DKC1	dyskeratosis congenita 1, dyskerin	-1.63	AJ010395
219324_at	TRIOBP /// NOL12	TRIO and F-actin binding protein /// nucleolar protein 12	-1.63	NM_024313
220051_at	PRSS21	protease, serine, 21 (testisin)	-1.63	NM_006799
221649_s_at	PPAN	peter pan homolog (Drosophila)	-1.63	BC000535
202715_at	CAD /// ARHGEF5 /// LOC653691	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase /// Rho guanine nucleotide exchange factor (GEF) 5 /// FLJ40722-like	-1.65	NM_004341
209930_s_at	NFE2	nuclear factor (erythroid-derived 2), 45 kDa	-1.65	L13974
210147_at	ART3	ADP-ribosyltransferase 3	-1.65	U47054
216449_x_at	HSP90B1	heat shock protein 90 kDa beta (Grp94), member 1	-1.65	AK025862
218156_s_at	TSR1	TSR1, 20S rRNA accumulation, homolog (S. cerevisiae)	-1.65	NM_018128
200659_s_at	PHB	prohibitin	-1.68	NM_002634
200895_s_at	FKBP4	FK506 binding protein 4, 59 kDa	-1.68	NM_002014
200935_at	CALR	calreticulin	-1.68	NM_004343
202345_s_at	FABP5 /// LOC728641 /// LOC729163 /// LOC731043 /// LOC732031	fatty acid binding protein 5 (psoriasis-associated) /// similar to Fatty acid-binding protein, epidermal (E-FABP) (Psoriasis-associated fatty acid-binding protein homolog) (PA-FABP) /// similar to Fatty acid-binding protein, epidermal (E-FABP) (Psoriasis-	-1.68	NM_001444
206111_at	RNASE2	ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin)	-1.68	NM_002934
209892_at	FUT4	fucosyltransferase 4 (alpha (1,3) fucosyltransferase, myeloid-specific)	-1.68	AF305083
217489_s_at	IL6R	interleukin 6 receptor	-1.68	S72848
200953_s_at	CCND2	cyclin D2	-1.7	NM_001759
204514_at	DPH2	DPH2 homolog (S. cerevisiae)	-1.7	NM_001384
206653_at	POLR3 G	polymerase (RNA) III (DNA directed) polypeptide G (32kD)	-1.7	BF062139
214369_s_at	RASGRP2	RAS guanyl releasing protein 2 (calcium and DAG-regulated)	-1.7	AI688812
218893_at	ISOC2	isochorismatase domain containing 2	-1.7	NM_024710
200894_s_at	FKBP4	FK506 binding protein 4, 59 kDa	-1.73	AA894574
203397_s_at	GALNT3	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3)	-1.73	BF063271
211715_s_at	BDH1	3-hydroxybutyrate dehydrogenase, type 1 /// 3-hydroxybutyrate dehydrogenase, type 1	-1.73	BC005844
219361_s_at	ISG20L1	interferon stimulated exonuclease gene 20 kDa-like 1	-1.73	NM_022767
201562_s_at	SORD /// LOC653381	sorbitol dehydrogenase /// similar to Sorbitol dehydrogenase (L-idoitol 2-dehydrogenase)	-1.75	NM_003104
203948_s_at	MPO	myeloperoxidase	-1.75	J02694
209710_at	GATA2	GATA binding protein 2	-1.75	AL563460

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Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
219295_s_at	PCOLCE2	procollagen C-endopeptidase enhancer 2	-1.75	NM_013363
221586_s_at	E2F5	E2F transcription factor 5, p130-binding	-1.75	U15642
202241_at	TRIB1	tribbles homolog 1 (Drosophila)	-1.78	NM_025195
202759_s_at	AKAP2 /// PALM2- AKAP2	A kinase (PRKA) anchor protein 2 /// PALM2-AKAP2 protein	-1.78	BE879367
205896_at	SLC22A4	solute carrier family 22 (organic cation transporter), member 4	-1.78	NM_003059
213524_s_at	G0S2	G0/G1switch 2	-1.78	NM_015714
218590_at	PEO1	progressive external ophthalmoplegia 1	-1.78	NM_021830
201841_s_at	HSPB1 /// MEIS3	heat shock 27 kDa protein 1 /// Meis1, myeloid ecotropic viral integration site 1 homolog 3 (mouse)	-1.8	NM_001540
204087_s_at	SLC5A6	solute carrier family 5 (sodium-dependent vitamin transporter), member 6	-1.8	NM_021095
205131_x_at	CLEC11A	C-type lectin domain family 11, member A	-1.8	NM_002975
205471_s_at	DACH1	dachshund homolog 1 (Drosophila)	-1.8	AW772082
210692_s_at	SLC43A3	solute carrier family 43, member 3	-1.8	BC003163
213142_x_at	LOC54103	hypothetical protein LOC54103	-1.8	AV700415
216950_s_at	FCGR1A	Fc fragment of IgG, high affinity Ia, receptor (CD64)	-1.8	X14355
205476_at	CCL20	chemokine (C-C motif) ligand 20	-1.83	NM_004591
209731_at	NTHL1	nth endonuclease III-like 1 (E. coli)	-1.83	U79718
60474_at	C20orf42	chromosome 20 open reading frame 42	-1.83	AA469071
201796_s_at	VARS	valyl-tRNA synthetase	-1.85	BE790854
209777_s_at	SLC19A1	solute carrier family 19 (folate transporter), member 1	-1.85	AF004354
201508_at	IGFBP4	insulin-like growth factor binding protein 4	-1.88	NM_001552
201695_s_at	NP	nucleoside phosphorylase	-1.88	NM_000270
204301_at	KBTBD11	kelch repeat and BTB (POZ) domain containing 11	-1.88	NM_014867
221648_s_at	—	—	-1.88	AK025651
203148_s_at	TRIM14	tripartite motif-containing 14	-1.9	NM_014788
211576_s_at	SLC19A1	solute carrier family 19 (folate transporter), member 1	-1.9	BC003068
214575_s_at	AZU1	azurocidin 1 (cationic antimicrobial protein 37)	-1.9	NM_001700
214011_s_at	HSPC111	hypothetical protein HSPC111	-1.93	BE314601
214511_x_at	FCGR1B	Fc fragment of IgG, high affinity Ib, receptor (CD64)	-1.93	L03419
216913_s_at	RRP12	ribosomal RNA processing 12 homolog (S. cerevisiae)	-1.93	AK021460
202760_s_at	AKAP2 /// PALM2-AKAP2	A kinase (PRKA) anchor protein 2 /// PALM2-AKAP2 protein	-1.95	NM_007203
206655_s_at	GP1BB /// SEPT5	glycoprotein Ib (platelet), beta polypeptide /// septin 5	-1.95	NM_000407
216667_at	RNASE2 /// LOC643332	ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin) /// similar to Nonsecretory ribonuclease precursor (Ribonuclease US) (Eosinophil-derived neurotoxin) (RNase UpI-2) (Ribonuclease 2) (RNase 2)	-1.95	X55989
204647_at	HOMER3	homer homolog 3 (Drosophila)	-1.98	NM_004838
210008_s_at	MRPS12	mitochondrial ribosomal protein S12	-1.98	AA513737
220688_s_at	MRT4	mRNA turnover 4 homolog (S. cerevisiae)	-1.98	NM_016183
204717_s_at	SLC29A2	solute carrier family 29 (nucleoside transporters), member 2	-2	AF034102
205419_at	EBI2	Epstein-Barr virus induced gene 2 (lymphocyte-specific G protein-coupled receptor)	-2	NM_004951
201195_s_at	SLC7A5	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5	-2.03	AB018009
208206_s_at	RASGRP2	RAS guanyl releasing protein 2 (calcium and DAG-regulated)	-2.03	NM_005825
209100_at	IFRD2	interferon-related developmental regulator 2	-2.03	BC001327
203023_at	HSPC111	hypothetical protein HSPC111	-2.05	NM_016391
204798_at	MYB	v-myb myeloblastosis viral oncogene homolog (avian)	-2.05	NM_005375
210140_at	CST7	cystatin F (leukocystatin)	-2.05	AF031824
203119_at	CCDC86	coiled-coil domain containing 86	-2.08	NM_024098
213395_at	MLC1	megalencephalic leukoencephalopathy with subcortical cysts 1	-2.13	AL022327
206851_at	RNASE3	ribonuclease, RNase A family, 3 (eosinophil cationic protein)	-2.18	NM_002935
206267_s_at	MATK	megakaryocyte-associated tyrosine kinase	-2.2	NM_002378
215806_x_at	TRGC2 /// TRGV9 /// TARP	T cell receptor gamma constant 2 /// T cell receptor gamma variable 9 /// TCR gamma alternate reading frame protein	-2.23	M13231

(continued)

Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
216920_s_at	TRGC2 /// TRGV9 /// TARP	T cell receptor gamma constant 2 /// T cell receptor gamma variable 9 /// TCR gamma alternate reading frame protein	-2.23	M27331
218305_at	IPO4	importin 4	-2.23	NM_024658
222150_s_at	LOC54103	hypothetical protein LOC54103	-2.23	AK026747
214452_at	BCAT1	branched chain aminotransferase 1, cytosolic	-2.25	NM_005504
215489_x_at	HOMER3	homer homolog 3 (Drosophila)	-2.25	AI871287
221270_s_at	QTRT1	queuine tRNA-ribosyltransferase 1 (tRNA-guanine transglycosylase) /// queuine tRNA-ribosyltransferase 1 (tRNA-guanine transglycosylase)	-2.3	NM_031209
200951_s_at	CCND2	cyclin D2	-2.33	AW026491
219568_x_at	SOX18	SRY (sex determining region Y)-box 18	-2.35	NM_018419
209813_x_at	TRGC2 /// TRGV9 /// TARP	T cell receptor gamma constant 2 /// T cell receptor gamma constant 2 /// T cell receptor gamma variable 9 /// T cell receptor gamma variable 9 /// TCR gamma alternate reading frame protein /// TCR gamma alternate reading frame protein	-2.38	M16768
211144_x_at	TRGC2 /// TRGV9 /// TARP	T cell receptor gamma constant 2 /// T cell receptor gamma variable 9 /// TCR gamma alternate reading frame protein	-2.38	M30894
219911_s_at	SLCO4A1	solute carrier organic anion transporter family, member 4A1	-2.38	NM_016354
206103_at	RAC3	ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	-2.4	NM_005052
207397_s_at	HOXD13	homeobox D13	-2.4	NM_000523
205130_at	RAGE	renal tumor antigen	-2.43	NM_014226
209906_at	C3AR1	complement component 3a receptor 1	-2.45	U62027
211382_s_at	TACC2	transforming, acidic coiled-coil containing protein 2	-2.45	AF220152
214390_s_at	BCAT1	branched chain aminotransferase 1, cytosolic	-2.48	AI652662
220112_at	ANKRD55	ankyrin repeat domain 55	-2.48	NM_024669
203548_s_at	LPL	lipoprotein lipase	-2.5	BF672975
210036_s_at	KCNH2	potassium voltage-gated channel, subfamily H (eag-related), member 2	-2.5	AB044806
221197_s_at	CHAT	choline acetyltransferase	-2.53	NM_020985
214240_at	GAL	galanin	-2.55	AL556409
210755_at	HGF	hepatocyte growth factor (hepapoietin A; scatter factor)	-2.6	U46010
209129_at	TRIP6	thyroid hormone receptor interactor 6	-2.65	AF000974
214788_x_at	DDN	dendrin	-2.73	AA731713
202382_s_at	GNPDA1	glucosamine-6-phosphate deaminase 1	-2.75	NM_005471
220798_x_at	PRG2	plasticity-related gene 2	-2.83	NM_024888
204163_at	EMILIN1	elastin microfibril interfacer 1	-2.85	NM_007046
219926_at	POPDC3	popeye domain containing 3	-2.9	NM_022361
218796_at	C20orf42	chromosome 20 open reading frame 42	-2.93	NM_017671
205472_s_at	DACH1	dachshund homolog 1 (Drosophila)	-2.95	NM_004392
211273_s_at	TBX1	T-box 1	-2.95	AF012130
209775_x_at	SLC19A1	solute carrier family 19 (folate transporter), member 1	-3.08	AI917627
209776_s_at	SLC19A1	solute carrier family 19 (folate transporter), member 1	-3.2	U15939
211966_at	COL4A2	collagen, type IV, alpha 2	-3.33	AA909035
207199_at	TERT	telomerase reverse transcriptase	-3.38	NM_003219
201667_at	GJA1	gap junction protein, alpha 1, 43 kDa (connexin 43)	-3.45	NM_000165
206277_at	P2RY2	purinergic receptor P2Y, G-protein coupled, 2	-3.5	NM_002564
211964_at	COL4A2	collagen, type IV, alpha 2	-3.55	X05610
219799_s_at	DHRS9	dehydrogenase/reductase (SDR family) member 9	-3.58	NM_005771
204420_at	FOSL1	FOS-like antigen 1	-3.6	BG251266
217143_s_at	TRA@ /// TRD@	T cell receptor alpha locus /// T cell receptor delta locus	-3.63	X06557
216191_s_at	TRA@ /// TRD@ /// BCL11B	T cell receptor alpha locus /// T cell receptor delta locus /// B-cell CLL/lymphoma 11B (zinc finger protein)	-3.65	X72501
207341_at	PRTN3	proteinase 3 (serine proteinase, neutrophil, Wegener granulomatosis autoantigen)	-3.7	NM_002777
222222_s_at	HOMER3	homer homolog 3 (Drosophila)	-3.7	AC002985
213589_s_at	B3GNTL1	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase-like 1	-3.85	AW468201
207067_s_at	HDC	histidine decarboxylase	-4	NM_002112

(continued)

Supplementary Table E2 (continued)

Probe set ID	Gene symbol	Gene title	Average SLR	Representative public ID
210254_at	MS4A3	membrane-spanning 4-domains, subfamily A, member 3 (hematopoietic cell-specific)	−4.03	L35848
205653_at	CTSG	cathepsin G	−4.35	NM_001911
213830_at	TRA@	T cell receptor alpha locus	−4.45	AW007751
205262_at	KCNH2	potassium voltage-gated channel, subfamily H (eag-related), member 2	−4.68	NM_000238
219491_at	LRFN4	leucine rich repeat and fibronectin type III domain containing 4	−5.08	NM_024036
209960_at	HGF	hepatocyte growth factor (hepapoietin A; scatter factor)	−6.6	X16323

SLR = signal log ratio.

Supplementary Table E3A. GO Categories increased in WEB-2170-treated vs untreated NB4 cells

GO Name	<i>p Value</i>
cell death	6.63E-05
death	7.30E-05
cell proliferation	2.08E-04
negative regulation of cell proliferation	3.08E-04
apoptosis	3.27E-04
programmed cell death	3.41E-04
regulation of apoptosis	0
regulation of programmed cell death	0
regulation of cell cycle	0.01
negative regulation of progression through cell cycle	0.01
positive regulation of biological process	0.01
positive regulation of apoptosis	0.01
positive regulation of programmed cell death	0.01
regulation of progression through cell cycle	0.01
induction of programmed cell death	0.02
induction of apoptosis	0.02
response to stress	0.02
negative regulation of cell-matrix adhesion	0.03
apoptotic program	0.04
cellular catabolism	0.04
regulation of signal transduction	0.04
positive regulation of caspase activity	0.05
caspase activation	0.05
regulation of caspase activity	0.05

Supplementary Table E3B. GO Categories decreased in WEB-2170-treated vs untreated NB4 cells

GO Name	<i>pValue</i>
ribosome biogenesis and assembly	2.00E-09
RNA metabolism	9.12E-07
rRNA metabolism	2.85E-06
cellular physiological process	6.75E-06
cell proliferation	3.43E-05
tRNA metabolism	2.10E-04
tRNA processing	2.25E-04
macromolecule metabolism	0
amine metabolism	0
anti-apoptosis	0
cellular biosynthesis	0.01
negative regulation of apoptosis	0.01
negative regulation of programmed cell death	0.01
cellular metabolism	0.01
di-, tri-valent inorganic cation homeostasis	0.01
protein import	0.01
amino acid metabolism	0.01
organelle organization and biogenesis	0.02
transcription from RNA polymerase II promoter	0.02
positive regulation of cell proliferation	0.03
regulation of cell cycle	0.03
cell cycle	0.03
regulation of apoptosis	0.03
regulation of programmed cell death	0.03
positive regulation of biological process	0.05