

Impact of Phosphodiesterase 4 Inhibition on the Operational Efficacy, Response Maxima and Kinetics of Indacaterol-induced Gene Expression Changes in BEAS-2B Airway Epithelial Cells: A Global Transcriptomic Analysis

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Running Head: Genomic effects of PDE4 inhibitors in airway epithelia

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ABBREVIATIONS: AE, adverse effect; ANOVA, analysis of variance; ASM, airways smooth muscle; AUC_{0-18h}, area under the curve from 0 to 18h; β 2A, 8-hydroxy-5-((*R*)-1-hydroxy-2-methylaminoethyl)-1*H*-quinolin-2-one; COPD, chronic obstructive pulmonary disease; CRE, cAMP response element; CREB, cAMP response element binding protein; DAVID, database for visualization and integrated discovery; DCITC, 5(2-(((1'-(4'-isothiocyanatophenylamino)thiocarbonyl)amino)-2-methylpropyl)amino-2-hydroxypropoxy)-3,4-dihydrocarbostyryl; DEGs, differentially-expressed genes; DMEM, Dulbecco's modified Eagle's medium; *E*, pharmacological effect; FCS, fetal calf serum; FDR, false discovery rate; GO, gene ontology; GSK 256066, 6-[3-(dimethylcarbamoyl)benzenesulphonyl]-4-[(3-methoxyphenyl)amino]-8-methylquinoline-3-carboxamide; HGNC, human genome nomenclature committee; ICS, inhaled corticosteroid; IL-6, interleukin-6; Ind+GSK, indacaterol and GSK 256066 in combination; KEGG, Kyoto encyclopedia of genes and genomes; LABA, long-acting β ₂-adrenoceptor agonist; LAMA, long-acting muscarinic receptor antagonist; *n*_H, Hill coefficient; PDE, phosphodiesterase; RNO, roflumilast *N*-oxide; Salm_{0.3}, salmeterol 0.3nM; Salm_{0.5}, salmeterol 0.5nM; Salm₁₀₀, salmeterol 100nM; SFM, serum-free medium; TAC, transcriptome analysis console; TPM, transcripts per million.

ABSTRACT

The effects of phosphodiesterase (PDE) 4 inhibitors on gene expression changes in BEAS-2B human airway epithelial cells are reported and discussed in relation to the mechanism(s) of action of roflumilast in chronic obstructive pulmonary disease (COPD). Microarray-based gene expression profiling failed to identify mRNA transcripts that were differentially regulated by the PDE4 inhibitor, GSK 256066 after 1, 2, 6 or 18h of exposure. However, real-time PCR analysis revealed that GSK 256066 was a weak stimulus and the negative microarray results reflected low statistical power due to small sample sizes. Furthermore, GSK 256066, roflumilast and its biologically-active metabolite, roflumilast *N*-oxide, generally potentiated gene expression changes produced by the long-acting β_2 -adrenoceptor agonists (LABAs), salmeterol, indacaterol and formoterol. Many of these genes encode proteins with anti-viral, anti-inflammatory and anti-bacterial activities that could contribute to the clinical efficacy of roflumilast in COPD. RNA-Seq experiments established that the sensitivity of genes to salmeterol varied by ~7.5-fold. Consequently, the degree to which a PDE4 inhibitor potentiated the effect of a given concentration of LABA was gene dependent. Operational model fitting of concentration-response curve data from cells subjected to fractional, β_2 -adrenoceptor inactivation determined that PDE4 inhibition increased the potency and doubled the efficacy of LABAs. Thus, adding-on roflumilast to standard triple therapy, as COPD guidelines recommend, may have clinical relevance especially in target tissues where LABAs behave as partial agonists. Collectively, these results suggest that the genomic impact of roflumilast, including its ability to augment LABA-induced gene expression changes, may contribute to its therapeutic activity in COPD.

Introduction

Phosphodiesterase (PDE) 4 inhibitors entered clinical development in the 1980s as potential anti-depressant drugs (Zeller et al., 1984) and, since that time, have suffered a high level of attrition due to a low therapeutic ratio and weak efficacy (Giembycz, 2008). Nevertheless, in April 2010, roflumilast became the first, selective, orally-active, PDE4 inhibitor to be approved for human use with chronic obstructive pulmonary disease (COPD) being a primary indication (Giembycz and Field, 2010; Gross et al., 2010; Wedzicha et al., 2016). The 2019 Global Initiative for Chronic Obstructive Lung Disease guidelines recommend that roflumilast be used as an add-on therapy in a specific sub-group of patients with COPD. These are categorised as high risk, having severe, symptomatic disease in whom exacerbations occur despite regular treatment with a combination of a long-acting β_2 -adrenoceptor agonist (LABA), a long-acting muscarinic receptor antagonist (LAMA) and an inhaled corticosteroid (ICS) (<http://goldcopd.org>). In this COPD phenotype, the therapeutic activity of roflumilast relies on its ability to improve airway calibre. However, PDE4 inhibitors do not promote acute bronchodilatation (Grootendorst et al., 2003), suggesting that the gain in lung function and associated reduction in exacerbation frequency are unrelated to direct airways smooth muscle (ASM) relaxation. Instead, preclinical studies and trials of roflumilast in human subjects suggest a primary mode of action is to suppress inflammation (Gamble et al., 2003; Giembycz and Newton, 2014; Grootendorst et al., 2007; Hatzelmann et al., 2010; Moodley et al., 2013).

Another selective, orally-active PDE4 inhibitor, apremilast, was approved in 2015 for the treatment of plaque psoriasis and psoriatic arthritis (Fala, 2015). Similar to the COPD phenotype for which roflumilast is indicated, these disorders are characterised by a chronic, systemic dysregulation of cytokine generation with attendant inflammation, implying that PDE4 inhibitors may share the same or a similar mechanism of action (Pincelli et al., 2018).

At a molecular level, inhibition of PDE4 increases the intracellular concentration of cAMP in target cells and tissues. While the downstream signalling pathways that ultimately lead to improved clinical outcomes are ill defined, cAMP is known to modulate gene expression by activating a family of transcription factors of which cAMP response element-binding protein (CREB) and activating

transcription factor-1 are prototypical examples (Zhang et al., 2005). Recently, we reported that the LABAs, indacaterol and salmeterol, promoted significant, and potentially beneficial, gene expression changes in BEAS-2B airway epithelial cells and human primary bronchial epithelia by mechanisms that involve canonical, G α /adenylyl cyclase/cAMP-dependent signalling (Yan et al., 2018). Therefore, logic dictates that PDE4 inhibitors may also provide clinical benefit by modulating gene expression (BinMahfouz et al., 2015; Giembycz and Maurice, 2014; Joshi et al., 2017; Moodley et al., 2013; Tannheimer et al., 2012). A genomic, anti-inflammatory mechanism of action also accommodates the likelihood that ASM is but one of several tissues that are therapeutic targets of orally-active PDE4 inhibitors. In this respect, the airway epithelium, which is considered a major player in COPD pathogenesis (Crystal, 2014), and extrapulmonary tissues including circulating leukocytes, the vascular endothelium and the bone marrow are attractive additional candidates. Indeed, the need for systemic exposure may help explain why PDE4 inhibitors developed for inhaled administration have, without exception, failed in clinical trials of COPD.

In this study, we hypothesised that PDE4 inhibitors work, in part, by genomic mechanisms and interact in additive or synergistic manner with LABAs. To test this idea, the transcriptomic signatures of two, highly selective PDE4 inhibitors, roflumilast *N*-oxide (RNO), the active metabolite of roflumilast (Hatzelmann et al., 2010), and GSK 256066 (6-[3-(dimethylcarbamoyl)benzenesulphonyl]-4-[(3-methoxyphenyl)amino]-8-methylquinoline-3-carboxamide; Tralau-Stewart et al., 2011) were obtained in BEAS-2B human airway epithelial cells treated alone and concurrently with a LABA. In addition, the impact of PDE4 inhibitors on the operational efficacy, magnitude of response and duration of action of LABA-induced gene expression changes was determined. BEAS-2B cells were selected for this investigation because they display gene expression profiles that mirror, to a large degree, those obtained in human primary bronchial epithelial cells treated with a variety of stimuli including LABAs (Yan et al., 2018).

Materials and Methods

Drugs and Reagents. GSK 256066, indacaterol and β 2A (8-hydroxy-5-((*R*)-1-hydroxy-2-methylaminoethyl)-1*H*-quinolin-2-one) were provided by Gilead Sciences (Seattle, WA). Salmeterol and formoterol were donated by GlaxoSmithKline (Stevenage, UK) and AstraZeneca (Mölndal, Sweden), respectively. Roflumilast and RNO were from Nycomed (Konstanz, Germany). DCITC (5(2-(((1'-(4'-isothiocyanatophenylamino)thiocarbonyl)amino)-2-methylpropyl)amino-2-hydroxypropoxy)-3,4-dihydrocarbostyryl) was a gift from Dr. Stephen Baker (University of Florida, FL). All drugs were dissolved in DMSO and diluted in serum-free medium (SFM). The highest concentration of DMSO used in these experiments (0.2% v/v) did not affect any output measured.

Generation of a CRE Reporter in BEAS-2B Cells. Cells were transfected with 8 μ g of plasmid DNA (pADneo2-C6-BGL) using Lipofectamine 2000 (Invitrogen, Burlington, ON, Canada) to generate 6 \times CRE BEAS-2B luciferase reporter cells as described previously (Meja et al., 2004).

Submersion Culture of BEAS-2B Cells. BEAS-2B cells were cultured under a 5% CO₂/air atmosphere at 37°C in 12- or 24-well plastic plates (Corning Life Sciences, Lowell, MA) containing keratinocyte-SFM (ThermoFisher Scientific, Burlington Ontario) supplemented with epidermal growth factor (5ng/ml), bovine pituitary extract (50 μ g/ml), penicillin (100mg/ml) and streptomycin (100IU/ml). When confluent, cells were growth-arrested for 24h in keratinocyte-SFM without supplements (Greer et al., 2013) and processed as described below. For RNA-seq and subsequent validation experiments, BEAS-2B cells were grown in Dulbecco's modified Eagle's/Ham's F12 medium containing 10% fetal bovine serum, 2.5mM L-glutamine and 14mM NaHCO₃ (all Invitrogen) until confluent, and for a further 24h in SFM.

Measurement of Luciferase Activity. 6 \times CRE BEAS-2B reporter cells were treated with PDE4 inhibitor (GSK 256066, roflumilast or RNO) or LABA (indacaterol, salmeterol or formoterol) alone and in the combinations indicated in the text. After 6h, cells were lysed in 1 \times firefly luciferase buffer (Biotium, Hayward, CA) and luciferase activity was measured by luminometry. Data are expressed as fold increase in enzyme activity relative to vehicle-treated samples matched for time.

Western Blot Analyses and ELISAs. Confluent BEAS-2B cells at 37°C were incubated with RNO (1µM) and/or salmeterol (100nM). At 60min, the culture medium was decanted and cells were lysed in HCl (0.1M). cAMP in the resulting lysates was measured by ELISAs (Enzo Life Sciences, Farmingdale, NY) according to the manufacturer's instructions. Alternatively, cells were incubated with GSK 256066 and indacaterol alone and in combination at the concentrations indicated. At 6h supernatants were collected and interleukin-6 (IL-6) was measured by ELISA (D6050; R&D Systems, Minneapolis, MN). Cells were lysed in 1× Laemmli buffer supplemented with phosphatase inhibitors (Sigma-Aldrich) and 1× complete protease inhibitor cocktail (Roche, Indianapolis, IN). The cell lysates were size fractionated on 10% acrylamide gels, electrotransferred onto reinforced 0.2µM nitrocellulose membranes (GE Healthcare, Waukesha, WI) and blocked with 5% milk in Tris-buffered saline containing 1% Tween 20. Subsequently, membranes were probed with antibodies against NR4A2 (PP-N1404-00), NR4A3 (PP-H7833-00; both Perseus Proteomics Inc., Tokyo), and GAPDH (MCA4739; Bio-Rad, Hercules, CA). After washing, membranes were incubated with horseradish peroxidase-conjugated, anti-mouse immunoglobulin (115-035-003; Jackson ImmunoResearch Laboratories Inc., West Grove, PA). Proteins were detected by chemiluminescence using SuperSignal™ West Pico PLUS chemiluminescent substrate (#34580, ThermoFisher Scientific), visualized by autoradiography and expressed relative to GAPDH. Preliminary studies verified the identity of NR4A2 and NR4A3 by gene silencing (data not shown).

Measurement of Gene Expression by Real-time PCR. BEAS-2B cells were treated with PDE4 inhibitor and/or LABA as described above. Total RNA was extracted (RNeasy Mini Kit, Qiagen Inc., Mississauga, ON, Canada) and reverse transcribed using a qscript cDNA synthesis kit according to the manufacturer's instructions (Quanta Biosciences, Gaithersburg, MD). Real-time PCR analysis of cDNA was performed using the primer sequences shown in supplemental table 1 as described previously (Joshi et al., 2017; Yan et al., 2018).

Gene Expression Profiling by Microarray. BEAS-2B cells were cultured for 1, 2, 6 and 18h ($N = 4$ at each time-point) with vehicle, GSK 256066 (10nM) and a concentration of indacaterol (10nM) that maximally activated 6×CRE reporter cells (Supplemental Fig. 1). Cells were also treated with

indacaterol and GSK 256066 in combination (Ind+GSK, both 10nM) under identical conditions. Total RNA was extracted (*vide supra*) and processed for gene expression profiling (Yan et al., 2018). The microarray images were scaled and normalised using the probe logarithmic intensity error algorithm in Transcriptome Analysis Console (TAC, v4.0; Affymetrix, Santa Clara, CA) and stored as .chp files. Signals from the four replicates for each probe set were averaged and the relative expression patterning was implemented in TAC. At each time-point, data from all treatments were analysed concurrently and visualized by generating volcano plots. The *P* statistic was adjusted using the Benjamini and Hochberg false discovery rate (FDR), with step-up procedure, and significance was set to the <0.1, <0.05 and <0.01 probability levels as indicated.

Gene Expression Profiling by RNA-Seq. BEAS-2B cells were treated for 2h with vehicle, RNO (1 μ M) and two, submaximal concentrations of salmeterol (0.3nM [Salm_{0.3}] and 0.5nM [Salm_{0.5}]) alone and in the presence of RNO (1 μ M). A maximally-effective concentration of salmeterol (100nM, Salm₁₀₀) was examined in parallel to define maximum responses. Total RNA was extracted as described above and a total of 28 samples (*N* = 4 per treatment group) were submitted to the Centre for Health Genomics and Informatics, University of Calgary, for sequencing.

RNA sequencing libraries were prepared using the NEBNext Ultra II Directional kit (New England Biolabs, Ipswich, MA) with the poly(A) mRNA magnetic isolation module as described by the manufacturer. The libraries were validated by using the D1000 Screen Tape assay on an Agilent 2200 TapeStation system (Agilent Technologies, Santa Clara, CA) and quantified with a Kapa qPCR Library Quantification kit for Illumina (Kapa Biosystems, Boston, MA). The libraries were pooled and sequenced across two consecutive, single end, 75 cycle sequencing runs on a NextSeq 500 instrument (Illumina, San Diego, CA) according to the manufacturer's instructions, generating approximately 33 million reads per sample.

Demultiplexing of the sequencing data and read quality of each sample were performed using bcl2fastq conversion software (v2.18.0.12, Illumina) and FastQC (v0.10.1) respectively. Good-quality reads were mapped to the reference human transcriptome (GRCh37/hg19 version) and quantified by using Kallisto

(v0.42.4) (Bray et al., 2016) with 100 bootstraps per sample. Differential expression analysis was performed at the transcript and gene level using the *R* package, Sleuth (v0.30.0) (Pimentel et al., 2017). Pairwise comparisons were performed between vehicle- and salmeterol (100nM)-treated samples, and differentially-expressed genes (DEGs) were identified based on a FDR-corrected *P* value of ≤ 0.05 . Induced (≥ 2 -fold) and repressed (≤ 0.5 -fold) genes were filtered to remove those expressed at ≤ 1 transcript per million (TPM) after Salm₁₀₀ and vehicle, respectively before subsequent analyses. Pairwise comparisons of these DEGs were performed between vehicle and all other treatments using the Wald test in Sleuth to estimate fold changes (derived from beta-values). Data were also expressed as a change in TPM as indicated.

Analysis of Gene Expression Profiles. The microarray and RNA-seq data have been deposited with NCBI's Gene Expression Omnibus and are freely available using accession codes GSE106710 and GSE126981 respectively. Unless stated otherwise, genes are referred to by the official human genome nomenclature committee (HGNC) symbols supplied by the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov). Functional annotation clustering of indacaterol- and Ind+GSK-regulated genes including associated enriched gene ontology (GO) terms was performed with the database for visualization and integrated discovery (DAVID) bioinformatics resources (v6.8) at medium stringency (Huang et al., 2009). Results are reported using the GO term that describes biological process (GOTERM_BP_DIRECT). When this descriptor was absent from a given gene cluster, molecular function (GOTERM_MF_DIRECT), cellular component (GOTERM_CC_DIRECT), UniProt Sequence Feature, Uniprot Key Word, InterPro or Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway was reported. Pseudogenes, hypothetical genes, noncoding RNAs and uncharacterised sequences lacking annotation were excluded from all analyses.

Curve Fitting. Monophasic $E/[A]$ curves were fit by least-squares, non-linear, iterative regression to the following form of the Hill equation (Eq. 1; Prism 6[®], GraphPad Software Inc, San Diego, CA):

$$E = E_{min} + \frac{(E_{max} - E_{min})}{1 + 10^{(p[A]_{50} - p[A])^{n_H}}} \quad (\text{Eq. 1})$$

where E is the pharmacological effect, E_{min} and E_{max} are the basal response and maximum response respectively, $p[A]$ is the negative log molar concentration of the compound of interest, $p[A]_{50}$ is a location parameter equal to the negative log molar concentration of compound producing $(E_{max} - E_{min})/2$ and n_H is the Hill coefficient of the $E/[A]$ curve at the $p[A]_{50}$ level.

Applying Fractional Receptor Depletion to Quantify the Impact of PDE4 Inhibition on the Efficacy of β_2 -Adrenoceptor Agonists. $E/[A]$ curves were constructed to salmeterol and β_2A , a quinolinone-based orthostere (Yoshizaki et al., 1976) present in many β_2 -adrenoceptor agonists, in the absence and presence of a PDE4 inhibitor. These experiments were performed in cells that had been pre-treated (60min) with vehicle or the alkylating agent, DCITC (100nM) and then washed in SFM (Deyrup et al., 1998). Each family of $E/[A]$ curves was fit simultaneously to the operational model of agonism (Eq. 2), which describes a theoretical relationship between E and agonist concentration (Black and Leff, 1983). Algebraically,

$$E = \frac{E_m \cdot \tau^n \cdot [A]^n}{(K_A + [A])^n + \tau^n \cdot [A]^n} \quad (\text{Eq. 2})$$

where E_m is the theoretical maximum response of the tissue, K_A is the agonist equilibrium dissociation constant, $[A]$ is agonist concentration, n is the slope of the relationship between the concentration of agonist-receptor complexes and response, and τ is the operational efficacy of the agonist. In these analyses, only τ was allowed to vary between individual $E/[A]$ curves; for all other parameters (i.e., E_m , K_A and n) a common value was assumed (Black and Leff, 1983; Leff et al., 1990).

Determination of Receptor Reserve. Occupancy-response curves in the absence and presence of a PDE4 inhibitor were constructed using K_A values determined by β_2 -adrenoceptor depletion. At each concentration of agonist, fractional receptor occupancy was determined assuming the binding of ligand to the β_2 -adrenoceptor was a non-cooperative process (Eq. 3) where R_A and R_t represent the number of agonist-occupied receptors and total number of receptors respectively.

$$R_A/R_t = [A]/(K_A + [A]) \quad (\text{Eq. 3})$$

Statistics. Data are presented as the mean \pm s.e. mean or as Box and Whisker plots of N independent

determinations. Differences in CRE reporter activity and gene expression changes were evaluated by using Student's *t*-test or repeated measures, one-way ANOVA as indicated. When the ANOVA *F*-test *P* value was <0.05, differences between groups were identified by using Tukey's multiple comparison test without Greenhouse-Geisser correction (Lew, 2007). The relationship between global changes in gene expression produced by two treatment interventions was determined by Pearson product moment correlation. Least squared perpendicular major axis (Deming) regression (Cornbleet and Gochman, 1979) was used to verify differences between treatments or treatment methods. In the text, the terms *synergy* and *synergistic* refer to a change in gene expression produced by a LABA and a PDE4 inhibitor in combination that is greater than the sum of their individual effects. The null hypothesis was rejected when $P < 0.05$.

Results

Effect of GSK 256066 on Global Gene Expression Changes. The microarray results of GSK 256066-treated BEAS-2B cells are displayed as volcano plots in supplemental figure 2 where induced and repressed genes are represented as red circles (>1.5 -fold) and blue circles (<0.67 -fold) respectively. Although many gene expression changes were apparent, and exceeded P values of 0.05 obtained by ANOVA, no probe set on the array was significantly different from vehicle at a Benjamini and Hochberg FDR of $<10\%$. Previously, we reported that PDE4 inhibitors can potentiate LABA-induced gene expression in BEAS-2B cells suggesting that a common pool of cAMP may regulate transcription (BinMahfouz et al., 2015; Moodley et al., 2013). Thus, these results reported here may indicate that GSK 256066 is a weak stimulus in these cells and that the small sample size lacked statistical power. To address this prospect, indacaterol (10nM)-regulated gene expression changes at 1, 2 and 6h were correlated against their counterparts in GSK 256066-treated BEAS-2B cells using FDRs of $<10\%$, $<5\%$ and $<1\%$ (Fig. 1A). This approach revealed significant correlations between the two drugs, which strengthened as the stringency of the FDR was increased. Furthermore, slopes of Deming regressions were shallow (0.23-0.36) at all time-points, which is consistent with weak transcriptional activity of GSK 256066 relative to indacaterol. Using the same RNA, the expression of 18 genes (labelled A to R) that were significantly (FDR $<5\%$) up-regulated by indacaterol at 2h (yellow circles in figure 1 and supplemental figure 2) were tested for their sensitivity to GSK 256066 by real-time PCR. These results are shown in supplemental figure 3 where the expression of each gene is plotted over time together with data from the probe set that gave the most robust increase on the microarray. Pearson's analyses indicated significant correlations between the microarray- and PCR-generated data at 1, 2 and 6h (Fig. 1B) although changes in gene expression were modest and did not reach statistical significance (Supplemental Fig. 3). However, repeating this experiment with a larger sample size established that most of these genes were significantly upregulated in BEAS-2B cells exposed to GSK 256066 (10nM) and roflumilast (1 μ M) for 1 and/or 2h (Supplemental Fig. 4).

Effect of GSK 256066 on Expression of the Indacaterol-regulated Transcriptome. Microarrays were also used to determine the effect of GSK 256066 (10nM) on the *number* of genes that were

significantly (FDR <10%) induced or repressed at 1, 2, 6 and 18h (Fig. 2A) by a concentration of indacaterol (10nM) that maximally activated 6×CRE reporter cells (Supplemental Fig. 1). Relative to time-matched, vehicle-treated cells, 181 DEGs were either up-regulated (135) or down-regulated (46) at 1h by >1.5-fold and <0.67-fold respectively. At 2h, the number of DEGs had increased to 351 (304 induced and 47 repressed), which had declined to 251 (206 induced and 45 repressed) by 6h. At 18h, 9 genes were up-regulated and 1 gene was down-regulated by indacaterol.

In the presence of GSK 256066, the number of indacaterol-regulated genes at 1 and 2h was similar to the gene count in BEAS-2B cells exposed to indacaterol alone (Fig. 2A). In contrast, at 6 and 18h the number of significant gene expression changes was considerably greater in cells exposed to Ind+GSK than to indacaterol (Fig. 2A). The Venn diagrams in figure 2B show that 41, 87, 86 and 60% of all genes induced or repressed by indacaterol were similarly regulated by Ind+GSK at 1, 2, 6 and 18h respectively. The corresponding values for genes induced or repressed by Ind+GSK that were also regulated by indacaterol were 56, 86, 55 and 30%. Analyses of data at all time-points revealed that ≥70% of all genes were regulated by both interventions (Fig. 2B).

Ontological Analysis and Functional Annotation Clustering. Categorization of indacaterol- and Ind+GSK-regulated transcripts (by probe set) at 1, 2, 6 and 18h was performed manually using six generic descriptors: (1) *transcriptional regulators* (red); (2) *transporters, ion channels and membrane receptors* (orange); (3) *metabolic proteins* (yellow); (4) *general signalling molecules, including translational regulators* (green); (5) *other functions* (blue); and (6) *not assigned* (purple). Annotated probe sets meeting the expression criteria (>1.5-fold, <0.67-fold; FDR <10%) were assigned HGNC gene symbols and are listed in supplemental tables 2 and 3. The number of induced and repressed genes within each general terms expressed as a percentage of the total number of significant gene expression changes is also presented as a pie chart at each time-point for each intervention.

To explore how downstream function may change with time, the number of DEGs assigned to each of the six terms described above was enumerated at 1, 2, 6 and 18h (Supplemental Fig. 5). Apart from repressed genes assigned to the term *receptors, ion channels and transporters*, the gene count in each

of the other categories mirrored the global effect of GSK 256066 on the indacaterol-regulated transcriptome (Fig. 2A). Breaking down these changes by category showed that indacaterol promoted a transient burst (peaking at 2h) in induced and repressed genes that are associated with transcriptional regulation and signalling. At 1, 2 and 18h the gene count was not materially affected by GSK 256066 whereas at 6h it was markedly increased (Supplemental Fig. 5). Indacaterol-regulated gene expression changes in the other categories occurred more slowly with the highest number recorded at 6h. Again, GSK 256066 did not affect the number of DEGs at the early or late time-points; only those appearing at 6h were increased in number (Supplemental Fig. 5).

Functional annotation clustering of genes that were differentially expressed in response to indacaterol and Ind+GSK across all time-points determined that the number of clusters and enriched GO terms within each cluster were similar (Supplemental Tables 4 & 5). Many of the most highly enriched terms, such as *positive regulation of transcription from RNA polymerase II promoter* (GO:0045944), relate to gene transcription and contain transcripts that encode sequence-specific transcription factors, co-activators, (co)repressors and allied regulators of gene expression. Of these, several encode transcriptional repressors including *KLF2*, *KLF4*, *KLF15*, *NR4A1*, *NR4A2* and *NR4A3*. Other enriched GO terms such as *transcription, DNA templated* (GO:0006351), *extracellular region* (GO:0005576), *integral component of plasma membrane* (GO:0005887), *peptidyl-threonine dephosphorylation* (GO:0035970) and *type I interferon signaling pathway* (GO:0060337) contained genes that may attenuate cytokine production (*CD200*, *DUSP1*, *SOC3*), protect against COPD exacerbations (*DMBT1*, *CRISPLD2*) and regulate oxidative stress, fibrosis and mucus secretion (*EGR1*, *TXNIP*).

Enriched GO and KEGG terms including *extracellular space* (GO:0005615), *cell-cell signaling* (GO:0007267), *cytokine activity* (GO:0005125), *positive regulation of tyrosine phosphorylation of stat3 protein* (GO:0042531) and *TNF signalling pathway* (HSA:04688) were populated with a variety of adverse effect (AE) genes notably *AREG*, *BDNF*, *CCL2*, *CCL20*, *CXCL2*, *CXCL3*, *CTGF*, *EDN1*, *IL6*, *IL11*, *IL15* and *IL20*.

A comprehensive analysis of indacaterol-regulated transcripts in BEAS-2B cells including functional annotation clustering has been reported previously (Yan et al., 2018) and those findings were largely replicated here in BEAS-2B cells treated with Ind+GSK (Supplemental Tables 2-5).

Effect of GSK 256066 on the Duration of Indacaterol-induced Gene Expression Changes. The global effect of PDE4 inhibition on the expression of the indacaterol-regulated transcriptome was further interrogated by comparing the magnitudes of all significant gene expression changes (by probe set) induced by Ind+GSK at 1, 2, 6 and 18h (no fold threshold at the FDR indicated) with the corresponding indacaterol data (Fig. 3). This analysis revealed significant correlations between the two treatments at each time-point. At 1 and 2h, GSK 256066 had little effect on those genes up-regulated by indacaterol (slopes of Deming regressions ~ 1) whereas at the two later time-points slopes of regressions were shallow in favour of Ind+GSK (Fig. 3C & D). The overall effect of this interaction is presented in figure 3E-H as areas under the curves of the mean change in gene expression over the total period of exposure (AUC_{0-18h}). For example, taking the 158 probe sets that were significantly upregulated by Ind+GSK at 1h, plotting the overall mean induction of the same probe sets at 2, 6 and 18h, and comparing these results with the indacaterol counterparts (Fig. 3E), revealed that GSK 256066 produced an overall enhancement of gene induction. Similar data were obtained for those genes significantly up-regulated by Ind+GSK at the other time-points (Fig. 3F-H). These outcomes were attributable to the persistence of gene expression changes at 1 and 2h, as well as the induction of a greater number of genes at 6 and 18h. In each case, the AUC_{0-18h} for the 1, 2, 6 and 18h data sets was 23, 21, 20 and 28% greater in cells treated with Ind+GSK compared to indacaterol alone respectively (Fig. 3E-H). Indacaterol-repressed genes were affected similarly (Supplemental Fig. 6).

The impact of GSK 256066 on the AUC_{0-18h} of the 259 probe sets that were significantly induced (>2 -fold; $FDR < 10\%$) by indacaterol at any time-point was converted to a fold change and presented as a heat map. As shown in figure 4, the effects of PDE4 inhibition were gene-dependent and formed a continuum that ranged from 2.5-fold for *DNAI1* to 0.21-fold for *UGT1A8/9*. Using cut-off levels of >1.1 -fold and <0.9 -fold, GSK 256066 variably increased and decreased respectively AUC_{0-18h} of 157

(61%) and 34 (13%) indacaterol-induced transcripts. The AUC_{0-18h} of the remaining 68 (26%) transcripts were unaffected (Fig. 4).

The effects of GSK 256066 on 18 indacaterol-induced genes (labelled A to R in figure 4) that spanned AUC_{0-18h} continuum were validated by real-time PCR using the same RNA (Fig. 5). For the majority (13/18) of these genes, GSK 256066 variably enhanced the indacaterol AUC_{0-18h} by maintaining transcript expression at the 6 and 18h time-points. However, the kinetics of other gene expression changes (i.e., *C5AR1*, *CRISPLD2*, *DMBT1*, *SOCS3*) were unaffected by GSK 256066 or even abbreviated (e.g. *BMP2*), which suggests gene-dependent differences in regulation by cAMP.

Effect of PDE4 Inhibition on the Magnitude of Gene Expression Changes produced by a Submaximal Concentration of a LABA. The experiments described in the previous section explored the impact of RNO in cells treated with a maximally-effective concentration of indacaterol (10nM; Supplemental Fig. 1). As this may have precluded an assessment of whether these drugs could interact in an additive or synergistic manner, the effects of a lower concentration of indacaterol (1nM; [A]₃₂) on the expression of nine genes was determined in the absence and presence of GSK 256066 (10nM) and roflumilast (1 μ M). In most cases, at 1 and/or 2h, the effect of the drugs in combination was greater than the LABA alone (Fig. 6A). When changes in expression produced by the drugs in combination were plotted against the sum of their individual effects, lines of Deming regressions deviated from unity raising the possibility that the PDE4 inhibitor and LABA interacted synergistically (Fig. 6B). A similar and more striking interaction occurred when indacaterol was substituted with a higher effective concentration of formoterol (30pM; [A]₄₅; Fig. 6A & B). These data are also presented as Box and Whisker plots to illustrate the variability in response to LABA and PDE4 inhibitor (Supplemental Fig. 4). The ability of GSK 256066 to enhance the effect of indacaterol was reproduced at the protein level using NR4A2, NR4A3 and IL-6 as representative examples (Fig. 6C).

The Salmeterol-Regulated Transcriptome and the Effect of RNO. RNA-seq was used to establish if PDE4 inhibitors augmented the expression of all LABA-regulated genes or a subpopulation. For these experiments, RNO and salmeterol were substituted for GSK 256066 and indacaterol to provide clinical

applicability and to gain further evidence that this interaction represents a class effect of LABAs and PDE4 inhibitors. Initially, the sensitivity of genes that comprise the LABA-regulated transcriptome to agonist was determined. This was achieved by comparing global gene expression changes in BEAS-2B cells treated for 2h with two, submaximal concentrations of salmeterol (Salm_{0.3} and Salm_{0.5}), which equated to a [A]₁₄ and [A]₃₆ on the 6×CRE reporter respectively, with a concentration of salmeterol (100nM; Salm₁₀₀) that defined maximal responses (Supplemental Fig. 1).

At a FDR of ≤5%, 180 and 16 genes were significantly induced (≥2-fold) and repressed (≤0.5-fold) respectively by Salm₁₀₀. Changes in gene expression produced by Salm_{0.3} expressed as a percentage of the corresponding Salm₁₀₀ data formed a continuum that ranged from 11.6% (*NPTX1*) to 83% (*TCF21*) for up-regulated genes (Fig. 7A), and from 37.6% (*C10orf10*) to 71.6% (*KRTAP2-3/KRTAP2-4*) for genes that were repressed (Supplemental Table 7). Assuming that (i) salmeterol is a full agonist on all DEGs; (ii) gene expression is described by symmetrical $E/[A]$ curves with $n_H = 1.8$ (Supplemental Fig. 1); and (iii) Salm₁₀₀ maximally induced or repressed all DEGs, then the sensitivity of genes within the salmeterol-regulated transcriptome varied by ~7.5-fold (Fig. 7A & B). In contrast, Salm_{0.5} was a strong stimulus in BEAS-2B cells and, unlike its modest effect on the 6×CRE reporter (Supplemental Fig. 1), promoted gene expression changes that were ≥58% of their respective maxima (Fig. 7A).

In BEAS-2B cells treated for 2h with RNO (1μM), 16 genes were differentially regulated (≥2-fold; ≤0.5-fold; FDR ≤5%) consistent with the superior sensitivity of RNA-seq over microarrays. Analysis of the 196 Salm₁₀₀-regulated genes (Supplemental Table 7) revealed strong correlations between gene expression changes produced by RNO and all concentrations of salmeterol tested (Supplemental Fig. 7). The additional finding that RNO augmented salmeterol-induced cAMP accumulation (Fig. 7C) implies that both drugs can regulate gene expression by a common mechanism that involves the activation of PKA (Yan et al., 2018). To explore that possibility, gene expression changes produced by salmeterol and RNO in combination and the sum of their individual effects were analysed by Deming regression (Fig. 8A & B). On most genes, the activity of salmeterol was augmented by RNO (1μM) in a synergistic manner, which was reflected by slopes that were steeper than the line-of-identity in favour of Salm_{0.3} + RNO (1.98) and Salm_{0.5} + RNO (1.24; Fig. 8A & B). However, the magnitudes of these

interactions varied and formed a continuum due to differences in the sensitivity of genes to salmeterol (Supplemental Tables 7 & 8). This is illustrated in figure 8C & D, which shows simulated salmeterol $E/[A]$ curves with n_H fixed to a value of 1.8 (*vide supra*) in the absence and presence of a concentration of RNO that displaced the control curve three-fold to the left. It can be seen that the degree to which RNO augments a given response depends where on the salmeterol $E/[A]$ curve the measurement is made and how it is calculated. On *NPTX1* and *TCF21*, which lie towards the extremes of the salmeterol sensitivity spectrum (Fig.7A), the impact of RNO differed markedly (Fig 8E & F). Thus, RNO augmented Salm_{0.3}-induced *NPTX1* and *TCF21* expression from 11.6 to 51% and from 83 to 97% of their maximum responses respectively.

Quantifying the Impact of RNO on the Efficacy of Salmeterol. Pre-treatment of 6×CRE BEAS-2B cells with RNO (1μM; 30 min) produced a modest activation of the reporter (<2-fold) and a 4.5-fold sinistral displacement of the mean salmeterol $E/[A]$ curve without affecting the maximum response (Fig 9A). To mimic a therapeutic target where receptor number is limiting, the effect of RNO was examined in cells subjected to fractional, irreversible β₂-adrenoceptor inactivation with DCITC (100nM; 60 min). In these experiments, the upper asymptote of the mean $E/[A]$ curve was significantly depressed (by 49%) and the potency of salmeterol was reduced by a factor of 8.5-fold. In the presence of RNO, the effects of receptor depletion were partially rescued; there was an increase in the potency of salmeterol and in the maximum response attained (Fig. 9A). Analysing this family of $E/[A]$ curves by operational model fitting determined that RNO had doubled the efficacy of salmeterol in the absence (τ : from 10.5 to 24) and presence (τ' : from 0.9 to 1.7) of DCITC (Table 1).

The operational model also provides a measure of agonist affinity. For salmeterol-induced reporter activation, this was calculated to be 3.7nM (Table 1). Substituting this value in to equation 3, which is a statement of the *Law of Mass Action*, provides a description of the relationship between receptor occupancy and response (Kenakin, 2016). For activation of 6×CRE BEAS-2B reporter cells, this relationship deviated significantly from the line-of-identity (Fig. 9B). Interpolation from the mean occupancy-response curve showed that 4, 13 and 25% receptor occupancy was required to generate 20, 50 and 80% of the maximal response, respectively and is consistent with a receptor reserve. In the

presence of RNO, the deviation from linearity was more pronounced; the salmeterol $K_A/[A]_{50}$ value was increased from 8 to 32 and the generation of 20, 50 and 80% of the maximal response now required only 1, 4 and 13% β_2 -adrenoceptor occupancy, respectively (Fig. 9B).

In cells treated with DCITC, salmeterol-induced reporter activation collapsed to a linear function of receptor occupancy. The $K_A/[A']_{50}$ value was ~ 1 and the receptor reserve present under control conditions was lost (Fig. 9B). In contrast, the sensitivity of receptor-depleted cells treated with RNO to salmeterol was partially restored. The occupancy-response relationship returned to a shallow rectangular hyperbola, where 15, 43 and 77% binding generated 20, 50 and 80% of the maximal response respectively, and the $K_A/[A']_{50}$ value was increased from 0.74 to 1.59 (Fig. 9B; Table 1).

GSK 256066 (10nM; 30min) had a similar impact on the operational efficacy and receptor reserve of β_2A (Fig. 9C & D; Table 1), the functionality that confers β_2 -adrenoceptor agonism (Yoshizaki et al., 1976) in indacaterol, carmoterol and abediterol. Thus, the interaction between salmeterol and RNO shown in figure 9A is likely to be generic to LABAs and PDE4 inhibitors.

On *bona fide* genes (i.e., *CRISPLD2*, *NR4A2*, *RGS2*), RNO produced sinistral displacements of the salmeterol $E/[A]$ curves in the absence and presence of DCITC consistent with increases in efficacy and receptor reserves (Fig. 9E-G). However, the quality of the data was not sufficiently robust for quantification by operational model fitting.

Discussion

The results of large scale, phase III clinical trials indicate that the PDE4 inhibitor, roflumilast, is beneficial in a subset of individuals with severe, bronchitic COPD in whom frequent exacerbations occur despite ICS/LABA combination therapy, even in the presence of a LAMA. These results are important because they illustrate that the ceiling of benefit, following an additional drug intervention, had not been attained (Martinez et al., 2015; Martinez et al., 2018). While the mechanism of action of roflumilast is unclear, its ability to improve lung function and reduce exacerbation frequency (Wedzicha et al., 2016), in the absence of direct bronchodilatation (Grootendorst et al., 2003), implies that suppression of inflammation plays a role (Gamble et al., 2003; Grootendorst et al., 2007). We have reported previously that LABAs promote changes in gene expression in human airway epithelial cells that may contribute to: (i) their clinical efficacy in obstructive lung diseases, especially when combined with an ICS (Giembycz and Newton, 2011; Giembycz and Newton, 2015; Rider et al., 2018), and (ii) the AEs that are associated with chronic β_2 -adrenoceptor agonist monotherapy (*vide infra*; Yan et al., 2018). This study extends those findings by establishing that PDE4 inhibitors also promoted changes in gene expression in BEAS-2B cells and, perhaps more importantly, increased the operational efficacy, enhanced the magnitude of response and variably altered gene expression kinetics induced by LABAs. Thus, if suppression of airways inflammation underpins the clinical activity of PDE4 inhibitors in COPD, genomic mechanisms may be involved.

The PDE4-Regulated Transcriptome. Immediate and delayed targets of cAMP signalling could equally contribute to the efficacy of PDE4 inhibitors. Accordingly, DEGs were identified in BEAS-2B cells exposed to GSK 256066 for 1, 2, 6 and 18h. GSK 256066 was chosen for this experiment because it is a potent, pan-PDE4 inhibitor with considerable selectivity (>30,000-fold) over all other PDE families and the *Cerep*[®] panel of receptors (Tralau-Stewart et al., 2011). At a concentration 3800 \times greater than its K_I for the inhibition of human PDE4B1 (Joshi et al., 2017), GSK 256066 did not affect gene expression even at a FDR <10%. While these data suggested that genomic mechanisms play little role in the mechanism of action of PDE4 inhibitors, further analyses ascertained that GSK 256066 was a weak stimulus in BEAS-2B cells and the small sample size used for the arrays lacked statistical

power to detect small changes in gene expression. Indeed, real-time PCR confirmed that many genes induced by indacaterol were also up-regulated by GSK 256066 and roflumilast.

The weak transcriptional activity of PDE4 inhibitors may reflect low basal adenylyl cyclase activity in BEAS-2B cells and questions the significance of genomic mechanisms *in vivo*. This is an important consideration given that roflumilast monotherapy was beneficial in clinical trials of COPD (Calverley et al., 2009). However, the modest *in vitro* effects described here are likely amplified *in vivo* because adenylyl cyclase activity in target cells and tissues will be higher. Indeed, many Gs-coupled receptors will be under tonic activation by various endogenous ligands including catecholamines, adenosine and prostaglandins (BinMahfouz et al., 2015; Greer et al., 2013; Kaur et al., 2008; Moodley et al., 2013; Wilson et al., 2009). Furthermore, any genomic effects of PDE4 inhibitors could be further enhanced by endogenous glucocorticoids given that these drugs can often summate or even synergise at a transcriptional level (BinMahfouz et al., 2015; Moodley et al., 2013). Thus, the clinical efficacy of roflumilast monotherapy may reflect its ability to enhance the activity of various endogenous ligands to produce a more robust gene expression signature than these *in vitro* data suggest.

Effect of PDE4 Inhibition on the LABA-Regulated Transcriptome. Consistent with this *in vivo* prediction, RNO and GSK 256066 enhanced the expression of a panel of formoterol- and indacaterol-induced genes in BEAS-2B cells and this was reproduced at the protein level using NR4A2, NR4A3 and IL-6 as representative examples. Operational model fitting determined that PDE4 inhibition doubled the efficacy of LABAs and, thereby, increased the β_2 -adrenoceptor reserve. Clinically, this finding could be described as “LABA sparing” where, in the presence of a PDE4 inhibitor, a lower agonist concentration is required to produce the same degree of gene induction or repression. To establish if this interaction extended to the LABA-regulated transcriptome or a subpopulation of DEGs, the effects of RNO on global gene expression changes produced by submaximal concentrations of salmeterol were determined by RNA-seq. In these experiments, RNO augmented the expression of the majority of DEGs. These included those with AE and therapeutic potential (*vide infra*), although the magnitude of effect varied because of the estimated 7.5-fold difference in their sensitivity to salmeterol. This was defined by *NPTX1* and *TCF21*, which lie towards the extremes of the sensitivity spectrum.

Thus, Salm_{0.3} alone and in the presence of RNO equated respectively to [A]_{11.6} and [A]₅₁ for *NPTX1* and [A]₈₃ and [A]₉₇ for *TCF21*. Collectively, these results support the idea that Gs-dependent signalling plays a dominant role in regulating β_2 -adrenoceptor-mediated gene expression. While non-canonical mechanisms cannot be excluded (see Penn et al., 2013), *cis*-acting CREs for the transcription factor, CREB are found in the promoter regions of a large number of cAMP-regulated genes, which support this proposal (Zhang et al., 2005). An additive or synergistic interaction of a PDE4 inhibitor with a LABA may be particularly important in target cells and tissues that express low β_2 -adrenoceptor number or where receptor-effector coupling efficiency is weak (Rabe et al., 1993). Indeed, modelling this scenario by rendering salmeterol and β_2A (the functionality that confers agonism in many LABAs) partial agonists with DCITC, revealed that PDE4 inhibitors partially rescued the associated loss in operational efficacy, increased the maximum response and produced sinistral displacements of LABA $E/[A]$ curves as the *Law of Mass Action* predicts.

GSK 256066 also prolonged the duration of many indacaterol-induced gene expression changes. This was prominent at 6h and often persisted to 18h when the level of mRNA transcripts induced or repressed by Ind+GSK was still greater than with indacaterol alone. A simple explanation of these data is that by maintaining the cAMP signal, PDE4 inhibitors likewise sustain gene transcription. However, GSK 256066 did not prolong the expression of all LABA-induced genes equally; in fact, for some genes the AUC_{0-18h} was unaffected or even decreased by GSK 256066. Thus, additional mechanisms that accommodate variable effects of PDE4 inhibition on gene expression kinetics must be entertained. One possibility is that the initial and delayed components of gene induction are regulated by temporally distinct transcriptional events that involve feed forward loops (Mangan and Alon, 2003). This type of regulation has been described for many genes including *DUSP1* (Lu et al., 2008) and can equally explain both prolongation and retardation of gene expression kinetics.

Genes with Therapeutic Potential. The LABA- and LABA+PDE4 inhibitor-regulated transcriptomes in BEAS-2B cells contained genes that may help reduce exacerbation frequency and the associated inflammation (Perera et al., 2007) that characterises the COPD phenotype that responds to roflumilast. In particular, several up-regulated genes encode proteins that suppress pro-inflammatory cytokine

generation such as *CD200*, *DUSP1* and *SOCS3* (Liu et al., 2007; Snelgrove et al., 2008; Yoshimura et al., 2018), whereas others may directly protect against bacterial and viral exacerbations. For example, the multifunctional, secreted protein, DMBT1, binds Gram-positive and Gram-negative bacteria and so could defend against microbial pathogens; it also inhibits the infectivity of human influenza A and immunodeficiency viruses (Madsen et al., 2010). Likewise, *CRISPLD2* encodes a secreted lipopolysaccharide-binding protein (Wang et al., 2009) that can neutralise the pathogenicity of Gram-negative bacteria and, thereby, down-regulate TLR4-mediated inflammation (Zhang et al., 2016). LABAs and PDE4 inhibitors also induced several genes that may encode negative feedback regulators of inflammation that include *KLF2*, *KLF4*, *KLF15* and the NR4A family of transcription factors (Rodriguez-Calvo et al., 2017; Sweet et al., 2018). Many of these genes are further upregulated when a LABA and/or a PDE4 inhibitor are combined with a glucocorticoid (Moodley et al., 2013; Rider et al., 2018), which may be relevant to understanding how these drugs work in a clinical setting (Giembycz & Newton, 2014).

Noteworthy DEGs down-regulated by indacaterol and Ind+GSK include *EGR1*. This gene is induced by cigarette smoke and is elevated in the lungs of subjects with severe COPD (Ning et al., 2004) with potential to promote mucus hypersecretion (Wang et al., 2017), inflammation, fibrosis and remodelling in the airways (Cho et al., 2006; Lee et al., 2004). *TXNIP* is another cigarette smoke-sensitive gene (Sun et al., 2018) that may contribute to the free radical burden that often prevails in COPD airways (Domej et al., 2014) by encoding an inhibitor of the oxidoreductase, thioredoxin 1 (Nishiyama et al., 1999). Therefore, the ability of PDE4 inhibitors and LABAs to repress *EGR1* and *TXNIP* could help arrest pro-inflammatory and fibrotic changes in the lungs and reduce oxidative stress, respectively.

Adverse-Effect Genes. Chronic, β_2 -adrenoceptor agonist monotherapy in asthma is associated with an increased risk of serious AEs (Cates et al., 2014; Pearce et al., 1991). The apparent *absence* of similar toxicity in subjects with COPD is, therefore, a paradox (Decramer et al., 2013). If genomic mechanisms contribute to these AEs in asthma as previously proposed (Ritchie et al., 2018; Yan et al., 2018), then how can these discrepant responses to treatment be rationalised? This question is pertinent given that the expression of putative AE genes was exaggerated by a PDE4 inhibitor. The profound differences in

aetiology, pathogenesis, inflammation and causes of exacerbations between the two diseases may provide an explanation (Decramer et al., 2013) such that these gene expression changes in COPD have less pathological relevance than in asthma. Alternatively, cells exposed chronically to cigarette smoke in a Th1-like inflammatory environment may respond to a LABA by expressing a less harmful transcriptome.

Conclusions. The results of this study implicate widespread changes in gene expression in the mechanism of action of PDE4 inhibitors in COPD. This effect may be particularly relevant when added on to a LABA or an ICS/LABA combination therapy. Nevertheless, a comparable genomic signature must be confirmed in airway epithelia harvested from individuals with COPD if this assertion to gain traction. Such *in vivo* investigations are necessary because they will reveal the genomic capacity of these drugs at therapeutically-relevant doses on a background of airways and extrapulmonary inflammation that is common in individuals exposed chronically to cigarette smoke. They will also provide valuable information on the extent to which cultured airway epithelial cells predict the genomic behaviour of their *in vivo* counterparts in response to drug interventions under pathological conditions. Finally, the anti-inflammatory activity of oral apremilast in plaque psoriasis and psoriatic arthritis suggests that systemic exposure could contribute to the mechanism of action of roflumilast and may help explain why inhaled PDE4 inhibitors are inactive in COPD.

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Footnotes

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Figure Legends

Fig. 1. Relationships between indacaterol- and GSK 256066-regulated gene expression changes in BEAS-2B cells. Panel A: Deming regressions at 1, 2 and 6h between changes in the expression of all genes (by probe set) regulated by indacaterol (10nM) at FDRs of <1, <5 and <10% and their counterparts in cells treated with GSK 256066 (10nM). Induced or repressed probes sets are shown as red or blue circles, respectively, and are plotted as fold on a log₂ scale where a value of 1 equates to baseline expression (horizontal and vertical dashed lines). Yellow circles represent genes that were validated by real-time PCR (Fig. 6; Supplemental Fig. 4). The letter in each yellow circle corresponds to a HGNC gene symbol and Affymetrix probe set ID code: **A.** *BMP2* (205289_at); **B.** *C5AR1* (220088_at); **C.** *CCL20* (205476_at); **D.** *CD200* (209582_s_at); **E.** *CRISPLD2* (221541_at); **F.** *DMBT1* (208250_s_at); **G.** *DUSP1* (201044_x_at); **H.** *FGFR2* (203638_at); **I.** *GAS1* (204456_s_at); **J.** *IL6* (205207_at); **K.** *NR4A2* (216248_s_at); **L.** *NR4A3* (209959_at); **M.** *PDE4D* (228962_at); **N.** *PDK4* (225702_at); **O.** *PRDMI* (228964_at); **P.** *RGS2* (202388_at); **Q.** *SGK1* (201739_at); **R.** *SOCS3* (206359_at); **S.** *EGR1* (227404_s_at); **T.** *TXNIP* (201008_s_at). Panel B: Correlations at 1, 2 and 6h of the changes in expression (in fold) of the same 18 genes (**A** to **R**) determined by microarray and PCR in BEAS-2B cells treated with GSK 256066 (10nM). Solid and dashed diagonal lines in each panel represent linear regression and the line-of-identity respectively.

Fig. 2. Comparative effects of indacaterol and Ind+GSK on the number of induced and repressed genes in BEAS-2B cells. Panel A: Time-course showing of the *number* of DEGs (>1.5-fold, <0.67-fold; FDR <10%) in cells treated for 1, 2, 6 and 18h with indacaterol (10nM), Ind+GSK (both 10nM) or vehicle. DEGs were identified using *Entrez Gene* and DAVID IDs and the number is shown in brackets at each time-point. Panel B: Proportional Venn diagrams showing the number of genes regulated by Ind+GSK (white set), indacaterol (black set) and both treatments (intersections) at each, and across all, time-points. See text for further details.

Fig. 3. Global effect of GSK 256066 on the indacaterol-induced transcriptome in BEAS-2B cells. Panels A-D: Genes (by probe set) that were significantly induced (>1-fold) by Ind+GSK at 1, 2, 6 and 18h at the FDR indicated were correlated against their counterparts in indacaterol-treated cells. The

black arrows in panels C and D indicate deviation from unity slope in favour of Ind+GSK (i.e. genes were induced more with Ind+GSK than with indacaterol alone). Panels E-H: Comparative global expression kinetics for the probe sets from panels A-D that were significantly upregulated by Ind+GSK at 1, 2, 6 and 18h, respectively with their counterparts in cells treated with indacaterol and GSK 256066 (areas shaded dark and light grey respectively). For example, in panel E, the global mean change in expression (in fold) of the 158 probe sets that were significantly upregulated by Ind+GSK at 1h was also calculated at the other three time-points, and at 1, 2, 6 and 18h in cells treated with indacaterol and GSK 256066. These calculations were replicated with the 519, 1055 and 39 probe sets that were significantly upregulated at 2, 6 and 18h (Panels F-H). The areas shaded green indicate the gain in AUC_{0-18h} produced by Ind+GSK over indacaterol alone. The AUC_{0-18h} for each intervention is indicated.

Fig. 4. Gene-dependent impact of PDE4 inhibition on the indacaterol AUC_{0-18h} in BEAS-2B cells. The AUC_{0-18h} of the 259 significantly up-regulated probe sets (FDR <10%; >2-fold at any time-point) were calculated in the absence and presence of GSK 256066 (10nM). The $AUC_{0-18h}^{Ind+GSK/Ind}$ are plotted on a linear scale as a heat map where red, blue and grey colours correspond to changes that are >1.1-fold (157 probe sets), <0.9-fold (34 probe sets) and from 0.9- to 1.1-fold (68 probe sets) respectively. Those genes validated by real-time PCR are shown on the right side of the panel where the letters assigned to HGNC symbols are consistent with the labelling used in figures 1 and 5 and in supplemental figures 2 and 3. *DNAI1* and *UGT1A8/9* represent genes at the extremes of this continuum where GSK 256066 maximally increased and decreased the indacaterol AUC_{0-18h} , respectively.

Fig. 5. Validation of the effect of GSK 256066 on gene induction kinetics produced by a maximally-effective concentration of indacaterol. BEAS-2B cells were treated for 1, 2, 6 and 18h with vehicle, GSK 256066 (GSK; 10nM), indacaterol (Ind; 10nM) and Ind+GSK (both 10nM). RNA was extracted and the expression of eighteen genes (selected from the 259 probe sets that were significantly induced by indacaterol, on the microarrays; Supplementary Table 6) was determined by real-time PCR. Gene expression changes were normalised to *GAPDH* and plotted as fold over time on a \log_2 scale where a value of 1 defines the baseline (dashed horizontal line). With the exception of *BMP2*, whose expression

kinetics in response to indacaterol was abbreviated by PDE4 inhibition, the green shaded areas indicate the gain in AUC produced by GSK 256066 when combined with indacaterol over indacaterol alone (shaded dark grey). The letters assigned to each HGNC gene symbol correspond to the same genes shown in figures 1 and 4 and in supplemental figures 2 and 3. Data represent the mean \pm s.e. mean of N independent determinations.

Fig. 6. Effect of PDE4 inhibition on gene expression changes produced by submaximal concentrations of indacaterol and formoterol. Panel A: BEAS-2B cells were pre-treated (30min) with either GSK 256066 (GSK; 10nM) or roflumilast (Rof; 1 μ M) and then exposed to either indacaterol (Ind; 1nM) or formoterol (Form; 30pM) for an additional 1 and 2h. RNA was extracted and the expression of nine genes was determined by real-time PCR. Data were normalised to *GAPDH* and are presented as the mean \pm s.e. mean of N independent determinations. Data were analysed by repeated measures, one-way ANOVA followed by Tukey's multiple comparisons test. * P <0.05, significantly different from vehicle (V). # P <0.05, significantly different from LABA. Panel B: The 2h data from panel A expressed as fold changes in gene expression in response to LABA and PDE4 inhibitor in combination were correlated by the method of Pearson against the sum of the responses produced by each drug alone. These data were also subjected to Deming regression (black line) where black arrows indicate deviations from the lines of identity (diagonal dashed lines). Panel C: BEAS-2B cells were treated with vehicle (V) or GSK 256066 (GSK) and indacaterol (Ind) alone and in combination at the concentrations (in nM) indicated. At 6h, IL-6 was measured in supernatants by ELISA and the levels of NR4A2 and NR4A3 were determined in cell lysates by western blotting and expressed relative to *GAPDH*. Data are expressed as Box and Whisker plots of N independent determinations and were analysed by repeated measures, one-way ANOVA followed by Tukey's multiple comparisons test. * P <0.05, significantly different from indacaterol. Representative westerns blots of NR4A2 and NR4A3 protein expression changes are also shown.

Fig. 7. Differential sensitivity of the LABA-regulated transcriptome to salmeterol. BEAS-2B cells were exposed to vehicle, Salm_{0.3}, Salm_{0.5} and Salm₁₀₀ (to define maximum responses) for 2h and gene expression changes were determined by RNA-seq ($N = 4$ for each intervention). Panel A (left): The

change from vehicle in the expression of genes upregulated (≥ 2 -fold; FDR $\leq 5\%$) by Salm_{0.3} and Salm_{0.5} were converted to a percentage of the counterpart Salm₁₀₀ data and presented as a heat map. The most (*TCF21*) and least (*NPTX1*) sensitive genes are indicated. Panel A (right): Simulated $E/[A]$ curves were established for each salmeterol-induced gene from their respective Salm_{0.3}/Salm₁₀₀ values with n_H constrained to a value of 1.8 (Supplemental Table 7). The degree to which each gene was upregulated by Salm_{0.3} (as a percentage of its Salm₁₀₀ counterpart) is shown as a red circle on each $E/[A]$ curve. Panel B: Salmeterol $E/[A]$ curve data from supplemental figure 1 that define activation of the 6×CRE BEAS-2B reporter with $n_H = 1.8$. Assuming that (i) salmeterol is a full agonist on all DEGs; (ii) changes in the expression of all DEGs are described by a symmetrical $E/[A]$ curve with $n_H = 1.8$; and (iii) Salm₁₀₀ maximally upregulated all DEGs, then the sensitivity between *NPTX1* and *TCF21* must differ by a factor of ~ 7.5 -fold (grey circles) with Salm_{0.3} being equivalent to $[A]_{11.6}$ and $[A]_{83}$ respectively. Panel C: BEAS-2B cells were incubated with vehicle (V) or RNO (1 μ M) and salmeterol (Salm; 100nM) alone and in combination. At 60min, the cells were lysed and cAMP measured by ELISA. Data are expressed as Box and Whisker plots of N independent determinations. Statistical analysis was by repeated measures, one-way ANOVA followed by Tukey's multiple comparisons test. * $P < 0.05$, significantly different from V. # $P < 0.05$, significantly different from Salm.

Fig. 8. Effect of RNO on salmeterol-induced gene expression changes in BEAS-2B cells determined by RNA-seq. Panels A & B: Impact of RNO (1 μ M) on gene expression changes (≥ 2 -fold; ≤ 0.5 -fold; FDR $\leq 5\%$) induced by salmeterol after 2h exposure. The effects of Salm_{0.3} + RNO and Salm_{0.5} + RNO were correlated by the method of Pearson against the sum of the responses produced by each drug alone and expressed as a change in TPM from vehicle. The data were also subjected to Deming regression (black line) where the black arrows indicate deviation from the line-of-identity (diagonal dashed line). The panels shaded grey show the same data with *KRT17* excluded from the analyses. Red and blue circles represent induced and repressed genes, respectively. Panels C & D: Simulated $E/[A]$ curves showing the effect of salmeterol alone and in the presence of RNO with n_H constrained to a value of 1.8. In these examples, RNO produced a 3-fold sinistral displacement of the salmeterol $E/[A]$ curve, which are shown in solid and dashed black respectively. Circles coloured blue and red show respectively the *fold*

$((\text{Salm} + \text{RNO})/\text{Salm})$ and *percentage* difference $((\text{Salm} + \text{RNO}) - \text{Salm})$ of salmeterol-induced responses (from -12 to -8M) produced by RNO plotted in 0.1 intervals of \log_{10} concentration, which are described by a symmetrical bell-shaped curve. The greatest change in fold (6.47; from $[\text{A}]_{3.4}$ to $[\text{A}]_{22}$) and percentage difference (47%; from $[\text{A}]_{30}$ to $[\text{A}]_{77}$) were produced with salmeterol at 50pM (-10.3M) and 200pM (-9.7M) respectively. Panels E and F: Relationship between those genes induced by $\text{Salm}_{0.3}$ (expressed a percentage of the Salm_{100} counterparts) and the degree to which the same gene was augmented by RNO given as a synergy index. This index is presented as a fold of the increase in TPM (i.e., $\text{Salm}_{0.3} + \text{RNO} / \Sigma(\text{Salm}_{0.3}, \text{RNO}) - \text{Vehicle (V)}$) in panel E and as a percentage difference (i.e., $\text{Salm}_{0.3} + \text{RNO} - (\Sigma(\text{Salm}_{0.3}, \text{RNO}) - \text{V})$) in panel F after normalization to the Salm_{100} data. Values above the horizontal dashed line in each panel indicate a synergistic interaction. Each upregulated gene (180 in total) is represented by a grey circle. Blue and red circles highlight *TCF21* and *NPTX1*, which lie towards the extremes of the sensitivity spectrum, with $\text{Salm}_{0.3}$ (-9.52M) being equal to $[\text{A}]_{83}$ and $[\text{A}]_{11.6}$ as indicated in figure 7C.

Fig. 9. Application of fractional, irreversible, β_2 -adrenoceptor inactivation to determine the impact of PDE4 inhibition on the pharmacodynamics of LABA-induced gene expression. Panels A & C: $E/[A]$ curves were constructed to salmeterol and $\beta_2\text{A}$ in the absence and presence of RNO (1 μM) and GSK 256066 (10nM) respectively in 6 \times CRE BEAS-2B cells that had been pre-treated (60min) with vehicle or DCITC (100nM) and then washed in SFM. The two families of curves were analyzed by operational model fitting from which estimates of K_A , τ , n , E_m and $p[\text{A}]_{50}$ (of the control curve) were derived (Table 1). The horizontal dashed lines represent baseline luciferase activity. The K_A of each agonist was used to calculate the relationship between fractional β_2 -adrenoceptor occupancy and reporter activation shown in panels B & D. The diagonal dashed line is the line-of-identity where luciferase activity is a linear function of receptor occupancy. Panels E-G: BEAS-2B cells were treated as described for the experiments shown in panels A-D. At 2h, RNA was harvested and real-time PCR performed for *CRISPLD2*, *NR4A2* and *RGS2*. The data were normalised to *GAPDH*, expressed as fold and used to construct $E/[A]$ curves. Data represent the mean \pm s.e. mean of N independent determinations.

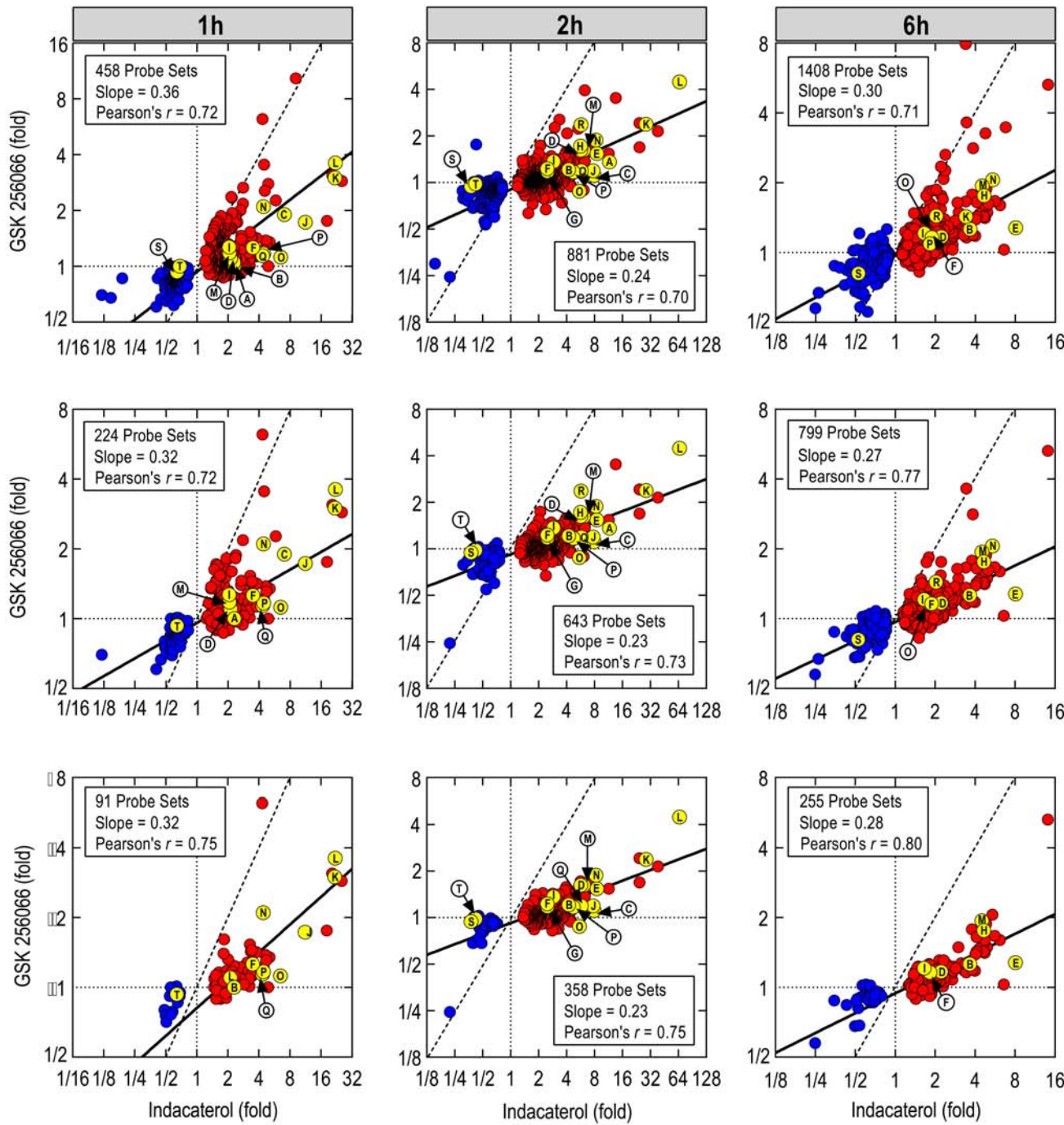
Table 1. Effect of PDE4 inhibition on the pharmacodynamic parameters that define salmeterol- and β_2 A-induced CRE-dependent reporter activation in BEAS-2B cells.

Treatment	Parameter Estimates									
	<i>N</i>	p[A] ₅₀	p[A'] ₅₀	p <i>K</i> _A	<i>K</i> _A /[A] ₅₀	<i>K</i> _A /[A'] ₅₀	<i>E</i> _m (fold)	<i>n</i>	logτ	logτ'
Salmeterol	6	9.33 ± 0.11	8.30 ± 0.04	8.43 ± 0.01	7.9	0.74	19.1 ± 0.5	2.01 ± 0.57	1.02 ± 0.10	-0.04 ± 0.03
Salmeterol + RNO		9.94 ± 0.13	8.63 ± 0.18		32.4	1.59			1.38 ± 0.21	0.24 ± 0.10
β_2 A	6	8.67 ± 0.04	7.32 ± 0.06	7.39 ± 0.06	19.0	0.85	14.0 ± 0.8	1.50 ± 0.15	1.26 ± 0.07	0.10 ± 0.03
β_2 A + GSK 256066		9.00 ± 0.04	7.85 ± 0.05		40.7	2.88			1.60 ± 0.09	0.38 ± 0.05

Agonist $E/[A]$ curves in the absence and presence of PDE4 inhibitor were constructed in cells treated with or without DCITC (100nM for 60min). The four curves in each family were analysed simultaneously by operational model fitting. p[A]₅₀ and p[A']₅₀ refer to the concentration (-log₁₀ M) of agonist that produced half maximum response in the absence and presence of DCITC respectively. Logτ and logτ' values refer to the operational efficacy of β_2 -adrenoceptor agonist before and after alkylation respectively. Parameters were derived from the data shown in figure 9A and C.

Figure 1

(A)



(B)

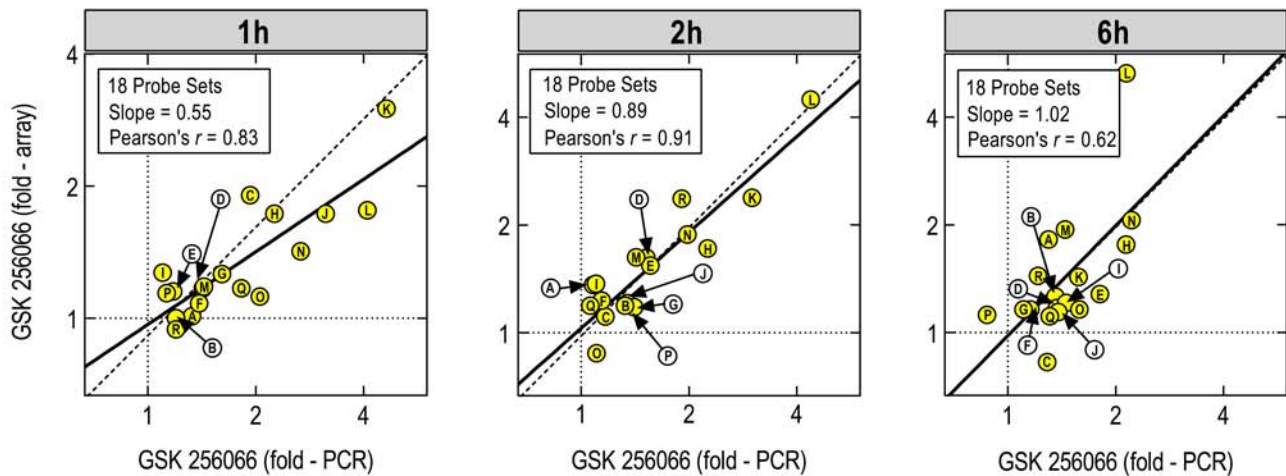
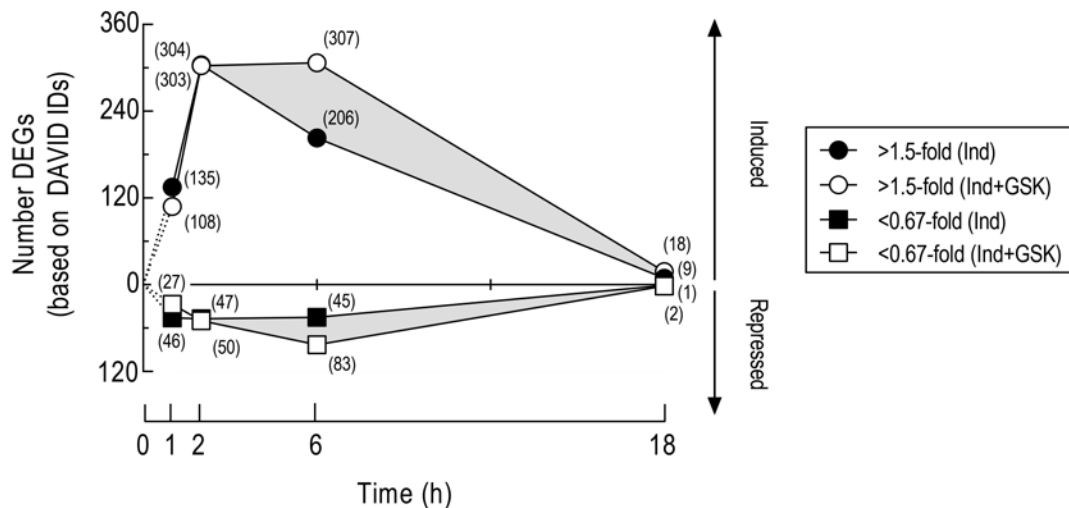


Figure 2

(A)



(B)

● Ind-regulated Genes ○ Ind+GSK-regulated Genes ● Ind- and Ind+GSK-regulated Genes

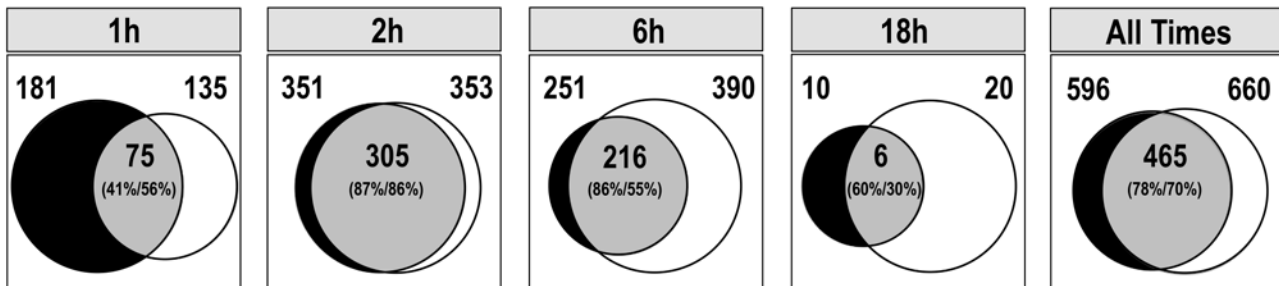


Figure 3

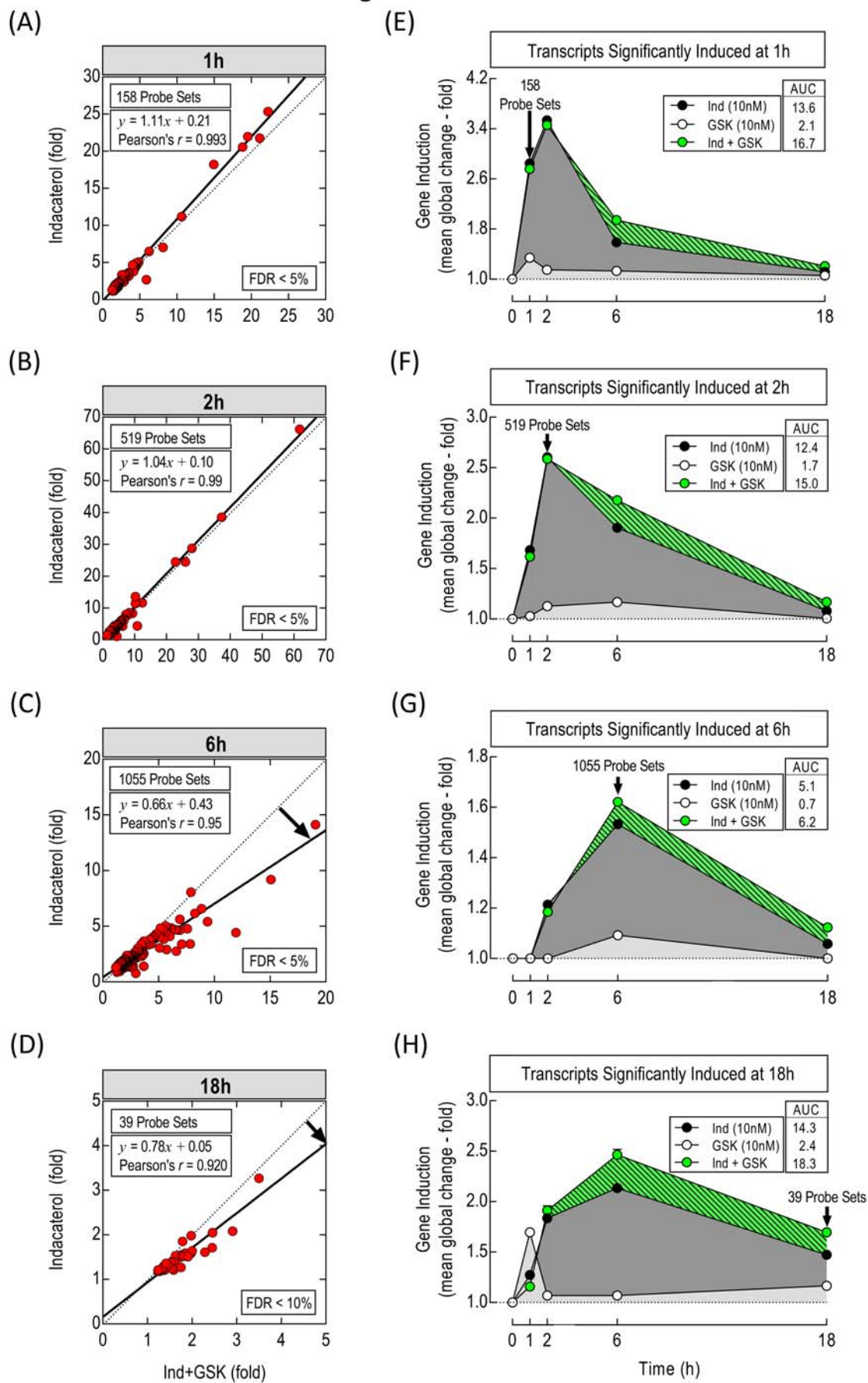


Figure 4

AUC_{0-18h} (fold)

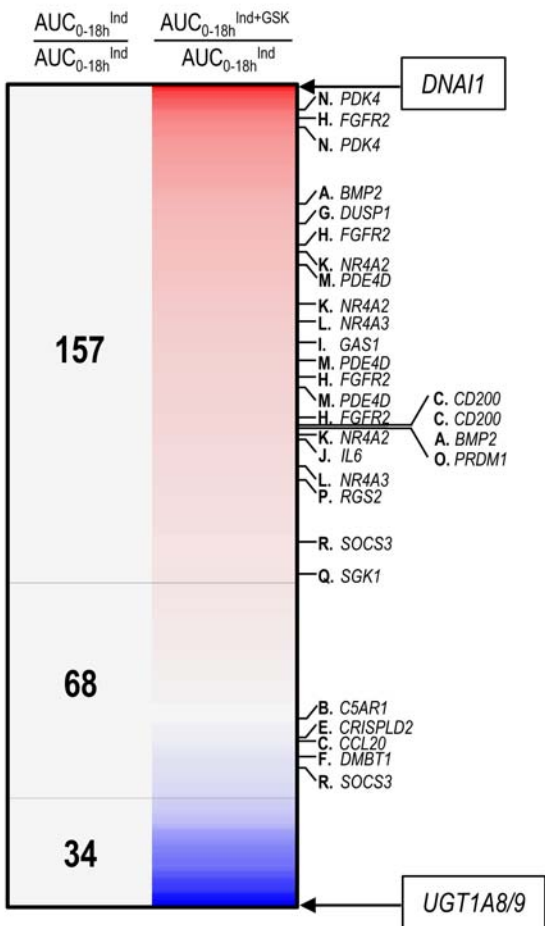
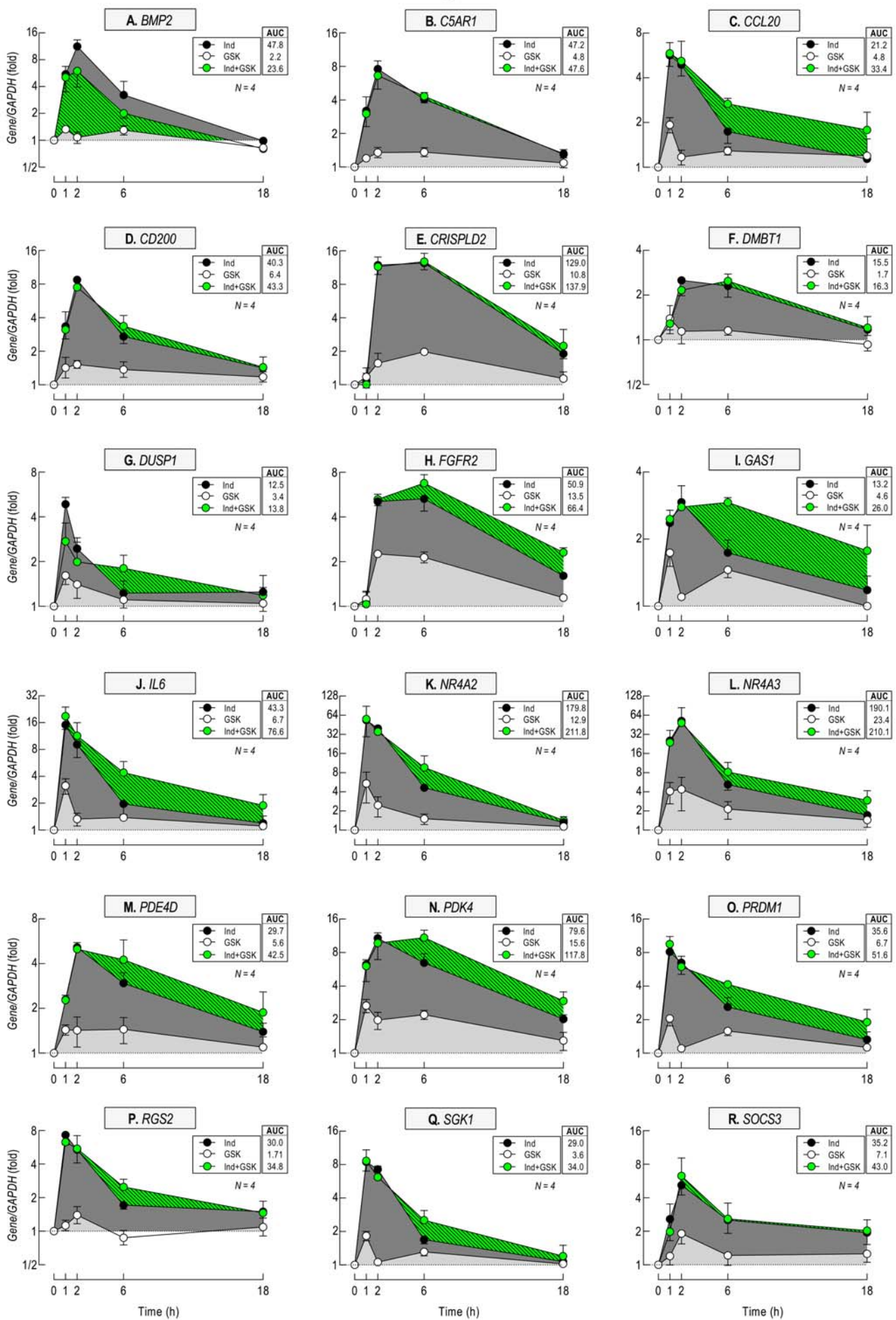
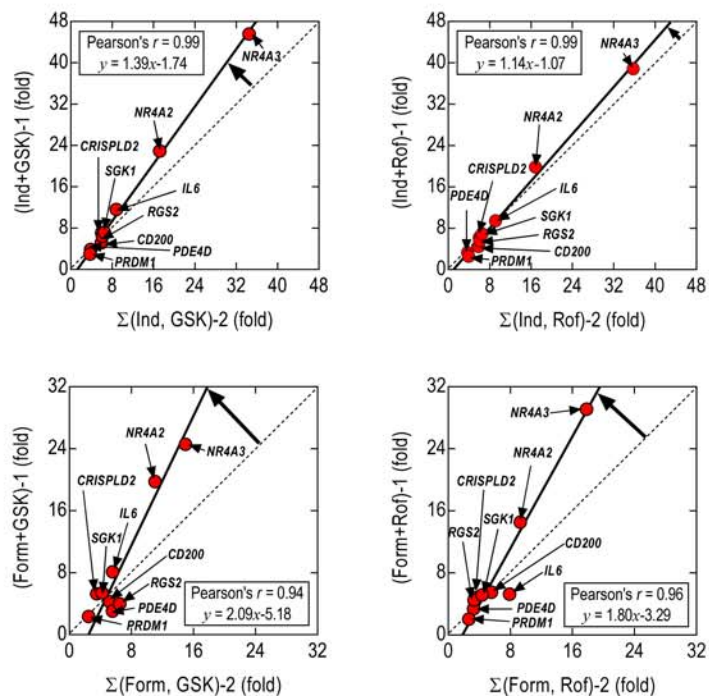
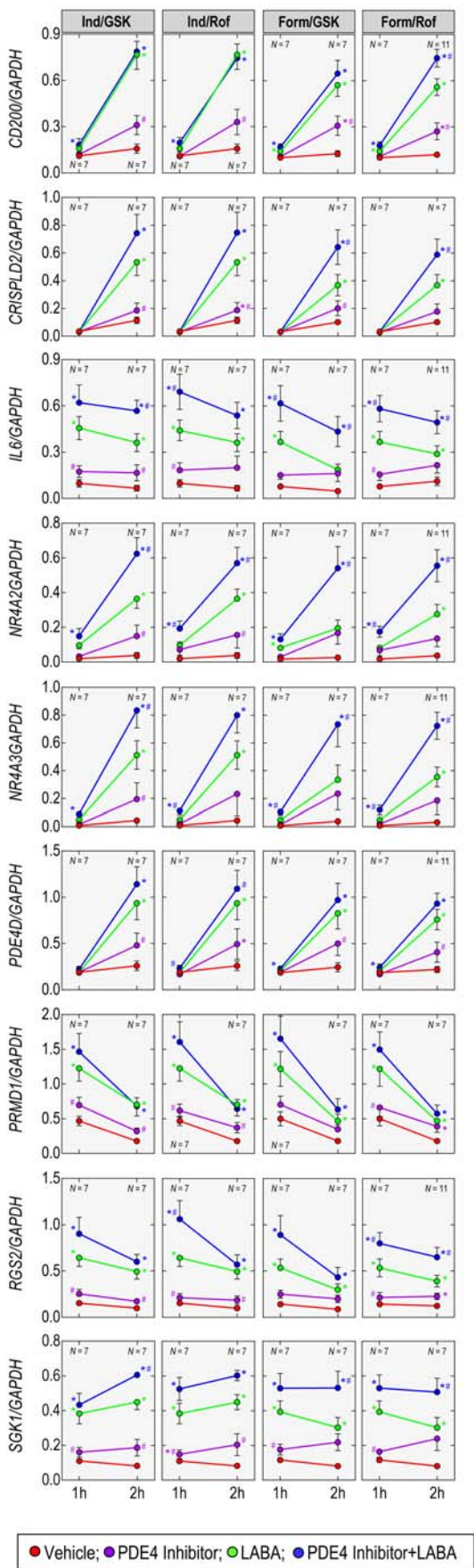


Figure 5



(A) **Figure 6** (B)



(C)

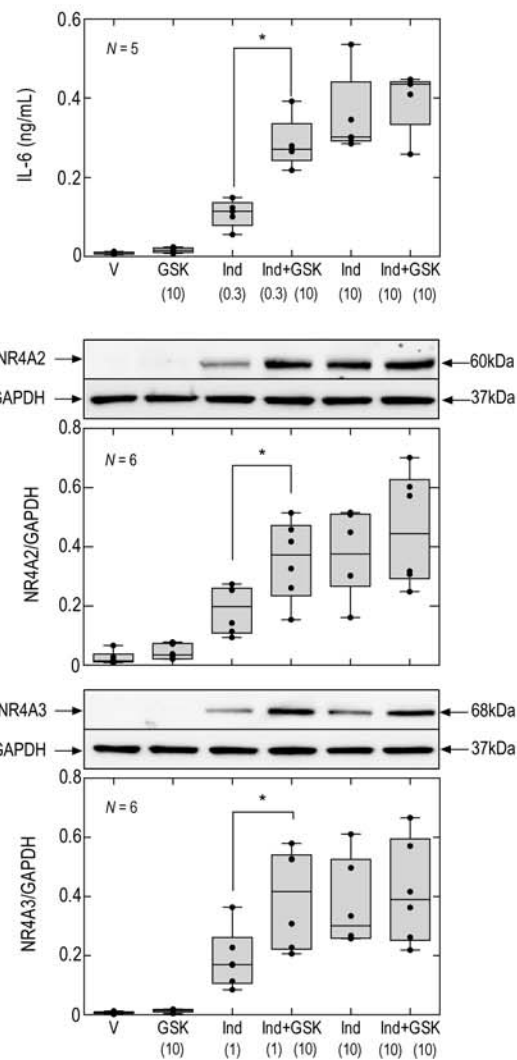
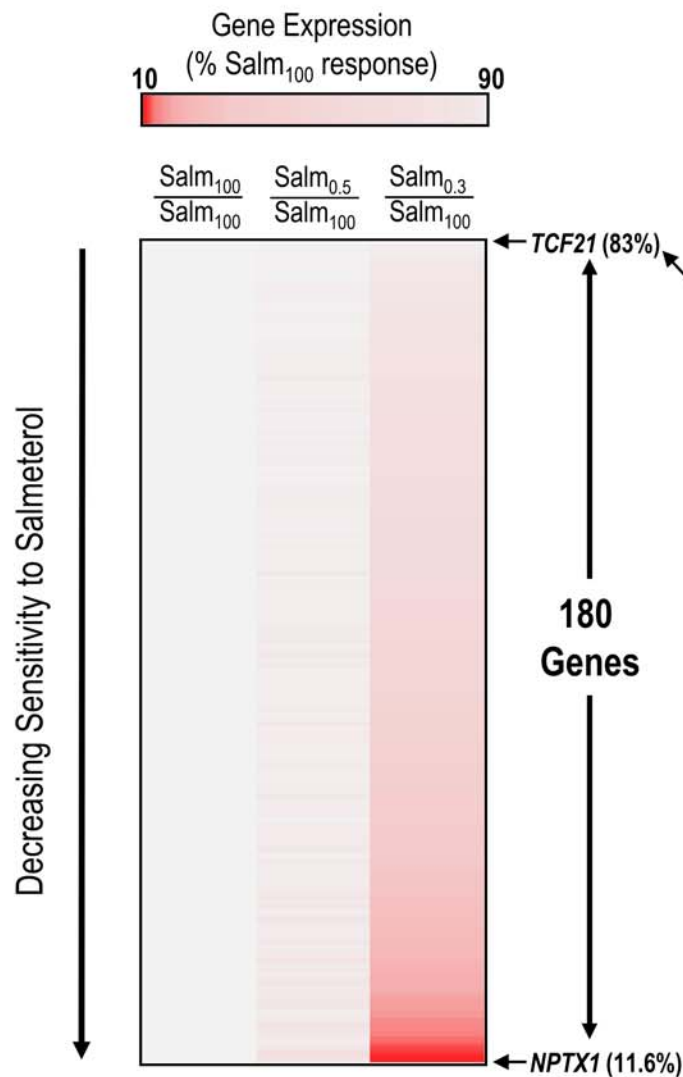
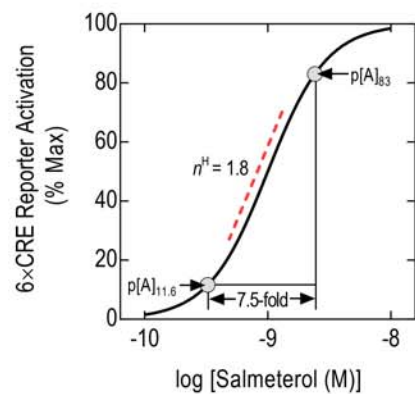


Figure 7

(A)



(B)



(C)

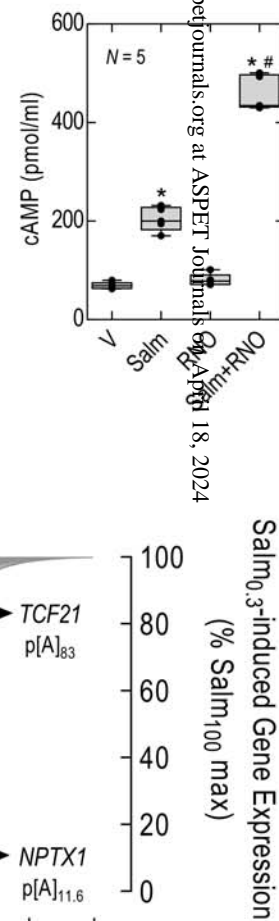
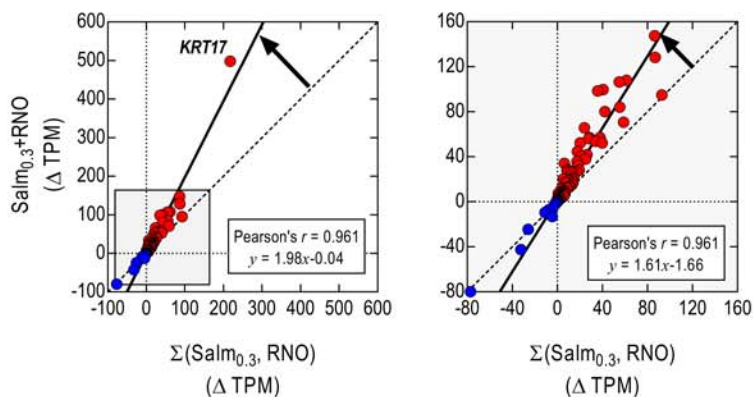
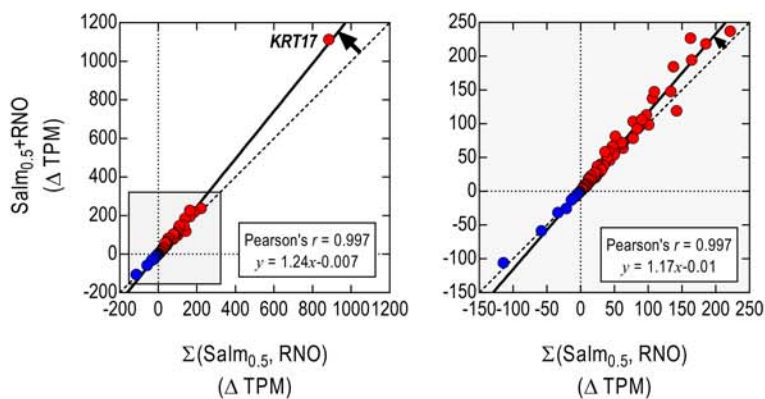


Figure 8

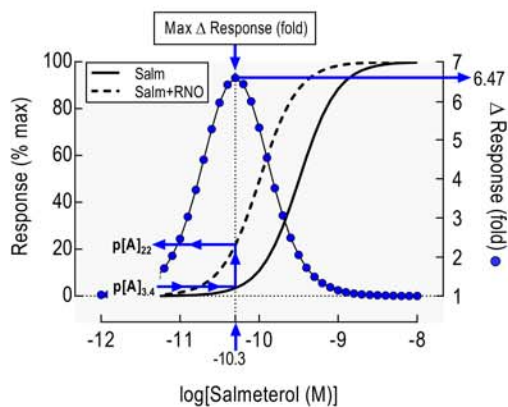
(A)



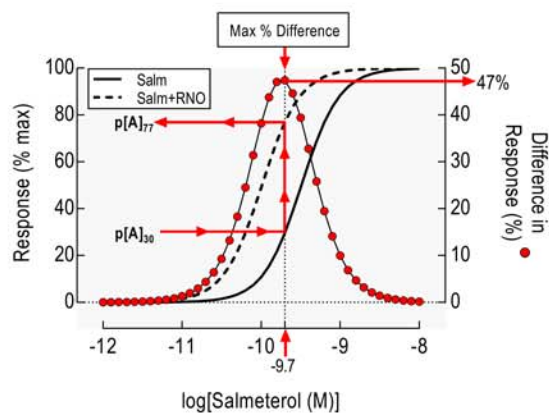
(B)



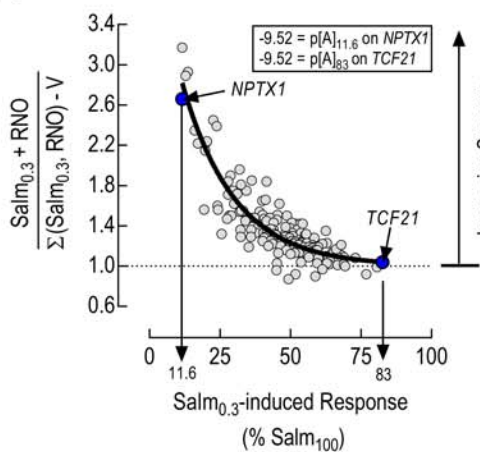
(C)



(D)



(E)



(F)

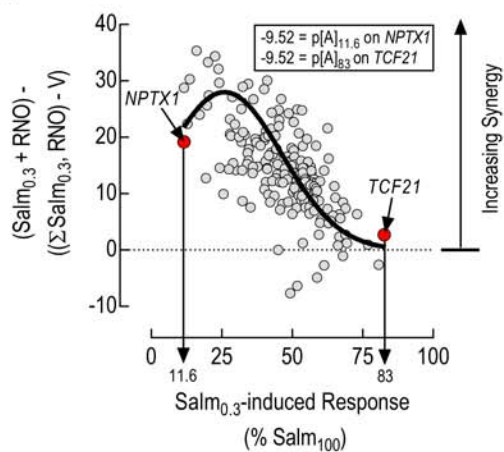
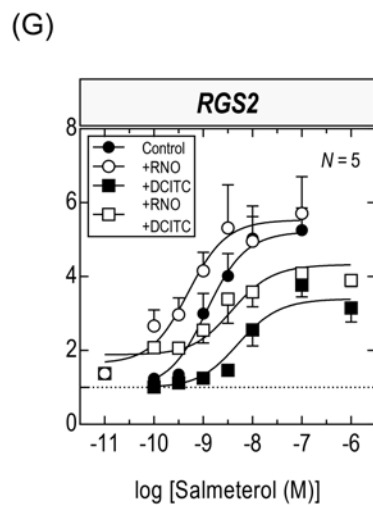
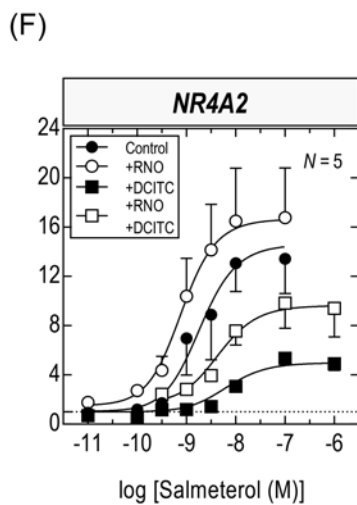
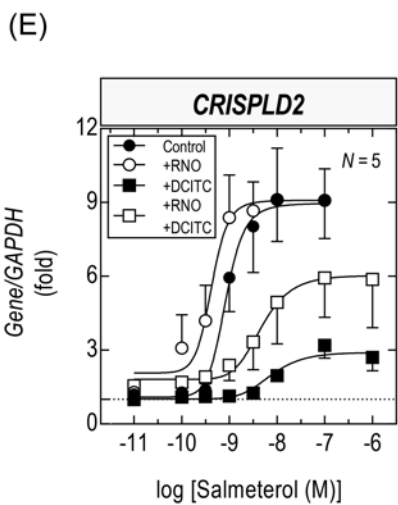
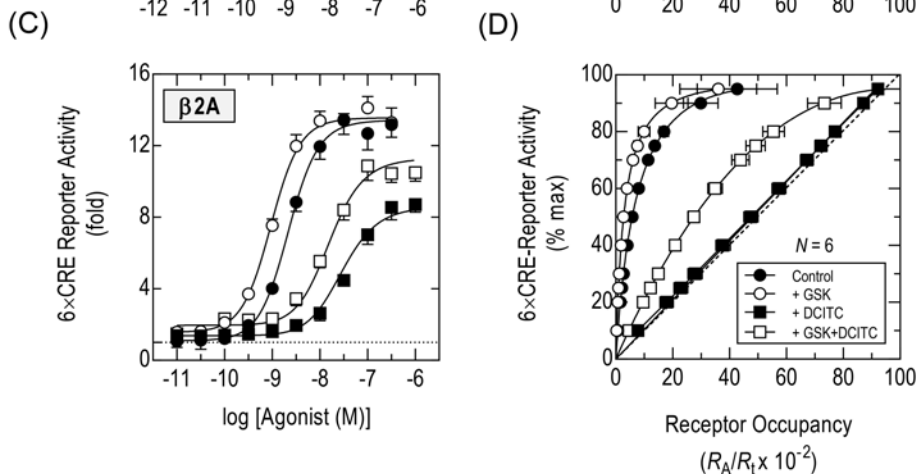
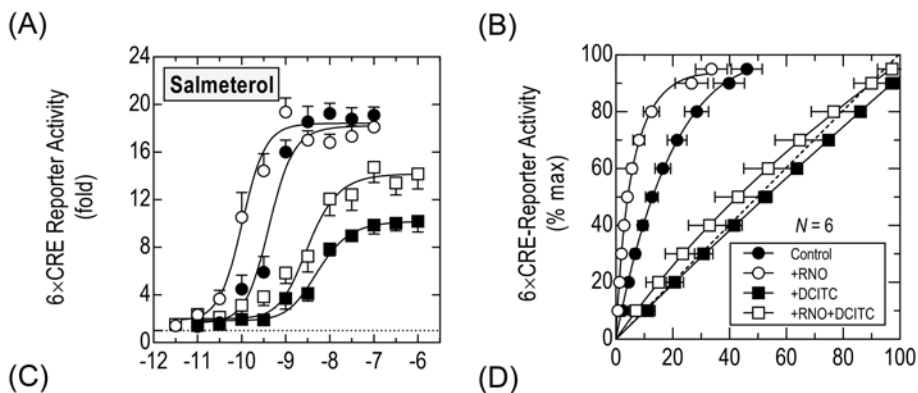


Figure 9



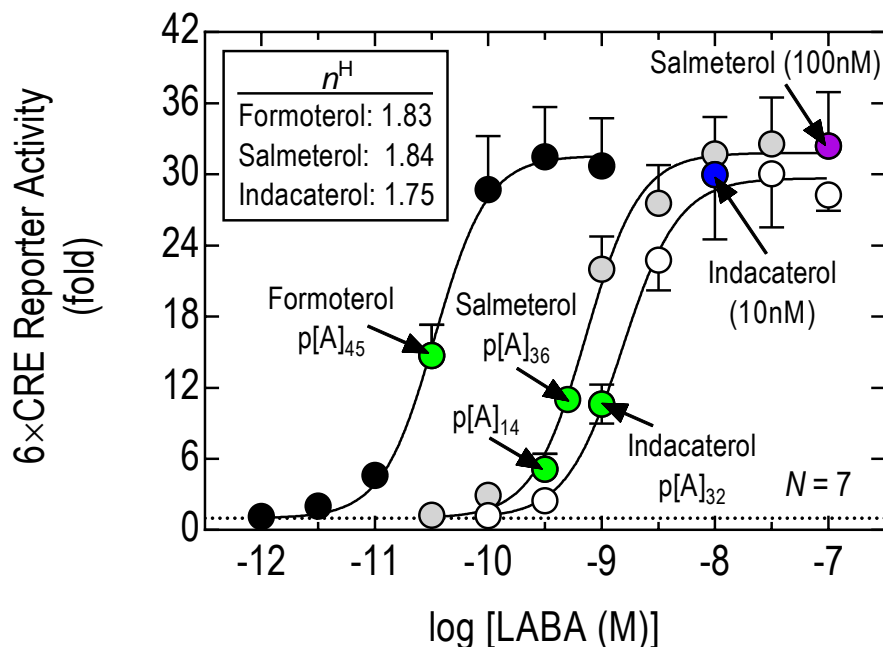
Supplemental Material

Impact of Phosphodiesterase 4 Inhibition on the Operational Efficacy, Response Maxima and Kinetics of Indacaterol-induced Gene Expression Changes in BEAS-2B Airway Epithelial Cells: A Global Transcriptomic Analysis

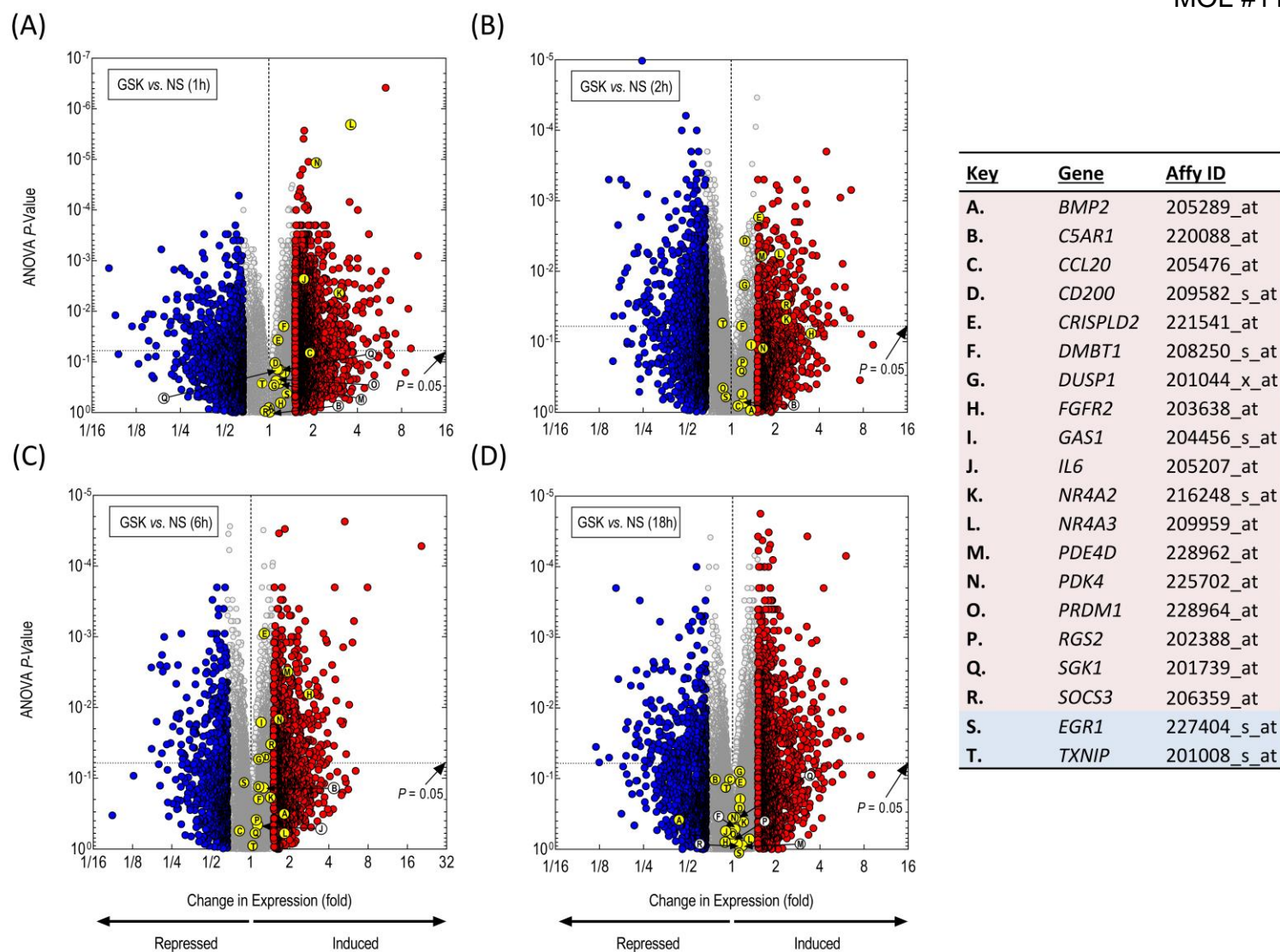
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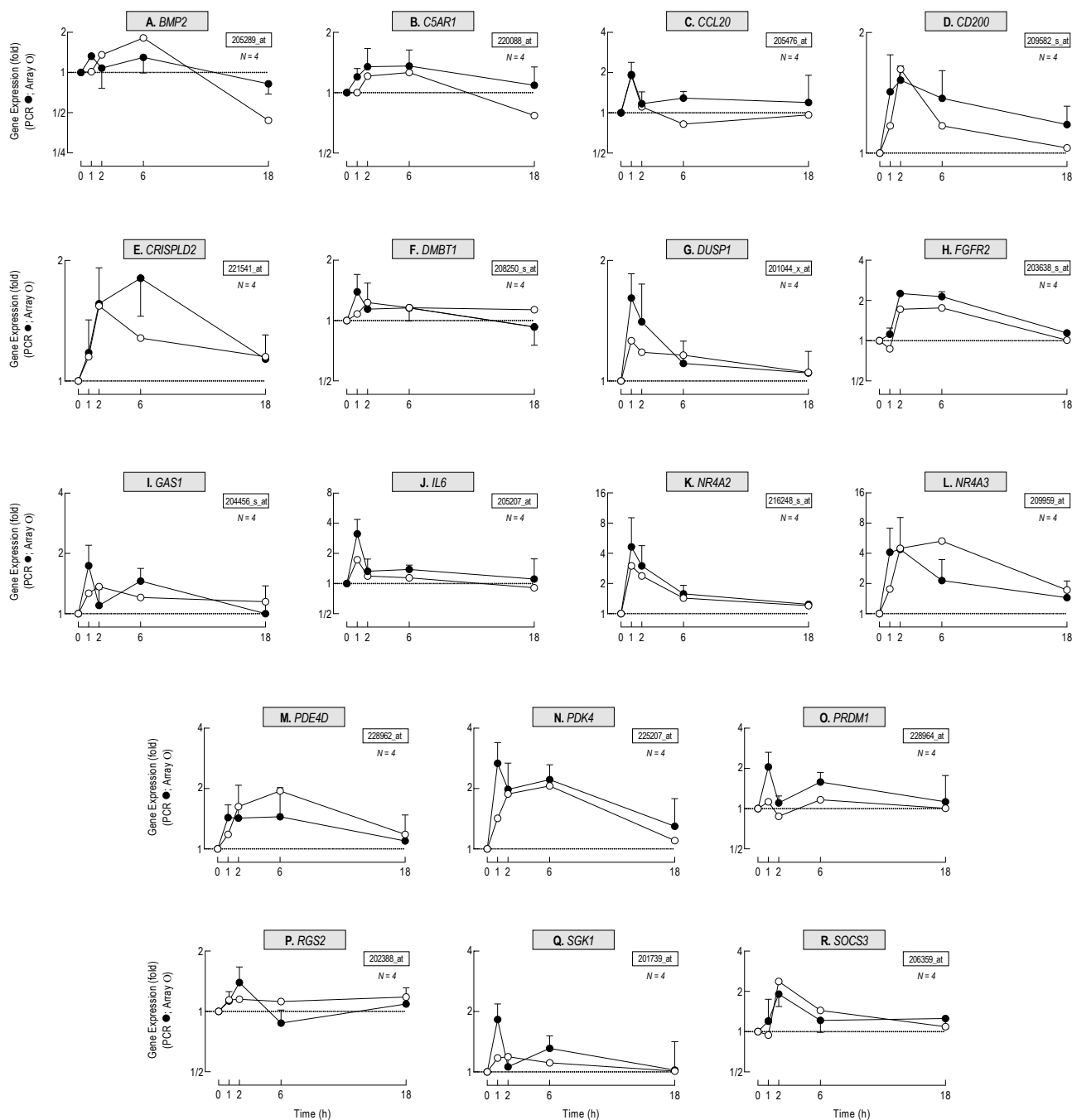
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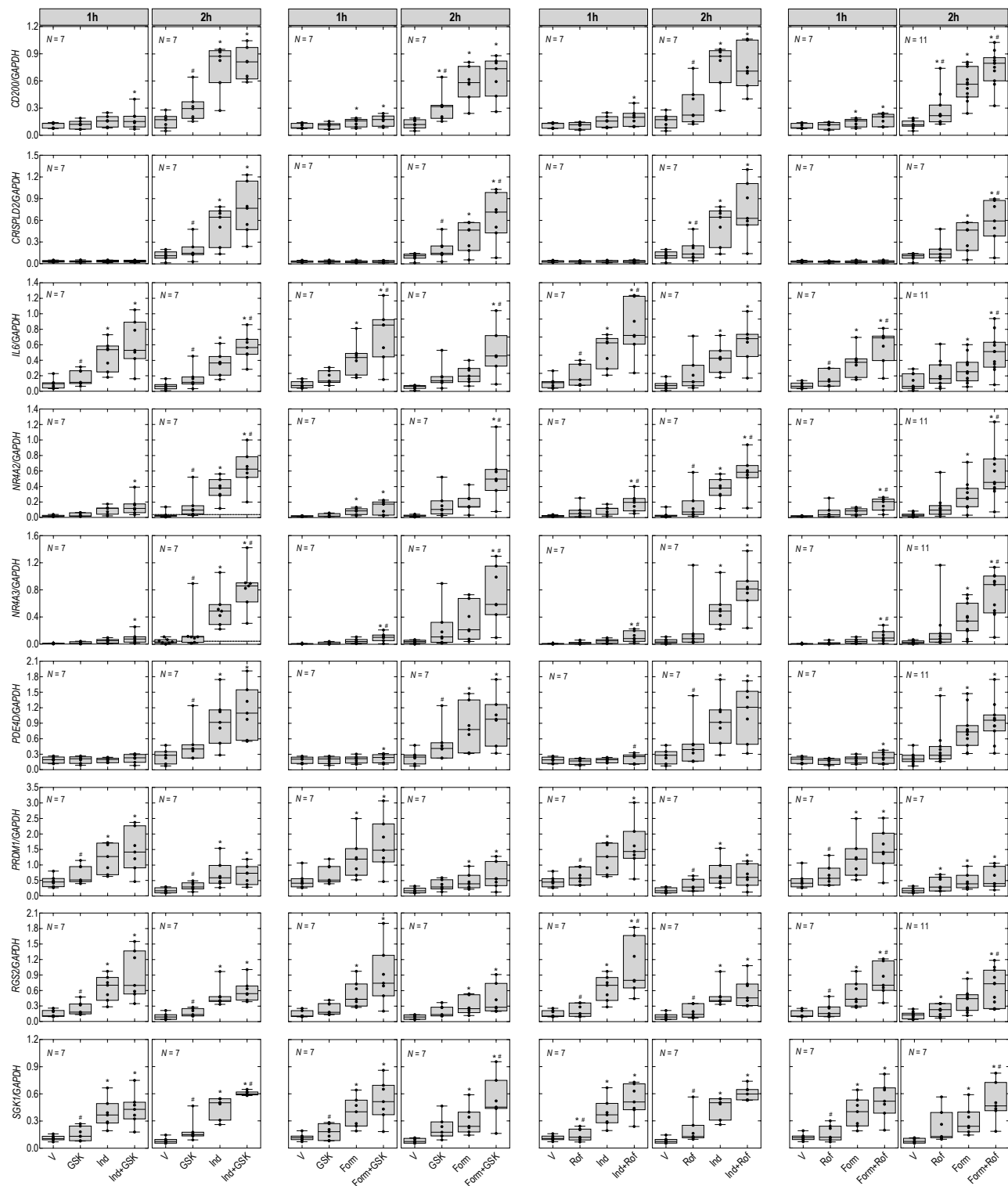
Supplemental Fig. 1. Effect of LABAs on the expression of luciferase activity in 6xCRE BEAS-2B reporter cells. $E/[A]$ curves were constructed to formoterol (black circles), indacaterol (white circles) and salmeterol (grey circles). The results shown in figures 1 to 5 were obtained with a maximally-effective concentration of indacaterol (10nM, blue circle). The results shown in figures 6, 7 and 8 were obtained with submaximal concentrations (green circles) of formoterol (30pM; $p[A]_{45}$), indacaterol (1nM; $p[A]_{32}$) and salmeterol (0.3nM; $p[A]_{14}$ and 0.5nM; $p[A]_{36}$) as indicated. In the RNA-seq experiment presented in figures 7 and 8, salmeterol (100nM, purple circle) was used to define maximal gene expression. Data points represent the mean \pm s.e. mean of N independent determinations. The horizontal dashed line represents baseline luciferase activity. N.B. All LABA $E/[A]$ curves were steep with Hill coefficients (n^H) significantly greater than unity slope.



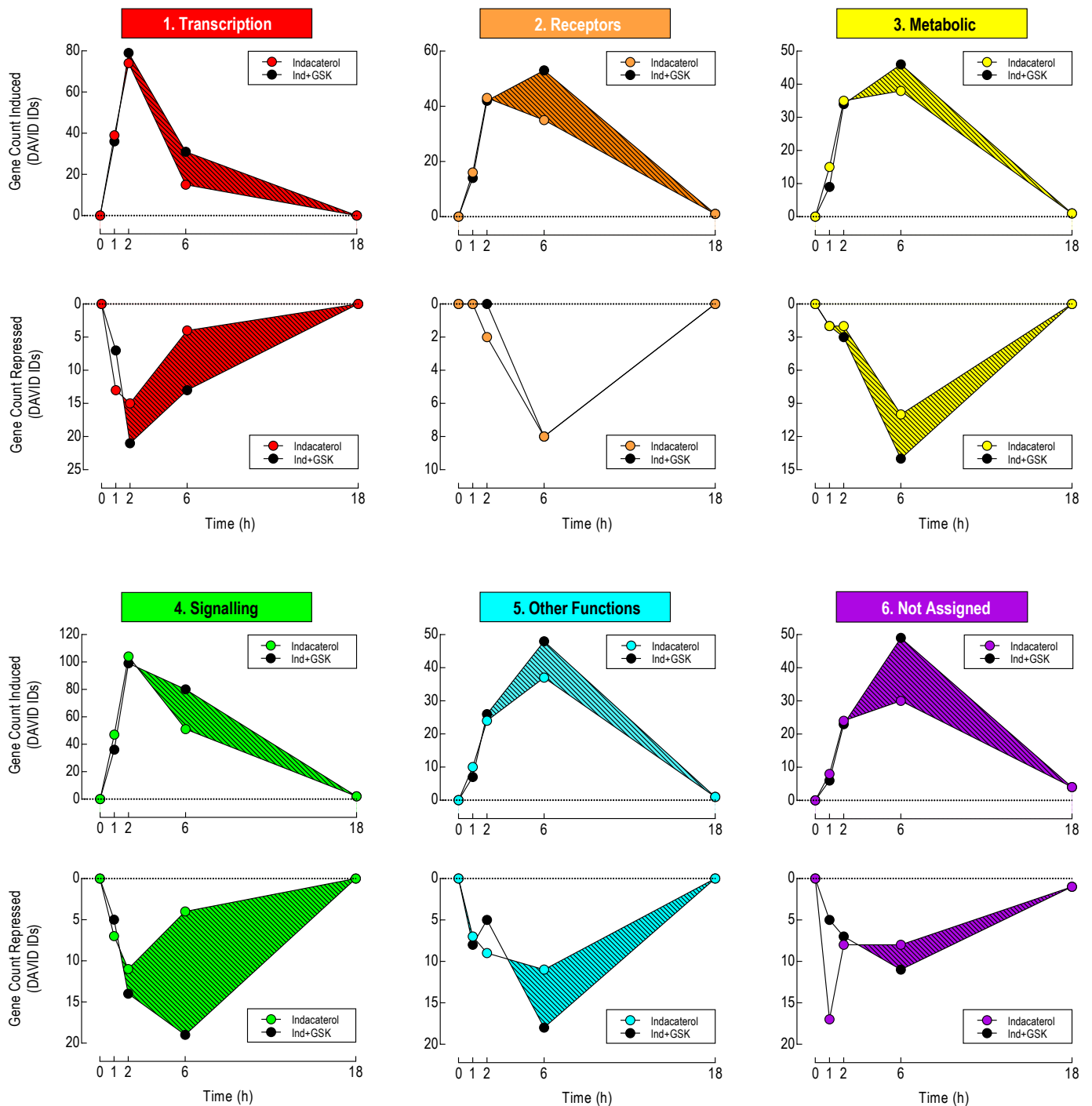
Supplemental Fig. 2. Volcano plots depicting GSK 256066-induced gene expression changes in BEAS-2B cells. cDNA from GSK 256066 (10nM)-treated cells was subjected to microarray and the relative expression patterning of probe sets at 1, 2, 6 and 18h was visualized by generating volcano plots (A to D respectively). Each probe set is represented by a circle coloured grey (transcript changes from >0.67-fold to <1.5-fold), red or blue (corresponding to transcripts that are either induced or repressed by >1.5-fold and <0.67-fold respectively). The letters in circles coloured yellow correspond to a HGNC gene symbol and Affymetrix probe set ID number (shown on the right side of the figure). The horizontal and vertical dashed lines in each panel indicate the ANOVA P -value set to a value of 0.05 and baseline gene expression respectively.



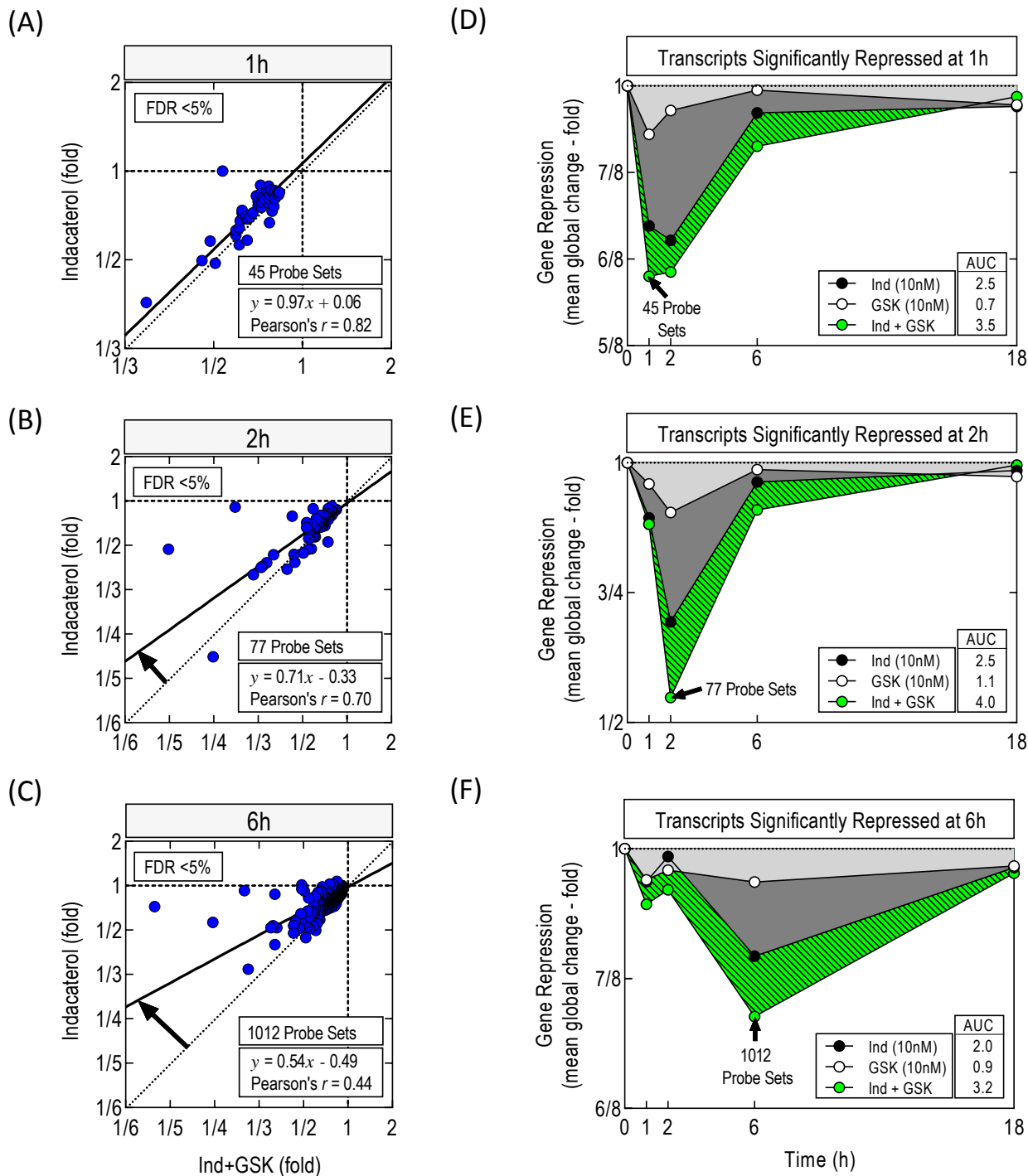
Supplemental Fig. 3. Validation of GSK 256066-induced gene expression changes. cDNA was prepared from BEAS-2B cells treated for 1, 2, 6 and 18h with GSK 256066 (10nM) or vehicle and subjected to gene expression profiling by microarray. Panels show the kinetics of 18 up-regulated genes (ordered alphabetically) plotted as fold on a \log_2 scale where a value of 1 indicates baseline expression (dashed horizontal lines). The open circles represent data taken directly from the microarray using the probe set that gave the most robust response relative to vehicle-treated, time-matched controls. These data were validated by PCR using the same cDNA, normalised to *GAPDH* and expressed as fold (filled black circles). Probe set IDs and their corresponding HGNC gene symbols are indicated in each panel. The letter preceding each gene symbol and in the circles coloured yellow in figure 1 and supplemental figure 2 refer to the same gene. PCR data are the mean \pm s.e. mean of *N* determinations.



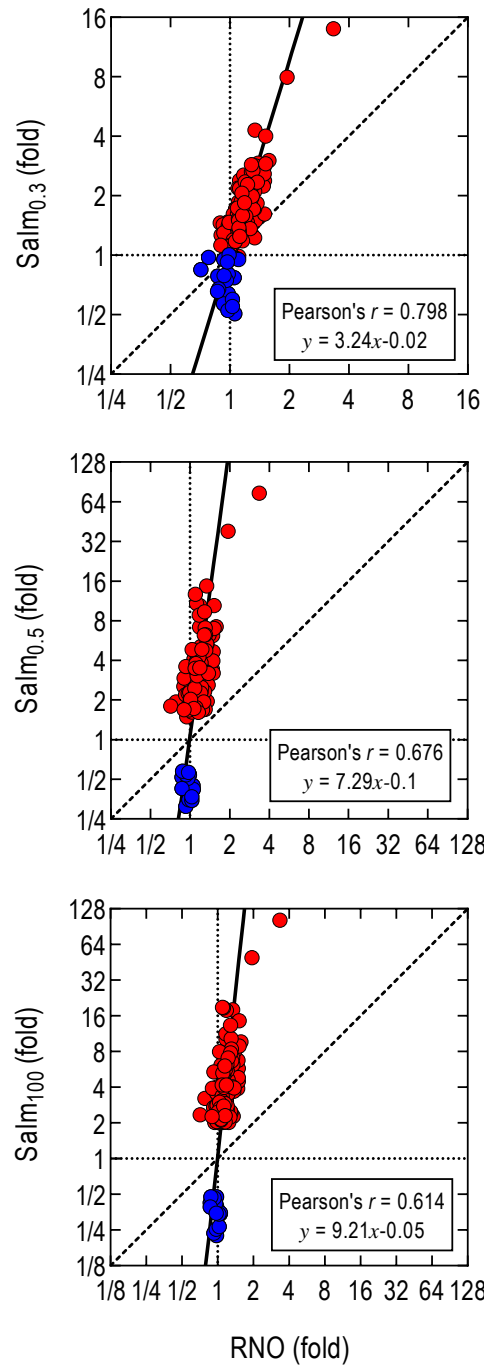
Supplemental Fig. 4. Effect of PDE4 inhibition on gene expression changes produced by submaximal concentrations of indacaterol and formoterol. BEAS-2B cells were pre-treated (30min) with either GSK 256066 (GSK; 10nM) or roflumilast (Rof; 1 μ M) and then exposed to either indacaterol (Ind; 1nM) or formoterol (Form; 30pM) for an additional 1 and 2h. RNA was extracted, cDNA prepared and the expression of nine indacaterol-induced genes was determined by real-time PCR, normalised to *GAPDH* and presented as Box and Whisker plots. Data are the mean \pm s.e. mean of *N* independent determinations. Statistical analysis was by repeated measures one-way ANOVA followed, when appropriate, by Tukey's multiple comparisons test. * P <0.05, significantly different from vehicle (V). # P <0.05, significantly different from LABA.



Supplemental Fig. 5. Comparative effects of indacaterol and Ind+GSK at 1, 2, 6 and 18h on the number of induced and repressed genes in BEAS-2B cells. cDNA was prepared from cells treated with indacaterol (10nM), Ind+GSK (both 10nM) or vehicle and subjected to gene expression profiling by microarray. Probe sets meeting the expression criteria (>1.5 -fold, <0.67 -fold; FDR $<10\%$) were analysed to identify DEGs (based on DAVID IDs). These were manually assigned to one of the six generic descriptors indicated and their number plotted at each time-point. The areas shaded in colours indicate the gain in gene count produced by Ind+GSK over indacaterol alone.



Supplemental Fig. 6. Global effect of GSK 256066 on the indacaterol-repressed transcriptome. Panels A-C: Genes (by probe set) that were significantly repressed (<1-fold; FDR <5%) by Ind+GSK at 1, 2 and 6h were correlated on a linear scale against their counterparts in indacaterol-treated cells. The black arrows in panels B and C indicate deviation from unity slope in favour of indacaterol (i.e., genes were repressed less than with Ind+GSK). Panels D-F: Comparative global expression kinetics for the probe sets from panels A-C that were significantly repressed by Ind+GSK at 1, 2 and 6h, respectively with their counterparts in cells treated with indacaterol (dark grey) and GSK 256066 (light grey). For example, in panel D, the global mean changes in expression (in fold) of the 45 probe sets that were significantly repressed by Ind+GSK at 1h was also calculated at the other two time-points, and at 1, 2 and 6h in cells treated with indacaterol and GSK 256066. This was repeated with the 72 and 1012 probe sets that were significantly upregulated at 2 and 6h (Panels E & F). The areas shaded green indicate the gain in AUC_{0-18h} produced by Ind+GSK compared to indacaterol alone. The AUC_{0-18h} for each intervention is indicated.



Supplemental Fig. 7. Relationships between salmeterol- and RNO-regulated gene expression changes in BEAS-2B cells. The panels show Pearson correlations and Deming regressions at 2h between gene expression changes produced by Salm_{0.3}, Salm_{0.5} and Salm₁₀₀ and their counterparts in cells treated with RNO (1 μ M). These data were generated by RNA-Seq and genes that were significantly induced (180, red circles) and repressed (16, blue circles) by Salm₁₀₀ (≥ 2 -fold; ≤ 0.5 -fold, FDR $\leq 5\%$) are presented (in fold) and plotted on a log₂ scale where a value of 1 equates to baseline expression (horizontal and vertical dashed lines). Solid and dashed diagonal lines represent linear regression and the line of identity respectively.

Supplemental TABLE 1. Primer pairs for real-time PCR.

Gene	Oligonucleotides	Accession Number(s)
<i>BMP2</i>		NM_001200.3
Forward	5' -CTACCAGAAACGAGTGGGAAA-3'	
Reverse	5' -GAAGCTCTGCTGAGGTGATAAA-3'	
<i>C5AR1</i>		NM_001736.3
Forward	5' -TCCTCCGGAACGTGTTGACT-3'	
Reverse	5' -AGCGCGTGAATGACTTGCT-3'	
<i>CCL20 (MIP3A)</i>		NM_001130046.1, NM_004591.2
Forward	5' -TGACATCAATGCTATCATCTTTCACA-3'	
Reverse	5' -TTTGCGCACACAGACAACCTTTT-3'	
<i>CD200</i>		NM_005944.5, NM_001004196.2
Forward	5' -GGACTGTGACCGACTTTAAGCAA-3'	
Reverse	5' -AGCAATAGCGGAACTGAAAACC-3'	
<i>CRISPLD2 (LGL)</i>		NM_031476.3
Forward	5' -CAAACCTTCCAGCTCATTCATG-3'	
Reverse	5' -GGTCGTGTAGCAGTCCAAATCC-3'	
<i>DMBT1</i>		NM_004406.2, NM_007329.2, NM_017579.2, NM_001320644.1
Forward	5' -GGTGGCATCCAACAACACTACAA-3'	
Reverse	5' -GTAGGATGGGCTGGAGAATGT-3'	
<i>DUSP1 (MKP1)</i>		NM_004417.3
Forward	5' -CGCGCAAGTCTTCTTCCCTCA-3'	
Reverse	5' -GATGCTTCGCTCTGCTTCA-3'	
<i>FGFR2</i>		NM_000141.4, NM_022970.3, NM_001144913.1, NM_023029.2, NM_001144914.1, NM_001144915.1, NM_001144916.1, NM_001144917.1, NM_001144918.1, NM_001144919.1
Forward	5' -CATCGCATTGGAGGCTACAAG-3'	
Reverse	5' -GGGACCACACTTTCATAATGAG-3'	
<i>GAPDH</i>		NM_002046.5, NM_001256799.2
Forward	5' -ATGGAAATCCCATCACCATCTT-3'	
Reverse	5' -CAGCATCGCCCCACTTG-3'	
<i>GAS1</i>		NM_002048.2
Forward	5' -CAGATTGTGCCAGTGAGGA-3'	
Reverse	5' -TCTGGGCCGAGATACAAACA-3'	

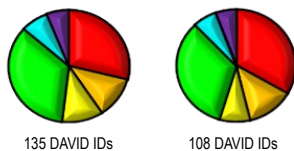
Gene	Oligonucleotides	Accession Number(s)
<i>IL6</i>		NM_000600.4, NM_001318095.1
Forward	5' -GAGTAGTGAGGAACAAGCCAG-3'	
Reverse	5' -GTCAGGGGTGGTTATTGCATC-3'	
<i>NR4A2 (NURR1)</i>		NM_006186.3
Forward	5' -GGCCCATGTGCGACTCCAA-3'	
Reverse	5' -GTCAGGGTTCGCCTGGAA-3'	
<i>NR4A3 (NORI)</i>		NM_006981.3, NM_173200.2, NM_173199.2
Forward	5' -GTAGACAAGAGACGTCGAAACC-3'	
Reverse	5' -CCTCTCCTCCCTTTCAGACTAT-3'	
<i>PDE4D</i>		NM_006203.4, NM_001104631.1, NM_001165899.1, NM_001197218.1, NM_001197219.1, NM_001197220.1, NM_001197221.1, NM_001197222.1, NM_001197223.1
Forward	5' -CTCTCTGAAATGAGTCGGTCTG-3'	
Reverse	5' -CCTTCTGAGTTGGAGAAGGAAT-3'	
<i>PDK4</i>		NM_002612.3
Forward	5' -GCTGTCCATGAAGCAGCTACTG-3'	
Reverse	5' -CGCAAAAATGCAAAAGAAGTTCT-3'	
<i>PRDM1</i>		NM_001198
Forward	5' -AACCAGGGAGGAAGAGATACA-3'	
Reverse	5' -GACTTGGGTGTGACCACATAA-3'	
<i>RGS2</i>		NM_002923
Forward	5' -CCTCAAAGCAAGGAAAAATATATACTGA-3'	
Reverse	5' -AGTTGTAAAGCAGCCACTTGTAGCT-3'	
<i>SGKI</i>		NM_001291995.1, NM_001143676.1, NM_001143677.1, NM_001143678.1, NM_005627.3, XM_011536071.1
Forward	5' -ATGGCCTGCCGCCTTTTTAT-3'	
Reverse	5' -CAGGAGGTGTCTTGCGGAAT-3'	
<i>SOCS3</i>		NM_003955.3
Forward	5' -GATTCTCCTTCAATTCCTCAGCTT-3'	
Reverse	5' -ATTAGTTCAGCATTCCCGAAGTGT-3'	

Official HGNC gene symbols are shown. When appropriate, common gene symbols are provided in parentheses. Generic primers were used for genes that encode multiple isoforms.

Supplemental TABLE 2. Transcripts induced by indacaterol and Ind+GSK in BEAS-2B cells. Genes, by probe set, are listed in decreasing order of induction after exposure of cells to indacaterol (10nM) and Ind+GSK (both 10nM) for 1, 2, 6 and 18h. Unshaded rows list transcripts that were significantly (FDR <10%) induced (>1.5-fold) by both treatments. Rows shaded grey highlight additional transcripts that were induced by indacaterol but not by Ind+GSK; rows shaded green highlight additional transcripts that were induced by Ind+GSK but not by indacaterol. All genes were manually assigned a colour that corresponds to one of six generic descriptors. Transcripts that lacked annotation were classified as *not assigned* (purple) and were excluded from all analyses. Pie charts at each time-point depict the number of indacaterol- and Ind+GSK-induced genes within each generic descriptor expressed as a fraction of the total number of significant gene expression changes. Genes validated by real-time PCR (Fig. 5+A1251) are underlined and shown in bold face.

GO Term	Color
Transcriptional Regulators	Red
Transporters, Ion Channels and Membrane Receptors	Orange
Metabolic Proteins	Yellow
General Signalling Molecules, including Translational Regulators	Green
Other Functions	Cyan
Not Assigned	Purple
MicroRNA	White

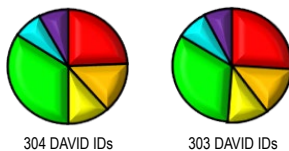
Treatment (1h)
 Ind: 173 Probe Sets (135 Genes)
 Ind+GSK: 139 Probe Sets (108 Genes)



Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value (Ind)	Fold change (Ind)	FDR P-Value (Ind+GSK)	Fold change (Ind+GSK)	UniGene Name	Function
204621_s_at	4929	<u>NR4A2</u>	2.10E-03	25.34	2.80E-03	22.26	nuclear receptor subfamily 4, group A, member 2	Red
207978_s_at	8013	<u>NR4A3</u>	2.40E-03	21.95	4.50E-03	19.54	nuclear receptor subfamily 4, group A, member 3	Red
216248_s_at	4929	<u>NR4A2</u>	1.40E-03	21.76	1.50E-03	21.15	nuclear receptor subfamily 4, group A, member 2	Red
204622_x_at	4929	<u>NR4A2</u>	1.60E-03	20.56	1.90E-03	18.84	nuclear receptor subfamily 4, group A, member 2	Red
209959_at	8013	<u>NR4A3</u>	2.80E-03	18.20	5.20E-03	14.96	nuclear receptor subfamily 4, group A, member 3	Red
205207_at	3569	<u>IL6</u>	5.78E-05	11.20	7.93E-05	10.63	interleukin 6	Green
205476_at	6364	<u>CCL20</u>	1.93E-02	7.04	2.45E-02	8.15	chemokine (C-C motif) ligand 20	Orange
228964_at	639	<u>PRDM1</u>	5.78E-05	6.48	7.93E-05	6.25	PR domain containing 1, with ZNF domain	Orange
208078_s_at	150094	<u>SIK1</u>	2.00E-04	5.07	2.00E-04	4.87	salt-inducible kinase 1	Yellow
209774_x_at	2920	<u>CXCL2</u>	5.78E-05	4.91	7.93E-05	4.48	serine/threonine-protein kinase SIK1	Yellow
239818_x_at	10221	<u>TRIB1</u>	5.00E-04	4.71	7.00E-04	4.65	chemokine (C-X-C motif) ligand 2	Yellow
232470_at	150094	<u>SIK1</u>	3.00E-04	4.65	6.00E-04	4.04	tribbles pseudokinase 1	Yellow
238378_at	285513	<u>GPRIN3</u>	1.10E-02	4.48	6.11E-02	3.08	salt-inducible kinase 1	Yellow
202241_at	10221	<u>TRIB1</u>	5.78E-05	4.46	7.93E-05	4.34	serine/threonine-protein kinase SIK1	Yellow
201739_at	6446	<u>SGK1</u>	1.00E-04	4.42	2.00E-04	4.39	tribbles pseudokinase 1	Yellow
205960_at	5166	<u>PKD4</u>	1.00E-04	4.41	3.00E-04	4.16	serum/glucocorticoid regulated kinase 1	Yellow
202388_at	5997	<u>RS2</u>	6.58E-05	4.33	7.93E-05	4.27	pyruvate dehydrogenase kinase, isozyme 4	Yellow
1557285_at	374	<u>AREG</u>	1.88E-02	3.79	2.13E-02	4.16	regulator of G-protein signaling 2	Yellow
225207_at	5166	<u>PKD4</u>	2.90E-03	3.78	4.60E-03	4.16	amphiregulin	Yellow
218995_s_at	1906	<u>EDN1</u>	2.00E-04	3.63	2.00E-04	3.51	pyruvate dehydrogenase kinase, isozyme 4	Yellow
201044_x_at	1843	<u>DUSP1</u>	2.00E-04	3.49	2.00E-04	3.37	endothelin 1	Yellow
222802_at	1906	<u>EDN1</u>	2.00E-04	3.47	2.00E-04	3.32	dual specificity phosphatase 1	Yellow
1555585_a_at	153745	<u>FAM71B</u>	8.10E-03	3.42	1.61E-02	3.09	endothelin 1	Yellow
227613_at	55422	<u>ZNF331</u>	2.60E-03	3.39	4.60E-03	3.12	family with sequence similarity 71, member B	Yellow
201169_s_at	8553	<u>BHLHE40</u>	2.00E-04	3.37	5.00E-04	2.88	zinc finger protein 331	Yellow
202340_x_at	3164	<u>NR4A1</u>	3.40E-03	3.35	1.55E-02	2.58	basic helix-loop-helix family, member e40	Yellow
211143_x_at	3164	<u>NR4A1</u>	1.30E-03	3.28	2.00E-03	2.89	nuclear receptor subfamily 4, group A, member 1	Yellow
213139_at	6591	<u>SNAI2</u>	6.58E-05	3.24	2.00E-04	2.88	nuclear receptor subfamily 4, group A, member 1	Yellow
219228_at	55422	<u>ZNF331</u>	3.40E-03	3.22	5.80E-03	2.95	snail family zinc finger 2	Yellow
244025_at	85450	<u>ITPR1</u>	6.00E-04	3.17	5.00E-04	3.52	zinc finger protein 331	Yellow
201170_s_at	8553	<u>BHLHE40</u>	7.07E-05	3.07	1.00E-04	2.90	inositol 1,4,5-trisphosphate receptor interacting protein	Yellow
224797_at	57561	<u>ARRDC3</u>	9.10E-03	2.88	5.20E-03	3.00	basic helix-loop-helix family, member e40	Yellow
205764_at	1452	<u>CSNK1A1</u>	2.51E-02	2.78	5.81E-02	2.28	arrestin domain containing 3	Yellow
203395_s_at	3280	<u>HES1</u>	1.40E-02	2.77	2.47E-02	2.69	casein kinase 1, alpha 1	Yellow
221841_s_at	9314	<u>KLF4</u>	3.50E-03	2.75	5.80E-03	2.64	hes family bHLH transcription factor 1	Yellow
225582_at	85450	<u>ITPR1</u>	3.00E-04	2.66	5.00E-04	2.50	Kruppel-like factor 4 (gut)	Yellow
203394_s_at	3280	<u>HES1</u>	4.70E-03	2.65	1.33E-02	2.49	hes family bHLH transcription factor 1	Yellow
238987_at	2683	<u>B4GALTL1</u>	1.16E-02	2.48	5.80E-03	2.91	inositol 1,4,5-trisphosphate receptor interacting protein	Yellow
205239_at	374	<u>AREG</u>	1.76E-02	2.41	2.27E-02	2.27	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1	Yellow
240413_at	149628	<u>PYHIN1</u>	2.32E-02	2.38	8.91E-02	2.06	amphiregulin	Yellow
203313_s_at	7050	<u>TGIF1</u>	7.00E-04	2.37	1.10E-03	2.17	pyrin and HIN domain family, member 1	Yellow
227337_at	353322	<u>ANKRD37</u>	7.00E-03	2.34	1.41E-02	2.18	TGFbeta-induced factor homeobox 1	Yellow
220088_at	728	<u>CSAR1</u>	2.60E-03	2.30	5.80E-03	2.26	ankyrin repeat domain 37	Yellow
36711_at	23764	<u>MAFF</u>	4.70E-03	2.29	8.30E-03	2.07	complement component 5a receptor 1	Yellow
201939_at	10769	<u>PLK2</u>	2.60E-03	2.23	2.40E-03	2.29	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F	Yellow
209582_s_at	4345	<u>CD200</u>	6.90E-03	2.21	1.27E-02	2.07	polo-like kinase 2	Yellow
1566901_at	7050	<u>TGIF1</u>	3.12E-02	2.21	3.97E-02	2.19	CD200 molecule	Yellow
202935_s_at	6662	<u>SOX9</u>	9.00E-04	2.19	5.00E-03	1.88	TGFbeta induced factor homeobox 1	Yellow
205193_at	23764	<u>MAFF</u>	1.49E-02	2.17	3.61E-02	1.90	SRY box 9	Yellow
209583_s_at	4345	<u>CD200</u>	5.00E-04	2.12	6.00E-04	2.07	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F	Yellow
204011_at	10253	<u>SPRY2</u>	8.00E-04	2.11	6.00E-04	2.19	CD200 molecule	Yellow
204491_at	5144	<u>PDE4D</u>	1.67E-02	2.11	2.26E-02	2.03	sprouty RTK signaling antagonist 2	Yellow
228962_at	5144	<u>PDE4D</u>	2.49E-02	2.06	2.92E-02	2.09	phosphodiesterase 4D, cAMP-specific	Yellow
204456_s_at	2619	<u>GAS1</u>	3.50E-02	2.05	4.01E-02	2.05	phosphodiesterase 4D, cAMP-specific	Yellow
205466_s_at	9957	<u>HS3ST1</u>	2.92E-02	2.04	5.61E-02	1.94	growth arrest-specific 1	Yellow
203574_at	4783	<u>NFIL3</u>	1.33E-02	2.02	2.56E-02	1.87	heparan sulfate (glucosamine) 3-O-sulfotransferase 1	Yellow
218177_at	57132	<u>CHMP1B</u>	1.63E-02	2.02	2.27E-02	1.92	nuclear factor, interleukin 3 regulated	Yellow
209457_at	1847	<u>DUSP5</u>	2.00E-03	2.01	2.60E-03	1.92	charged multivesicular body protein 1B	Yellow
216604_s_at	23428	<u>SLC7A8</u>	6.90E-03	2.01	9.90E-03	1.85	dual specificity phosphatase 5	Yellow
212977_at	57007	<u>ACKR3</u>	2.20E-03	1.99	4.10E-03	1.93	solute carrier family 7 (amino acid transporter light chain, L system), member 8	Yellow
205027_s_at	1326	<u>MAP3K8</u>	2.29E-02	1.99	3.38E-02	1.93	atypical chemokine receptor 3	Yellow
206758_at	1907	<u>EDN2</u>	1.88E-02	1.98	4.02E-02	1.70	mitogen-activated protein kinase kinase 8	Yellow
206382_s_at	627	<u>BONF</u>	3.60E-03	1.97	5.50E-03	1.93	endothelin 2	Yellow
230748_at	9120	<u>SLC16A6</u>	2.20E-02	1.96	5.64E-02	1.81	brain-derived neurotrophic factor	Yellow
207826_s_at	3399	<u>ID3</u>	5.10E-03	1.95	8.30E-03	1.90	solute carrier family 16, member 6	Yellow
206706_at	4908	<u>NTF3</u>	8.00E-04	1.94	1.10E-03	1.79	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein	Yellow
218631_at	60370	<u>AVP11</u>	9.00E-04	1.93	1.10E-03	1.86	neurotrophin 3	Yellow
218178_s_at	57132	<u>CHMP1B</u>	1.80E-03	1.93	2.50E-03	1.86	arginine vasopressin-induced 1	Yellow
202936_s_at	6662	<u>SOX9</u>	1.90E-03	1.93	1.56E-02	1.59	charged multivesicular body protein 1B	Yellow
208937_s_at	3397	<u>ID1</u>	1.21E-02	1.91	3.06E-02	1.69	SRY box 9	Yellow
218810_at	80149	<u>ZC3H12A</u>	9.20E-03	1.90	1.56E-02	1.71	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	Yellow
208960_s_at	1316	<u>KLF6</u>	6.00E-04	1.88	8.00E-04	1.82	zinc finger CCCH-type containing 12A	Yellow
202023_at	1942	<u>EFNA1</u>	3.00E-04	1.86	4.00E-04	1.82	Kruppel-like factor 6	Yellow
215111_s_at	8848	<u>TSC22D1</u>	1.03E-02	1.85	1.38E-02	1.83	ephrin-A1	Yellow
218723_s_at	28984	<u>RGCC</u>	1.33E-02	1.85	3.61E-02	1.61	TSC22 domain family, member 1	Yellow
239058_at	2303	<u>FOXO2</u>	1.49E-02	1.85	2.45E-02	1.73	regulator of cell cycle	Yellow
232746_at	57007	<u>ACKR3</u>	4.43E-02	1.84	4.01E-02	2.12	forkhead box C2	Yellow
225557_at	64651	<u>CSRN1P</u>	2.20E-03	1.83	2.40E-03	1.79	atypical chemokine receptor 3	Yellow
207850_at	2921	<u>CXCL3</u>	9.80E-03	1.83	1.20E-02	1.83	cysteine-serine-rich nuclear protein 1	Yellow
1552948_at	148870	<u>CDC27</u>	9.80E-03	1.82	1.56E-02	1.77	chemokine (C-X-C motif) ligand 3	Yellow
220987_s_at	81788	<u>NUAK2</u>	2.00E-03	1.81	2.80E-03	1.73	coiled-coil domain containing 27	Yellow
							A kinase (PRKA) interacting protein 1	Yellow
							NUAK family, SNF1-like kinase, 2	Yellow

202149_at	4739	<i>NEDD9</i>	8.40E-03	1.81	1.69E-02	1.71	neural precursor cell expressed, developmentally down-regulated 9
202431_s_at	4609	<i>MYC</i>	6.00E-04	1.80	1.00E-03	1.73	v-myc avian myelocytomatosis viral oncogene homolog
220266_s_at	9314	<i>KLIF4</i>	4.10E-02	1.80	5.61E-02	1.93	Kruppel-like factor 4 (gut)
220299_s_at	6515	<i>SLC2A3</i>	3.34E-02	1.78	7.68E-02	1.60	solute carrier family 2 (facilitated glucose transporter), member 3
204014_at	1846	<i>DUSP4</i>	1.20E-02	1.77	2.65E-02	1.58	dual specificity phosphatase 4
210836_x_at	5144	<i>PDE4D</i>	1.90E-02	1.77	1.86E-02	1.78	phosphodiesterase 4D, cAMP-specific
1555832_s_at	1316	<i>KLIF6</i>	1.40E-03	1.76	1.40E-03	1.73	Kruppel-like factor 6
203708_at	5142	<i>PDE4B</i>	1.96E-02	1.76	3.01E-02	1.68	phosphodiesterase 4B, cAMP-specific
226034_at	1846	<i>DUSP4</i>	6.90E-03	1.75	1.11E-02	1.63	dual specificity phosphatase 4
230472_at	79192	<i>IRK1</i>	6.90E-03	1.75	9.10E-03	1.69	iroquois homeobox 1
202150_s_at	4739	<i>NEDD9</i>	2.18E-02	1.74	3.97E-02	1.60	neural precursor cell expressed, developmentally down-regulated 9
235849_at	286133	<i>SCARAS5</i>	6.63E-02	1.71	1.97E-02	1.99	scavenger receptor class A, member 5
1553613_s_at	2296	<i>FOXO1</i>	1.60E-03	1.69	8.40E-03	1.50	forkhead box C1
233379_at	79899	<i>PRRS5</i>	8.33E-02	1.69	5.42E-02	1.93	proline rich 5 like
1554980_a_at	467	<i>ATF3</i>	1.80E-02	1.68	4.20E-02	1.55	activating transcription factor 3
215990_s_at	604	<i>BCL6</i>	1.90E-02	1.68	3.10E-02	1.63	B-cell CLL/lymphoma 6
222162_s_at	9510	<i>ADAMTS1</i>	2.20E-02	1.68	2.27E-02	1.75	ADAM metalloproteinase with thrombospondin type 1 motif 1
202497_x_at	6515	<i>SLC2A3</i>	2.97E-02	1.68	5.12E-02	1.61	solute carrier family 2 (facilitated glucose transporter), member 3
216236_s_at	144195	<i>SLC2A14</i>	2.98E-02	1.68	8.19E-02	1.53	solute carrier family 2 (facilitated glucose transporter), member 14
224605_at	1316	<i>KLIF6</i>	2.30E-03	1.67	3.00E-03	1.65	Kruppel-like factor 6
203140_at	604	<i>BCL6</i>	2.60E-03	1.67	4.50E-03	1.64	B-cell CLL/lymphoma 6
224657_at	54206	<i>ERRF1</i>	1.45E-02	1.65	2.65E-02	1.58	ERBB receptor feedback inhibitor 1
204931_at	6943	<i>TCF21</i>	1.88E-02	1.65	3.89E-02	1.53	transcription factor 21
204284_at	5507	<i>PPP1R3C</i>	5.76E-02	1.65	7.79E-02	1.54	protein phosphatase 1, regulatory subunit 3C
201041_s_at	1843	<i>DUSP1</i>	6.00E-04	1.64	5.00E-04	1.68	dual specificity phosphatase 1
227443_at	286343	<i>LURAP1L</i>	7.04E-02	1.64	9.28E-02	1.56	leucine rich adaptor protein 1-like
222088_s_at	6515	<i>SLC2A14</i>	6.27E-02	1.63	9.05E-02	1.57	solute carrier family 2 (facilitated glucose transporter), member 14
222379_at	23704	<i>SLC2A3</i>					solute carrier family 2 (facilitated glucose transporter), member 3
225720_at	171024	<i>KCNE4</i>	1.88E-02	1.61	4.20E-02	1.59	potassium channel, voltage gated subfamily E regulatory beta subunit 4
208961_s_at	1316	<i>SYNPO2</i>	8.98E-02	1.61	4.94E-02	1.78	synaptotagmin 2
225606_at	10018	<i>KLIF6</i>	1.80E-03	1.60	2.30E-03	1.60	Kruppel-like factor 6
226140_s_at	220213	<i>BCL2L11</i>	2.32E-02	1.60	5.47E-02	1.50	BCL2-like 11 (apoptosis facilitator)
201328_at	2114	<i>OTUD1</i>	8.90E-03	1.56	1.70E-02	1.51	OTU deubiquitinase 1
228325_at	23514	<i>ETS2</i>	7.00E-03	1.55	1.66E-02	1.50	v-ets avian erythroblastosis virus E26 oncogene homolog 2
228462_at	153572	<i>SHDR</i>	1.03E-02	1.55	9.50E-03	1.60	scaffolding protein involved in DNA repair
207980_s_at	10370	<i>IRK2</i>	1.33E-02	1.55	1.44E-02	1.58	iroquois homeobox 2
212230_at	8613	<i>CITED2</i>	1.11E-02	1.54	1.38E-02	1.52	Cbp/p300-interacting transactivator, with Glu/Asp rich carboxy-terminal domain, 2
202704_at	10140	<i>PLPP3</i>	3.27E-02	1.54	3.97E-02	1.52	phospholipid phosphatase 3
209101_at	1490	<i>TOB1</i>	5.18E-02	1.54	3.36E-02	1.61	transducer of ERBB2, 1
228167_at	89857	<i>CTGF</i>	5.89E-02	1.54	6.11E-02	1.52	connective tissue growth factor
206999_at	3595	<i>KLHL6</i>	7.24E-02	1.53	1.76E-01	1.30	kelch-like family member 6
229004_at	170689	<i>IL12RB2</i>	4.25E-02	1.52	4.01E-02	1.56	interleukin 12 receptor, beta 2
		<i>ADAMTS15</i>	1.88E-02	1.51	2.27E-02	1.58	ADAM metalloproteinase with thrombospondin type 1 motif 15
239145_at	84330	<i>ZNF414</i>	1.00E-01	6.62	3.39E-01	2.68	zinc finger protein 414
233972_s_at	55079	<i>FEZF2</i>	8.52E-02	4.90	4.73E-01	2.22	FEZ family zinc finger 2
239530_at	119	<i>ADD2</i>	6.44E-02	2.64	1.69E-01	1.77	adducin 2 (beta)
210632_s_at	6442	<i>SGCA</i>	9.68E-02	2.35	1.48E-01	2.15	sarcoglycan alpha
205290_s_at	650	<i>BMIP2</i>	7.04E-02	2.27	1.69E-01	1.83	bone morphogenetic protein 2
1559987_at	124540	<i>MSI2</i>	8.27E-02	2.27	1.09E-01	2.09	musashi RNA binding protein 2
242543_at	284948	<i>SH2D6</i>	8.83E-02	2.19	2.96E-01	1.45	SH2 domain containing 6
229152_at	260436	<i>FDCSP</i>	4.70E-02	2.17	1.27E-01	1.80	follicular dendritic cell secreted protein
1555118_at	956	<i>ENTPD3</i>	7.24E-02	2.15	1.07E-01	1.89	ectonucleoside triphosphate diphosphohydrolase 3
239367_at	627	<i>BDNF</i>	1.30E-03	2.10	1.87E-01	1.62	brain-derived neurotrophic factor
220125_at	27019	<i>DNAI1</i>	5.65E-02	2.10	2.30E-03	1.97	dynein, axonemal, intermediate chain 1
	1139	<i>CHRFAM7A</i>					CHRNA7 (Exons 5-10) And FAM7A (Exons A-E) Fusion
236385_at	89832	<i>CHRNA7</i>	3.12E-02	1.93	1.44E-01	1.66	cholinergic receptor, nicotinic alpha 7
	101929970	<i>LOC101929970</i>					CHRNA7-FAM7A fusion protein
229110_at	25769	<i>SLC2A2</i>	5.09E-02	1.93	2.03E-01	1.47	solute carrier family 24 (sodium/potassium/calcium exchanger), member 2
202672_s_at	467	<i>ATF3</i>	5.76E-02	1.93	1.02E-01	1.59	activating transcription factor 3
234583_at	10752	<i>CHL1</i>	6.34E-02	1.83	5.55E-01	1.25	cell adhesion molecule L1-like
205815_at	5068	<i>REG3A</i>	8.98E-02	1.79	1.65E-01	1.67	regenerating islet-derived 3 alpha
231035_s_at	220213	<i>OTUD1</i>	3.90E-02	1.74	1.08E-01	1.50	OTU deubiquitinase 1
211962_s_at	677	<i>ZFP36L1</i>	9.92E-02	1.73	1.02E-01	1.68	ZFP36 ring finger protein-like 1
1553422_s_at	54715	<i>RBFOX1</i>	5.93E-02	1.70	1.18E-01	1.50	RNA binding protein, fox-1 homolog (C. elegans) 1
213170_at	2882	<i>GPX7</i>	4.29E-02	1.68	1.08E-01	1.53	glutathione peroxidase 7
207981_s_at	2104	<i>ESRRG</i>	4.29E-02	1.67	2.20E-01	1.33	estrogen-related receptor gamma
213284_at	677	<i>ZFP36L1</i>	5.24E-02	1.66	2.62E-01	1.28	ZFP36 ring finger protein-like 1
221766_s_at	55603	<i>FAM46A</i>	5.09E-02	1.64	7.49E-02	1.47	family with sequence similarity 46, member A
229373_at	3274	<i>HRH2</i>	1.63E-02	1.63	6.88E-02	1.44	histamine receptor H2
205929_at	10223	<i>GPA33</i>	6.88E-02	1.62	1.02E-01	1.53	glycoprotein A33 (transmembrane)
1554420_at	467	<i>ATF3</i>	9.65E-02	1.62	1.01E-01	1.62	activating transcription factor 3
219371_s_at	10365	<i>KLIF2</i>	4.72E-02	1.61	7.49E-02	1.44	Kruppel-like factor 2
1553378_a_at	256957	<i>HEATR9</i>	5.39E-02	1.60	1.13E-01	1.50	HEAT repeat containing 9
234928_x_at	864	<i>RUNX3</i>	6.63E-02	1.60	3.58E-01	1.18	runt-related transcription factor 3
206374_at	1850	<i>DUSP8</i>	2.31E-02	1.59	9.62E-02	1.33	dual specificity phosphatase 8
1431_at	1571	<i>CYP2E1</i>	1.67E-02	1.58	4.80E-02	1.46	cytochrome P450, family 2, subfamily E, polypeptide 1
218880_at	2355	<i>FOSL2</i>	4.79E-02	1.58	1.07E-01	1.37	FOS-like antigen 2
211302_s_at	5142	<i>PDE4B</i>	8.43E-02	1.58	1.37E-01	1.45	phosphodiesterase 4B, cAMP-specific
239381_at	5650	<i>KLK7</i>	9.47E-02	1.58	1.79E-01	1.39	kallikrein related peptidase 7
203438_at	8614	<i>STC2</i>	1.63E-02	1.57	3.53E-02	1.48	stanniocalcin 2
229552_at	8739	<i>HRK</i>	8.49E-02	1.56	1.02E-01	1.51	harakiri, BCL2 interacting protein
	283454	<i>LOC283454</i>					uncharacterized LOC283454
212143_s_at	3486	<i>IGFBP3</i>	3.90E-02	1.55	9.06E-02	1.44	insulin like growth factor binding protein 3
228188_at	2355	<i>FOSL2</i>	8.83E-02	1.55	9.28E-02	1.48	FOS-like antigen 2
230493_at	387914	<i>SHISA2</i>	8.30E-03	1.54	1.66E-02	1.47	shisa family member 2
202628_s_at	5054	<i>SERPINE1</i>	2.60E-03	1.53	8.50E-03	1.42	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1
203973_s_at	1052	<i>CEBPD</i>	7.00E-03	1.53	1.38E-02	1.45	CCAAT/enhancer binding protein (C/EBP), delta
231958_at	132001	<i>TAMM41</i>	3.78E-02	1.53	4.09E-01	1.05	TAM41 mitochondrial translocator assembly and maintenance homolog
229800_at	9201	<i>DCLK1</i>	1.63E-02	1.52	5.15E-02	1.42	doublecortin-like kinase 1
212226_s_at	8613	<i>PLPP3</i>	1.72E-02	1.52	2.89E-02	1.48	phospholipid phosphatase 3
206170_at	154	<i>ADRB2</i>	1.63E-02	1.51	4.43E-02	1.43	adrenoceptor beta 2, surface
230372_at	3037	<i>HAS2</i>	2.25E-02	1.51	3.85E-02	1.47	hyaluronan synthase 2
204015_s_at	1846	<i>DUSP4</i>	2.41E-02	1.51	3.22E-02	1.48	dual specificity phosphatase 4
230773_x_at	79750	<i>ZNF385D</i>	3.60E-02	1.51	1.27E-01	1.36	zinc finger protein 385D
208293_x_at	1444	<i>CSHL1</i>	6.70E-02	1.51	3.40E-01	1.21	chorionic somatomammotropin hormone-like 1
235182_at	140862	<i>ISM1</i>	9.00E-02	1.51	3.67E-01	1.31	isthmin 1, angiogenesis inhibitor
1565800_x_at	117177	<i>RAB31P</i>	1.95E-01	2.68	3.45E-02	5.89	RAB3A interacting protein
204938_s_at	5350	<i>PLN</i>	1.25E-01	2.05	5.61E-02	2.57	phospholamban
219388_at	79977	<i>GRHL2</i>	2.12E-01	1.59	9.93E-02	1.95	grainyhead-like transcription factor 2
215025_at	4916	<i>NTRK3</i>	3.24E-01	1.39	8.86E-02	1.84	neurotrophic tyrosine kinase, receptor, type 3
223563_at	54584	<i>GNB1L</i>	1.47E-01	1.53	9.28E-02	1.72	guanine nucleotide binding protein (G protein), beta polypeptide 1-like
210504_at	10661	<i>KLIF1</i>	1.14E-01	1.36	2.89E-02	1.66	Kruppel-like factor 1 (erythroid)
220819_at	79981	<i>FRMD1</i>	8.43E-02	1.45	1.68E-02	1.64	FERM domain containing 1
220509_at	64062	<i>RBM26</i>	1.74E-01	1.49	8.67E-02	1.63	RNA binding motif protein 26
1557085_at	219990	<i>OOSP2</i>	2.42E-01	1.32	6.03E-02	1.61	oocyte secreted protein 2
219682_s_at	6926	<i>TBX3</i>	9.65E-02	1.47	5.89E-02	1.61	T-box 3
216281_at	23405	<i>DICER1</i>	1.55E-01	1.39	4.90E-02	1.58	dicer 1, ribonuclease type III
223218_s_at	64332	<i>NFKBIZ</i>	9.73E-02	1.46	5.53E-02	1.55	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta
236554_x_at	147138	<i>MTC8</i>	3.57E-01	1.18	1.67E-02	1.53	transmembrane channel like 8
213260_at	2296	<i>FOXO1</i>	1.02E-01	1.50	8.00E-02	1.52	forkhead box C1
1559429_a_at	255798	<i>SMCO1</i>	1.71E-01	1.34	6.10E-02	1.52	single-pass membrane protein with coiled-coil domains 1
1553505_at	144568	<i>A2M1L</i>	1.67E-02	1.48	1.66E-02	1.52	alpha-2-macroglobulin-like 1

Treatment (2h)
 Ind: 483 Probe Sets (304 Genes)
 Ind+GSK: 479 Probe Sets (303 Genes)



Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value (Ind)	Fold change (Ind)	FDR P-Value (Ind+GSK)	Fold change (Ind+GSK)	UniGene Name	Function
209959_at	8013	NR4A3	6.05E-05	66.19	7.80E-05	61.82	nuclear receptor subfamily 4, group A, member 3	
207978_s_at	8013	NR4A3	4.57E-05	38.53	4.84E-05	37.30	nuclear receptor subfamily 4, group A, member 3	
216248_s_at	4929	NR4A2	7.00E-04	28.71	6.00E-04	27.98	nuclear receptor subfamily 4, group A, member 2	
204622_x_at	4929	NR4A2	2.00E-04	24.49	2.00E-04	22.83	nuclear receptor subfamily 4, group A, member 2	
204621_s_at	4929	NR4A2	1.70E-03	24.45	1.60E-03	25.95	nuclear receptor subfamily 4, group A, member 2	
203639_s_at	2263	FGFR2	1.51E-02	13.55	2.43E-02	10.25	fibroblast growth factor receptor 2	
205289_at	650	BMP2	1.45E-02	11.62	1.36E-02	12.41	bone morphogenetic protein 2	
221541_at	83716	CRISPLD2	5.25E-06	8.50	5.99E-06	8.33	cysteine-rich secretory protein LCCL domain containing 2	
225207_at	5166	PKD4	1.00E-04	8.30	1.00E-04	9.33	pyruvate dehydrogenase kinase, isozyme 4	
205476_at	6364	CCL20	3.00E-04	7.94	6.00E-04	7.25	chemokine (C-C motif) ligand 20	
205207_at	3569	IL6	1.90E-03	7.75	2.00E-03	7.75	interleukin 6	
205960_at	5166	PKD4	3.00E-03	6.74	3.10E-03	6.75	pyruvate dehydrogenase kinase, isozyme 4	
232470_at	150094	SIK1	2.00E-04	6.56	2.00E-04	6.38	salt-inducible kinase 1	
	102724428	LOC102724428					serine/threonine-protein kinase SIK1	
208078_s_at	150094	SIK1					salt-inducible kinase 1	
	102724428	LOC102724428	1.11E-05	6.31	1.01E-05	6.64	serine/threonine-protein kinase SIK1	
218541_s_at	56892	C8orf4	1.81E-02	6.12	1.77E-02	6.60	chromosome 8 open reading frame 4	
228962_at	5144	PDE4D	8.63E-05	6.12	9.09E-05	5.88	phosphodiesterase 4D, cAMP-specific	
201739_at	6446	SGK1	6.05E-05	5.78	7.80E-05	5.53	serum/glucocorticoid regulated kinase 1	
206359_at	9021	SOCS3	1.44E-02	5.73	1.32E-02	5.75	suppressor of cytokine signaling 3	
209582_s_at	4345	CD200	2.00E-04	5.71	2.00E-04	5.56	CD200 molecule	
203638_s_at	2263	FGFR2	1.20E-03	5.67	1.40E-03	5.56	fibroblast growth factor receptor 2	
228964_at	639	PRDM1	1.11E-05	5.50	1.17E-05	5.76	PR domain containing 1, with ZNF domain	
211401_s_at	2263	FGFR2	5.23E-02	5.37	5.12E-02	6.11	fibroblast growth factor receptor 2	
204491_at	5144	PDE4D	5.15E-05	5.25	4.12E-05	5.31	phosphodiesterase 4D, cAMP-specific	
227697_at	9021	SOCS3	2.11E-02	5.04	2.32E-02	4.80	suppressor of cytokine signaling 3	
225582_at	85450	ITPRIP	1.35E-05	4.75	1.83E-05	4.52	inositol 1,4,5-trisphosphate receptor interacting protein	
210837_s_at	5144	PDE4D	2.00E-04	4.75	2.00E-04	4.58	phosphodiesterase 4D, cAMP-specific	
202388_at	5997	RG52	9.78E-05	4.75	1.00E-04	4.58	regulator of G-protein signaling 2	
210836_x_at	5144	PDE4D	9.33E-05	4.52	1.00E-04	4.48	phosphodiesterase 4D, cAMP-specific	
244025_at	85450	ITPRIP	3.00E-04	4.49	2.00E-04	4.73	inositol 1,4,5-trisphosphate receptor interacting protein	
205290_s_at	650	BMP2	1.20E-03	4.45	7.00E-04	5.11	bone morphogenetic protein 2	
209774_x_at	2920	CXCL2	1.80E-03	4.40	3.10E-03	3.73	chemokine (C-X-C motif) ligand 2	
205330_at	4330	MM1	1.20E-03	4.40	1.20E-03	4.32	meningioma (disrupted in balanced translocation) 1	
230748_at	9120	SLC16A6	1.00E-04	4.32	1.00E-04	4.03	solute carrier family 16, member 6	
209583_s_at	4345	CD200	1.11E-05	4.30	1.01E-05	4.35	CD200 molecule	
227613_at	54222	ZNF331	2.00E-04	4.30	2.00E-04	4.24	zinc finger protein 331	
207038_at	9120	SLC16A6	3.20E-03	4.29	3.20E-03	4.32	solute carrier family 16, member 6	
220088_at	728	CSAR1	5.00E-04	4.23	6.00E-04	4.11	complement component 5a receptor 1	
211143_x_at	3164	NR4A1	5.00E-04	4.17	6.00E-04	4.17	nuclear receptor subfamily 4, group A, member 1	
219228_at	54222	ZNF331	3.00E-04	4.12	3.00E-04	4.02	zinc finger protein 331	
229552_at	8739	HRK	3.00E-04	4.08	3.00E-04	3.87	harakiri, BCL2 interacting protein	
	283454	LOC283454					uncharacterized LOC283454	
239367_at	627	BDNF	3.74E-05	4.05	4.76E-05	3.92	brain-derived neurotrophic factor	
213182_x_at	1028	CDKN1C	2.68E-02	4.02	3.11E-02	4.04	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
202340_x_at	3164	NR4A1	1.60E-03	3.97	2.60E-03	3.42	nuclear receptor subfamily 4, group A, member 1	
219911_s_at	28231	SLC04A1	2.40E-03	3.84	3.80E-03	3.56	solute carrier organic anion transporter family, member 4A1	
1559141_s_at	157693	FAM87A	8.00E-03	3.81	3.20E-02	3.01	family with sequence similarity 87, member A	
	400728	FAM87B					family with sequence similarity 87, member B	
219534_x_at	1028	CDKN1C	1.81E-02	3.76	3.20E-02	3.01	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
224828_at	80315	CPEB4	3.00E-04	3.74	2.49E-02	3.61	cytoplasmic polyadenylation element binding protein 4	
229709_at	483	ATP1B3	6.20E-03	3.73	2.00E-04	3.89	ATPase, Na ⁺ /K ⁺ transporting, beta 3 polypeptide	
206382_s_at	627	BDNF	1.00E-04	3.72	1.48E-02	3.12	brain-derived neurotrophic factor	
219682_s_at	6926	TBX3	9.99E-05	3.59	1.00E-04	3.74	T-box 3	
203549_s_at	4023	LPL	2.00E-04	3.57	1.00E-04	3.50	lipoprotein lipase	
224829_at	80315	CPEB4	2.00E-04	3.53	2.00E-04	3.60	cytoplasmic polyadenylation element binding protein 4	
216894_x_at	1028	CDKN1C	7.80E-03	3.47	2.00E-04	3.37	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
206865_at	8739	HRK	2.00E-04	3.47	1.13E-02	3.31	harakiri, BCL2 interacting protein	
239818_x_at	10221	TRIB1	2.00E-04	3.46	2.00E-04	2.93	tribbles pseudokinase 1	
218177_at	57132	CHMP1B	2.00E-04	3.39	5.00E-04	3.00	charged multivesicular body protein 1B	
218995_s_at	1906	EDN1	8.59E-05	3.36	2.00E-04	3.40	endothelin 1	
1552755_at	157983	C9orf66	8.11E-02	3.35	8.77E-05	3.38	chromosome 9 open reading frame 66	
216236_s_at	6515	SLC2A14	9.78E-05	3.35	1.00E-04	3.05	solute carrier family 2 (facilitated glucose transporter), member 14	
	144195	SLC2A3					solute carrier family 2 (facilitated glucose transporter), member 3	
213348_at	1028	CDKN1C	8.70E-03	3.32	1.30E-02	3.12	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
213006_at	1052	CEBPD	8.00E-04	3.32	9.00E-04	3.24	CCAAT/enhancer binding protein (C/EBP), delta	
202241_at	10221	TRIB1	3.74E-05	3.31	4.76E-05	3.26	tribbles pseudokinase 1	
209631_s_at	2861	GPR37	2.00E-04	3.30	2.00E-04	3.23	G protein-coupled receptor 37 (endothelin receptor type B-like)	
202497_x_at	6515	SLC2A3	2.00E-04	3.30	3.00E-04	3.11	solute carrier family 2 (facilitated glucose transporter), member 3	
228128_x_at	5069	PAPPA	4.00E-04	3.28	2.00E-04	4.04	pregnancy-associated plasma protein A, pappalysin 1	
201981_at	5069	PAPPA	2.68E-02	3.21	1.92E-02	3.69	pregnancy-associated plasma protein A, pappalysin 1	
203548_s_at	4023	LPL	2.00E-04	3.18	2.00E-04	3.26	lipoprotein lipase	
224831_at	80315	CPEB4	2.00E-04	3.17	1.00E-04	3.69	cytoplasmic polyadenylation element binding protein 4	
	6515	SLC2A14					solute carrier family 2 (facilitated glucose transporter), member 14	
222088_s_at	144195	SLC2A3	3.00E-04	3.16	4.00E-04	2.89	solute carrier family 2 (facilitated glucose transporter), member 3	
228325_at	23514	SPIDR	8.00E-04	3.16	1.00E-03	2.88	scaffolding protein involved in DNA repair	
220483_s_at	25897	RNF19A	5.00E-04	3.13	1.10E-03	2.86	ring finger protein 19A, RBR E3 ubiquitin protein ligase	
202499_s_at	6515	SLC2A3	5.00E-04	3.11	7.00E-04	2.88	solute carrier family 2 (facilitated glucose transporter), member 3	
224942_at	5069	PAPPA	7.00E-04	3.09	7.00E-04	2.98	pregnancy-associated plasma protein A, pappalysin 1	
202498_s_at	6515	SLC2A3	1.00E-03	3.04	1.10E-03	2.75	solute carrier family 2 (facilitated glucose transporter), member 3	
224940_s_at	5069	PAPPA	8.00E-04	3.03	4.00E-04	3.86	pregnancy-associated plasma protein A, pappalysin 1	
239123_at	8848	TSC22D1	1.21E-02	3.03	1.82E-02	3.12	TSC22 domain family, member 1	
218178_s_at	57132	CHMP1B	1.77E-05	3.00	2.93E-05	2.88	charged multivesicular body protein 1B	
203984_s_at	842	CASP9	4.80E-03	2.99	7.80E-03	2.79	caspase 9	
222802_at	1906	EDN1	8.34E-05	2.98	7.80E-05	3.07	endothelin 1	
226614_s_at	83648	FAM167A	5.00E-04	2.96	6.00E-04	2.91	family with sequence similarity 167, member A	
205027_s_at	1326	MAP3K8	1.70E-03	2.93	1.00E-03	3.02	mitogen-activated protein kinase kinase kinase 8	
204456_s_at	2619	GAS1	5.50E-03	2.91	6.50E-03	2.74	growth arrest-specific 1	
212226_s_at	8613	PLPP3	6.82E-05	2.90	8.77E-05	2.78	phospholipid phosphatase 3	
218723_s_at	28984	RGCC	1.02E-02	2.89	2.43E-02	2.63	regulator of cell cycle	
212977_at	57007	ACKR3	9.84E-05	2.87	1.00E-04	2.83	atypical chemokine receptor 3	
208228_s_at	2263	FGFR2	1.00E-04	2.86	1.00E-04	3.29	fibroblast growth factor receptor 2	
225516_at	6542	SLC7A2	1.00E-04	2.84	1.00E-04	2.81	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2	
209355_s_at	8613	PLPP3	7.59E-05	2.83	9.09E-05	2.76	phospholipid phosphatase 3	
225544_at	6926	TBX3	1.00E-04	2.82	2.00E-04	2.73	T-box 3	
230472_at	79192	IRX1	7.00E-04	2.81	7.00E-04	2.82	iroquois homeobox 1	
210775_x_at	842	CASP9	5.20E-03	2.77	8.70E-03	2.58	caspase 9	
237187_at	8739	HRK	3.20E-03	2.77	3.20E-03	2.62	harakiri, BCL2 interacting protein	
224941_at	5069	PAPPA	2.60E-03	2.77	1.00E-03	3.37	pregnancy-associated plasma protein A, pappalysin 1	
225606_at	10018	BCL2L11	1.00E-04	2.76	1.00E-04	2.91	BCL2-like 11 (apoptosis facilitator)	
219316_s_at	55640	FLVCR2	2.20E-03	2.72	2.70E-03	2.60	feline leukemia virus subgroup C cellular receptor family, member 2	
1553613_s_at	2296	FOXC1	1.54E-05	2.67	3.05E-05	2.50	forkhead box C1	
209681_at	10560	SLC19A2	4.50E-03	2.67	4.30E-03	2.51	solute carrier family 19 (thiamine transporter), member 2	
235085_at	157285	PRAG1	5.20E-03	2.65	6.70E-03	2.55	homolog of rat pragra of Rnd2	
214446_at	22936	ELL2	1.02E-02	2.63	1.26E-02	2.45	elongation factor, RNA polymerase II, 2	
209189_at	2353	FOS	6.00E-03	2.63	1.69E-02	2.10	FBJ murine osteosarcoma viral oncogene homolog	

223085_at	25897	<i>RNF19A</i>	2.00E-04	2.62	2.00E-04	2.59	ring finger protein 19A, RBR E3 ubiquitin protein ligase
222015_at	1454	<i>CSNK1E</i>					casein kinase 1, epsilon
	102800317	<i>LOC400927-CSNK1E</i>	5.00E-04	2.61	6.00E-04	2.63	LOC400927-CSNK1E readthrough
227443_at	286343	<i>LURAP1L</i>	1.36E-02	2.61	1.78E-02	2.46	leucine rich adaptor protein 1-like
205239_at	374	<i>AREG</i>	4.20E-03	2.60	3.80E-03	2.67	amphiregulin
218880_at	2355	<i>FOSL2</i>	3.00E-04	2.60	5.00E-04	2.50	FOS-like antigen 2
224325_at	8325	<i>FZD8</i>	9.00E-03	2.60	1.04E-02	2.44	frizzled class receptor 8
227099_s_at	387763	<i>C1orf96</i>	6.76E-02	2.59	9.32E-02	2.36	chromosome 11 open reading frame 96
227188_at	59271	<i>EVA1C</i>	8.50E-03	2.59	1.05E-02	2.54	eva-1 homolog C (C. elegans)
206924_at	3589	<i>ILL1</i>	3.00E-03	2.59	7.40E-03	2.33	interleukin 11
229004_at	170689	<i>ADAMTS15</i>	9.99E-05	2.58	1.00E-04	2.55	ADAM metalloproteinase with thrombospondin type 1 motif 15
214438_at	3142	<i>HLX</i>	3.38E-02	2.57	2.49E-02	2.74	H2.0-like homeobox
36711_at	23764	<i>MAFF</i>	1.00E-04	2.57	1.00E-04	2.56	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F
205193_at	23764	<i>MAFF</i>	7.00E-04	2.57	7.00E-04	2.56	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F
227337_at	353322	<i>ANKRD37</i>	3.00E-04	2.56	4.00E-04	2.50	ankyrin repeat domain 37
220225_at	50805	<i>IRX4</i>	6.60E-03	2.56	6.60E-03	2.73	iroquois homeobox 4
218631_at	60370	<i>AVP1J</i>	6.05E-05	2.55	7.80E-05	2.41	arginine vasopressin-induced 1
225987_at	79689	<i>STEAP4</i>	4.00E-04	2.54	4.00E-04	2.54	STEAP family member 4
230398_at	84951	<i>TNS4</i>	1.11E-02	2.54	2.25E-02	2.43	tenascin 4
215111_s_at	8848	<i>TSC22D1</i>	4.60E-03	2.53	5.50E-03	2.46	TSC22 domain family, member 1
205409_at	2355	<i>FOSL2</i>	5.70E-03	2.52	7.80E-03	2.51	FOS-like antigen 2
1553133_at	203228	<i>C9orf72</i>	2.60E-03	2.51	3.60E-03	2.38	chromosome 9 open reading frame 72
212230_at	8613	<i>PLPPP3</i>	3.26E-05	2.51	2.96E-05	2.58	phospholipid phosphatase 3
201044_x_at	1843	<i>DUSP1</i>	2.00E-04	2.50	2.00E-04	2.41	dual specificity phosphatase 1
208250_s_at	1755	<i>DMBT1</i>	8.63E-05	2.48	1.00E-04	2.34	deleted in malignant brain tumors 1
236911_at	57494	<i>RIMKLB</i>	2.53E-02	2.48	2.76E-02	2.39	ribosomal modification protein rimK-like family member B
202150_s_at	4739	<i>NEDD9</i>	4.00E-04	2.47	9.00E-04	2.24	neural precursor cell expressed, developmentally down-regulated 9
202723_s_at	2308	<i>FOXO1</i>	3.20E-03	2.46	3.80E-03	2.24	forkhead box O1
202768_at	2354	<i>FOSB</i>	7.40E-03	2.43	1.46E-02	2.06	FBJ murine osteosarcoma viral oncogene homolog B
206404_at	2254	<i>FGF9</i>	4.00E-04	2.42	4.00E-04	2.25	fibroblast growth factor 9
213221_s_at	23235	<i>SIK2</i>	3.30E-03	2.42	3.10E-03	2.45	salt-inducible kinase 2
205466_s_at	9957	<i>HS3ST1</i>	2.21E-02	2.42	6.03E-02	2.08	heparan sulfate (glucosamine) 3-O-sulfotransferase 1
201169_s_at	8553	<i>BHLHE40</i>	5.60E-03	2.39	1.28E-02	2.23	basic helix-loop-helix family, member e40
210136_at	4155	<i>MBP</i>	7.00E-04	2.39	8.00E-04	2.42	myelin basic protein
202149_at	4739	<i>NEDD9</i>	3.00E-04	2.38	6.00E-04	2.17	neural precursor cell expressed, developmentally down-regulated 9
203574_at	4783	<i>NFIL3</i>	5.00E-04	2.38	7.00E-04	2.28	nuclear factor, interleukin 3 regulated
223379_s_at	26524	<i>LATS2</i>	3.00E-04	2.37	5.00E-04	2.14	large tumor suppressor kinase 2
207626_s_at	6542	<i>SLC7A2</i>	3.00E-04	2.37	1.40E-03	2.03	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2
213139_at	6591	<i>SNAI2</i>	5.20E-03	2.37	8.70E-03	2.28	snail family zinc finger 2
224797_at	57561	<i>ARRDC3</i>	5.80E-03	2.36	3.70E-03	2.33	arrestin domain containing 3
215990_s_at	604	<i>BCL6</i>	9.30E-03	2.36	9.10E-03	2.18	B-cell CLL/lymphoma 6
231035_s_at	220213	<i>OTUD1</i>	3.70E-03	2.36	5.40E-03	2.14	OTU deubiquitinase 1
226858_at	1454	<i>CSNK1E</i>					casein kinase 1, epsilon
	102800317	<i>LOC400927-CSNK1E</i>	4.00E-04	2.34	4.00E-04	2.37	LOC400927-CSNK1E readthrough
209101_at	1490	<i>CTGF</i>	3.00E-04	2.34	3.00E-04	2.42	connective tissue growth factor
231067_s_at	9590	<i>AKAP12</i>	1.51E-02	2.33	1.72E-02	2.20	A kinase (PKA) anchor protein 12
220335_x_at	23491	<i>CE53</i>	1.70E-03	2.33	1.60E-03	2.22	carboxylesterase 3
216627_s_at	2683	<i>BAGALTI</i>	6.80E-03	2.32	1.10E-02	2.41	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1
218881_s_at	2355	<i>FOSL2</i>	3.00E-03	2.32	3.40E-03	2.38	FOS-like antigen 2
237252_at	7056	<i>THBD</i>	1.58E-02	2.32	4.81E-02	1.96	thrombomodulin
208536_s_at	10018	<i>BCL2L11</i>	2.11E-02	2.28	1.69E-02	2.29	BCL2-like 11 (apoptosis facilitator)
203796_s_at	605	<i>BCL7A</i>	4.00E-04	2.28	9.00E-04	1.99	B-cell CLL/lymphoma 7A
212099_at	388	<i>RHOB</i>	4.00E-04	2.28	5.00E-04	2.29	ras homolog family member B
203313_s_at	7050	<i>TGIF1</i>	6.00E-04	2.28	6.00E-04	2.28	TGF-beta-induced factor homeobox 1
229720_at	573	<i>BAG1</i>	1.50E-03	2.25	1.70E-03	2.15	BCL2-associated athanogene
1558143_a_at	10018	<i>BCL2L11</i>	5.00E-03	2.25	4.80E-03	2.43	BCL2-like 11 (apoptosis facilitator)
219195_at	10891	<i>PPARGC1A</i>	1.14E-02	2.24	3.58E-02	2.05	peroxisome proliferator-activated receptor gamma, coactivator 1 alpha
223430_at	23235	<i>SIK2</i>	1.84E-02	2.23	2.89E-02	2.15	salt-inducible kinase 2
207213_s_at	9099	<i>USP2</i>	3.00E-03	2.23	3.10E-03	2.33	ubiquitin specific peptidase 2
238987_at	2683	<i>BAGALTI</i>	8.84E-02	2.22	1.35E-02	3.09	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1
228625_at	163732	<i>CITE4D</i>	4.00E-04	2.22	5.00E-04	2.18	Cbp/p300-interacting transactivator, with Glu/Asp rich carboxy-terminal domain, 4
225955_at	284207	<i>METRNL</i>	1.00E-04	2.22	1.00E-04	2.20	meteorin, glial cell differentiation regulator-like
1554544_a_at	4155	<i>MBP</i>	7.00E-04	2.21	6.00E-04	2.35	myelin basic protein
200731_s_at	7803	<i>PTPAA1</i>	1.09E-02	2.21	7.30E-03	2.32	protein tyrosine phosphatase type IVA, member 1
203887_s_at	7056	<i>THBD</i>	1.69E-02	2.21	3.62E-02	1.95	thrombomodulin
202023_at	1942	<i>EFNA1</i>	2.00E-04	2.20	2.00E-04	2.14	ephrin-A1
221841_s_at	9314	<i>KLf4</i>	9.90E-03	2.20	1.38E-02	2.22	Kruppel-like factor 4 (gut)
206472_s_at	7090	<i>TLE3</i>	8.63E-02	2.19	4.54E-02	2.25	transducin-like enhancer of split 3
201170_s_at	8553	<i>BHLHE40</i>	4.00E-04	2.18	8.00E-04	2.03	basic helix-loop-helix family, member e40
202672_s_at	467	<i>ATF3</i>	8.00E-04	2.17	1.80E-03	2.05	activating transcription factor 3
228188_at	2355	<i>FOSL2</i>	8.00E-04	2.17	6.00E-04	2.16	FOS-like antigen 2
221011_s_at	81606	<i>LBH</i>	3.00E-04	2.17	4.00E-04	2.08	limb bud and heart development
222784_at	64093	<i>SMOC1</i>	3.10E-02	2.17	1.88E-02	2.46	SPARC related modular calcium binding 1
226575_at	58499	<i>ZNF462</i>	1.00E-03	2.17	1.20E-03	2.14	zinc finger protein 462
219433_at	54880	<i>BCOR</i>	1.35E-02	2.16	9.10E-03	2.15	BCL6 corepressor
205870_at	624	<i>BDKRB2</i>	3.27E-02	2.16	7.41E-02	2.07	bradykinin receptor B2
204014_at	1846	<i>DUSP4</i>	5.20E-03	2.16	7.00E-03	1.93	dual specificity phosphatase 4
225262_at	2355	<i>FOSL2</i>	1.00E-04	2.16	1.00E-04	2.12	FOS-like antigen 2
209184_s_at	8660	<i>IRS2</i>	7.00E-04	2.15	7.00E-04	2.07	insulin receptor substrate 2
213260_at	2296	<i>FOXO1</i>	5.34E-05	2.14	7.80E-05	2.07	forkhead box O1
200732_s_at	7803	<i>PTPAA1</i>	2.30E-03	2.14	3.00E-03	2.10	protein tyrosine phosphatase type IVA, member 1
206035_at	5966	<i>REL</i>	2.90E-03	2.13	8.10E-03	1.88	v-rel avian reticuloendotheliosis viral oncogene homolog
205896_at	6583	<i>SLC22A4</i>	2.08E-02	2.13	2.78E-02	1.99	solute carrier family 22 (organic cation/zwitterion transporter), member 4
203290_at	3117	<i>HLA-DQA1</i>	3.73E-02	2.12	3.39E-02	2.24	major histocompatibility complex, class II, DQ alpha 1
1553962_s_at	388	<i>RHOB</i>	1.40E-03	2.12	1.30E-03	2.33	ras homolog family member B
212143_s_at	3486	<i>IGFBP3</i>	1.70E-03	2.11	2.60E-03	2.02	insulin like growth factor binding protein 3
204032_at	8412	<i>BCAR3</i>	4.00E-03	2.10	3.30E-03	2.08	breast cancer anti-estrogen resistance 3
211631_x_at	2683	<i>BAGALTI</i>	3.66E-02	2.09	5.08E-02	2.16	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1
209772_s_at	100133941	<i>CD24</i>	3.00E-04	2.09	4.00E-04	2.07	CD24 molecule
224572_s_at	359948	<i>IRF2BP2</i>	3.00E-04	2.09	5.00E-04	2.04	interferon regulatory factor 2 binding protein 2
233002_at	57718	<i>PPP4R4</i>	1.53E-02	2.09	6.38E-02	1.81	protein phosphatase 4, regulatory subunit 4
207826_s_at	3399	<i>ID3</i>	1.10E-03	2.08	1.40E-03	1.98	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein
233379_at	79899	<i>PRRS5</i>	1.35E-02	2.08	4.50E-03	2.50	proline rich 5 like
225999_at	57494	<i>RIMKLB</i>	3.10E-03	2.08	3.10E-03	2.12	ribosomal modification protein rimK-like family member B
203140_at	604	<i>BCL6</i>	9.00E-04	2.07	9.00E-04	2.08	B-cell CLL/lymphoma 6
223566_s_at	54880	<i>BCOR</i>	5.30E-03	2.07	7.10E-03	2.00	BCL6 corepressor
227458_at	29126	<i>CD274</i>	3.20E-03	2.07	7.20E-03	1.91	CD274 molecule
202724_s_at	2308	<i>FOXO1</i>	1.80E-03	2.07	1.30E-03	2.16	forkhead box O1
205051_s_at	3815	<i>KIT</i>	2.70E-03	2.07	5.00E-03	1.94	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
205157_s_at	3872	<i>KRT17</i>	3.12E-02	2.07	3.41E-02	1.96	keratin 17, type I
225407_at	4155	<i>MBP</i>	8.00E-04	2.07	9.00E-04	1.97	myelin basic protein
223834_at	29126	<i>CD274</i>	5.60E-03	2.06	1.17E-02	1.91	CD274 molecule
209457_at	1847	<i>DUSP5</i>	1.90E-03	2.06	3.20E-03	1.94	dual specificity phosphatase 5
230348_at	26524	<i>LATS2</i>	7.70E-03	2.06	1.31E-02	1.95	large tumor suppressor kinase 2
204284_at	5507	<i>PPP1R3C</i>	2.53E-02	2.06	2.97E-02	2.01	protein phosphatase 1, regulatory subunit 3C
218113_at	23670	<i>TMEM22</i>	7.00E-04	2.06	5.00E-04	2.07	transmembrane protein 2
227529_s_at	9590	<i>AKAP12</i>	9.90E-03	2.05	1.16E-02	1.92	A kinase (PKA) anchor protein 12
203795_s_at	605	<i>BCL7A</i>	3.50E-03	2.05	3.30E-03	2.02	B-cell CLL/lymphoma 7A
219383_at	79899	<i>PRRS5</i>	1.70E-03	2.05	1.70E-03	1.93	proline rich 5 like
223916_s_at	54880	<i>BCOR</i>	3.60E-02	2.04	2.99E-02	2.04	BCL6 corepressor
216598_s_at	6347	<i>CCL2</i>	2.10E-03	2.03	2.70E-03	2.10	chemokine (C-C motif) ligand 2
201925_s_at	1604	<i>CD55</i>	1.99E-02	2.03	1.48E-02	2.12	CD55 molecule, decay accelerating factor for complement (Cromer blood group)
228462_at	153572	<i>IRX2</i>	6.00E-04	2.03	6.00E-04	2.04	iroquois homeobox 2
220540_at	60598	<i>KCNK15</i>	7.93E-02	2.03	7.15E-02	2.17	potassium channel, two pore domain subfamily K, member 15
231798_at	9241	<i>NOG</i>	6.00E-04	2.03	4.00E-04	2.09	noggin
217584_at	4864	<i>NPC1</i>	2.11E-02	2.03	1.53E-02	2.13	Niemann-Pick disease, type C1
228284_at	7088	<i>TLE1</i>	4.00E-03	2.03	5.20E-03	1.95	transducin-like enhancer of split 1 (E[sp1] homolog, Drosophila)
203708_at	5142	<i>PDE4B</i>	2.22E-02	2.02	2.93E-02	1.89	phosphodiesterase 4B, cAMP-specific
225919_s_at	203228	<i>C9orf72</i>	3.44E-02	2.01	4.19E-02	1.89	chromosome 9 open reading frame 72
225626_at	55824	<i>PAG1</i>	5.80E-02	2.01	7.77E-02	1.78	phosphoprotein membrane anchor with glycosphingolipid microdomains 1



1554980_a_at	467	<i>ATF3</i>	8.00E-04	2.00	2.20E-03	1.86	activating transcription factor 3
1555590_a_at	1604	<i>CD55</i>	6.90E-03	2.00	9.90E-03	1.82	CD55 molecule, decay accelerating factor for complement (Cromer blood group)
213844_a_at	3202	<i>HOXA5</i>	9.00E-03	2.00	7.10E-03	2.22	homeobox A5
206864_s_at	8739	<i>HRK</i>	5.00E-04	2.00	5.00E-04	2.06	harakiri, BCL2 interacting protein
1555486_a_at	79899	<i>PRRS1</i>	2.00E-04	2.00	3.00E-04	1.98	proline rich 5 like
204654_s_at	7020	<i>TFAP2A</i>	6.70E-03	2.00	8.10E-03	2.03	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)
239178_s_at	2254	<i>FGF9</i>	2.11E-02	1.99	1.48E-02	2.06	fibroblast growth factor 9
203108_s_at	9052	<i>GPRC5A</i>	6.00E-04	1.99	6.00E-04	2.04	G protein-coupled receptor, class C, group 5, member A
220187_s_at	79689	<i>STEAP4</i>	9.40E-03	1.99	2.69E-02	1.67	STEAP family member 4
229337_s_at	9099	<i>USP2</i>	2.33E-02	1.99	5.18E-02	1.84	ubiquitin specific peptidase 2
236352_s_at	245806	<i>VGLL2</i>	1.53E-02	1.99	3.44E-02	1.79	vestigial-like family member 2
242162_at	164781	<i>DAW1</i>	1.51E-02	1.98	1.67E-02	2.18	dynein assembly factor with WDR repeat domains 1
226206_at	7975	<i>MAFK</i>	3.00E-04	1.98	3.00E-04	1.94	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog K
235421_at	1326	<i>MAP3K8</i>	4.99E-02	1.98	1.55E-02	2.43	mitogen-activated protein kinase kinase kinase 8
224570_s_at	359948	<i>IRF2BP2</i>	3.20E-03	1.97	2.60E-03	2.05	interferon regulatory factor 2 binding protein 2
229889_at	388341	<i>LIRC75A</i>	1.78E-02	1.97	1.68E-02	1.99	leucine rich repeat containing 75A
228293_at	91614	<i>DEPDC7</i>	1.70E-03	1.96	1.10E-03	2.11	DEP domain containing 7
201328_at	2114	<i>ETS2</i>	7.00E-04	1.96	1.30E-03	1.85	v-ets avian erythroblastosis virus E26 oncogene homolog 2
210162_s_at	4772	<i>NFATC1</i>	8.00E-04	1.96	3.30E-03	1.78	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1
219737_s_at	5101	<i>PCDH9</i>	6.30E-03	1.96	4.80E-03	2.06	protocadherin 9
218691_s_at	8572	<i>PDLIM4</i>	1.00E-01	1.96	9.04E-02	1.98	PDZ and LIM domain 4
212444_at	9052	<i>GPRC5A</i>	8.00E-04	1.95	1.20E-03	1.96	G protein-coupled receptor, class C, group 5, member A
228812_at	5966	<i>REL</i>	6.90E-03	1.95	7.80E-03	1.83	v-rel avian reticuloendotheliosis viral oncogene homolog
222343_s_at	10018	<i>BCL2L11</i>	5.00E-03	1.94	6.70E-03	1.90	BCL2-like 11 (apoptosis facilitator)
224826_at	56261	<i>GPCPD1</i>	2.40E-03	1.94	4.10E-03	1.82	glycerophosphocholine phosphodiesterase 1
203372_s_at	8835	<i>SOCS2</i>	6.82E-02	1.94	9.48E-02	1.86	suppressor of cytokine signaling 2
226034_at	1846	<i>DUSP4</i>	1.60E-03	1.93	2.20E-03	1.87	dual specificity phosphatase 4
224835_at	56261	<i>GPCPD1</i>	4.20E-03	1.93	4.10E-03	1.97	glycerophosphocholine phosphodiesterase 1
215034_s_at	4071	<i>TM4SF1</i>	2.90E-02	1.93	6.38E-02	1.67	transmembrane 4 L six family member 1
227530_at	9590	<i>AKAP12</i>	1.16E-02	1.92	1.22E-02	1.86	A kinase (PKA) anchor protein 12
208650_s_at	100133941	<i>CD24</i>	4.10E-03	1.92	4.20E-03	1.90	CD24 molecule
225408_at	4155	<i>MBP</i>	1.00E-03	1.92	9.00E-04	2.02	myelin basic protein
206036_s_at	5966	<i>REL</i>	6.80E-03	1.92	9.10E-03	1.78	v-rel avian reticuloendotheliosis viral oncogene homolog
205074_at	6584	<i>SLC22A5</i>	4.20E-03	1.92	5.10E-03	1.88	solute carrier family 22 (organic cation/carnitine transporter), member 5
231183_s_at	128710	<i>SLX4IP</i>	3.54E-02	1.92	3.20E-02	2.04	SLX4 interacting protein
205286_at	7022	<i>TFAP2C</i>	3.09E-02	1.92	5.08E-02	1.76	transcription factor AP-2 gamma (activating enhancer binding protein 2 gamma)
209185_s_at	8660	<i>IRS2</i>	2.00E-04	1.91	4.00E-04	1.84	insulin receptor substrate 2
210095_s_at	3486	<i>IGFBP3</i>	9.00E-04	1.90	1.70E-03	1.82	insulin like growth factor binding protein 3
216268_s_at	182	<i>JAG1</i>	8.50E-03	1.90	4.00E-03	1.91	jagged 1
212236_x_at	3872	<i>KRT17</i>	2.53E-02	1.90	2.65E-02	1.94	keratin 17, type I
201416_at	6659	<i>SOX4</i>	1.80E-03	1.90	2.00E-03	1.86	SRY box 4
231899_at	85463	<i>ZC3H12C</i>	2.80E-03	1.90	3.10E-03	1.87	zinc finger CCHC-type containing 12C
204679_at	3775	<i>KCNK1</i>	1.20E-03	1.89	1.50E-03	1.86	potassium channel, two pore domain subfamily K, member 1
235242_at	5966	<i>REL</i>	5.90E-03	1.89	5.60E-03	1.85	v-rel avian reticuloendotheliosis viral oncogene homolog
230493_at	387914	<i>SHISA2</i>	2.70E-03	1.89	2.40E-03	1.98	shisa family member 2
203888_at	7056	<i>THBD</i>	4.19E-02	1.89	6.62E-02	1.80	thrombomodulin
227405_s_at	8325	<i>FZD8</i>	5.57E-02	1.88	1.11E-01	1.78	frizzled class receptor 8
205992_s_at	3600	<i>IL15</i>	4.20E-03	1.88	5.60E-03	1.85	interleukin 15
224571_s_at	359948	<i>IRF2BP2</i>	4.20E-03	1.88	4.80E-03	1.78	interferon regulatory factor 2 binding protein 2
206706_at	4908	<i>NTF3</i>	3.80E-03	1.88	3.70E-03	1.86	neurotrophin 3
231823_s_at	285590	<i>SH3PXD2B</i>	3.06E-02	1.88	4.51E-02	1.90	SH3 and PX domains 2B
203373_s_at	8835	<i>SOCS2</i>	1.21E-02	1.88	3.30E-02	1.67	suppressor of cytokine signaling 2
213003_s_at	23514	<i>SPDR</i>	6.71E-02	1.88	4.80E-02	1.91	scaffolding protein involved in DNA repair
226208_at	57688	<i>ZSWIM6</i>	5.20E-03	1.88	5.60E-03	1.85	zinc finger, SWIM-type containing 6
203003_s_at	4209	<i>MEF2D</i>	1.05E-02	1.87	2.41E-02	1.68	myocyte enhancer factor 2D
226140_s_at	220213	<i>OTUD1</i>	3.00E-04	1.87	4.00E-04	1.88	OTU deubiquitinase 1
204015_s_at	1846	<i>DUSP4</i>	4.30E-03	1.86	8.70E-03	1.73	dual specificity phosphatase 4
239058_at	2303	<i>FOXO2</i>	2.21E-02	1.86	2.85E-02	1.84	forkhead box C2
201939_at	10769	<i>PLK2</i>	9.00E-04	1.86	9.00E-04	1.82	polo-like kinase 2
1553965_x_at	388	<i>RHOB</i>	1.53E-02	1.86	1.35E-02	2.03	ras homolog family member B
222783_s_at	64093	<i>SMOCC1</i>	1.05E-02	1.86	1.45E-02	1.85	SPARC related modular calcium binding 1
244007_at	58499	<i>ZNF462</i>	1.60E-03	1.86	7.00E-04	1.95	zinc finger protein 462
235849_at	286133	<i>SCARA5</i>	6.50E-03	1.85	9.00E-04	2.35	scavenger receptor class A, member 5
202897_at	140885	<i>SIRPA</i>	2.18E-02	1.85	5.07E-02	1.70	signal-regulatory protein alpha
229529_at	6943	<i>TCF21</i>	9.40E-03	1.85	2.21E-02	1.70	transcription factor 21
216379_x_at	100133941	<i>CD24</i>	8.00E-04	1.84	1.70E-03	1.75	CD24 molecule
204602_at	22943	<i>DKK1</i>	5.26E-02	1.84	9.97E-02	1.73	dickkopf WNT signaling pathway inhibitor 1
222258_s_at	23677	<i>SH3BP4</i>	1.10E-03	1.84	2.00E-03	1.75	SH3-domain binding protein 4
202935_s_at	6662	<i>SOX9</i>	2.55E-02	1.84	7.95E-02	1.60	SRY box 9
224963_at	1836	<i>SLC26A2</i>	1.60E-03	1.83	9.00E-04	1.87	solute carrier family 26 (anion exchanger), member 2
205294_at	10458	<i>BAlAP2</i>	1.30E-03	1.82	2.60E-03	1.72	BAl1-associated protein 2
209099_x_at	182	<i>JAG1</i>	4.50E-03	1.82	3.60E-03	1.84	jagged 1
206765_at	3759	<i>KCNJ2</i>	3.48E-02	1.82	2.56E-02	1.90	potassium channel, inwardly rectifying subfamily J, member 2
203180_at	220	<i>ALDH1A3</i>	6.85E-02	1.81	9.30E-02	1.81	aldehyde dehydrogenase 1 family, member A3
208651_x_at	100133941	<i>CD24</i>	3.60E-02	1.81	9.90E-03	2.10	CD24 molecule
229800_at	9201	<i>DCLK1</i>	1.00E-03	1.80	1.80E-03	1.70	doublecortin-like kinase 1
228501_at	117248	<i>GALNT15</i>	1.84E-02	1.80	3.68E-02	1.72	polypeptide N-acetylgalactosaminyltransferase 15
204698_at	3669	<i>ISG20</i>	2.75E-02	1.80	6.68E-02	1.69	interferon stimulated exonuclease gene 20kDa
212831_at	1955	<i>MEGF9</i>	8.50E-03	1.80	8.70E-03	1.77	multiple EGF-like-domains 9
217678_at	23657	<i>SLC7A11</i>	6.00E-04	1.80	6.00E-04	1.76	solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11
202936_s_at	6662	<i>SOX9</i>	7.10E-03	1.80	1.66E-02	1.65	SRY box 9
204908_s_at	602	<i>BCL3</i>	2.90E-02	1.79	3.33E-02	1.74	B-cell CLL/lymphoma 3
201926_s_at	1604	<i>CD55</i>	3.07E-02	1.79	3.27E-02	1.70	CD55 molecule, decay accelerating factor for complement (Cromer blood group)
204678_s_at	3775	<i>KCNK1</i>	5.08E-02	1.79	6.56E-02	1.80	potassium channel, two pore domain subfamily K, member 1
1554822_at	57157	<i>PHF7</i>	8.10E-03	1.79	5.22E-02	1.50	putative homeodomain transcription factor 2
224973_at	55603	<i>FAM46A</i>	7.89E-02	1.78	9.66E-02	1.68	family with sequence similarity 46, member A
204472_at	2669	<i>GEM</i>	6.90E-03	1.78	5.47E-02	1.51	GTP binding protein overexpressed in skeletal muscle
203394_s_at	3280	<i>HES1</i>	5.78E-02	1.78	9.46E-02	1.73	hes family bHLH transcription factor 1
226164_x_at	57494	<i>RIMKLB</i>	8.37E-02	1.78	5.07E-02	1.70	ribosomal modification protein rimK-like family member B
266_s_at	100133941	<i>CD24</i>	4.13E-02	1.77	2.43E-02	1.82	CD24 molecule
228759_at	64764	<i>CREB3L2</i>	1.74E-02	1.77	3.07E-02	1.73	cAMP responsive element binding protein 3-like 2
221766_s_at	55603	<i>FAM46A</i>	4.30E-03	1.77	5.80E-03	1.64	family with sequence similarity 46, member A
223380_s_at	26524	<i>LATS2</i>	1.10E-03	1.77	7.00E-04	1.87	large tumor suppressor kinase 2
237724_at	162333	<i>MARCH10</i>	5.94E-02	1.76	9.38E-02	1.67	membrane associated ring finger 10
203044_at	22856	<i>CHSY1</i>	5.00E-04	1.76	7.00E-04	1.73	chondroitin sulfate synthase 1
227755_s_at	2081	<i>ERN1</i>	1.50E-03	1.76	1.30E-03	1.81	endoplasmic reticulum to nucleus signaling 1
219889_at	10023	<i>FRA11</i>	1.05E-02	1.76	9.90E-03	1.78	frequently rearranged in advanced T-cell lymphomas 1
227032_at	5362	<i>PLXNA2</i>	5.04E-02	1.76	3.98E-02	1.79	plexin A2
204197_s_at	864	<i>RUNX3</i>	9.90E-03	1.76	3.59E-02	1.54	runt-related transcription factor 3
238029_s_at	151473	<i>SLC16A14</i>	3.00E-03	1.76	3.20E-03	1.75	solute carrier family 16, member 14
202387_at	573	<i>BAG1</i>	7.00E-04	1.75	9.00E-04	1.78	BCL2-associated athanogene
236361_at	117248	<i>GALNT15</i>	1.73E-02	1.75	7.41E-02	1.52	polypeptide N-acetylgalactosaminyltransferase 15
218469_at	26585	<i>GREM1</i>	1.60E-03	1.75	1.10E-03	1.82	gremlin 1, DAN family BMP antagonist
224569_s_at	359948	<i>IRF2BP2</i>	3.70E-03	1.75	4.10E-03	1.77	interferon regulatory factor 2 binding protein 2
202861_at	5187	<i>PER1</i>	2.77E-02	1.75	4.59E-02	1.64	period circadian clock 1
209771_x_at	100133941	<i>CD24</i>	6.00E-04	1.74	9.00E-04	1.70	CD24 molecule
225978_at	57494	<i>RIMKLB</i>	1.50E-03	1.74	2.60E-03	1.63	ribosomal modification protein rimK-like family member B
201418_s_at	6659	<i>SOX4</i>	1.02E-02	1.74	1.03E-02	1.74	SRY box 4
230824_at	162333	<i>MARCH10</i>	1.79E-02	1.73	1.36E-02	1.77	membrane associated ring finger 10
206374_at	1850	<i>DUSP8</i>	2.83E-02	1.73	5.07E-02	1.63	dual specificity phosphatase 8
218696_at	9451	<i>EIF2AK3</i>	6.98E-02	1.73	6.02E-02	1.73	eukaryotic translation initiation factor 2-alpha kinase 3
201329_s_at	2114	<i>ETS2</i>	1.50E-03	1.73	2.20E-03	1.66	v-ets avian erythroblastosis virus E26 oncogene homolog 2
218468_s_at	26585	<i>GREM1</i>	9.00E-04	1.73	8.00E-04	1.79	gremlin 1, DAN family BMP antagonist
209098_s_at	182	<i>JAG1</i>	1.89E-02	1.73	1.03E-02	1.73	jagged 1
206750_at	7975	<i>MAFK</i>	2.02E-02	1.73	2.80E-02	1.63	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog K
200730_s_at	7803	<i>PTPAA1</i>	8.50E-03	1.73	6.70E-03	1.77	protein tyrosine phosphatase type IVA, member 1
203439_s_at	8614	<i>STC2</i>	1.00E-03	1.73	8.00E-04	1.75	stanniocalcin 2
205035_at	9150	<i>CTDP1</i>	1.08E-02	1.72	4.69E-02	1.54	CTD phosphatase subunit 1
224657_at	54206	<i>ERRF1</i>	4.10E-03	1.72	6.10E-03	1.69	ERBB receptor feedback inhibitor 1
204011_at	10253	<i>SPRY2</i>	1.69E-02	1.72	1.41E-02	1.83	sprouty RTK signaling antagonist 2

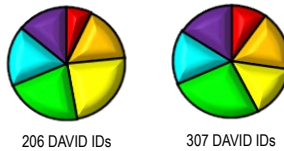


222549_at	9076	<i>CLDN1</i>	4.70E-03	1.71	9.70E-03	1.53	claudin 1
210350_x_at	3621	<i>ING1</i>	4.14E-02	1.71	4.68E-02	1.60	inhibitor of growth family member 1
231559_at	4837	<i>NNMT</i>	1.79E-02	1.71	1.09E-02	1.80	nicotinamide N-methyltransferase
202679_at	4864	<i>NPC1</i>	3.00E-03	1.71	5.10E-03	1.63	Niemann-Pick disease, type C1
222662_at	79660	<i>PPP1R3B</i>	3.79E-02	1.71	9.63E-02	1.68	protein phosphatase 1, regulatory subunit 3B
239615_at	6584	<i>SLC22A5</i>	6.40E-03	1.71	2.73E-02	1.55	solute carrier family 22 (organic cation/carnitine transporter), member 5
209921_at	23657	<i>SLC7A11</i>	6.00E-04	1.71	6.00E-04	1.68	solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11
238542_at	80328	<i>ULBP2</i>	1.60E-03	1.71	2.30E-03	1.66	UL16 binding protein 2
202628_s_at	5054	<i>SERPINE1</i>	1.50E-03	1.70	1.80E-03	1.60	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1
213624_at	10924	<i>SMPDL3A</i>	4.45E-02	1.70	5.01E-02	1.72	sphingomyelin phosphodiesterase, acid-like 3A
213668_s_at	6659	<i>SOX4</i>	3.35E-02	1.70	2.71E-02	1.72	SRY box 4
203973_s_at	1052	<i>CEBPD</i>	4.00E-04	1.69	6.00E-04	1.66	CCAAT/enhancer binding protein (C/EBP), delta
242767_at	29995	<i>LMCO1</i>	1.65E-02	1.69	1.95E-02	1.77	LIM and cysteine-rich domains 1
202431_s_at	4609	<i>MYC</i>	3.90E-03	1.69	5.00E-03	1.67	v-myc avian myelocytomatosis viral oncogene homolog
204595_s_at	6781	<i>STC1</i>	3.52E-02	1.69	2.67E-02	1.74	stanniocalcin 1
221577_x_at	9518	<i>GDF15</i>	1.00E-02	1.68	1.32E-02	1.68	growth differentiation factor 15
201195_s_at	8140	<i>SLC7A5</i>	2.11E-02	1.68	2.71E-02	1.63	solute carrier family 7 (amino acid transporter light chain, L system), member 5
202181_at	9766	<i>SUSD6</i>	2.70E-03	1.68	3.60E-03	1.64	sushi domain containing 6
227195_at	84858	<i>ZNF503</i>	1.87E-02	1.68	3.82E-02	1.54	zinc finger protein 503
204039_at	1050	<i>CEBPA</i>	7.58E-02	1.67	2.21E-02	1.93	CCAAT/enhancer binding protein (C/EBP), alpha
241985_at	133746	<i>JMY</i>	1.35E-02	1.67	6.42E-02	1.44	junction mediating and regulatory protein, p53 cofactor
201810_s_at	9467	<i>SH3BP5</i>	3.00E-03	1.67	7.00E-03	1.54	SH3-domain binding protein 5 (BTK-associated)
211475_s_at	573	<i>BAG1</i>	9.00E-04	1.66	1.10E-03	1.68	BCL2-associated athanogene
1552487_a_at	646	<i>BNC1</i>	5.20E-03	1.66	1.19E-02	1.53	basonuclin 1
212830_at	1955	<i>MEGF9</i>	4.30E-03	1.66	5.10E-03	1.68	multiple EGF-like-domains 9
203438_at	8614	<i>STC2</i>	2.02E-02	1.66	6.61E-02	1.52	stanniocalcin 2
204931_at	6943	<i>TCF21</i>	3.10E-03	1.66	4.00E-03	1.63	transcription factor 21
209386_at	4071	<i>TM4SF1</i>	7.20E-03	1.66	6.40E-03	1.66	transmembrane 4 L six family member 1
204198_s_at	864	<i>RUNX3</i>	2.13E-02	1.65	4.77E-02	1.54	runt-related transcription factor 3
206511_s_at	10736	<i>SIX2</i>	1.55E-02	1.65	4.61E-02	1.49	SIX homeobox 2
224126_at	84068	<i>SLC10A7</i>	9.42E-02	1.65	2.35E-01	1.57	solute carrier family 10, member 7
204653_at	7020	<i>TFAP2A</i>	3.10E-03	1.64	6.00E-03	1.57	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)
209864_at	23401	<i>FRAT2</i>	1.43E-02	1.63	1.93E-02	1.62	frequently rearranged in advanced T-cell lymphomas 2
204512_at	3096	<i>HVPEP1</i>	9.40E-03	1.63	6.10E-03	1.68	human immunodeficiency virus type I enhancer binding protein 1
212641_at	3097	<i>HVPEP2</i>	2.27E-02	1.63	2.07E-02	1.64	human immunodeficiency virus type I enhancer binding protein 2
225263_at	9394	<i>HS6ST1</i>	9.40E-03	1.63	1.44E-02	1.55	heparan sulfate 6-O-sulfotransferase 1
202464_s_at	5209	<i>PFKFB3</i>	6.30E-03	1.63	8.70E-03	1.61	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3
225056_at	57568	<i>SIPA1L2</i>	6.39E-02	1.63	1.10E-01	1.56	signal-induced proliferation-associated 1 like 2
212614_at	84159	<i>ARID5B</i>	2.20E-03	1.62	1.70E-03	1.60	AT rich interactive domain 5B (MRF1-like)
235122_at	59269	<i>HVPEP3</i>	3.98E-02	1.62	1.92E-02	1.71	human immunodeficiency virus type I enhancer binding protein 3
205945_at	3570	<i>IL6R</i>	1.99E-02	1.62	6.22E-02	1.52	interleukin 6 receptor
209808_x_at	3621	<i>ING1</i>	5.60E-03	1.62	6.00E-03	1.54	inhibitor of growth family member 1
33304_at	3669	<i>ISG20</i>	2.93E-02	1.62	6.72E-02	1.57	interferon stimulated exonuclease gene 20kDa
225688_s_at	90102	<i>PLDLR2</i>	9.83E-02	1.62	5.07E-02	1.62	pleckstrin homology-like domain, family B, member 2
204286_s_at	5366	<i>PMAIP1</i>	9.50E-02	1.62	8.61E-02	1.61	phorbol-12-myristate-13-acetate-induced protein 1
205097_at	1836	<i>SLC26A2</i>	5.20E-03	1.62	6.00E-03	1.57	solute carrier family 26 (anion exchanger), member 2
227867_at	129293	<i>TRABD2A</i>	3.98E-02	1.62	6.33E-02	1.64	Trab domain containing 2A
211205_x_at	8394	<i>PIP5K1A</i>	1.60E-02	1.61	5.34E-02	1.45	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha
229344_x_at	57494	<i>RIMKLB</i>	3.63E-02	1.61	3.17E-02	1.64	ribosomal modification protein rimk-like family member B
201417_at	6659	<i>SOX4</i>	3.80E-03	1.61	6.00E-03	1.61	SRY box 4
243259_at	6314	<i>ATXN7</i>	5.79E-02	1.60	9.23E-02	1.52	ataxin 7
233506_at	9689	<i>BZW1</i>	4.39E-02	1.60	5.63E-02	1.52	basic leucine zipper and W2 domains 1
202883_s_at	5519	<i>PPP2R1B</i>	2.33E-02	1.60	4.21E-02	1.53	protein phosphatase 2, regulatory subunit A, beta
226101_at	5581	<i>PRKCE</i>	7.10E-03	1.60	1.29E-02	1.54	protein kinase C, epsilon
213988_s_at	6303	<i>SAT1</i>	7.21E-02	1.60	7.72E-02	1.48	spermidine/spermine N1-acetyltransferase 1
226492_at	80031	<i>SEMA6D</i>	3.05E-02	1.60	2.06E-02	1.66	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D
207332_s_at	7037	<i>TFRC</i>	1.09E-02	1.60	1.78E-02	1.60	transferrin receptor
209387_s_at	4071	<i>TM4SF1</i>	4.82E-02	1.60	2.53E-02	1.69	transmembrane 4 L six family member 1
1555007_s_at	144406	<i>WDR66</i>	2.10E-03	1.60	2.90E-03	1.57	WD repeat domain 66
1553096_s_at	10018	<i>BCL2L11</i>	2.70E-02	1.59	7.50E-03	1.67	BCL2-like 11 (apoptosis facilitator)
206581_at	646	<i>BNC1</i>	5.90E-03	1.59	4.00E-03	1.65	basonuclin 1
203628_at	3480	<i>IGF1R</i>	2.33E-02	1.59	2.23E-02	1.55	insulin-like growth factor 1 receptor
1554833_at	55784	<i>MCTP2</i>	1.37E-02	1.59	3.43E-02	1.47	multiple C2 domains, transmembrane 2
202838_at	2517	<i>FUCA1</i>	6.90E-03	1.58	2.88E-02	1.48	fucosidase, alpha-L-1, tissue
205227_at	3556	<i>IL1RAP</i>	3.40E-02	1.58	2.51E-02	1.57	interleukin 1 receptor accessory protein
229092_at	7026	<i>NR2F2</i>	9.40E-03	1.58	7.90E-03	1.65	nuclear receptor subfamily 2, group F, member 2
202886_s_at	5519	<i>PPP2R1B</i>	3.98E-02	1.58	7.90E-03	1.49	protein phosphatase 2, regulatory subunit A, beta
209758_s_at	8076	<i>MFAP5</i>	3.33E-02	1.57	6.68E-02	1.44	microfibrillar associated protein 5
202238_s_at	4837	<i>NNMT</i>	1.05E-02	1.57	1.53E-02	1.48	nicotinamide N-methyltransferase
36829_at	5187	<i>PER1</i>	6.70E-03	1.57	1.28E-02	1.56	period circadian clock 1
216074_x_at	23286	<i>WWC1</i>	1.21E-02	1.57	1.31E-02	1.56	WW and C2 domain containing 1
241969_at	84159	<i>ARID5B</i>	8.15E-02	1.56	8.10E-03	1.94	AT rich interactive domain 5B (MRF1-like)
200920_s_at	694	<i>BTG1</i>	5.60E-03	1.56	5.20E-03	1.57	B-cell translocation gene 1, anti-proliferative
224822_at	10395	<i>DLC1</i>	4.00E-03	1.56	7.60E-03	1.50	DLC1 Rho GTPase activating protein
222866_s_at	55640	<i>FLVCR2</i>	1.17E-02	1.56	1.69E-02	1.58	feline leukemia virus subgroup C cellular receptor family, member 2
230492_s_at	56261	<i>GPCPD1</i>	6.02E-02	1.56	5.47E-02	1.58	glycerophosphocholine phosphodiesterase 1
212642_s_at	3097	<i>HVPEP2</i>	1.19E-02	1.56	8.70E-03	1.60	human immunodeficiency virus type I enhancer binding protein 2
201811_x_at	9467	<i>SH3BP5</i>	2.90E-03	1.56	4.20E-03	1.52	SH3-domain binding protein 5 (BTK-associated)
203221_at	7088	<i>TLE1</i>	3.05E-02	1.56	4.91E-02	1.53	transducin-like enhancer of split 1 (E[spl1] homolog, Drosophila)
226982_at	22936	<i>ELL2</i>	2.12E-02	1.55	3.92E-02	1.48	elongation factor, RNA polymerase II, 2
214212_x_at	10979	<i>FERMT2</i>	1.64E-02	1.55	3.96E-02	1.47	fermitin family member 2
243358_at	3480	<i>IGF1R</i>	4.20E-03	1.55	3.30E-03	1.56	insulin-like growth factor 1 receptor
203542_s_at	687	<i>KLF9</i>	2.90E-03	1.55	2.20E-03	1.60	Kruppel-like factor 9
226844_at	79817	<i>MOB3B</i>	6.55E-02	1.55	1.59E-01	1.41	MOB kinase activator 3B
204285_s_at	5366	<i>PMAIP1</i>	2.30E-02	1.55	1.99E-02	1.59	phorbol-12-myristate-13-acetate-induced protein 1
213280_at	23108	<i>RAP1GAP2</i>	6.00E-03	1.55	4.10E-03	1.58	RAP1 GTPase activating protein 2
220924_s_at	54407	<i>SLC38A2</i>	1.30E-03	1.55	2.50E-03	1.49	solute carrier family 38, member 2
225033_at	6482	<i>ST3GAL1</i>	4.92E-02	1.55	1.82E-01	1.33	ST3 beta-galactoside alpha-2,3-sialyltransferase 1
204596_s_at	6781	<i>STC1</i>	8.05E-02	1.55	5.18E-02	1.61	stanniocalcin 1
202644_s_at	7128	<i>TNFAIP3</i>	7.49E-02	1.55	1.18E-01	1.50	tumor necrosis factor, alpha-induced protein 3
209946_at	7424	<i>VEGFC</i>	1.51E-02	1.55	1.66E-02	1.59	vascular endothelial growth factor C
214014_at	10435	<i>CDC42EP2</i>	2.21E-02	1.54	1.49E-02	1.50	CDC42 effector protein (Rho GTPase binding) 2
208072_s_at	8527	<i>DGKD</i>	1.62E-02	1.54	1.59E-02	1.56	diacylglycerol kinase, delta 130kDa
1554966_a_at	11259	<i>FIUP1L</i>	2.75E-02	1.54	6.97E-02	1.51	filamin A interacting protein 1-like
230788_at	2651	<i>GCNT2</i>	1.74E-02	1.54	3.92E-02	1.49	glucosaminyl (N-acetyl) transferase 2, l-branching enzyme (l blood group)
203821_at	1839	<i>HBEFG</i>	7.30E-03	1.54	3.35E-02	1.41	heparin-binding EGF-like growth factor
208960_s_at	1316	<i>KLF6</i>	2.30E-03	1.54	2.40E-03	1.59	Kruppel-like factor 6
210805_x_at	861	<i>RUNX1</i>	8.70E-03	1.54	1.55E-02	1.39	runt-related transcription factor 1
202896_s_at	100506403	<i>LOC100506403</i>					uncharacterized LOC100506403
202896_s_at	140885	<i>SIRPA</i>	1.09E-02	1.54	1.67E-02	1.49	signal-regulatory protein alpha
212290_at	6541	<i>SLC7A1</i>	6.23E-02	1.54	1.83E-01	1.46	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1
221291_at	80328	<i>ULBP2</i>	3.12E-02	1.54	6.27E-02	1.39	UL16 binding protein 2
236557_bt	253461	<i>ZBTB38</i>	2.75E-02	1.54	6.85E-02	1.51	zinc finger and BTB domain containing 38
218865_at	64757	<i>MARCI</i>	5.90E-03	1.53	1.42E-02	1.47	mitochondrial amidoxime reducing component 1
203097_s_at	9693	<i>RAPGEF2</i>	2.30E-03	1.53	2.00E-03	1.56	Rap guanine nucleotide exchange factor 2
203096_s_at	9693	<i>RAPGEF2</i>	1.59E-02	1.53	2.03E-02	1.51	Rap guanine nucleotide exchange factor 2
209481_at	54861	<i>SNRK</i>	3.00E-03	1.53	5.50E-03	1.46	SNF related kinase
205990_s_at	7474	<i>WNT5A</i>	2.83E-02	1.53	1.77E-02	1.72	wingless-type MMTV integration site family, member 5A
210517_s_at	9590	<i>AKAP12</i>	1.14E-02	1.52	1.67E-02	1.46	A kinase (PRKA) anchor protein 12
201508_at	3487	<i>IGFBP4</i>	3.82E-02	1.52	3.62E-02	1.54	insulin like growth factor binding protein 4
208415_x_at	3621	<i>ING1</i>	8.80E-03	1.52	9.80E-03	1.49	inhibitor of growth family member 1
231849_at	144501	<i>KRT80</i>	8.60E-03	1.52	2.96E-02	1.44	keratin 80, type II
210762_s_at	10395	<i>DLC1</i>	8.60E-03	1.51	1.28E-02	1.48	DLC1 Rho GTPase activating protein
203627_at	3480	<i>IGF1R</i>	6.88E-02	1.51	3.17E-02	1.65	insulin-like growth factor 1 receptor
233487_s_at	56262	<i>LRRCSA</i>	6.00E-03	1.51	1.67E-02	1.43	leucine rich repeat containing 8 family, member A
210845_s_at	5329	<i>PLAUR</i>	4.00E-03	1.51	6.20E-03	1.47	plasminogen activator, urokinase receptor
226563_at	4087	<i>SMAD2</i>	3.93E-02	1.51	8.49E-02	1.37	SMAD family member 2
208083_s_at	3694	<i>ITGB6</i>	7.49E-02	4.05	8.13E-01	1.63	integrin beta 6
100505984	100505984	<i>LOC100505984</i>					uncharacterized LOC100505984
228340_at	7090	<i>TLE3</i>	5.60E-02	2.69	1.04E-01	2.55	transducin-like enhancer of split 3



208606_s_at	54361	WNT4	9.27E-02	2.32	1.88E-01	1.95	wingless-type MMTV integration site family, member 4
1556185_a_at	79689	STEAP4	3.99E-02	2.12	1.05E-01	1.96	STEAP family member 4
241547_at	29974	A1CF	4.11E-02	2.02	9.07E-01	1.16	APOBEC1 complementation factor
238419_at	90102	PHLDB2	8.17E-02	1.91	1.17E-01	1.63	pleckstrin homology-like domain, family B, member 2
204597_x_at	6781	STC1	8.49E-02	1.90	1.24E-01	1.84	stanniocalcin 1
242329_at	9586	CREB5	9.69E-02	1.86	2.25E-01	1.67	cAMP responsive element binding protein 5
401317	LOC401317						uncharacterized LOC401317
227354_at	55824	PAG1	7.54E-02	1.84	1.92E-01	1.58	phosphoprotein membrane anchor with glycosphingolipid microdomains 1
204684_at	4884	NPTX1	6.04E-02	1.75	1.37E-01	1.63	neuronal pentraxin I
226333_at	3570	IL6R	4.04E-02	1.73	1.03E-01	1.61	interleukin 6 receptor
220266_s_at	9314	KLFA	7.49E-02	1.73	1.60E-01	1.69	Kruppel-like factor 4 (gut)
218810_at	80149	ZC3H12A	3.60E-02	1.70	1.26E-01	1.55	zinc finger CCHC-type containing 12A
230330_at	8493	PPM1D	2.06E-02	1.69	1.01E-01	1.46	protein phosphatase, Mg2+/Mn2+ dependent, 1D
1559140_at	157693	FAM87A					family with sequence similarity 87, member A
400728	FAM87B		7.49E-02	1.65	2.21E-01	1.61	family with sequence similarity 87, member B
217371_s_at	3600	IL15	8.39E-02	1.62	1.18E-01	1.57	interleukin 15
210511_s_at	3624	INHBA	5.57E-02	1.61	7.86E-01	1.12	inhibin beta A
203220_s_at	7088	TFE1	5.26E-02	1.61	1.81E-01	1.49	transducin-like enhancer of split 1 (E[sp1] homolog, Drosophila)
214595_at	3755	KCNK1	5.38E-02	1.60	2.48E-01	1.46	potassium channel, voltage gated modifier subfamily G, member 1
219657_s_at	51274	KLIF	5.04E-02	1.58	1.70E-01	1.46	Kruppel-like factor 3 (basic)
212272_at	23175	LPIN1	6.14E-02	1.57	1.05E-01	1.41	lipin 1
1553134_s_at	203228	C9orf72	8.79E-02	1.56	2.83E-01	1.25	chromosome 9 open reading frame 72
224978_s_at	57602	USP36	9.13E-02	1.56	1.11E-01	1.54	ubiquitin specific peptidase 36
203592_s_at	10272	FSTL3	7.79E-02	1.53	1.04E-01	1.52	folliculin-like 3 (secreted glycoprotein)
203759_at	6484	ST3GAL4	2.19E-02	1.53	1.03E-01	1.36	ST3 beta-galactoside alpha-2,3-sialyltransferase 4
212823_s_at	26030	PLEKHG3	6.70E-02	1.52	1.25E-01	1.40	pleckstrin homology domain containing, family G (with RhoGef domain) member 3
216049_at	22836	RHOBTB3	6.50E-02	1.51	7.07E-01	1.20	Rho-related BTB domain containing 3
235598_at	4087	SMAD2	6.82E-02	1.51	2.01E-01	1.40	SMAD family member 2
213873_at	10402	ST3GAL6	7.38E-02	1.51	2.22E-01	1.40	ST3 beta-galactoside alpha-2,3-sialyltransferase 6
1566930_at	64216	TFB2M	8.47E-01	1.07	1.39E-02	4.40	transcription factor B2, mitochondrial
224917_at	81671	VMP1					vacuole membrane protein 1
406991	MIR21		1.78E-01	2.26	6.64E-02	2.77	microRNA 21
203563_at	60312	AFAP1	2.30E-01	1.85	3.49E-02	2.15	actin filament associated protein 1
1566901_at	7050	TGIF1	1.94E-01	1.70	6.57E-02	2.07	TGFB induced factor homeobox 1
211466_at	4781	NFIB	4.26E-01	1.43	1.69E-02	1.93	nuclear factor I/B
214586_at	2861	GPR37	1.53E-01	1.62	4.06E-02	1.91	G protein-coupled receptor 37 (endothelin receptor type B-like)
219132_at	57161	PELI2	1.87E-01	1.57	3.82E-02	1.91	pellino E3 ubiquitin protein ligase family member 2
230090_at	2668	GDNF	1.65E-01	1.62	9.22E-02	1.89	glial cell derived neurotrophic factor
202704_at	10140	TOB1	7.65E-02	1.50	2.29E-02	1.75	transducer of ERBB2, 1
243109_at	55784	MCTP2	1.57E-01	1.52	9.94E-02	1.64	multiple C2 domains, transmembrane 2
211965_at	677	ZFP36L1	1.61E-01	1.32	1.92E-02	1.61	ZFP36 ring finger protein-like 1
239486_at	5966	REL	1.85E-01	1.51	7.18E-02	1.60	v-rel avian reticuloendotheliosis viral oncogene homolog
229812_at	84196	USP48	4.92E-02	1.51	1.94E-02	1.57	ubiquitin specific peptidase 48
225133_at	51274	KLIF3	4.38E-02	1.50	2.63E-02	1.57	Kruppel-like factor 3 (basic)
205585_at	2120	ETV6	1.81E-01	1.44	9.97E-02	1.57	ets variant 6
239710_at	55137	FIGN	2.88E-02	1.50	1.39E-02	1.55	fidgetin
216511_s_at	6934	TCF7L2	4.96E-02	1.46	3.35E-02	1.54	transcription factor 7-like 2 (T-cell specific, HMG-box)
204516_at	6314	ATXN7	5.94E-02	1.50	3.26E-02	1.53	ataxin 7
226066_at	4286	MITF	1.30E-02	1.49	9.70E-03	1.53	microphthalmia-associated transcription factor
210869_s_at	4162	MWCM	2.53E-02	1.48	3.66E-02	1.53	melanoma cell adhesion molecule
213085_s_at	23286	WWC1	4.20E-03	1.50	4.10E-03	1.52	WW and C2 domain containing 1
216035_x_at	6934	TCF7L2	5.21E-02	1.49	2.27E-02	1.51	transcription factor 7-like 2 (T-cell specific, HMG-box)
201041_s_at	1843	USP1	3.30E-03	1.47	2.90E-03	1.51	dual specificity phosphatase 1
225330_at	3480	IGF1R	1.32E-01	1.43	4.61E-02	1.51	insulin-like growth factor 1 receptor
222162_s_at	9510	ADAMTS1	8.44E-02	1.42	5.60E-02	1.50	ADAM metalloproteinase with thrombospondin type 1 motif 1

Treatment (6h)
 Ind: 320 Probe Sets (206 Genes)
 Ind+GSK: 456 Probe Sets (307 Genes)



Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value (Ind)	Fold change (Ind)	FDR P-Value (Ind+GSK)	Fold change (Ind+GSK)	UniGene Name	Function
209959_at	8013	NR4A3	5.00E-04	14.13	2.00E-04	19.07	nuclear receptor subfamily 4, group A, member 3	
221541_at	83716	CRISPLD2	5.31E-08	8.05	3.78E-08	7.90	cysteine-rich secretory protein LCCL domain containing 2	
219049_at	55790	CSGALNACT1	3.00E-04	6.58	9.99E-05	8.85	chondroitin sulfate N-acetylgalactosaminyltransferase 1	
228128_x_at	5069	PAPPA	1.00E-04	6.16	2.63E-05	8.26	pregnancy-associated plasma protein A, pappalysin 1	
222784_at	64093	SMOC1	1.00E-04	5.62	5.10E-05	6.90	SPARC related modular calcium binding 1	
225207_at	5166	PKD4	7.00E-04	5.41	1.00E-04	9.39	pyruvate dehydrogenase kinase, isozyme 4	
239461_at	117248	GALNT15	4.05E-02	5.02	1.67E-02	5.63	polypeptide N-acetylgalactosaminyltransferase 15	
222783_s_at	64093	SMOC1	1.00E-04	4.93	6.79E-05	5.64	SPARC related modular calcium binding 1	
243438_at	27115	PDE7B	8.50E-03	4.85	3.00E-03	6.14	phosphodiesterase 7B	
205421_at	6581	SLC22A3	5.51E-02	4.77	9.60E-03	7.58	solute carrier family 22 (organic cation transporter), member 3	
1556185_a_at	79689	STEAP4	5.00E-04	4.73	2.00E-04	5.42	STEAP family member 4	
224942_at	5069	PAPPA	3.00E-04	4.69	9.99E-05	6.51	pregnancy-associated plasma protein A, pappalysin 1	
224940_s_at	5069	PAPPA	3.00E-04	4.68	9.99E-05	6.62	pregnancy-associated plasma protein A, pappalysin 1	
203638_s_at	2263	FGFR2	1.40E-03	4.65	3.00E-04	6.11	fibroblast growth factor receptor 2	
224941_at	5069	PAPPA	5.00E-04	4.64	9.99E-05	6.91	pregnancy-associated plasma protein A, pappalysin 1	
228962_at	5144	PDE4D	1.30E-03	4.51	3.00E-04	5.65	phosphodiesterase 4D, cAMP-specific	
230109_at	27115	PDE7B	3.00E-04	4.31	1.00E-04	4.79	phosphodiesterase 7B	
201981_at	5069	PAPPA	7.00E-04	4.10	1.00E-04	6.01	pregnancy-associated plasma protein A, pappalysin 1	
238649_at	26207	PITPNC1	2.20E-03	4.10	9.00E-04	4.61	phosphatidylinositol transfer protein, cytoplasmic 1	
228501_at	117248	GALNT15	1.60E-03	4.02	4.00E-04	5.07	polypeptide N-acetylgalactosaminyltransferase 15	
203549_s_at	4023	LPL	3.00E-04	3.99	1.00E-04	4.46	lipoprotein lipase	
211401_s_at	2263	FGFR2	4.96E-02	3.85	1.27E-02	5.47	fibroblast growth factor receptor 2	
203548_s_at	4023	LPL	1.00E-03	3.82	3.00E-04	4.33	lipoprotein lipase	
213050_at	23242	COBL	5.00E-04	3.79	2.00E-04	4.19	cordon-bleu WH2 repeat protein	
220088_at	728	CSAR1	9.00E-04	3.65	3.00E-04	3.68	complement component 5a receptor 1	
225987_at	79689	STEAP4	3.00E-04	3.44	1.00E-04	3.82	STEAP family member 4	
236361_at	117248	GALNT15	6.20E-03	3.41	1.80E-03	4.32	polypeptide N-acetylgalactosaminyltransferase 15	
205960_at	5166	PKD4	2.24E-02	3.40	2.90E-03	7.85	pyruvate dehydrogenase kinase, isozyme 4	
229709_at	483	ATP1B3	8.00E-03	3.39	4.40E-03	3.44	ATPase, Na+/K+ transporting, beta 3 polypeptide	
216248_s_at	4929	NR4A2	6.53E-02	3.39	2.90E-03	7.07	nuclear receptor subfamily 4, group A, member 2	
225516_at	6542	SLC7A2	1.00E-04	3.33	2.63E-05	4.06	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2	
208606_s_at	54361	WNT4	6.96E-02	3.27	2.38E-02	3.53	wingless-type MMTV integration site family, member 4	
213182_x_at	1028	CDKN1C	3.10E-03	3.14	1.10E-03	3.54	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
205501_at	10846	PDE10A	5.43E-05	3.00	2.46E-05	3.12	phosphodiesterase 10A	
220540_at	60598	KCNK15	2.79E-02	2.93	8.90E-03	3.18	potassium channel, two pore domain subfamily K, member 15	
219093_at	55022	PIDI	3.90E-03	2.86	1.10E-03	3.30	phosphotyrosine interaction domain containing 1	
204491_at	5144	PDE4D	1.03E-02	2.82	1.60E-03	3.42	phosphodiesterase 4D, cAMP-specific	
219534_x_at	1028	CDKN1C	1.40E-03	2.75	3.00E-04	3.25	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
216894_x_at	1028	CDKN1C	3.00E-04	2.74	1.00E-04	3.10	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
213348_at	1028	CDKN1C	9.00E-04	2.73	3.00E-04	3.17	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	
220187_at	79689	STEAP4	7.00E-04	2.70	2.00E-04	3.14	STEAP family member 4	
223484_at	84419	C15orf48	9.39E-02	2.69	9.43E-02	2.28	chromosome 15 open reading frame 48	
239650_at	344148	NCKAP5	1.11E-02	2.68	3.20E-03	2.89	NCK-associated protein 5	
237939_at	2044	EPHA5	3.00E-04	2.64	1.00E-04	2.92	EPH receptor A5	
230748_at	9120	SLC16A6	1.63E-02	2.55	1.50E-03	3.67	solute carrier family 16, member 6	
207038_at	9120	SLC16A6	1.72E-02	2.49	1.40E-03	3.64	solute carrier family 16, member 6	
222015_at	1454	CSNK1E					casein kinase 1, epsilon	
102800317	LOC400927-CSNK1E		5.00E-04	2.45	2.00E-04	2.54	LOC400927-CSNK1E readthrough	

216627_s_at	2683	<i>B4GALT1</i>	2.40E-03	2.44	6.00E-04	2.81	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1
210102_at	4013	<i>VWASA</i>	2.93E-02	2.41	7.60E-03	2.56	von Willebrand factor A domain containing 5A
229093_at	4846	<i>NOS3</i>	6.78E-02	2.38	2.45E-02	2.92	nitric oxide synthase 3
228132_at	84448	<i>ABLIM2</i>	3.00E-04	2.36	2.00E-04	2.42	actin binding LIM protein family, member 2
236300_at	5139	<i>PDE3A</i>	1.30E-03	2.35	6.00E-04	2.46	phosphodiesterase 3A, cGMP-inhibited
238029_s_at	151473	<i>SLC16A14</i>	1.90E-03	2.35	5.00E-04	2.64	solute carrier family 16, member 14
210836_x_at	5144	<i>PDE4D</i>	1.06E-02	2.35	1.20E-03	2.75	phosphodiesterase 4D, cAMP-specific
1555007_s_at	144406	<i>WDR66</i>	3.00E-04	2.34	1.00E-04	2.46	WD repeat domain 66
228507_at	5139	<i>PDE3A</i>	2.20E-03	2.34	6.00E-04	2.56	phosphodiesterase 3A, cGMP-inhibited
208228_s_at	2263	<i>FGFR2</i>	2.60E-03	2.32	2.00E-04	3.34	fibroblast growth factor receptor 2
209583_s_at	4345	<i>CD200</i>	2.80E-03	2.32	4.00E-04	2.86	CD200 molecule
229414_at	26207	<i>PITPNC1</i>	3.25E-02	2.32	1.17E-02	2.49	phosphatidylinositol transfer protein, cytoplasmic 1
1553199_at	138009	<i>DCAF4L2</i>	6.02E-02	2.31	4.71E-02	2.30	DDB1 and CUL4 associated factor 4-like 2
224071_at	50604	<i>IL20</i>	6.00E-02	2.30	3.21E-02	2.25	interleukin 20
225978_at	57494	<i>RIMKLB</i>	3.00E-04	2.29	2.00E-04	2.30	ribosomal modification protein rimk-like family member B
1555006_at	144406	<i>WDR66</i>	1.11E-02	2.28	4.50E-03	2.38	WD repeat domain 66
229552_at	8739	<i>HRK</i>	1.20E-03	2.24	3.00E-04	2.64	harakiri, BCL2 interacting protein
	283454	<i>LOC283454</i>					uncharacterized LOC283454
208425_s_at	26115	<i>TANC2</i>	1.20E-03	2.24	3.00E-04	2.49	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2
209582_s_at	4345	<i>CD200</i>	1.20E-03	2.22	2.00E-04	2.71	CD200 molecule
232267_at	283383	<i>ADGRD1</i>	8.60E-03	2.22	4.80E-03	2.16	adhesion G protein-coupled receptor D1
1552736_a_at	81832	<i>NETO1</i>	3.00E-04	2.21	1.00E-04	2.44	neuropilin (NRP) and tolloid (TLL)-like 1
218177_at	57132	<i>CHMP1B</i>	2.94E-02	2.18	2.50E-03	3.06	charged multivesicular body protein 1B
205003_at	9732	<i>DOCK4</i>	1.92E-02	2.17	5.80E-03	2.37	dedicator of cytokinesis 4
227099_s_at	387763	<i>CI1orf96</i>	1.80E-03	2.16	5.00E-04	2.48	chromosome 11 open reading frame 96
206389_s_at	5139	<i>PDE3A</i>	2.40E-03	2.16	1.10E-03	2.25	phosphodiesterase 3A, cGMP-inhibited
209772_s_at	100133941	<i>CD24</i>	1.00E-04	2.15	6.79E-05	2.20	CD24 molecule
206356_s_at	2774	<i>GNAL</i>	1.20E-03	2.15	6.00E-04	2.21	guanine nucleotide binding protein, alpha activating activity polypeptide, olfactory type
218589_at	10161	<i>LPAR6</i>	1.13E-02	2.15	1.70E-03	2.66	lysophosphatidic acid receptor 6
228325_at	23514	<i>SPIDR</i>	4.55E-02	2.15	4.80E-03	2.80	scaffolding protein involved in DNA repair
235367_at	84665	<i>MYPN</i>	9.00E-04	2.13	6.00E-04	2.12	myopalladin
213006_at	1052	<i>CEBPD</i>	7.22E-02	2.13	1.01E-02	2.81	CCAAT/enhancer binding protein (C/EBP), delta
224952_at	26115	<i>TANC2</i>	3.00E-04	2.12	9.99E-05	2.15	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2
203628_at	3480	<i>IGF1R</i>	9.00E-04	2.10	2.00E-04	2.21	insulin-like growth factor 1 receptor
213436_at	1268	<i>CNR1</i>	1.30E-03	2.10	3.00E-04	2.43	cannabinoid receptor 1 (brain)
218865_at	64757	<i>MARCI</i>	3.00E-04	2.09	9.99E-05	2.30	mitochondrial amidoxime reducing component 1
207626_s_at	6542	<i>SLC7A2</i>	1.55E-02	2.09	4.40E-03	2.36	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2
220335_x_at	23491	<i>CE53</i>	3.00E-04	2.08	9.99E-05	2.21	carboxylesterase 3
205157_s_at	3872	<i>KRT17</i>	1.63E-02	2.08	7.70E-03	2.12	keratin 17, type I
230398_at	84951	<i>TNS4</i>	4.36E-02	2.07	8.20E-03	2.40	tensin 4
205896_at	6583	<i>SLC22A4</i>	9.20E-03	2.06	5.50E-03	1.98	solute carrier family 22 (organic cation/zwitterion transporter), member 4
	150094	<i>SIK1</i>	7.78E-02	2.06	4.50E-03	2.81	salt-inducible kinase 1
208078_s_at	102724428	<i>LOC102724428</i>					serine/threonine-protein kinase SIK1
208651_x_at	100133941	<i>CD24</i>	2.05E-02	2.05	4.80E-03	2.34	CD24 molecule
1568949_at	26207	<i>PITPNC1</i>	8.20E-03	2.03	4.70E-03	2.13	phosphatidylinositol transfer protein, cytoplasmic 1
206359_at	9021	<i>SOC33</i>	4.68E-02	2.03	1.63E-02	2.17	suppressor of cytokine signaling 3
208650_s_at	100133941	<i>CD24</i>	8.00E-03	2.02	4.10E-03	2.06	CD24 molecule
201810_s_at	9467	<i>SH3BP5</i>	1.20E-03	2.01	3.00E-04	2.23	SH3-domain binding protein 5 (BTK-associated)
226858_at	1454	<i>CSNK1E</i>	5.00E-04	2.00	2.00E-04	2.10	casein kinase 1, epsilon
	102800317	<i>LOC400927-CSNK1E</i>					LOC400927-CSNK1E readthrough
224963_at	1836	<i>SLC26A2</i>	9.00E-04	2.00	2.00E-04	2.12	solute carrier family 26 (anion exchanger), member 2
236440_at	81832	<i>NETO1</i>	1.30E-03	2.00	3.00E-04	2.24	neuropilin (NRP) and tolloid (TLL)-like 1
211631_x_at	2683	<i>B4GALT1</i>	3.50E-03	1.99	8.00E-04	2.28	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1
206864_s_at	8739	<i>HRK</i>	3.00E-04	1.98	1.00E-04	2.03	harakiri, BCL2 interacting protein
236087_at	84448	<i>ABLIM2</i>	1.20E-03	1.98	8.00E-04	1.96	actin binding LIM protein family, member 2
266_s_at	100133941	<i>CD24</i>	2.84E-02	1.98	6.60E-03	2.19	CD24 molecule
210837_s_at	5144	<i>PDE4D</i>	7.29E-02	1.98	8.50E-03	2.71	phosphodiesterase 4D, cAMP-specific
237724_at	162333	<i>MARCH10</i>	2.61E-02	1.97	1.78E-02	2.02	membrane associated ring finger 10
206388_at	5139	<i>PDE3A</i>	5.00E-04	1.96	2.00E-04	2.17	phosphodiesterase 3A, cGMP-inhibited
226865_at	84898	<i>PLXDC2</i>	1.40E-03	1.96	1.10E-03	1.91	plexin domain containing 2
242444_at	114904	<i>CIQTNF6</i>	1.31E-02	1.96	4.70E-03	2.02	C1q and tumor necrosis factor related protein 6
238919_at	5101	<i>PCDH9</i>	3.88E-02	1.95	5.50E-03	2.44	protocadherin 9
200731_s_at	7803	<i>PTPAA1</i>	8.85E-02	1.95	1.00E-02	2.26	protein tyrosine phosphatase type IVA, member 1
224393_s_at	27439	<i>TMEM121B</i>	8.80E-02	1.95	3.10E-02	2.12	transmembrane Protein 121B
225728_at	8470	<i>SORBS2</i>	1.57E-02	1.94	5.40E-03	2.04	sorbin and SH3 domain containing 2
203627_at	3480	<i>IGF1R</i>	9.00E-04	1.93	2.00E-04	2.25	insulin-like growth factor 1 receptor
213438_at	23114	<i>NFASC</i>	1.30E-03	1.93	5.00E-04	1.93	neurofascin
213765_at	8076	<i>MFAP5</i>	1.20E-03	1.91	9.00E-04	1.77	microfibrillar associated protein 5
202952_s_at	8038	<i>ADAM12</i>	3.00E-04	1.90	3.00E-04	1.65	ADAM metalloproteinase domain 12
220343_at	27115	<i>PDE7B</i>	3.00E-04	1.89	9.99E-05	1.98	phosphodiesterase 7B
214807_at	84898	<i>PLXDC2</i>	1.63E-02	1.89	1.77E-02	1.70	plexin domain containing 2
219155_at	26207	<i>PITPNC1</i>	1.93E-02	1.89	7.10E-03	2.02	phosphatidylinositol transfer protein, cytoplasmic 1
206865_at	8739	<i>HRK</i>	3.31E-02	1.89	3.70E-03	2.15	harakiri, BCL2 interacting protein
216379_x_at	100133941	<i>CD24</i>	3.10E-03	1.88	2.00E-03	1.89	CD24 molecule
210397_at	1672	<i>DEFB1</i>	7.30E-03	1.88	2.50E-03	1.87	defensin, beta 1
228964_at	639	<i>PRDM1</i>	1.71E-02	1.88	8.00E-04	2.33	PR domain containing 1, with ZNF domain
225330_at	3480	<i>IGF1R</i>	4.50E-02	1.88	6.50E-03	2.02	insulin-like growth factor 1 receptor
214595_at	3755	<i>CNGC1</i>	7.60E-03	1.87	3.20E-03	1.98	potassium channel, voltage gated modifier subfamily G, member 1
223571_at	114904	<i>CIQTNF6</i>	1.35E-02	1.87	6.10E-03	1.90	C1q and tumor necrosis factor related protein 6
226614_s_at	83648	<i>FAM167A</i>	3.00E-04	1.86	9.99E-05	1.91	family with sequence similarity 167, member A
213924_at	2774	<i>GNAL</i>	8.20E-03	1.86	2.00E-03	2.03	guanine nucleotide binding protein, alpha activating activity polypeptide, olfactory type
213764_s_at	8076	<i>MFAP5</i>	1.82E-02	1.86	1.02E-02	1.85	microfibrillar associated protein 5
221272_s_at	81563	<i>CIorf21</i>	3.20E-03	1.85	2.90E-03	1.74	chromosome 1 open reading frame 21
242162_at	164781	<i>DAWI</i>	8.60E-03	1.85	4.50E-03	2.17	dynein assembly factor with WDR repeat domains 1
237187_at	8739	<i>HRK</i>	9.00E-04	1.84	2.00E-04	2.14	harakiri, BCL2 interacting protein
227529_s_at	9590	<i>AKAP12</i>	1.72E-02	1.84	5.00E-03	1.96	A kinase (PKA) anchor protein 12
227276_at	84898	<i>PLXDC2</i>	1.30E-03	1.83	5.00E-04	1.91	plexin domain containing 2
206355_at	2774	<i>GNAL</i>	1.60E-03	1.83	4.00E-04	2.07	guanine nucleotide binding protein, alpha activating activity polypeptide, olfactory type
208250_s_at	1755	<i>DMBT1</i>	3.10E-03	1.83	9.00E-04	1.82	deleted in malignant brain tumors 1
212236_x_at	3872	<i>KRT17</i>	4.52E-02	1.83	2.25E-02	1.83	keratin 17, type I
1563933_a_at	200150	<i>PLDS</i>	5.00E-04	1.82	6.00E-04	1.69	phospholipase D family, member 5
229180_at	23286	<i>WWC1</i>	1.30E-03	1.82	9.00E-04	1.82	WW and C2 domain containing 1
209771_x_at	100133941	<i>CD24</i>	2.20E-03	1.82	1.70E-03	1.79	CD24 molecule
237217_at	92949	<i>ADAMTSL1</i>	8.20E-03	1.82	6.20E-03	1.76	ADAMTS like 1
202388_at	5997	<i>RGS2</i>	7.25E-02	1.82	1.69E-02	2.19	regulator of G-protein signaling 2
201811_x_at	9467	<i>SH3BP5</i>	2.10E-03	1.81	5.00E-04	2.01	SH3-domain binding protein 5 (BTK-associated)
225999_at	57494	<i>RIMKLB</i>	2.48E-02	1.81	5.70E-03	1.78	ribosomal modification protein rimk-like family member B
218178_s_at	57132	<i>CHMP1B</i>	3.03E-02	1.81	4.30E-03	2.21	charged multivesicular body protein 1B
209016_s_at	3855	<i>KRT7</i>	9.00E-04	1.80	3.00E-04	1.85	keratin 7, type II
1562713_a_at	81832	<i>NETO1</i>	3.30E-03	1.80	9.00E-04	1.93	neuropilin (NRP) and tolloid (TLL)-like 1
208335_s_at	2532	<i>ACKR1</i>	1.03E-02	1.80	4.40E-03	2.01	atypical chemokine receptor 1 (Duffy blood group)
229403_at	2683	<i>B4GALT1</i>	7.27E-02	1.80	4.63E-02	1.84	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1
243243_at	2719	<i>GPC3</i>	1.48E-02	1.79	1.30E-02	1.56	glypican 3
221577_x_at	9518	<i>GDF15</i>	2.43E-02	1.79	6.60E-03	1.86	growth differentiation factor 15
200732_s_at	7803	<i>PTPAA1</i>	2.92E-02	1.79	4.50E-03	2.25	protein tyrosine phosphatase type IVA, member 1
213425_at	7474	<i>WNT5A</i>	7.78E-02	1.79	8.10E-03	2.21	wingless-type MMTV integration site family, member 5A
205139_s_at	10090	<i>UST</i>	8.29E-02	1.79	2.28E-02	1.94	uronyl-2-sulfotransferase
229529_at	6943	<i>TCF21</i>	9.00E-04	1.78	1.10E-03	1.66	transcription factor 21
226777_at	8038	<i>ADAM12</i>	1.30E-03	1.78	1.50E-03	1.75	ADAM metalloproteinase domain 12
225328_at	114907	<i>FBXO32</i>	1.70E-03	1.78	3.00E-04	2.02	F-box protein 32
226834_at	79827	<i>CLMP</i>	6.30E-03	1.78	1.60E-03	1.91	CXADR-like membrane protein
223475_at							

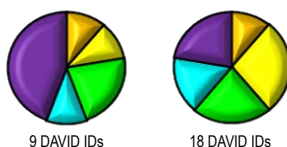
236038_at	57484	<i>RNF150</i>	3.89E-02	1.76	1.62E-02	1.77	ring finger protein 150
220092_s_at	84168	<i>ANTXR1</i>	7.00E-04	1.75	3.00E-04	1.72	anthrax toxin receptor 1
229720_at	573	<i>BAG1</i>	1.10E-03	1.75	2.00E-04	1.91	BCL2-associated athanogene
203710_at	3708	<i>ITPR1</i>	6.40E-03	1.75	2.90E-03	1.87	inositol 1,4,5-trisphosphate receptor, type 1
215303_at	9201	<i>DCLK1</i>	2.60E-03	1.74	2.00E-03	1.73	doublecortin-like kinase 1
219383_at	79899	<i>PRRS1</i>	3.10E-03	1.74	4.00E-04	1.98	proline rich 5 like
228731_at	2977	<i>GLUCY1A2</i>	8.87E-02	1.74	4.64E-02	1.71	guanylate cyclase 1, soluble, alpha 2
212143_s_at	3486	<i>IGFBP3</i>	3.80E-03	1.73	1.70E-03	1.79	insulin like growth factor binding protein 3
230962_at	9201	<i>DCLK1</i>	7.30E-03	1.72	2.00E-03	1.90	doublecortin-like kinase 1
225520_at	25902	<i>MTHFD1L</i>	8.00E-03	1.72	6.90E-03	1.56	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-like
238455_at	84898	<i>PLXDC2</i>	1.15E-02	1.72	3.20E-03	1.89	plexin domain containing 2
227530_at	9590	<i>AKAP12</i>	2.20E-02	1.72	8.50E-03	1.78	A kinase (PKA) anchor protein 12
236201_at	55304	<i>SPTLC3</i>	6.71E-02	1.72	2.35E-02	1.81	serine palmitoyltransferase, long chain base subunit 3
241950_at	23286	<i>WWC1</i>	8.80E-03	1.71	4.20E-03	1.73	WW and C2 domain containing 1
217678_at	23657	<i>SLC7A11</i>	1.40E-02	1.71	6.50E-03	1.65	solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11
202478_at	28951	<i>TRIB2</i>	2.78E-02	1.71	7.40E-03	1.85	tribbles pseudokinase 2
212906_at	57476	<i>GRAMD1B</i>	9.87E-02	1.71	2.73E-02	1.85	GRAM domain containing 1B
202897_at	140885	<i>SIRPA</i>	6.80E-03	1.70	2.40E-03	1.75	signal-regulatory protein alpha
209277_at	7980	<i>TFPI2</i>	2.12E-02	1.70	3.60E-03	1.88	tissue factor pathway inhibitor 2
231559_at	4837	<i>NNMT</i>	2.35E-02	1.70	7.40E-03	1.84	nicotinamide N-methyltransferase
203180_at	220	<i>ALDH1A3</i>	1.20E-03	1.69	3.00E-04	1.82	aldehyde dehydrogenase 1 family, member A3
224959_at	1836	<i>SLC26A2</i>	4.50E-03	1.69	1.10E-03	1.78	solute carrier family 26 (anion exchanger), member 2
219911_s_at	28231	<i>SLC04A1</i>	1.35E-02	1.69	2.50E-03	1.89	solute carrier organic anion transporter family, member 4A1
202238_s_at	4837	<i>NNMT</i>	1.57E-02	1.69	4.30E-03	1.90	nicotinamide N-methyltransferase
209758_s_at	8076	<i>MFAP5</i>	3.00E-04	1.68	2.00E-04	1.60	microfibrillar associated protein 5
202679_at	4864	<i>NPC1</i>	9.00E-04	1.68	2.00E-04	1.71	Niemann-Pick disease, type C1
205399_at	9201	<i>DCLK1</i>	2.00E-03	1.68	1.00E-03	1.67	doublecortin-like kinase 1
230493_at	387914	<i>SHISA2</i>	2.70E-03	1.68	3.00E-04	1.98	shisa family member 2
213849_s_at	5521	<i>PPP2R2B</i>	3.10E-03	1.68	3.30E-03	1.58	protein phosphatase 2, regulatory subunit B, beta
227867_at	129293	<i>TRABD2A</i>	1.50E-02	1.68	4.60E-03	1.77	Trab domain containing 2A
215034_s_at	4071	<i>TM4SF1</i>	2.07E-02	1.68	1.64E-02	1.60	transmembrane 4 L six family member 1
203984_s_at	842	<i>CASP9</i>	6.44E-02	1.68	3.98E-02	1.68	caspase 9
226281_at	92737	<i>DNER</i>	6.89E-02	1.68	3.48E-02	1.61	delta/notch like EGF repeat containing
201925_s_at	1604	<i>CD55</i>	7.41E-02	1.68	1.09E-02	1.79	CD55 molecule, decay accelerating factor for complement (Cromer blood group)
203865_s_at	104	<i>ADARB1</i>	9.00E-04	1.67	4.00E-04	1.62	adenosine deaminase, RNA-specific, B1
216074_x_at	23286	<i>WWC1</i>	4.90E-03	1.67	1.60E-03	1.77	WW and C2 domain containing 1
219825_at	56603	<i>CYP26B1</i>	6.80E-03	1.67	4.20E-03	1.77	cytochrome P450, family 26, subfamily B, polypeptide 1
206707_x_at	9750	<i>FAM65B</i>	1.36E-02	1.67	1.94E-02	1.52	family with sequence similarity 65, member B
228461_at	344558	<i>SH3RF3</i>	1.20E-03	1.66	4.00E-04	1.73	SH3 domain containing ring finger 3
209676_at	7035	<i>TFPI</i>	2.22E-02	1.66	3.30E-03	1.76	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)
214199_at	6441	<i>SFTPD</i>	5.72E-02	1.66	7.60E-03	2.01	surfactant protein D
209829_at	9750	<i>FAM65B</i>	7.78E-02	1.66	1.78E-02	1.99	family with sequence similarity 65, member B
206866_at	1002	<i>CDH4</i>	1.20E-03	1.65	6.00E-04	1.62	cadherin 4, type 1, R-cadherin (retinal)
223125_s_at	81563	<i>C1orf21</i>	2.00E-03	1.65	1.80E-03	1.58	chromosome 1 open reading frame 21
1555486_a_at	79899	<i>PRRS1</i>	2.90E-03	1.65	5.00E-04	1.84	proline rich 5 like
213258_at	7035	<i>TFPI</i>	2.90E-03	1.65	8.00E-04	1.74	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)
222073_at	1285	<i>COL4A3</i>	3.90E-03	1.65	2.50E-03	1.59	collagen, type IV, alpha 3 (Goodpasture antigen)
204456_s_at	2619	GAS1	4.60E-03	1.65	5.00E-04	1.96	growth arrest-specific 1
215646_s_at	1462	<i>VCAN</i>	7.22E-02	1.65	2.38E-02	1.62	versican
213085_s_at	23286	<i>WWC1</i>	8.00E-04	1.64	3.00E-04	1.72	WW and C2 domain containing 1
213988_s_at	6303	<i>SAT1</i>	2.49E-02	1.64	4.40E-03	1.90	spermidine/spermine N1-acetyltransferase 1
217546_at	4499	<i>MT1M</i>	3.96E-02	1.64	9.70E-03	2.00	metallothionein 1M
219737_s_at	5101	<i>PCDH9</i>	7.13E-02	1.64	1.09E-02	1.92	protocadherin 9
224783_at	283991	<i>UBALD2</i>	9.00E-04	1.63	4.00E-04	1.66	UBA-like domain containing 2
225540_at	4133	<i>MAP2</i>	1.20E-03	1.63	9.00E-04	1.61	microtubule associated protein 2
202723_s_at	2308	<i>FOXO1</i>	4.30E-03	1.63	8.00E-04	1.81	forkhead box O1
232206_at	54986	<i>ULK4</i>	3.00E-04	1.62	3.00E-04	1.53	unc-51 like kinase 4
219714_s_at	55799	<i>CACNA2D3</i>	5.00E-04	1.62	4.00E-04	1.53	calcium channel, voltage-dependent, alpha 2/delta subunit 3
229585_at	92949	<i>ADAMTSL1</i>	3.40E-03	1.62	4.00E-04	1.85	ADAMTS like 1
216598_s_at	6347	<i>CCL2</i>	6.70E-03	1.62	2.90E-03	1.56	chemokine (C-C motif) ligand 2
205795_at	9369	<i>NRXN3</i>	9.80E-03	1.62	1.58E-02	1.47	neurexin 3
209355_s_at	8613	<i>PLPP3</i>	1.17E-02	1.62	1.10E-03	1.92	phospholipid phosphatase 3
216944_s_at	3708	<i>ITPR1</i>	3.78E-02	1.62	5.20E-03	1.71	inositol 1,4,5-trisphosphate receptor, type 1
238419_at	90102	<i>PHLDB2</i>	4.08E-02	1.62	3.90E-03	1.92	pleckstrin homology-like domain, family B, member 2
206002_at	10149	<i>ADGRG2</i>	7.00E-04	1.61	9.00E-04	1.50	adhesion G protein-coupled receptor G2
226506_at	79875	<i>THSD4</i>	1.80E-03	1.61	2.40E-03	1.54	thrombospondin type 1 domain containing 4
36711_at	23764	<i>MAFF</i>	2.14E-02	1.61	2.50E-03	1.75	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F
231067_s_at	9590	<i>AKAP12</i>	2.39E-02	1.61	8.50E-03	1.75	A kinase (PKA) anchor protein 12
210775_x_at	842	<i>CASP9</i>	4.69E-02	1.61	2.88E-02	1.65	caspase 9
229228_at	9586	<i>CREB5</i>	6.56E-02	1.61	1.34E-02	1.75	cAMP responsive element binding protein 5
225803_at	114907	<i>FBXO32</i>	4.60E-03	1.60	1.70E-03	1.66	F-box protein 32
207826_s_at	3399	<i>ID3</i>	9.50E-03	1.60	1.00E-03	1.89	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein
209278_s_at	7980	<i>TFPI2</i>	1.71E-02	1.60	6.20E-03	1.64	tissue factor pathway inhibitor 2
201508_at	3487	<i>IGFBP4</i>	9.00E-04	1.59	1.00E-04	1.79	insulin like growth factor binding protein 4
209276_s_at	2745	<i>GLRX</i>	1.80E-03	1.59	5.00E-04	1.68	glutaredoxin
225989_at	26091	<i>HERC4</i>	3.10E-03	1.59	2.00E-03	1.59	HECT and RLD domain containing E3 ubiquitin protein ligase 4
229649_at	9369	<i>NRXN3</i>	3.90E-03	1.59	4.50E-03	1.44	neurexin 3
210592_s_at	6303	<i>SAT1</i>	1.97E-02	1.59	3.70E-03	1.65	spermidine/spermine N1-acetyltransferase 1
238877_at	2070	<i>EYA4</i>	2.67E-02	1.59	1.14E-02	1.60	EYA transcriptional coactivator and phosphatase 4
213624_at	10924	<i>SMPDL3A</i>	3.36E-02	1.59	5.40E-03	1.65	sphingomyelin phosphodiesterase, acid-like 3A
204039_at	1050	<i>CEBPA</i>	5.67E-02	1.59	1.09E-02	1.80	CCAAT/enhancer binding protein (C/EBP), alpha
204288_s_at	8470	<i>SORBS2</i>	5.74E-02	1.59	2.26E-02	1.67	sorbin and SH3 domain containing 2
226931_at	83857	<i>TMTC1</i>	7.00E-04	1.58	2.00E-04	1.66	transmembrane and tetratricopeptide repeat containing 1
209386_at	4071	<i>TM4SF1</i>	1.38E-02	1.58	6.80E-03	1.59	transmembrane 4 L six family member 1
224480_s_at	84803	<i>GPA73</i>	2.18E-02	1.58	2.50E-03	1.87	glycerol 3-phosphate acyltransferase 3
202479_s_at	28951	<i>TRIB2</i>	8.42E-02	1.58	2.80E-02	1.72	tribbles pseudokinase 2
205074_at	6584	<i>SLC22A5</i>	2.60E-03	1.57	1.20E-03	1.59	solute carrier family 22 (organic cation/carnitine transporter), member 5
238733_at	4193	<i>MDM2</i>	5.00E-03	1.57	7.00E-04	1.78	MDM2 proto-oncogene, E3 ubiquitin protein ligase
212226_s_at	8613	<i>PLPP3</i>	8.80E-03	1.57	1.10E-03	1.77	phospholipid phosphatase 3
221731_x_at	1462	<i>VCAN</i>	1.31E-02	1.57	5.20E-03	1.58	versican
33304_at	3669	<i>ISG20</i>	1.46E-02	1.57	5.00E-03	1.67	interferon stimulated exonuclease gene 20kDa
232124_at	729085	<i>FAM198A</i>	2.16E-02	1.57	2.71E-02	1.53	family with sequence similarity 198, member A
228293_at	91614	<i>DEPDC7</i>	4.93E-02	1.57	1.78E-02	1.65	DEP domain containing 7
228933_at	4810	<i>NHS</i>	6.40E-02	1.57	1.48E-02	1.79	Nance-Horan syndrome (congenital cataracts and dental anomalies)
203108_at	9052	<i>GPCR5A</i>	5.00E-04	1.56	3.00E-04	1.57	G protein-coupled receptor, class C, group 5, member A
230193_at	144406	<i>WDR66</i>	3.20E-03	1.56	2.90E-03	1.58	WD repeat domain 66
207528_s_at	23657	<i>SLC7A11</i>	6.60E-03	1.56	1.67E-02	1.41	solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11
204698_at	3669	<i>ISG20</i>	1.29E-02	1.56	3.50E-03	1.70	interferon stimulated exonuclease gene 20kDa
205870_at	624	<i>BDKRB2</i>	4.44E-02	1.56	5.10E-03	1.92	bradykinin receptor B2
223402_at	54935	<i>DUSP23</i>	1.50E-03	1.55	3.00E-04	1.72	dual specificity phosphatase 23
202387_at	573	<i>BAG1</i>	1.60E-03	1.55	6.00E-04	1.61	BCL2-associated athanogene
209087_x_at	4162	<i>MCAM</i>	4.60E-03	1.55	1.20E-03	1.59	melanoma cell adhesion molecule
242624_at	84448	<i>ABLIM2</i>	8.00E-03	1.55	3.30E-03	1.58	actin binding LIM protein family, member 2
217623_at	91807	<i>MYLK3</i>	1.30E-02	1.55	1.98E-02	1.43	myosin light chain kinase 3
202724_s_at	2308	<i>FOXO1</i>	1.57E-02	1.55	1.40E-03	1.78	forkhead box O1
200730_s_at	7803	<i>PTP4A1</i>	5.37E-02	1.55	8.60E-03	1.76	protein tyrosine phosphatase type IVA, member 1
210869_s_at	4162	<i>MCAM</i>	2.10E-03	1.54	7.00E-04	1.63	melanoma cell adhesion molecule
210095_s_at	3486	<i>IGFBP3</i>	2.90E-03	1.54	1.20E-03	1.61	insulin like growth factor binding protein 3
226431_at	150864	<i>FAM117B</i>	3.70E-03	1.54	1.80E-03	1.62	family with sequence similarity 117, member B
228625_at	163732	<i>CITFD4</i>	1.01E-02	1.54	5.00E-04	1.95	Cbp/p300-interacting transactivator, with Glu/Asp rich carboxy-terminal domain, 4
202237_at	4837	<i>NNMT</i>	1.36E-02	1.54	3.30E-03	1.66	nicotinamide N-methyltransferase
228813_at	9759	<i>HDAC4</i>	1.57E-02	1.54	1.38E-02	1.52	histone deacetylase 4
213790_at	8038	<i>ADAM12</i>	2.61E-02	1.54	8.20E-03	1.66	ADAM metallopeptidase domain 12
243358_at	3480	<i>IGF1R</i>	2.64E-02	1.54	3.80E-03	1.80	insulin-like growth factor 1 receptor
213508_at	171546	<i>SPTSSA</i>	4.14E-02	1.54	9.80E-03	1.65	serine palmitoyltransferase, small subunit A
225496_s_at	54843	<i>SYTL2</i>	5.37E-02	1.54	8.20E-02	1.34	synaptotagmin-like 2
211475_s_at	573	<i>BAG1</i>	1.40E-03	1.53	7.00E-04	1.56	BCL2-associated athanogene
202254_at	26037	<i>SIPA1L1</i>	5.70E-03	1.53	5.20E-03	1.47	signal-induced proliferation-associated 1 like 1
201858_s_at	5552	<i>SRGN</i>	6.80E-03	1.53	2.10E-03	1.62	serglycin
1555950_a_at	1604	<i>CD55</i>	1.74E-02	1.53	5.40E-03	1.56	CD55 molecule, decay accelerating factor for complement (Cromer blood group)



227657_at	57484	<i>RNF150</i>	3.90E-02	1.53	2.13E-02	1.52	ring finger protein 150
229812_at	84196	<i>USP48</i>	4.12E-02	1.53	1.18E-02	1.53	ubiquitin specific peptidase 48
231015_at	28999	<i>KLF15</i>	7.74E-02	1.53	1.23E-02	1.60	Kruppel-like factor 15
218113_at	23670	<i>TMEM2</i>	9.95E-02	1.53	1.64E-02	1.66	transmembrane protein 2
226322_at	83857	<i>TMTC1</i>	1.70E-03	1.52	5.00E-04	1.58	transmembrane and tetra-ricopeptide repeat containing 1
219501_at	55068	<i>ENOX1</i>	2.20E-03	1.52	2.00E-03	1.44	ecto-NOX disulfide-thiol exchanger 1
210015_s_at	4133	<i>MAP2</i>	2.60E-03	1.52	1.20E-03	1.54	microtubule associated protein 2
208055_s_at	26091	<i>HERC4</i>	2.69E-02	1.52	1.09E-02	1.54	HECT and RLD domain containing E3 ubiquitin protein ligase 4
226811_at	54855	<i>FAM46C</i>	8.29E-02	1.51	2.01E-02	1.64	family with sequence similarity 46, member C
203455_s_at	6303	<i>SAT1</i>	9.47E-02	1.52	1.32E-02	1.68	spermidine/spermine N1-acetyltransferase 1
220227_at	1002	<i>CDH4</i>	1.30E-03	1.51	8.00E-04	1.53	cadherin 4, type 1, R-cadherin (retinal)
229310_at	114818	<i>KHLH29</i>	1.00E-02	1.51	2.40E-03	1.60	kelch-like family member 29
210664_s_at	7035	<i>TLPI</i>	2.43E-02	1.51	6.10E-03	1.61	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)
209683_at	81553	<i>FAM49A</i>	4.80E-02	1.51	1.63E-02	1.68	family with sequence similarity 49, member A
228796_at	131034	<i>CNPE4</i>	5.13E-02	1.51	8.15E-02	1.43	copine IV
205193_at	23764	<i>MAFF</i>	8.39E-02	1.51	7.00E-03	1.77	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F
205462_s_at	3241	<i>HPCAL1</i>	1.30E-03	1.50	6.00E-04	1.53	hippocalcin-like 1
239352_at	55117	<i>SLC6A15</i>	4.30E-03	1.50	1.15E-02	1.36	solute carrier family 6 (neutral amino acid transporter), member 15
213280_at	23108	<i>RAP1GAP2</i>	2.18E-02	1.50	2.50E-03	1.67	RAP1 GTPase activating protein 2
220148_at	64577	<i>ALDH8A1</i>	4.05E-02	1.50	1.00E-02	1.61	aldehyde dehydrogenase 8 family, member A1
233506_at	9689	<i>BZW1</i>	9.02E-02	1.50	4.65E-02	1.52	basic leucine zipper and W2 domains 1
1565657_at	54918	<i>CMTM6</i>	9.35E-02	6.78	2.12E-01	3.80	CKLF-like MARVEL transmembrane domain containing 6
211119_at	2100	<i>ESR2</i>	3.77E-02	3.44	4.40E-01	1.49	estrogen receptor 2 (ER beta)
237804_at	8701	<i>DNAH11</i>	4.79E-02	3.41	1.02E-01	2.17	dynein, axonemal, heavy chain 11
221305_s_at	54576	<i>UGT1A8</i>	9.20E-02	2.27	5.55E-01	1.27	UDP glucuronosyltransferase 1 family, polypeptide A8
206616_s_at	53616	<i>ADAM22</i>	2.07E-02	2.22	1.06E-01	1.67	ADAM metalloproteinase domain 22
1554199_at	5800	<i>PTPRO</i>	4.44E-02	2.20	1.27E-01	1.73	protein tyrosine phosphatase, receptor type, O
207430_s_at	4477	<i>MSMB</i>	9.32E-02	2.03	3.57E-01	1.57	microseminoprotein, beta
215703_at	1080	<i>CFTR</i>	8.96E-02	1.92	4.16E-01	1.33	cystic fibrosis transmembrane conductance regulator
1559997_x_at	201191	<i>SAMD14</i>	6.77E-02	1.89	5.54E-01	1.44	sterile alpha motif domain containing 14
219743_at	23493	<i>HEY2</i>	5.53E-02	1.82	1.12E-01	1.49	hes-related family bHLH transcription factor with YRPW motif 2
1554744_at	114769	<i>CARD16</i>	2.64E-02	1.79	3.97E-01	1.24	caspase recruitment domain family, member 16
1560253_at	56956	<i>LHX9</i>	8.92E-02	1.79	1.87E-01	1.57	LIM homeobox 9
214842_s_at	213	<i>ALB</i>	4.74E-02	1.76	3.84E-01	1.21	albumin
208108_s_at	554	<i>AVPR2</i>	4.26E-02	1.65	1.08E-01	1.42	arginine vasopressin receptor 2
211682_x_at	54490	<i>UGT2B28</i>	4.95E-02	1.59	2.50E-01	1.31	UDP glucuronosyltransferase 2 family, polypeptide B28
207978_s_at	8013	<i>NR4A3</i>	1.34E-01	9.20	2.44E-02	15.07	nuclear receptor subfamily 4, group A, member 3
204621_s_at	4929	<i>NR4A2</i>	2.40E-01	2.76	1.48E-02	6.59	nuclear receptor subfamily 4, group A, member 2
218541_s_at	56892	<i>C8orf4</i>	2.21E-01	4.25	6.66E-02	6.13	chromosome 8 open reading frame 4
205289_at	650	<i>BMP2</i>	1.57E-01	4.46	5.18E-02	5.97	bone morphogenetic protein 2
204622_x_at	4929	<i>NR4A2</i>	1.01E-01	2.90	5.40E-03	5.72	nuclear receptor subfamily 4, group A, member 2
209720_s_at	6317	<i>SERPINB3</i>	1.16E-01	4.82	4.74E-02	5.15	serpin peptidase inhibitor, clade B (ovalbumin), member 3
203639_s_at	2263	<i>FGFR2</i>	1.78E-01	3.06	9.70E-03	5.09	fibroblast growth factor receptor 2
211550_at	1956	<i>EGFR</i>	1.08E-01	5.72	8.15E-02	4.56	epidermal growth factor receptor
220393_at	51557	<i>LGSN</i>	2.82E-01	2.92	8.56E-02	4.15	lensin, lens protein with glutamine synthetase domain
1569262_x_at	90025	<i>UBE3D</i>	4.19E-01	2.22	6.63E-02	3.35	ubiquitin protein ligase E3D
224215_s_at	28514	<i>DLL1</i>	3.75E-01	1.62	5.10E-02	3.03	delta-like 1 (Drosophila)
239123_at	8848	<i>TSC22D1</i>	1.63E-01	1.41	1.70E-03	2.73	TSC22 domain family, member 1
232361_s_at	26298	<i>EHF</i>	2.80E-01	2.38	9.35E-02	2.72	ets homologous factor
232470_at	102724428	<i>LOC102724428</i>	4.21E-01	1.47	1.09E-02	2.56	serine/threonine-protein kinase SIK1
232265_at	222255	<i>ATXN7L1</i>	7.53E-01	1.28	8.72E-02	2.46	salt-inducible kinase 1
235066_at	4134	<i>MAP4</i>	1.56E-01	2.25	5.77E-02	2.46	microtubule associated protein 4
205206_at	3730	<i>ANOS1</i>	1.05E-01	2.07	1.95E-02	2.43	anosmin 1
225801_at	114907	<i>FBXO32</i>	1.54E-01	2.34	9.44E-02	2.33	F-box protein 32
218723_s_at	28984	<i>RGCC</i>	1.48E-01	1.92	4.00E-02	2.32	regulator of cell cycle
230865_at	167410	<i>LIX1</i>	3.88E-01	1.42	1.77E-02	2.29	limb and CNS expressed 1
205207_at	3569	<i>IL6</i>	5.18E-01	1.50	5.41E-02	2.22	interleukin 6
244025_at	85450	<i>ITPR1</i>	1.06E-01	1.62	4.80E-03	2.21	inositol 1,4,5-trisphosphate receptor interacting protein
208153_s_at	2196	<i>FAT2</i>	2.89E-01	1.84	7.74E-02	2.20	FAT atypical cadherin 2
212856_at	23151	<i>GRAMD4</i>	2.62E-01	1.66	3.33E-02	2.18	GRAM domain containing 4
240362_at	51660	<i>MPC1</i>	1.56E-01	1.66	2.29E-02	2.15	mitochondrial pyruvate carrier 1
244403_at	23418	<i>CRB1</i>	5.66E-01	1.47	6.84E-02	2.14	crumbs family member 1, photoreceptor morphogenesis associated
240709_at	23544	<i>SEZ6L</i>	3.47E-01	1.32	6.70E-03	2.05	seizure related 6 homolog (mouse)-like
225582_at	85450	<i>ITPR1</i>	1.05E-01	1.58	7.20E-03	1.97	inositol 1,4,5-trisphosphate receptor interacting protein
206633_at	1134	<i>CHRNA1</i>	1.77E-01	1.65	8.61E-02	1.95	cholinergic receptor, nicotinic alpha 1
209612_s_at	125	<i>ADH1B</i>	1.46E-01	1.64	3.16E-02	1.94	alcohol dehydrogenase 1B (class I), beta polypeptide
207526_s_at	9173	<i>IL1RL1</i>	2.94E-01	1.62	7.50E-02	1.93	interleukin 1 receptor-like 1
237956_s_at	133874	<i>Csorf58</i>	2.11E-01	1.76	7.23E-02	1.92	chromosome 5 open reading frame 58
203394_s_at	3280	<i>HES1</i>	1.17E-01	1.25	2.00E-03	1.91	hes family bHLH transcription factor 1
201645_at	3371	<i>TNC</i>	1.73E-01	2.08	6.49E-02	1.91	tenascin C
227697_at	9021	<i>SOC3</i>	1.31E-01	1.91	4.35E-02	1.91	suppressor of cytokine signaling 3
227188_at	59271	<i>EVA1C</i>	1.15E-01	1.60	1.74E-02	1.91	eva-1 homolog C (C. elegans)
209613_s_at	125	<i>ADH1B</i>	3.31E-01	1.44	3.56E-02	1.90	alcohol dehydrogenase 1B (class I), beta polypeptide
209631_s_at	2861	<i>GPR37</i>	2.95E-01	1.45	5.08E-02	1.87	G protein-coupled receptor 37 (endothelin receptor type B-like)
201044_x_at	1843	<i>DUSP1</i>	1.14E-01	1.45	6.00E-03	1.85	dual specificity phosphatase 1
219195_at	10891	<i>PPARGCIA</i>	5.04E-02	1.42	4.40E-03	1.84	peroxisome proliferator-activated receptor gamma, coactivator 1 alpha
223816_at	57864	<i>SLC46A2</i>	4.93E-01	1.33	7.11E-02	1.83	solute carrier family 46, member 2
1565602_at	5101	<i>PCDH9</i>	1.24E-01	1.68	8.61E-02	1.83	protocadherin 9
204882_at	9938	<i>ARHGAP25</i>	3.14E-01	1.45	6.30E-02	1.82	Rho GTPase activating protein 25
201739_at	6446	<i>SGK1</i>	1.20E-01	1.53	1.77E-02	1.82	serum/glucocorticoid regulated kinase 1
203395_s_at	3280	<i>HES1</i>	1.41E-01	1.40	7.80E-03	1.81	hes family bHLH transcription factor 1
204463_s_at	1909	<i>EDNRA</i>	2.41E-01	1.79	8.97E-02	1.81	endothelin receptor type A
215815_at	8896	<i>BUD31</i>	1.77E-01	1.48	4.20E-02	1.80	BUD31 homolog
205920_at	6533	<i>SLC6A6</i>	5.72E-01	1.29	8.97E-02	1.80	solute carrier family 6 (neurotransmitter transporter), member 6
209189_at	2353	<i>FOS</i>	1.77E-01	1.60	3.10E-02	1.80	FBJ murine osteosarcoma viral oncogene homolog
236539_at	26191	<i>PTPN22</i>	8.47E-02	1.45	7.80E-03	1.78	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)
222450_at	56937	<i>PM2EP1</i>	4.25E-02	1.44	4.90E-03	1.78	prostate transmembrane protein, androgen induced 1
233968_at	140880	<i>CST11</i>	5.56E-01	1.21	1.93E-02	1.76	cytostatin 11
204684_at	4884	<i>NPTX1</i>	1.35E-01	1.70	2.64E-02	1.76	neuronal pentraxin I
244435_at	642938	<i>FAM196A</i>	5.93E-01	1.47	8.83E-02	1.75	family with sequence similarity 196, member A
235887_at	3090	<i>HIC1</i>	1.21E-01	1.35	3.60E-03	1.75	hypermethylated in cancer 1
212230_at	8613	<i>PLPP3</i>	3.63E-02	1.47	2.90E-03	1.74	phospholipid phosphatase 3
211828_s_at	23043	<i>TNIK</i>	1.27E-01	1.76	4.92E-02	1.74	TRAF2 and NCK interacting kinase
214725_at	157869	<i>SBSPON</i>	8.65E-01	1.16	6.07E-02	1.73	somatomedin B and thrombospondin type 1 domain containing
215111_s_at	8848	<i>TSC22D1</i>	5.20E-03	1.49	4.00E-04	1.72	TSC22 domain family, member 1
205992_s_at	3600	<i>IL15</i>	1.49E-01	1.45	1.83E-02	1.72	interleukin 15
205990_s_at	7474	<i>WNT5A</i>	8.52E-02	1.43	8.60E-03	1.72	wingless-type MMTV integration site family, member 5A
203973_s_at	1052	<i>CEBPD</i>	2.33E-02	1.49	2.30E-03	1.71	CCAAT/enhancer binding protein (C/EBP), delta
227900_at	868	<i>CSBL</i>	2.85E-01	1.42	4.20E-02	1.71	Cbl proto-oncogene B, E3 ubiquitin protein ligase
224797_at	57561	<i>ARRDC3</i>	5.04E-01	1.26	3.17E-02	1.71	arrestin domain containing 3
217371_s_at	3600	<i>IL15</i>	2.76E-01	1.46	2.77E-02	1.70	interleukin 15
201982_s_at	5069	<i>PAPPA</i>	4.29E-01	1.21	3.44E-02	1.70	pregnancy-associated plasma protein A, pappalysin 1
214641_at	1285	<i>COL4A3</i>	3.87E-02	1.49	4.60E-03	1.69	collagen, type IV, alpha 3 (Goodpasture antigen)
213596_at	837	<i>CASP4</i>	1.97E-01	1.33	1.05E-02	1.69	caspase 4
204619_s_at	1462	<i>VCAN</i>	1.66E-01	1.49	4.54E-02	1.68	versican
242153_at	55132	<i>LARP1B</i>	4.51E-01	1.42	4.81E-02	1.67	La ribonucleoprotein domain family, member 1B
205559_s_at	5125	<i>CSK5</i>	1.21E-01	1.49	3.06E-02	1.66	proprotein convertase subtilisin/kexin type 5
204908_s_at	602	<i>BCL3</i>	2.53E-01	1.43	3.73E-02	1.66	B-cell CLL/lymphoma 3
208234_x_at	2263	<i>FGFR2</i>	3.10E-01	1.46	6.93E-02	1.65	fibroblast growth factor receptor 2
200733_s_at	7803	<i>PTP4A1</i>	2.47E-01	1.42	3.72E-02	1.65	protein tyrosine phosphatase type IVA, member 1
235916_at	219539	<i>YPEL4</i>	1.34E-01	1.34	1.24E-02	1.65	yippee like 4
238987_at	2683	<i>B4GALT1</i>	6.57E-01	1.29	3.27E-02	1.64	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1
231325_at	137970	<i>UNC5D</i>	4.60E-01	1.21	9.37E-02	1.64	unc-5 netrin receptor D
213221_s_at	23235	<i>SIK2</i>	5.87E-02	1.48	9.40E-03	1.63	salt-inducible kinase 2
227032_at	5362	<i>PLXNA2</i>	1.71E-02	1.47	3.10E-03	1.63	pelin A2
219316_s_at	55640	<i>FLVCR2</i>	1.75E-02	1.36	1.60E-03	1.63	feline leukemia virus subgroup C cellular receptor family, member 2
225842_at	22822	<i>PHLDA1</i>	2.33E-01	1.41	2.41E-02	1.62	pleckstrin homology-like domain, family A, member 1

223058_at	83641	FAM107B	8.60E-03	1.48	1.60E-03	1.61	family with sequence similarity 107, member B
225688_s_at	90102	PHLDB2	6.85E-02	1.48	8.50E-03	1.61	pleckstrin homology-like domain, family B, member 2
226158_at	54800	KLHL24	2.85E-01	1.44	6.43E-02	1.61	kelch-like family member 24
228340_at	7090	TLE3	2.41E-02	1.44	3.90E-03	1.61	transducin-like enhancer of split 3
205792_at	8839	WISP2	7.85E-02	1.43	1.38E-02	1.61	WNT1 inducible signaling pathway protein 2
211143_x_at	3164	NR4A1	6.35E-01	1.28	9.99E-02	1.61	nuclear receptor subfamily 4, group A, member 1
224325_at	8325	FZD8	7.36E-02	1.42	1.78E-02	1.60	frizzled class receptor 8
226034_at	1846	DUSP4	1.39E-01	1.41	9.70E-03	1.60	dual specificity phosphatase 4
220225_at	50805	IRX4	2.17E-01	1.34	2.74E-02	1.60	iroquois homeobox 4
230472_at	79192	IRX1	4.99E-01	1.21	2.45E-02	1.60	iroquois homeobox 1
216604_s_at	23428	SLC7A8	6.12E-01	1.14	3.40E-03	1.60	solute carrier family 7 (amino acid transporter light chain, L system), member 8
205225_at	2099	ESR1	1.32E-01	1.56	5.03E-02	1.60	estrogen receptor 1
205083_at	316	AOX1	1.83E-01	1.49	8.15E-02	1.59	aldehyde oxidase 1
219256_s_at	54436	SH3TC1	2.15E-01	1.38	2.79E-02	1.59	SH3 domain and tetratricopeptide repeats 1
238825_at	93953	ACRC	7.81E-02	1.37	8.10E-03	1.59	acidic repeat containing
219564_at	3773	KCNJ16	5.86E-01	1.15	9.76E-02	1.59	potassium channel, inwardly rectifying subfamily J, member 16
228082_at	79827	CLMP	1.83E-01	1.51	7.24E-02	1.59	CXADR-like membrane protein
204014_at	1846	DUSP4	2.13E-01	1.45	3.24E-02	1.58	dual specificity phosphatase 4
209681_at	10560	SLC19A2	2.44E-01	1.45	2.26E-02	1.58	solute carrier family 19 (thiamine transporter), member 2
231964_at	636	BICD1	9.00E-03	1.41	1.70E-03	1.58	bicaudal D homolog 1 (Drosophila)
242443_at	79882	ZC3H14	5.48E-02	1.36	8.50E-03	1.58	zinc finger CCCH-type containing 14
203795_s_at	605	BCL7A	1.48E-01	1.35	6.80E-03	1.58	B-cell CLL/lymphoma 7A
209774_x_at	2920	CKL2	4.33E-01	1.28	9.97E-02	1.58	chemokine (C-X-C motif) ligand 2
211571_s_at	1462	VCAN	1.02E-01	1.69	5.38E-02	1.58	versican
201195_s_at	8140	SLC7A5	1.20E-03	1.47	3.00E-04	1.57	solute carrier family 7 (amino acid transporter light chain, L system), member 5
202965_s_at	827	CAPN6	3.24E-02	1.47	1.26E-02	1.56	calpain 6
206011_at	834	CASP1	3.57E-02	1.45	9.20E-03	1.56	caspase 1
1566678_at	4313	MMP2	1.03E-01	1.45	3.18E-02	1.56	matrix metalloproteinase 2
244506_at	83857	TMTC1	4.41E-02	1.45	1.30E-02	1.56	transmembrane and tetratricopeptide repeat containing 1
241986_at	168667	BMPER	6.74E-01	1.22	9.36E-02	1.56	BMP binding endothelial regulator
205239_at	374	AREG	2.73E-01	1.52	7.74E-02	1.56	amphiregulin
225606_at	10018	BCL2L11	8.63E-02	1.32	6.60E-03	1.55	BCL2-like 11 (apoptosis facilitator)
212769_at	7090	TLE3	1.92E-01	1.32	3.33E-02	1.55	transducin-like enhancer of split 3
201418_s_at	6659	SOX4	7.13E-02	1.29	5.20E-03	1.55	SRY box 4
239178_at	2254	FGF9	2.39E-01	1.45	4.15E-02	1.54	fibroblast growth factor 9
220603_s_at	55784	MCTP2	2.79E-02	1.40	3.50E-03	1.54	multiple C2 domains, transmembrane 2
226559_at	389792	IER5L	2.39E-01	1.32	2.17E-02	1.54	immediate early response 5-like
204602_at	22943	DKK1	3.88E-02	1.49	1.42E-02	1.53	dickkopf WNT signaling pathway inhibitor 1
209102_s_at	26959	HBP1	5.00E-04	1.48	2.00E-04	1.53	HMG-box transcription factor 1
234008_s_at	23491	CE53	4.67E-02	1.47	2.60E-02	1.53	carboxylesterase 3
206382_s_at	627	BDNF	1.59E-01	1.46	1.79E-02	1.53	brain-derived neurotrophic factor
230383_x_at	162394	FN5	8.50E-03	1.45	2.10E-03	1.53	schlafen family member 5
206871_at	1991	ELANE	4.85E-01	1.32	9.75E-02	1.53	elastase, neutrophil expressed
225645_at	26298	EHF	4.00E-01	1.22	7.79E-02	1.53	ets homologous factor
213228_at	8622	PDE8B	3.30E-03	1.49	2.90E-03	1.52	phosphodiesterase 8B
222835_at	79875	THSD4	8.70E-03	1.45	2.90E-03	1.52	thrombospondin type 1 domain containing 4
223605_at	83733	SLC25A18	9.60E-02	1.39	3.02E-02	1.52	solute carrier family 25 (glutamate carrier), member 18
220025_at	10716	TBR1	2.76E-01	1.39	5.45E-02	1.52	T-box, brain, 1
212298_at	8829	NRP1	1.51E-01	1.37	2.41E-02	1.52	neuropilin 1
208072_s_at	8527	DGKD	9.71E-02	1.34	1.34E-02	1.52	diacylglycerol kinase, delta 130kDa
239367_at	627	BDNF	1.71E-01	1.33	1.38E-02	1.52	brain-derived neurotrophic factor
202701_at	649	BMP1	1.82E-02	1.32	1.20E-03	1.52	bone morphogenetic protein 1
227443_at	286343	LURAP1L	7.07E-02	1.32	5.40E-03	1.52	leucine rich adaptor protein 1-like
201703_s_at	5514	PPP1R10	2.41E-02	1.32	1.70E-03	1.52	protein phosphatase 1, regulatory subunit 10
221234_s_at	60468	BACH2	5.33E-01	1.30	7.36E-02	1.52	BTB and CNC homology 1, basic leucine zipper transcription factor 2
228451_at	100128071	FAM229A	4.50E-02	1.49	2.39E-02	1.51	family with sequence similarity 229, member A
212258_s_at	6595	SMARCA2	1.34E-01	1.49	8.56E-02	1.51	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, 2
207327_at	2070	EYA4	1.03E-02	1.46	4.40E-03	1.51	EYA transcriptional coactivator and phosphatase 4
223059_s_at	83641	FAM107B	2.81E-02	1.45	6.20E-03	1.51	family with sequence similarity 107, member B
238445_x_at	146664	MGAT5B	7.25E-02	1.42	1.74E-02	1.51	mannosyl (alpha-1,6)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase, isozyme B
203077_s_at	4087	SMAD2	9.01E-02	1.41	1.08E-02	1.51	SMAD family member 2
226438_at	6641	SNR1	2.18E-02	1.41	5.80E-03	1.51	syn trophin, beta 1 (dystrophin-associated protein A1, 59kDa, basic component 1)
202023_at	1942	EFNA1	7.04E-02	1.36	9.20E-03	1.51	ephrin-A1
228269_x_at	30818	KCNIP3	9.68E-02	1.30	1.09E-02	1.51	Kv channel interacting protein 3, calsenilin
208168_s_at	1118	CHIT1	5.67E-01	1.18	8.68E-02	1.51	chitinase 1 (chitotrioidase)
216235_s_at	1909	EDNRA	1.29E-01	1.47	7.87E-02	1.50	endothelin receptor type A
202304_at	22862	FNDC3A	2.37E-01	1.40	5.30E-02	1.50	fibronectin type III domain containing 3A
223315_at	59277	NTN4	2.35E-01	1.39	5.90E-02	1.50	netrin 4
223660_at	140	ADORA3	6.67E-01	1.11	2.01E-02	1.50	adenosine A3 receptor
205883_at	57413	TMIGD3	2.37E-01	1.40	5.30E-02	1.50	transmembrane and immunoglobulin domain containing 3
	7704	ZBTB16	1.13E-02	1.35	1.60E-03	1.50	zinc finger and BTB domain containing 16

Treatment (18h)
 Ind: 9 Probe Sets (9 Genes)
 Ind+GSK: 21 Probe Sets (18 Genes)



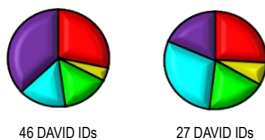
Affy Probe Set ID	Entrez Gene ID	Official Gene Symbol	FDR P-Value	Fold change	FDR P-Value	Fold change	UniGene Name	Function
237328_at	55195	C14orf105	9.76E-02	3.27	5.85E-02	3.50	chromosome 14 open reading frame 105	
220006_at	79825	EFCC1	4.21E-02	1.98	3.82E-02	1.98	EF-hand and coiled-coil domain containing 1	
237222_at	123722	FSD2	9.76E-02	1.85	6.45E-02	1.79	fibronectin type III and SPRY domain containing 2	
208335_s_at	2532	ACKR1	3.93E-02	1.59	2.00E-03	1.98	atypical chemokine receptor 1 (Duffy blood group)	
220227_at	1002	CDH4	3.67E-02	1.55	2.60E-03	1.76	cadherin 4, type 1, R-cadherin (retinal)	
220335_x_at	23491	CE53	3.53E-02	1.53	2.60E-03	1.63	carboxylesterase 3	
1556420_s_at	388403	YPPEL2	4.21E-02	2.24	1.04E-01	1.82	yppee like 2	
216639_at	27286	SRPX2	7.81E-02	2.02	2.33E-01	1.43	sushi-repeat containing protein, X-linked 2	
1554202_x_at	57010	CABP4	9.76E-02	1.54	4.41E-01	1.15	calcium binding protein 4	
222784_at	64093	SMOC1	3.19E-01	2.08	5.85E-02	2.91	SPARC related modular calcium binding 1	
222783_s_at	64093	SMOC1	3.51E-01	2.05	8.71E-02	2.46	SPARC related modular calcium binding 1	
225207_at	5166	PKDK	3.81E-01	1.71	5.85E-02	2.45	pyruvate dehydrogenase kinase, isozyme 4	
224942_at	5069	PAPPA	4.02E-01	1.61	6.94E-02	2.29	pregnancy-associated plasma protein A, pappalysin 1	
1552932_at	171389	NLRP6	2.84E-01	1.64	5.85E-02	2.00	NLR family, pyrin domain containing 6	
203548_s_at	4023	LPL	3.73E-01	1.51	7.60E-02	1.91	lipoprotein lipase	
221541_at	83716	CRISPLD2	2.61E-01	1.59	4.84E-02	1.85	cysteine-rich secretory protein LCCL domain containing 2	
201981_at	5069	PAPPA	3.81E-01	1.52	7.55E-02	1.82	pregnancy-associated plasma protein A, pappalysin 1	
201508_at	3487	IGFBP4	2.84E-01	1.53	5.85E-02	1.78	insulin like growth factor binding protein 4	
209016_s_at	3855	KRT7	3.51E-01	1.27	4.84E-02	1.75	keratin 7, type II	
206866_at	1002	CDH4	3.93E-02	1.49	2.60E-03	1.72	cadherin 4, type 1, R-cadherin (retinal)	
210102_at	4013	VWASA	4.20E-01	1.21	4.58E-02	1.59	von Willebrand factor A domain containing 5A	
209772_s_at	100133941	CD24	2.14E-01	1.33	1.56E-02	1.55	CD24 molecule	
1569351_at	55084	SOBP	3.81E-01	1.24	5.85E-02	1.55	sine oculis binding protein homolog	
205542_at	26872	STEAP1	1.86E-01	1.38	4.10E-02	1.53	six transmembrane epithelial antigen of the prostate 1	

*N.B. Some genes are recognised by more than one probe set and some probe sets recognise more than one gene.

Supplemental TABLE 3. Transcripts repressed by indacaterol and Ind+GSK in BEAS-2B cells. Genes, by probe set, are listed in decreasing order of repression after exposure of cells to indacaterol (10nM) and Ind+GSK (both 10nM) for 1, 2, 6 and 18h. Unshaded rows list transcripts that were significantly (FDR <10%) repressed (<0.67-fold) by both treatments. Rows shaded grey highlight additional transcripts that were repressed by indacaterol but not by Ind+GSK; rows shaded green highlight additional transcripts that were repressed by Ind+GSK but not by indacaterol. All genes were manually assigned a colour that corresponds to one of six generic descriptors. Transcripts that lacked annotation were classified as *not assigned* (purple) and were excluded from all analyses. Pie charts at each time-point depict the number of indacaterol- and Ind+GSK-repressed genes within each generic descriptor expressed as a fraction of the total number of significant gene expression changes.

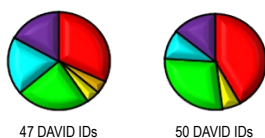
GO Term	
Transcriptional Regulators	Red
Transporters, Ion Channels and Membrane Receptors	Orange
Metabolic Proteins	Yellow
General Signalling Molecules, including Translational Regulators	Green
Other Functions	Cyan
Not Assigned	Purple
Pseudogene	White

Treatment (1h)
Ind: 39 Probe Sets (46 Genes)
Ind+GSK: 30 Probe Sets (27 Genes)



Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value	Fold change	FDR P-Value	Fold change	UniGene Name	Function
236862_at	57120	GOPC	7.67E-02	0.44	6.53E-02	0.41	golgi-associated PDZ and coiled-coil motif containing	Red
237943_at	23023	TMCC1	1.26E-02	0.49	1.71E-02	0.51	transmembrane and coiled-coil domain family 1	Orange
237469_at	7153	TOP2A	7.00E-03	0.50	1.69E-02	0.47	topoisomerase (DNA) II alpha	Yellow
218657_at	51195	RARGFFL1	8.58E-02	0.51	9.83E-02	0.55	Rap guanine nucleotide exchange factor like 1	Green
1558124_at	134492	NUDCD2	5.91E-02	0.53	8.85E-02	0.56	NudC domain containing 2	Cyan
244427_at	9493	KIF23	6.70E-03	0.55	1.38E-02	0.58	kinesin family member 23	Red
201693_s_at	1958	EGR1	7.00E-03	0.56	2.40E-03	0.49	early growth response 1	Orange
236841_at	100287171	WASHC1	3.27E-02	0.57	7.96E-02	0.63	WAS protein family homolog 1	Yellow
201009_s_at	10628	TXNIP	1.02E-02	0.60	5.70E-03	0.57	thioredoxin interacting protein	Green
228455_at	64783	RBM15	3.95E-02	0.61	3.87E-02	0.58	RNA binding motif protein 15	Cyan
242922_at	408050	NODAL3	7.19E-02	0.63	9.64E-02	0.63	NODAL modulator 3	Red
201008_s_at	10628	TXNIP	2.90E-03	0.64	1.10E-03	0.59	thioredoxin interacting protein	Orange
1565703_at	4089	SMAD4	6.24E-02	0.65	9.06E-02	0.66	SMAD family member 4	Yellow
201466_s_at	3725	JUN	3.80E-02	0.65	2.57E-02	0.61	jun proto-oncogene	Green
201694_s_at	1958	EGR1	1.17E-02	0.66	8.30E-03	0.63	early growth response 1	Cyan
219545_at	65987	KCTD14	8.43E-02	0.66	5.12E-02	0.62	potassium channel tetramerization domain containing 14	Red
	100532726	NDUFC2-KCTD14					NDUFC2-KCTD14 readthrough	Orange
210919_at	23239	PHLP1	7.23E-02	0.15	7.78E-01	0.73	PH domain and leucine rich repeat protein phosphatase 1	Yellow
1569262_x_at	90025	UBE3D	5.12E-02	0.19	2.42E-01	0.39	ubiquitin protein ligase E3D	Green
236811_at	63946	DMRTC2	9.40E-02	0.41	9.53E-01	1.03	DMRT-like family C2	Cyan
1557852_at	1912	PHC2	7.80E-03	0.51	1.71E-01	0.71	polyhomeotic homolog 2 (Drosophila)	Red
1561720_at	9400	RECCO5	5.67E-02	0.55	2.80E-01	0.77	RecQ helicase-like 5	Orange
220084_at	55195	CCDC198	5.65E-02	0.58	2.90E-01	0.72	coiled-Coil Domain Containing 198	Yellow
239194_at	84277	DNAJC30	9.91E-02	0.58	2.37E-01	0.71	DnaJ (Hsp40) homolog, subfamily C, member 30	Green
214918_at	4670	HNRNPM	8.11E-02	0.60	1.22E-01	0.65	heterogeneous nuclear ribonucleoprotein M	Cyan
240452_at	2935	GSPT1	5.04E-02	0.60	1.02E-01	0.68	G1 to S phase transition 1	Red
230998_at	11335	CBX3	9.92E-02	0.61	1.36E-01	0.65	chromobox homolog 3	Orange
231292_at	493861	EID3	9.51E-02	0.61	2.53E-01	0.79	EP300 interacting inhibitor of differentiation 3	Green
228393_s_at	55900	ZNF302	4.43E-02	0.61	1.56E-01	0.74	zinc finger protein 302	Cyan
	55672	NBPF1					neuroblastoma breakpoint family member 1	Red
	728841	NBPF8					neuroblastoma breakpoint family, member 8	Orange
	400818	NBPF9					neuroblastoma breakpoint family, member 9	Yellow
	100132406	NBPF10					neuroblastoma breakpoint family, member 10	Green
	200030	NBPF11					neuroblastoma breakpoint family, member 11	Cyan
1569519_at	149013	NBPF12	8.16E-02	0.63	6.80E-01	0.13	neuroblastoma breakpoint family, member 12	Red
	25832	NBPF14					neuroblastoma breakpoint family, member 14	Orange
	101060226	NBPF19					neuroblastoma breakpoint family, member 19	Yellow
	101060684	NBPF26					neuroblastoma breakpoint family, member 26	Green
	100996763	LOC100996763					notch Homolog 2 N-Terminal-Like Protein	Cyan
	102724250	LOC102724250					neuroblastoma breakpoint family member 1	Red
1570173_at	25896	INTS7	3.50E-02	0.63	1.02E-01	0.72	integrator complex subunit 7	Orange
242111_at	56339	METTL3	3.50E-03	0.63	3.87E-02	0.73	methyltransferase like 3	Yellow
1561965_at	6629	SNRPB2	2.30E-02	0.63	2.60E-01	0.81	small nuclear ribonucleoprotein polypeptide B	Green
229423_at	1111	CHEK1	9.47E-02	0.64	1.02E-01	0.67	checkpoint kinase 1	Cyan
1559993_at	81855	SFXN3	8.94E-02	0.65	1.88E-01	0.69	sideroflexin 3	Red
232055_at	94081	SFXN1	8.11E-02	0.65	1.40E-01	0.64	sideroflexin 1	Orange
239044_at	81533	ITFG1	2.20E-03	0.65	6.24E-02	0.79	integrin alpha FG-GAP repeat containing 1	Yellow
239071_at	5928	RBBP4	7.29E-02	0.66	2.48E-01	0.79	retinoblastoma binding protein 4	Green
206683_at	7718	ZNF165	9.17E-02	0.66	1.36E-01	0.70	zinc finger protein 165	Cyan
155349_at	196528	ARID2	9.47E-02	0.67	1.32E-01	0.69	AT rich interactive domain 2 (ARID, RFX-like)	Red
1555210_at	56986	DTWD1	5.24E-01	0.79	8.59E-02	0.46	DTW domain containing 1	Orange
1552321_a_at	85478	CCDC65	8.99E-01	0.91	8.29E-02	0.47	coiled-coil domain containing 65	Yellow
242261_at	3658	IREB2	1.81E-01	0.54	9.74E-02	0.50	iron responsive element binding protein 2	Green
240551_at	84878	ZBTB45	2.75E-01	0.66	8.59E-02	0.52	zinc finger and BTB domain containing 45	Cyan
243361_at	140890	SREK1	3.87E-01	0.75	8.59E-02	0.53	splicing regulatory glutamine/lysine-rich protein 1	Red
1562775_at	83594	NUDT12	1.90E-01	0.71	5.61E-02	0.57	nudix hydrolase 12	Orange
219389_at	55061	SUSD4	9.28E-01	1.05	9.70E-02	0.58	sushi domain containing 4	Yellow
227404_s_at	1958	EGR1	8.16E-02	0.68	3.25E-02	0.60	early growth response 1	Green
214978_s_at	8497	PPPIA4	1.34E-01	0.69	2.29E-02	0.60	PTPRF interacting protein alpha 4	Cyan
239286_at	1009	CDH11	8.98E-01	1.05	7.68E-02	0.63	cadherin 11, type 2, OB-cadherin (osteoblast)	Red
214477_at	4298	MLLT1	2.78E-01	0.72	7.83E-02	0.63	myeloid/lymphoid or mixed-lineage leukemia; translocated to, 1	Orange
201010_s_at	10628	TXNIP	3.10E-03	0.68	1.10E-03	0.64	thioredoxin interacting protein	Yellow
230444_at	5150	PDE7A	1.96E-01	0.78	2.91E-02	0.66	phosphodiesterase 7A	Green
235476_at	286827	TRIM59	7.19E-02	0.75	3.66E-02	0.67	tripartite motif containing 59	Cyan

Treatment (2h)
Ind: 51 Probe Sets (47 Genes)
Ind+GSK: 59 Probe Sets (50 Genes)



Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value	Fold change	FDR P-Value	Fold change	UniGene Name	Function
232328_at	79818	ZNF552	1.70E-03	0.22	3.50E-03	0.25	zinc finger protein 552	Red
227404_s_at	1958	EGR1	7.00E-04	0.38	3.00E-04	0.32	early growth response 1	Orange
201009_s_at	10628	TXNIP	7.00E-04	0.40	3.00E-04	0.34	thioredoxin interacting protein	Yellow
201694_s_at	1958	EGR1	3.00E-04	0.40	2.00E-04	0.34	early growth response 1	Green
201008_s_at	10628	TXNIP	3.00E-04	0.42	1.00E-04	0.36	thioredoxin interacting protein	Cyan
1556300_s_at	6492	SIM1	2.20E-03	0.42	6.90E-03	0.46	single-minded family bHLH transcription factor 1	Red
201010_s_at	10628	TXNIP	3.00E-04	0.45	1.00E-04	0.38	thioredoxin interacting protein	Orange
206876_at	6492	SIM1	5.20E-03	0.45	5.60E-03	0.46	single-minded family bHLH transcription factor 1	Yellow
237469_at	7153	TOP2A	2.00E-04	0.46	4.00E-04	0.51	topoisomerase (DNA) II alpha	Green
244427_at	9493	KIF23	1.50E-03	0.48	7.50E-03	0.56	kinesin family member 23	Cyan
215508_at	699	BUB1	7.38E-02	0.54	5.07E-02	0.55	BUB1 mitotic checkpoint serine/threonine kinase	Red
204826_at	899	CCNF	3.40E-03	0.54	4.10E-03	0.54	cyclin F	Orange

240432_x_at	8609	<i>KLF7</i>	1.02E-02	0.54	5.65E-02	0.65	Kruppel-like factor 7 (ubiquitous)	
1553883_at	7652	<i>ZNF99</i>	4.47E-02	0.55	4.77E-02	0.55	zinc finger protein 99	
201693_s_at	1958	<i>EGR1</i>	1.95E-02	0.55	2.91E-02	0.58	early growth response 1	
232735_s_at	284615	<i>ANKRD34A</i>	4.00E-03	0.56	3.60E-03	0.57	ankyrin repeat domain 34A	
208025_s_at	8091	<i>HMG2A</i>	1.30E-03	0.56	1.80E-03	0.56	high mobility group AT-hook 2	
219544_at	79866	<i>BORA</i>	2.80E-03	0.59	1.40E-03	0.54	bora, aurora kinase A activator	
227687_at	219844	<i>HVLS1</i>	2.40E-03	0.61	7.00E-04	0.53	hydrolethalus syndrome 1	
201896_s_at	84722	<i>PSRC1</i>	9.00E-04	0.61	7.00E-04	0.58	proline/serine-rich coiled-coil 1	
218192_at	51447	<i>IPK2</i>	5.40E-03	0.63	5.20E-03	0.62	inositol hexakisphosphate kinase 2	
238220_at	7403	<i>KDMS6A</i>	7.53E-02	0.63	3.66E-02	0.52	lysine (K)-specific demethylase 6A	
1552546_a_at	137994	<i>LETM2</i>	2.06E-02	0.63	7.20E-03	0.58	leucine zipper-EF-hand containing transmembrane protein 2	
216061_x_at	5155	<i>PDGFB</i>	1.13E-02	0.63	1.13E-02	0.64	platelet-derived growth factor beta polypeptide	
218726_x_at	55355	<i>HJURP</i>	9.20E-03	0.65	6.90E-03	0.61	Holliday junction recognition protein	
204349_at	9443	<i>MED7</i>	3.98E-02	0.65	4.21E-02	0.64	mediator complex subunit 7	
235476_at	286827	<i>TRIM59</i>	8.20E-03	0.65	2.70E-03	0.56	tripartite motif containing 59	
225283_at	91947	<i>ARRDC4</i>	4.50E-03	0.66	1.90E-03	0.63	arrestin domain containing 4	
216345_at	23053	<i>ZSWIM8</i>	5.53E-02	0.34	6.30E-01	0.72	zinc finger, SWIM-type containing 8	
1569262_x_at	90025	<i>UBE3D</i>	6.85E-02	0.36	8.85E-01	0.77	ubiquitin protein ligase E3D	
230673_at	93035	<i>PKHD1L1</i>	9.18E-02	0.40	7.46E-01	0.69	polycystic kidney and hepatic disease 1 (autosomal recessive)-like 1	
1555591_at	80119	<i>PIF1</i>	6.70E-02	0.49	1.89E-01	0.55	PIF1 5'-to-3' DNA helicase	
216109_at	23389	<i>MED13L</i>	1.30E-02	0.51	2.28E-01	0.65	mediator complex subunit 13-like	
1566111_at	9780	<i>PIEZO1</i>	1.20E-03	0.51	8.40E-01	0.90	piezo-type mechanosensitive ion channel component 1	
206115_at	1960	<i>EGR3</i>	5.78E-02	0.52	4.95E-01	0.63	early growth response 3	
1552880_at	89866	<i>SEC16B</i>	2.49E-02	0.53	4.88E-01	0.74	SEC16 homolog B, endoplasmic reticulum export factor	
215175_at	22990	<i>PCNX</i>	1.12E-02	0.53	3.32E-01	0.74	pecanex homolog (Drosophila)	
238049_at	65983	<i>GRAMD3</i>	4.99E-02	0.55	1.03E-01	0.59	GRAM domain containing 3	
232912_at	160897	<i>GPR180</i>	8.34E-02	0.57	2.09E-01	0.64	G protein-coupled receptor 180	
220709_at	80032	<i>ZNF556</i>	7.18E-02	0.57	3.37E-01	0.66	zinc finger protein 556	
	23049	<i>NPIP84</i>	440345				nuclear pore complex interacting protein family, member B4	
	440345	<i>NPIP85</i>	440354				nuclear pore complex interacting protein family, member B5	
	440354	<i>SMG1</i>	595101				SMG1 phosphatidylinositol 3-kinase-related kinase	
	641298	<i>SMG1P1</i>	641298				SMG1 pseudogene 1	
	100132247	<i>SMG1P2</i>	641298				SMG1 pseudogene 2	
244766_at	100271836	<i>SMG1P3</i>	6.15E-02	0.57	2.30E-01	0.67	SMG1 pseudogene 3	
	100506060	<i>SMG1P5</i>					SMG1 pseudogene 5	
	101060596	<i>SMG1P7</i>					SMG1 pseudogene 7	
	105369244	<i>LOC101060596</i>					serine/threonine-protein kinase SMG1-like	
	105369244	<i>LOC105369244</i>					serine/threonine-protein kinase SMG1-like	
	105369278	<i>LOC105369278</i>					serine/threonine-protein kinase SMG1-like	
228892_at	153769	<i>SH3RF2</i>	9.78E-02	0.60	2.77E-01	0.66	SH3 domain containing ring finger 2	
207286_at	9662	<i>CEP135</i>	2.57E-02	0.61	3.51E-01	0.75	centrosomal protein 135kDa	
230462_at	8650	<i>NUMB</i>	3.38E-02	0.62	5.05E-01	0.79	numb homolog (Drosophila)	
235690_at	84622	<i>ZNF594</i>	7.49E-02	0.63	1.11E-01	0.65	zinc finger protein 594	
227801_at	286827	<i>TRIM59</i>	7.00E-03	0.64	1.89E-02	0.67	tripartite motif containing 59	
216081_at	3910	<i>LAMA4</i>	6.14E-02	0.65	4.51E-01	0.76	laminin, alpha 4	
235165_at	84612	<i>PAR6B</i>	7.48E-02	0.65	3.05E-01	0.74	par-6 family cell polarity regulator beta	
233782_at	10238	<i>DCAF7</i>	1.69E-02	0.65	6.97E-02	0.71	DDB1 and CUL4 associated factor 7	
214918_at	4670	<i>HNRNPM</i>	6.42E-02	0.66	5.74E-01	0.72	heterogeneous nuclear ribonucleoprotein M	
1552794_a at	284306	<i>ZNF547</i>	6.66E-02	0.66	5.31E-02	0.70	zinc finger protein 547	
1566449_at	57554	<i>LRRC7</i>	4.27E-01	0.48	3.17E-02	0.20	leucine rich repeat containing 7	
230808_at	2339	<i>FNIT4</i>	8.14E-01	0.88	9.90E-03	0.28	farnesyltransferase, CAAX box, alpha	
1552461_at	169966	<i>FAM46D</i>	5.30E-01	0.75	4.05E-02	0.45	family with sequence similarity 46, member D	
223185_s_at	79365	<i>BHLHE41</i>	4.39E-01	0.71	6.02E-02	0.52	basic helix-loop-helix family, member e41	
213894_at	221981	<i>THSD7A</i>	5.07E-01	0.76	8.86E-02	0.54	thrombospondin type 1 domain containing 7A	
228827_at	862	<i>RUNX1T1</i>	4.84E-01	0.73	7.65E-02	0.56	RUNX1 Translocation Partner 1	
208893_s_at	1848	<i>DUSP6</i>	3.06E-02	0.67	9.90E-03	0.59	dual specificity phosphatase 6	
214639_s_at	3198	<i>HOXA1</i>	1.41E-01	0.71	2.49E-02	0.59	homeobox A1	
216727_at	11329	<i>STK38</i>	2.49E-01	0.67	9.82E-02	0.61	serine/threonine kinase 38	
204827_s_at	899	<i>CCNF</i>	7.86E-02	0.68	3.51E-02	0.61	cyclin F	
225687_at	81610	<i>FAM83D</i>	3.20E-03	0.69	7.00E-04	0.62	family with sequence similarity 83, member D	
232254_s_at	55632	<i>GZE3</i>	1.82E-01	0.70	6.22E-02	0.62	G2/M-phase specific E3 ubiquitin protein ligase	
1570364_at	163051	<i>ZNF709</i>	9.90E-01	-0.96	9.42E-02	0.63	zinc finger protein 709	
230468_s_at	54964	<i>C1orf56</i>	7.04E-01	0.88	6.58E-02	0.63	chromosome 1 open reading frame 56	
204962_s_at	1058	<i>CENPA</i>	3.20E-03	0.68	1.70E-03	0.63	centromere protein A	
201466_s_at	3725	<i>JUN</i>	1.17E-01	0.69	7.08E-02	0.63	jun proto-oncogene	
225346_at	80298	<i>MTERF2</i>	4.80E-02	0.68	1.67E-02	0.63	mitochondrial transcription termination factor 2	
232745_x_at	79925	<i>SPEF2</i>	5.93E-01	0.75	9.63E-02	0.64	sperm flagellar 2	
236550_s_at	282890	<i>ZNF311</i>	4.17E-01	0.75	6.40E-02	0.64	zinc finger protein 311	
216468_s_at	91120	<i>ZNF682</i>	1.38E-01	0.68	6.97E-02	0.64	zinc finger protein 682	
204092_s_at	6790	<i>AURKA</i>	5.10E-03	0.67	2.20E-03	0.64	aurora kinase A	
219635_at	80095	<i>ZNF606</i>	4.00E-01	0.79	6.40E-02	0.65	zinc finger protein 606	
208079_s_at	6790	<i>AURKA</i>	7.00E-03	0.70	3.50E-03	0.65	aurora kinase A	
203378_at	51585	<i>PCF11</i>	5.26E-02	0.75	8.10E-03	0.65	PCF11 cleavage and polyadenylation factor subunit	
221520_s_at	55143	<i>CDC48</i>	2.20E-02	0.67	1.53E-02	0.66	cell division cycle associated 8	
204244_s_at	10926	<i>DBF4</i>	2.22E-02	0.71	1.07E-02	0.66	DBF4 zinc finger	
204350_s_at	9443	<i>MED7</i>	1.20E-02	0.68	6.40E-03	0.66	mediator complex subunit 7	
231950_at	26149	<i>ZNF658</i>	9.50E-02	0.68	7.08E-02	0.66	zinc finger protein 658	
226661_at	157313	<i>CDC42</i>	5.40E-03	0.72	2.30E-03	0.66	cell division cycle associated 2	
227285_at	148523	<i>CIART</i>	3.66E-01	0.76	8.59E-02	0.66	circadian associated repressor of transcription	
236957_a at	157313	<i>CDC42</i>	1.03E-01	0.76	2.26E-02	0.67	cell division cycle associated 2	

Treatment (6h)
Ind: 51 Probe Sets (45 Genes)
Ind+GSK: 102 Probe Sets (83 Genes)



45 DAVID IDs

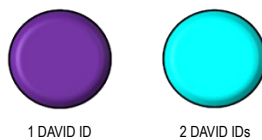


83 DAVID IDs

Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value	Fold change	FDR P-Value	Fold change	UniGene Name	Function
204823_at	89795	<i>NAV3</i>	8.00E-04	0.35	2.00E-04	0.31	neuron navigator 3	
1552658_a_at	89795	<i>NAV3</i>	7.00E-04	0.43	2.00E-04	0.38	neuron navigator 3	
217262_s_at	9620	<i>CELSR1</i>	6.07E-02	0.46	9.75E-02	0.60	cadherin, EGF LAG seven-pass G-type receptor 1	
223204_at	51313	<i>FAM198B</i>	1.31E-02	0.46	1.04E-02	0.51	family with sequence similarity 198, member B	
1552546_a_at	137994	<i>LETM2</i>	1.82E-02	0.48	5.50E-03	0.45	leucine zipper-EF-hand containing transmembrane protein 2	
219872_at	51313	<i>FAM198B</i>	1.00E-04	0.50	5.00E-04	0.58	family with sequence similarity 198, member B	
231053_at	3745	<i>KCNB1</i>	5.67E-02	0.51	2.70E-02	0.54	potassium channel, voltage gated Shab related subfamily B, member 1	
201694_s_at	1958	<i>EGR1</i>	1.74E-02	0.51	9.00E-04	0.38	early growth response 1	
218864_at	7145	<i>TNS1</i>	4.60E-03	0.52	3.60E-03	0.52	tensin 1	
204439_at	10964	<i>IFI44L</i>	1.67E-02	0.52	2.54E-02	0.56	interferon-induced protein 44-like	
227404_s_at	1958	<i>EGR1</i>	1.33E-02	0.53	4.00E-04	0.37	early growth response 1	
214453_s_at	10561	<i>IFI44</i>	9.90E-03	0.54	1.24E-02	0.59	interferon-induced protein 44	
211006_s_at	3745	<i>KCNB1</i>	2.14E-02	0.55	6.20E-03	0.46	potassium channel, voltage gated Shab related subfamily B, member 1	
215649_s_at	4598	<i>MVK</i>	1.80E-03	0.55	3.00E-04	0.49	mevalonate kinase	
204363_at	2152	<i>F3</i>	5.74E-02	0.57	3.43E-02	0.59	coagulation factor III (thromboplastin, tissue factor)	
223749_at	114898	<i>CIQTNF2</i>	2.83E-02	0.57	1.93E-02	0.61	C1q and tumor necrosis factor related protein 2	
1556361_s_at	81573	<i>ANKRD13C</i>	1.51E-02	0.58	4.80E-03	0.53	ankyrin repeat domain 13C	
222071_s_at	353189	<i>SILCO4C1</i>	3.53E-02	0.60	7.80E-03	0.59	solute carrier organic anion transporter family, member 4C1	
233234_at	57528	<i>KCTD16</i>	6.71E-02	0.61	2.88E-02	0.61	potassium channel tetramerization domain containing 16	
211520_s_at	2890	<i>GRIA1</i>	1.61E-02	0.62	7.88E-02	0.66	glutamate receptor, ionotropic, AMPA 1	
206825_at	5021	<i>OXTR</i>	1.60E-03	0.62	6.00E-04	0.59	oxytocin receptor	
233907_s_at	56256	<i>SERTAD4</i>	9.00E-03	0.62	4.80E-03	0.62	SERTA domain containing 4	
235315_at	8848	<i>TSC22D1</i>	6.53E-02	0.62	2.01E-02	0.56	TSC22 domain family, member 1	
204056_s_at	4598	<i>MVK</i>	1.60E-03	0.63	3.00E-04	0.55	mevalonate kinase	
1559060_a_at	96459	<i>FNIP1</i>	5.54E-02	0.63	3.11E-02	0.61	folliculin interacting protein 1	
1554018_at	10457	<i>GPHNB</i>	8.38E-02	0.64	3.43E-02	0.56	glycoprotein (transmembrane) nmb	
240869_at	3745	<i>KCNB1</i>	6.88E-02	0.64	1.37E-02	0.53	potassium channel, voltage gated Shab related subfamily B, member 1	
226603_at	219285	<i>KCNB1</i>	1.40E-02	0.64	3.04E-02	0.65	sterile alpha motif domain containing 9-like	
211018_at	4047	<i>LSS</i>	6.70E-03	0.65	3.50E-03	0.65	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	
211019_s_at	4047	<i>LSS</i>	1.70E-03	0.65	6.00E-04	0.63	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	

227055_at	196410	<i>METTL7B</i>	2.79E-02	0.65	2.15E-02	0.68	methyltransferase like 7B
236344_at	5137	<i>PDE1C</i>	1.40E-02	0.65	1.00E-02	0.68	phosphodiesterase 1C, calmodulin-dependent 70kDa
235760_at	64324	<i>NSD1</i>	4.41E-02	0.66	2.40E-02	0.68	nuclear receptor binding SET domain protein 1
230708_at	144185	<i>PRICKLE1</i>	2.70E-02	0.66	5.60E-03	0.60	prickle homolog 1
231600_at	387837	<i>CLEC12B</i>	3.31E-02	0.26	3.61E-01	0.68	C-type lectin domain family 12, member B
207134_x_at	7177	<i>TPSAB1</i>	7.04E-02	0.41	6.77E-01	0.88	tryptase alpha/beta 1
	64499	<i>TPSB2</i>					tryptase beta 2 (gene/pseudogene)
223317_at	84266	<i>ALKBH7</i>	4.09E-02	0.47	1.79E-01	0.62	alkB homolog 7
214978_s_at	8497	<i>PPFIA4</i>	6.39E-02	0.48	2.65E-01	0.58	PTPRF interacting protein alpha 4
220208_at	4599	<i>MX1</i>	7.05E-02	0.53	2.11E-01	0.73	MX dynamin-like GTPase 1
206757_at	8654	<i>PDE5A</i>	9.95E-02	0.55	6.13E-01	0.81	phosphodiesterase 5A, cGMP-specific
206553_at	4939	<i>OAS2</i>	8.63E-02	0.57	3.43E-01	0.82	2'-5'-oligoadenylate synthetase 2
229337_at	9099	<i>USP2</i>	7.04E-02	0.57	1.06E-01	0.65	ubiquitin specific peptidase 2
220381_at	79822	<i>ARHGAP28</i>	7.11E-02	0.58	2.83E-01	0.78	Rho GTPase activating protein 28
205552_s_at	4938	<i>OAS1</i>	7.12E-02	0.58	1.86E-01	0.65	2'-5'-oligoadenylate synthetase 1
232666_at	4940	<i>OAS3</i>	4.19E-02	0.60	1.23E-01	0.61	2'-5'-oligoadenylate synthetase 3
237767_at	10160	<i>FARP1</i>	5.51E-02	0.62	4.58E-01	0.83	FERM, ARH/RhoGEF and pleckstrin domain protein 1
204938_s_at	5350	<i>PLN</i>	6.15E-02	0.63	1.20E-01	0.68	phospholamban
237691_x_at	2027	<i>ENO3</i>	1.51E-02	0.63	2.30E-01	0.83	enolase 3 (beta, muscle)
1559449_a_at	9534	<i>ZNF254</i>	5.51E-02	0.64	1.71E-01	0.76	zinc finger protein 254
235544_x_at	284069	<i>FAM171A2</i>	7.04E-02	0.65	4.24E-01	0.82	family with sequence similarity 171, member A2
229767_at	6904	<i>TBCD</i>	1.07E-02	0.67	1.38E-01	0.83	tubulin folding cofactor D
228368_at	57569	<i>ARHGAP20</i>	2.81E-01	0.51	4.11E-02	0.37	Rho GTPase activating protein 20
204814_at	8618	<i>CADPS</i>	7.61E-01	0.84	3.63E-02	0.38	Ca++-dependent secretion activator
219250_s_at	23767	<i>FLRT3</i>	1.56E-01	0.61	1.11E-02	0.49	fibronectin leucine rich transmembrane protein 3
244725_at	63951	<i>DMRTA1</i>	3.95E-01	0.60	8.29E-02	0.49	DMRT-like family A1
210099_at	20	<i>ABCA2</i>	7.13E-01	0.89	9.90E-03	0.51	ATP binding cassette subfamily A member 2
1554328_at	252983	<i>STXB4</i>	1.90E-01	0.57	5.86E-02	0.52	syntaxin binding protein 4
215231_at	51422	<i>PRKAG2</i>	1.60E-01	0.52	8.20E-02	0.53	protein kinase, AMP-activated, gamma 2 non-catalytic subunit
222076_at	1839	<i>HBEGF</i>	3.94E-01	0.78	4.00E-02	0.53	heparin-binding EGF-like growth factor
217452_s_at	8707	<i>B3GALT2</i>	2.05E-01	0.50	8.82E-02	0.55	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase 2
231786_at	3209	<i>HOXA13</i>	4.88E-01	0.75	9.38E-02	0.56	homeobox A13
232365_at	6477	<i>SIAH1</i>	2.93E-01	0.69	5.94E-02	0.56	siah E3 ubiquitin protein ligase 1
1554686_at	27067	<i>STAU2</i>	9.01E-02	0.68	1.00E-02	0.56	staufen double-stranded RNA binding protein 2
221993_s_at	115939	<i>TSR3</i>	8.54E-01	1.04	8.56E-02	0.56	TSR3, 20S rRNA accumulation, homolog (S. cerevisiae)
203766_s_at	25802	<i>LMOD1</i>	3.28E-01	0.79	6.80E-03	0.58	leiomodulin 1 (smooth muscle)
239744_at	5998	<i>RG53</i>	2.78E-01	0.81	7.10E-03	0.58	regulator of G-protein signaling 3
200865_at	8665	<i>EIF3F</i>	2.24E-01	0.74	1.51E-02	0.58	eukaryotic translation initiation factor 3, subunit F
1560467_at	344838	<i>PAQR9</i>	2.07E-01	0.62	5.69E-02	0.60	progesterin and adipoQ receptor family member IX
226065_at	144165	<i>PRICKLE1</i>	2.18E-02	0.73	8.00E-04	0.60	prickle homolog 1
1559022_at	9813	<i>EFCAB14</i>	4.09E-01	0.69	5.30E-02	0.61	EF-hand calcium binding domain 14
	105378698	<i>LOC105378698</i>					uncharacterized LOC105378698
224469_s_at	64423	<i>INF2</i>	1.65E-02	0.67	2.10E-03	0.61	inverted formin, FH2 and WH2 domain containing
212168_at	10137	<i>RBM12</i>	7.18E-02	0.71	5.10E-03	0.61	RNA binding motif protein 12
1566739_at	51196	<i>PLCE1</i>	3.84E-02	0.67	8.10E-03	0.61	phospholipase C, epsilon 1
225173_at	93663	<i>ARHGAP18</i>	1.69E-02	0.74	6.00E-04	0.61	Rho GTPase activating protein 18
1569675_at	5450	<i>BTG4</i>	1.71E-01	0.69	4.45E-02	0.61	B-cell translocation gene 4
	54766	<i>POU2AF1</i>					POU class 2 associating factor 1
229292_at	57669	<i>EPB415</i>	1.92E-01	0.72	3.92E-02	0.61	erythrocyte membrane protein band 4.1 like 5
226069_at	144165	<i>PRICKLE1</i>	5.87E-02	0.68	1.01E-02	0.61	prickle homolog 1
220300_at	5998	<i>RG53</i>	6.87E-01	0.88	1.48E-02	0.62	regulator of G-protein signaling 3
228906_at	80312	<i>TEF1</i>	7.91E-02	0.69	8.20E-03	0.62	tet methylcytosine dioxygenase 1
242767_at	29895	<i>LMCD1</i>	3.31E-02	0.70	4.30E-03	0.62	LIM and cysteine-rich domains 1
203027_s_at	4597	<i>MVD</i>	9.90E-03	0.70	7.00E-04	0.62	mevalonate (diphospho) decarboxylase
230044_s_at	5833	<i>PCYT2</i>	4.17E-02	0.68	9.80E-03	0.63	phosphate cytidylyltransferase 2, ethanolamine
1555131_a_at	8863	<i>PER3</i>	9.90E-03	0.70	3.10E-03	0.63	period circadian clock 3
212170_at	10137	<i>RBM12</i>	2.50E-03	0.73	2.00E-04	0.63	RNA binding motif protein 12
1570238_at	84503	<i>ZNF527</i>	5.72E-01	0.79	4.97E-02	0.63	zinc finger protein 527
206987_x_at	8817	<i>FGF18</i>	2.93E-01	0.72	7.11E-02	0.63	fibroblast growth factor 18
235828_at	153768	<i>PRELID2</i>	4.28E-02	0.72	2.50E-03	0.63	PRELI domain containing 2
211029_x_at	8817	<i>FGF18</i>	2.00E-01	0.68	3.13E-02	0.63	fibroblast growth factor 18
222853_at	23767	<i>FLRT3</i>	3.43E-01	0.79	1.26E-02	0.63	fibronectin leucine rich transmembrane protein 3
219042_at	11178	<i>LZTS1</i>	2.46E-01	0.79	1.83E-02	0.63	leucine zipper, putative tumor suppressor 1
47550_at	11178	<i>LZTS1</i>	2.28E-02	0.74	3.00E-03	0.63	leucine zipper, putative tumor suppressor 1
241470_x_at	9182	<i>RASSF9</i>	1.08E-01	0.59	9.43E-02	0.63	Ras association (RalGDS/AF-6) domain family (N-terminal) member 9
223063_at	84886	<i>C1orf198</i>	1.24E-02	0.71	1.80E-03	0.64	chromosome 1 open reading frame 198
1554966_a_at	11259	<i>FLIPL1</i>	1.44E-01	0.65	4.79E-02	0.64	filamin A interacting protein 1-like
225171_at	93663	<i>ARHGAP18</i>	9.01E-02	0.75	1.20E-02	0.64	Rho GTPase activating protein 18
1552721_a_at	2246	<i>FGF1</i>	4.74E-02	0.72	1.62E-02	0.64	fibroblast growth factor 1 (acidic)
219821_s_at	54438	<i>FGOD1</i>	5.30E-03	0.72	6.00E-04	0.64	glucose-fructose oxidoreductase domain containing 1
206290_s_at	6000	<i>RG57</i>	3.06E-02	0.72	5.80E-03	0.64	regulator of G-protein signaling 7
227088_at	8654	<i>PDE5A</i>	2.12E-01	0.81	3.19E-02	0.65	phosphodiesterase 5A, cGMP-specific
214704_at	22980	<i>TCF25</i>	7.86E-01	0.91	6.10E-02	0.65	transcription factor 25 (basic helix-loop-helix)
230047_at	143872	<i>ARHGAP42</i>	2.06E-01	0.75	5.34E-02	0.65	Rho GTPase activating protein 42
222797_at	56896	<i>DPYSL5</i>	2.64E-01	0.73	4.64E-02	0.65	dihydropyrimidinase-like 5
219515_at	56980	<i>PRDM10</i>	3.36E-02	0.75	2.90E-03	0.65	PR domain containing 10
225166_at	93663	<i>ARHGAP18</i>	6.94E-02	0.73	7.60E-03	0.65	Rho GTPase activating protein 18
208240_s_at	2246	<i>FGF1</i>	5.30E-03	0.68	2.30E-03	0.65	fibroblast growth factor 1 (acidic)
1554036_at	9841	<i>ZBTB24</i>	3.20E-01	0.75	3.21E-02	0.65	zinc finger and BTB domain containing 24
1559409_a_at	57545	<i>CC2D2A</i>	1.20E-01	0.62	6.94E-02	0.66	coiled-coil and C2 domain containing 2A
231234_at	1075	<i>CTSC</i>	3.55E-01	0.74	8.14E-02	0.66	cathepsin C
204135_at	11259	<i>FLIPL1</i>	1.16E-01	0.68	6.68E-02	0.66	filamin A interacting protein 1-like
202245_at	4047	<i>LSS</i>	1.80E-03	0.70	5.00E-04	0.66	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)
203824_at	7103	<i>TSPAN8</i>	1.90E-01	0.73	4.50E-02	0.66	tetraspanin 8
236937_at	23355	<i>VP58</i>	8.63E-02	0.73	1.46E-02	0.66	vacuolar protein sorting 8 homolog (S. cerevisiae)
210544_s_at	224	<i>ALDH3A2</i>	6.18E-02	0.80	2.20E-03	0.66	aldehyde dehydrogenase 3 family, member A2
1555600_s_at	80832	<i>APOLA</i>	1.07E-01	0.75	3.21E-02	0.66	apolipoprotein L 4
227702_at	260293	<i>CYP4X1</i>	2.93E-01	0.72	2.17E-02	0.66	cytochrome P450, family 4, subfamily X, polypeptide 1
220615_s_at	55711	<i>FAR2</i>	1.97E-01	0.79	1.32E-02	0.66	fatty acyl-CoA reductase 2
209279_s_at	50814	<i>NSDHL</i>	1.83E-02	0.75	1.30E-03	0.66	NAD(P) dependent steroid dehydrogenase-like
237056_at	387755	<i>INSC</i>	4.00E-01	0.77	9.06E-02	0.67	inscuteable homolog (Drosophila)
229674_at	56256	<i>SERTAD4</i>	1.22E-01	0.68	4.95E-02	0.67	SERTA domain containing 4

Treatment (18h)
Ind: 1 Probe Set (1 Gene)
Ind+GSK: 2 Probe Sets (2 Genes)



Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	FDR P-Value	Fold change	FDR P-Value	Fold change	UniGene Name	Function
240876_x_at	145645	<i>C15orf43</i>	9.51E-02	0.51	9.43E-01	1.04	chromosome 15 open reading frame 43	
213240_s_at	3851	<i>KRT4</i>	2.84E-01	0.53	7.60E-02	0.48	keratin 4, type II	
221748_s_at	7145	<i>TNS1</i>	2.55E-01	0.72	5.85E-02	0.67	tensin 1	

*N.B. Some genes are recognised by more than one probe set and some probe sets recognise more than one gene.

Supplemental TABLE 4. Functional annotation clustering of genes induced by indacaterol and Ind+GSK in BEAS-2B cells. Genes, by probe set, that were significantly (FDR <10%) induced (>1.5-fold) by indacaterol (10nM) and Ind+GSK (both 10nM) at all time-points were subjected to functional annotation clustering using DAVID bioinformatics resources. Clusters for each treatment intervention are listed in decreasing order of enrichment. Within each cluster, GO terms are listed in decreasing order of significance. When a GO term was absent from a given gene cluster, UniProt Sequence Feature, Uniprot Key Words, InterPro and/or KEGG pathway are cited. "Count" refers to the number of genes in each GO term or equivalent.

Indacaterol (10nM)

724 Probe Sets Analysed

Annotation Cluster 1		Enrichment Score: 6.23	Count	P-Value	Benjamini
GOTERM_CC_DIRECT	extracellular space		60	1.1E-06	3.2E-04
GOTERM_CC_DIRECT	extracellular region		60	2.0E-04	1.5E-02
Annotation Cluster 2		Enrichment Score: 4.67	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	positive regulation of transcription from RNA polymerase II promoter		60	8.4E-11	2.3E-07
GOTERM_BP_DIRECT	negative regulation of transcription from RNA polymerase II promoter		48	6.2E-10	8.4E-07
GOTERM_BP_DIRECT	transcription from RNA polymerase II promoter		33	1.1E-06	7.2E-04
GOTERM_BP_DIRECT	transcription, DNA-templated		55	1.7E-01	8.9E-01
GOTERM_CC_DIRECT	nucleus		156	5.6E-04	2.8E-02
GOTERM_MF_DIRECT	sequence-specific DNA binding		37	2.0E-08	1.4E-05
GOTERM_MF_DIRECT	transcription factor activity, sequence-specific DNA binding		50	9.3E-07	3.1E-04
GOTERM_MF_DIRECT	DNA binding		39	7.2E-01	1.0E+00
Annotation Cluster 3		Enrichment Score: 3.74	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	transcription factor activity, RNA polymerase II core promoter proximal region sequence-specific binding		5	2.2E-03	1.0E-01
Annotation Cluster 4		Enrichment Score: 3.27	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cell-cell signaling		18	1.6E-04	1.8E-02
GOTERM_MF_DIRECT	growth factor activity		14	1.8E-04	2.0E-02
GOTERM_MF_DIRECT	cytokine activity		12	4.2E-03	1.5E-01
Annotation Cluster 5		Enrichment Score: 2.8	Count	P-Value	Benjamini
GOTERM_CC_DIRECT	integral component of plasma membrane		62	1.1E-06	1.7E-04
GOTERM_CC_DIRECT	plasma membrane		113	2.2E-02	4.6E-01
GOTERM_CC_DIRECT	integral component of membrane		113	7.7E-01	9.9E-01
Annotation Cluster 6		Enrichment Score: 2.18	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	amino acid transport		8	1.7E-05	3.1E-03
GOTERM_BP_DIRECT	leukocyte migration		9	9.7E-03	2.5E-01
GOTERM_BP_DIRECT	L-amino acid transport		3	3.3E-02	4.7E-01
GOTERM_BP_DIRECT	neutral amino acid transport		3	3.8E-02	5.1E-01
GOTERM_BP_DIRECT	cellular amino acid metabolic process		3	2.5E-01	9.5E-01
GOTERM_BP_DIRECT	transport		10	4.7E-01	1.0E+00
GOTERM_MF_DIRECT	amino acid transmembrane transporter activity		7	9.6E-04	6.3E-02
GOTERM_MF_DIRECT	antiporter activity		4	1.4E-02	3.2E-01
GOTERM_MF_DIRECT	L-amino acid transmembrane transporter activity		3	3.9E-02	5.3E-01
Annotation Cluster 7		Enrichment Score: 2.09	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cAMP catabolic process		5	3.8E-04	3.0E-02
GOTERM_MF_DIRECT	3',5'-cyclic-AMP phosphodiesterase activity		5	3.9E-04	3.3E-02
GOTERM_MF_DIRECT	cAMP binding		5	2.6E-03	1.1E-01
GOTERM_MF_DIRECT	3',5'-cyclic-nucleotide phosphodiesterase activity		4	1.8E-02	3.7E-01
Annotation Cluster 8		Enrichment Score: 2.01	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	quaternary ammonium group transport		3	5.6E-03	1.7E-01
GOTERM_MF_DIRECT	quaternary ammonium group transmembrane transporter activity		3	5.7E-03	1.8E-01
Annotation Cluster 9		Enrichment Score: 1.97	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cellular response to corticotropin-releasing hormone stimulus		3	8.2E-03	2.3E-01
GOTERM_BP_DIRECT	steroid hormone mediated signaling pathway		5	4.9E-02	5.8E-01
GOTERM_BP_DIRECT	intracellular receptor signaling pathway		4	6.4E-02	6.5E-01
GOTERM_BP_DIRECT	transcription initiation from RNA polymerase II promoter		7	1.6E-01	8.8E-01
GOTERM_MF_DIRECT	RNA polymerase II transcription factor activity, ligand-activated sequence-specific DNA binding		5	1.1E-02	3.1E-01

GOTERM_MF_DIRECT	steroid hormone receptor activity	6	1.2E-02	3.0E-01
Annotation Cluster		Enrichment Score: 1.83	Count	P-Value Benjamini
GOTERM_MF_DIRECT	symporter activity	7	1.5E-03	7.4E-02
GOTERM_BP_DIRECT	sodium ion transport	7	1.4E-02	3.0E-01
Annotation Cluster		Enrichment Score: 1.56	Count	P-Value Benjamini
GOTERM_MF_DIRECT	transmembrane transporter activity	3	3.4E-01	9.6E-01
Annotation Cluster		Enrichment Score: 1.54	Count	P-Value Benjamini
GOTERM_BP_DIRECT	endoderm formation	6	5.6E-06	1.4E-03
GOTERM_BP_DIRECT	peptidyl-threonine dephosphorylation	4	2.0E-03	8.8E-02
GOTERM_BP_DIRECT	peptidyl-tyrosine dephosphorylation	7	3.3E-02	4.7E-01
GOTERM_BP_DIRECT	inactivation of MAPK activity	3	1.2E-01	8.2E-01
GOTERM_BP_DIRECT	dephosphorylation	5	1.6E-01	8.7E-01
GOTERM_MF_DIRECT	phosphatase activity	5	1.6E-02	3.5E-01
GOTERM_MF_DIRECT	protein tyrosine phosphatase activity	7	3.6E-02	5.2E-01
GOTERM_MF_DIRECT	MAP kinase tyrosine/serine/threonine phosphatase activity	3	3.9E-02	5.3E-01
GOTERM_MF_DIRECT	protein tyrosine/serine/threonine phosphatase activity	3	2.3E-01	9.1E-01
Annotation Cluster		Enrichment Score: 1.45	Count	P-Value Benjamini
KEGG_PATHWAY	TNF signaling pathway	12	2.3E-04	2.4E-02
KEGG_PATHWAY	Rheumatoid arthritis	7	4.2E-02	3.7E-01
KEGG_PATHWAY	Intestinal immune network for IgA production	3	4.0E-01	8.4E-01
KEGG_PATHWAY	Herpes simplex infection	7	4.4E-01	8.4E-01
Annotation Cluster		Enrichment Score: 1.43	Count	P-Value Benjamini
GOTERM_CC_DIRECT	anchored component of plasma membrane	4	2.6E-02	4.5E-01
Annotation Cluster		Enrichment Score: 1.4	Count	P-Value Benjamini
UP_KEYWORDS	Lipoprotein	29	2.4E-02	2.2E-01
UP_SEQ_FEATURE	lipid moiety-binding region:S-palmitoyl cysteine	10	2.5E-02	7.5E-01
UP_KEYWORDS	Palmitate	12	1.0E-01	4.7E-01
Annotation Cluster		Enrichment Score: 1.34	Count	P-Value Benjamini
GOTERM_MF_DIRECT	E-box binding	3	2.0E-01	8.9E-01
Annotation Cluster		Enrichment Score: 1.31	Count	P-Value Benjamini
UP_KEYWORDS	Extracellular matrix	13	1.2E-02	1.4E-01
INTERPRO	Thrombospondin, type 1 repeat	6	1.8E-02	4.8E-01
INTERPRO	Peptidase M12B, ADAM-TS	3	1.1E-01	8.7E-01
INTERPRO	ADAM-TS Spacer 1	3	1.1E-01	8.7E-01

Indacaterol (10nM) + GSK 256066 (10nM)

781 Probe Sets Analysed

Annotation Cluster 1		Enrichment Score: 5.78	Count	P-Value Benjamini
UP_SEQ_FEATURE	domain:Leucine-zipper	15	8.0E-07	3.9E-04
INTERPRO	Basic-leucine zipper domain	11	9.8E-07	8.6E-04
UP_SEQ_FEATURE	DNA-binding region:Basic motif	17	3.1E-06	1.1E-03
Annotation Cluster 2		Enrichment Score: 5.37	Count	P-Value Benjamini
GOTERM_BP_DIRECT	negative regulation of transcription from RNA polymerase II promoter	55	6.0E-12	1.7E-08
GOTERM_BP_DIRECT	positive regulation of transcription from RNA polymerase II promoter	64	7.0E-11	1.0E-07
GOTERM_MF_DIRECT	transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding	26	4.4E-09	2.9E-06
GOTERM_MF_DIRECT	transcription factor activity, sequence-specific DNA binding	58	1.0E-08	3.3E-06
GOTERM_BP_DIRECT	transcription from RNA polymerase II promoter	39	1.4E-08	9.9E-06
GOTERM_CC_DIRECT	nucleus	172	2.7E-04	1.4E-02
GOTERM_BP_DIRECT	transcription, DNA-templated	59	2.1E-01	9.3E-01
GOTERM_MF_DIRECT	DNA binding	41	7.9E-01	1.0E+00
Annotation Cluster 3		Enrichment Score: 3.66	Count	P-Value Benjamini
GOTERM_CC_DIRECT	extracellular space	68	6.0E-08	1.9E-05
GOTERM_CC_DIRECT	integral component of plasma membrane	62	2.5E-05	2.7E-03
GOTERM_CC_DIRECT	extracellular region	65	1.7E-04	1.1E-02
GOTERM_CC_DIRECT	plasma membrane	129	4.3E-03	1.2E-01
GOTERM_CC_DIRECT	integral component of membrane	128	6.4E-01	9.8E-01
Annotation Cluster 4		Enrichment Score: 2.63	Count	P-Value Benjamini

GOTERM_MF_DIRECT	3',5'-cyclic-AMP phosphodiesterase activity	6	3.1E-05	2.9E-03
GOTERM_BP_DIRECT	cAMP catabolic process	6	3.2E-05	5.0E-03
GOTERM_MF_DIRECT	3',5'-cyclic-nucleotide phosphodiesterase activity	5	2.9E-03	1.2E-01
GOTERM_MF_DIRECT	cAMP binding	5	3.4E-03	1.3E-01

Annotation Cluster 5		Enrichment Score: 2.24	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	amino acid transport		9	3.0E-06	8.6E-04
GOTERM_BP_DIRECT	leukocyte migration		9	1.7E-02	3.2E-01
GOTERM_BP_DIRECT	L-amino acid transport		3	3.9E-02	5.0E-01
GOTERM_BP_DIRECT	neutral amino acid transport		3	4.6E-02	5.3E-01
GOTERM_BP_DIRECT	cellular amino acid metabolic process		4	9.0E-02	7.2E-01
GOTERM_BP_DIRECT	transport		11	4.4E-01	1.0E+00
GOTERM_MF_DIRECT	amino acid transmembrane transporter activity		8	2.3E-04	1.4E-02
GOTERM_MF_DIRECT	antiporter activity		4	1.7E-02	3.9E-01
GOTERM_MF_DIRECT	L-amino acid transmembrane transporter activity		3	4.5E-02	5.5E-01

Annotation Cluster 6		Enrichment Score: 2.06	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	regulation of cell growth		8	5.5E-03	1.7E-01
GOTERM_MF_DIRECT	insulin-like growth factor binding		4	1.1E-02	3.2E-01

Annotation Cluster 7		Enrichment Score: 2	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	quaternary ammonium group transmembrane transporter activity		3	6.7E-03	2.2E-01
GOTERM_BP_DIRECT	quaternary ammonium group transport		3	6.7E-03	1.9E-01

Annotation Cluster 8		Enrichment Score: 1.83	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	symporter activity		8	3.8E-04	2.2E-02
GOTERM_BP_DIRECT	transmembrane transport		8	4.7E-01	1.0E+00

Annotation Cluster 9		Enrichment Score: 1.77	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	symporter activity		8	3.8E-04	2.2E-02
GOTERM_BP_DIRECT	sodium ion transport		7	2.1E-02	3.7E-01

Annotation Cluster		Enrichment Score: 1.59	Count	P-Value	Benjamini
UP_SEQ_FEATURE	domain:CUB 2		5	1.2E-02	6.6E-01
UP_SEQ_FEATURE	domain:CUB 1		5	1.2E-02	6.6E-01
INTERPRO	CUB domain		5	5.2E-02	7.0E-01

Annotation Cluster		Enrichment Score: 1.56	Count	P-Value	Benjamini
INTERPRO	Thrombospondin, type 1 repeat		8	1.3E-03	1.4E-01
UP_SEQ_FEATURE	domain:TSP type-1 2		5	2.5E-02	8.0E-01
UP_SEQ_FEATURE	domain:TSP type-1 1		5	2.5E-02	8.0E-01
UP_SEQ_FEATURE	domain:TSP type-1 3		4	6.3E-02	8.9E-01
UP_SEQ_FEATURE	domain:TSP type-1		3	9.4E-02	9.4E-01
INTERPRO	Peptidase M12B, ADAM-TS		3	1.3E-01	8.8E-01
INTERPRO	ADAM-TS Spacer 1		3	1.3E-01	8.8E-01

Annotation Cluster		Enrichment Score: 1.56	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	transmembrane transporter activity		3	3.8E-01	9.5E-01

Annotation Cluster		Enrichment Score: 1.46	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	vasoconstriction		4	9.7E-03	2.4E-01
GOTERM_BP_DIRECT	artery smooth muscle contraction		3	2.3E-02	3.7E-01
GOTERM_BP_DIRECT	positive regulation of cytosolic calcium ion concentration		8	6.8E-02	6.3E-01
GOTERM_BP_DIRECT	regulation of vasoconstriction		3	9.8E-02	7.4E-01

Annotation Cluster		Enrichment Score: 1.45	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cellular response to corticotropin-releasing hormone stimulus		3	9.9E-03	2.4E-01
GOTERM_BP_DIRECT	steroid hormone mediated signaling pathway		5	6.5E-02	6.3E-01
GOTERM_BP_DIRECT	intracellular receptor signaling pathway		4	8.0E-02	6.8E-01
GOTERM_BP_DIRECT	transcription initiation from RNA polymerase II promoter		6	3.8E-01	9.9E-01
GOTERM_MF_DIRECT	RNA polymerase II transcription factor activity, ligand-activated		5	1.5E-02	3.6E-01
	sequence-specific DNA binding				
GOTERM_MF_DIRECT	steroid hormone receptor activity		5	6.1E-02	6.0E-01

Annotation Cluster		Enrichment Score: 1.43	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	protein phosphorylation		25	1.3E-03	7.1E-02
GOTERM_BP_DIRECT	protein autophosphorylation		10	4.1E-02	5.1E-01
GOTERM_BP_DIRECT	peptidyl-serine phosphorylation		8	5.0E-02	5.6E-01
GOTERM_MF_DIRECT	protein kinase activity		16	5.8E-02	5.8E-01
GOTERM_MF_DIRECT	protein serine/threonine kinase activity		15	1.3E-01	7.4E-01
GOTERM_MF_DIRECT	ATP binding		38	7.0E-01	1.0E+00

<u>Annotation Cluster</u>		<u>Enrichment Score: 1.36</u>	<u>Count</u>	<u>P-Value</u>	<u>Benjamini</u>
GOTERM_BP_DIRECT	positive regulation of tyrosine phosphorylation of Stat3 protein		7	4.7E-04	3.4E-02

<u>Annotation Cluster</u>		<u>Enrichment Score: 1.35</u>	<u>Count</u>	<u>P-Value</u>	<u>Benjamini</u>
GOTERM_BP_DIRECT	endoderm formation		6	9.0E-06	2.0E-03
GOTERM_BP_DIRECT	peptidyl-threonine dephosphorylation		3	3.3E-02	4.6E-01
GOTERM_BP_DIRECT	peptidyl-tyrosine dephosphorylation		7	4.9E-02	5.5E-01
GOTERM_BP_DIRECT	inactivation of MAPK activity		3	1.4E-01	8.5E-01
GOTERM_BP_DIRECT	dephosphorylation		4	4.0E-01	9.9E-01
GOTERM_MF_DIRECT	phosphatase activity		5	2.1E-02	4.0E-01
GOTERM_MF_DIRECT	MAP kinase tyrosine/serine/threonine phosphatase activity		3	4.5E-02	5.5E-01
GOTERM_MF_DIRECT	protein tyrosine phosphatase activity		7	5.1E-02	5.6E-01
GOTERM_MF_DIRECT	protein tyrosine/serine/threonine phosphatase activity		3	2.6E-01	8.9E-01

<u>Annotation Cluster</u>		<u>Enrichment Score: 1.31</u>	<u>Count</u>	<u>P-Value</u>	<u>Benjamini</u>
KEGG_PATHWAY	TNF signaling pathway		12	4.4E-04	1.8E-02
KEGG_PATHWAY	Rheumatoid arthritis		7	5.7E-02	3.8E-01
KEGG_PATHWAY	Intestinal immune network for IgA production		3	4.3E-01	8.2E-01
KEGG_PATHWAY	Herpes simplex infection		7	5.2E-01	8.5E-01

Supplemental TABLE 5. Functional annotation clustering of genes repressed by indacaterol and Ind+GSK in BEAS-2B cells. Genes, by probe set, that were significantly (FDR <10%) repressed (>0.67-fold) by indacaterol (10nM) and Ind+GSK (both 10nM) at all time-points were subjected to functional annotation clustering using DAVID bioinformatics resources. Clusters for each treatment intervention are listed in decreasing order of enrichment. Within each cluster, GO terms are listed in decreasing order of significance. "Count" refers to the number of genes in each GO term or equivalent.

Indacaterol (10nM)

131 Probe Sets Analysed

Annotation Cluster 1		Enrichment Score: 2.12	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cell division		7	1.7E-02	9.0E-01
GOTERM_BP_DIRECT	mitotic nuclear division		5	5.7E-02	9.7E-01
Annotation Cluster 2		Enrichment Score: 1.96	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	type I interferon signaling pathway		6	3.5E-05	2.4E-02
GOTERM_MF_DIRECT	2'-5'-oligoadenylate synthetase activity		3	2.0E-04	4.2E-02
GOTERM_BP_DIRECT	response to virus		6	4.6E-04	1.5E-01
GOTERM_MF_DIRECT	nucleotidyltransferase activity		3	1.1E-02	4.4E-01
GOTERM_BP_DIRECT	defense response to virus		5	1.6E-02	9.4E-01
GOTERM_BP_DIRECT	negative regulation of viral genome replication		3	2.3E-02	8.7E-01
GOTERM_MF_DIRECT	double-stranded RNA binding		3	5.0E-02	7.4E-01
GOTERM_BP_DIRECT	interferon-gamma-mediated signaling pathway		3	6.5E-02	9.7E-01
GOTERM_MF_DIRECT	transferase activity		3	1.1E-01	9.3E-01
GOTERM_BP_DIRECT	immune response		4	4.5E-01	1.0E+00
Annotation Cluster 3		Enrichment Score: 1.41	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	metal ion binding		23	3.8E-03	3.3E-01
GOTERM_CC_DIRECT	intracellular		16	1.6E-02	7.4E-01
GOTERM_BP_DIRECT	transcription, DNA-templated		20	1.7E-02	8.7E-01
GOTERM_MF_DIRECT	transcription factor activity, sequence-specific DNA binding		12	2.5E-02	5.9E-01
GOTERM_BP_DIRECT	regulation of transcription, DNA-templated		16	2.8E-02	8.9E-01
GOTERM_MF_DIRECT	DNA binding		17	3.4E-02	6.5E-01
GOTERM_MF_DIRECT	nucleic acid binding		10	1.2E-01	9.4E-01
GOTERM_CC_DIRECT	nucleus		40	1.4E-01	9.4E-01

Indacaterol (10nM) + GSK 256066 (10nM)

177 Probe Sets Analysed

Annotation Cluster 1		Enrichment Score: 2.55	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cell division		9	6.2E-03	6.3E-01
GOTERM_BP_DIRECT	mitotic nuclear division		7	1.3E-02	6.9E-01
GOTERM_CC_DIRECT	midbody		4	7.6E-02	8.3E-01
Annotation Cluster 2		Enrichment Score: 1.72	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	cholesterol biosynthetic process		4	3.2E-03	4.7E-01
Annotation Cluster 3		Enrichment Score: 1.7	Count	P-Value	Benjamini
GOTERM_BP_DIRECT	transcription, DNA-templated		28	2.1E-03	5.7E-01
GOTERM_MF_DIRECT	DNA binding		24	3.2E-03	6.0E-01
GOTERM_BP_DIRECT	regulation of transcription, DNA-templated		22	6.2E-03	5.6E-01
GOTERM_MF_DIRECT	metal ion binding		24	3.5E-02	8.2E-01
GOTERM_MF_DIRECT	nucleic acid binding		13	6.7E-02	8.4E-01
GOTERM_CC_DIRECT	intracellular		16	8.3E-02	8.2E-01
GOTERM_CC_DIRECT	nucleus		49	1.2E-01	8.9E-01
GOTERM_MF_DIRECT	zinc ion binding		11	3.8E-01	1.0E+00
Annotation Cluster 4		Enrichment Score: 1.46	Count	P-Value	Benjamini
GOTERM_MF_DIRECT	3',5'-cyclic-nucleotide phosphodiesterase activity		3	1.3E-02	7.1E-01

Supplemental TABLE 6. Effect of GSK 256066 on the kinetics of indacaterol-induced gene expression changes. The AUC_{0-18h} of all significant indacaterol (Ind)-induced gene expression changes (FDR <10%), by probe set, was calculated in BEAS-2B cells in the absence and presence of GSK 256066 (GSK; 10nM). The difference in these values (i.e., Ind+GSK/Ind) for each probe set is listed ranked highest to lowest; values >1 and <1 indicate an increase and decreased respectively of the indacaterol AUC_{0-18h} . This analysis was restricted to transcripts that were induced by >2-fold. Genes underlined and in bold face were validated by real-time PCR (Fig. 5).

Affy Probe Set ID*	Entrez Gene ID	Official Gene Symbol	AUC_{0-18h} Ind	AUC_{0-18h} Ind+GSK	AUC_{0-18h} Ind+GSK/Ind	UniGene Name
220125_at	27019	<i>DNAI1</i>	2.2	5.6	2.5	dynein, axonemal, intermediate chain 1
239123_at	8848	<i>TSC22D1</i>	8.8	20.3	2.3	TSC22 domain family, member 1
216604_s_at	23428	<i>SLC7A8</i>	3.1	6.6	2.1	solute carrier family 7 (amino acid transporter light chain, L system), member 8
203394_s_at	2380	<i>HES1</i>	5.3	11.1	2.1	hes family bHLH transcription factor 1
205960_at	5166	<i>PDK4</i>	39.5	78.5	2.0	<i>pyruvate dehydrogenase kinase, isozyme 4</i>
202768_at	2354	<i>FOSB</i>	4.4	8.6	2.0	FBJ murine osteosarcoma viral oncogene homolog B
238987_at	2683	<i>B4GALT1</i>	6.7	12.9	1.9	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1
209720_s_at	6317	<i>SERPINB3</i>	33.1	61.9	1.9	serpin peptidase inhibitor, clade B (ovalbumin), member 3
1569262_x_at	90025	<i>UBE3D</i>	9.8	17.4	1.8	ubiquitin protein ligase E3D
208228_s_at	2263	<i>FGFR2</i>	15.6	27.4	1.8	<i>fibroblast growth factor receptor 2</i>
205421_at	6581	<i>SLC22A3</i>	33.6	58.3	1.7	solute carrier family 22 (organic cation transporter), member 3
1558143_a_at	10018	<i>BCL2L11</i>	4.3	7.3	1.7	BCL2-like 11 (apoptosis facilitator)
235066_at	4134	<i>MAP4</i>	9.4	15.8	1.7	microtubule associated protein 4
225207_at	5166	<i>PDK4</i>	60.6	99.8	1.6	<i>pyruvate dehydrogenase kinase, isozyme 4</i>
205870_at	624	<i>BDKRB2</i>	7.3	12.0	1.6	bradykinin receptor B2
232361_s_at	26298	<i>EHF</i>	11.6	19.0	1.6	ets homologous factor
220393_at	51557	<i>LGSN</i>	26.5	42.2	1.6	lensin, lens protein with glutamine synthetase domain
219195_at	10891	<i>PPARGC1A</i>	6.3	10.0	1.6	peroxisome proliferator-activated receptor gamma, coactivator 1 alpha
224941_at	5069	<i>PAPPA</i>	35.4	55.6	1.6	pregnancy-associated plasma protein A, pappalysin 1
1565800_x_at	117177	<i>RAB31P</i>	14.5	22.7	1.6	RAB3A interacting protein
224572_s_at	359948	<i>IRF2BP2</i>	3.4	5.3	1.6	interferon regulatory factor 2 binding protein 2
203290_at	3117	<i>HLA-DQA1</i>	6.5	10.1	1.6	major histocompatibility complex, class II, DQ alpha 1
201981_at	5069	<i>PAPPA</i>	33.5	51.7	1.5	pregnancy-associated plasma protein A, pappalysin 1
207038_at	9120	<i>SLC16A6</i>	20.9	32.0	1.5	solute carrier family 16, member 6
217584_at	4864	<i>NPC1</i>	3.2	4.9	1.5	Niemann-Pick disease, type C1
224940_s_at	5069	<i>PAPPA</i>	37.4	56.4	1.5	pregnancy-associated plasma protein A, pappalysin 1
224797_at	57561	<i>ARRDC3</i>	7.1	10.7	1.5	arrestin domain containing 3
1553199_at	138009	<i>DCAF4L2</i>	9.7	14.6	1.5	DDB1 and CUL4 associated factor 4-like 2
229093_at	4846	<i>NOS3</i>	10.2	15.2	1.5	nitric oxide synthase 3
224942_at	5069	<i>PAPPA</i>	38.4	57.0	1.5	pregnancy-associated plasma protein A, pappalysin 1
1557285_at	374	<i>AREG</i>	10.5	15.5	1.5	amphiregulin
228625_at	163732	<i>CITED4</i>	8.4	12.4	1.5	Cbp/p300-interacting transactivator, with Glu/Asp rich carboxy-terminal domain, 4
208536_s_at	10018	<i>BCL2L11</i>	5.4	7.8	1.4	BCL2-like 11 (apoptosis facilitator)
218589_at	10161	<i>LPAR6</i>	11.9	17.1	1.4	lysophosphatidic acid receptor 6
232470_at	150094	<i>SIK1</i>	23.4	33.6	1.4	salt-inducible kinase 1
218177_at	57132	<i>CHMP1B</i>	17.2	24.3	1.4	charged multivesicular body protein 1B
203395_s_at	3280	<i>HES1</i>	7.1	10.0	1.4	hes family bHLH transcription factor 1
228128_x_at	5069	<i>PAPPA</i>	49.9	69.2	1.4	pregnancy-associated plasma protein A, pappalysin 1
205290_s_at	650	<i>BMP2</i>	13.2	18.3	1.4	<i>bone morphogenetic protein 2</i>
209631_s_at	2861	<i>GPR37</i>	10.9	15.1	1.4	G protein-coupled receptor 37 (endothelin receptor type B-like)
213006_at	1052	<i>CEBPD</i>	16.4	22.7	1.4	CCAAT/enhancer binding protein (C/EBP), delta
244025_at	85450	<i>ITPRIP</i>	15.4	21.2	1.4	inositol 1,4,5-trisphosphate receptor interacting protein
224917_at	81671	<i>VMP1</i>	6.8	9.3	1.4	vacuole membrane protein 1
219049_at	55790	<i>CSGALNACT1</i>	47.0	64.2	1.4	chondroitin sulfate N-acetylgalactosaminyltransferase 1
201044_x_at	1843	<i>DUSP1</i>	9.9	13.5	1.4	<i>dual specificity phosphatase 1</i>
208335_s_at	2532	<i>ACKR1</i>	11.2	15.2	1.4	atypical chemokine receptor 1 (Duffy blood group)
200732_s_at	7803	<i>PTP4A1</i>	10.1	13.7	1.4	protein tyrosine phosphatase type IVA, member 1
205409_at	2355	<i>FOSL2</i>	4.3	5.8	1.3	FOS-like antigen 2
203795_s_at	605	<i>BCL7A</i>	5.2	7.0	1.3	B-cell CLL/lymphoma 7A
222784_at	64093	<i>SMOC1</i>	46.4	62.3	1.3	SPARC related modular calcium binding 1
205206_at	3730	<i>ANOS1</i>	10.6	14.2	1.3	anosmin 1
203638_s_at	2263	<i>FGFR2</i>	43.8	58.4	1.3	<i>fibroblast growth factor receptor 2</i>
231798_at	9241	<i>NOG</i>	4.8	6.4	1.3	noggin
204621_s_at	4929	<i>NR4A2</i>	98.4	131.0	1.3	<i>nuclear receptor subfamily 4, group A, member 2</i>
220225_at	50805	<i>IRX4</i>	6.8	9.0	1.3	iroquois homeobox 4
213436_at	1268	<i>CNR1</i>	9.9	13.1	1.3	cannabinoid receptor 1 (brain)
227188_at	59271	<i>EVA1C</i>	9.4	12.4	1.3	eva-1 homolog C (C. elegans)
236911_at	57494	<i>RIMKLB</i>	4.7	6.2	1.3	ribosomal modification protein rimK-like family member B
210837_s_at	5144	<i>PDE4D</i>	19.2	25.3	1.3	<i>phosphodiesterase 4D, cAMP-specific</i>
202724_s_at	2308	<i>FOXO1</i>	7.6	10.0	1.3	forkhead box O1
219316_s_at	55640	<i>FLVCR2</i>	7.0	9.2	1.3	feline leukemia virus subgroup C cellular receptor family, member 2
223430_at	23235	<i>SIK2</i>	4.8	6.3	1.3	salt-inducible kinase 2
210102_at	4013	<i>VWA5A</i>	12.8	16.7	1.3	von Willebrand factor A domain containing 5A
207213_s_at	9099	<i>USP2</i>	3.7	4.8	1.3	ubiquitin specific peptidase 2
214438_at	3142	<i>HLX</i>	5.1	6.6	1.3	H2.0-like homeobox
218541_s_at	56892	<i>C8orf4</i>	44.5	57.6	1.3	chromosome 8 open reading frame 4
243438_at	27115	<i>PDE7B</i>	34.1	43.8	1.3	phosphodiesterase 7B
225516_at	6542	<i>SLC7A2</i>	23.7	30.4	1.3	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2
208078_s_at	150094	<i>SIK1</i>	26.6	33.8	1.3	salt-inducible kinase 1
216627_s_at	2683	<i>B4GALT1</i>	16.1	20.4	1.3	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1
216248_s_at	4929	<i>NR4A2</i>	109.9	139.0	1.3	<i>nuclear receptor subfamily 4, group A, member 2</i>
209184_s_at	8660	<i>IRS2</i>	5.7	7.2	1.3	insulin receptor substrate 2
211631_x_at	2683	<i>B4GALT1</i>	12.3	15.5	1.3	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1
1555585_a_at	153745	<i>FAM71B</i>	13.9	17.4	1.3	family with sequence similarity 71, member B
209355_s_at	8613	<i>PLPP3</i>	9.6	12.0	1.3	phospholipid phosphatase 3
211143_x_at	3164	<i>NR4A1</i>	12.2	15.2	1.2	nuclear receptor subfamily 4, group A, member 1
207626_s_at	6542	<i>SLC7A2</i>	11.9	14.8	1.2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2
207978_s_at	8013	<i>NR4A3</i>	188.8	234.9	1.2	<i>nuclear receptor subfamily 4, group A, member 3</i>
205193_at	23764	<i>MAFF</i>	9.1	11.3	1.2	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F
1552736_a_at	81832	<i>NETO1</i>	10.0	12.4	1.2	neuropilin (NRP) and tolloid (TLL)-like 1
204456_s_at	2619	<i>GAS1</i>	12.9	16.0	1.2	<i>growth arrest-specific 1</i>

200731_s_at	7803	<i>PTP4A1</i>	12.0	14.8	1.2	protein tyrosine phosphatase type IVA, member 1
205330_at	4330	<i>MN1</i>	10.8	13.3	1.2	meningioma (disrupted in balanced translocation) 1
219093_at	55022	<i>PID1</i>	17.3	21.2	1.2	phosphotyrosine interaction domain containing 1
219383_at	79899	<i>PRR5L</i>	8.5	10.4	1.2	proline rich 5 like
230398_at	84951	<i>TNS4</i>	14.7	18.0	1.2	tensin 4
228962_at	5144	<i>PDE4D</i>	43.7	53.4	1.2	phosphodiesterase 4D, cAMP-specific
208425_s_at	26115	<i>TANC2</i>	10.4	12.7	1.2	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2
203639_s_at	2263	<i>FGFR2</i>	46.9	57.2	1.2	fibroblast growth factor receptor 2
204032_at	8412	<i>BCAR3</i>	3.2	3.9	1.2	breast cancer anti-estrogen resistance 3
239650_at	344148	<i>NCKAP5</i>	13.5	16.4	1.2	NCK-associated protein 5
224831_at	80315	<i>CPEB4</i>	8.4	10.2	1.2	cytoplasmic polyadenylation element binding protein 4
203548_s_at	4023	<i>LPL</i>	31.3	37.9	1.2	lipoprotein lipase
204491_at	5144	<i>PDE4D</i>	27.9	33.8	1.2	phosphodiesterase 4D, cAMP-specific
205003_at	9732	<i>DOCK4</i>	9.5	11.5	1.2	dedicator of cytokinesis 4
211401_s_at	2263	<i>FGFR2</i>	42.7	51.7	1.2	fibroblast growth factor receptor 2
209583_s_at	4345	<i>CD200</i>	21.6	26.1	1.2	CD200 molecule
227099_s_at	387763	<i>C11orf96</i>	14.9	18.0	1.2	chromosome 11 open reading frame 96
224829_at	80315	<i>CPEB4</i>	7.8	9.4	1.2	cytoplasmic polyadenylation element binding protein 4
222783_s_at	64093	<i>SMOC1</i>	39.9	48.0	1.2	SPARC related modular calcium binding 1
1566901_at	7050	<i>TGIF1</i>	4.0	4.8	1.2	TGFB induced factor homeobox 1
206865_at	8739	<i>HRK</i>	13.5	16.2	1.2	harakiri, BCL2 interacting protein
228507_at	5139	<i>PDE3A</i>	11.5	13.8	1.2	phosphodiesterase 3A, cGMP-inhibited
213221_s_at	23235	<i>SIK2</i>	7.6	9.1	1.2	salt-inducible kinase 2
1556185_a_at	79689	<i>STEAP4</i>	35.6	42.4	1.2	STEAP family member 4
209582_s_at	4345	<i>CD200</i>	23.5	28.0	1.2	CD200 molecule
205289_at	650	<i>BMP2</i>	59.7	70.9	1.2	bone morphogenetic protein 2
228964_at	639	<i>PRDM1</i>	25.0	29.7	1.2	PR domain containing 1, with ZNF domain
222802_at	1906	<i>EDN1</i>	9.2	10.9	1.2	endothelin 1
204622_x_at	4929	<i>NR4A2</i>	95.0	112.5	1.2	nuclear receptor subfamily 4, group A, member 2
218113_at	23670	<i>TMEM2</i>	6.7	7.9	1.2	transmembrane protein 2
205207_at	3569	<i>IL6</i>	31.5	37.1	1.2	interleukin 6
1568949_at	26207	<i>PITPNC1</i>	7.9	9.3	1.2	phosphatidylinositol transfer protein, cytoplasmic 1
218995_s_at	1906	<i>EDN1</i>	9.8	11.5	1.2	endothelin 1
225582_at	85450	<i>ITPRIP</i>	16.3	19.1	1.2	inositol 1,4,5-trisphosphate receptor interacting protein
204011_at	10253	<i>SPRY2</i>	4.7	5.5	1.2	sprouty RTK signaling antagonist 2
225262_at	2355	<i>FOSL2</i>	5.3	6.2	1.2	FOS-like antigen 2
227337_at	353322	<i>ANKRD37</i>	6.5	7.6	1.2	ankyrin repeat domain 37
202241_at	10221	<i>TRIB1</i>	11.3	13.2	1.2	tribbles pseudokinase 1
223566_s_at	54880	<i>BCOR</i>	4.4	5.1	1.2	BCL6 corepressor
213182_x_at	1028	<i>CDKN1C</i>	25.9	30.0	1.2	cyclin-dependent kinase inhibitor 1C (p57, Kip2)
213348_at	1028	<i>CDKN1C</i>	21.5	24.9	1.2	cyclin-dependent kinase inhibitor 1C (p57, Kip2)
203549_s_at	4023	<i>LPL</i>	32.5	37.6	1.2	lipoprotein lipase
1554544_a_at	4155	<i>MBP</i>	4.5	5.2	1.2	myelin basic protein
209959_at	8013	<i>NR4A3</i>	282.2	325.0	1.2	nuclear receptor subfamily 4, group A, member 3
224828_at	80315	<i>CPEB4</i>	8.6	9.9	1.2	cytoplasmic polyadenylation element binding protein 4
237187_at	8739	<i>HRK</i>	12.1	13.9	1.1	harakiri, BCL2 interacting protein
240413_at	149628	<i>PYHIN1</i>	5.5	6.3	1.1	pyrin and HIN domain family, member 1
202388_at	5997	<i>RGS2</i>	20.4	23.3	1.1	regulator of G-protein signaling 2
213050_at	23242	<i>COBL</i>	27.5	31.4	1.1	cordon-bleu WH2 repeat protein
203313_s_at	7050	<i>TGIF1</i>	5.7	6.5	1.1	TGFB-induced factor homeobox 1
219433_at	54880	<i>BCOR</i>	5.0	5.7	1.1	BCL6 corepressor
238649_at	26207	<i>PITPNC1</i>	25.3	28.8	1.1	phosphatidylinositol transfer protein, cytoplasmic 1
202723_s_at	2308	<i>FOXO1</i>	9.5	10.8	1.1	forkhead box O1
210632_s_at	6442	<i>SGCA</i>	5.1	5.8	1.1	sarcoglycan alpha
201925_s_at	1604	<i>CD55</i>	8.1	9.2	1.1	CD55 molecule, decay accelerating factor for complement (Cromer blood group)
228340_at	7090	<i>TLE3</i>	7.4	8.4	1.1	transducin-like enhancer of split 3
230109_at	27115	<i>PDE7B</i>	29.6	33.6	1.1	phosphodiesterase 7B
1553962_s_at	388	<i>RHOB</i>	5.3	6.0	1.1	ras homolog family member B
216894_x_at	1028	<i>CDKN1C</i>	21.5	24.3	1.1	cyclin-dependent kinase inhibitor 1C (p57, Kip2)
226575_at	58499	<i>ZNF462</i>	6.2	7.0	1.1	zinc finger protein 462
219534_x_at	1028	<i>CDKN1C</i>	22.0	24.8	1.1	cyclin-dependent kinase inhibitor 1C (p57, Kip2)
1555006_at	144406	<i>WDR66</i>	12.8	14.4	1.1	WD repeat domain 66
225987_at	79689	<i>STEAP4</i>	26.5	29.8	1.1	STEAP family member 4
206359_at	9021	<i>SOCS3</i>	21.6	24.2	1.1	suppressor of cytokine signaling 3
209772_s_at	100133941	<i>CD24</i>	14.2	15.9	1.1	CD24 molecule
224325_at	8325	<i>FZD8</i>	7.5	8.4	1.1	frizzled class receptor 8
206472_s_at	7090	<i>TLE3</i>	4.2	4.7	1.1	transducin-like enhancer of split 3
208606_s_at	54361	<i>WNT4</i>	22.5	25.1	1.1	wingless-type MMTV integration site family, member 4
206389_s_at	5139	<i>PDE3A</i>	10.5	11.7	1.1	phosphodiesterase 3A, cGMP-inhibited
226858_at	1454	<i>CSNK1E</i>	11.4	12.7	1.1	casein kinase 1, epsilon
36711_at	23764	<i>MAFF</i>	10.5	11.7	1.1	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F
229720_at	573	<i>BAG1</i>	9.3	10.3	1.1	BCL2-associated athanogene
205501_at	10846	<i>PDE10A</i>	15.5	17.1	1.1	phosphodiesterase 10A
237939_at	2044	<i>EPHA5</i>	14.6	16.1	1.1	EPH receptor A5
201739_at	6446	<i>SGK1</i>	19.6	21.6	1.1	serum/glucocorticoid regulated kinase 1
205157_s_at	3872	<i>KRT17</i>	11.9	13.1	1.1	keratin 17, type I
239818_x_at	10221	<i>TRIB1</i>	12.0	13.2	1.1	tribbles pseudokinase 1
203574_at	4783	<i>NFIL3</i>	6.2	6.8	1.1	nuclear factor, interleukin 3 regulated
239461_at	117248	<i>GALNT15</i>	39.7	43.5	1.1	polypeptide N-acetylglactosaminyltransferase 15
239367_at	627	<i>BDNF</i>	11.8	12.9	1.1	brain-derived neurotrophic factor
219911_s_at	28231	<i>SLCO4A1</i>	13.1	14.3	1.1	solute carrier organic anion transporter family, member 4A1
229709_at	483	<i>ATP1B3</i>	27.0	29.3	1.1	ATPase, Na ⁺ /K ⁺ transporting, beta 3 polypeptide
220335_x_at	23491	<i>CES3</i>	15.4	16.7	1.1	carboxylesterase 3
225919_s_at	203228	<i>C9orf72</i>	3.7	4.0	1.1	chromosome 9 open reading frame 72
201645_at	3371	<i>TNC</i>	12.6	13.6	1.1	tenascin C
209681_at	10560	<i>SLC19A2</i>	8.0	8.6	1.1	solute carrier family 19 (thiamine transporter), member 2
220540_at	60598	<i>KCNK15</i>	22.1	23.7	1.1	potassium channel, two pore domain subfamily K, member 15
201939_at	10769	<i>PLK2</i>	4.2	4.5	1.1	polo-like kinase 2
224952_at	26115	<i>TANC2</i>	9.9	10.6	1.1	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2
206356_s_at	2774	<i>GNAL</i>	12.2	13.0	1.1	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type
227529_s_at	9590	<i>AKAP12</i>	9.1	9.7	1.1	A kinase (PRKA) anchor protein 12
228132_at	84448	<i>ABLIM2</i>	12.4	13.2	1.1	actin binding LIM protein family, member 2
224071_at	50604	<i>IL20</i>	12.7	13.5	1.1	interleukin 20
231067_s_at	9590	<i>AKAP12</i>	8.0	8.5	1.1	A kinase (PRKA) anchor protein 12

1553133_at	203228	<i>C9orf72</i>	6.5	6.9	1.1	chromosome 9 open reading frame 72
227613_at	55422	<i>ZNF331</i>	13.0	13.8	1.1	zinc finger protein 331
214446_at	22936	<i>ELL2</i>	6.6	7.0	1.1	elongation factor, RNA polymerase II, 2
226614_s_at	83648	<i>FAM167A</i>	12.3	13.0	1.1	family with sequence similarity 167, member A
237252_at	7056	<i>THBD</i>	7.0	7.4	1.1	thrombomodulin
222015_at	1454	<i>CSNK1E</i>	16.9	17.7	1.0	casein kinase 1, epsilon
202340_x_at	3164	<i>NR4A1</i>	14.2	14.8	1.0	nuclear receptor subfamily 4, group A, member 1
236300_at	5139	<i>PDE3A</i>	12.2	12.7	1.0	phosphodiesterase 3A, cGMP-inhibited
209774_x_at	2920	<i>CXCL2</i>	16.4	16.9	1.0	chemokine (C-X-C motif) ligand 2
205239_at	374	<i>AREG</i>	10.7	11.0	1.0	amphiregulin
210775_x_at	842	<i>CASP9</i>	10.7	11.0	1.0	caspace 9
203984_s_at	842	<i>CASP9</i>	11.3	11.6	1.0	caspace 9
225801_at	114907	<i>FBXO32</i>	11.7	12.0	1.0	F-box protein 32
219228_at	55422	<i>ZNF331</i>	13.0	13.3	1.0	zinc finger protein 331
223379_s_at	26524	<i>LATS2</i>	4.5	4.6	1.0	large tumor suppressor kinase 2
233972_s_at	55079	<i>FEZF2</i>	5.6	5.7	1.0	FEZ family zinc finger 2
209189_at	2353	<i>FOS</i>	11.6	11.8	1.0	FBJ murine osteosarcoma viral oncogene homolog
225955_at	284207	<i>METRNL</i>	5.8	5.9	1.0	meteorin, glial cell differentiation regulator-like
232267_at	283383	<i>ADGRD1</i>	10.1	10.2	1.0	adhesion G protein-coupled receptor D1
229414_at	26207	<i>PITPNC1</i>	12.9	13.0	1.0	phosphatidylinositol transfer protein, cytoplasmic 1
209457_at	1847	<i>DUSP5</i>	3.8	3.8	1.0	dual specificity phosphatase 5
218881_s_at	2355	<i>FOSL2</i>	5.0	5.0	1.0	FOS-like antigen 2
220088_at	728	<i>CSAR1</i>	31.1	31.1	1.0	complement component 5a receptor 1
221011_s_at	81606	<i>LBH</i>	5.0	5.0	1.0	limb bud and heart development
223085_at	25897	<i>RNF19A</i>	6.1	6.1	1.0	ring finger protein 19A, RBR E3 ubiquitin protein ligase
227458_at	29126	<i>CD274</i>	3.2	3.2	1.0	CD274 molecule
221541_at	83716	<i>CRISPLD2</i>	78.9	78.7	1.0	cysteine-rich secretory protein LCCL domain containing 2
205476_at	6364	<i>CCL20</i>	29.8	29.5	1.0	chemokine (C-C motif) ligand 20
216598_s_at	6347	<i>CCL2</i>	8.8	8.7	1.0	chemokine (C-C motif) ligand 2
225999_at	57494	<i>RIMKLB</i>	8.7	8.6	1.0	ribosomal modification protein rimK-like family member B
225544_at	6926	<i>TBX3</i>	7.1	7.0	1.0	T-box 3
208250_s_at	1755	<i>DMBT1</i>	12.5	12.3	1.0	deleted in malignant brain tumors 1
235085_at	157285	<i>PRAG1</i>	4.9	4.8	1.0	homolog of rat pragma of Rnd2
212099_at	388	<i>RHOB</i>	4.8	4.7	1.0	ras homolog family member B
206404_at	2254	<i>FGF9</i>	7.5	7.2	1.0	fibroblast growth factor 9
227697_at	9021	<i>SOC33</i>	19.0	18.2	1.0	suppressor of cytokine signaling 3
202498_s_at	6515	<i>SLC2A3</i>	7.0	6.7	1.0	solute carrier family 2 (facilitated glucose transporter), member 3
210136_at	4155	<i>MBP</i>	5.8	5.5	0.9	myelin basic protein
225407_at	4155	<i>MBP</i>	5.3	5.0	0.9	myelin basic protein
213139_at	6591	<i>SNAI2</i>	8.6	8.1	0.9	snail family zinc finger 2
205896_at	6583	<i>SLC22A4</i>	13.2	12.4	0.9	solute carrier family 22 (organic cation/zwitterion transporter), member 4
228284_at	7088	<i>TLE1</i>	3.3	3.1	0.9	transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila)
230348_at	26524	<i>LATS2</i>	3.3	3.1	0.9	large tumor suppressor kinase 2
203887_s_at	7056	<i>THBD</i>	6.2	5.8	0.9	thrombomodulin
201169_s_at	8553	<i>BHLHE40</i>	5.9	5.5	0.9	basic helix-loop-helix family, member e40
206924_at	3589	<i>IL11</i>	6.5	6.0	0.9	interleukin 11
211550_at	1956	<i>EGFR</i>	44.1	40.6	0.9	epidermal growth factor receptor
207430_s_at	4477	<i>MSMB</i>	7.4	6.8	0.9	microseminoprotein, beta-
221841_s_at	9314	<i>KLF4</i>	5.5	5.0	0.9	Kruppel-like factor 4 (gut)
201170_s_at	8553	<i>BHLHE40</i>	5.2	4.7	0.9	basic helix-loop-helix family, member e40
203796_s_at	605	<i>BCL7A</i>	5.6	5.0	0.9	B-cell CLL/lymphoma 7A
235367_at	84665	<i>MYPN</i>	13.1	11.5	0.9	myopalladin
220483_s_at	25897	<i>RNF19A</i>	7.3	6.4	0.9	ring finger protein 19A, RBR E3 ubiquitin protein ligase
223916_s_at	54880	<i>BCOR</i>	4.0	3.5	0.9	BCL6 corepressor
1552755_at	157983	<i>C9orf66</i>	8.7	7.5	0.9	chromosome 9 open reading frame 66
204938_s_at	5350	<i>PLN</i>	4.7	4.0	0.9	phospholamban
237328_at	55195	<i>C14orf105</i>	18.6	15.5	0.8	chromosome 14 open reading frame 105
223484_at	84419	<i>C15orf48</i>	20.8	17.3	0.8	chromosome 15 open reading frame 48
205051_s_at	3815	<i>KIT</i>	4.1	3.3	0.8	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
1559141_s_at	57693; 400728	<i>FAM87A</i>	11.2	8.7	0.8	family with sequence similarity 87, member A; family with sequence similarity 87, member B
225626_at	55824	<i>PAG1</i>	2.9	2.1	0.7	phosphoprotein membrane anchor with glycosphingolipid microdomains 1
1556420_s_at	388403	<i>YPEL2</i>	8.4	6.0	0.7	yippee like 2
206616_s_at	53616	<i>ADAM22</i>	10.3	7.2	0.7	ADAM metallopeptidase domain 22
1559987_at	124540	<i>MSI2</i>	4.6	3.1	0.7	musashi RNA binding protein 2
233002_at	57718	<i>PPP4R4</i>	13.4	8.9	0.7	protein phosphatase 4, regulatory subunit 4
1554199_at	5800	<i>PTPRO</i>	8.7	5.5	0.6	protein tyrosine phosphatase, receptor type, O
208083_s_at	3694	<i>ITGB6</i>	9.2	5.8	0.6	integrin beta 6
202935_s_at	6662	<i>SOX9</i>	4.9	3.0	0.6	SRY box 9
223834_at	29126	<i>CD274</i>	4.3	2.6	0.6	CD274 molecule
238378_at	285513	<i>GPRIN3</i>	7.0	4.1	0.6	GPRIN family member 3
205466_s_at	9957	<i>HS3ST1</i>	8.6	5.0	0.6	heparan sulfate (glucosamine) 3-O-sulfotransferase 1
206035_at	5966	<i>REL</i>	4.5	2.6	0.6	v-rel avian reticuloendotheliosis viral oncogene homolog
216639_at	27286	<i>SRPX2</i>	14.5	8.0	0.6	sushi-repeat containing protein, X-linked 2
1565657_at	54918	<i>CMTM6</i>	50.0	24.9	0.5	CKLF-like MARVEL transmembrane domain containing 6
239530_at	119	<i>ADD2</i>	9.7	4.8	0.5	adducin 2 (beta)
242543_at	284948	<i>SH2D6</i>	2.5	1.1	0.4	SH2 domain containing 6
237804_at	8701	<i>DNAH11</i>	20.0	8.3	0.4	dynein, axonemal, heavy chain 11
241547_at	29974	<i>A1CF</i>	4.2	1.7	0.4	APOBEC1 complementation factor
211119_at	2100	<i>ESR2</i>	34.9	13.8	0.4	estrogen receptor 2 (ER beta)
1555118_at	956	<i>ENTPD3</i>	6.1	2.2	0.4	ectonucleoside triphosphate diphosphohydrolase 3
205764_at	1452	<i>CSNK1A1</i>	15.6	4.4	0.3	casein kinase 1, alpha 1
239145_at	84330	<i>ZNF414</i>	27.0	7.1	0.3	zinc finger protein 414
229152_at	260436	<i>FDSCP</i>	11.0	2.5	0.2	follicular dendritic cell secreted protein
221305_s_at	54576; 54600	<i>UGT1A8</i>	11.9	2.5	0.2	UDP glucuronosyltransferase 1 family, polypeptide A8; UDP glucuronosyltransferase 1 family, polypeptide A9

Supplemental TABLE 7. Differential sensitivity of genes to salmeterol. DEGs (≥ 2 -fold, ≤ 0.5 -fold; FDR $\leq 5\%$) were identified in BEAS-2B cells by RNA-Seq after 2h exposure to a maximally-effective concentration of salmeterol (Salm₁₀₀). The magnitude of gene expression changes produced by Salm_{0.3} was then expressed as a percentage of the corresponding Salm₁₀₀ data. These values are listed in increasing order of sensitivity (righthand column) with *NPTX1* and *TCF21* being the least and most sensitive induced genes (pink shading) respectively and *C10orf10* and *KRTAP2-4/KRTAP2-5* being the least and most sensitive repressed genes (blue shading) respectively.

<i>Official Gene Symbol</i>	Salm _{0.3} (fold change)	Salm ₁₀₀ (fold change)	(Salm _{0.3} /Salm ₁₀₀) $\times 100$
<i>NPTX1</i>	2.19	18.90	11.6
<i>FLRT3</i>	2.08	17.88	11.6
<i>IL6</i>	2.39	18.64	12.8
<i>NR4A3</i>	14.03	102.54	13.7
<i>NR4A2</i>	7.94	49.52	16.0
<i>NPPC</i>	1.22	7.11	17.2
<i>RRAD</i>	1.99	10.27	19.4
<i>SGK1</i>	2.64	13.36	19.8
<i>STC1</i>	1.61	8.00	20.1
<i>CXCL2</i>	1.25	6.11	20.5
<i>RGS2</i>	2.55	11.24	22.7
<i>ZNF331</i>	4.29	18.00	23.8
<i>RAB3A</i>	1.30	5.39	24.1
<i>CRISPLD2</i>	2.48	10.20	24.3
<i>PSD4</i>	1.71	6.68	25.6
<i>CD200</i>	4.00	14.52	27.5
<i>KRT16</i>	1.72	6.15	28.0
<i>RHOB</i>	1.59	5.70	27.9
<i>TBX3</i>	1.49	5.28	28.2
<i>FGF18</i>	0.96	3.34	28.7
<i>C11orf96</i>	1.54	5.31	29.0
<i>ARTN</i>	0.95	3.20	29.7
<i>DAW1</i>	0.97	3.23	30.0
<i>PDE4D</i>	3.01	9.65	31.2
<i>SLFN1</i>	2.68	8.40	31.9
<i>KRT17</i>	1.64	5.13	32.0
<i>UBE2QL1</i>	2.28	7.06	32.3
<i>NFATC2</i>	1.27	3.92	32.4
<i>IL11</i>	2.91	8.94	32.6
<i>LOC102724428/SIK1</i>	2.04	6.28	32.5
<i>GEM</i>	1.24	3.73	33.2
<i>WNT4</i>	2.06	6.06	34.0
<i>ITPRIP</i>	1.71	4.99	34.3
<i>CBARP</i>	1.28	3.73	34.3
<i>MN1</i>	1.38	4.00	34.5
<i>CD24</i>	1.85	5.35	34.6
<i>ITPKB</i>	1.95	5.54	35.2
<i>GAS1</i>	2.93	8.11	36.1
<i>RND1</i>	0.85	2.35	36.2
<i>AREG</i>	1.61	4.47	36.0
<i>TM4SF1</i>	2.87	7.78	36.9
<i>PPP1R3C</i>	2.17	5.82	37.3
<i>SLC16A6</i>	2.35	6.23	37.7
<i>ADAMTS15</i>	1.73	4.47	38.7
<i>MEDAG</i>	1.40	3.58	39.1
<i>ST3GAL1</i>	1.20	2.99	40.1
<i>FOSB</i>	1.18	2.95	40.0
<i>ANKRD37</i>	1.47	3.66	40.2
<i>GPCPD1</i>	1.65	4.08	40.4
<i>CYP26B1</i>	1.82	4.47	40.7
<i>CPEB4</i>	1.59	3.92	40.6
<i>SLC2A3</i>	1.25	3.07	40.7
<i>NR4A1</i>	2.77	6.73	41.2
<i>PLPP3</i>	2.38	5.78	41.2
<i>AVP1</i>	2.23	5.43	41.1
<i>SOCS3</i>	1.66	4.00	41.5
<i>TSC22D1</i>	1.73	4.17	41.5
<i>EDN2</i>	1.01	2.43	41.6
<i>PRDM1</i>	1.47	3.53	41.6
<i>KCNG1</i>	1.62	3.84	42.2
<i>REL</i>	1.43	3.36	42.6
<i>DUSP1</i>	1.72	4.03	42.7
<i>EFNA1</i>	1.45	3.41	42.5
<i>CASP9</i>	1.21	2.81	43.1
<i>SLCO4A1</i>	1.24	2.89	42.9

ACTC1	1.40	3.20	43.8
ZNF620	1.84	4.17	44.1
FZD8	1.22	2.77	44.0
ISG20	1.57	3.53	44.5
ID3	1.48	3.34	44.3
PMEPA1	1.23	2.75	44.7
FLVCR2	1.51	3.34	45.2
JAG1	1.28	2.85	44.9
USP2	1.25	2.77	45.1
JUNB	0.99	2.19	45.2
TOB1	1.12	2.46	45.5
ATF3	1.30	2.87	45.3
DMBT1	2.83	6.19	45.7
DEPDC7	2.11	4.63	45.6
FAM167A	1.83	3.94	46.4
CD274	1.45	3.14	46.2
IRX1	1.78	3.81	46.7
AKAP12	1.71	3.61	47.4
LATS2	1.67	3.53	47.3
CHMP1B	1.57	3.27	48.0
METRNL	1.31	2.71	48.3
ARRDC3	1.58	3.27	48.3
DIO2	1.40	2.89	48.4
SNAI2	1.01	2.07	48.8
EDNRA	1.83	3.71	49.3
LPL	1.61	3.25	49.5
TGIF1	1.32	2.66	49.6
WNT10B	1.13	2.27	49.8
SYNPO	1.34	2.68	50.0
ING1	1.16	2.33	49.8
ACKR3	1.78	3.53	50.4
HLX	1.17	2.33	50.2
GPR37	1.21	2.39	50.6
CITED4	2.10	4.14	50.7
PPP1R3B	1.61	3.18	50.6
PTP4A1	1.25	2.46	50.8
RDH10	1.13	2.23	60.7
BCL2L11	1.77	3.46	51.2
B4GALT1	1.12	2.17	51.6
FOXC1	1.34	2.60	51.5
ARMS2	1.27	2.45	51.8
PER1	1.59	3.07	51.8
SHISA2	1.46	2.83	51.6
OTUD1	1.52	2.91	52.2
EPHB3	1.41	2.69	52.4
EPGN	1.42	2.69	52.8
ETS2	1.41	2.68	52.6
CHSY1	1.38	2.60	53.1
IGFBP4	1.23	2.31	53.2
PDE4B	2.58	4.82	53.5
KLF4	1.41	2.64	53.4
BDNF	1.97	3.66	53.6
BCL3	1.32	2.45	53.9
MISP	1.39	2.58	53.9
MAP3K8	1.21	2.25	53.8
KBTBD11	1.22	2.25	54.2
TLE3	1.12	2.06	54.4
CES3	1.73	3.18	54.4
NFKBIZ	1.21	2.23	54.3
PLK2	1.24	2.27	54.6
MALSU1	1.22	2.23	54.7
ULBP2	1.17	2.14	54.7
ODC1	1.13	2.06	54.9
DDIT4	2.01	3.63	55.4
ISL2	1.43	2.57	55.6
DUSP10	1.21	2.17	55.8
SNRK	1.53	2.71	56.5
PTGES	1.36	2.41	56.4
TMEM2	1.23	2.19	56.2
KLHL21	1.13	2.01	56.2
FAM46A	1.26	2.22	56.8
COL3A1	1.51	2.66	56.8
S1PR1	1.58	2.79	56.6
GRAMD1B	1.15	2.01	57.2
CEBPD	2.23	3.89	57.3
SLC19A2	1.29	2.25	57.3
NTF3	1.39	2.39	58.2

<i>FST</i>	1.36	2.35	57.9
<i>IL6R</i>	1.22	2.11	57.8
<i>LBH</i>	1.45	2.51	57.8
<i>TNFRSF1B</i>	1.18	2.04	57.8
<i>DUSP8</i>	1.33	2.28	58.3
<i>SIRPA</i>	1.43	2.45	58.4
<i>SLC38A2</i>	1.37	2.33	58.8
<i>PLEKHA2</i>	1.33	2.27	58.6
<i>BTG1</i>	1.30	2.22	58.6
<i>SMOC1</i>	1.72	2.93	58.7
<i>TMEM190</i>	2.35	3.94	59.6
<i>MAFK</i>	1.23	2.06	59.7
<i>RNF125</i>	1.56	2.60	60.0
<i>PRAG1</i>	1.46	2.45	59.6
<i>AMACR</i>	1.34	2.23	60.1
<i>SCG2</i>	1.37	2.23	61.4
<i>EDN1</i>	1.42	2.31	61.5
<i>NFIL3</i>	1.25	2.00	62.5
<i>MITF</i>	1.36	2.16	63.0
<i>NUAK2</i>	1.33	2.11	63.0
<i>IRX2</i>	1.27	2.03	62.6
<i>TMEM217</i>	1.38	2.17	63.6
<i>MEGF9</i>	1.46	2.27	64.3
<i>KLF9</i>	1.37	2.11	64.9
<i>FGF9</i>	1.56	2.39	65.3
<i>CCL2</i>	1.51	2.28	66.2
<i>BCL7A</i>	1.82	2.73	66.7
<i>TSKU</i>	1.41	2.11	66.8
<i>SETD1B</i>	1.38	2.06	67.0
<i>LURAP1L</i>	1.56	2.30	67.8
<i>PHLDA3</i>	1.37	2.01	68.2
<i>WDR66</i>	1.59	2.31	68.8
<i>ZNF462</i>	1.65	2.38	69.3
<i>PKDCC</i>	1.39	2.01	69.2
<i>ARID5B</i>	1.48	2.03	72.9
<i>IL24</i>	1.93	2.50	77.2
<i>FRAT2</i>	1.64	2.04	80.4
<i>TCF21</i>	1.88	2.27	83.0
<i>C10orf10</i>	1.01	0.38	37.6
<i>TXNIP</i>	0.93	0.35	37.6
<i>FOSL1</i>	0.57	0.23	40.0
<i>EGR1</i>	0.54	0.23	42.6
<i>ANKRD34A</i>	0.77	0.34	44.1
<i>RGS4</i>	0.60	0.27	45.0
<i>KLF10</i>	0.52	0.25	48.1
<i>HYLS1</i>	0.78	0.42	53.8
<i>JUN</i>	0.75	0.42	56.0
<i>KRTAP1-5</i>	0.79	0.47	59.4
<i>BHLHE41</i>	0.80	0.48	60.0
<i>METTL7B</i>	0.66	0.39	59.0
<i>SPRY4</i>	0.55	0.34	61.8
<i>DUSP6</i>	0.64	0.40	62.5
<i>HES1</i>	0.51	0.35	68.6
<i>KRTAP2-3/KRTAP2-4</i>	0.67	0.48	71.6

Supplemental TABLE 8. Effects of RNO on salmeterol-induced gene expression changes. DEGs (≥ 2 -fold; ≤ 0.5 ; FDR $\leq 5\%$) were identified in BEAS-2B cells by RNA-Seq after 2h exposure to a maximally-effective concentration of salmeterol (Salm₁₀₀; Supplemental Table 7). The expression levels of the same genes in response to vehicle (V), RNO (1 μ M), Salm_{0.3} and Salm_{0.3}+RNO are shown (irrespective of FDR) and are given in TPM. The columns shaded grey show synergy indices of the 180 genes upregulated by Salm₁₀₀. These are expressed as either changes in gene expression produced by Salm_{0.3} and RNO in combination relative to the sum (Σ) of their individual effects, or changes in gene expression produced by Salm_{0.3} and RNO in combination minus the sum (Σ) of their individual effects. The higher the value the greater was the effect of RNO on Salm_{0.3}-induced gene induction.

Induced Genes	Synergy Indices								
	Official Gene Symbol	Vehicle (V)	Salm ₁₀₀	RNO	Salm _{0.3}	Salm _{0.3} + RNO	Σ (Salm _{0.3} , RNO) - V	Salm _{0.3} + RNO	(Salm _{0.3} + RNO) -
								Σ (Salm _{0.3} , RNO) - V	Σ (Salm _{0.3} , RNO) - V
<i>FLRT3</i>	0.12	2.26	0.15	0.27	0.95	0.30	3.17	28.76	
<i>NR4A2</i>	0.64	32.44	1.27	5.32	17.41	5.95	2.93	35.33	
<i>NR4A3</i>	0.61	62.92	2.07	8.61	29.13	10.07	2.89	30.29	
<i>IL6</i>	3.47	65.49	3.88	8.43	23.50	8.84	2.66	22.39	
<i>NPTX1</i>	0.08	1.51	0.09	0.19	0.49	0.20	2.45	19.21	
<i>RGS2</i>	4.88	55.07	5.72	12.74	32.52	13.58	2.39	34.39	
<i>STC1</i>	0.18	1.50	0.23	0.32	0.87	0.37	2.35	33.33	
<i>ZNF331</i>	5.49	99.63	7.41	23.80	57.72	25.72	2.24	32.12	
<i>RAB3A</i>	0.56	3.07	0.52	0.78	1.65	0.74	2.23	29.64	
<i>CXCL2</i>	0.52	3.28	0.57	0.69	1.64	0.74	2.22	27.44	
<i>SGK1</i>	18.39	243.56	23.61	49.00	116.79	54.22	2.15	25.69	
<i>NPPC</i>	0.12	1.00	0.17	0.20	0.49	0.25	1.96	24.00	
<i>RND1</i>	0.42	1.01	0.30	0.42	0.57	0.30	1.90	26.73	
<i>FGF18</i>	0.39	1.29	0.43	0.37	0.76	0.41	1.85	27.13	
<i>EDN2</i>	0.80	1.94	0.76	0.81	1.42	0.77	1.84	33.51	
<i>CBARP</i>	2.58	9.74	2.68	3.30	6.27	3.40	1.84	29.47	
<i>LOC102724428/SIK1</i>	32.35	203.29	38.72	66.72	132.00	73.09	1.81	28.98	
<i>RHOB</i>	31.72	179.65	36.96	50.52	97.47	55.76	1.75	23.22	
<i>ARTN</i>	0.64	2.11	0.63	0.64	1.10	0.63	1.75	22.27	
<i>KRT16</i>	0.44	2.77	0.47	0.76	1.36	0.79	1.72	20.58	
<i>FOSB</i>	4.68	13.81	4.78	5.45	9.49	5.55	1.71	28.53	
<i>TBX3</i>	2.55	13.44	2.84	3.83	6.84	4.12	1.66	20.24	
<i>SLFN1</i>	0.28	2.32	0.37	0.80	1.47	0.89	1.65	25.00	
<i>NR4A1</i>	18.52	125.86	27.54	51.70	98.59	60.72	1.62	30.09	
<i>CD274</i>	1.71	5.38	1.53	2.51	3.77	2.33	1.62	26.77	
<i>DAW1</i>	0.55	1.83	0.43	0.55	0.69	0.43	1.60	14.21	
<i>RRAD</i>	0.20	2.12	0.26	0.42	0.75	0.48	1.56	12.74	
<i>KRT17</i>	284.11	1465.71	319.24	466.31	782.42	501.44	1.56	19.17	
<i>CRISPLD2</i>	2.40	23.85	2.87	5.83	9.77	6.30	1.55	14.55	
<i>GEM</i>	7.40	27.67	8.48	9.21	15.95	10.29	1.55	20.46	
<i>PDE4D</i>	1.10	10.67	1.75	3.33	6.12	3.98	1.54	20.06	
<i>IL11</i>	25.22	222.67	38.39	73.51	133.20	86.68	1.54	20.89	
<i>MEDAG</i>	0.41	1.48	0.36	0.62	0.86	0.57	1.51	19.59	
<i>ANKRD37</i>	1.30	4.73	1.23	1.88	2.73	1.81	1.51	19.45	
<i>TOB1</i>	48.73	120.64	49.13	54.55	82.75	54.95	1.51	23.04	
<i>JUNB</i>	12.40	26.79	13.59	12.10	19.94	13.29	1.50	24.82	
<i>C11orf96</i>	0.18	1.04	0.20	0.30	0.48	0.32	1.50	15.38	
<i>SNAI2</i>	4.11	8.75	4.18	4.21	6.40	4.28	1.50	24.23	
<i>SLC2A3</i>	26.52	81.90	28.85	33.22	52.83	35.55	1.49	21.10	
<i>TM4SF1</i>	39.60	308.99	50.92	114.74	187.00	126.06	1.48	19.72	
<i>CD24</i>	30.69	159.56	33.85	56.06	87.78	59.22	1.48	17.90	
<i>PPP1R3C</i>	3.32	19.41	3.73	7.29	11.41	7.70	1.48	19.11	
<i>DUSP1</i>	52.17	210.86	69.67	89.78	158.71	107.28	1.48	24.39	
<i>REL</i>	2.29	7.76	2.52	3.29	5.19	3.52	1.47	21.52	
<i>GPCPD1</i>	3.58	14.67	3.96	5.93	9.25	6.31	1.47	20.04	
<i>ITPRIP</i>	5.54	27.69	6.27	9.52	15.01	10.25	1.46	17.19	
<i>ATF3</i>	17.07	49.14	18.00	22.33	34.05	23.26	1.46	21.96	
<i>TSC22D1</i>	32.97	138.61	36.08	57.81	89.07	60.92	1.46	20.31	
<i>CD200</i>	0.84	12.34	1.34	3.42	5.69	3.92	1.45	14.34	
<i>MN1</i>	0.52	2.02	0.52	0.71	1.03	0.71	1.45	15.84	
<i>PER1</i>	7.84	24.21	9.32	12.49	20.01	13.97	1.43	24.95	
<i>ADAMTS15</i>	1.54	6.69	1.73	2.69	4.12	2.88	1.43	18.54	
<i>GPR37</i>	1.37	3.26	1.49	1.63	2.49	1.75	1.42	22.70	
<i>WNT4</i>	0.16	1.05	0.19	0.35	0.54	0.38	1.42	15.24	
<i>ZNF620</i>	4.20	17.64	4.98	7.79	12.14	8.57	1.42	20.24	
<i>KLF4</i>	1.39	3.75	1.64	1.99	3.17	2.24	1.42	24.80	
<i>WNT10B</i>	0.90	2.10	0.81	1.03	1.32	0.94	1.40	18.10	
<i>UBE2QL1</i>	0.15	1.06	0.18	0.35	0.53	0.38	1.39	14.15	
<i>FZD8</i>	0.72	2.03	0.70	0.89	1.20	0.87	1.38	16.26	
<i>EFNA1</i>	14.49	48.99	16.04	20.90	30.91	22.45	1.38	17.27	
<i>CASP9</i>	5.02	14.27	5.47	6.10	8.97	6.55	1.37	16.96	
<i>SLC16A6</i>	2.32	14.56	2.78	5.44	8.05	5.90	1.36	14.77	
<i>ISG20</i>	1.57	5.52	1.84	2.45	3.71	2.72	1.36	17.93	
<i>OTUD1</i>	17.90	52.30	20.74	27.25	40.93	30.09	1.36	20.73	
<i>GAS1</i>	10.81	87.19	15.05	31.68	48.79	35.92	1.36	14.76	
<i>CPEB4</i>	6.19	24.27	6.95	9.89	14.46	10.65	1.36	15.70	
<i>PRDM1</i>	0.35	1.25	0.43	0.52	0.81	0.60	1.35	16.80	
<i>TGIF1</i>	28.31	75.09	31.59	37.40	54.42	40.68	1.34	18.30	
<i>NFIL3</i>	16.45	33.07	17.12	20.69	28.51	21.36	1.33	21.62	
<i>MAP3K8</i>	3.19	7.16	3.29	3.88	5.30	3.98	1.33	18.44	
<i>PPP1R3B</i>	3.31	10.60	3.62	5.34	7.52	5.65	1.33	17.64	
<i>ARRDC3</i>	7.48	24.68	7.96	11.91	16.47	12.39	1.33	16.53	
<i>PSD4</i>	0.56	3.73	0.73	0.96	1.50	1.13	1.33	9.92	
<i>LPL</i>	0.68	2.27	0.71	1.08	1.47	1.11	1.32	15.86	
<i>JAG1</i>	0.84	2.37	0.88	1.08	1.48	1.12	1.32	15.19	

DDIT4	13.41	48.99	16.81	27.11	40.15	30.51	1.32	19.68
AVP1	36.31	196.51	47.18	81.00	120.43	91.87	1.31	14.53
PTP4A1	35.73	88.00	38.01	44.66	61.47	46.94	1.31	16.51
CHMP1B	26.75	87.60	29.72	42.20	58.81	45.17	1.30	15.57
AREG	2.42	10.78	3.59	3.89	6.53	5.06	1.29	13.64
RDH10	13.00	29.07	13.53	14.72	19.66	15.25	1.29	15.17
ING1	9.51	22.18	9.95	11.08	14.84	11.52	1.29	14.97
PLPP3	10.45	60.00	15.59	24.85	38.61	29.99	1.29	14.37
DUSP8	7.11	16.29	8.14	9.45	13.49	10.48	1.29	18.48
PMEPA1	2.28	6.28	2.39	2.82	3.77	2.93	1.29	13.38
NFATC2	0.59	2.31	0.54	0.76	0.91	0.71	1.28	8.66
CHSY1	18.31	47.63	19.99	25.17	34.37	26.85	1.28	15.79
CYP26B1	3.91	17.66	4.55	7.09	9.86	7.73	1.28	12.06
ID3	4.32	14.45	4.61	6.42	8.55	6.71	1.27	12.73
LATS2	30.47	107.83	36.11	51.10	72.29	56.74	1.27	14.42
SLC04A1	1.66	4.73	1.79	2.07	2.78	2.20	1.26	12.26
AKAP12	40.32	146.18	46.00	68.67	93.92	74.35	1.26	13.39
KBTBD11	2.15	4.85	2.19	2.64	3.38	2.68	1.26	14.43
ST3GAL1	1.73	5.20	1.80	2.08	2.71	2.15	1.26	10.77
PTGES	2.13	5.16	2.24	2.89	3.76	3.00	1.25	14.73
ISL2	1.92	4.93	2.21	2.75	3.81	3.04	1.25	15.62
METRNL	38.13	103.70	39.83	49.99	64.69	51.69	1.25	12.54
NFKBIZ	2.07	4.62	2.25	2.52	3.37	2.70	1.25	14.50
ACKR3	39.84	140.15	46.55	70.97	96.85	77.68	1.25	13.68
BCL3	7.38	18.12	8.69	9.72	13.67	11.03	1.24	14.57
ETS2	23.58	62.99	25.82	33.51	44.16	35.75	1.24	13.35
DMBT1	1.45	9.02	1.95	4.15	5.74	4.65	1.23	12.08
B4GALT1	29.19	63.39	29.32	32.79	40.62	32.92	1.23	12.15
FAM46A	4.27	9.46	4.47	5.37	6.87	5.57	1.23	13.74
IRX1	4.88	18.75	5.76	8.72	11.84	9.60	1.23	11.95
NUAK2	4.46	9.48	5.13	5.96	8.17	6.63	1.23	16.24
TLE3	1.62	3.36	1.62	1.80	2.21	1.80	1.23	12.20
SOCS3	14.01	56.88	15.92	23.33	30.85	25.24	1.22	9.86
BDNF	11.54	42.38	14.73	23.02	32.03	26.21	1.22	13.73
MALSU1	64.62	144.56	67.70	79.01	100.27	82.09	1.22	12.58
COL3A1	0.43	1.14	0.50	0.66	0.89	0.73	1.22	14.04
EDN1	6.19	14.47	6.57	9.03	11.45	9.41	1.22	14.10
HLX	1.68	3.89	1.61	1.95	2.28	1.88	1.21	10.28
DUSP10	1.62	3.60	1.74	1.99	2.55	2.11	1.21	12.22
BCL2L1	9.60	32.91	10.54	16.90	21.56	17.84	1.21	11.30
ACTC1	0.32	1.04	0.35	0.45	0.58	0.48	1.21	9.62
PLK2	30.09	68.21	32.76	37.61	48.55	40.28	1.21	12.12
IL6R	3.86	8.16	4.09	4.74	5.99	4.97	1.21	12.50
EPGN	0.88	2.39	0.84	1.27	1.48	1.23	1.20	10.46
SLC19A2	3.97	8.93	4.23	5.14	6.47	5.40	1.20	11.98
KCNG1	1.09	4.23	1.16	1.76	2.19	1.83	1.20	8.51
SIRPA	24.58	60.42	26.00	35.31	43.91	36.73	1.20	11.88
ODC1	121.00	248.95	122.22	137.58	165.80	138.80	1.19	10.85
MAFK	33.80	69.37	36.02	41.58	52.28	43.80	1.19	12.22
FOXC1	15.05	39.21	16.04	20.22	25.30	21.21	1.19	10.43
ITPKB	1.25	6.89	1.51	2.45	3.23	2.71	1.19	7.55
SNRK	9.11	24.82	10.07	13.96	17.78	14.92	1.19	11.52
LBH	26.42	66.66	27.65	38.33	47.06	39.56	1.19	11.25
CITED4	27.44	113.62	36.67	58.01	79.72	67.24	1.19	10.98
NTF3	6.57	15.93	6.58	9.15	10.84	9.16	1.18	10.55
BTG1	9.86	21.95	10.23	12.87	15.63	13.24	1.18	10.89
EPHB3	0.54	1.46	0.58	0.77	0.95	0.81	1.17	9.59
IGFBP4	96.88	221.58	96.33	118.67	137.54	118.12	1.16	8.76
FAM167A	1.98	7.85	2.33	3.61	4.60	3.96	1.16	8.15
SLC38A2	169.93	395.81	194.32	232.35	298.23	256.74	1.16	10.48
DIO2	1.63	4.56	1.78	2.27	2.81	2.42	1.16	8.55
GRAMD1B	0.75	1.54	0.71	0.86	0.95	0.82	1.16	8.44
CES3	1.06	3.40	1.14	1.84	2.22	1.92	1.16	8.82
KLF9	9.79	20.67	11.50	13.38	17.43	15.09	1.16	11.32
FST	10.70	25.25	11.03	14.55	17.17	14.88	1.15	9.07
PDE4B	0.82	3.95	1.23	2.13	2.92	2.54	1.15	9.62
SHISA2	6.92	19.53	6.92	10.14	11.60	10.14	1.14	7.48
DEPDC7	8.47	38.95	10.36	17.85	22.52	19.74	1.14	7.14
PLEKHA2	10.36	23.48	10.96	13.76	16.35	14.36	1.14	8.48
PRAG1	16.07	39.32	17.94	23.53	28.83	25.40	1.14	8.72
ULBP2	7.43	16.02	7.89	8.71	10.38	9.17	1.13	7.55
FGF9	4.67	11.20	5.46	7.30	9.13	8.09	1.13	9.29
TMEM2	24.45	53.61	26.37	30.18	36.18	32.10	1.13	7.61
CEBPD	34.56	134.26	50.97	77.09	105.28	93.50	1.13	8.77
SYNPO	2.41	6.41	2.56	3.24	3.80	3.39	1.12	6.40
PHLDA3	29.30	59.25	32.29	40.26	48.26	43.25	1.12	8.46
KLHL21	10.05	20.31	10.44	11.45	13.15	11.84	1.11	6.45
IRX2	36.74	74.80	40.47	46.74	55.93	50.47	1.11	7.30
TNFRSF1B	0.58	1.15	0.65	0.67	0.82	0.74	1.11	6.96
S1PR1	4.48	12.50	5.39	7.10	8.84	8.01	1.10	6.64
WDR66	18.49	42.72	21.39	29.52	35.58	32.42	1.10	7.40
BCL7A	13.51	36.91	15.50	24.53	28.85	26.52	1.09	6.31
MEGF9	11.82	26.74	13.10	17.29	20.20	18.57	1.09	6.10
AMACR	5.96	13.31	6.68	7.99	9.43	8.71	1.08	5.41
ARID5B	17.63	35.67	20.14	26.06	30.84	28.57	1.08	6.36
SETD1B	2.95	6.05	3.28	4.05	4.72	4.38	1.08	5.62
TMEM217	2.43	5.26	2.68	3.34	3.86	3.59	1.08	5.13
RNF125	0.72	1.86	0.81	1.12	1.30	1.21	1.07	4.84
MITF	5.08	10.95	5.52	6.89	7.85	7.33	1.07	4.75
TMEM190	0.78	3.33	1.07	1.86	2.24	2.15	1.04	2.70
FLVCR2	0.87	2.84	0.96	1.29	1.43	1.38	1.04	1.76
TSKU	9.66	20.38	10.30	13.64	14.76	14.28	1.03	2.36
PKDCC	2.01	4.07	2.56	2.83	3.49	3.38	1.03	2.70

<i>TCF21</i>	6.77	15.39	7.72	12.73	14.10	13.68	1.03	2.73
<i>MISP</i>	1.00	2.46	1.13	1.34	1.50	1.47	1.02	1.22
<i>ZNF462</i>	7.15	17.04	8.47	11.80	13.33	13.12	1.02	1.23
<i>CCL2</i>	109.39	248.37	147.68	163.94	204.25	202.23	1.01	0.81
<i>USP2</i>	0.63	1.75	0.71	0.77	0.85	0.85	1.00	0.00
<i>LURAP1L</i>	4.14	9.52	4.81	6.49	7.06	7.16	0.99	-1.05
<i>FRAT2</i>	4.65	9.51	5.21	7.62	7.93	8.18	0.97	-2.63
<i>SCG2</i>	0.49	1.11	0.62	0.67	0.77	0.80	0.96	-2.70
<i>SMOC1</i>	0.84	2.45	0.99	1.40	1.43	1.55	0.92	-4.90
<i>IL24</i>	4.73	11.82	6.10	9.15	10.63	10.52	0.92	0.93
<i>ARMS2</i>	0.76	1.88	0.97	0.98	1.07	1.19	0.90	-6.38
<i>EDNRA</i>	0.42	1.57	0.58	0.77	0.81	0.93	0.87	-7.64

Repressed Genes

<i>Official Gene Symbol</i>	Vehicle	Salm ₁₀₀	RNO	Salm _{0.3}	Salm _{0.3} +RNO	$\Sigma(\text{Salm}_{0.3}, \text{RNO})$
<i>C10orf10</i>	2.17	0.84	2.12	2.26	1.37	2.21
<i>ANKRD34A</i>	1.45	0.49	1.52	1.11	0.91	1.18
<i>TXNIP</i>	46.22	16.15	44.92	43.08	33.19	41.78
<i>KRTAP1-5</i>	2.16	1.04	2.00	1.69	1.23	1.53
<i>RGS4</i>	9.53	2.65	9.70	5.69	4.90	5.86
<i>JUN</i>	109.95	46.26	105.57	82.11	67.44	77.73
<i>SPRY4</i>	2.92	1.05	3.02	1.65	1.59	1.75
<i>HYLS1</i>	6.30	2.71	5.48	4.97	3.88	4.15
<i>FOSL1</i>	153.43	36.46	142.48	87.20	72.52	76.25
<i>DUSP6</i>	4.70	1.88	4.62	3.01	2.80	2.93
<i>BHLHE41</i>	1.60	0.77	1.57	1.28	1.20	1.25
<i>EGR1</i>	15.72	3.59	15.43	8.50	8.66	8.21
<i>KLF10</i>	51.57	13.29	50.15	27.09	27.08	25.67
<i>KRTAP2-3/KRTAP2-4</i>	24.79	11.98	21.76	16.86	15.24	13.83
<i>METTL7B</i>	3.81	1.48	3.33	2.51	2.35	2.03
<i>HES1</i>	3.63	1.26	3.65	1.80	2.36	1.82