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# Gene Expression Profiling Identifies Lobe-Specific and Common Disruptions of Multiple Gene Networks in Testosterone-Supported, 17β-Estradiol– or Diethylstilbestrol-Induced Prostate Dysplasia in Noble Rats[1,2]

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## Abstract

The xenoestrogen diethylstilbestrol (DES) is commonly believed to mimic the action of the natural estrogen 17β-estradiol ($E_2$). To determine if these two estrogens exert similar actions in prostate carcinogenesis, we elevated circulating levels of estrogen in Noble (NBL) rats with $E_2$/DES–filled implants, while maintaining physiological levels of testosterone (T) in the animals with T-filled implants. The two estrogens induced dysplasia in a lobe-specific manner, with $E_2$ targeting only the lateral prostate (LP) and DES impacting only the ventral prostate (VP). Gene expression profiling identified distinct and common $E_2$-disrupted *versus* DES-disrupted gene networks in each lobe. More importantly, hierarchical clustering analyses revealed that T + $E_2$ treatment primarily affected the gene expression pattern in the LP, whereas T + DES treatment primarily affected the gene expression profile in the VP. Gene ontology analyses and pathway mapping suggest that the two hormone treatments disrupt unique and/or common cellular processes, including cell development, proliferation, motility, apoptosis, and estrogen signaling, which may be linked to dysplasia development in the rat prostate. These findings suggest that the effects of xenoestrogens and natural estrogens on the rat prostate are more divergent than previously suspected and that these differences may explain the lobe-specific carcinogenic actions of the hormones.

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## Introduction

Androgens are essential to the growth and functioning of the normal prostate and undoubtedly play a key role in prostate carcinogenesis [1]. Emerging evidence shows that estrogens also have a critical role in prostatic diseases, including prostate cancer (PCa) [2,3]. The incidence of PCa increases dramatically with age in human males, whose testosterone (T) levels in both the circulation and in prostate decline, whereas those of 17β-estradiol ($E_2$) remain relatively stable [2–4]. Thus, the age-associated alterations in the sex hormone milieu toward an *estrogen predominance* have been proposed as an endogenous risk factor for prostate carcinogenesis. Dynamic changes in the expression of estrogen receptor-β during PCa progression in humans

Abbreviations: C/EBP, CCAAT/enhancer binding protein; DES, diethylstilbestrol; $E_2$, 17β-estradiol; LP, lateral prostate; NBL, Noble; PCa, prostate cancer; PCR, polymerase chain reaction; VP, ventral prostate

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[5,6] also suggest the involvement of estrogen signaling in the malignant transformation of the prostate. Moreover, the findings of aberrant activation of aromatase expression in benign prostatic hyperplasia and PCa [3,7] further advance the concept that local production of estrogens is pivotal in the pathobiology of this gland.

Humans are exposed to xenoestrogens from various sources, including food, drugs, and other exogenous venues. Xenoestrogens are believed to cause endocrine disruptions that lead to pathogenesis in reproductive end organs [8,9]. One agent of public health concern is diethylstilbestrol (DES), a synthetic estrogen, which was widely used as a growth-promoting animal feed additive [10]. Epidemiological studies have established a strong association between maternal exposure to DES and increased risk of vaginal, cervical, and perhaps breast cancers in DES daughters [11,12]. It remains uncertain, however, whether prenatal exposure to DES elevates cancer risk in men [13]. Transient exposure of neonatal rodents to estrogen increases susceptibility of the prostate to inflammation and cancer development later in life [14]. Together, these findings strongly suggest that natural or synthetic estrogen–mediated endocrine disruption leads to the evolution of prostatic diseases, including PCa.

We have established the T plus estrogen–induced dysplasia/carcinoma model in Noble (NBL) rats as a robust study system for deciphering the contributions of estrogens, in adulthood, on the pathogenesis of dysplasia, a precancerous lesion, and adenocarcinoma of the prostate [15,16]. In this model, estrogens are administered through subcutaneous implants of hormone-filled Silastic capsules with the coimplantation of T-filled capsules to maintain physiological levels of this androgen in the circulation [17]. It is well known that increased exposure to estrogens leads to a decline in circulating levels of T through the hypothalamic–pituitary–gonadal axis. The topographical localization of premalignant/malignant lesions within the rat prostate gland has been found to be dependent on the type of estrogens used. Under the same exogenous androgen support, $E_2$ induces epithelial dysplasia and adenocarcinoma in the lateral prostate (LP) but not in the ventral prostate (VP) [16–19], whereas synthetic DES specifically targets the VP but not the LP [19,20]. Why two different estrogens induce lobe-specific carcinogenic actions in the prostate remains unclear. To address this issue, we conducted gene expression profiling analyses on the LP and VP of NBL rats exposed to T + $E_2$ or T + DES. The experimental design and the application of a bioinformatic tool of gene network mapping enabled us to identify lobe-specific and common estrogen–mediated disruptions in multiple biologic networks/pathways that may be linked to prostate carcinogenesis and explain the distinctive action of the two estrogens.

## Materials and Methods

### *Animals and Hormonal Treatment*

The animal usage protocol was approved by the Institutional Animal Care Committee at the University of Cincinnati. Male NBL rats (5–6 weeks old) were purchased from Charles River Laboratories (Kingston, NY), kept under standard conditions, and treated as previously reported [16,19,20]. Briefly, animals were randomized into three groups ($n$ = 5 for each group). Rats in the T + $E_2$ treatment group received subcutaneous implants of two pieces of 2-cm-long Silastic capsules containing T (Sigma, St Louis, MO) and one piece of 1-cm-long capsules packed with $E_2$ (Sigma), whereas the T + DES treatment group received the same number of Silastic capsules of the same length filled with T and DES (Sigma). Age-matched untreated control rats were implanted with empty capsules. At the end of a 16-week treatment period, animals were sacrificed with an overdose of isoflurane, and VPs and LPs were excised. One half of each lobe was processed for histologic examination, and the other half was snap-frozen for RNA extraction.

### *Microarray Hybridization*

The Atlas Glass Rat 3.8 I Microarray (Clontech, Palo Alto, CA) carrying 3800 named rat genes (spotted oligonucleotides) were used as the gene chip platform. The Atlas Glass Fluorescent Labeling Kit (Clontech) was used for synthesizing and purifying fluorescent-labeled cDNA probes for hybridization to glass microarrays. The labeling and hybridization procedures were performed in accordance with the manufacturer's instruction manual. In brief, amino-modified first-strand cDNA probes were synthesized with aminoallyl–2′-deoxyuridine 5′-triphosphate incorporation. Then Cy3 fluorescent dye was coupled to the cDNAs derived from individual prostatic lobes, whereas Cy5 dye was conjugated to the universal rat reference RNA obtained from Stratagene (La Jolla, CA). Equal quantities of two labeled probes were mixed and hybridized in a Corning microarray hybridization chamber (Corning, Corning, NY) at 50°C overnight (≥16 hours). Spikes of positive control probes were also included as an internal control for the process of cDNA probe synthesis and the dye-coupled reaction. Finally, the signal was obtained using a microarray scanner (GenePix 4000B; Axon Instruments, Foster City, CA). A probe coverage of >90% was achieved for all arrays. Five animal replicates for each treatment/tissue group (T + $E_2$–treated VP or LP, T + DES–treated VP and LP, and untreated VP and LP) were used to conduct a 30-microarray analysis to assess changes in the gene expression pattern due to treatment and lobe specificity.

### *Microarray Data Normalization and Analysis*

The data were analyzed to identify differentially expressed genes in 1) the T + $E_2$–treated LPs and VPs compared with untreated controls and 2) the T + DES–treated LPs and VPs compared with untreated controls. Five biologic replicate arrays for each experimental condition, all *versus* universal reference, were performed. R statistical software and the *limma* Bioconductor package [21] were used for analysis. Data normalization was performed in two steps separately for each microarray [22–24]. First, background-adjusted intensities were log-transformed, and the differences ($M$) and averages ($A$) of log-transformed values were calculated as $M = \log_2(X_1) - \log_2(X2)$ and $A = [\log_2(X_1) + \log_2(X_2)]/2$, where $X_1$ and $X_2$ denote the Cy5 and Cy3 intensities, respectively. Second, normalization was performed by fitting the array-specific local regression model of $M$ as a function of $A$ and obtaining residuals. The statistical analysis was performed for each gene separately by fitting a one-way analysis of variance (ANOVA) model with treatment. Estimated fold changes were calculated from the ANOVA model; an intensity-based empirical Bayes method was used to modify the resulting $t$-statistics from each comparison [25]. This method obtains more precise estimates of variance by pooling information across genes and by accounting for the dependency of variance on probe intensity level. Genes with a false discovery rate (FDR) <0.05 [26] were considered to be significantly differentially expressed. Clustering was performed using normalized, centered sample ratios. The gene list used for clustering consisted of all genes having an FDR <0.05 for at least one comparison (1063 genes). T + $E_2$ and T + DES samples were each clustered using the Ward clustering method and Euclidean dissimilarity metric with 1063 genes.

### *Identification of Estrogen-Regulated Gene Expression*

Genes differentially regulated in the different lobes with T + DES and T + $E_2$ treatment were identified separately in each drug treatment. Gene lists were generated according to their expression signature in different gene expression clusters; each group was described in the Results section.

### *Pathway and Network Analysis*

Biologic relationships between differentially expressed genes were mapped by Ingenuity Pathway Analysis (IPA) 3.1 software (www.ingenuity.com). Gene lists of different patterns of gene expression in response to T + $E_2$ and T + DES treatments (as described in the Results section) were uploaded to the IPA Web application in an Excel file format containing expression data and GenBank accession number as identifier. The biologic relationship of uploaded genes was mapped with IPA software into networks according to the published literature in the database. A score was assigned to each network in the data set to estimate the relevance of the network to the uploaded gene list. A higher score means that the network is more relevant to the gene list entered by the user [27]. The two highest score networks were selected in this study, and genes in these two networks were selected for further post hoc analysis.

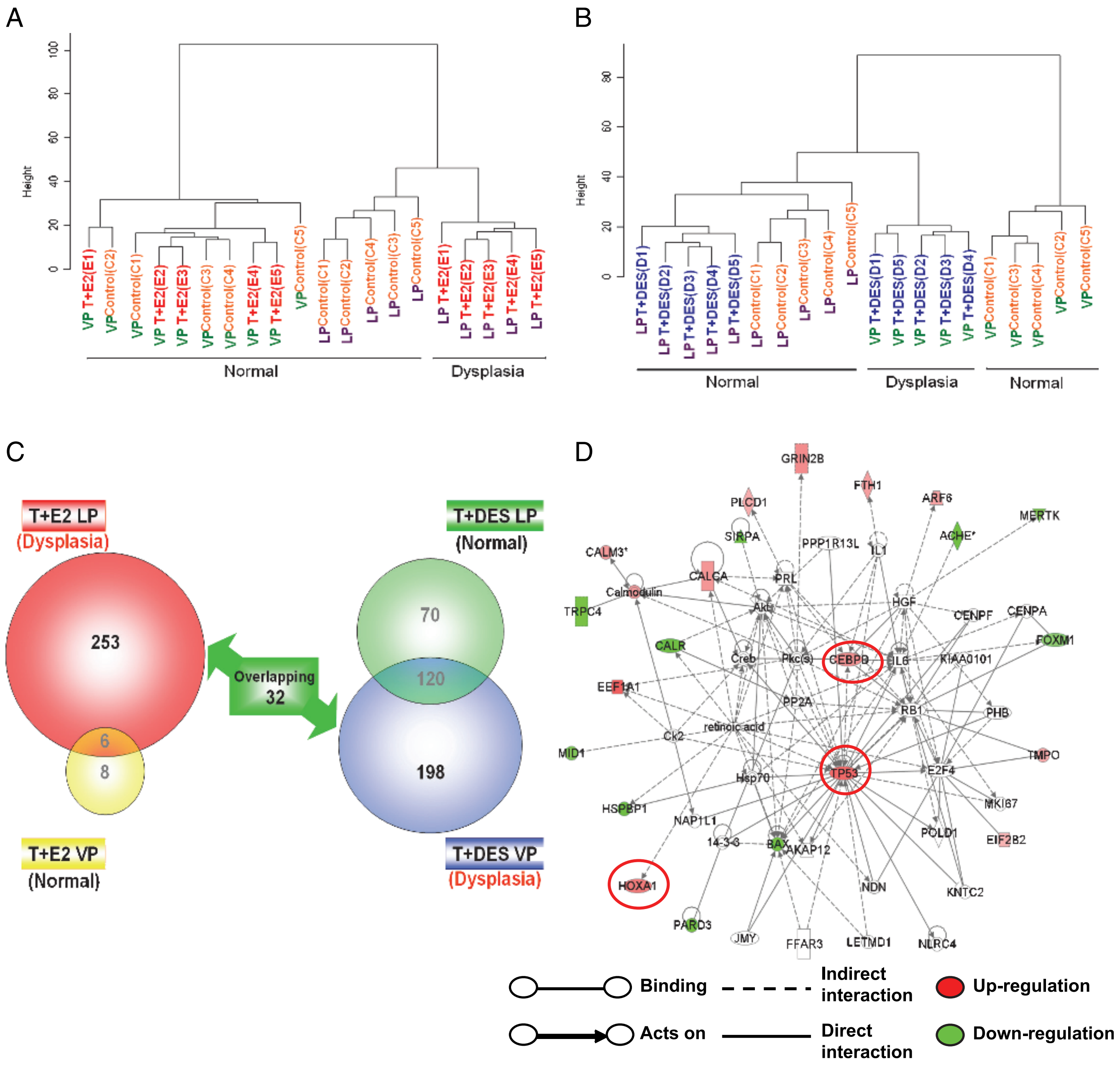


**Figure 1.** Hierarchical clustering analysis of T + $E_2$ and T + DES gene expression data set. (A) Dendrogram of T + $E_2$ expression data set in LP and VP. (B) Dendrogram of T + DES expression data set in LP and VP. (C) Venn diagram showing the number of genes differentially expressed in each treatment group compared with the respective untreated control. (D) Gene interaction network of a subset of differentially expressed genes that are common in both LP and VP dysplasia. Genes bordered with red were validated by quantitative real-time PCR.

**Table 1.** T + $E_2$–Induced LP Dysplasia Panel: Genes Whose Expression Selectively Changed following T + $E_2$ Treatment in the LPs Harboring Dysplasia, but not in the VPs.

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| prohibitin* | 25344 | *PHB* | 3.42 | Cell death; cell signaling; cellular growth and proliferation; gene transcription |
| nuclease-sensitive element binding protein 1* | 29206 | *NSEP1* | 3.08 | Cell death; gene transcription |
| potassium channel, subfamily K, member 9* | 84429 | *KCNK9* | 3.08 | Cell death |
| *vesicle-associated membrane protein 2** | 24803 | *VAMP2* | 2.97 | Cell death; cellular assembly and organization; cellular movement |
| cytochrome *c* oxidase subunit IV isoform 1* | 29445 | *COX4I1* | 2.71 | Others/unclassified |
| PR-Vbeta1* | 498341 | *PR-Vbeta1* | 2.68 | Others/unclassified |
| melanocortin 5 receptor* | 25726 | *MC5R* | 2.47 | Cell signaling |
| glutamate receptor, ionotropic, kainate 3* | 298521 | *GRIK3* | 2.45 | Cell signaling |
| 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4* | 54283 | *PFKFB4* | 2.41 | Others/unclassified |
| potassium voltage–gated channel, Shaw-related subfamily, member 1* | 25327 | *KCNC1* | 2.39 | Molecular transport |
| actin alpha cardiac 1* | 29275 | *ACTC1* | 2.34 | Others/unclassified |
| *eukaryotic translation elongation factor 1 alpha 1** | 171361 | *EEF1A1* | 2.31 | Cell death, protein synthesis |
| ATPase, $Na^+/K^+$ transporting, alpha 3 polypeptide* | 24213 | *ATP1A3* | 2.29 | Inflammation; molecular transport |
| gamma-aminobutyric acid A receptor, rho 1* | 29694 | *GABRR1* | 2.25 | Cell death; cell signaling |
| guanylate cyclase 1, soluble, alpha 3* | 25201 | *GUCY1A3* | 2.25 | Cellular movement |
| transforming growth factor alpha* | 24827 | *TGFA* | 2.24 | Biomolecule metabolism; cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription; molecular transport; protein synthesis |
| ribosomal protein S12* | 65139 | *RPS12* | 2.20 | Protein synthesis |
| *tumor protein p53** | 24842 | *TP53* | 2.16 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; cellular response to therapeutics; DNA replication, recombination and repair; free radical scavenging; gene transcription; inflammation; molecular transport; post–translational modification; protein synthesis; RNA post–transcriptional modification |
| nuclear receptor subfamily 3, group C, member 2* | 25672 | *NR3C2* | 2.13 | Biomolecule metabolism; cell signaling; gene transcription; molecular transport; protein synthesis |
| secretory carrier membrane protein 1* | 29521 | *SCAMP1* | 2.09 | Cellular assembly and organization |
| CEA-related cell adhesion molecule 1* | 81613 | *CEACAM1* | 2.08 | Cell death; cell signaling; cellular growth and proliferation; cellular movement; inflammation |
| olfactory marker protein* | 24612 | *OMP* | 2.08 | Cell signaling |
| guanine nucleotide binding protein, alpha z subunit* | 25740 | *GNAZ* | 2.05 | Cell signaling; cellular development; cellular movement; molecular transport; biomolecule metabolism |
| phosphodiesterase 1C* | 81742 | *PDE1C* | 2.04 | Others/unclassified |
| ribosomal protein S3a* | 29288 | *RPS3A* | 2.04 | Cell death; cellular development; cellular growth and proliferation; protein synthesis |
| insulin-like 6* | 50546 | *IL1RAP* | 1.95 | Cell signaling |
| A kinase (PRKA) anchor protein 14* | 60332 | *AKAP14* | 1.94 | Others/unclassified |
| CD38 antigen* | 25668 | *CD38* | 1.94 | Cell cycle; cell death; cell signaling; cellular development; cellular growth and proliferation; cellular movement; biomolecule metabolism; molecular transport; post–translational modification |
| p21 (CDKN1A)–activated kinase 1* | 29431 | *PAK1* | 1.93 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular movement |
| regenerating islet–derived 3 alpha* | 171162 | *REG3G* | 1.93 | Others/unclassified |
| ubiquitin-conjugating enzyme E2I* | 25573 | *UBE2I* | 1.93 | Cell signaling; gene transcription; protein synthesis |
| ATPase, $H^+$ transporting, V1 subunit F* | 116664 | *ATP6V1F* | 1.91 | Molecular transport |
| *homeo box A1** | 25607 | *HOXA1* | 1.89 | Cell death; cellular development; cellular movement; gene transcription |
| regenerating islet–derived 3 gamma* | 24620 | *REG3G* | 1.89 | Others/unclassified |
| Fas apoptotic inhibitory molecule 2* | 246274 | *FAIM2* | 1.86 | Cell death |
| barrier to autointegration factor 1* | 114087 | *BANF1* | 1.85 | DNA replication, recombination, and repair |
| *thyroid hormone receptor alpha** | 81812 | *THRA* | 1.85 | Biomolecule metabolism; cell death; cell morphology; cellular development; free radical scavenging; gene transcription; protein synthesis |
| neuromedin B receptor* | 25264 | *NMBR* | 1.83 | Others/unclassified |
| ATPase, $Na^+/K^+$ transporting, beta 2 polypeptide* | 24214 | *ATP1B2* | 1.82 | Others/unclassified |
| Chondroitin sulfate proteoglycan 5* | 50568 | *CSPG5* | 1.81 | Cell signaling |
| MAD homolog 7 (*Drosophila*)* | 81516 | *SMAD7* | 1.78 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; gene transcription |
| tachykinin receptor 2* | 25007 | *TACR2* | 1.78 | Others/unclassified |
| alanyl (membrane) aminopeptidase* | 81641 | *ANPEP* | 1.76 | Cell death; cell morphology; cellular development; cellular movement; protein synthesis |
| growth hormone–releasing hormone* | 29446 | *GHRH* | 1.75 | Cell morphology; cell signaling; cellular growth and proliferation; biomolecule metabolism; molecular transport |
| protein kinase N1* | 29355 | *PKN1* | 1.75 | Cell signaling; cellular growth and proliferation; cellular movement; gene transcription |
| slit homolog 3 (*Drosophila*)* | 83467 | *SLIT3* | 1.74 | Others/unclassified |
| dopamine receptor 2* | 24318 | *DRD2* | 1.72 | Cell death; cell signaling; cellular growth and proliferation; cellular movement; gene transcription; inflammation; biomolecule metabolism |
| glutathione peroxidase 3* | 64317 | *GPX3* | 1.72 | Cellular growth and Proliferation; Post–translational modification; protein synthesis |
| vasoactive intestinal peptide receptor 1* | 24875 | *VIPR1* | 1.71 | Cell death; cell signaling; cellular growth and proliferation; cellular movement; biomolecule metabolism; molecular transport |
| amphiphysin 1* | 60668 | *AMPH* | 1.70 | Cell signaling; cellular assembly and organization; cellular movement; gene transcription |
| G protein beta subunit–like* | 64226 | *GBL* | 1.70 | Others/unclassified |

**Table 1.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| heat shock 70 kDa protein 5* | 25617 | *HSPA5* | 1.69 | Cell death; cellular growth and proliferation; inflammation |
| hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1* | 29632 | *HSD3B2* | 1.68 | Others/unclassified |
| POU domain, class 3, transcription factor 2* | 29588 | *POU3F2* | 1.68 | Cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| ribosomal protein S9* | 81772 | *RPS9* | 1.64 | Protein synthesis |
| glucocorticoid modulatory element binding protein 2* | 83635 | *GMEB2* | 1.63 | Gene transcription |
| *glutamate receptor, ionotropic, NMDA2B** | 24410 | *GRIN2B* | 1.63 | Cell signaling |
| solute carrier family 8 (sodium/calcium exchanger), member 3* | 140448 | *SLC8A3* | 1.63 | Cell death; cell signaling |
| ATPase, Ca$^{2+}$ transporting, ubiquitous* | 25391 | *ATP2A3* | 1.62 | Others/unclassified |
| *CTD-binding SR-like rA1** | 56081 | *SR-A1* | 1.60 | Others/unclassified |
| solute carrier family 2 (facilitated glucose transporter), member 2* | 25351 | *SLC2A2* | 1.60 | Cell death |
| calcineurin binding protein 1* | 94165 | *CABIN1* | 1.59 | Cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; gene transcription; inflammation; biomolecule metabolism; molecular transport |
| heterogeneous nuclear ribonucleoprotein A1* | 29578 | *LOC144983* | 1.59 | Others/unclassified |
| casein kinase 1, gamma 1* | 64086 | *CSNK1G1* | 1.57 | Others/unclassified |
| potassium inwardly rectifying channel, subfamily J, member 10* | 29718 | *KCNJ10* | 1.56 | Cell morphology; cellular development; inflammation; molecular transport |
| potassium large conductance calcium–activated channel, subfamily M, beta member 1* | 29747 | *KCNMB1* | 1.56 | Cell signaling; molecular transport |
| potassium voltage–gated channel, Shaw-related subfamily, member 3* | 117101 | *KCNC3* | 1.56 | Molecular transport |
| *CCAAT/enhancer binding protein (C/EBP), delta** | 25695 | *CEBPD* | 1.55 | Cell death; cellular development; cellular growth and proliferation; gene transcription; inflammation |
| guanine nucleotide binding protein, beta 3* | 60449 | *GNB3* | 1.55 | Cell signaling |
| ribosomal protein S19* | 29287 | *RPS19* | 1.54 | Cellular development; cellular growth and proliferation; cellular movement; protein synthesis |
| aquaporin 5* | 25241 | *AQP5* | 1.53 | Inflammation |
| chloride channel Kb* | 79430 | *CLCNKB* | 1.53 | Others/unclassified |
| fatty acid binding protein 3* | 79131 | *FABP3* | 1.52 | Cellular growth and proliferation; biomolecule metabolism; molecular transport |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2* | 116744 | *EDG2* | 1.51 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| *killer cell lectin–like receptor subfamily B member 1B** | 25192 | *KLRB1* | 1.51 | Cell death |
| suppression of tumorigenicity 18* | 266680 | *ST18* | 1.50 | Gene transcription |
| pregnancy upregulated nonubiquitously expressed CaM kinase* | 29660 | *PNCK* | 1.49 | Others/unclassified |
| Arg/Abl–interacting protein ArgBP2* | 114901 | *SORBS2* | 1.48 | Cell death; cell morphology; cell signaling |
| sodium channel, voltage-gated, type IV, alpha polypeptide* | 25722 | *SCN4A* | 1.48 | Molecular transport |
| *calcitonin/calcitonin–related polypeptide, alpha** | 24241 | *CALCA* | 1.47 | Cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; gene transcription; inflammation; biomolecule metabolism; molecular transport |
| RASD family, member 2* | 171099 | *RASD2* | 1.47 | Others/unclassified |
| spondin 1* | 64456 | *SPON1* | 1.46 | Others/unclassified |
| sulfotransferase family, cytosolic, 1C, member 2* | 171072 | *SULT1C2* | 1.46 | Others/unclassified |
| acyl-CoA synthetase long-chain family member 4* | 113976 | *ACSL4* | 1.45 | Cell death |
| aldehyde dehydrogenase family 1, subfamily A2* | 116676 | *ALDH1A2* | 1.45 | Cell death; cellular development; cellular growth and proliferation; biomolecule metabolism |
| CD3 antigen, zeta polypeptide* | 25300 | *CD247* | 1.45 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; gene transcription; inflammation; post–translational modification |
| discs, large homolog 4 (*Drosophila*)* | 29495 | *DLG4* | 1.45 | Cell signaling; cellular assembly and organization |
| *calmodulin 3* | 24244 | *CALM3* | 1.43 | Cell signaling; cellular growth and proliferation |
| carboxypeptidase E* | 25669 | *CPE* | 1.43 | Biomolecule metabolism; molecular transport |
| phosphofructokinase, muscle* | 65152 | *PFKM* | 1.42 | Others/unclassified |
| translocase of outer mitochondrial membrane 20 homology (yeast)* | 266601 | *TOMM20* | 1.42 | Others/unclassified |
| complement component 1, q subcomponent, beta polypeptide* | 29687 | *C1QB* | 1.40 | Others/unclassified |
| regulator of G-protein signaling 19* | 59293 | *RGS19* | 1.40 | Cell signaling; cellular development; biomolecule metabolism; protein synthesis |
| Carcinoembryonic antigen gene family (CGM3)* | 24256 | *PSG18* | 1.39 | Others/unclassified |
| gamma-glutamyl hydrolase* | 25455 | *GGH* | 1.39 | Others/unclassified |
| *N*-acetyltransferase 8 (camello like)* | 64570 | *NAT8* | 1.37 | Others/unclassified |
| pyrimidinergic receptor P2Y, G-protein–coupled, 6* | 117264 | *P2RY6* | 1.37 | Others/unclassified |
| protein tyrosine phosphatase, receptor type, K, extracellular region* | 360302 | *PTPRK* | 1.36 | Cellular growth and proliferation |
| cytochrome *P*450, 4a12* | 266674 | *CYP4A22* | 1.35 | Others/unclassified |

**Table 1.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| gamma-aminobutyric acid A receptor, alpha 1* | 29705 | *GABRA1* | 1.35 | Cell morphology; cell signaling |
| *ferritin, heavy polypeptide 1** | 25319 | *FTH1* | 1.34 | Cell death; cell morphology; cellular growth and proliferation; DNA replication, recombination, and repair; free radical scavenging; cell death; cell morphology; cellular growth and proliferation; free radical scavenging |
| guanylate cyclase 1, soluble, beta 2* | 25206 | *GUCY1B2* | 1.34 | Others/unclassified |
| proteasome (prosome, macropain) 28 subunit, beta* | 29614 | *PSME2* | 1.31 | Cell signaling; cellular growth and proliferation |
| small inducible cytokine A4* | 116637 | *CCL4* | 1.31 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; inflammation biomolecule metabolism |
| *ADP-ribosylation factor 6** | 79121 | *ARF6* | 1.30 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular movement; biomolecule metabolism; molecular transport; protein trafficking |
| mannan-binding lectin serine protease 2 | 64459 | *MASP2* | 1.30 | Others/unclassified |
| *dopamine receptor 4** | 25432 | *DRD4* | 1.29 | Cell signaling; biomolecule metabolism; molecular transport |
| ATP synthase, $H^+$ transporting, mitochondrial $F_1$ complex, delta subunit* | 245965 | *ATP5D* | 1.26 | Energy production; molecular transport; biomolecule metabolism |
| calponin 1 | 65204 | *CNN1* | 1.26 | Cellular assembly and organization; cellular growth and proliferation; cellular movement |
| hydroxyacid oxidase 2 (long chain) | 84029 | *HAO2* | 1.25 | Others/unclassified |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.23 | Cell cycle; cell death; cell signaling; cellular development; cellular growth and proliferation; cellular movement; inflammation |
| *potassium voltage–gated channel, subfamily H (eag-related), member 7** | 170739 | *KCNH7* | 1.23 | Others/unclassified |
| Ras association (RalGDS/AF-6) domain family 5 | 54355 | *RASSF5* | 1.23 | Cell cycle; cell death; cellular growth and proliferation |
| *thymopoietin* | 25359 | *TMPO* | 1.22 | Cell cycle; cellular assembly and organization; DNA replication, recombination, and repair; gene transcription |
| polypyrimidine tract binding protein 1 | 29497 | *PTBP1* | 1.19 | Protein synthesis |
| protein kinase C and casein kinase substrate in neurons 2 | 124461 | *PACSIN2* | 1.16 | Cell morphology; cell signaling; cellular assembly and organization |
| leptin receptor overlapping transcript | 56766 | *LEPROT* | 1.15 | Others/unclassified |
| *phospholipase C, delta 1* | 24655 | *PLCD1* | 1.15 | Biomolecule metabolism; cellular growth and proliferation |
| synaptonemal complex protein SC65 | 59101 | *SC65* | 1.15 | Others/unclassified |
| ADP-ribosylation factor 5 | 79117 | *ARF5* | 1.14 | Molecular transport; protein trafficking |
| crystallin, beta $B_2$ | 25422 | *CRYBB2* | 1.11 | Others/unclassified |
| prolactin-like protein L | 171556 | *PRLPL* | 1.10 | Others/unclassified |
| protein phosphatase 3, catalytic subunit, beta isoform | 24675 | *PPP3CB* | 1.09 | Cell death; cellular development; inflammation |
| calpain 3 | 29155 | *CAPN3* | 1.07 | Protein synthesis |
| cathepsin D | 171293 | *CTSD* | 1.07 | Cell death; cellular growth and proliferation; free radical scavenging; inflammation; molecular transport; protein synthesis |
| *eukaryotic translation initiation factor 2B, subunit 2 beta* | 84005 | *EIF2B2* | 1.07 | Cellular development; cellular growth and proliferation; protein synthesis |
| calcitonin/calcitonin–related polypeptide, alpha | 24241 | *CALCA* | −1.13 | Cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; gene transcription; inflammation; biomolecule metabolism; molecular transport |
| *forkhead box M1* | 58921 | *FOXM1* | −1.13 | Cell cycle; cell death; cell morphology; cellular growth and proliferation; gene transcription |
| *adrenal secretory serine protease precursor* | 64565 | *TMPRSS11D* | −1.14 | Others/unclassified |
| *MAP-kinase activating death domain* | 94193 | *MADD* | −1.19 | Cell death; cellular growth and proliferation |
| *calmodulin 3* | 24244 | *CALM3* | −1.22 | Cell signaling; cellular growth and proliferation |
| neural visinin–like $Ca^{2+}$–binding protein type 3* | 50871 | *HPCAL1* | −1.28 | Others/unclassified |
| fertility protein SP22 | 117287 | *PARK7* | −1.30 | Cell death; cell signaling; cellular growth and proliferation |
| actin, beta* | 81822 | *ACTB* | −1.31 | Cellular growth and proliferation; cellular movement |
| G-protein–coupled receptor 37* | 117549 | *GPR37* | −1.33 | Cell death; cell signaling |
| glycogen synthase kinase 3 alpha* | 50686 | *GSK3A* | −1.34 | Cellular movement |
| ribosomal protein L22 | 81768 | *RPL22* | −1.34 | Protein synthesis |
| actinin alpha 4* | 63836 | *ACTN4* | −1.35 | Cell death; cellular growth and proliferation; cellular movement |
| *midline 1** | 54252 | *MID1* | −1.35 | Cellular assembly and organization |
| dipeptidase 1 (renal)* | 94199 | *DPEP1* | −1.36 | Others/unclassified |
| polymeric immunoglobulin receptor* | 25046 | *PIGR* | −1.36 | Cell signaling; cellular growth and proliferation; cellular movement |
| adducin 2 (beta)* | 24171 | *ADD2* | −1.38 | Cellular development; cellular growth and proliferation; inflammation; molecular transport |
| *c-mer protooncogene tyrosine kinase** | 65037 | *MERTK* | −1.38 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation |
| caspase 7* | 64026 | *CASP7* | −1.39 | Cell death; protein synthesis |
| ddx5 gene | 287765 | *DDX5* | −1.40 | Cell death; cellular growth and proliferation; gene transcription |
| vesicle docking protein* | 56042 | *VDP* | −1.40 | Cellular assembly and organization; molecular transport; protein trafficking |
| *acetylcholinesterase** | 83817 | *ACHE* | −1.41 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; DNA replication, recombination, and repair; post–translational modification; protein synthesis |
| phenylalkylamine $Ca^{2+}$ antagonist (emopamil) binding protein* | 117278 | *EBP* | −1.41 | Cellular development |
| phosphodiesterase 4C, cAMP-specific* | 290646 | *PDE4C* | −1.41 | Inflammation |
| transition protein 2* | 24840 | *TNP2* | −1.44 | Others/unclassified |
| casein kinase 1, alpha 1* | 113927 | *CSNK1A1* | −1.45 | Cell death |
| nuclear receptor subfamily 4, group A, member 3 | 58853 | *NR4A3* | −1.46 | Cellular development; cellular growth and proliferation; gene transcription |

**Table 1.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| phospholipase C, beta 3* | 29322 | *PLCB3* | −1.46 | Biomolecule metabolism; cellular movement; molecular transport |
| myelin-associated oligodendrocytic basic protein* | 25037 | *MOBP* | −1.47 | Others/unclassified |
| retinoic acid receptor, alpha* | 24705 | *RARA* | −1.47 | Cell death; cell signaling; cellular development; cellular growth and proliferation; cellular movement; biomolecule metabolism; gene transcription; inflammation |
| putative pheromone receptor Go-VN13C* | 286986 | *EG665255* | −1.48 | Others/unclassified |
| prolyl 4-hydroxylase, beta polypeptide* | 25506 | *P4HB* | −1.49 | Cell death |
| protein kinase, lysine-deficient 1* | 116477 | *WNK1* | −1.49 | Molecular transport |
| Pyruvate carboxylase* | 25104 | *PC* | −1.49 | Others/unclassified |
| ribosomal protein S15* | 29285 | *RPS15* | −1.49 | Others/unclassified |
| ATP synthase, $H^+$ transporting, mitochondrial F1 complex, O subunit* | 192241 | *ATP5O* | −1.50 | Others/unclassified |
| *granzyme M (lymphocyte met-ase 1)** | 29252 | *GZMM* | −1.50 | Cell death |
| metastasis-associated 1* | 64520 | *MTA1* | −1.50 | Cell morphology; cell signaling; cellular growth and proliferation; cellular movement; gene transcription |
| Rous sarcoma oncogene* | 83805 | *SRC* | −1.50 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription; biomolecule metabolism; molecular transport; protein synthesis |
| *neurexophilin 3** | 59315 | *NXPH3* | −1.51 | Others/unclassified |
| phosphodiesterase 4A* | 25638 | *PDE4A* | −1.51 | Cell death; cell signaling; cellular development; inflammation; molecular transport; biomolecule metabolism |
| calcium channel, voltage-dependent, alpha 1I subunit* | 56827 | *CACNA1I* | −1.52 | Cell signaling |
| *transient receptor potential cation channel, subfamily C, member 4** | 84494 | *TRPC4* | −1.53 | Others/unclassified |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide* | 29753 | *YWHAE* | −1.53 | Cell cycle; cell signaling; cellular movement |
| polymerase (RNA) II (DNA-directed) polypeptide G* | 117017 | *POLR2G* | −1.54 | Gene transcription |
| F-box only protein 2* | 85273 | *FBXO2* | −1.55 | Cellular growth and proliferation; protein synthesis |
| apolipoprotein C-I* | 25292 | *APOC1* | −1.56 | Biomolecule metabolism; molecular transport |
| proprotein convertase subtilisin/kexin type 3* | 54281 | *FURIN* | −1.56 | Cell signaling; cellular growth and proliferation; cellular movement; protein synthesis |
| chemokine orphan receptor 1* | 84348 | *CXCR7* | −1.57 | Cellular growth and proliferation; cellular movement |
| heat shock protein, alpha-crystallin–related, B6* | 192245 | *HSPB6* | −1.57 | Others/unclassified |
| interleukin 5* | 24497 | *IL5* | −1.57 | Cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription; molecular transport |
| interleukin enhancer binding factor 3* | 84472 | *ILF3* | −1.57 | Cellular growth and proliferation; gene transcription |
| protein tyrosine phosphatase, receptor type, F* | 360406 | *PTPRF* | −1.57 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular growth and proliferation; cellular movement |
| *par-3 (partitioning defective 3) homolog (C. elegans)** | 81918 | *PARD3* | −1.58 | Cell morphology; cell signaling; cellular development; gene Transcription |
| ribosomal protein L27* | 64306 | *RPL27* | −1.58 | Others/unclassified |
| linker for activation of T cells* | 81511 | *LAT* | −1.59 | Biomolecule metabolism; cell death; cell morphology; cell signaling; cellular development; gene transcription; molecular transport |
| nuclear factor I/C* | 29228 | *NFIC* | −1.59 | Gene transcription |
| potassium voltage–gated channel, shaker-related subfamily, beta member 1* | 29737 | *KCNAB1* | −1.59 | Molecular transport |
| *Bcl2-associated X protein** | 24887 | *BAX* | −1.60 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular response to therapeutics; DNA replication, recombination, and repair; free radical scavenging; inflammation; biomolecule metabolism; molecular transport |
| carboxylesterase 1* | 29225 | *ES22* | −1.60 | Others/unclassified |
| ribosomal protein L10A* | 81729 | *RPL10A* | −1.60 | Others/unclassified |
| upstream of NRAS* | 117180 | *CSDE1* | −1.60 | Others/unclassified |
| nucleoporin 62* | 65274 | *NUP62* | −1.61 | Cell death; cell signaling; cellular growth and proliferation; gene transcription |
| eukaryotic translation initiation factor 2B, subunit 4 delta* | 117019 | *EIF2B4* | −1.62 | Cellular development; protein synthesis |
| apolipoprotein A–V* | 140638 | *APOA5* | −1.63 | Biomolecule metabolism; molecular transport |
| myosin IE* | 25484 | *MYO1E* | −1.64 | Others/unclassified |
| paired box gene 8* | 81819 | *PAX8* | −1.64 | Cellular development; gene transcription |
| prion protein* | 24686 | *PRNP* | −1.64 | Cell death; cellular development; cellular growth and proliferation; cellular movement |
| amelogenin X chromosome* | 29160 | *AMELX* | −1.67 | Others/unclassified |
| Unc4.1 homeobox (*C. elegans*)* | 29375 | *UNCX4.1* | −1.67 | Cell death |
| cofilin 1* | 29271 | *CFL1* | −1.68 | Cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; molecular transport; protein trafficking |
| caudal type homeo box 1* | 171042 | *CDX1* | −1.69 | Others/unclassified |
| phosphatidylinositol-4-phosphate 5-kinase, type II, alpha* | 116723 | *PIP5K2A* | −1.70 | Biomolecule metabolism; molecular transport |
| platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit* | 114113 | *PAFAH1B3* | −1.70 | Cell death; cellular development; biomolecule metabolism |
| *protein tyrosine phosphatase, nonreceptor type substrate 1** | 25528 | *SIRPA* | −1.70 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription; inflammation |
| *acetylcholinesterase** | 83817 | *ACHE* | −1.71 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; DNA replication, recombination, and repair; post–translational modification; protein synthesis |
| ribosomal protein L36* | 58927 | *RPL36* | −1.71 | Others/unclassified |

**Table 1.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| G-protein–coupled receptor 24* | 83567 | *MCHR1* | −1.72 | Cell signaling; molecular transport; biomolecule metabolism |
| epididymal retinoic acid–binding protein* | 29552 | *LCN5* | −1.73 | Biomolecule metabolism |
| gap junction membrane channel protein beta 4* | 117055 | *GJB4* | −1.75 | Others/unclassified |
| zinc finger protein 111* | 170849 | *ZNF227* | −1.75 | Others/unclassified |
| cleavage and polyadenylation–specific factor 4* | 252943 | *CPSF4* | −1.76 | Cellular growth and proliferation |
| ADP-ribosylation factor 1* | 64310 | *ARF1* | −1.77 | Cellular assembly and organization; cellular growth and proliferation; biomolecule metabolism; molecular transport; protein trafficking |
| coagulation factor X* | 29243 | *F10* | −1.77 | Cell signaling; cellular movement; inflammation; biomolecule metabolism; molecular transport |
| ephrin A1* | 94268 | *EFNA1* | −1.77 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement |
| rabaptin 5* | 54190 | *RABEP1* | −1.78 | Others/unclassified |
| allograft inflammatory factor 1* | 29427 | *AIF1* | −1.79 | Cell death; cell morphology; cellular development; cellular growth and proliferation |
| Cbp/p300–interacting transactivator with Glu/Asp–rich carboxy-terminal domain 1* | 64466 | *CITED1* | −1.79 | Cellular development; cellular growth and proliferation; gene transcription |
| testis enhanced gene transcript* | 24822 | *TEGT* | −1.79 | Cell death |
| neurogenic differentiation 2* | 54276 | *NEUROD2* | −1.80 | Cellular development; gene transcription |
| heat shock 10 kDa protein 1* | 25462 | *HSPE1* | −1.83 | Cell death |
| *hsp70-interacting protein** | 246146 | *HSPBP1* | −1.83 | Others/unclassified |
| *calreticulin** | 64202 | *CALR* | −1.84 | Cell death; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription; molecular transport; protein trafficking |
| discoidin domain receptor family, member 1* | 25678 | *DDR1* | −1.84 | Cell death; cellular development; cellular growth and proliferation; cellular movement |
| myosin ID* | 25485 | *MYO1D* | −1.84 | Others/unclassified |
| ribosomal protein L28* | 64638 | *RPL28* | −1.84 | Others/unclassified |
| gap junction membrane channel protein alpha 3* | 79217 | *GJA3* | −1.85 | Cell morphology; cell signaling; cellular development |
| hairy and enhancer of split 3 (*Drosophila*)* | 64628 | *HES3* | −1.85 | Cellular development; gene transcription |
| ornithine decarboxylase antizyme 1* | 25502 | *OAZ1* | −1.87 | Cell death; cellular growth and proliferation |
| a disintegrin and metallopeptidase domain 1a* | 56777 | *ADAM1A* | −1.89 | Cellular movement |
| mucosal vascular addressin cell adhesion molecule 1* | 54266 | *MADCAM1* | −1.89 | Cell signaling; cellular development; cellular movement; inflammation |
| membrane protein, palmitoylated 3 (MAGUK p55 subfamily member 3)* | 114202 | *MPP3* | −1.90 | Others/unclassified |
| sulfotransferase family 4A, member 1* | 58953 | *SULT4A1* | −1.90 | Others/unclassified |
| CCAAT/enhancer binding protein (C/EBP), alpha* | 24252 | *CEBPA* | −1.91 | Cell cycle; cell death; cellular development; cellular growth and proliferation; cellular response to therapeutics; gene transcription; biomolecule metabolism; molecular transport |
| SNF-related kinase* | 170837 | *SNRK* | −1.92 | Cellular development |
| ADP-ribosylation factor 3* | 140940 | *ARF3* | −1.94 | Molecular transport; protein trafficking |
| aspartyl-tRNA synthetase* | 116483 | *DARS* | −1.94 | Cell cycle; cell signaling; protein synthesis |
| glycine cleavage system protein H (aminomethyl carrier)* | 171133 | *GCSH* | −1.94 | Biomolecule metabolism; post–translational modification |
| 3-hydroxyisobutyrate dehydrogenase* | 63938 | *HIBADH* | −1.96 | Others/unclassified |
| preoptic regulatory factor-2* | 286903 | *KIAA1688* | −1.96 | Others/unclassified |
| amino-terminal enhancer of split* | 29466 | *AES* | −1.97 | Cell death; gene transcription |
| ribosomal protein L29* | 29283 | *RPL29* | −1.99 | Others/unclassified |
| quinoid dihydropteridine reductase* | 64192 | *QDPR* | −2.01 | Others/unclassified |
| complexin 2* | 116657 | *CPLX2* | −2.02 | Cellular assembly and organization; cellular movement |
| hairy and enhancer of split 2 (*Drosophila*)* | 29567 | *HES2* | −2.02 | Gene transcription |
| transmembrane 4 superfamily member 11* | 64364 | *PLLP* | −2.02 | Molecular transport |
| ferritin light chain 1* | 29292 | *FTL* | −2.03 | Cellular growth and proliferation |
| growth hormone–releasing hormone receptor* | 25321 | *GHRHR* | −2.04 | Cell signaling; cellular growth and proliferation; molecular transport; biomolecule metabolism |
| membrane protein, palmitoylated 2 (MAGUK p55 subfamily member 2)* | 85275 | *MPP2* | −2.04 | Cell signaling |
| ribosomal protein S27* | 94266 | *RPS27* | −2.05 | Cell signaling; cellular growth and proliferation; protein synthesis |
| translocase of inner mitochondrial membrane 22 homolog (yeast)* | 79463 | *TIMM22* | −2.06 | Others/unclassified |
| sec22 homolog* | 117513 | *SEC22A* | −2.08 | Molecular transport; protein trafficking |
| transmembrane protein with EGF-like and two follistatin-like domains 1* | 63845 | *TMEFF1* | −2.11 | Cellular growth and proliferation |
| paired-like homeodomain transcription factor 3* | 29609 | *PITX3* | −2.12 | Cellular development; gene transcription |
| fibrinogen, gamma polypeptide* | 24367 | *FGG* | −2.25 | Cell signaling |
| neurogenic differentiation 1* | 29458 | *NEUROD1* | −2.26 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| steroid-sensitive gene 1* | 64387 | *CCDC80* | −2.31 | Others/unclassified |
| ubiquitin A-52 residue ribosomal protein fusion product 1* | 64156 | *UBA52* | −2.33 | Gene transcription; protein synthesis |
| synuclein, gamma* | 64347 | *SNCG* | −2.42 | Cell death; cell morphology; cellular growth and proliferation; cellular movement |

*The change in expression was significant compared with untreated control ($P < .05$). Gene names in italics are common in both panels of T + $E_2$–treated LP and T + DES–treated VP.

**Table 2.** T + DES–Induced VP Dysplasia Panel: Genes Whose Expression Selectively Changed following T + DES Treatment in the VPs Harboring Dysplasia, but not in the LPs.

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| glutathione peroxidase 3* | 64317 | _GPX3_ | 17.188 | Cellular development; cellular growth and proliferation; post–translational modification; protein synthesis |
| _ferritin, heavy polypeptide 1_* | 25319 | _FTH1_ | 6.304 | Cell death; cell morphology; cellular growth and proliferation; DNA replication, recombination, and repair; free radical scavenging; post–translational modification |
| protein phosphatase 2a, catalytic subunit, alpha isoform* | 24672 | _PPP2CA_ | 3.388 | Biomolecule metabolism; cell death; cellular growth and proliferation; post–translational modification |
| monocarboxylate transporter* | 80878 | _SLC16A3_ | 2.263 | Others/unclassified |
| nuclease-sensitive element binding protein 1* | 29206 | _NSEP1_ | 1.898 | Cell death; gene transcription |
| _thymopoietin_* | 25359 | _TMPO_ | 1.814 | Cell cycle; DNA replication, recombination, and repair; gene transcription |
| _homeo box A1_* | 25607 | _HOXA1_ | 1.586 | Cell death; cellular development; cellular movement; gene transcription |
| cystatin C* | 25307 | _CST3_ | 1.585 | Cell death; cellular development; cellular growth and proliferation |
| _thyroid hormone receptor alpha_* | 81812 | _THRA_ | 1.583 | Cell death; cell morphology; cellular development; free radical scavenging; gene transcription |
| tubulin, alpha 1* | 64158 | _TUBA1A_ | 1.580 | Inflammation |
| _phospholipase C, delta 1_* | 24655 | _PLCD1_ | 1.532 | Cellular growth and proliferation |
| glutamate receptor, metabotropic 7* | 81672 | _GRM7_ | 1.481 | Cell signaling |
| _potassium voltage–gated channel, subfamily H (eag-related), member 7_* | 170739 | _KCNH7_ | 1.481 | Others/unclassified |
| plasminogen activator, urokinase* | 25619 | _PLAU_ | 1.461 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; inflammation |
| _vesicle-associated membrane protein 2_ | 24803 | _VAMP2_ | 1.452 | Cell signaling; cellular assembly and organization; cellular movement; molecular transport |
| glyceraldehyde-3-phosphate dehydrogenase* | 24383 | _GAPDH_ | 1.401 | Others/unclassified |
| protein phosphatase 1F (PP2C domain containing)* | 287931 | _PPM1F_ | 1.392 | Biomolecule metabolism; cell death; post–translational modification |
| _tumor protein p53_* | 24842 | _TP53_ | 1.379 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and; organization; cellular development; cellular growth and proliferation; cellular movement; cellular response to therapeutics; DNA replication, recombination, and repair; free radical scavenging; gene transcription; inflammation; post–translational modification; protein synthesis |
| opioid receptor, mu 1* | 25601 | _OPRM1_ | 1.375 | Cell death; cell signaling; cellular growth and proliferation; cellular movement; inflammation |
| _calcitonin/calcitonin–related polypeptide, alpha_* | 24241 | _CALCA_ | 1.361 | Cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; gene transcription; inflammation |
| testis-specific protein* | 192229 | _C3ORF34_ | 1.357 | Others/unclassified |
| _eukaryotic translation initiation factor 2B, subunit 2 beta_* | 84005 | _EIF2B2_ | 1.334 | Cellular development; cellular growth and proliferation |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide* | 25576 | _YWHAH_ | 1.333 | Cellular assembly and organization; gene transcription |
| glucagon-like peptide 1 receptor | 25051 | _GLP1R_ | 1.328 | Cell death; gene transcription; inflammation |
| transient receptor potential cation channel, subfamily C, member 2* | 64573 | _TRPC2_ | 1.322 | Others/unclassified |
| _dopamine receptor 4_* | 25432 | _DRD4_ | 1.311 | Cell signaling |
| early growth response 3* | 25148 | _EGR3_ | 1.289 | Cell death; cell signaling; cellular development; cellular growth and proliferation; gene transcription |
| _glutamate receptor, ionotropic, NMDA2B_* | 24410 | _GRIN2B_ | 1.248 | Cell morphology; cell signaling |
| chemokine (C–X–C motif) ligand 5* | 60665 | _CXCL6_ | 1.236 | Cell signaling; cellular movement |
| myosin IC | 65261 | _MYO1C_ | 1.190 | Cell morphology |
| breast cancer anti–estrogen resistance 1 | 25414 | _BCAR1_ | 1.190 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement |
| aryl hydrocarbon receptor nuclear translocator 2 | 25243 | _ARNT2_ | 1.172 | Gene transcription |
| _CCAAT/enhancer binding protein (C/EBP), delta_ | 25695 | _CEBPD_ | 1.151 | Cell cycle; cell death; cellular development; cellular growth and proliferation; gene transcription; inflammation; biomolecule metabolism; molecular transport |
| _CTD-binding SR-like rA1_ | 56081 | _SR-A1_ | 1.148 | Others/unclassified |
| _ADP-ribosylation factor 6_ | 79121 | _ARF6_ | 1.142 | Cell death; cell morphology; cellular assembly and organization; cellular movement |
| _calmodulin 3_ | 24244 | _CALM3_ | 1.138 | Cell death; cellular growth and proliferation; post–translational modification |
| synaptotagmin 3 | 25731 | _SYT3_ | 1.115 | Cell signaling; cellular assembly and organization; cellular movement; molecular transport |
| dynein, cytoplasmic, light chain 1 | 58945 | _DYNLL1_ | 1.090 | Cell death; cell morphology; cellular assembly and organization |
| MAD homolog 7 (_Drosophila_) | 81516 | _SMAD7_ | 1.062 | Cell cycle; cell death; cell morphology; cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| v-maf musculoaponeurotic fibrosarcom oncogene family, protein B (avian) | 54264 | _MAFB_ | 1.062 | Cell death; cellular development; cellular movement; gene transcription |
| _calmodulin 3_ | 24244 | _CALM3_ | 1.060 | Cellular growth and proliferation; post–translational modification |
| thymosin, beta 10 | 50665 | _TMSB10_ | 1.059 | Cell death; cellular assembly and organization; cellular growth and proliferation |

**Table 2.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| aldehyde dehydrogenase family 1, subfamily A2 | 116676 | *ALDH1A2* | 1.035 | Cell death; cellular development; cellular growth and proliferation |
| syntaxin 1B2 | 24923 | *STX1B2* | 1.032 | Others/unclassified |
| aldolase A | 24189 | *ALDOA* | −1.013 | Others/unclassified |
| prosaposin | 25524 | *PSAP* | −1.031 | Cell cycle; cell death; cellular growth and proliferation; biomolecule metabolism; molecular transport; post–translational modification |
| vesicle-associated membrane protein 2 | 24803 | *VAMP2* | −1.031 | Cell death; cell signaling; cellular assembly and organization; cellular movement; molecular transport |
| Rous sarcoma oncogene | 83805 | *SRC* | −1.070 | Biomolecule metabolism; cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; gene transcription; molecular transport; post–translational modification |
| *acetylcholinesterase* | 83817 | *ACHE* | −1.072 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; DNA replication, recombination, and repair; post–translational modification; protein synthesis |
| Max interacting protein 1 | 25701 | *MXI1* | −1.120 | Cell morphology; cellular growth and proliferation; gene transcription |
| betacellulin | 64022 | *BTC* | −1.137 | Cell cycle; cell death; cell signaling; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair |
| argininosuccinate synthetase | 25698 | *ASS1* | −1.165 | Others/unclassified |
| nuclear receptor subfamily 1, group D, member 2 | 259241 | *NR1D2* | −1.170 | Gene transcription |
| stannin | 29140 | *SNN* | −1.242 | Cell death |
| phosphatase and tensin homolog* | 50557 | *PTEN* | −1.272 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription inflammation; biomolecule metabolism; molecular transport; post–translational modification |
| solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 7* | 116638 | *SLC17A7* | −1.287 | Cell signaling |
| carnitine palmitoyltransferase 1, liver* | 25757 | *CPT1A* | −1.291 | Biomolecule metabolism |
| isopentenyl-diphosphate delta isomerase* | 89784 | *IDI1* | −1.294 | Others/unclassified |
| LIM homeobox protein 5 | 124451 | *LHX5* | −1.317 | Others/unclassified |
| calpain, small subunit 1* | 29156 | *CAPNS1* | −1.318 | Cell death; cellular assembly and organization; cellular growth and proliferation; cellular movement |
| filaggrin | 24641 | *FLG* | −1.325 | Cellular assembly and organization |
| microsomal glutathione *S*-transferase 1 | 171341 | *MGST1* | −1.329 | Biomolecule metabolism |
| *protein tyrosine phosphatase, nonreceptor type substrate 1** | 25528 | *SIRPA* | −1.330 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription; inflammation |
| neurofibromatosis 2 | 25744 | *NF2* | −1.333 | Cell death; cellular growth and proliferation; cellular movement |
| Notch gene homolog 3 (*Drosophila*)* | 56761 | *NOTCH3* | −1.335 | Cellular development; gene transcription |
| *killer cell lectin–like receptor subfamily B member 1B** | 25192 | *KLRB1* | −1.338 | Cell death |
| basic transcription element binding protein 1* | 117560 | *KLF9* | −1.339 | Gene transcription |
| regulating synaptic membrane exocytosis 1* | 84556 | *RIMS1* | −1.353 | Cell morphology; cell signaling; cellular assembly and organization; cellular movement; molecular transport |
| transglutaminase 1* | 60335 | *TGM1* | −1.376 | Biomolecule metabolism; cell death; cellular development; post–translational modification |
| translocase of inner mitochondrial membrane 23 homolog (yeast)* | 54312 | *TIMM23* | −1.393 | Others/unclassified |
| lysozyme | 25211 | *LYZ* | −1.399 | Others/unclassified |
| solute carrier family 25 (mitochondrial carrier; oxoglutarate carrier), member 11* | 64201 | *SLC25A11* | −1.407 | Others/unclassified |
| hydroxysteroid 11-beta dehydrogenase 1* | 25116 | *HSD11B1* | −1.407 | Cellular development; cellular growth and proliferation |
| potassium intermediate/small conductance calcium–activated channel, subfamily N, member 3* | 54263 | *KCNN3* | −1.412 | Cell signaling |
| B-cell leukemia/lymphoma 2* | 24224 | *BCL2* | −1.413 | Cell cycle; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; cellular response to therapeutics; DNA replication, recombination, and repair; biomolecule metabolism; gene transcription; inflammation; molecular transport; post–translational modification |
| hyperpolarization-activated, cyclic nucleotide–gated $K^+$ 4* | 59266 | *HCN4* | −1.415 | Cell signaling |
| perforin 1 (pore-forming protein)* | 50669 | *PRF1* | −1.417 | Cell death; cell morphology; cell signaling; DNA replication, recombination, and repair; inflammation |
| *calcitonin/calcitonin–related polypeptide, alpha** | 24241 | *CALCA* | −1.433 | Cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; gene transcription; inflammation |
| nuclear RNA export factor 1* | 59087 | *NXF1* | −1.436 | Protein synthesis |
| fibroblast growth factor 14* | 63851 | *FGF14* | −1.439 | Others/unclassified |
| solute carrier family 7 (cationic amino acid transporter, y+ system), member 3* | 29485 | *SLC7A3* | −1.455 | Others/unclassified |

**Table 2.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| ATP synthase, H$^+$ transporting, mitochondrial $F_0$ complex, subunit b, isoform 1* | 171375 | *ATP5F1* | –1.456 | Cellular growth and proliferation |
| septin 3* | 56003 | *SEPT3* | –1.468 | Others/unclassified |
| cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)* | 54239 | *CHRNB2* | –1.469 | Cell signaling |
| wild-type p53–induced gene 1* | 64394 | *ZMAT3* | –1.480 | Cell death; cellular growth and proliferation; DNA replication, recombination, and repair |
| glutamate receptor, ionotropic, kainate 4* | 24406 | *GRIK4* | –1.482 | Cell signaling |
| Kruppel-like factor 15* | 85497 | *KLF15* | –1.488 | Gene transcription |
| aquaporin 6* | 29170 | *AQP6* | –1.496 | Others/unclassified |
| unc-5 homolog A (*C. elegans*)* | 60629 | *UNC5A* | –1.498 | Cell death |
| integrin beta 4* | 25724 | *ITGB4* | –1.502 | Cell death; cell morphology; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| peptidylprolyl isomerase A* | 25518 | *PPIA* | –1.526 | Cell death; cellular development; cellular growth and proliferation; cellular movement; DNA replication, recombination, and repair; inflammation; post–translational modification |
| FXYD domain–containing ion transport regulator 6* | 63847 | *FXYD6* | –1.562 | Others/unclassified |
| ribosomal protein L37* | 81770 | *RPL37* | –1.579 | Others/unclassified |
| RT1 class II, locus Da* | 294269 | *HLA-DRA* | –1.580 | Cell signaling; inflammation |
| FK506 binding protein 12-rapamycin–associated protein 1* | 56718 | *FRAP1* | –1.596 | Biomolecule metabolism; cell cycle; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription; inflammation; post–translational modification; protein synthesis |
| *eukaryotic translation elongation factor 1 alpha 1** | 171361 | *EEF1A1* | –1.618 | Cell death; protein synthesis |
| glutathione *S*-transferase theta 1* | 25260 | *GSTT1* | –1.622 | Biomolecule metabolism |
| solute carrier family 4, member 1* | 24779 | *SLC4A1* | –1.630 | Cell death; cellular growth and proliferation |
| fibroblast growth factor 17* | 29368 | *FGF17* | –1.642 | Cellular growth and proliferation |
| *forkhead box M1** | 58921 | *FOXM1* | –1.646 | Cell cycle; cell death; cell morphology; cellular growth and proliferation; gene transcription |
| ATPase, class II, type 9A* | 84011 | *ATP9A* | –1.649 | Others/unclassified |
| phosphorylase kinase, gamma 2 (testis)* | 140671 | *PHKG2* | –1.679 | Biomolecule metabolism; post–translational modification |
| arrestin, beta 1* | 25387 | *ARRB1* | –1.683 | Cellular movement |
| rhoB gene* | 64373 | *RHOB* | –1.684 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| *par-3 (partitioning defective 3) homolog (C. elegans)** | 81918 | *PARD3* | –1.686 | Cell morphology; cell signaling; cellular assembly and organization; cellular development; gene transcription |
| ribosomal protein L21* | 79449 | *RPL21* | –1.687 | Others/unclassified |
| RAS protein–specific guanine nucleotide–releasing factor 1* | 192213 | *RASGRF1* | –1.715 | Cell morphology; cell signaling; cellular growth and proliferation; gene transcription |
| *acetylcholinesterase** | 83817 | *ACHE* | –1.741 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; DNA replication, recombination, and repair; post–translational modification; protein synthesis |
| ribosomal protein L18* | 81766 | *RPL18* | –1.741 | Others/unclassified |
| *granzyme M (lymphocyte met-ase 1)** | 29252 | *GZMM* | –1.745 | Cell death |
| *Bcl2-associated X protein** | 24887 | *BAX* | –1.746 | Cell cycle; cell death; cell morphology; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular response to therapeutics; DNA replication, recombination, and repair; free radical scavenging; inflammation; biomolecule metabolism; molecular transport; protein synthesis |
| legumain* | 63865 | *LGMN* | –1.749 | Cellular movement |
| RAB6A, member RAS oncogene family* | 84379 | *RAB6A* | –1.752 | Cellular assembly and organization |
| matrix metalloproteinase 16* | 65205 | *MMP16* | –1.763 | Cellular movement; inflammation |
| olfactory receptor 226* | 65140 | *OR6A2* | –1.770 | Others/unclassified |
| mitogen-activated protein kinase 14* | 81649 | *MAPK14* | –1.775 | Biomolecule metabolism; cell cycle; cell death; cell morphology; cellular development; cellular growth and proliferation; cellular movement; gene transcription; inflammation; post–translational modification |
| *c-mer protooncogene tyrosine kinase** | 65037 | *MERTK* | –1.780 | Biomolecule metabolism; cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; post–translational modification |
| clathrin, heavy polypeptide (Hc)* | 54241 | *CLTC* | –1.786 | Cell morphology; cellular growth and proliferation |
| *transient receptor potential cation channel, subfamily C, member 4** | 84494 | *TRPC4* | –1.793 | Others/unclassified |
| carnitine palmitoyltransferase 1b* | 25756 | *CPT1B* | –1.795 | Biomolecule metabolism |
| PDZ and LIM domain 1 (elfin)* | 54133 | *PDLIM1* | –1.796 | Gene transcription |
| fatty acid amide hydrolase* | 29347 | *FAAH* | –1.798 | Cell death; inflammation |
| fatty acid binding protein 4, adipocyte* | 79451 | *FABP4* | –1.820 | Gene transcription |
| protein tyrosine phosphatase, nonreceptor type 12* | 117255 | *PTPN12* | –1.826 | Biomolecule metabolism; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular movement; post–translational modification |
| potassium voltage–gated channel, Shab-related subfamily, member 2* | 117105 | *KCNB2* | –1.834 | Others/unclassified |

**Table 2.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| glutathione _S_-transferase, pi 2* | 29438 | *GSTP1* | −1.856 | Cell death; cellular growth and proliferation; biomolecule metabolism; gene transcription |
| Fc receptor, IgG, alpha chain transporter* | 29558 | *FCGRT* | −1.870 | Cell signaling; molecular transport |
| voltage-gated channel like 1* | 266760 | *VGCNL1* | −1.871 | Others/unclassified |
| prostaglandin D$_2$ synthase* | 25526 | *PTGDS* | −1.888 | Cell death; cell morphology |
| _MAP-kinase activating death domain_* | 94193 | *MADD* | −1.934 | Cell death; cellular growth and proliferation |
| neogenin* | 81735 | *NEO1* | −1.935 | Cellular growth and proliferation; cellular movement; gene transcription |
| calbindin 1* | 83839 | *CALB1* | −1.950 | Cell death; cell morphology; cell signaling |
| guanylate cyclase 2e* | 79222 | *GUCY2D* | −1.957 | Others/unclassified |
| _adrenal secretory serine protease precursor_* | 64565 | *TMPRSS11D* | −1.971 | Others/unclassified |
| ubc2e ubiquitin–conjugating enzyme* | 641452 | *Ube2d2* | −1.986 | Others/unclassified |
| neuroblastoma, suppression of tumorigenicity 1* | 50594 | *NBL1* | −2.003 | Cellular movement |
| collagen, type 1, alpha 1* | 29393 | *COL1A1* | −2.023 | Cell morphology; cellular growth and proliferation; cellular movement |
| homeodomain interacting protein kinase 3* | 83617 | *HIPK3* | −2.034 | Biomolecule metabolism; cell signaling; post–translational modification |
| intercellular adhesion molecule 1* | 25464 | *ICAM1* | −2.052 | Cell death; cell morphology; cell signaling; cellular development; cellular growth and proliferation; cellular movement; inflammation |
| cyclin-dependent kinase 5* | 140908 | *CDK5* | −2.134 | Biomolecule metabolism; cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; molecular transport; post–translational modification |
| ATPase, Cu$^{2+}$ transporting, beta polypeptide* | 24218 | *ATP7B* | −2.137 | Cell death |
| Jun D protooncogene* | 24518 | *JUND* | −2.159 | Cell death; cell morphology; cellular growth and proliferation; gene transcription |
| _neurexophilin 3_* | 59315 | *NXPH3* | −2.168 | Others/unclassified |
| heterogeneous nuclear ribonucleoprotein methyltransferase–like 3 (_S. cerevisiae_)* | 89820 | *PRMT3* | −2.171 | Biomolecule metabolism; post–translational modification |
| _midline 1_* | 54252 | *MID1* | −2.180 | Cellular assembly and; organization |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1* | 24565 | *ABCC1* | −2.191 | Cell death; cellular movement; inflammation; biomolecule metabolism; molecular transport |
| prothymosin alpha* | 29222 | *PTMA* | −2.313 | Cell cycle; cell death; cellular development; cellular growth and proliferation; gene transcription |
| ubiquilin 1* | 114590 | *UBQLN1* | −2.322 | Others/unclassified |
| similar to Leydig cell tumor 10 kDa protein* | 288913 | *C19ORF53* | −2.346 | Others/unclassified |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein* | 25587 | *ID2* | −2.357 | Cell cycle; cell death; cell morphology; cellular development; cellular growth and proliferation; cellular movement; gene transcription |
| lectin, galactose binding, soluble 1* | 56646 | *LGALS1* | −2.385 | Cell cycle; cell death; cell morphology; cellular development; cellular growth and proliferation; cellular movement gene transcription; inflammation; post–translational modification |
| _calreticulin_* | 64202 | *CALR* | −2.401 | Cell cycle; cell death; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement; gene transcription; post–translational modification |
| carbonic anhydrase 5* | 54233 | *CA5A* | −2.427 | Inflammation |
| mitogen-activated protein kinase 13* | 29513 | *MAPK13* | −2.438 | Cell death; cell morphology; gene transcription; inflammation |
| cytochrome _P_450, family 19, subfamily a, polypeptide 1* | 25147 | *CYP19A1* | −2.440 | Cell death; cell morphology; cellular development; cellular growth and proliferation; cellular movement; gene transcription; biomolecule metabolism |
| nucleobindin 1* | 84595 | *NUCB1* | −2.513 | Others/unclassified |
| tropomodulin 2* | 58814 | *TMOD2* | −2.563 | Cell signaling; cellular assembly and organization |
| apolipoprotein B editing complex 1* | 25383 | *APOBEC1* | −2.655 | Others/unclassified |
| solute carrier family 7 (cationic amino acid transporter, y+ system), member 7* | 83509 | *SLC7A7* | −2.720 | Cell signaling; cellular growth and proliferation |
| _hsp70-interacting protein_* | 246146 | *HSPBP1* | −2.772 | Post–translational modification |
| Rsec5 protein* | 171455 | *EXOC2* | −2.779 | Cell signaling; molecular transport |
| MAD homolog 9 (_Drosophila_)* | 85435 | *SMAD9* | −2.815 | Others/unclassified |
| ERM-binding phosphoprotein* | 59114 | *SLC9A3R1* | −2.851 | Cell signaling; cellular growth and proliferation |
| low-density lipoprotein receptor–related protein 3* | 89787 | *LRP3* | −2.869 | Others/unclassified |
| Rab geranylgeranyl transferase, a subunit* | 58983 | *RABGGTA* | −2.890 | Biomolecule metabolism; post–translational modification |
| cadherin EGF LAG seven-pass G-type receptor 2* | 83465 | *CELSR2* | −2.923 | Others/unclassified |
| tropomyosin 4* | 24852 | *TPM4* | −3.019 | Cellular movement |
| cytochrome _P_450, family 2, subfamily e, polypeptide 1* | 25086 | *CYP2E1* | −3.161 | Cell death; biomolecule metabolism |
| CEA-related cell adhesion molecule 9* | 116711 | *CEACAM9* | −3.207 | Others/unclassified |
| discoidin domain receptor family, member 2* | 83573 | *DDR2* | −3.253 | Others/unclassified |
| phosphoglucomutase 1* | 24645 | *PGM1* | −3.308 | Others/unclassified |
| gamma-glutamyl carboxylase* | 81716 | *GGCX* | −3.455 | Post–translational modification |
| Cplx1 complexin 1* | 64832 | *CPLX1* | −3.464 | Cell signaling; cellular assembly; and organization; cellular movement; molecular transport |
| septin 9* | 83788 | *SEPT9* | −3.781 | Cell cycle; protein synthesis |
| matrix metallopeptidase 8* | 63849 | *MMP8* | −3.785 | Cell death, cellular movement |
| thyroid hormone receptor interactor 10* | 116717 | *TRIP10* | −4.232 | Cell death |
| carboxylesterase 3* | 113902 | *CES1* | −4.325 | Others/unclassified |
| cyclin-dependent kinase 2* | 362817 | *CDK2* | −4.458 | Biomolecule metabolism; cell cycle; cell death; cell morphology; cellular development; cellular growth and proliferation; DNA replication, recombination, and repair; gene transcription; post–translational modification |

**Table 2.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | Functions |
|---|---|---|---|---|
| monoamine oxidase B* | 25750 | *MAOB* | −4.873 | Cell death |
| solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12* | 50676 | *SLC6A12* | −5.287 | Others/unclassified |
| peroxiredoxin 1* | 117254 | *PRDX1* | −5.360 | Cell death; cell morphology; cellular growth and proliferation; gene transcription; post–translational modification |
| ADP-ribosylation factor 4* | 79120 | *ARF4* | −5.374 | Others/unclassified |
| glypican 3* | 25236 | *GPC3* | −5.638 | Cell death; cellular growth and proliferation |
| protein kinase C, delta binding protein* | 85332 | *PRKCDBP* | −6.059 | Others/unclassified |
| cd86 antigen* | 56822 | *CD86* | −6.118 | Cell signaling; cellular development; cellular growth and proliferation; cellular movement; gene transcription; inflammation |
| Sjogren syndrome antigen B* | 81783 | *SSB* | −6.131 | Gene transcription; protein synthesis |
| secretoglobin, family 2A, member 1* | 25010 | *PSBP1* | −6.227 | Others/unclassified |
| procollagen, type I, alpha 2* | 84352 | *COL1A2* | −7.076 | Cell morphology |
| A kinase (PRKA) anchor protein 1* | 114124 | *AKAP1* | −8.502 | Cell death |
| methionine adenosyltransferase II, alpha* | 171347 | *MAT2A* | −9.474 | Others/unclassified |
| FXYD domain–containing ion transport regulator 1* | 58971 | *FXYD1* | −9.644 | Cellular growth and proliferation; gene transcription |
| CD24 antigen* | 25145 | *CD24* | −11.299 | Cell death; cell morphology; cell signaling; cellular assembly and organization; cellular development; cellular growth and proliferation; cellular movement |
| nuclear receptor subfamily 1, group I, member 2* | 84385 | *NR1I2* | −11.958 | Biomolecule metabolism; gene transcription; inflammation; molecular transport; post–translational modification |
| glial cell line derived neurotrophic factor family receptor alpha 1* | 25454 | *GFRA1* | −17.708 | Cell death; cell morphology; cellular development; cellular; growth and proliferation; cellular movement |
| cell division cycle 25 homolog A (*S. cerevisiae*)* | 171102 | *CDC25A* | −19.859 | Cell cycle; cell death; cell morphology; cellular growth and proliferation; dna replication, recombination, and repair |
| 5-hydroxytryptamine (serotonin) receptor 5B* | 79247 | *HTR5B* | −22.285 | Others/unclassified |
| NSFL1 (p97) cofactor (p47)* | 83809 | *NSFL1C* | −22.400 | Others/unclassified |
| membrane and microfilament–associated protein p58* | 207121 | *RGD: 727794* | −49.533 | Cellular assembly and organization |

*The change in expression was significant compared with untreated control ($P < .05$). Gene names in italics are common in both panels of T + $E_2$–treated LP and T + DES–treated VP.

### *Reverse Transcription and Real-Time Quantitative Polymerase Chain Reaction*

The total RNA from each sample of prostate tissue was reverse-transcribed into cDNA using Superscript III (Invitrogen, Carlsbad, CA). Specific primers were designed using either Primer Express 3 (Applied Biosystems, Foster City, CA) or Primer3 software [28]; the sequence of the primer is listed in Table W1. Real-time quantitative polymerase chain reaction (q-PCR) was performed on the 7900HT Fast Real-Time PCR System (ABI Biosystems) using the Power SYBR Green PCR master mix (Applied Biosystems). Polymerase chain reaction was performed in a total volume of 10 μl containing 50 ng of total cDNA, 1× Power SYBR Green PCR master mix, and a final primer concentration of 800 nM. The relative expression level was analyzed by the $\Delta\Delta C_t$ method [29] and one-way ANOVA followed by Tukey post hoc analysis, where $P < .05$ was considered statistically significant.

## Results

### *T + $E_2$ and T + DES Treatments Differentially Induced Dysplasia in LP and VP, Respectively*

The expected physiological and histologic changes resulting from T + $E_2$ and T + DES treatment were observed as reported previously [15,18–20]. Dysplasia was observed in the T + $E_2$–treated LPs (100% incidence) and T + DES–treated VPs (100% incidence), whereas no preneoplastic lesions were observed in T + $E_2$–treated VPs and T + DES LPs. In T + $E_2$–treated LPs, the dysplastic lesions were often accompanied by inflammatory infiltrates [17].

### *Hierarchical Clustering Identified Differential Action of $E_2$ and DES in the Two Prostate Lobes*

Unsupervised hierarchical clustering was performed for each hormone treatment group (T + $E_2$ or T + DES) to determine the relatedness of replicate LP and VP samples ($n = 5$ per group) according to similarity in gene expression patterns among the 1063 genes with a significant difference in expression across samples, without prior knowledge of gene and sample identity.

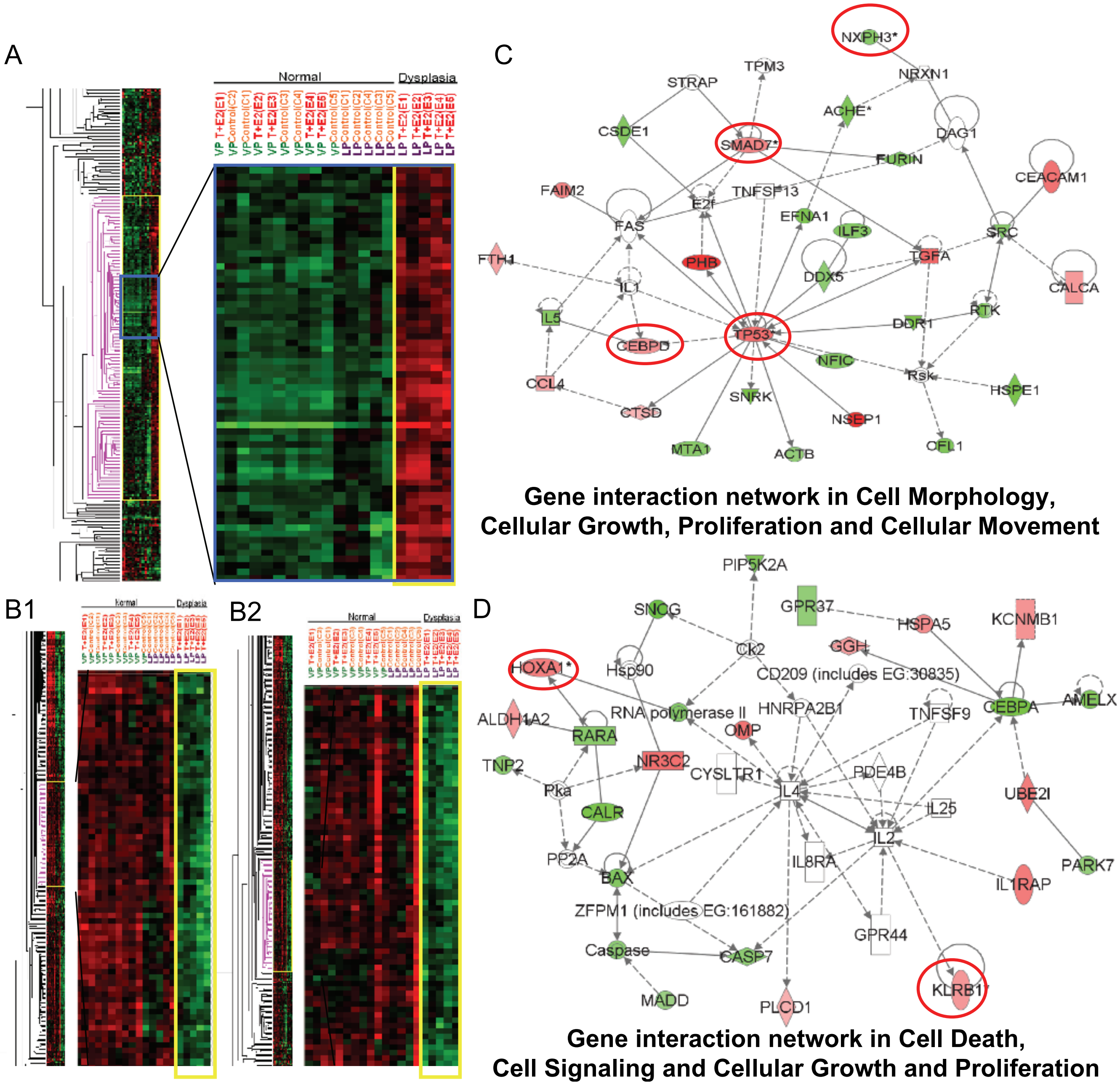
Hierarchical clustering of samples showed that all LPs treated with T + $E_2$ formed one cluster distinct from the cluster containing all untreated LPs. The hormone treatment, however, did not partition the hormone-treated and -untreated VPs, which formed a single large cluster (Figure 1*A*). These results indicate that the T + $E_2$ treatment induced changes in gene expression mainly in the LP and had little, if any, effect on the gene expression pattern in the VP.

In a similar manner, T + DES treatment segregated only the VPs into two distinct clusters (treated and untreated) and did not partition the LPs into distinctive groups (Figure 1*B*). These findings indicate that the hormone treatment altered primarily the gene expression pattern in the VP and had little effect on LP gene expression. It is interesting that the gene expression pattern in the VP after T + DES treatment appeared to more closely resemble that observed in the LPs, as the T + DES–treated VPs formed a cluster more closely linked to the LP cluster than the one comprising untreated VPs.

### *Identification of Estrogen-Induced Differentially Expressed Genes Related to Dysplasia in Rat LP or VP*

We used the following criteria to identify two panels of dysplasia-related genes: 1) the T + $E_2$–induced LP dysplasia panel contains genes whose expression changed following T + $E_2$ treatment in the LPs harboring dysplasia but excludes those whose expression also changed in the VPs with no dysplastic changes (253 genes; Figure 1*C*, *left*; Table 1), and 2) the T + DES–induced VP dysplasia panel includes genes whose expression changed after T + DES treatment in the VPs harboring dysplasia but excludes those whose expression also changed in the LPs without dysplasia (198 genes; Figure 1*C*, *right*; Table 2).

Image plots (Figure 2, *A*, and *B1* and *B2*) showed the up- and downregulated genes in the T + $E_2$–induced LP dysplasia panel (253 genes), respectively. Although genes in this panel were distributed among 27 IPA networks, two major networks with the highest relevancy scores were identified: one related to cell morphology, cellular growth, proliferation, and movement (Figure 2*C*), and the other related to apoptosis and cell signaling (Figure 2*D*). From these two networks, six genes were selected for post hoc confirmation by real-time q-PCR (Figure 3). All six genes showed the predicted expression patterns. Significant differences ($P$ < .01/.05) were observed between the transcript levels in the T + $E_2$–treated and –untreated LPs, whereas no significant differences ($P$ > .05) in the transcript levels



Gene interaction network in Cell Morphology, Cellular Growth, Proliferation and Cellular Movement

Gene interaction network in Cell Death, Cell Signaling and Cellular Growth and Proliferation

**Figure 2.** Heat maps and gene interaction networks of differentially expressed genes found exclusively in the LP dysplasia following T + $E_2$ treatment. Red and green denote upregulated and downregulated expression, respectively, as compared with the overall gene's mean value normalized to the universal rat reference RNA. Columns represent data from a single prostate sample, and rows correspond to a single gene probe. (A) A single cluster of upregulated genes identified in the T + $E_2$ LP dysplasia, marked with pink (*left panel*); a selected region (blue box) of this cluster is enlarged (*right panel*). (B1 and B2) Two separate downregulated gene clusters observed only in T + $E_2$ LP dysplasia, marked with pink (*left panels*); selected clusters are magnified (*right panels*). (C and D) Two representative gene interaction networks (with the highest relevancy scores) generated by IPA analysis from the differentially expressed genes in the T + $E_2$ LP dysplasia panel. Green indicates downregulated; red, upregulated. Genes bordered in red were validated by real-time q-PCR. See Figure 1 for key to IPA network.

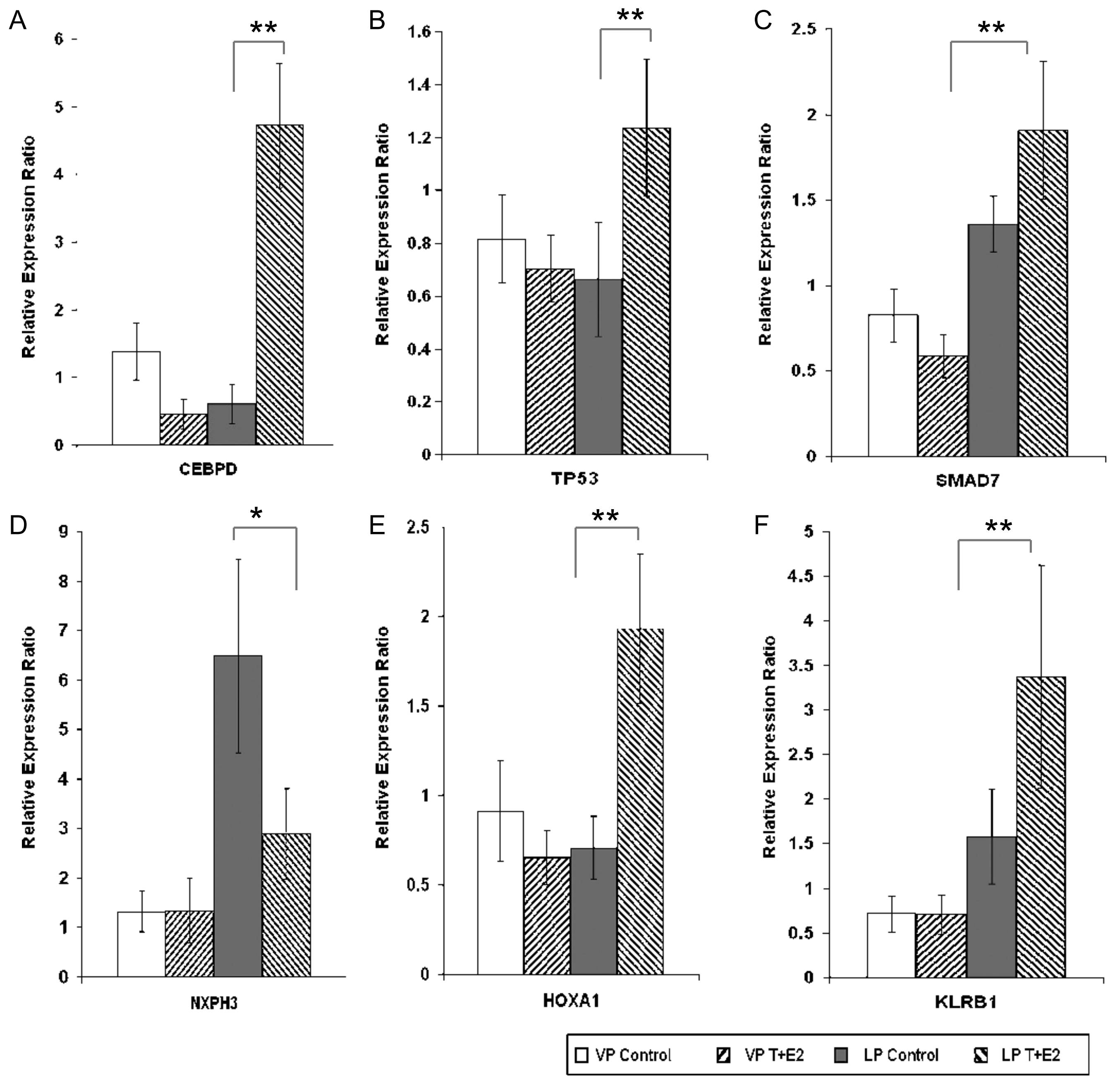


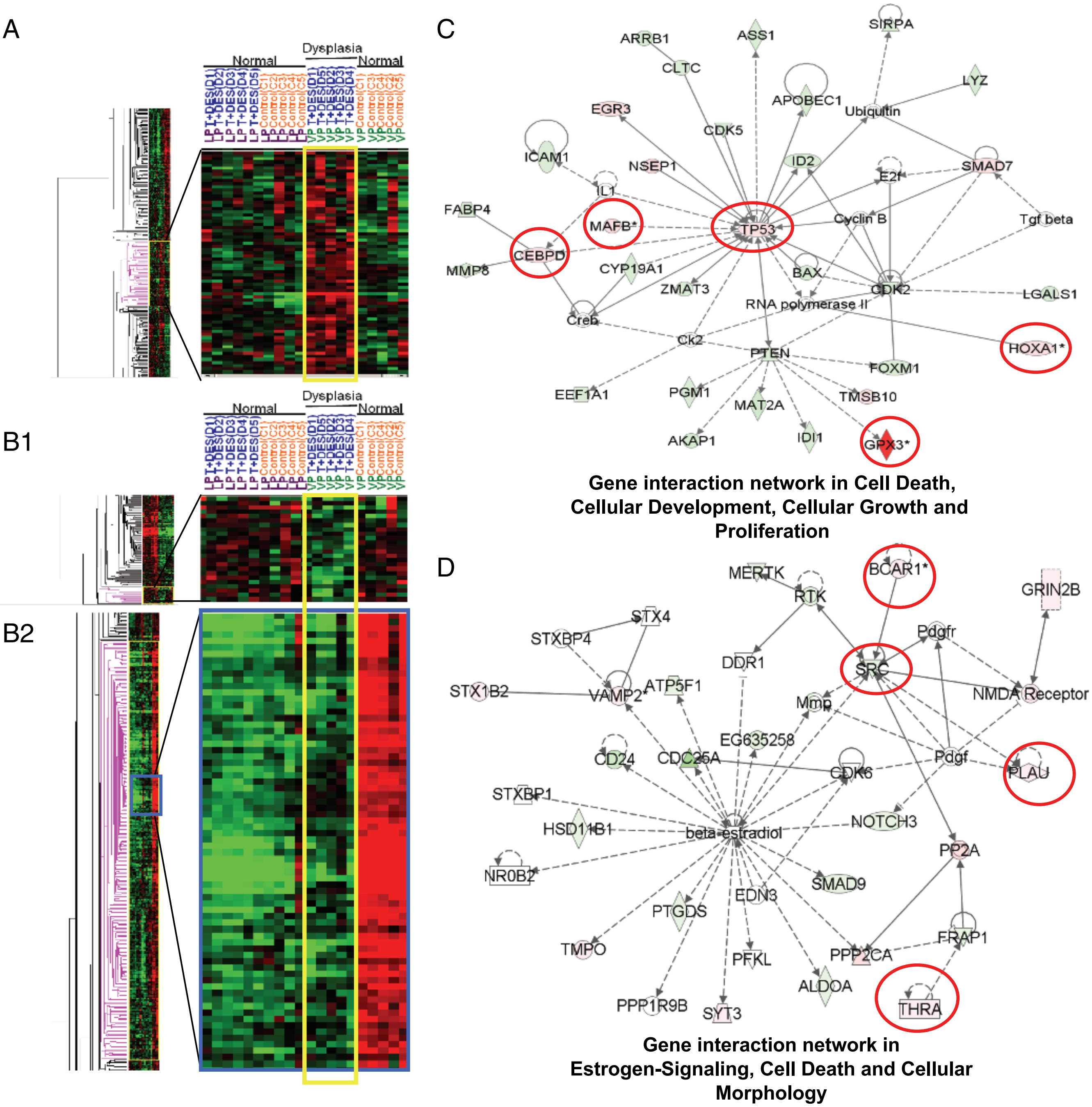
**Figure 3.** Post hoc real-time q-PCR analyses of selected genes in the T + $E_2$ LP dysplasia panel. Data were normalized to the levels of Rpl19. Bars indicate standard deviations (SD) of three to five animals in each treatment group. *$P < .05$, **$P < .01$ by one-way ANOVA with Tukey post hoc analysis.

were observed between the treated and untreated VP groups. These genes are the CCAAT/enhancer binding protein-delta (*Cebpd*), the tumor protein *Tp53*, MAD homolog 7 (*Smad7*), homeobox A1 (*Hoxa1*), killer cell lectin–like receptor subfamily B member 1 (*Klrb1*), and neurexophilin 3 (*Nxph3*). Notably, the q-PCR data correlated well with those obtained by microarray analyses (Figure W1*A*). T + $E_2$–response genes found in VP, in contrast to those found in the LP, were not mapped to any particular IPA networks (data not shown).

Image plots illustrated distinctive upregulated (Figure 4*A*) and downregulated (Figure 4, *B1* and *B2*) genes in the T + DES–induced VP dysplasia panel. In addition, a unique set of genes was exclusively repressed by T + DES in the VP harboring dysplasia (Figure 4*B2*). These genes were also underexpressed in LPs compared with the untreated VPs. Genes in the T + DES–treated VP panel (198 genes) mapped primarily to two major networks related to 1) apoptosis, cellular development, growth, and proliferation and 2) estrogen signaling, as they exhibited the highest relevancy scores (Figure 4, *C* and *D*, respectively). From the two networks, nine genes were selected for post hoc confirmation by q-PCR analyses that correlated well with those obtained by microarrays (Figure W1*B*). All nine genes showed significant increases in transcript levels ($P < .01/.05$) in the VP with T + DES treatment and exhibited little or no change in expression ($P > .05$) in the LPs of the treated group compared with untreated controls

(Figure 5). They include *Cebpd*, *Tp53*, v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (*Mafb*), *Hoxa1*, breast cancer anti–estrogen resistance 1 (*Bcar1*), plasminogen activator urokinase (*Plau*), thyroid hormone receptor alpha (*Thra*), glutathione peroxidase 3 (*Gpx3*), and v-*src* sarcoma viral oncogene homolog (*Src*).

Only 32 genes were found to be common in both dysplasia-related panels (Figure 1*C*), and 23 (of 32) genes formed a unique gene network when mapped by IPA (Figure 1*D*). We postulate that this gene network is central to $E_2$- or DES-induced dysplasia in the LP or VP.



**Gene interaction network in Cell Death, Cellular Development, Cellular Growth and Proliferation**

**Gene interaction network in Estrogen-Signaling, Cell Death and Cellular Morphology**

**Figure 4.** Heat maps and gene interaction networks of differentially expressed genes found uniquely in the VP dysplasia following T + DES treatment. (A) A single cluster of upregulated genes identified only in the T + DES VP dysplasia, marked with pink (*left panel*), and the selected cluster enlarged (*right panel*). (B1 and B2) Clusters of downregulated genes in the VP but not in the LP following T + DES exposure. Interestingly, a single cluster (B2, *left panel*) corresponds to the downregulated genes in the T + DES–treated VP and is also underexpressed in both untreated and treated LPs. A selected region (*blue box*) of this cluster is enlarged (*right panel*). (C and D) Two representative gene interaction networks (with the highest relevancy scores) generated by IPA analysis from the differentially expressed genes in the T + DES VP dysplasia panel. Green indicates downregulated; red, upregulated. Genes bordered with red were validated by real-time q-PCR. See Figure 1 for key to IPA network.

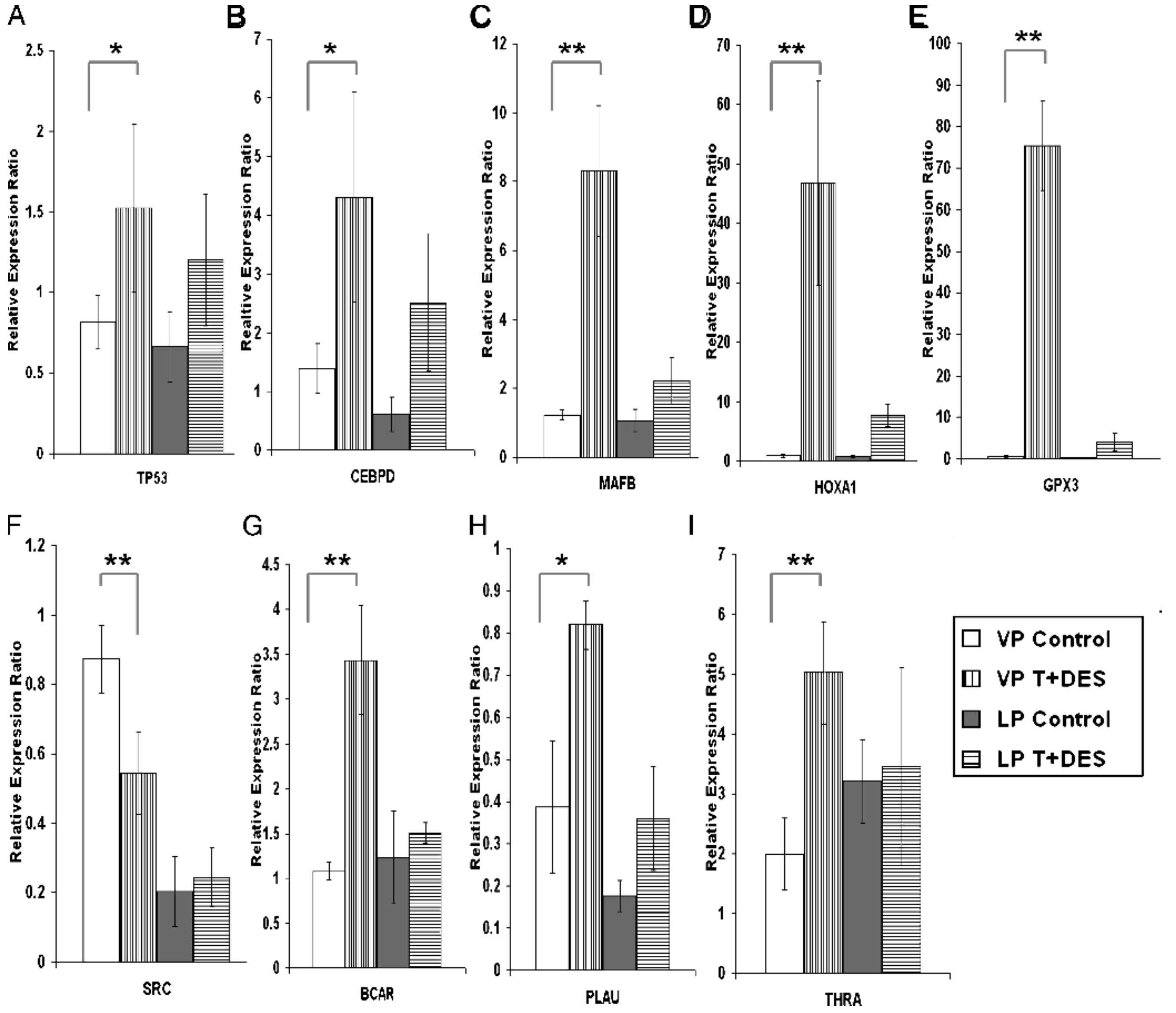


**Figure 5.** Post hoc validation of selected genes in the T + DES VP dysplasia panel by real-time q-PCR. The data were normalized to the levels of Rpl19. Bars indicated standard deviations (SD) of three to five animals in each treatment group. $^*P < .05$, $^{**}P < .01$ by one-way ANOVA with Tukey post hoc analysis.

### *Identification of Estrogen-induced Differentially Expressed Genes That Are Not Related to Dysplasia in Rat LP or VP*

We also identified two sets of hormone-induced genes that are not related to dysplasia. These genes exhibited differential expression in the VP following T + $E_2$ treatment (14 genes; Figure 1*C*, *left bottom*) and in the LP following T + DES treatment (190 genes; Figure 1*C*, *right bottom*). They are published in Tables W2 and W3.

### *Genes Insensitive to the T + $E_2$ and T + DES Treatments*

Two sets of 156 and 80 genes were identified as insensitive in the LP and/or VP to T + $E_2$ or T + DES treatment, respectively (Figure 6, *A–C*; Tables W4 and W5). Forty-one genes were found in both hormone-insensitive panels and mapped to an IPA network (Figure 6*D*) that includes the androgen receptor (Ar), a key regulator of prostate function.

## Discussion

Exposure of the human prostate to estrogen may increase as men age [2–4] or with increased exposure to dietary estrogens such as DES or zeranol residues in meat, bisphenol A from food containers, or phytoestrogens [9]. The NBL rat provides a relevant model for elucidating mechanisms underlying carcinogenesis caused by such exposures, such as dysplasia and PCa, that consistently developed in the LP or the VP following chronic T–supported treatment with $E_2$ or DES, respectively [15,18–20]. In the present study, we assessed transcriptional profiles elicited by the xenoestrogen DES in comparison with those of the endogenous hormone $E_2$ and observed prostatic lobe–specific differential responses to the two estrogens in NBL rats. Hierarchical clustering revealed that the T + $E_2$ treatment principally affects the LP gene expression profile whereas the T + DES targets that of the VP. Two distinct panels of dysplasia-related genes were identified: the T + $E_2$ LP panel (253 genes) and the T + DES VP panel (198 genes), with only 32 overlapping genes. These findings indicate that the two estrogens alter gene expression profiles only in the prostatic lobe that develops dysplasia following each of the hormonal treatments. These findings imply a functional divergence of the two estrogens with respect to their oncogenic actions in the rat prostate. Thus, endocrine disruption of gene expression and dysplasia induction of the two estrogens are categorically different [9], although they may share some biologic convergence [30].

The IPA analysis identified distinct gene interaction networks based on differential expression profiles. It classified genes into functional categories and suggested a possible mechanistic linkage among the differentially expressed genes. We also used this tool to help prioritize genes for confirmation. The T + $E_2$ treatment altered the expression of LP genes primarily in two major networks: one related to cell morphology, cellular growth, proliferation, and movement, and the other related to apoptosis and cell signaling. Exposure to T + DES also affected expression of genes in a similar network associated with apoptosis, cellular development, growth, and proliferation. Intriguingly, it also altered the expression of a set of genes linked to $E_2$, a finding that may explain why, after T + DES treatment, gene expression profiles in the VP shifted closer to those in the treated and untreated LPs, which are under the influence of natural estrogen. By

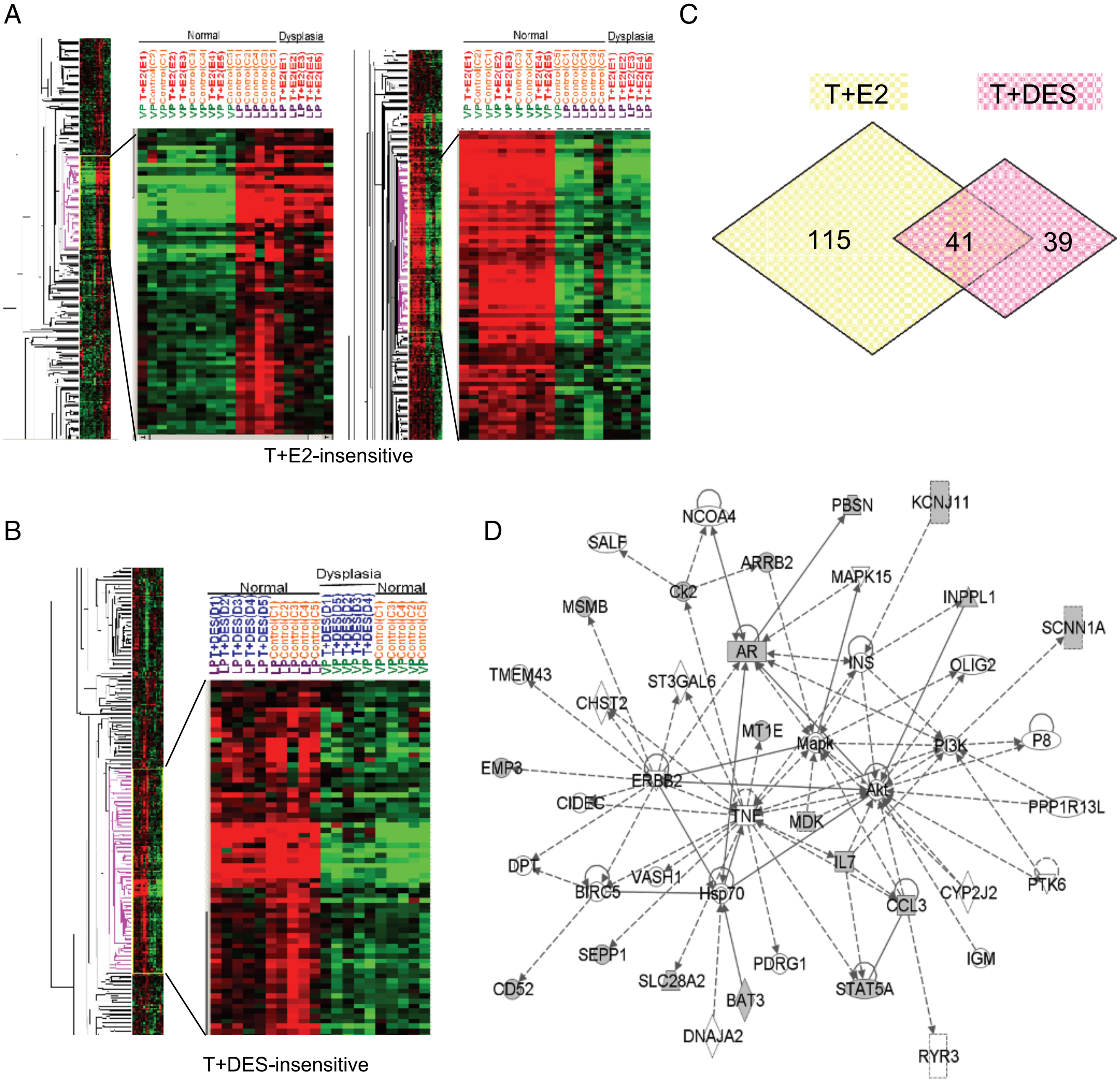


**Figure 6.** Heat maps of genes insensitive to (A) T + $E_2$ or (B) T + DES. (C) Venn diagram showing the number of genes insensitive to T + $E_2$ and/or T + DES treatment. Note that 41 genes are found in common in both hormone-insensitive panels and mapped to an IPA network (D) that includes the Ar, a key regulator of prostate function. Gray indicates no change in gene expression levels compared with those in untreated counterparts. See Figure 1 for key to IPA network.

first mapping genes to the IPA network before selecting genes for confirmation, we were able to validate most of the expression changes in the microarrays with real-time q-PCR. In this regard, we confirmed three genes (*Cebpd*, *Hoxa1*, and *Tp53*) common in the two dysplasia panels. Importantly, these three genes were upregulated only in the prostatic lobes that developed dysplasia, i.e., the T + $E_2$–treated LP and the T + DES–treated VP. Other lobe-specific genes that were confirmed were *Smad7*, *Klb1*, and *Nxph3* in the T + $E_2$–treated LP and *Mafb*, *Src*, *Bcar1*, *Gpx3*, *Plau*, and *Thra* in T + DES–treated VP. Our findings suggest that these gene expression changes induced by T + $E_2$/DES treatment could be causative factors of dysplasia development. However, it remains possible that these gene expression changes are simply part of the neoplastic transformation process. Future studies employing laser capture–microdissected samples to establish the temporal relationship between change in gene expression pattern and evolution of dysplasia may shed new light on the cause–effect link between the two.

Among all these validated genes, *Cebpd*, *Hoxa1*, and *Tp53* are the ones upregulated in common in the two dysplasia panels. CCAAT/enhancer binding proteins (C/EBP) are a highly conserved family of basic leucine zipper transcription factors; six members (C/EBP-alpha to -zeta) have been identified to date. This protein family plays a critical role in cell proliferation, apoptosis, and inflammation, depending on the cell type and specific physiological stress [31]. The precise functional role of C/EBP-delta, in particular, in normal prostate biology and PCa remains poorly understood. *Cebpd* was shown to be an androgen-repressed gene in the normal rat prostate [32,33], supporting its role as an apoptotic mediator and/or a negative regulator of cell proliferation. In a human androgen–dependent PCa xenograft, androgen withdrawal, however, resulted in a decline in the expression of C/EBP-delta [32]. Most published studies focus on the androgenic regulation of C/EBP-delta; this is, therefore, the first report of the association of estrogen-mediated upregulation of C/EBP-delta gene expression with the early phase of prostate carcinogenesis. A recent study showed overexpression of C/EBP-beta, another member of the family, in proliferative inflammatory atrophy in human prostate specimens, suggesting its role in the inflammation-associated carcinogenesis in the prostate [34]. In microarray data, we observed downregulation of C/EBP-alpha (*Cebpa*) only in T + $E_2$–treated dysplastic LPs, corroborating its putative suppressive function in epithelial tumorigenesis [35]. Together, these findings raise the possibility that an orchestrated deregulation of C/EBP-family transcripts is involved in the pathogenesis of PCa in humans and rodents.

Homeobox gene (*HOX*) is a family of transcription factors related to growth and development. In rodents and humans, 39 members of the *HOX* gene family have been assigned to four gene clusters (A–D) and are numbered according to their expression along the anterior–posterior axis. *Hox13* was shown to be involved in cell differentiation during normal prostate development [36], whereas upregulations of *HOXC* have been observed in PCa cells [37,38]. Knockdown of *HOXC6* gene expression led to apoptosis of PCa cells [39], and overexpression of the *HOXC8* gene correlated with the loss of tumor differentiation in human PCa [37]. Increased expression of the *HOXA1* transcript was detected in human clinical cervical cancer samples and in several cervical cell lines compared with expression in normal tissues [40,41]. Our data suggest that ectopic expression of *Hoxa1* is related to the evolution of dysplasia in both LP and VP and that the detailed roles of *Hoxa1* in PCa require further study.

*Tp53* is a well-known tumor-suppressive transcription factor and acts as a gatekeeper in signaling pathways involved in monitoring cellular stress such as DNA damage and in the determination of congruous responses (DNA repair, cell growth arrest, or apoptosis) to specific physiological stress. Previous studies demonstrated that mutation of *Tp53* is not necessarily as late an event in prostate carcinogenesis as previously reported; it is also frequently found in high-grade prostate intraepithelial *neoplasia*, a precursor lesion of PCa [42,43]. In this regard, we observed upregulation of *Tp53* gene expression in dysplastic rat prostate glands treated with sex hormone, implying a role in early prostate tumorigenesis, but whether these glands express wild-type or mutated *Tp53* is not known. Alternatively, the induction of *Tp53* expression may be a compensatory response to cellular stress imposed by hormonal changes. We recently demonstrated that T + $E_2$ treatment induced oxidative and nitrosative stress, accompanied by DNA and protein damages, specifically in the LP, which is susceptible to dysplasia/cancer induction [17].

*Smad7*, an inhibitory Smad, is rapidly induced by TGF-β, thereby creating a negative feedback loop to a variety of TGF-β signaling responses, including proliferation, differentiation, apoptosis, inflammation, tissue remodeling, angiogenesis, and cell adhesion [44]. Disruption of the TGF-β signaling cascade by aberrant overexpression of this negative modulator leads to increased tumorigenicity in colon cancer cells by blocking TGF-β–mediated growth inhibition and apoptosis [45]. In contrast, *Smad7* has been shown to mediate apoptosis induced by TGF-β in PCa cells [46], perhaps through crosstalking with other cellular signaling cascades such as the p38 mitogen-activated protein kinase [47] and β-catenin/Wnt [48] pathways. In our study, upregulation of *Smad7* in the dysplastic LP (also in the T + DES VP microarray data) suggests perturbations of TGF-β feedback regulation and thus the loss of balance between cell proliferation and apoptosis in the early phase of prostate carcinogenesis.

A particularly interesting gene network found in the T + DES–treated VP (Figure 4, *B1* and *B2*) is related to $E_2$ signaling. Members include *Src*, *Bcar1*, and *Plau*. *Src*, a nonreceptor protein tyrosine kinase, triggers the nongenomic estrogen signaling leading to activation of ERK1/2 and cell proliferation in prostate epithelial cells [49,50]. It remains to be determined if the downregulation of *Src* by DES represents a classic negative feedback loop. The *Bcar1* interacts and modulates *Src* activity [51]. An increase in *Bcar1* gene expression, as observed in the rat dysplastic VP, has also been reported in human PCa [52]. The coordinated dysregulation of both *Src* (downregulation) and *Bcar1* (upregulation) may reflect a disruption of the *Src*-dependent signaling pathway during the early development of PCa, a notion further supported by the altered expression of *Plau*, a downstream target of *Src* [53]. Interestingly, both *Bcar1* and *Plau* are involved in cell survival and migration [54,55].

Our group recently demonstrated significant oxidative stress and inflammation in the T + $E_2$–treated NBL rat LP [17,56]. The microarray data show a relatively small fraction of genes related to redox homeostasis and immune response, possibly due to inherent limitations of the type and coverage size (about 3800 genes) of the array chips we selected. However, T + $E_2$ treatment was found to upregulate *Klrb1* in the LP. This gene, also known as *NKR-P1A/CD161* in humans, encodes a natural killer (NK) cell C-type lectin–like receptor that regulates NK cell functions. *KLRB1* is expressed not only in NK cells but also in immune cell types, such as T cells, monocytes, and dendritic cells [57]. Thus, it is likely that increased expression of *Klrb1* in LP with T + $E_2$ treatment is due to the infiltration of immune cells [17].

The observation of a dramatic induction of *Gpx3* in the VP dysplasia panel, as shown by microarray (>17-fold) and q-PCR (>70-fold), is consistent with our previous report of a marked elevation of GPX enzyme activity and lipid peroxidation in this lobe after T + DES treatment [56]. Hence, the activation in this glutathione-associated detoxification enzyme might be a response to hormone-induced oxidative stress in the gland or represent a cytoprotective mechanism, adapted by dysplastic cells, against oxidative insults. An elevation of *GPX3* expression, but not of *GPX1* and *GPX2*, was found in precancerous lesions of *NKX3.1* mutant mouse prostate [58]. Taken together, these findings suggest that *GPX3* is specifically involved in early prostatic transformation that has a mechanistic link to oxidative stress.

In summary, we showed that genes such as *Cebpd*, *Tp53*, and *Hoxa1* are at the core of disrupted biologic networks related to hormone-induced dysplasia. Unbiased gene profiling clearly demonstrated differential susceptibility of the LP and VP to natural and xenoestrogen with regard to alterations in gene expression and induction of dysplasia. Our data suggest more functional divergence between DES and $E_2$ in the disruption of prostatic functions than that previously suspected. Methodologically, the combined utility of expression profiling and gene network mapping provides an instrumental platform for transcriptome studies.

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**Table W1.** Primers Used for Real-Time q-PCR.

| Name | Sequence | Accession No. | $T_m$ | Product Size (bp) |
|---|---|---|---|---|
| BCAR_UP1 | CCAGGTTCCCAGGACATCTA | NM_012931.1 | 59.92 | |
| BCAR_LP1 | TGCTCACAGAAGGAGGAACA | NM_012931.1 | 59.55 | 214 |
| CEBPD_UP1 | CAGGAGATGCAGCAGAAGC | NM_013154.1 | 59.83 | |
| CEBPD_LP1 | GTATCGGTCGTTCGGAGTCT | NM_013154.1 | 59.17 | 198 |
| Gpx3_UP1 | ACCAATTTGGCAAACAGGAG | NM_022525.2 | 59.97 | |
| Gpx3_LP1 | TCAAAGAGCTGGAAATTAGGC | NM_022525.2 | 59.18 | 110 |
| Hoxa1_UP2 | TTCTCCAGCGCAGACCTT | NM_013075.1 | 59.66 | |
| Hoxa1_LP2 | CCCACGTAGCCATACTCTCC | NM_013075.1 | 59.57 | 84 |
| KLRB1_UP1 | TGGATAAACGGCTCGACTTT | NM_173292.1 | 59.71 | |
| KLRB1_LP1 | GCACTTTGTCCTGTGAGACG | NM_173292.1 | 59.47 | 94 |
| MAFB_UP2 | AACGCGTCCAGCAGAAACAT | NM_019316.1 | 59 | |
| MAFB_LP2 | CTGCTCCACCTGCTGAATGA | NM_019316.1 | 59 | 65 |
| Nxph3_UP1 | CTGCTGCTTCGTGTTCCTAGT | NM_021679.1 | 52.38 | |
| Nxph3_LP1 | CATCATGCTCAGGGTCCTC | NM_021679.1 | 57.89 | 95 |
| PLAU_UP1 | AGCTGCCCAAAGAAATTCAA | NM_013085.2 | 59.82 | |
| PLAU_LP1 | TGGTGTCAGTATTGGCCTTTC | NM_013085.2 | 59.99 | 106 |
| SMAD7_UP1 | AGAGGCTGTGTTGCTGTGAA | NM_030858.1 | 59.62 | |
| SMAD7_LP1 | GAGGAAGGTACAGCGTCTGG | NM_030858.1 | 59.87 | 172 |
| SRC_UP1 | TGTGGAGCGGATGAACTATG | NM_031977.1 | 59.67 | |
| SRC_LP1 | TGATGGTGAACCTGCCATAC | NM_031977.1 | 59.37 | 197 |
| Thra_T1_UP1 | ACAAGGCCACCGGTTATCAC | NM_001017960.1 | 58 | |
| Thra_T1_LP1 | GCGAAAGAAGCCCTTGCA | NM_001017960.1 | 59 | 62 |
| TP53_UP1 | ACGTGCTCACACTGGCTAAA | NM_030989.1 | 59.51 | |
| TP53_LP1 | GGAGCTCGATGCTCATATCC | NM_030989.1 | 59.76 | 189 |

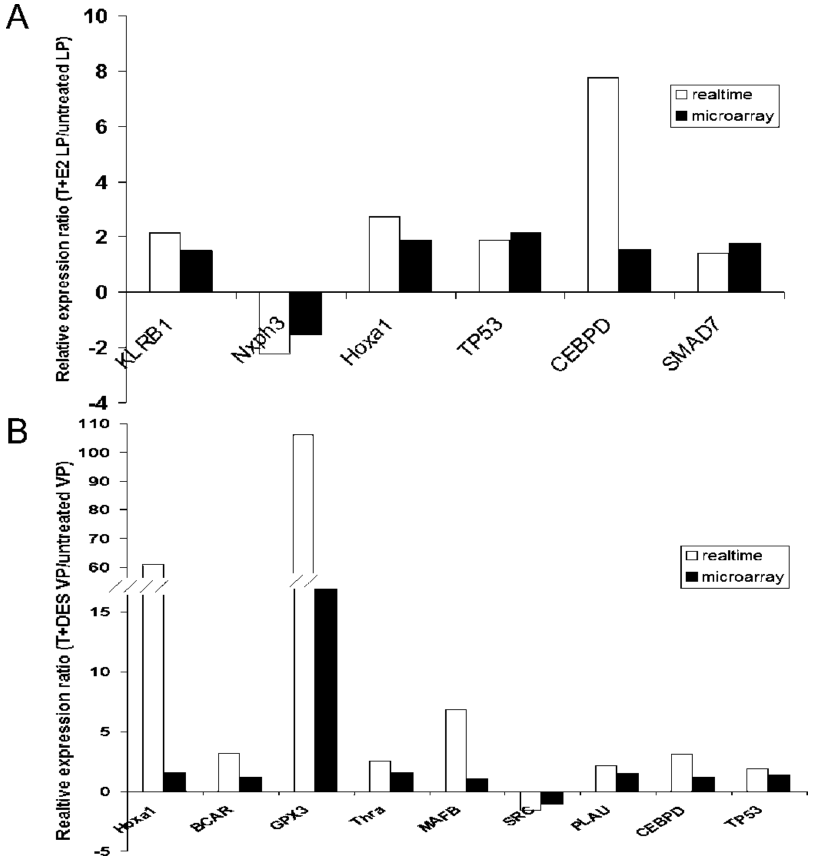

**Figure W1.** Comparison of real-time q-PCR to microarray findings. Genes selected from (A) T + $E_2$–induced LP dysplasia and (B) T + DES–induced VP dysplasia panels.

**Table W2.** Genes Whose Expression Altered following T + $E_2$ in the VPs with No Dysplastic Changes.

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + $E_2$ VP *vs* VP | T + $E_2$ VP *vs* VP | T + $E_2$ VP *vs* VP |
| **Cell morphology** | | | | | |
| contactin-associated protein 1 | 84008 | *CNTNAP1* | 2.33 | .0125 | 0.739395415 |
| **Cell to cell signaling and interaction** | | | | | |
| contactin-associated protein 1 | 84008 | *CNTNAP1* | 2.33 | .0125 | 0.739395415 |
| **Cellular growth and proliferation** | | | | | |
| potassium voltage–gated channel, shaker-related subfamily, member 5 | 25470 | *KCNA5* | −1.83 | .0227 | 0.766365976 |
| solute carrier family 12, member 2 | 83629 | *SLC12A2* | 1.57 | .0142 | 0.739395415 |
| **Molecular transport** | | | | | |
| potassium voltage–gated channel, shaker-related subfamily, member 5 | 25470 | *KCNA5* | −1.83 | .0227 | 0.766365976 |
| solute carrier family 12, member 2 | 83629 | *SLC12A2* | 1.57 | .0142 | 0.739395415 |
| **Carbohydrate metabolism** | | | | | |
| lysozyme | 25211 | *LYZ* | −1.55 | .1027 | 0.916873843 |
| **Cellular assembly and organization** | | | | | |
| potassium voltage–gated channel, shaker-related subfamily, member 5 | 25470 | *KCNA5* | −1.83 | .0227 | 0.766365976 |
| mucin 5, subtypes A and C, tracheobronchial/gastric | 65188 | *MUC5AC* | 1.70 | .0134 | 0.739395415 |
| **Small molecule biochemistry** | | | | | |
| ornithine decarboxylase antizyme inhibitor | 58961 | *AZIN1* | 1.51 | .0801 | 0.886144389 |
| solute carrier family 12, member 2 | 83629 | *SLC12A2* | 1.57 | .0142 | 0.739395415 |
| lysozyme | 25211 | *LYZ* | −1.55 | .1027 | 0.916873843 |
| **Cell death** | | | | | |
| solute carrier family 12, member 2 | 83629 | *SLC12A2* | 1.57 | .0142 | 0.739395415 |
| SH3-domain kinase binding protein 1 | 84357 | *SH3KBP1* | −1.56 | .0011 | 0.443416906 |
| **Cellular function and maintenance** | | | | | |
| potassium voltage–gated channel, shaker-related subfamily, member 5 | 25470 | *KCNA5* | −1.83 | .0227 | 0.766365976 |
| mucin 5, subtypes A and C, tracheobronchial/gastric | 65188 | *MUC5AC* | 1.70 | .0134 | 0.739395415 |
| **Cell signaling** | | | | | |
| major histocompatibility complex, class II, DM beta | 294273 | *HLA-DMB* | 1.51 | .0185 | 0.739395415 |
| **Drug metabolism** | | | | | |
| solute carrier family 12, member 2 | 83629 | *SLC12A2* | 1.57 | .0142 | 0.739395415 |
| **Lipid metabolism** | | | | | |
| solute carrier family 12, member 2 | 83629 | *SLC12A2* | 1.57 | .0142 | 0.739395415 |

We propose that these genes were not related to dysplasia development.

Genes were categorized according to their cellular functions (in bold and italics).

**Table W3.** Genes that Showed Altered Levels of Expression following T + DES in the LPs with No Dysplastic Changes.

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| **Cell morphology** | | | | | |
| actin alpha cardiac 1 | 29275 | *ACTC1* | 2.30 | .0000 | 0.000248913 |
| actinin alpha 4 | 63836 | *ACTN4* | –1.62 | .0004 | 0.015327409 |
| adducin 2 (beta) | 24171 | *ADD2* | –1.50 | .0023 | 0.046831092 |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | –1.33 | .0048 | 0.067126523 |
| allograft inflammatory factor 1 | 29427 | *AIF1* | –1.58 | .0001 | 0.007642386 |
| alanyl (membrane) aminopeptidase | 81641 | *ANPEP* | 1.23 | .0662 | 0.309192141 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| cofilin 1 | 29271 | *CFL1* | –1.39 | .0163 | 0.137582819 |
| discs, large homolog 4 (*Drosophila*) | 29495 | *DLG4* | 1.28 | .0138 | 0.12501336 |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2 | 116744 | *EDG2* | 1.50 | .0006 | 0.020782669 |
| ephrin A1 | 94268 | *EFNA1* | –1.33 | .0595 | 0.29465518 |
| espin | 56227 | *ESPN* | –1.65 | .0004 | 0.015327409 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| gap junction membrane channel protein alpha 3 | 79217 | *GJA3* | –1.67 | .0003 | 0.013918065 |
| interleukin 5 | 24497 | *IL5* | –1.52 | .0526 | 0.275768333 |
| potassium inwardly rectifying channel, subfamily J, member 10 | 29718 | *KCNJ10* | 1.57 | .0002 | 0.011445829 |
| NK6 transcription factor–related, locus 1 (*Drosophila*) | 65193 | *NKX6-1* | –1.31 | .0144 | 0.128278942 |
| protein kinase C and casein kinase substrate in neurons 2 | 124461 | *PACSIN2* | 1.27 | .0261 | 0.187905149 |
| p21 (CDKN1A)–activated kinase1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 6 | 25509 | *PAX6* | –1.72 | .0000 | 0.001014633 |
| synuclein, gamma | 64347 | *SNCG* | –1.83 | .0014 | 0.034901656 |
| Arg/Abl–interacting protein Arg BP2 | 114901 | *SORBS2* | 1.20 | .0883 | 0.361834544 |
| transition protein 2 | 24840 | *TNP2* | –1.46 | .0025 | 0.048139684 |
| ubiquitin A-52 residue ribosomal protein fusion product 1 | 64156 | *UBA52* | –1.94 | .0001 | 0.004893344 |
| ubiquitin-conjugating enzyme E2I | 25573 | *UBE2I* | 1.53 | .0001 | 0.008104491 |
| vesicle docking protein | 56042 | *VDP* | –1.33 | .0114 | 0.114843401 |
| **Cellular movement** | | | | | |
| actin, beta | 81822 | *ACTB* | –1.34 | .0132 | 0.121186877 |
| actinin alpha 4 | 63836 | *ACTN4* | –1.62 | .0004 | 0.015327409 |
| a disintegrin and metallopeptidase domain 1a | 56777 | *ADAM1A* | –1.69 | .0007 | 0.023296301 |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | –1.33 | .0048 | 0.067126523 |
| alanyl (membrane) aminopeptidase | 81641 | *ANPEP* | 1.23 | .0662 | 0.309192141 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| cofilin 1 | 29271 | *CFL1* | –1.39 | .0163 | 0.137582819 |
| calponin 1 | 65204 | *CNN1* | –1.04 | .7878 | 0.930382649 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| chemokine orphan receptor 1 | 84348 | *CXCR7* | –1.57 | .0008 | 0.025012801 |
| discoidin domain receptor family, member 1 | 25678 | *DDR1* | –1.75 | .0000 | 0.002145778 |
| defensin beta 1 | 83687 | *DEFB1* | –1.15 | .1095 | 0.409029443 |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2 | 116744 | *EDG2* | 1.50 | .0006 | 0.020782669 |
| ephrin A1 | 94268 | *EFNA1* | –1.33 | .0595 | 0.29465518 |
| coagulation factor X | 29243 | *F10* | –1.80 | .0004 | 0.016178933 |
| proprotein convertase subtilisin/kexin type 3 | 54281 | *FURIN* | –1.46 | .0026 | 0.048296067 |
| guanine nucleotide binding protein, alpha z subunit | 25740 | *GNAZ* | 1.46 | .0041 | 0.060465974 |
| glycogen synthase kinase 3 alpha | 50686 | *GSK3A* | –1.27 | .0048 | 0.066546045 |
| guanylate cyclase 1, soluble, alpha 3 | 25201 | *GUCY1A3* | 2.07 | .0000 | 0.000248913 |
| interleukin 5 | 24497 | *IL5* | –1.52 | .0526 | 0.275768333 |
| mucosal vascular addressin cell adhesion molecule 1 | 54266 | *MADCAM1* | –1.53 | .0051 | 0.068231134 |
| metastasis-associated 1 | 64520 | *MTA1* | –1.40 | .0225 | 0.172625732 |
| NK6 transcription factor–related, locus 1 (*Drosophila*) | 65193 | *NKX6-1* | –1.31 | .0144 | 0.128278942 |
| nuclear receptor subfamily 4, group A, member 3 | 58853 | *NR4A3* | –1.51 | .0383 | 0.23317558 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 6 | 25509 | *PAX6* | –1.72 | .0000 | 0.001014633 |
| polymeric immunoglobulin receptor | 25046 | *PIGR* | –1.35 | .0066 | 0.080018243 |
| protein kinase N1 | 29355 | *PKN1* | 1.51 | .0001 | 0.005817694 |
| phospholipase C, beta 3 | 29322 | *PLCB3* | –1.54 | .0020 | 0.043467607 |
| prion protein | 24686 | *PRNP* | –1.33 | .1183 | 0.42614185 |
| protein tyrosine phosphatase, receptor type, F | 360406 | *PTPRF* | –1.44 | .0029 | 0.050810807 |
| retinoic acid receptor, alpha | 24705 | *RARA* | –1.45 | .0003 | 0.0125346 |
| slit homolog 3 (*Drosophila*) | 83467 | *SLIT3* | 1.51 | .0005 | 0.017227903 |
| synuclein, gamma | 64347 | *SNCG* | –1.83 | .0014 | 0.034901656 |
| ventral anterior homeobox 1 | 64571 | *VAX1* | –1.52 | .0001 | 0.007642386 |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide | 29753 | *YWHAE* | –1.54 | .0014 | 0.034901656 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| **Cell signaling** | | | | | |
| adrenergic receptor, alpha 2c | 24175 | *ADRA2C* | −1.35 | .0729 | 0.3262758 |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | −1.33 | .0048 | 0.067126523 |
| calcineurin binding protein 1 | 94165 | *CABIN1* | 1.47 | .0000 | 0.004028913 |
| calcium channel, voltage-dependent, T type, alpha 1 G subunit | 29717 | *CACNA1G* | −1.50 | .0002 | 0.011161422 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2 | 116744 | *EDG2* | 1.50 | .0006 | 0.020782669 |
| ephrin A1 | 94268 | *EFNA1* | −1.33 | .0595 | 0.29465518 |
| gamma-aminobutyric acid A receptor, rho 1 | 29694 | *GABRR1* | 1.87 | .0000 | 0.000345513 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| guanine nucleotide binding protein, beta 3 | 60449 | *GNB3* | 1.68 | .0000 | 0.002364708 |
| glutamate receptor, ionotropic, kainate 3 | 298521 | *GRIK3* | 2.06 | .0000 | 2.51e–06 |
| G protein–coupled receptor 24 | 83567 | *MCHR1* | −1.52 | .0002 | 0.00962618 |
| protein kinase C and casein kinase substrate in neurons 2 | 124461 | *PACSIN2* | 1.27 | .0261 | 0.187905149 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| fertility protein SP22 | 117287 | *PARK7* | −1.22 | .2198 | 0.566510451 |
| phosphodiesterase 4A | 25638 | *PDE4A* | −1.55 | .0011 | 0.030023803 |
| protein kinase N1 | 29355 | *PKN1* | 1.51 | .0001 | 0.005817694 |
| Arg/Abl–interacting protein Arg BP2 | 114901 | *SORBS2* | 1.20 | .0883 | 0.361834544 |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide | 29753 | *YWHAE* | −1.54 | .0014 | 0.034901656 |
| **Cellular growth and proliferation** | | | | | |
| allograft inflammatory factor 1 | 29427 | *AIF1* | −1.58 | .0001 | 0.007642386 |
| calcium channel, voltage-dependent, T type, alpha 1 G subunit | 29717 | *CACNA1G* | −1.50 | .0002 | 0.011161422 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| CD63 antigen | 29186 | *CD63* | −1.10 | .4195 | 0.737185743 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| Cbp/p300–interacting transactivator with Glu/Asp–rich carboxy-terminal domain 1 | 64466 | *CITED1* | −1.53 | .0019 | 0.042644963 |
| calponin 1 | 65204 | *CNN1* | −1.04 | .7878 | 0.930382649 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| chemokine orphan receptor 1 | 84348 | *CXCR7* | −1.57 | .0008 | 0.025012801 |
| discoidin domain receptor family, member 1 | 25678 | *DDR1* | −1.75 | .0000 | 0.002145778 |
| ddx5 gene | 287765 | *DDX5* | −1.27 | .1781 | 0.520336467 |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2 | 116744 | *EDG2* | 1.50 | .0006 | 0.020782669 |
| ephrin A1 | 94268 | *EFNA1* | −1.33 | .0595 | 0.29465518 |
| F-box only protein 2 | 85273 | *FBXO2* | −1.42 | .0115 | 0.114843401 |
| growth hormone–releasing hormone receptor | 25321 | *GHRHR* | −1.59 | .0255 | 0.186284598 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| metastasis-associated 1 | 64520 | *MTA1* | −1.40 | .0225 | 0.172625732 |
| nuclear receptor subfamily 4, group A, member 3 | 58853 | *NR4A3* | −1.51 | .0383 | 0.23317558 |
| paired box gene 6 | 25509 | *PAX6* | −1.72 | .0000 | 0.001014633 |
| polymeric immunoglobulin receptor | 25046 | *PIGR* | −1.35 | .0066 | 0.080018243 |
| protein tyrosine phosphatase, receptor type, F | 360406 | *PTPRF* | −1.44 | .0029 | 0.050810807 |
| retinoic acid receptor, alpha | 24705 | *RARA* | −1.45 | .0003 | 0.0125346 |
| synuclein, gamma | 64347 | *SNCG* | −1.83 | .0014 | 0.034901656 |
| ventral anterior homeobox 1 | 64571 | *VAX1* | −1.52 | .0001 | 0.007642386 |
| zinc finger protein of the cerebellum 1 | 64618 | *ZIC1* | −1.54 | .0002 | 0.00960067 |
| **Cell to cell signaling and interaction** | | | | | |
| a disintegrin and metallopeptidase domain 1a | 56777 | *ADAM1A* | −1.69 | .0007 | 0.023296301 |
| adrenergic receptor, alpha 2c | 24175 | *ADRA2C* | −1.35 | .0729 | 0.3262758 |
| amelogenin X chromosome | 29160 | *AMELX* | −1.71 | .0000 | 0.000345513 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| cofilin 1 | 29271 | *CFL1* | −1.39 | .0163 | 0.137582819 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| discoidin domain receptor family, member 1 | 25678 | *DDR1* | −1.75 | .0000 | 0.002145778 |
| discs, large homolog 4 (*Drosophila*) | 29495 | *DLG4* | 1.28 | .0138 | 0.12501336 |
| ephrin A1 | 94268 | *EFNA1* | −1.33 | .0595 | 0.29465518 |
| coagulation factor X | 29243 | *F10* | −1.80 | .0004 | 0.016178933 |
| fibrinogen, gamma polypeptide | 24367 | *FGG* | −1.79 | .0067 | 0.080887122 |
| proprotein convertase subtilisin/kexin type 3 | 54281 | *FURIN* | −1.46 | .0026 | 0.048296067 |
| gap junction membrane channel protein alpha 3 | 79217 | *GJA3* | −1.67 | .0003 | 0.013918065 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| mucosal vascular addressin cell adhesion molecule 1 | 54266 | *MADCAM1* | −1.53 | .0051 | 0.068231134 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| polymeric immunoglobulin receptor | 25046 | *PIGR* | −1.35 | .0066 | 0.080018243 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| proteasome (prosome, macropain) 28 subunit, beta | 29614 | *PSME2* | 1.40 | .0008 | 0.025480573 |
| retinoic acid receptor, alpha | 24705 | *RARA* | –1.45 | .0003 | 0.0125346 |
| Rhesus blood group CE and D | 60414 | *RHD* | –1.45 | .0030 | 0.050810807 |
| ubiquitin A-52 residue ribosomal protein fusion product 1 | 64156 | *UBA52* | –1.94 | .0001 | 0.004893344 |
| ubiquitin-conjugating enzyme E2I | 25573 | *UBE2I* | 1.53 | .0001 | 0.008104491 |
| ventral anterior homeobox 1 | 64571 | *VAX1* | –1.52 | .0001 | 0.007642386 |
| **Cellular function and maintenance** | | | | | |
| blocked early in transport 1 homolog (*S. cerevisiae*) like | 54400 | *BET1L* | –1.31 | .0707 | 0.321228605 |
| calcineurin binding protein 1 | 94165 | *CABIN1* | 1.47 | .0000 | 0.004028913 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| cofilin 1 | 29271 | *CFL1* | –1.39 | .0163 | 0.137582819 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| ephrin A1 | 94268 | *EFNA1* | –1.33 | .0595 | 0.29465518 |
| fibrinogen, gamma polypeptide | 24367 | *FGG* | –1.79 | .0067 | 0.080887122 |
| interleukin 5 | 24497 | *IL5* | –1.52 | .0526 | 0.275768333 |
| protein kinase C and casein kinase substrate in neurons 2 | 124461 | *PACSIN2* | 1.27 | .0261 | 0.187905149 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| protein tyrosine phosphatase, receptor type, F | 360406 | *PTPRF* | –1.44 | .0029 | 0.050810807 |
| retinoic acid receptor, alpha | 24705 | *RARA* | –1.45 | .0003 | 0.0125346 |
| ubiquitin-conjugating enzyme E2I | 25573 | *UBE2I* | 1.53 | .0001 | 0.008104491 |
| vesicle docking protein | 56042 | *VDP* | –1.33 | .0114 | 0.114843401 |
| **Cellular assembly and organization** | | | | | |
| actin, beta | 81822 | *ACTB* | –1.34 | .0132 | 0.121186877 |
| actin alpha cardiac 1 | 29275 | *ACTC1* | 2.30 | .0000 | 0.000248913 |
| actinin alpha 4 | 63836 | *ACTN4* | –1.62 | .0004 | 0.015327409 |
| a disintegrin and metallopeptidase domain 1a | 56777 | *ADAM1A* | –1.69 | .0007 | 0.023296301 |
| ADP-ribosylation factor 1 | 64310 | *ARF1* | –1.51 | .0042 | 0.06161559 |
| blocked early in transport 1 homolog (*S. cerevisiae*) like | 54400 | *BET1L* | –1.31 | .0707 | 0.321228605 |
| calcineurin binding protein 1 | 94165 | *CABIN1* | 1.47 | .0000 | 0.004028913 |
| calpain 3 | 29155 | *CAPN3* | –1.06 | .6514 | 0.868611888 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| cofilin 1 | 29271 | *CFL1* | –1.39 | .0163 | 0.137582819 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| discs, large homolog 4 (*Drosophila*) | 29495 | *DLG4* | 1.28 | .0138 | 0.12501336 |
| phenylalkylamine $Ca^{2+}$ antagonist (emopamil) binding protein | 117278 | *EBP* | –1.24 | .1023 | 0.394501794 |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2 | 116744 | *EDG2* | 1.50 | .0006 | 0.020782669 |
| ephrin A1 | 94268 | *EFNA1* | –1.33 | .0595 | 0.29465518 |
| espin | 56227 | *ESPN* | –1.65 | .0004 | 0.015327409 |
| fibrinogen, gamma polypeptide | 24367 | *FGG* | –1.79 | .0067 | 0.080887122 |
| protein kinase C and casein kinase substrate in neurons 2 | 124461 | *PACSIN2* | 1.27 | .0261 | 0.187905149 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 6 | 25509 | *PAX6* | –1.72 | .0000 | 0.001014633 |
| protein tyrosine phosphatase, receptor type, F | 360406 | *PTPRF* | –1.44 | .0029 | 0.050810807 |
| Rhesus blood group CE and D | 60414 | *RHD* | –1.45 | .0030 | 0.050810807 |
| Arg/Abl–interacting protein Arg BP2 | 114901 | *SORBS2* | 1.20 | .0883 | 0.361834544 |
| transition protein 2 | 24840 | *TNP2* | –1.46 | .0025 | 0.048139684 |
| ubiquitin-conjugating enzyme E2I | 25573 | *UBE2I* | 1.53 | .0001 | 0.008104491 |
| ventral anterior homeobox 1 | 64571 | *VAX1* | –1.52 | .0001 | 0.007642386 |
| vesicle docking protein | 56042 | *VDP* | –1.33 | .0114 | 0.114843401 |
| **Cellular development** | | | | | |
| adducin 2 (beta) | 24171 | *ADD2* | –1.50 | .0023 | 0.046831092 |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | –1.33 | .0048 | 0.067126523 |
| allograft inflammatory factor 1 | 29427 | *AIF1* | –1.58 | .0001 | 0.007642386 |
| alanyl (membrane) aminopeptidase | 81641 | *ANPEP* | 1.23 | .0662 | 0.309192141 |
| calcitonin/calcitonin–related polypeptide, alpha | 24241 | *CALCA* | 1.57 | .0002 | 0.00960067 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | –1.53 | .0095 | 0.101978652 |
| cofilin 1 | 29271 | *CFL1* | –1.39 | .0163 | 0.137582819 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| discoidin domain receptor family, member 1 | 25678 | *DDR1* | –1.75 | .0000 | 0.002145778 |
| phenylalkylamine $Ca^{2+}$ antagonist (emopamil) binding protein | 117278 | *EBP* | –1.24 | .1023 | 0.394501794 |
| endothelial differentiation, lysophosphatidic acid G-protein–coupled receptor, 2 | 116744 | *EDG2* | 1.50 | .0006 | 0.020782669 |
| ephrin A1 | 94268 | *EFNA1* | –1.33 | .0595 | 0.29465518 |
| eukaryotic translation initiation factor 2B, subunit 4 delta | 117019 | *EIF2B4* | –1.32 | .0626 | 0.302985912 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| potassium inwardly rectifying channel, subfamily J, member 10 | 29718 | *KCNJ10* | 1.57 | .0002 | 0.011445829 |
| neurogenic differentiation 2 | 54276 | *NEUROD2* | −1.47 | .0457 | 0.259241663 |
| NK6 transcription factor–related, locus 1 (*Drosophila*) | 65193 | *NKX6-1* | −1.31 | .0144 | 0.128278942 |
| nuclear receptor subfamily 4, group A, member 3 | 58853 | *NR4A3* | −1.51 | .0383 | 0.23317558 |
| platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit | 114113 | *PAFAH1B3* | −1.59 | .0007 | 0.021362381 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 6 | 25509 | *PAX6* | −1.72 | .0000 | 0.001014633 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| retinoic acid receptor, alpha | 24705 | *RARA* | −1.45 | .0003 | 0.0125346 |
| SNF-related kinase | 170837 | *SNRK* | −1.68 | .0002 | 0.01079459 |
| zinc finger protein of the cerebellum 1 | 64618 | *ZIC1* | −1.54 | .0002 | 0.00960067 |
| **Vitamin and mineral metabolism** | | | | | |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | −1.33 | .0048 | 0.067126523 |
| calcium channel, voltage-dependent, T type, alpha 1 G subunit | 29717 | *CACNA1G* | −1.50 | .0002 | 0.011161422 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide | 29753 | *YWHAE* | −1.54 | .0014 | 0.034901656 |
| gamma-glutamyl hydrolase | 25455 | *GGH* | 1.05 | .6924 | 0.88871634 |
| **Nucleic acid metabolism** | | | | | |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| G protein–coupled receptor 24 | 83567 | *MCHR1* | −1.52 | .0002 | 0.00962618 |
| phosphodiesterase 4A | 25638 | *PDE4A* | −1.55 | .0011 | 0.030023803 |
| heat shock 10 kDa protein 1 | 25462 | *HSPE1* | −1.53 | .0302 | 0.202134203 |
| **Cell cycle** | | | | | |
| allograft inflammatory factor 1 | 29427 | *AIF1* | −1.58 | .0001 | 0.007642386 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| cofilin 1 | 29271 | *CFL1* | −1.39 | .0163 | 0.137582819 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| aspartyl-tRNA synthetase | 116483 | *DARS* | −1.43 | .0353 | 0.221986221 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| nuclear receptor subfamily 4, group A, member 3 | 58853 | *NR4A3* | −1.51 | .0383 | 0.23317558 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 6 | 25509 | *PAX6* | −1.72 | .0000 | 0.001014633 |
| protein tyrosine phosphatase, receptor type, F | 360406 | *PTPRF* | −1.44 | .0029 | 0.050810807 |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide | 29753 | *YWHAE* | −1.54 | .0014 | 0.034901656 |
| **Cell death** | | | | | |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| NK6 transcription factor–related, locus 1 (*Drosophila*) | 65193 | *NKX6-1* | −1.31 | .0144 | 0.128278942 |
| ornithine decarboxylase antizyme 1 | 25502 | *OAZ1* | −1.61 | .0040 | 0.059747718 |
| prolyl 4-hydroxylase, beta polypeptide | 25506 | *P4HB* | −1.29 | .0491 | 0.266073897 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| retinoic acid receptor, alpha | 24705 | *RARA* | −1.45 | .0003 | 0.0125346 |
| **Cellular compromise** | | | | | |
| adducin 2 (beta) | 24171 | *ADD2* | −1.50 | .0023 | 0.046831092 |
| cofilin 1 | 29271 | *CFL1* | −1.39 | .0163 | 0.137582819 |
| calponin 1 | 65204 | *CNN1* | −1.04 | .7878 | 0.930382649 |
| cytotoxic T-lymphocyte–associated protein 4 | 63835 | *CTLA4* | 1.25 | .0618 | 0.301897804 |
| ephrin A1 | 94268 | *EFNA1* | −1.33 | .0595 | 0.29465518 |
| G-protein–coupled receptor 37 | 117549 | *GPR37* | −1.24 | .0689 | 0.316311201 |
| heat shock 10 kDa protein 1 | 25462 | *HSPE1* | −1.53 | .0302 | 0.202134203 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| potassium inwardly rectifying channel, subfamily J, member 10 | 29718 | *KCNJ10* | 1.57 | .0002 | 0.011445829 |
| mucosal vascular addressin cell adhesion molecule 1 | 54266 | *MADCAM1* | −1.53 | .0051 | 0.068231134 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| synuclein, gamma | 64347 | *SNCG* | −1.83 | .0014 | 0.034901656 |
| Arg/Abl–interacting protein Arg BP2 | 114901 | *SORBS2* | 1.20 | .0883 | 0.361834544 |
| **Gene expression** | | | | | |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| Cbp/p300–interacting transactivator with Glu/Asp–rich carboxy-terminal domain 1 | 64466 | *CITED1* | −1.53 | .0019 | 0.042644963 |
| ddx5 gene | 287765 | *DDX5* | −1.27 | .1781 | 0.520336467 |
| glucocorticoid modulatory element binding protein 2 | 83635 | *GMEB2* | 1.44 | .0013 | 0.033527564 |
| hairy and enhancer of split 2 (*Drosophila*) | 29567 | *HES2* | −1.66 | .0001 | 0.008055371 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| interleukin enhancer binding factor 3 | 84472 | *ILF3* | −1.45 | .0041 | 0.060465974 |
| neurogenic differentiation 2 | 54276 | *NEUROD2* | −1.47 | .0457 | 0.259241663 |
| nuclear factor I/C | 29228 | *NFIC* | −1.54 | .0000 | 0.001390745 |
| nuclear receptor subfamily 3, group C, member 2 | 25672 | *NR3C2* | 1.57 | .0025 | 0.048296067 |
| nuclear receptor subfamily 4, group A, member 3 | 58853 | *NR4A3* | −1.51 | .0383 | 0.23317558 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 6 | 25509 | *PAX6* | −1.72 | .0000 | 0.001014633 |
| paired box gene 8 | 81819 | *PAX8* | −1.50 | .0027 | 0.049209986 |
| protein kinase N1 | 29355 | *PKN1* | 1.51 | .0001 | 0.005817694 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| retinoic acid receptor, alpha | 24705 | *RARA* | −1.45 | .0003 | 0.0125346 |
| retinoblastoma binding protein 7 | 83712 | *RBBP7* | −1.15 | .2769 | 0.626562643 |
| suppression of tumorigenicity 18 | 266680 | *ST18* | 1.16 | .3190 | 0.656804744 |
| telomerase-associated protein 1 | 64523 | *TEP1* | −1.53 | .0024 | 0.047008762 |
| ubiquitin A-52 residue ribosomal protein fusion product 1 | 64156 | *UBA52* | −1.94 | .0001 | 0.004893344 |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide | 29753 | *YWHAE* | −1.54 | .0014 | 0.034901656 |
| **Amino acid metabolism** | | | | | |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | −1.33 | .0048 | 0.067126523 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| glycine cleavage system protein H (aminomethyl carrier) | 171133 | *GCSH* | −1.43 | .0131 | 0.120934801 |
| gamma-glutamyl hydrolase | 25455 | *GGH* | 1.05 | .6924 | 0.88871634 |
| glycogen synthase kinase 3 alpha | 50686 | *GSK3A* | −1.27 | .0048 | 0.066546045 |
| prolyl 4-hydroxylase, beta polypeptide | 25506 | *P4HB* | −1.29 | .0491 | 0.266073897 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| paired box gene 8 | 81819 | *PAX8* | −1.50 | .0027 | 0.049209986 |
| protein kinase N1 | 29355 | *PKN1* | 1.51 | .0001 | 0.005817694 |
| **Post–translational modification** | | | | | |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | −1.33 | .0048 | 0.067126523 |
| glycine cleavage system protein H (aminomethyl carrier) | 171133 | *GCSH* | −1.43 | .0131 | 0.120934801 |
| glycogen synthase kinase 3 alpha | 50686 | *GSK3A* | −1.27 | .0048 | 0.066546045 |
| prolyl 4-hydroxylase, beta polypeptide | 25506 | *P4HB* | −1.29 | .0491 | 0.266073897 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| protein kinase N1 | 29355 | *PKN1* | 1.51 | .0001 | 0.005817694 |
| **Carbohydrate metabolism** | | | | | |
| apolipoprotein A-V | 140638 | *APOA5* | −1.43 | .0022 | 0.045371928 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| guanine nucleotide binding protein, alpha z subunit | 25740 | *GNAZ* | 1.46 | .0041 | 0.060465974 |
| neuromedin B receptor | 25264 | *NMBR* | 1.66 | .0005 | 0.017227903 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| **Cellular response to therapeutics** | | | | | |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| **DNA replication, recombination, and repair** | | | | | |
| cofilin 1 | 29271 | *CFL1* | −1.39 | .0163 | 0.137582819 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| **Drug metabolism** | | | | | |
| apolipoprotein A-V | 140638 | *APOA5* | −1.43 | .0022 | 0.045371928 |
| phenylalkylamine $Ca^{2+}$ antagonist (emopamil) binding protein | 117278 | *EBP* | −1.24 | .1023 | 0.394501794 |
| gamma-glutamyl hydrolase | 25455 | *GGH* | 1.05 | .6924 | 0.88871634 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| insulin-like 6 | 50546 | *IL1RAP* | 1.56 | .0002 | 0.01079459 |
| fertility protein SP22 | 117287 | *PARK7* | −1.22 | .2198 | 0.566510451 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| **Energy production** | | | | | |
| heat shock 10 kDa protein 1 | 25462 | *HSPE1* | −1.53 | .0302 | 0.202134203 |
| Pyruvate carboxylase | 25104 | *PC* | −1.68 | .0005 | 0.017227903 |
| **Lipid metabolism** | | | | | |
| adrenergic receptor, alpha 2c | 24175 | *ADRA2C* | −1.35 | .0729 | 0.3262758 |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | −1.33 | .0048 | 0.067126523 |
| apolipoprotein A-V | 140638 | *APOA5* | −1.43 | .0022 | 0.045371928 |
| apolipoprotein C-I | 25292 | *APOC1* | −1.45 | .0040 | 0.060048723 |
| ADP-ribosylation factor 1 | 64310 | *ARF1* | −1.51 | .0042 | 0.06161559 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| cytochrome *P*450, 4a12 | 266674 | *CYP4A22* | 1.29 | .0127 | 0.118852704 |
| phenylalkylamine $Ca^{2+}$ antagonist (emopamil) binding protein | 117278 | *EBP* | −1.24 | .1023 | 0.394501794 |
| coagulation factor X | 29243 | *F10* | −1.80 | .0004 | 0.016178933 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| growth hormone–releasing hormone receptor | 25321 | *GHRHR* | −1.59 | .0255 | 0.186284598 |
| CCA2 protein | 246211 | *HSD3B7* | −1.14 | .2909 | 0.639015905 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit | 114113 | *PAFAH1B3* | −1.59 | .0007 | 0.021362381 |
| phosphatidylinositol-4-phosphate 5-kinase, type II, alpha | 116723 | *PIP5K2A* | −1.54 | .0028 | 0.050001834 |
| **Molecular transport** | | | | | |
| adducin 2 (beta) | 24171 | *ADD2* | −1.50 | .0023 | 0.046831092 |
| apolipoprotein A-V | 140638 | *APOA5* | −1.43 | .0022 | 0.045371928 |
| apolipoprotein C-I | 25292 | *APOC1* | −1.45 | .0040 | 0.060048723 |
| ADP-ribosylation factor 1 | 64310 | *ARF1* | −1.51 | .0042 | 0.06161559 |
| ADP-ribosylation factor 3 | 140940 | *ARF3* | −1.73 | .0015 | 0.035552435 |
| ATPase, $H^+$ transporting, V1 subunit F | 116664 | *ATP6V1F* | 1.82 | .0000 | 0.002117528 |
| calcium channel, voltage-dependent, T type, alpha 1 G subunit | 29717 | *CACNA1G* | −1.50 | .0002 | 0.011161422 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| cofilin 1 | 29271 | *CFL1* | −1.39 | .0163 | 0.137582819 |
| gamma-glutamyl hydrolase | 25455 | *GGH* | 1.05 | .6924 | 0.88871634 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| guanine nucleotide binding protein, alpha z subunit | 25740 | *GNAZ* | 1.46 | .0041 | 0.060465974 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| potassium voltage–gated channel, Shaw-related subfamily, member 1 | 25327 | *KCNC1* | 1.88 | .0000 | 0.001278795 |
| potassium voltage–gated channel, Shaw-related subfamily, member 3 | 117101 | *KCNC3* | 1.28 | .0499 | 0.267188376 |
| potassium inwardly rectifying channel, subfamily J, member 10 | 29718 | *KCNJ10* | 1.57 | .0002 | 0.011445829 |
| potassium large conductance calcium–activated channel, subfamily M, beta member 1 | 29747 | *KCNMB1* | 1.45 | .0016 | 0.037292397 |
| G protein–coupled receptor 24 | 83567 | *MCHR1* | −1.52 | .0002 | 0.00962618 |
| neuromedin B receptor | 25264 | *NMBR* | 1.66 | .0005 | 0.017227903 |
| nuclear receptor subfamily 3, group C, member 2 | 25672 | *NR3C2* | 1.57 | .0025 | 0.048296067 |
| ornithine decarboxylase antizyme 1 | 25502 | *OAZ1* | −1.61 | .0040 | 0.059747718 |
| fertility protein SP22 | 117287 | *PARK7* | −1.22 | .2198 | 0.566510451 |
| paired box gene 8 | 81819 | *PAX8* | −1.50 | .0027 | 0.049209986 |
| phosphodiesterase 4A | 25638 | *PDE4A* | −1.55 | .0011 | 0.030023803 |
| phosphatidylinositol-4-phosphate 5-kinase, type II, alpha | 116723 | *PIP5K2A* | −1.54 | .0028 | 0.050001834 |
| phospholipase C, beta 3 | 29322 | *PLCB3* | −1.54 | .0020 | 0.043467607 |
| transmembrane 4 superfamily member 11 | 64364 | *PLLP* | −1.89 | .0001 | 0.007928851 |
| RAB10, member RAS oncogene family | 50993 | *RAB10* | −1.26 | .1155 | 0.421950743 |
| vesicle docking protein | 56042 | *VDP* | −1.33 | .0114 | 0.114843401 |
| protein kinase, lysine-deficient 1 | 116477 | *WNK1* | −1.23 | .0401 | 0.239581758 |
| tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide | 29753 | *YWHAE* | −1.54 | .0014 | 0.034901656 |
| **Protein degradation** | | | | | |
| alanyl (membrane) aminopeptidase | 81641 | *ANPEP* | 1.23 | .0662 | 0.309192141 |
| calpain 3 | 29155 | *CAPN3* | −1.06 | .6514 | 0.868611888 |
| F-box only protein 2 | 85273 | *FBXO2* | −1.42 | .0115 | 0.114843401 |
| proprotein convertase subtilisin/kexin type 3 | 54281 | *FURIN* | −1.46 | .0026 | 0.048296067 |
| ubiquitin A-52 residue ribosomal protein fusion product 1 | 64156 | *UBA52* | −1.94 | .0001 | 0.004893344 |
| **Protein synthesis** | | | | | |
| ubiquitin A-52 residue ribosomal protein fusion product 1 | 64156 | *UBA52* | −1.94 | .0001 | 0.004893344 |
| alanyl (membrane) aminopeptidase | 81641 | *ANPEP* | 1.23 | .0662 | 0.309192141 |
| proprotein convertase subtilisin/kexin type 3 | 54281 | *FURIN* | −1.46 | .0026 | 0.048296067 |
| F-box only protein 2 | 85273 | *FBXO2* | −1.42 | .0115 | 0.114843401 |
| calpain 3 | 29155 | *CAPN3* | −1.06 | .6514 | 0.868611888 |
| eukaryotic translation initiation factor 2B, subunit 4 delta | 117019 | *EIF2B4* | −1.32 | .0626 | 0.302985912 |
| aspartyl-tRNA synthetase | 116483 | *DARS* | −1.43 | .0353 | 0.221986221 |
| ribosomal protein L41 | 124440 | *RPL41* | 1.11 | .5675 | 0.833181167 |
| ribosomal protein S27 | 94266 | *RPS27* | −1.90 | .0001 | 0.00504934 |
| ribosomal protein L22 | 81768 | *RPL22* | −1.28 | .1257 | 0.438278138 |
| ribosomal protein L24 | 64307 | *RPL24* | −1.21 | .2217 | 0.567754925 |
| ribosomal protein L4 | 64302 | *RPL4* | −1.42 | .0425 | 0.248528309 |
| **Protein trafficking** | | | | | |
| ADP-ribosylation factor 1 | 64310 | *ARF1* | −1.51 | .0042 | 0.06161559 |
| cofilin 1 | 29271 | *CFL1* | −1.39 | .0163 | 0.137582819 |
| vesicle docking protein | 56042 | *VDP* | −1.33 | .0114 | 0.114843401 |
| ADP-ribosylation factor 3 | 140940 | *ARF3* | −1.73 | .0015 | 0.035552435 |
| RAB10, member RAS oncogene family | 50993 | *RAB10* | −1.26 | .1155 | 0.421950743 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| protein tyrosine phosphatase, receptor type, F | 360406 | *PTPRF* | −1.44 | .0029 | 0.050810807 |
| **RNA damage and repair** | | | | | |
| telomerase-associated protein 1 | 64523 | *TEP1* | −1.53 | .0024 | 0.047008762 |
| **RNA post–transcriptional modification** | | | | | |
| telomerase-associated protein 1 | 64523 | *TEP1* | −1.53 | .0024 | 0.047008762 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| **Small molecule biochemistry** | | | | | |
| glycine cleavage system protein H (aminomethyl carrier) | 171133 | *GCSH* | −1.43 | .0131 | 0.120934801 |
| neuromedin B receptor | 25264 | *NMBR* | 1.66 | .0005 | 0.017227903 |
| guanine nucleotide binding protein, alpha z subunit | 25740 | *GNAZ* | 1.46 | .0041 | 0.060465974 |
| nuclear receptor subfamily 3, group C, member 2 | 25672 | *NR3C2* | 1.57 | .0025 | 0.048296067 |
| apolipoprotein C-I | 25292 | *APOC1* | −1.45 | .0040 | 0.060048723 |
| apolipoprotein A-V | 140638 | *APOA5* | −1.43 | .0022 | 0.045371928 |
| platelet-activating factor acetylhydrolase, isoform 1b, alpha1 subunit | 114113 | *PAFAH1B3* | −1.59 | .0007 | 0.021362381 |
| prion protein | 24686 | *PRNP* | −1.33 | .1183 | 0.42614185 |
| ornithine decarboxylase antizyme 1 | 25502 | *OAZ1* | −1.61 | .0040 | 0.059747718 |
| phosphatidylinositol-4-phosphate 5-kinase, type II, alpha | 116723 | *PIP5K2A* | −1.54 | .0028 | 0.050001834 |
| CCA2 protein | 246211 | *HSD3B7* | −1.14 | .2909 | 0.639015905 |
| interleukin 5 | 24497 | *IL5* | −1.52 | .0526 | 0.275768333 |
| aspartyl-tRNA synthetase | 116483 | *DARS* | −1.43 | .0353 | 0.221986221 |
| adrenergic receptor, alpha 2c | 24175 | *ADRA2C* | −1.35 | .0729 | 0.3262758 |
| cytochrome *P*450, 4a12 | 266674 | *CYP4A22* | 1.29 | .0127 | 0.118852704 |
| coagulation factor X | 29243 | *F10* | −1.80 | .0004 | 0.016178933 |
| heat shock 10 kDa protein 1 | 25462 | *HSPE1* | −1.53 | .0302 | 0.202134203 |
| paired box gene 8 | 81819 | *PAX8* | −1.50 | .0027 | 0.049209986 |
| phospholipase C, beta 3 | 29322 | *PLCB3* | −1.54 | .0020 | 0.043467607 |
| CCAAT/enhancer binding protein (C/EBP), alpha | 24252 | *CEBPA* | −1.53 | .0095 | 0.101978652 |
| gamma-glutamyl hydrolase | 25455 | *GGH* | 1.05 | .6924 | 0.88871634 |
| prolyl 4-hydroxylase, beta polypeptide | 25506 | *P4HB* | −1.29 | .0491 | 0.266073897 |
| fertility protein SP22 | 117287 | *PARK7* | −1.22 | .2198 | 0.566510451 |
| phenylalkylamine $Ca^{2+}$ antagonist (emopamil) binding protein | 117278 | *EBP* | −1.24 | .1023 | 0.394501794 |
| ADP-ribosylation factor 1 | 64310 | *ARF1* | −1.51 | .0042 | 0.06161559 |
| acetylcholinesterase | 83817 | *ACHE* | −1.61 | .0009 | 0.026111212 |
| adrenergic receptor kinase, beta 1 | 25238 | *ADRBK1* | −1.33 | .0048 | 0.067126523 |
| small inducible cytokine A4 | 116637 | *CCL4* | 1.50 | .0017 | 0.038035447 |
| growth hormone–releasing hormone | 29446 | *GHRH* | 1.87 | .0000 | 0.000562125 |
| glycogen synthase kinase 3 alpha | 50686 | *GSK3A* | −1.27 | .0048 | 0.066546045 |
| insulin-like 6 | 50546 | *IL1RAP* | 1.56 | .0002 | 0.01079459 |
| G protein–coupled receptor 24 | 83567 | *MCHR1* | −1.52 | .0002 | 0.00962618 |
| p21 (CDKN1A)–activated kinase 1 | 29431 | *PAK1* | 1.99 | .0000 | 0.001151782 |
| phosphodiesterase 4A | 25638 | *PDE4A* | −1.55 | .0011 | 0.030023803 |
| protein kinase N1 | 29355 | *PKN1* | 1.51 | .0001 | 0.005817694 |
| sulfotransferase family, cytosolic, 1C, member 2 | 171072 | *SULT1C2* | 1.40 | .0066 | 0.080018243 |
| **Others/unclassified** | | | | | |
| acetylcholinesterase | 83817 | *ACHE* | −1.61 | .0009 | 0.026111212 |
| A kinase (PRKA) anchor protein 14 | 60332 | *AKAP14* | 1.75 | .0000 | 0.000345513 |
| ADP-ribosylation factor 5 | 79117 | *ARF5* | 1.18 | .1270 | 0.441864518 |
| ATP synthase, $H^+$ transporting, mitochondrial $F_1$ complex, O subunit | 192241 | *ATP5O* | −1.21 | .1429 | 0.469959614 |
| barrier to autointegration factor 1 | 114087 | *BANF1* | 1.94 | .0000 | 0.000627148 |
| complement component 1, q subcomponent, beta polypeptide | 29687 | *C1QB* | 1.33 | .0055 | 0.071144019 |
| calcium channel, voltage-dependent, alpha 1I subunit | 56827 | *CACNA1I* | −1.49 | .0013 | 0.033306477 |
| calcitonin/calcitonin–related polypeptide, alpha | 24241 | *CALCA* | 1.57 | .0002 | 0.00960067 |
| steroid-sensitive gene 1 | 64387 | *CCDC80* | −1.68 | .0010 | 0.027773162 |
| caudal type homeobox 1 | 171042 | *CDX1(includesEG:171042)* | −1.38 | .0779 | 0.339542448 |
| chloride channel Kb | 79430 | *CLCNKB* | 1.34 | .0202 | 0.162131033 |
| cytochrome *c* oxidase subunit IV isoform 1 | 29445 | *COX4I1* | 2.01 | .0000 | 0.000345513 |
| cleavage and polyadenylation–specific factor 4 | 252943 | *CPSF4* | −1.47 | .0363 | 0.225382474 |
| upstream of NRAS | 117180 | *CSDE1* | −1.48 | .0027 | 0.049042265 |
| casein kinase 1, alpha 1 | 113927 | *CSNK1A1* | −1.48 | .0010 | 0.027890942 |
| chondroitin sulfate proteoglycan 5 | 50568 | *CSPG5* | 1.42 | .0130 | 0.12061056 |
| cytochrome *P*450, family 2, subfamily c, polypeptide 7 | 29298 | *CYP2C9* | 1.52 | .0030 | 0.050810807 |
| dipeptidase 1 (renal) | 94199 | *DPEP1* | −1.15 | .2356 | 0.588068112 |
| putative pheromone receptor Go-VN13C | 286986 | *EG665255* | −1.30 | .0159 | 0.136403128 |
| carboxylesterase 1 | 29225 | *ES22* | −1.53 | .0138 | 0.12501336 |
| Ena-vasodilator–stimulated phosphoprotein | 79115 | *EVL* | −1.48 | .0006 | 0.020979393 |
| Fas apoptotic inhibitory molecule 2 | 246274 | *FAIM2* | 1.74 | .0000 | 0.000313065 |
| gap junction membrane channel protein beta 4 | 117055 | *GJB4* | −1.62 | .0026 | 0.048592575 |
| galectin-related interfiber protein | 117130 | *GRIFIN* | −1.14 | .1826 | 0.525238789 |

**Table W3.** (*continued*)

| Gene Names | Locus ID | Symbol | Fold Changes | *P* | FDR |
|---|---|---|---|---|---|
| | | | T + DES LP *vs* LP | T + DES LP *vs* LP | T + DES LP *vs* LP |
| general transcription factor IIa 2 | 83828 | *GTF2A2* | −1.52 | .0018 | 0.040904546 |
| 3-hydroxyisobutyrate dehydrogenase | 63938 | *HIBADH* | −1.63 | .0092 | 0.099998918 |
| neural visinin–like $Ca^{2+}$–binding protein type 3 | 50871 | *HPCAL1* | −1.39 | .0014 | 0.034901656 |
| hydroxy-delta-5-steroid dehydrogenase, 3 beta-andosteroid delta-isomerase 1 | 29632 | *HSD3B2(includesEG:3284)* | 1.59 | .0132 | 0.121186877 |
| interferon, alpha-inducible protein 27–like | 170512 | *IFI27* | −1.33 | .0082 | 0.092474595 |
| potassium voltage–gated channel, shaker-related subfamily, beta member 1 | 29737 | *KCNAB1* | −1.47 | .0009 | 0.026111212 |
| potassium channel, subfamily K, member 9 | 84429 | *KCNK9* | 2.54 | .0000 | 3.18e−05 |
| preoptic regulatory factor-2 | 286903 | *KIAA1688* | −1.86 | .0000 | 0.001310057 |
| epididymal retinoic acid–binding protein | 29552 | *LCN5* | −1.33 | .1328 | 0.451496546 |
| leptin receptor overlapping transcript | 56766 | *LEPROT* | 1.23 | .0800 | 0.344030409 |
| Alpha-1,6-mannosyl-glycoprotein2-beta-*N*-acetylglucosaminyltransferase | 94273 | *MGAT2* | −1.49 | .0003 | 0.013861053 |
| membrane protein, palmitoylated 2 (MAGUK p55 subfamily member 2) | 85275 | *MPP2* | −1.54 | .0013 | 0.033527564 |
| membrane protein, palmitoylated 3 (MAGUK p55 subfamily member 3) | 114202 | *MPP3* | −1.78 | .0000 | 0.00238426 |
| myosin ID | 25485 | *MYO1D* | −1.86 | .0000 | 0.002259596 |
| myosin IE | 25484 | *MYO1E* | −1.49 | .0045 | 0.063968949 |
| *N*-acetyltransferase 8 (camello-like) | 64570 | *NAT8* | 1.60 | .0005 | 0.018001605 |
| nuclear factor I/X | 81524 | *NFIX* | −1.40 | .0020 | 0.043375551 |
| phosphodiesterase 4C, cAMP-specific | 290646 | *PDE4C* | −1.56 | .0015 | 0.035439407 |
| phosphofructokinase, muscle | 65152 | *PFKM* | 1.41 | .0036 | 0.05720289 |
| phospholipase C, delta 4 | 140693 | *PLCD4* | 1.06 | .5888 | 0.839859691 |
| pregnancy upregulated nonubiquitously expressed CaM kinase | 29660 | *PNCK* | 1.82 | .0000 | 0.004388703 |
| protein phosphatase 1, regulatory subunit 10 | 65045 | *PPP1R10* | −1.45 | .0110 | 0.112064665 |
| protein phosphatase 3, catalytic subunit, beta isoform | 24675 | *PPP3CB* | −1.05 | .6773 | 0.882757484 |
| prolactin-like protein L | 171556 | *PRLPL* | 1.11 | .3118 | 0.65353078 |
| PR-Vbeta1 | 498341 | *PR-Vbeta1* | 2.20 | .0000 | 3.18e−05 |
| Carcinoembryonic antigen gene family (CGM3) | 24256 | *PSG18* | 1.61 | .0001 | 0.00831627 |
| quinoid dihydropteridine reductase | 64192 | *QDPR* | −1.70 | .0343 | 0.218922533 |
| rabaptin 5 | 54190 | *RABEP1* | −1.46 | .0204 | 0.162411357 |
| RASD family, member 2 | 171099 | *RASD2* | 1.13 | .2983 | 0.645268138 |
| Ras association (RalGDS/AF-6) domain family 5 | 54355 | *RASSF5* | 1.15 | .1864 | 0.528802493 |
| ribosomal protein L10A | 81729 | *RPL10A(includesEG:81729)* | −1.40 | .0364 | 0.225382474 |
| ribosomal protein L27 | 64306 | *RPL27* | −1.33 | .0245 | 0.181311206 |
| ribosomal protein L28 | 64638 | *RPL28* | −1.65 | .0005 | 0.019279688 |
| ribosomal protein L29 | 29283 | *RPL29(includesEG:29283)* | −1.66 | .0011 | 0.029296571 |
| ribosomal protein S12 | 65139 | *RPS12* | 1.55 | .0012 | 0.0316706 |
| ribosomal protein S15 | 29285 | *RPS15* | −1.37 | .0212 | 0.16563314 |
| ribosomal protein S21 | 81775 | *RPS21* | −1.04 | .7860 | 0.92990797 |
| ribosomal protein S27a | 81777 | *RPS27A* | 1.09 | .5567 | 0.826186782 |
| ribosomal protein S9 | 81772 | *RPS9* | 1.46 | .0018 | 0.039884914 |
| spondin 1 | 64456 | *SPON1* | 1.46 | .0006 | 0.021028906 |
| sulfotransferase family 4A, member 1 | 58953 | *SULT4A1* | −1.45 | .0008 | 0.025012801 |
| synaptogyrin 2 | 89815 | *SYNGR2* | −1.47 | .0016 | 0.038035447 |
| tachykinin receptor 2 | 25007 | *TACR2* | 1.27 | .0327 | 0.212543742 |
| testis-enhanced gene transcript | 24822 | *TEGT* | −1.63 | .0004 | 0.015893027 |
| translocase of inner mitochondrial membrane 22 homolog (yeast) | 79463 | *TIMM22* | −1.48 | .0054 | 0.07023214 |
| transmembrane protein with EGF-like and two follistatin-like domains 1 | 63845 | *TMEFF1* | −1.85 | .0059 | 0.075505805 |
| translocase of outerm itochondrial membrane 20 homolog (yeast) | 266601 | *TOMM20* | 1.18 | .1323 | 0.451237424 |
| vesicle-associated membrane protein 2 | 24803 | *VAMP2* | 2.23 | .0000 | 0.002259596 |
| zinc finger protein 111 | 170849 | *ZNF227* | −1.69 | .0006 | 0.019354079 |

We propose that these genes was unlikely to be related to dysplasia induction.

Genes were categorized according to their cellular functions (in bold and italics).

**Table W4.** T + $E_2$–Insensitive Panel: Genes that Showed No Significant Changes in Their Expression Levels in the LPs or/and VPs following T + $E_2$ Treatment Relative to Their Respective Untreated Controls.

| Gene Names | Locus ID | Symbol |
|---|---|---|
| **Cellular movement** | | |
| arrestin, beta 2 | 25388 | *ARRB2* |
| androgen receptor | 24208 | *AR* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| interleukin 7 | 25647 | *IL7* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| neuropilin 2 | 81527 | *NRP2* |
| midkine | 81517 | *MDK* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| peptide YY (mapped) | 287730 | *PYY* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| protein tyrosine phosphatase, nonreceptor type 12 | 117255 | *PTPN12* |
| calcium and integrin binding 1 (calmyrin) | 81823 | *CIB1* |
| neogenin | 81735 | *NEO1* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| activated leukocyte cell adhesion molecule | 79559 | *ALCAM* |
| matrix metalloproteinase 16 | 65205 | *MMP16* |
| complexin 1 | 64832 | *CPLX1* |
| rhoB gene | 64373 | *RHOB* |
| legumain | 63865 | *LGMN* |
| matrix metallopeptidase 8 | 63849 | *MMP8* |
| cd86 antigen | 56822 | *CD86* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| neuroblastoma, suppression of tumorigenicity 1 | 50594 | *NBL1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| collagen, type 1, alpha 1 | 29393 | *COL1A1* |
| calpain, small subunit 1 | 29156 | *CAPNS1* |
| neurofibromatosis 2 | 25744 | *NF2* |
| synaptotagmin 3 | 25731 | *SYT3* |
| integrin beta 4 | 25724 | *ITGB4* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| paired box gene 6 | 25509 | *PAX6* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| cytochrome *P*450, family 19, subfamily a, polypeptide 1 | 25147 | *CYP19A1* |
| CD24 antigen | 25145 | *CD24* |
| tropomyosin 4 | 24852 | *TPM4* |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| **Cell death** | | |
| arrestin, beta 2 | 25388 | *ARRB2* |
| androgen receptor | 24208 | *AR* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| interleukin 7 | 25647 | *IL7* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| midkine | 81517 | *MDK* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| peptide YY (mapped) | 287730 | *PYY* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| calcium and integrin binding 1 (calmyrin) | 81823 | *CIB1* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| rhoB gene | 64373 | *RHOB* |
| matrix metallopeptidase 8 | 63849 | *MMP8* |
| cd86 antigen | 56822 | *CD86* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| calpain, small subunit 1 | 29156 | *CAPNS1* |
| neurofibromatosis 2 | 25744 | *NF2* |
| integrin beta 4 | 25724 | *ITGB4* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| paired box gene 6 | 25509 | *PAX6* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| cytochrome *P*450, family 19, subfamily a, polypeptide 1 | 25147 | *CYP19A1* |
| CD24 antigen | 25145 | *CD24* |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| metallothionein 1a | 24567 | *MT1E* |
| metallothionein 3 | 117038 | *MT3* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| calcitonin receptor | 116506 | *CALCR* |
| epithelial membrane protein 3 | 81505 | *EMP3* |
| persephin | 25525 | *PSPN* |
| HLA-B–associated transcript 3 | 94342 | *BAT3* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| cell division cycle 25 homolog A (*S. cerevisiae*) | 171102 | *CDC25A* |
| protein tyrosine phosphatase, nonreceptor type 23 | 117552 | *PTPN23* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| thyroid hormone receptor interactor 10 | 116717 | *TRIP10* |
| A kinase (PRKA) anchor protein 1 | 114124 | *AKAP1* |
| calbindin 1 | 83839 | *CALB1* |
| wild-type p53–induced gene 1 | 64394 | *ZMAT3* |
| unc-5 homolog A (*C. elegans*) | 60629 | *UNC5A* |
| transglutaminase 1 | 60335 | *TGM1* |
| mitogen-activated protein kinase 13 | 29513 | *MAPK13* |
| glutathione *S*-transferase, pi 2 | 29438 | *GSTP1* |
| fatty acid amide hydrolase | 29347 | *FAAH* |
| prothymosin alpha | 29222 | *PTMA* |
| stannin | 29140 | *SNN* |
| monoamine oxidase B | 25750 | *MAOB* |
| prostaglandin $D_2$ synthase | 25526 | *PTGDS* |
| glypican 3 | 25236 | *GPC3* |
| cytochrome *P*450, family 2, subfamily e, polypeptide 1 | 25086 | *CYP2E1* |
| ATPase, $Cu^{2+}$ transporting, beta polypeptide | 24218 | *ATP7B* |
| **Cell cycle** | | |
| androgen receptor | 24208 | *AR* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| interleukin 7 | 25647 | *IL7* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| midkine | 81517 | *MDK* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| rhoB gene | 64373 | *RHOB* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| neurofibromatosis 2 | 25744 | *NF2* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| paired box gene 6 | 25509 | *PAX6* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| calcitonin receptor | 116506 | *CALCR* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| cell division cycle 25 homolog A (*S. cerevisiae*) | 171102 | *CDC25A* |
| prothymosin alpha | 29222 | *PTMA* |
| collagen, type 1, alpha 1 | 29393 | *COL1A1* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| septin 9 | 83788 | *SEPT9* |
| **Cell morphology** | | |
| androgen receptor | 24208 | *AR* |
| interleukin 7 | 25647 | *IL7* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |

**Table W4.** (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| rhoB gene | 64373 | *RHOB* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| paired box gene 6 | 25509 | *PAX6* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| cell division cycle 25 homolog A (*S. cerevisiae*) | 171102 | *CDC25A* |
| collagen, type 1, alpha 1 | 29393 | *COL1A1* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| calcium and integrin binding 1 (calmyrin) | 81823 | *CIB1* |
| integrin beta 4 | 25724 | *ITGB4* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| cytochrome *P*450, family 19, subfamily a, polypeptide 1 | 25147 | *CYP19A1* |
| CD24 antigen | 25145 | *CD24* |
| protein tyrosine phosphatase, nonreceptor type 23 | 117552 | *PTPN23* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| calbindin 1 | 83839 | *CALB1* |
| mitogen-activated protein kinase 13 | 29513 | *MAPK13* |
| prostaglandin $D_2$ synthase | 25526 | *PTGDS* |
| protein tyrosine phosphatase, nonreceptor type 12 | 117255 | *PTPN12* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| RAS protein–specific guanine nucleotide–releasing factor 1 | 192213 | *RASGRF1* |
| procollagen, type I, alpha 2 | 84352 | *COL1A2* |
| ERM-binding phosphoprotein | 59114 | *SLC9A3R1* |
| clathrin, heavy polypeptide (Hc) | 54241 | *CLTC* |
| **Cellular growth and proliferation** | | |
| androgen receptor | 24208 | *AR* |
| interleukin 7 | 25647 | *IL7* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| rhoB gene | 64373 | *RHOB* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| paired box gene 6 | 25509 | *PAX6* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| cell division cycle 25 homolog A (*S. cerevisiae*) | 171102 | *CDC25A* |
| collagen, type 1, alpha 1 | 29393 | *COL1A1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| integrin beta 4 | 25724 | *ITGB4* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| cytochrome *P*450, family 19, subfamily a, polypeptide 1 | 25147 | *CYP19A1* |
| CD24 antigen | 25145 | *CD24* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| RAS protein–specific guanine nucleotide–releasing factor 1 | 192213 | *RASGRF1* |
| ERM-binding phosphoprotein | 59114 | *SLC9A3R1* |
| clathrin, heavy polypeptide (Hc) | 54241 | *CLTC* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| midkine | 81517 | *MDK* |
| neurofibromatosis 2 | 25744 | *NF2* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| calcitonin receptor | 116506 | *CALCR* |
| prothymosin alpha | 29222 | *PTMA* |
| peptide YY (mapped) | 287730 | *PYY* |

**Table W4.** (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| cd86 antigen | 56822 | *CD86* |
| calpain, small subunit 1 | 29156 | *CAPNS1* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| metallothionein 1a | 24567 | *MT1E* |
| metallothionein 3 | 117038 | *MT3* |
| epithelial membrane protein 3 | 81505 | *EMP3* |
| wild-type p53–induced gene 1 | 64394 | *ZMAT3* |
| glutathione *S*-transferase, pi 2 | 29438 | *GSTP1* |
| glypican 3 | 25236 | *GPC3* |
| neogenin | 81735 | *NEO1* |
| legumain | 63865 | *LGMN* |
| beta-microseminoprotein | 29311 | *MSMB* |
| solute carrier family 7 (cationic amino acid transporter, y+ system), member 7 | 83509 | *SLC7A7* |
| nuclear factor I/X | 81524 | *NFIX* |
| insulin-induced gene 1 | 64194 | *INSIG1* |
| FXYD domain–containing ion transport regulator 1 | 58971 | *FXYD1* |
| fibroblast growth factor 17 | 29368 | *FGF17* |
| solute carrier family 4, member 1 | 24779 | *SLC4A1* |
| **Molecular transport** | | |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| ERM-binding phosphoprotein | 59114 | *SLC9A3R1* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| calcitonin receptor | 116506 | *CALCR* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| insulin-induced gene 1 | 64194 | *INSIG1* |
| solute carrier family 4, member 1 | 24779 | *SLC4A1* |
| calbindin 1 | 83839 | *CALB1* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| A kinase (PRKA) anchor protein 1 | 114124 | *AKAP1* |
| cytochrome *P*450, family 2, subfamily e, polypeptide 1 | 25086 | *CYP2E1* |
| ATPase, $Cu^{2+}$ transporting, beta polypeptide | 24218 | *ATP7B* |
| carbonic anhydrase 2 | 54231 | *CA2* |
| solute carrier family 32 (GABA vesicular transporter), member 1 | 83612 | *SLC32A1* |
| potassium inwardly rectifying channel, subfamily J, member 11 | 83535 | *KCNJ11* |
| solute carrier family 30 (zinc transporter), member 2 | 25362 | *SLC30A2* |
| sodium channel, nonvoltage-gated, type I, alpha polypeptide | 25122 | *SCNN1A* |
| potassium voltage–gated channel, Shab-related subfamily, member 2 | 117105 | *KCNB2* |
| nuclear receptor subfamily 1, group I, member 2 | 84385 | *NR1I2* |
| transient receptor potential cation channel, subfamily C, member 2 | 64573 | *TRPC2* |
| hyperpolarization-activated, cyclic nucleotide–gated $K^+$ 4 | 59266 | *HCN4* |
| solute carrier family 14 (urea transporter), member 1 | 54301 | *SLC14A1* |
| potassium intermediate/small conductance calcium–activated channel, subfamily N, member 3 | 54263 | *KCNN3* |
| solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12 | 50676 | *SLC6A12* |
| potassium inwardly rectifying channel, subfamily J, member 3 | 50599 | *KCNJ3* |
| **DNA replication, recombination, and repair** | | |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| cell division cycle 25 homolog A (*S. cerevisiae*) | 171102 | *CDC25A* |

**Table W4.** (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| **Cellular assembly and organization** | | |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| A kinase (PRKA) anchor protein 1 | 114124 | *AKAP1* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| rhoB gene | 64373 | *RHOB* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| CD24 antigen | 25145 | *CD24* |
| peptide YY (mapped) | 287730 | *PYY* |
| thyroid hormone receptor interactor 10 | 116717 | *TRIP10* |
| complexin 1 | 64832 | *CPLX1* |
| synaptotagmin 3 | 25731 | *SYT3* |
| LIM motif–containing protein kinase 2 | 29524 | *LIMK2* |
| coronin, actin-binding protein, 1B | 29474 | *CORO1B* |
| synapsin III | 29130 | *SYN3* |
| **Cell signaling** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| A kinase (PRKA) anchor protein 1 | 114124 | *AKAP1* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| ERM-binding phosphoprotein | 59114 | *SLC9A3R1* |
| calcitonin receptor | 116506 | *CALCR* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| calbindin 1 | 83839 | *CALB1* |
| potassium inwardly rectifying channel, subfamily J, member 11 | 83535 | *KCNJ11* |
| transient receptor potential cation channel, subfamily C, member 2 | 64573 | *TRPC2* |
| homeodomain interacting protein kinase 3 | 83617 | *HIPK3* |
| **Nucleic acid metabolism** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| calcitonin receptor | 116506 | *CALCR* |
| **Small molecule biochemistry** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| calcitonin receptor | 116506 | *CALCR* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| homeodomain interacting protein kinase 3 | 83617 | *HIPK3* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| LIM motif–containing protein kinase 2 | 29524 | *LIMK2* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| insulin-induced gene 1 | 64194 | *INSIG1* |
| solute carrier family 4, member 1 | 24779 | *SLC4A1* |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| ATPase, $Cu^{2+}$ transporting, beta polypeptide | 24218 | *ATP7B* |
| carbonic anhydrase 2 | 54231 | *CA2* |
| solute carrier family 32 (GABA vesicular transporter), member 1 | 83612 | *SLC32A1* |
| nuclear receptor subfamily 1, group I, member 2 | 84385 | *NR1I2* |
| solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12 | 50676 | *SLC6A12* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| metallothionein 1a | 24567 | *MT1E* |
| metallothionein 3 | 117038 | *MT3* |
| neogenin | 81735 | *NEO1* |
| protein tyrosine phosphatase, nonreceptor type 12 | 117255 | *PTPN12* |
| transglutaminase 1 | 60335 | *TGM1* |
| fatty acid amide hydrolase | 29347 | *FAAH* |
| monoamine oxidase B | 25750 | *MAOB* |
| phosphorylase kinase, gamma 2 (testis) | 140671 | *PHKG2* |
| solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 7 | 116638 | *SLC17A7* |
| Rab geranylgeranyl transferase, a subunit | 58983 | *RABGGTA* |
| **Cellular development** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| calcitonin receptor | 116506 | *CALCR* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| LIM motif–containing protein kinase 2 | 29524 | *LIMK2* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| carbonic anhydrase 2 | 54231 | *CA2* |
| protein tyrosine phosphatase, nonreceptor type 12 | 117255 | *PTPN12* |
| transglutaminase 1 | 60335 | *TGM1* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| rhoB gene | 64373 | *RHOB* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| CD24 antigen | 25145 | *CD24* |
| androgen receptor | 24208 | *AR* |
| interleukin 7 | 25647 | *IL7* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| paired box gene 6 | 25509 | *PAX6* |
| integrin beta 4 | 25724 | *ITGB4* |
| cytochrome *P*450, family 19, subfamily a, polypeptide 1 | 25147 | *CYP19A1* |
| prothymosin alpha | 29222 | *PTMA* |
| cd86 antigen | 56822 | *CD86* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| calcium and integrin binding 1 (calmyrin) | 81823 | *CIB1* |
| neuropilin 2 | 81527 | *NRP2* |
| Notch gene homolog 3 (*Drosophila*) | 56761 | *NOTCH3* |
| **Post–Translational Modification** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| LIM motif–containing protein kinase 2 | 29524 | *LIMK2* |
| protein tyrosine phosphatase, nonreceptor type 12 | 117255 | *PTPN12* |
| transglutaminase 1 | 60335 | *TGM1* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| interleukin 7 | 25647 | *IL7* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| homeodomain interacting protein kinase 3 | 83617 | *HIPK3* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| nuclear receptor subfamily 1, group I, member 2 | 84385 | *NR1I2* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| phosphorylase kinase, gamma 2 (testis) | 140671 | *PHKG2* |
| Rab geranylgeranyl transferase, a subunit | 58983 | *RABGGTA* |
| gamma-glutamyl carboxylase | 81716 | *GGCX* |

**Table W4.** (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| **Cellular function and maintenance** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| interleukin 7 | 25647 | *IL7* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| CD24 antigen | 25145 | *CD24* |
| prothymosin alpha | 29222 | *PTMA* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| peptide YY (mapped) | 287730 | *PYY* |
| complexin 1 | 64832 | *CPLX1* |
| synaptotagmin 3 | 25731 | *SYT3* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| Rsec5 protein | 171455 | *EXOC2* |
| **Cell to cell signaling and interaction** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| interleukin 7 | 25647 | *IL7* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| CD24 antigen | 25145 | *CD24* |
| prothymosin alpha | 29222 | *PTMA* |
| peptide YY (mapped) | 287730 | *PYY* |
| complexin 1 | 64832 | *CPLX1* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| glial cell line–derived neurotrophic factor family receptor alpha 1 | 25454 | *GFRA1* |
| androgen receptor | 24208 | *AR* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| integrin beta 4 | 25724 | *ITGB4* |
| cd86 antigen | 56822 | *CD86* |
| calcium and integrin binding 1 (calmyrin) | 81823 | *CIB1* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| solute carrier family 4, member 1 | 24779 | *SLC4A1* |
| neogenin | 81735 | *NEO1* |
| solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 7 | 116638 | *SLC17A7* |
| calbindin 1 | 83839 | *CALB1* |
| hyperpolarization-activated, cyclic nucleotide–gated K$^+$ 4 | 59266 | *HCN4* |
| potassium intermediate/small conductance calcium–activated channel, subfamily N, member 3 | 54263 | *KCNN3* |
| RAS protein–specific guanine nucleotide–releasing factor 1 | 192213 | *RASGRF1* |
| midkine | 81517 | *MDK* |
| glypican 3 | 25236 | *GPC3* |
| activated leukocyte cell adhesion molecule | 79559 | *ALCAM* |
| tropomodulin 2 | 58814 | *TMOD2* |
| cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal) | 54239 | *CHRNB2* |
| **Gene expression** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| prothymosin alpha | 29222 | *PTMA* |
| v-*myc* myelocytomatosis viral–related oncogene, neuroblastoma-derived (avian) (mapped) | 298894 | *MYCN* |
| lectin, galactose binding, soluble 1 | 56646 | *LGALS1* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| androgen receptor | 24208 | *AR* |
| Inhibitor of DNA binding 2, dominant negative helix–loop–helix protein | 25587 | *ID2* |
| integrin beta 4 | 25724 | *ITGB4* |
| cd86 antigen | 56822 | *CD86* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| neogenin | 81735 | *NEO1* |
| RAS protein–specific guanine nucleotide–releasing factor 1 | 192213 | *RASGRF1* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| nuclear receptor subfamily 1, group I, member 2 | 84385 | *NR1I2* |
| rhoB gene | 64373 | *RHOB* |
| paired box gene 6 | 25509 | *PAX6* |
| cytochrome *P*450, family 19, subfamily a, polypeptide 1 | 25147 | *CYP19A1* |
| Notch gene homolog 3 (*Drosophila*) | 56761 | *NOTCH3* |
| glutathione *S*-transferase, pi 2 | 29438 | *GSTP1* |
| nuclear factor I/X | 81524 | *NFIX* |
| FXYD domain–containing ion transport regulator 1 | 58971 | *FXYD1* |
| mitogen-activated protein kinase 13 | 29513 | *MAPK13* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| proteasome (prosome, macropain) 26S subunit, non-ATPase, 9 | 161475 | *PSMD9* |
| basic transcription element binding protein 1 | 117560 | *KLF9* |
| Kruppel-like factor 15 | 85497 | *KLF15* |
| general transcription factor IIa 2 | 83828 | *GTF2A2* |
| Sjogren syndrome antigen B | 81783 | *SSB* |
| fatty acid binding protein 4, adipocyte | 79451 | *FABP4* |
| PDZ and LIM domain 1 (elfin) | 54133 | *PDLIM1* |
| **Amino acid metabolism** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| cyclin-dependent kinase 2 | 362817 | *CDK2* |
| nuclear receptor subfamily 1, group I, member 2 | 84385 | *NR1I2* |
| cyclin-dependent kinase 5 | 140908 | *CDK5* |
| solute carrier family 4, member 1 | 24779 | *SLC4A1* |
| solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 7 | 116638 | *SLC17A7* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| LIM motif–containing protein kinase 2 | 29524 | *LIMK2* |
| protein tyrosine phosphatase, nonreceptor type 12 | 117255 | *PTPN12* |
| transglutaminase 1 | 60335 | *TGM1* |
| homeodomain interacting protein kinase 3 | 83617 | *HIPK3* |
| phosphorylase kinase, gamma 2 (testis) | 140671 | *PHKG2* |
| Rab geranylgeranyl transferase, a subunit | 58983 | *RABGGTA* |
| solute carrier family 32 (GABA vesicular transporter), member 1 | 83612 | *SLC32A1* |
| **Lipid metabolism** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| phosphatase and tensin homolog | 50557 | *PTEN* |
| nuclear receptor subfamily 1, group I, member 2 | 84385 | *NR1I2* |
| transglutaminase 1 | 60335 | *TGM1* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| neogenin | 81735 | *NEO1* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| arrestin, beta 1 | 25387 | *ARRB1* |
| insulin-induced gene 1 | 64194 | *INSIG1* |
| fatty acid amide hydrolase | 29347 | *FAAH* |
| **Cellular compromise** | | |
| ATP-binding cassette, subfamily C (CFTR/MRP), member 1 | 24565 | *ABCC1* |
| fatty acid amide hydrolase | 29347 | *FAAH* |
| mitogen-activated protein kinase 14 | 81649 | *MAPK14* |
| RAS protein–specific guanine nucleotide–releasing factor 1 | 192213 | *RASGRF1* |
| peroxiredoxin 1 | 117254 | *PRDX1* |
| metallothionein 1a | 24567 | *MT1E* |
| metallothionein 3 | 117038 | *MT3* |

Table W4. (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| cytochrome *P*450, family 2, subfamily e, polypeptide 1 | 25086 | *CYP2E1* |
| **Vitamin and mineral metabolism** | | |
| insulin-like growth factor 1 | 24482 | *IGF1* |
| endothelial differentiation sphingolipid G-protein–coupled receptor 1 | 29733 | *EDG1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| intercellular adhesion molecule 1 | 25464 | *ICAM1* |
| calbindin 1 | 83839 | *CALB1* |
| peptidylprolyl isomerase A | 25518 | *PPIA* |
| calcitonin receptor | 116506 | *CALCR* |
| A kinase (PRKA) anchor protein 1 | 114124 | *AKAP1* |
| ERM-binding phosphoprotein | 59114 | *SLC9A3R1* |
| potassium inwardly rectifying channel, subfamily J, member 11 | 83535 | *KCNJ11* |
| transient receptor potential cation channel, subfamily C, member 2 | 64573 | *TRPC2* |
| **Drug metabolism** | | |
| ATPase, $Cu^{2+}$ transporting, beta polypeptide | 24218 | *ATP7B* |
| **Others/unclassified** | | |
| solute carrier family 5 (sodium-dependent vitamin transporter), member 6 | 170551 | *SLC5A6* |
| solute carrier family 28 (sodium-coupled nucleoside transporter), member 2 | 60423 | *SLC28A2* |
| selenoprotein P, plasma, 1 | 29360 | *SEPP1* |
| etoile, Sam68-like protein SLM-2 | 64015 | *KHDRBS3* |
| ubc2e ubiquitin–conjugating enzyme | 641452 | *UBE2D2* |
| RT1 class II, locus Da | 294269 | *HLA-DRA* |
| similar to Leydig cell tumor 10 kDa protein | 288913 | *C19ORF53* |
| voltage-gated channel like 1 | 266760 | *VGCNL1* |
| guanine nucleotide binding protein (G protein), gamma 8 subunit | 245986 | *GNG8* |
| membrane and microfilament–associated protein p58 | 207121 | *RGD:727794* |
| seminal vesicle secretion 3 | 192239 | *SEMG2* |
| methionine adenosyltransferase II, alpha | 171347 | *MAT2A* |
| LIM homeobox protein 5 | 124451 | *LHX5* |
| CD52 antigen | 117054 | *CD52* |
| CEA-related cell adhesion molecule 9 | 116711 | *CEACAM9* |
| ubiquilin 1 | 114590 | *UBQLN1* |
| carboxylesterase 3 | 113902 | *CES1* |
| synaptogyrin 2 | 89815 | *SYNGR2* |
| low-density lipoprotein receptor–related protein 3 | 89787 | *LRP3* |
| MAD homolog 9 (*Drosophila*) | 85435 | *SMAD9* |
| protein kinase C, delta binding protein | 85332 | *PRKCDBP* |
| nucleobindin 1 | 84595 | *NUCB1* |
| RAB6A, member RAS oncogene family | 84379 | *RAB6A* |
| ATPase, class II, type 9A | 84011 | *ATP9A* |
| NSFL1 (p97) cofactor (p47) | 83809 | *NSFL1C* |
| tripartite motif protein 3 | 83616 | *TRIM3* |
| discoidin domain receptor family, member 2 | 83573 | *DDR2* |
| cadherin EGF LAG seven-pass G-type receptor 2 | 83465 | *CELSR2* |
| 5-hydroxytryptamine (serotonin) receptor 5B | 79247 | *HTR5B* |
| ADP-ribosylation factor 4 | 79120 | *ARF4* |
| olfactory receptor 226 | 65140 | *OR6A2* |
| probasin | 54193 | *PBSN* |
| mini chromosome maintenance deficient 6 (*S. cerevisiae*) | 29685 | *MCM6* |
| argininosuccinate synthetase | 25698 | *ASS1* |
| sialyltransferase 8 C | 25547 | *ST8SIA3* |
| apolipoprotein B editing complex 1 | 25383 | *APOBEC1* |
| lysozyme | 25211 | *LYZ* |
| secretoglobin, family 2A, member 1 | 25010 | *PSBP1* |
| phosphoglucomutase 1 | 24645 | *PGM1* |
| filaggrin | 24641 | *FLG* |
| malate dehydrogenase 1, NAD (soluble) | 24551 | *MDH1* |

Genes were categorized according to their cellular functions (in bold and italics).

**Table W5.** T + DES–Insensitive Panel: Genes Whose Expression Levels Were Not Significantly Changed in the LPs or/and VPs following T + DES Treatment Relative to Their Respective Untreated Controls.

| Gene Names | Locus ID | Symbol |
|---|---|---|
| **Amino acid metabolism** | | |
| solute carrier family 32 (GABA vesicular transporter), member 1 | 83612 | *SLC32A1* |
| **Carbohydrate metabolism** | | |
| protein kinase, AMP-activated, alpha 2 catalytic subunit | 78975 | *PRKAA2* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| interleukin 7 | 25647 | *IL7* |
| **Cell cycle** | | |
| interleukin 7 | 25647 | *IL7* |
| myogenic differentiation 1 | 337868 | *MYOD1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| calcitonin receptor | 116506 | *CALCR* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| midkine | 81517 | *MDK* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| androgen receptor | 24208 | *AR* |
| **Cell death** | | |
| interleukin 7 | 25647 | *IL7* |
| myogenic differentiation 1 | 337868 | *MYOD1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| calcitonin receptor | 116506 | *CALCR* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| midkine | 81517 | *MDK* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| androgen receptor | 24208 | *AR* |
| protein kinase, AMP-activated, alpha 2 catalytic subunit | 78975 | *PRKAA2* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| metallothionein 3 | 117038 | *MT3* |
| HLA-B–associated transcript 3 | 94342 | *BAT3* |
| nuclear receptor subfamily 2, group F, member 1 | 81808 | *NR2F1* |
| linker for activation of T cells | 81511 | *LAT* |
| epithelial membrane protein 3 | 81505 | *EMP3* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| xanthine dehydrogenase | 29289 | *XDH* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| milk fat globule–EGF factor 8 protein | 25277 | *MFGE8* |
| early growth response 4 | 25129 | *EGR4* |
| transthyretin | 24856 | *TTR* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| metallothionein 1a | 24567 | *MT1E* |
| benzodiazepine receptor, peripheral | 24230 | *TSPO* |
| **Cell morphology** | | |
| myogenic differentiation 1 | 337868 | *MYOD1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| nuclear receptor subfamily 2, group F, member 1 | 81808 | *NR2F1* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| potassium inwardly rectifying channel, subfamily J, member 11 | 83535 | *KCNJ11* |
| lumican | 81682 | *LUM* |
| neuropilin 2 | 81527 | *NRP2* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| persephin | 25525 | *PSPN* |
| **Cell signaling** | | |
| linker for activation of T cells | 81511 | *LAT* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| **Cell to cell signaling and interaction** | | |
| linker for activation of T cells | 81511 | *LAT* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| neuropilin 2 | 81527 | *NRP2* |
| interleukin 7 | 25647 | *IL7* |
| midkine | 81517 | *MDK* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| xanthine dehydrogenase | 29289 | *XDH* |
| milk fat globule–EGF factor 8 protein | 25277 | *MFGE8* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| pleckstrin homology, Sec7 and coiled/coil domains 1 | 116691 | *PSCD1* |
| a disintegrin and metalloproteinase domain 15 (metargidin) | 57025 | *ADAM15* |
| **Cellular assembly and organization** | | |
| neuropilin 2 | 81527 | *NRP2* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| xanthine dehydrogenase | 29289 | *XDH* |
| milk fat globule–EGF factor 8 protein | 25277 | *MFGE8* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| nuclear receptor subfamily 2, group F, member 1 | 81808 | *NR2F1* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| lumican | 81682 | *LUM* |
| androgen receptor | 24208 | *AR* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| metallothionein 1a | 24567 | *MT1E* |
| **Cellular compromise** | | |
| xanthine dehydrogenase | 29289 | *XDH* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| metallothionein 1a | 24567 | *MT1E* |
| linker for activation of T cells | 81511 | *LAT* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| metallothionein 3 | 117038 | *MT3* |
| early growth response 4 | 25129 | *EGR4* |
| **Cellular development** | | |
| xanthine dehydrogenase | 29289 | *XDH* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| linker for activation of T cells | 81511 | *LAT* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| neuropilin 2 | 81527 | *NRP2* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| nuclear receptor subfamily 2, group F, member 1 | 81808 | *NR2F1* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| androgen receptor | 24208 | *AR* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| interleukin 7 | 25647 | *IL7* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| myogenic differentiation 1 | 337868 | *MYOD1* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| calcitonin receptor | 116506 | *CALCR* |
| interferon-induced transmembrane protein 2 (1–8D) | 114709 | *IFITM2* |
| CD164 antigen | 83689 | *CD164* |
| etoile, Sam68-like protein SLM-2 | 64015 | *KHDRBS3* |
| carbonic anhydrase 2 | 54231 | *CA2* |
| testis-specific protein, Y-linked | 25223 | *TSPY1* |
| histone 1, H1t | 24438 | *HIST1H1T* |
| **Cellular function and maintenance** | | |
| linker for activation of T cells | 81511 | *LAT* |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| nuclear receptor subfamily 2, group F, member 1 | 81808 | *NR2F1* |
| androgen receptor | 24208 | *AR* |
| interleukin 7 | 25647 | *IL7* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| myogenic differentiation 1 | 337868 | *MYOD1* |
| high mobility group box transcription factor 1 | 27080 | *HBP1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| **Cellular growth and proliferation** | | |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| androgen receptor | 24208 | *AR* |
| interleukin 7 | 25647 | *IL7* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |

**Table W5.** (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| myogenic differentiation 1 | 337868 | *MYOD1* |
| casein kinase II, alpha 1 polypeptide | 116549 | *CSNK2A1* |
| xanthine dehydrogenase | 29289 | *XDH* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| calcitonin receptor | 116506 | *CALCR* |
| CD164 antigen | 83689 | *CD164* |
| testis-specific protein, Y-linked | 25223 | *TSPY1* |
| metallothionein 1a | 24567 | *MT1E* |
| metallothionein 3 | 117038 | *MT3* |
| early growth response 4 | 25129 | *EGR4* |
| lumican | 81682 | *LUM* |
| midkine | 81517 | *MDK* |
| a disintegrin and metalloproteinase domain 15 (metargidin) | 57025 | *ADAM15* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| epithelial membrane protein 3 | 81505 | *EMP3* |
| nucleosome assembly protein 1–like 1 | 89825 | *NAP1L1* |
| solute carrier family 29 (nucleoside transporters), member 1 | 63997 | *SLC29A1* |
| beta-microseminoprotein | 29311 | *MSMB* |
| ferritin light chain 1 | 29292 | *FTL* |
| **Cellular movement** | | |
| chemokine (C–C motif) ligand 3 | 25542 | *CCL3* |
| androgen receptor | 24208 | *AR* |
| interleukin 7 | 25647 | *IL7* |
| xanthine dehydrogenase | 29289 | *XDH* |
| thioredoxin reductase 2 | 50551 | *PAX3* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| neuropilin 2 | 81527 | *NRP2* |
| **DNA replication, recombination, and repair** | | |
| androgen receptor | 24208 | *AR* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| phosphodiesterase 5A, cGMP-specific | 171115 | *PDE5A* |
| **Drug metabolism** | | |
| androgen receptor | 24208 | *AR* |
| xanthine dehydrogenase | 29289 | *XDH* |
| solute carrier family 29 (nucleoside transporters), member 1 | 63997 | *SLC29A1* |
| solute carrier family 28 (sodium-coupled nucleoside transporter), member 2 | 60423 | *SLC28A2* |
| **Free radical scavenging** | | |
| xanthine dehydrogenase | 29289 | *XDH* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| **Gene expression** | | |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| androgen receptor | 24208 | *AR* |
| structure-specific recognition protein 1 | 81785 | *SSRP1* |
| interleukin 7 | 25647 | *IL7* |
| myosin heavy chain 11 | 24582 | *MYH11* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| myogenic differentiation 1 | 337868 | *MYOD1* |
| nuclear receptor subfamily 2, group F, member 1 | 81808 | *NR2F1* |
| **Lipid metabolism** | | |
| androgen receptor | 24208 | *AR* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| xanthine dehydrogenase | 29289 | *XDH* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| protein kinase, AMP-activated, alpha 2 catalytic subunit | 78975 | *PRKAA2* |
| nuclear receptor binding factor 1 | 29470 | *MECR* |
| selenoprotein P, plasma, 1 | 29360 | *SEPP1* |
| **Molecular transport** | | |
| androgen receptor | 24208 | *AR* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| xanthine dehydrogenase | 29289 | *XDH* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| protein kinase, AMP-activated, alpha 2 catalytic subunit | 78975 | *PRKAA2* |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| interleukin 7 | 25647 | *IL7* |
| solute carrier family 29 (nucleoside transporters), member 1 | 63997 | *SLC29A1* |
| solute carrier family 28 (sodium-coupled nucleoside transporter), member 2 | 60423 | *SLC28A2* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| carbonic anhydrase 2 | 54231 | *CA2* |
| potassium inwardly rectifying channel, subfamily J, member 11 | 83535 | *KCNJ11* |
| solute carrier family 5 (sodium-dependent vitamin transporter), member 6 | 170551 | *SLC5A6* |
| solute carrier family 32 (GABA vesicular transporter), member 1 | 83612 | *SLC32A1* |
| solute carrier family 30 (zinc transporter), member 2 | 25362 | *SLC30A2* |
| sodium channel, nonvoltage-gated, type I, alpha polypeptide | 25122 | *SCNN1A* |
| **Nucleic acid metabolism** | | |
| xanthine dehydrogenase | 29289 | *XDH* |
| solute carrier family 29 (nucleoside transporters), member 1 | 63997 | *SLC29A1* |
| solute carrier family 28 (sodium-coupled nucleoside transporter), member 2 | 60423 | *SLC28A2* |
| nuclear receptor binding factor 1 | 29470 | *MECR* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| phosphodiesterase 5A, cGMP-specific | 171115 | *PDE5A* |
| **Post–translational modification** | | |
| xanthine dehydrogenase | 29289 | *XDH* |
| **RNA post–transcriptional modification** | | |
| Fanconi anemia, complementation group C | 24361 | *FANCC* |
| **Small molecule biochemistry** | | |
| xanthine dehydrogenase | 29289 | *XDH* |
| solute carrier family 29 (nucleoside transporters), member 1 | 63997 | *SLC29A1* |
| solute carrier family 28 (sodium-coupled nucleoside transporter), member 2 | 60423 | *SLC28A2* |
| nuclear receptor binding factor 1 | 29470 | *MECR* |
| arrestin, beta 2 | 25388 | *ARRB2* |
| phosphodiesterase 5A, cGMP-specific | 171115 | *PDE5A* |
| androgen receptor | 24208 | *AR* |
| signal transducer and activator of transcription 5A | 24918 | *STAT5A* |
| mannoside acetyl glucosaminyltransferase 3 | 29582 | *MGAT3* |
| protein kinase, AMP-activated, alpha 2 catalytic subunit | 78975 | *PRKAA2* |
| interleukin 7 | 25647 | *IL7* |
| neurotrophic tyrosine kinase, receptor, type 3 | 29613 | *NTRK3* |
| carbonic anhydrase 2 | 54231 | *CA2* |
| solute carrier family 5 (sodium-dependent vitamin transporter), member 6 | 170551 | *SLC5A6* |
| solute carrier family 32 (GABA vesicular transporter), member 1 | 83612 | *SLC32A1* |
| inositol polyphosphate phosphatase–like 1 | 65038 | *INPPL1* |
| selenoprotein P, plasma, 1 | 29360 | *SEPP1* |
| metallothionein 1a | 24567 | *MT1E* |
| metallothionein 3 | 117038 | *MT3* |
| ferritin light chain 1 | 29292 | *FTL* |
| **Vitamin and mineral metabolism** | | |
| solute carrier family 5 (sodium-dependent vitamin transporter), member 6 | 170551 | *SLC5A6* |
| linker for activation of T cells | 81511 | *LAT* |
| **Others/unclassified** | | |
| guanine nucleotide binding protein (G protein), gamma 8 subunit | 245986 | *GNG8* |
| H1 histone family, member 4 | 201097 | *H1F4* |
| glutaminase 2 (liver, mitochondrial) | 192268 | *GLS2* |
| seminal vesicle secretion 3 | 192239 | *SEMG2* |
| proteasome (prosome, macropain) 26S subunit, non-ATPase, 9 | 161475 | *PSMD9* |
| protein tyrosine phosphatase, nonreceptor type 23 | 117552 | *PTPN23* |
| CD52 antigen | 117054 | *CD52* |

Table W5. (*continued*)

| Gene Names | Locus ID | Symbol |
|---|---|---|
| ribosomal protein L6 | 117042 | *RPL6* |
| importin 13 | 116458 | *IPO13* |
| general transcription factor IIa 2 | 83828 | *GTF2A2* |
| tripartite motif protein 3 | 83616 | *TRIM3* |
| ribosomal protein L5 | 81763 | *RPL5* |
| ribosomal protein S8 | 65136 | *RPS8* |
| defensin beta 3 | 64389 | *DEFB4* |
| ribosomal protein L31 | 64298 | *RPL31* |
| ribosomal protein L35a | 57809 | *RPL35A* |
| solute carrier family 14 (urea transporter), member 1 | 54301 | *SLC14A1* |
| probasin | 54193 | *PBSN* |
| mini chromosome maintenance-deficient 6 (*S. cerevisiae*) | 29685 | *MCM6* |
| proteasome (prosome, macropain) subunit, beta type 3 | 29676 | *PSMB3* |
| peptidyl arginine deiminase, type II | 29511 | *PADI2* |
| coronin, actin-binding protein, 1B | 29474 | *CORO1B* |
| ribosomal protein S26 | 27139 | *RPS26* |
| sialyltransferase 8 C | 25547 | *ST8SIA3* |
| crystallin, beta B2 | 25422 | *CRYBB2* |
| glutamate-ammonia ligase (glutamine synthase) | 24957 | *CCDC92* |
| malate dehydrogenase 1, NAD (soluble) | 24551 | *MDH1* |

Genes were categorized according to their cellular functions (in bold and italics).