OPEN ACCESS Freely available online

PLOS ONE

Genome-Wide Analysis Using Exon Arrays Demonstrates an Important Role for Expression of Extra-Cellular Matrix, Fibrotic Control and Tissue Remodelling Genes in Dupuytren's Disease

Helen B. Forrester[1☯], Peter Temple-Smith[2,3,6☯], Seungmin Ham[2,3], David de Kretser[4,5], Graeme Southwick[5,6], Carl N. Sprung[1]*

1 Centre for Innate Immunology and Infectious Disease, Monash Institute of Medical Research, Monash University, Clayton, Victoria, Australia, **2** Department of Obstetrics and Gynaecology, Southern Clinical School, Monash University, Monash Medical Centre, Clayton, Victoria, Australia, **3** Prince Henry's Institute, Clayton, Victoria, Australia, **4** Centre for Reproduction and Development, Monash Institute of Medical Research, Clayton, Victoria, Australia, **5** Department of Anatomy and Developmental Biology, Monash University, Clayton, Victoria, Australia, **6** Melbourne Institute of Plastic Surgery, Malvern, Victoria, Australia

Abstract

Dupuytren's disease (DD) is a classic example of pathological fibrosis which results in a debilitating disorder affecting a large sector of the human population. It is characterized by excessive local proliferation of fibroblasts and over-production of collagen and other components of extracellular matrix (ECM) in the palmar fascia. The fibrosis progressively results in contracture of elements between the palmar fascia and skin causing flexion deformity or clawing of the fingers and a severe reduction in hand function. While much is known about the pathogenesis and surgical treatment of DD, little is known about the factors that cause its onset and progression, despite many years of research. Gene expression patterns in DD patients now offers the potential to identify genes that direct the pathogenesis of DD. In this study we used primary cultures of fibroblasts derived from excisional biopsies of fibrotic tissue from DD patients to compare the gene expression profiles on a genome-wide basis with normal control fibroblasts. Our investigations have identified genes that may be involved with DD pathogenesis including some which are directly relevant to fibrosis. In particular, these include significantly reduced expression levels of three matrix metallopeptidases (*MMP1*, *MMP3*, *MMP16*), follistatin, and *STAT1*, and significantly increased expression levels of fibroblast growth factors (*FGF9*, *FGF11*), a number of collagen genes and other ECM genes in DD patient samples. Many of these gene products are known to be involved in fibrosis, tumour formation and in the normal processes of tissue remodelling. In addition, alternative splicing was identified in some DD associated genes. These highly sensitive genomic investigations provide new insight into the molecular mechanisms that may underpin the development and progression of DD.

Citation: Forrester HB, Temple-Smith P, Ham S, de Kretser D, Southwick G, et al. (2013) Genome-Wide Analysis Using Exon Arrays Demonstrates an Important Role for Expression of Extra-Cellular Matrix, Fibrotic Control and Tissue Remodelling Genes in Dupuytren's Disease. PLoS ONE 8(3): e59056. doi:10.1371/journal.pone.0059056

Editor: Andrea Dardis, University Hospital S. Maria della Misericordia, Udine, Italy

Received September 29, 2012; **Accepted** February 11, 2013; **Published** March 12, 2013

Funding: This project was supported through the 2010 round of the Priority-driven Collaborative Cancer Research Scheme (grant 1002743) and funded by the Australian Government Department of Health and Ageing with the assistance of Cancer Australia. Also, this work was supported by the Australian National Health and Medical Research Council (grant numbers 145780, 288713; http://www.nhmrc.gov.au/); the Australian National Breast Cancer Foundation (grant PG-08-06; http://www.nbcf.org.au/); and the National Institute of Health (grant 5U19AI067773-07) and a grant from the Advanced Plastic Surgery Education Foundation. Support was also provided by the Victorian Government's Operational Infrastructure Support Program. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: carl.sprung@monash.edu

☯ These authors contributed equally to this work.

Introduction

Dupuytren's disease (DD) is a classic example of a pathological fibrotic disease characterized by excessive proliferation of fibroblasts and over-production of collagen and other components of extracellular matrix (ECM) in the hand [1,2,3]. DD typically starts in individuals between the age of 35 and 50 with the formation of one or more subcutaneous nodules in the palmar fascia that develop cords of fibrotic tissue impacting on the function of the metacarpophalangeal and proximal interphalangeal joints [1,2,3]. With time the developing fibrosis causes contracture of the palmar fascia resulting in flexion deformity of particularly the 4th and 5th digits with a severe reduction in hand function [4,5,6,7,8]. DD occurs in all racial groups but has a higher prevalence in populations with Caucasian ancestry [9,10,11]. Evidence from the pattern of inheritance observed in different populations suggests that it is heritable as an autosomal dominant or autosomal recessive with variable penetrance [12,13,14].

Males are three times more likely to develop DD and are also more likely to have greater disease severity [15,16]. DD affects more than 2% of individuals in a population with the incidence in some cohorts, for example, Belgian and German men over 50 and

men over 60 in Australia and Scotland, exceeding 20% (http:www.dupuytren-online.info/dupuytren_age_distribution.html) [12,13,17,18]. The predominance of DD in males may be related to expression of androgen receptors in Dupuytren fascia [16]. Other risk factors include manual labor with vibration exposure, prior hand trauma, alcoholism, smoking, diabetes mellitus, hyperlipidemia, Peyronie's disease of the penis, and complex regional pain syndrome [19].

Currently, the most effective treatment is palmar fasciectomy, which involves surgical resection of fibrotic bands and rearrangement of skin using flaps or interrupting normal skin topography by full thickness grafts. Unfortunately, with time, the recurrence rate is high and disease progression is inevitable, requiring further surgery. Other surgical options include simple transcutaneous division of a Dupuytren's band by needle or knife fasciotomy [20,21], with a high recurrence rate of about 3% in the first year and more than 50% by year 4. More recently, a nonsurgical treatment using subcutaneous injections of Clostridium-derived collagenase has been used [22,23,24].

While the descriptive pathogenesis of DD is understood [1,16], the factors causing its onset and progression remain unclear [16,25]. Fibrogenic cytokines that cause growth and differentiation of fibroblasts and production of ECM, such as epidermal growth factor (EGF), transforming growth factor-alpha and –beta (TGF-α, TGF-β) and platelet-derived growth factor (PDGF), have been implicated in DD [26,27]. Gene expression has also been investigated in various tissues or primary cells from DD patients using various experimental approaches and designs, and different gene expression platforms and methods of analysis [28]. Most have identified candidate genes, but many of the older gene expression studies did not have the sensitivity or depth of coverage [29]. Recent use of higher density arrays has confirmed and extended some gene expression profiles in DD patient tissues and identified additional candidate genes [28,30,31,32]. These include genes associated with tissue remodelling such as matrix metalloproteinases [28,29,31,33,34], those which have roles in the ECM, including fibronectin (*FBI*) laminins (*LAMB1*), integrins and thrombospondin (*THDS2*) [32] and others in which the link between the altered expression at both the transcriptional and translational levels like myoglobin and the tyrosine kinase orphan receptor 2 (*ROR2*) is less clear in terms of pathogenesis [30]. Some collagen genes show higher transcript levels in DD cord or nodal tissue [28,29,31,32,35] while other genes that have been implicated in DD include *ADAMT* (A disintergrin and metalloproteinase with thrombospondin motifs) genes [33,34,36], proteoglycans 4 (*PRG4*), A disintegrin and metalloproteinase domain 12 (*ADAM12*), fibulin-1 (*FBLN1*), and tenascin C (*TNC*) genes [36,37].

DD development and progression has been linked to genes associated with various signalling pathways (e.g., the sonic hedgehog pathway) [28] and others involved in the TGFβ signalling pathway (*TGFβ1, KLF6, SMADs*), known to be involved in proliferation, differentiation and fibrosis [32,38,39]. In contrast, known inhibitors of the TGFβ signalling pathway have been negatively associated with DD [40]. Genes in the AKT (*POSTN, RACK1, VCP*) and β-catenin and Wnt signalling pathways (*CTNNB1, WNT2, WNT4, RSPO2, SFRP1, SFRP4, ZIC1*) have also been implicated in DD [41,42]. *MAFB*, a tissue development and cellular differentiation transcription factor, was increased in 50% of DD tissue but not in controls [35]. While most of these expression studies have used biopsied primary tissue, some investigations have narrowed their focus to a specific fibrogenic cell type involved, namely fibroblasts [36,37].

Increased collagen expression has been found in DD patients [31,35,43] and recently collagenase has been used to treat DD [4,25,44] with initial studies showing that collagenase injections, though initially painful, are generally effective in reducing the effects of DD.

In previous studies, the use of tissue biopsies containing multiple cell types or short term culturing prior to processing raises the issue of heterogeneity in samples leading to increased noise and decreased assay sensitivity. In this study, we have use DD patient-derived cultured primary fibroblast cells to examine gene expression to identify new genes linked to the development of DD. The use of homogeneous populations of fibroblasts from DD patients provide an unique tissue source to identify genes linking to the development of DD as it removes the potential "noise" associated with the use of biopsies containing multiple cell types and effectively eliminates background and improves gene expression profiles. These data from genome-wide gene expression profiles were then compared to those from a complementary series of control primary fibroblast cells. Use of these control samples eliminated any DD genetic effect that may occur when adjacent tissue is used as a control. The novel use of exon arrays has identified new candidate genes associated with DD that provide further insights into this complex debilitating disorder.

Materials and Methods

Ethics statement

The study was approved by the Cabrini Human Research Ethics Committee (Approval #08-29-01-08) and confirmed by the Monash University Human Monash University Ethics Committee.

Primary cells

Primary fibroblasts were obtained from cord biopsies taken from five DD patients with extensive fibrosis of the palmar fascia during radical palmar fasciectomy. Of the five DD patients, four were male aged 37 to 75 years old and were stage 2 or 4, and one was female aged 54 and stage 1. Control primary fibroblast cells were derived from thigh skin punch biopsies from 6 individual females unaffected by DD [45]. Biopsies from the DD patients were minced finely, plated out into T25 Falcon flasks (BD Biosciences) containing 4–5 ml of DMEM/F12 medium (Invitrogen) with 5% serum and grown to confluence at 37°C in 4.5–5% CO_2. Fibroblasts from these cultures were harvested using standard procedures, washed in medium, and replated in 12 ml of medium at a concentration of 5×10^5 cells/ml in T75 Falcon flasks. Culture medium in each flask was changed once or twice weekly and cultures were grown to ~80% confluency before harvesting. For most patient samples, the cell cultures had undergone less than five passages since initiation, but had been grown to confluence in culture for several months. Most control cell samples had been grown in culture for less than ten passages. All patients gave written informed consent for their tissues to be used in this study.

RNA Isolation

Ten million fibroblasts from each DD and control cell line were pelleted, resuspended in 3 ml PBS with an equal volume of Trizol (Invitrogen, Carlsbad, CA, USA), mixed and incubated at room temperature for 15 minutes. Chloroform was then added and the mixture was centrifuged to separate the aqueous from the organic layer. The aqueous layer was mixed with an equal volume of 70 percent ethanol and loaded on to an RNeasy column (Qiagen, Venlo, The Netherlands). The RNA extraction was continued using the RNeasy method as per the manufacture's recommendation except that the procedure was started at the step where Buffer RW1 is added. RNA concentration and integrity was

determined using a bioanalyzer (Agilent, Santa Clara, CA, USA). RNA was determined to be high enough quality for exon array analysis if a minimum RIN of 8.5 was obtained.

Exon arrays

GeneChip Human Exon 1.0 ST Array analysis was performed on samples from 4 DD patients and 6 control patient (10 arrays) as per the GeneChip Whole Transcript (WT) Sense Target labelling assay instructions (Affymetrix, Santa Clara, CA, USA). The rRNA from 1 μg of total RNA was reduced using a RiboMinus Human/Mouse Transcriptome Isolation Kit (Invitrogen, Carlsbad, CA, USA). For this investigation we analysed the 'core set' that is defined by over 228,000 probe set regions (Affymetrix.com). Array quality was assessed using Expression Console (Affymetrix.com). For differential gene expression, all exon arrays were normalized with robust multi-array average (RMA) background correction and quantile normalization, and overall transcript expression was estimated using an exon RMA linear model [46]. Gene expression levels were determined using AS ANOVA or ANOVA algorithms provided in the Partek Genomics Suite statistical analysis package (Partek, St Louis, MO, USA). Array data and normalized expression values have been deposited in the gene expression omnibus database: accession number GSE41524.

Transcriptional validation

All primer sequences for candidate exons or genes (see Table S1) were designed using NCBI primer blast (ncbi.nih). cDNA was prepared from total RNA using Superscript III as per manufacturer's recommendation (Invitrogen, San Diego, USA). Normal PCR amplification for each sample was carried out using GoTaq Green Master Mix containing GoTaq DNA polymerase (Promega, Wisconsin, USA), 200 nM primers, 8 ng cDNA with a cycling protocol of 94°C: 3 min; ((94°C: 30 sec; 60°C: 30 sec; 72°C: 30 sec)×35); 72°C: 7 min. Products were run on a 2% agarose gel to determine amplification of the proper sized product. Real-time PCR was performed using these primers under the following conditions: Power SYBR Green Master Mix (Applied Biosystems, United Kingdom) was mixed with 5 to 10 ng of cDNA (per sample) and 2 pmol of each primer; the cycling steps used in the PCR were 95°C: 10 min; ((95°C: 15 sec; 60°C: 60 sec)×40); with a melting curve temperature ramp following.

Alpha smooth muscle actin staining

DD and control primary fibroblasts were plated on glass cover slips in 6 well plates. Attached cells were washed twice with PBS and fixed with cold methanol for 20 mins at 4°C and washed twice with PBS. Cells were incubated with Image-iT ™ FX Signal Enhancer (Invitrogen #I36933) for 1 hour at room temperature and then washed twice with PBS. Cell preparations were incubated overnight at 4°C with anti-αSMA antibody (abcam #ab5694) diluted with 5% BSA in PBS (1:100), washed twice with PBS and incubated for 1 hour at room temperature with Alexa Fluor 488 goat anti-rabbit (1:1000; Invitrogen #A11006) and Hoechst 33342 (1:2000) diluted in 5% BSA in PBS. Cells were washed twice with PBS and mounted with Fluorsave (Calbiochem #345789). Images were taken with a Nikon C1 inverted microscope.

Results

Genome-wide exon expression profiles

Whole genome Affymetrix exon arrays were used to determine gene expression profiles in DD patient primary fibroblasts. For these studies, the filtered 'core' set of probe selection regions (PSRs; RefSeq transcripts and full length mRNAs; Affymetrix.com), which include well-documented exon regions, were used for analysis.

Comparison of expression profiles from DD patient-derived primary fibroblast cells with those of the six control primary fibroblast cells from patients with no history of DD identified 307 genes with significantly higher, and 1288 genes with significantly lower, transcript levels (ANOVA p-values <0.05 after multiple test correction) and fold changes exceeding 2.0 in DD (Tables 1, 2: top 50 and Tables S1, S2: full list). Cluster analysis and heat maps for individual samples for the top genes (p-value <0.05 after multiple test correction and top 50 increased and decreased genes) showed a clear difference in Dupuytren's disease fibroblast gene expression when compared to normal fibroblasts (Figure 1). Many of these expression differences were associated with ECM genes (e.g., *COMP*, collagen) but other genes showing differences encoded for proteins that influence fibrosis (e.g., follistatin), tissue remodelling (e.g., collagenases and matrix metallopeptidase proteins) and signalling pathways (e.g., *STAT1*, *WNT2* and *WNT4*), growth factors (e.g., *FGF9*) and cell movement (e.g., *KIF* genes). Genes that showed differential expression and were located on the Y chromosome were eliminated from analysis. Furthermore, validated genes with differential expression were found to have no gender bias.

Metalloproteinase and Collagen Genes

The top gene identified in these gene expression studies was matrix metallopeptidase protein 1 (*MMP1*). This interstitial collagenase had a 56 fold reduction in expression levels in DD fibroblasts (Figure 2, Table 2). qRT-PCR using five DD and five control samples confirmed that *MMP1* expression was significantly lower in DD samples ($p<0.05$; Figure 3). Microarray gene expression analysis of other MMPs, (e.g. *MMP3*: Table 2, and

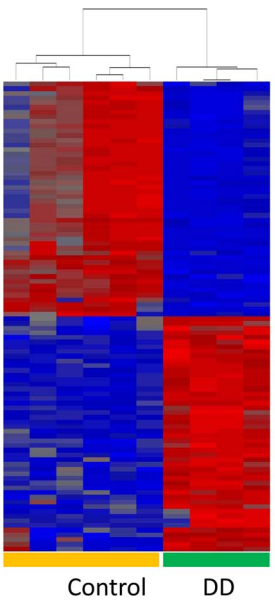

Figure 1. Dupuytren's disease (DD) samples show many genes that are differentially expressed compared to control samples. Cluster analysis and heat map of the top 50 genes showing highest or lowest gene expression in DD patient fibroblasts compared to controls. Genes are represented on individual rows while columns represent control or DD patient samples. Transcript levels that are relatively higher (red) or lower (blue) are color coded.
doi:10.1371/journal.pone.0059056.g001

Table 1. Top 50 genes that show higher gene expression in DD samples based on largest expression level difference from controls.

Gene Symbol	Gene ID (RefSeq)	p-value	Fold-Change(Control vs. DD)	Fold change direction
VCAM1	NM_001078	5.07E-11	−35.1342	CL down vs DD
COMP	NM_000095	8.61E-21	−34.3401	CL down vs DD
SFRP4	NM_003014	1.10E-02	−30.7416	CL down vs DD
CHI3L1	NM_001276	2.86E-16	−20.9531	CL down vs DD
DDIT4	NM_019058	7.80E-10	−17.4606	CL down vs DD
SCRG1	NM_007281	3.50E-19	−14.576	CL down vs DD
C10orf10	NM_007021	4.36E-04	−13.2329	CL down vs DD
FGF9	NM_002010	4.57E-03	−11.8243	CL down vs DD
FMOD	NM_002023	1.91E-03	−9.95692	CL down vs DD
KRT34	NM_021013	1.53E-06	−9.59421	CL down vs DD
CHAC1	NM_024111	7.00E-03	−9.54938	CL down vs DD
CADM1	NM_014333	2.71E-10	−9.35959	CL down vs DD
THBS4	NM_003248	1.40E-30	−8.74083	CL down vs DD
PTPRD	NM_002839	5.86E-29	−8.59582	CL down vs DD
CRLF1	NM_004750	1.98E-27	−8.46392	CL down vs DD
SPON1	NM_006108	4.48E-09	−7.64994	CL down vs DD
PAPPA2	NM_020318	1.11E-36	−7.16121	CL down vs DD
ANGPTL4	NM_139314	2.96E-11	−6.89301	CL down vs DD
PFKFB4	NM_004567	6.37E-23	−6.27251	CL down vs DD
DACT1	NM_016651	1.06E-15	−6.24109	CL down vs DD
C7orf68	NM_013332	9.42E-04	−5.78641	CL down vs DD
NRCAM	NM_001193582	6.68E-23	−5.72873	CL down vs DD
SLC2A5	NM_003039	1.97E-25	−5.64975	CL down vs DD
NDUFA4L2	NM_020142	2.48E-03	−5.64615	CL down vs DD
IL26	NM_018402	1.15E-04	−5.58784	CL down vs DD
CILP2	NM_153221	5.12E-24	−5.41481	CL down vs DD
ANKRD37	NM_181726	0.000196107	−5.39884	CL down vs DD
DAPK1	NM_004938	3.24E-09	−5.29651	CL down vs DD
CPA4	NM_016352	3.85E-02	−5.18093	CL down vs DD
RBP4	NM_006744	2.47E-04	−5.17563	CL down vs DD
LOXL3	NM_032603	2.70E-03	−5.08977	CL down vs DD
MOCOS	NM_017947	4.29E-08	−5.00414	CL down vs DD
ASPHD2	NM_020437	1.16E-06	−4.91587	CL down vs DD
UNC5B	NM_170744	1.68E-08	−4.90931	CL down vs DD
WNT2	NM_003391	1.39E-05	−4.82891	CL down vs DD
SPAG4	NM_003116	7.90E-23	−4.60329	CL down vs DD
RDH10	NM_172037	1.31E-02	−4.58245	CL down vs DD
TRIB3	NM_021158	3.67E-09	−4.46002	CL down vs DD
APLN	NM_017413	2.06E-08	−4.34215	CL down vs DD
MSC	NM_005098	5.40E-04	−4.33854	CL down vs DD
MTHFD2	NR_027405	2.00E-03	−4.3355	CL down vs DD
CPZ	NM_001014448	6.94E-11	−4.28206	CL down vs DD
COL15A1	NM_001855	1.18E-03	−4.26303	CL down vs DD
SLC7A5	NM_003486	2.08E-06	−4.25905	CL down vs DD
PDLIM3	NM_014476	4.79E-05	−4.22887	CL down vs DD
TFAP2B	NM_003221	3.30E-09	−4.17167	CL down vs DD
CXCL16	NM_022059	1.19E-07	−4.15755	CL down vs DD
PRG4	NM_005807	1.76E-10	−4.15362	CL down vs DD

Table 1. Cont.

Gene Symbol	Gene ID (RefSeq)	p-value	Fold-Change(Control vs. DD)	Fold change direction
SLC2A1	NM_006516	4.14E-09	−4.13188	CL down vs DD
CBS	NM_000071	1.10E-07	−4.1273	CL down vs DD

DD: Dupuytren's disease; CL: control.
doi:10.1371/journal.pone.0059056.t001

MMP16: Table S2) also showed lower expression levels in the DD group. Conversely, 24 collagen genes, including *COL15A1* (Figure 2 and 3, Table 1), *COL5A1*, *COL5A2*, *COL4A1*, *COL4A2*, *COL4A4* (Table S1), *COL1A1*, and *COL3A1* (Figure S1) showed significantly higher level of expression in the DD patient-derived fibroblasts. There was also an increase in expression of fibromodulin (*FMOD*) (Figure 4 and Table 1), a gene product that interacts with collagen fibrils and is involved in the formation of the ECM, the collagen chaperone, *SERPINH1* (Table S2), and *LOXL3*, a catalyst for crosslinks in collagen and elastin (Table 1). RT-PCR analysis showed that the *COL15A1* levels varied greatly between the individual DD patients (between 12.5 and 1450) and this was reflected in the large SEM (Figure 3). However, there was a clear difference between the two groups with the lowest DD *COL15A1* expression levels being 3.2 fold higher than the highest control patient expression levels and a p-value of 0.008 (Mann-Whitney U-test). This variation was not associated with differences in age, stage or gender of the DD patients. Other metalloproteinases, *ADAM15*, *ADAMST10*, *ADAMST2* and *ADAMTS3*, had increased transcription levels (approximately 2.3 to 2.5 fold) in DD fibroblasts (Figure S1). However, these genes are also involved in increasing cell adhesion and decreasing cell mobility (see "Cell adhesion, cell-to-cell, and cell-to-matrix interaction genes" below).

Follistatin and TGFβ Super Family Genes

Array analysis showed that follistatin (*FST*) mRNA levels were significantly lower in DD fibroblasts (Figure 5) compared to controls. These results were verified using qRT-PCR (Figure 3) which showed that DD fibroblasts had a relative follistatin gene expression that was ~10% of controls. The gene expression of *INHBA*, which codes for the β_A subunit component of activin and inhibin proteins, also showed lower levels in the DD fibroblasts compared to controls (Figures 3 and 5). However, qRT-PCR results indicated that the expression levels of *INHBB*, which codes for the β_B subunit of activin and inhibin proteins, varied greatly between individuals in both DD and control patient cells, so the difference between the groups was not significant (data not shown). *BMP4*, another member of the transforming growth factor family which codes for bone morphogenetic protein 4 had increased levels in DD (Figure S1).

Other ECM and tissue remodelling genes

Transcripts from other genes involved in ECM and tissue remodelling also had different gene expression levels in DD compared to control fibroblasts. For example, cartilage oligomeric matrix protein (*COMP*), spondin 1 ECM protein (*SPON1*), cartilage intermediate layer proteins (*CLIP* and *CLIP2*), sarcoglycan (*SGCG*), elastin (*ELN*) and ficolin collagen/fibrinogen domain containing lectin 2 (hucolin: *FCN2*), and tumour necrosis factor, alpha-induced protein 6 (*TNFAIP6*), all had significantly higher levels of gene transcripts in DD compared to control fibroblasts (Figure S1). Angiopoietin-like 4 (*ANGPTL4*), a glycosylated, secreted protein that has a fibrinogen C-terminal domain and has many functions including inhibition of proliferation, migration and tubule formation in endothelial cells had higher levels of gene transcripts in DD (Figure S1). In addition, several genes involved in the re-absorption or re-modelling of ECM were significantly lower in DD. For example, the level of gene expression for cathepsin K (*CTSK*), a lysosomal cysteine proteinase involved in bone remodelling and resorption and possibly involved in ECM re-absorption, was significantly lower in DD samples. Plasmin-mediated matrix remodelling protein, tissue factor pathway inhibitor 2 (*TFPI2*), and *TFPI* transcripts were expressed at significantly lower levels in DD (Figure S1). There are also examples of ECM gene transcripts that were significantly lower in DD compared to control fibroblasts including laminin alpha 4 (*LAMA4*), fibronectin type III domain containing 3A (*FNDC3A*), and fibronectin leucine rich transmembrane protein (*FLRT2*) (Figure S1).

Cell adhesion, cell-to-cell, and cell-to-matrix interaction genes

Genes coding for protein products that are involved in cell adhesion, cell-to-cell, and cell-to-matrix interactions had higher gene expression in DD fibroblasts than in controls (Figure 4, Table 1). These included vascular cell adhesion gene (*VCAM1*), which showed a 30-fold increase (Figure 4), cell adhesion molecule 1 (*CADM1*), chitinase 3 like 1 (*CHI3L1*), thrombospondin 4 (*THBS4*) (Figure 4), and neuronal cell adhesion molecule (NRCAM). In contrast, transcription levels of podocalyxin-like (*PODXL*) gene, a negative regulator of cell adhesion, was significantly lower in DD samples (Figure S1). Transcripts of several membrane glycoproteins involved in cell adhesion, integrin (ITG), alpha 11 gene (*ITGA11*), were significantly higher in DD (up 4.5 fold). However, the expression levels of some other integrin genes, for example, *ITGA2*, *ITGA6*, and *ITGA4*, were reduced 7.6–, 5.8- and 5.4-fold, respectively, in DD fibroblasts (Figure S1). Several metalloproteinases, *ADAM15*, *ADAMST10*, *ADAMST2* and *ADAMTS3* had increased transcription levels in DD fibroblasts (Figure S1).

Rho-associated genes

Rho-kinases are involved in cytoskeletal rearrangement and cell motility. Several Rho-associated genes showed lower levels of transcripts in DD compared to controls. These included Rho-associated, coiled-coil containing protein kinase 1 (*ROCK1*) which stabilises actin in cells, Rho GTPase activating protein 11A (*ARHGAP11A*), sema domain immunoglobulin domain (Ig) short basic domain, secreted (semaphorin) 3A (*SEMA3A:* found in human tumour cell lines) and DEP domain containing 1 (*DEPDC1*), a transcriptional corepressor (Figure S1).

Microtubule-based movement (KIFs) genes

Six genes in the kinesin family (*KIF11*, *KIF13A*, *KIF14*, *KIF18A*, *KIF20B*, and *KIF23*) that encode proteins involved in microtubule-based cellular movement showed significantly lower levels of

Table 2. Top 50 genes that show lower gene expression in DD samples based on largest expression level difference from controls.

Gene Symbol	Gene ID (RefSeq)	p-value	Fold-Change(Control vs. DD)	Fold change direction
MMP1	NM_002421	8.63E-14	56.6277	CL up vs DD
SEMA3A	NM_006080	1.63E-24	32.9807	CL up vs DD
KIT	NM_000222	0	19.8159	CL up vs DD
MMP3	NM_002422	2.75E-14	18.5218	CL up vs DD
PBK	NM_018492	1.02E-04	14.2813	CL up vs DD
TFPI	NM_006287	1.47E-18	14.109	CL up vs DD
SERPINB2	NM_001143818	1.32E-08	14.0724	CL up vs DD
TFPI2	NM_006528	9.40E-04	13.4744	CL up vs DD
KIF11	NM_004523	2.38E-05	13.0349	CL up vs DD
TOP2A	NM_001067	4.95E-36	12.6288	CL up vs DD
CTSK	NM_000396	1.26E-07	12.4257	CL up vs DD
TRPC4	NM_016179	6.46E-05	11.8229	CL up vs DD
IL13RA2	NM_000640	1.40E-04	11.7517	CL up vs DD
ANLN	NM_018685	2.06E-23	11.0621	CL up vs DD
DLGAP5	NM_001146015	3.47E-23	10.8337	CL up vs DD
LPHN2	NM_012302	2.54E-38	10.8311	CL up vs DD
CENPF	NM_016343	1.35E-22	9.51298	CL up vs DD
EEA1	NM_003566	3.44E-16	9.30826	CL up vs DD
KIF20B	NM_016195	9.28E-30	9.06	CL up vs DD
SMC2	NM_001042550	4.04E-18	8.26822	CL up vs DD
HMCN1	NM_031935	0.00E+00	8.08127	CL up vs DD
ROCK1	NM_005406	4.43E-20	8.07519	CL up vs DD
NCAPG	NM_022346	9.35E-26	7.93099	CL up vs DD
KIF23	NM_138555	3.38E-27	7.87122	CL up vs DD
GALNT5	NM_014568	4.63E-02	7.74798	CL up vs DD
MKI67	NM_002417	7.71E-16	7.68071	CL up vs DD
CASC5	NM_170589	0.00E+00	7.52791	CL up vs DD
CKAP2	NM_018204	1.64E-30	7.5254	CL up vs DD
ASPM	NM_018136	0.00E+00	7.37628	CL up vs DD
KIF18A	NM_031217	9.13E-06	7.28334	CL up vs DD
SCIN	NM_001112706	2.34E-11	7.28039	CL up vs DD
MELK	NM_014791	2.78E-22	7.11972	CL up vs DD
VPS13C	NM_020821	0.00E+00	7.1057	CL up vs DD
TTK	NM_003318	2.62E-16	7.00696	CL up vs DD
CENPK	NM_022145	1.49E-08	6.94789	CL up vs DD
HELLS	NM_018063	2.60E-27	6.94526	CL up vs DD
SHCBP1	NM_024745	2.66E-21	6.74075	CL up vs DD
CEP55	NM_018131	5.33E-15	6.70633	CL up vs DD
KITLG	NM_000899	3.62E-03	6.60831	CL up vs DD
RECQL	NM_002907	1.09E-21	6.56328	CL up vs DD
PODXL	NM_001018111	1.32E-20	6.47796	CL up vs DD
HMMR	NM_001142556	9.34E-16	6.46258	CL up vs DD
CD109	NM_133493	2.08E-02	6.42551	CL up vs DD
ECT2	NM_018098	2.02E-16	6.42206	CL up vs DD
NUF2	NM_145697	3.60E-21	6.40957	CL up vs DD
KIF5B	NM_004521	2.43E-27	6.31599	CL up vs DD
ITGA2	NM_002203	1.59E-16	6.27779	CL up vs DD
GAS2L3	NM_174942	1.09E-09	6.27478	CL up vs DD
GGH	NM_003878	5.16E-04	6.25643	CL up vs DD

Table 2. Cont.

Gene Symbol	Gene ID (RefSeq)	p-value	Fold-Change(Control vs. DD)	Fold change direction
DST	NM_015548	0.00E+00	6.25435	CL up vs DD
FAM111B	NM_198947	3.78E-06	6.22711	CL up vs DD

DD: Dupuytren's disease; CL: control.
doi:10.1371/journal.pone.0059056.t002

expression in the DD patient fibroblasts (Figure S1). Reduced expression of several KIF genes detailed in the microarray profiles (Figure 2) have also been confirmed using qRT-PCR (Figure 3).

Fibroblast growth factor genes

Higher expression levels (12-fold) of the fibroblast growth factor 9 gene (*FGF9*; glia-activating factor) (Figure 4), which is involved in growth stimulation and tissue repair, was observed in DD samples compared with controls and confirmed by qRT-PCR (Figure 3). *FGF11* gene expression was also increased significantly in DD fibroblasts (Figure S1).

KRT34 and other KRT genes

Expression levels of KRT34, a keratin gene for which the protein product is a major structural component of hair and nails, were significantly higher in DD patient samples compared to controls (Figure 4) and these increased expression levels were confirmed using qRT-PCR (Figure 3). Other keratin family genes that also showed significantly higher expression levels in DD patient fibroblasts included *KRT7*, *KRT16*, *KRT18*, *KRT19*, *KRT33A*, *KRT33B*, and *KRT81* (Table 1, Table S2, Figure S1).

Wnt signalling genes

WNT2 had a higher level of gene expression in DD fibroblasts than in controls (Figure 5). Secreted frizzled-related protein 4 (*SFRP4*), a potential modulator (inhibitor) of Wnt signalling, was another gene that showed a significantly higher level of gene transcripts in DD, but a related gene in this pathway (*SFRP1*) showed decreased expression in DD patients. There was also a significant reduction in transcripts of the ribonucleotide reductase M2 (*RRM2*) and *RSP03* genes in DD patient fibroblasts compared with controls (Figure S1). *RSPO3* is a member of the thrombospondin type 1 repeat supergene family and an activator of the β-catenin signalling cascade and *RRM2* is an inhibitor of the Wnt pathway. DNA-damage-inducible transcript 4 (*DDIT4*), an inhibitor of cell growth, also shows an increase in expression in DD fibroblasts.

Cell cycle genes

A large number of cell cycle genes had significantly reduced levels of transcripts in DD fibroblasts (Table S1). These included genes associated with mitosis, such as cyclin-dependent kinase 1 (*CDK1* or *CDC2*), *DLGAP5* (M phase), *CENPK*, *CENPF* (G2 phase), *MK167*, *NCAPG*, *CEP55*, *ASPM*, *SMC2*, *TPX2*, *CCDC99*, *RRM2* (DNA replication), *NUF2*, *NDC80* (mitotic sister chromatid segregation), *GAS2L3* (cell cycle arrest), *TOPO2A*, epithelial cell transforming sequence 2 oncogene (*ECT2*; G2 and M phase), and TTK protein kinase (TTK) and cancer susceptibility candidate 5 (*CASC5*), both essential for spindle-assembly checkpoint signalling and for correct chromosome alignment. However, one cell cycle gene, *CCND2* (G1/S transition), was expressed at significantly higher levels in DD than in control fibroblasts (Figure S1).

Innate immune response genes

Several genes involved in the innate immune response had lower levels of transcripts in DD fibroblasts. The transcription factor, STAT1, had a lower number of transcripts in the DD patient samples and this was confirmed by qRT-PCR (Figures 3 and 5).

Alternative splicing

Exon arrays identified transcript variants and provided a comparison of the expression of these variants between control and DD fibroblasts. Genes likely to have alternative transcripts include *THBS4*, *KRT34*, *TIRAP*, *KIF23* and *KIF14* and others (Figures 2, 4, 5 and S1). Some exons in these variants showed very little difference in expression between the samples which was especially common at the beginning of the transcript. For example, in the first region (located in exon 1) of the *THBS4* gene, there was little difference between control and DD fibroblasts, whereas the remaining exons in the gene showed a very distinct and large expression difference (Figure 4). In DD patients the *THBS4* transcript that was increased would code for a protein missing approximately the first 92 amino acids (aa) from the N-terminus. In the *KRT34* gene, the first PSR remained unchanged (within exon 1) and there was an increase in the other PSRs in DD (Figure 4). This increased *KRT34* transcript codes for a protein missing approximately the first 43 aa of the N-terminal. The *TIRAP* transcript in DD patients increased after the first two PSRs which were located in the first two exons (Figure 5). However, only the 5′ untranslated region (5′UTR) of the gene was involved, so the resulting protein was predicted to be unchanged. The expression profiles for both *KIF14* and *KIF23* indicated that the regions of the first three and one PSR, respectively (exon 1 in both genes), were unchanged but all the following PSRs were decreased in DD (Figure 2). Similar examples for other genes are shown in Figure S1.

Alpha smooth muscle actin analysis

Both control and DD fibroblasts were positive for anti-αSMA staining and there was no noticeable difference in the intensity between the samples (Figure S2). *ACTA2* gene expression was the same for both cell type and *ACTA1* gene expression was only slightly higher in the DD patient cells than in the controls.

Discussion

This study examined gene transcription at the exon level on a genome wide scale in DD patient fibroblasts. Each exon array provided extensive whole genome transcript coverage and allowed robust data acquisition for gene expression analysis superior to gene expression platforms used in earlier publications [29,32,35,37,47]. Of the more than 15,000 genes tested, 302 had significantly higher transcript levels (>2 fold) in DD and 1276 had lower transcript levels (>−2 fold) in DD when compared with controls.

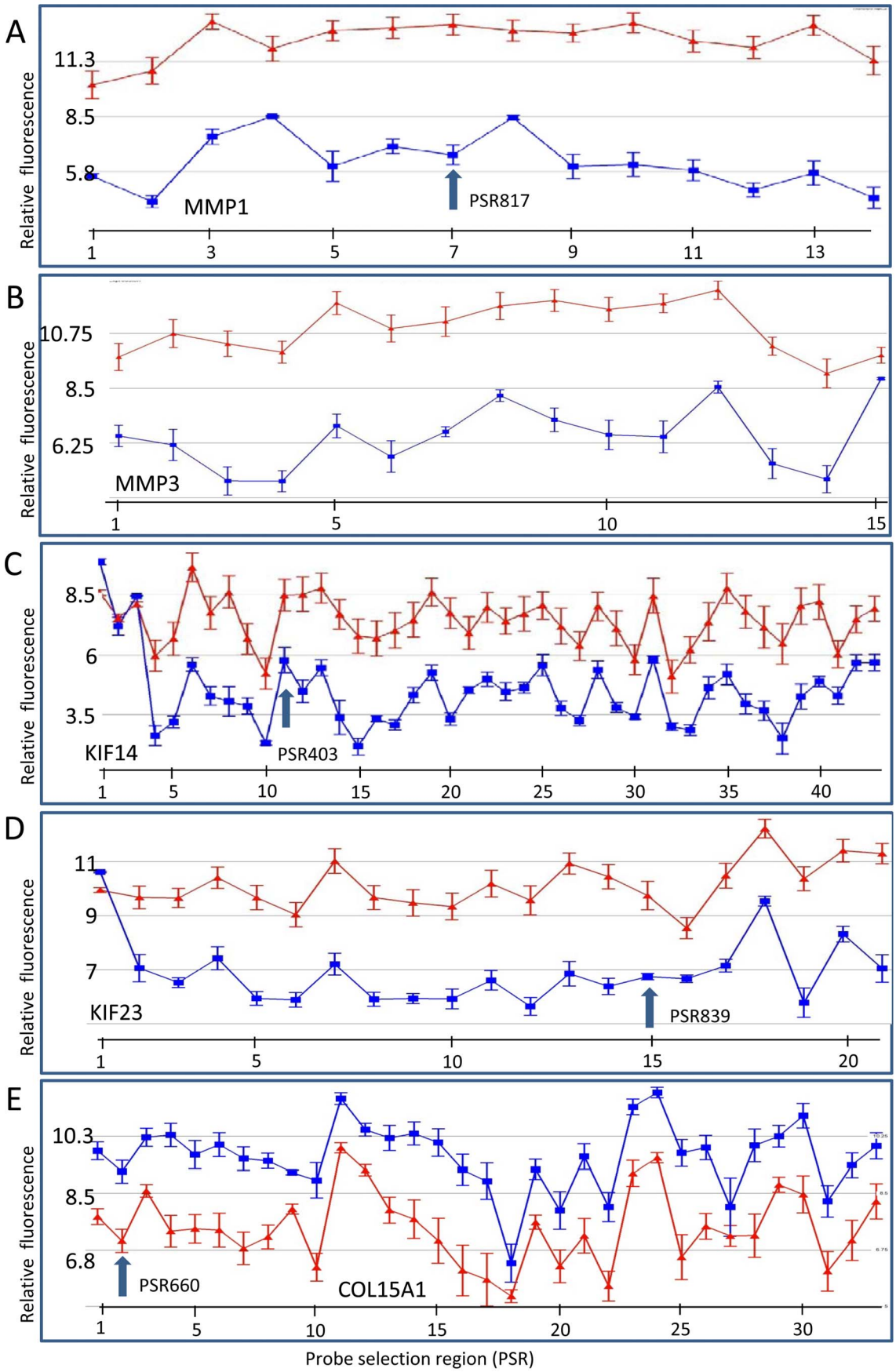
A
11.3
8.5
5.8
Relative fluorescence
MMP1
PSR817
1
3
5
7
9
11
13
B
10.75
8.5
6.25
Relative fluorescence
MMP3
1
5
10
15
C
8.5
6
3.5
Relative fluorescence
KIF14
PSR403
1
5
10
15
20
25
30
35
40
D
11
9
7
Relative fluorescence
KIF23
PSR839
1
5
10
15
20
E
10.3
8.5
6.8
Relative fluorescence
PSR660
COL15A1
1
5
10
15
20
25
30
Probe selection region (PSR)

Figure 2. The gene expression for several genes associated with collagen metabolism are modulated differently in DD patient fibroblasts compared to control fibroblasts. (A) *MMP1*, (B) *MMP3*, (C) *KIF14*, (D) *KIF23* and (E) *COL15A1*. Relative PSR fluorescence (y-axis) is plotted for each PSR (points along x-axis). Samples were either from DD fibroblast (blue) or skin fibroblasts from patients without DD (red). PSRs are oriented 5′ to 3′ across the gene from left to right on the x-axis. Relative expression levels are plotted on a $\log_2$ scale. Arrow represents a PSR region that was used for subsequent PCR validation. Four separate samples from different individuals were used for the DD cohort and six different individuals' samples for control fibroblasts. Error bars = SEM. Analysis was performed as described in the Materials and Methods section. Actual PSR numbers are shown in Figure S1.
doi:10.1371/journal.pone.0059056.g002

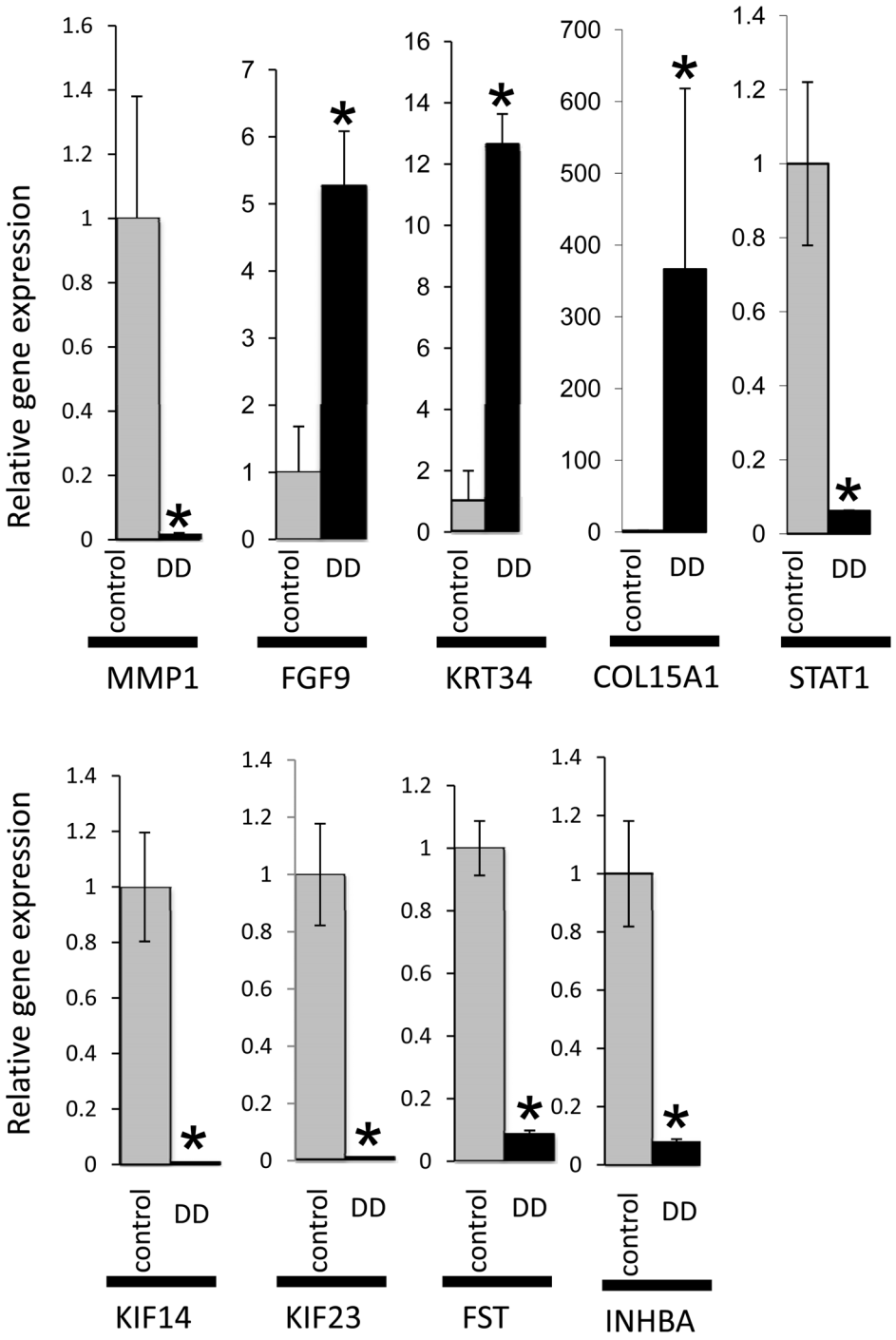

Figure 3. qRT-PCR validation of gene expression in fibroblasts from DD and control cells. The relative fold change in *MMP1*, *FGF9*, *KRT34*, *COL15A1*, *STAT1*, *KIF14*, *KIF23*, *FST* and *INHBA* gene expression in DD fibroblasts compared to control fibroblasts. The p-values using an unpaired t-test are: 0.019, 0.001, 0.03, 0.012, 0.03, 0.02, 0.00003, and 0.0058 for *MMP1*, *FGF9*, *KRT34*, STAT1, *KIF14*, *KIF23*, *FST* and *INHBA* respectively (n = 5 for both control and DD, except for *STAT1* where n = 3 for DD). The p-value using Mann-Whitney U test is 0.008 for *COL15A1*. Error bars represent the SEM.
doi:10.1371/journal.pone.0059056.g003

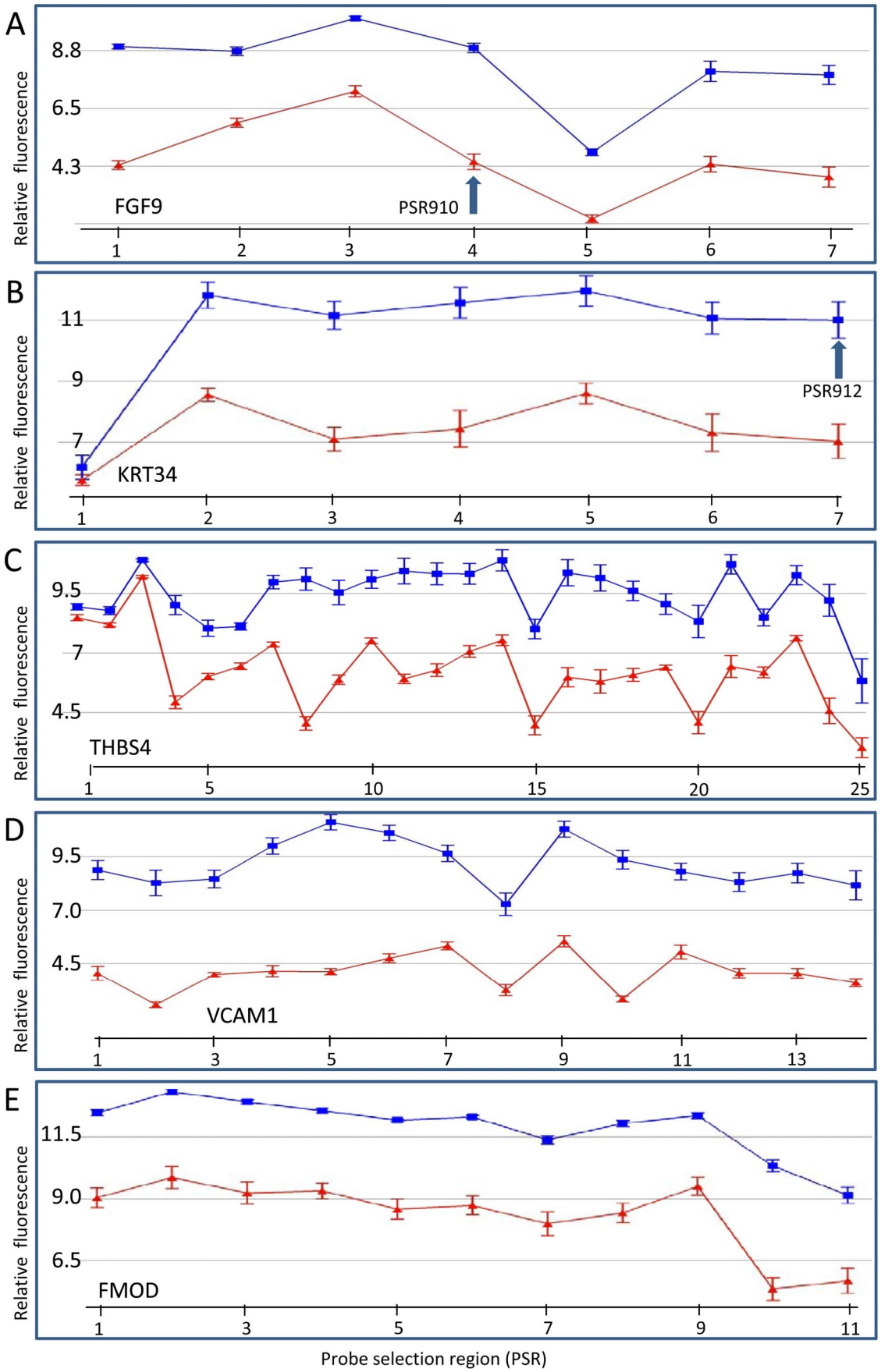
A
8.8
6.5
4.3
Relative fluorescence
FGF9
PSR910
1
2
3
4
5
6
7
B
11
9
7
Relative fluorescence
KRT34
PSR912
1
2
3
4
5
6
7
C
9.5
7
4.5
Relative fluorescence
THBS4
1
5
10
15
20
25
D
9.5
7.0
4.5
Relative fluorescence
VCAM1
1
3
5
7
9
11
13
E
11.5
9.0
6.5
Relative fluorescence
FMOD
1
3
5
7
9
11
Probe selection region (PSR)

Figure 4. The gene expression of several genes that are modulated differently in DD patient fibroblasts compared to control fibroblasts. (A) *FGF9,* (B) *KRT34,* (C) *THBS4,* (D) *VCAM1* and (E) *FMOD.* Relative PSR fluorescence (y-axis) is plotted for each PSR (points along x-axis). Samples were either from DD fibroblast (blue) or skin fibroblasts from patients without DD (red). PSRs are oriented 5′ to 3′ across the gene from left to right on the x-axis. Relative expression levels are plotted on a $\log_2$ scale. Arrow represents a PSR region that was used for subsequent PCR validation. Four separate samples from different individuals were used for the DD cohort and six different individuals' samples for control fibroblasts. Error bars = SEM. Actual PSR numbers are shown in Figure S1.
doi:10.1371/journal.pone.0059056.g004

Most of the previous studies have compared expression levels in tissue biopsies between diseased regions and unaffected regions from the same patients [28,29,31,32,33,35,36,47] and a few of these studies also included comparisons with tissue samples from carpal tunnel release patients [28,31,35], another soft tissue hand disease associated with diabetes [48]. Few previous studies have compared expression levels in primary fibroblasts derived from the affected and unaffected regions of DD patients [49] or from the two patient types [37,43]. One compared the tissue between DD patients and hand trauma patients [30]. Variation in the expression levels found can be accounted for by the differences in the cells contained in the tissue samples that were compared. In the tissue biopsies, the cell population consists of other cell types as well as fibroblasts. In addition, fibroblasts present in the DD tissue samples are in the diseased environment and expression levels may be influenced by the extensive cellular matrix and cell density. Differences in gene expression levels of primary fibroblast cells from diseased and non-diseased areas have been shown to decrease after 4 to 6 passages [50]. These different comparisons provide information about different aspects of the disease. The primary fibroblast cells used as controls in our study were derived from skin punch biopsies taken from the thigh and may elicit some fibroblast specific expression differences due to cell derivation from skin of a different region [51], but these cells are derived from cancer patients with no history of Dupuytren's disease or other soft tissue diseases and had no major scarring after radiation therapy. Variation between our findings and others may reflect genetic susceptibility to DD in addition to the disease state.

The major collagen found in the palmar fascia tissue is type I but in Dupuytren's nodules it has been reported that there is an increase in collagen and in particular, a higher proportion of type III compared to type I [52]. However, Murrell et al., 1991 found that the fibroblast cells (passage 3) from DD tissue and carpal tunnel control tissue did not show any noticeable difference in their collagen production and suggested that the increase in collagen type III to type I ratio found in the tissue samples was due to inhibition of collagen type I production in the fibroblasts growing in higher density as found in the DD tissue [53]. They demonstrated that an increase in fibroblast density resulted in an increase in the ratio of collagen type III to type I due to a decrease in collagen type I production. The fibroblasts used in the present study were grown to approximately the same density to avoid issues in expression differences associated with cell density.

Compelling evidence shows that the collagen-associated transcripts are a key component of progression of DD [28,31,32,35,43,47]. Satish et al (2008) [37] found *COL15A1* transcripts were lower in DD samples which is the opposite to our results. However, Satish et al (2008) were comparing DD and carpal tunnel syndrome derived fibroblasts and the differences between our studies may be due to the differences in our controls. Some past studies have also shown a higher level of expression of various collagen genes in DD [28,31,32,35,43,47]. Our analysis indicates a number of other collagens that showed higher levels in DD samples compared to controls. However, it is possible that some of the highly expressed collagen transcripts (e.g. *COL15A1*) are binding to the similar PSR sets for other collagen genes which would then also manifest as increased in DD patients.

Modulated expression levels in matrix metalloproteinase (MMP) genes is a common finding in previous studies although results vary depending on the experimental design [29,31,33,36,49]. Various MMP genes have been shown to have a higher expression level in DD and a few others have been shown to have lower expression. For example, *MMP2* has previously been shown to have a higher expression in DD [28,29]. We found a decrease in the expression level of *MMP16* in DD. MMP16 protein activates MMP2 protein which in turn degrades type III collagen. We also found a substantial decrease in *MMP1* gene expression in DD compared to the gene expression of control fibroblasts obtained from patients with no signs of DD. However, Johnston et. al. (2007) [33] found a higher expression level of *MMP1* in DD compared to carpal tunnel syndrome tissue samples. MMP1 protein functions as an interstitial collagenase to break down interstitial collagen types I, II and III. The expression levels of the *MMP3* (stromelysin) gene, which codes for a protein that is able to activate the MMP1 protein [54] was also down in DD cells. Rehmen et al (2008) [31] who compared DD and carpal fascia tissue (from patients with carpal tunnel syndrome), also found a decrease in expression level of MMP3 in DD. We speculate that a low level of activated MMP1 proteins in DD may cause an accumulation of type I, II, and III collagens in the ECM due to an inability to break them down. In addition, low levels of MMP16 protein may decrease the activation of MMP2 and increase the build-up of collagen type III.

These findings provide compelling evidence that the development and progression of DD is closely associated with significant up-regulation of a broad group of collagen genes and down-regulation of matrix metalloproteinase and other collagenase genes which are required in remodelling the ECM. They also extend the understanding of the likely genetic origins of DD and provided the experimental rationale for the recent use of injectible collagenase from *Clostridium histolyticum* in the non-surgical treatment of DD which has been found to be effective in controlling DD despite the associated pain tolerated by patients [44]. A twelve month follow-up study of this treatment indicated that some patients had debilitating pain and deep tissue scarring and adhesion [55]. Longer term studies are now required with this treatment to examine its effectiveness in preventing recurrence of DD and also to assess any negative consequences or non-specific effects of the treatment. More specific collagenases such as active MMP1 and MMP2 proteins may be better candidates for therapeutic treatment.

Other ECM components may also be involved in DD. Our findings show that transcripts of cathepsin K (*CTSK*), a lysosomal cysteine proteinase involved in bone and possibly ECM remodelling and resorption, are also lower in DD samples. Other matrix remodelling genes such as plasmin-mediated matrix remodelling protein, tissue factor pathway inhibitor 2 (*TFPI2*) and *TFPI* transcripts were also expressed at significantly lower levels in DD samples. BMP4, which has increased transcription levels in DD fibroblasts, induces cartilage and bone formation but also has been shown to regulate tissue remodelling and fibrosis [56]. The proteoglycan gene *PRG4* was found to have higher expression

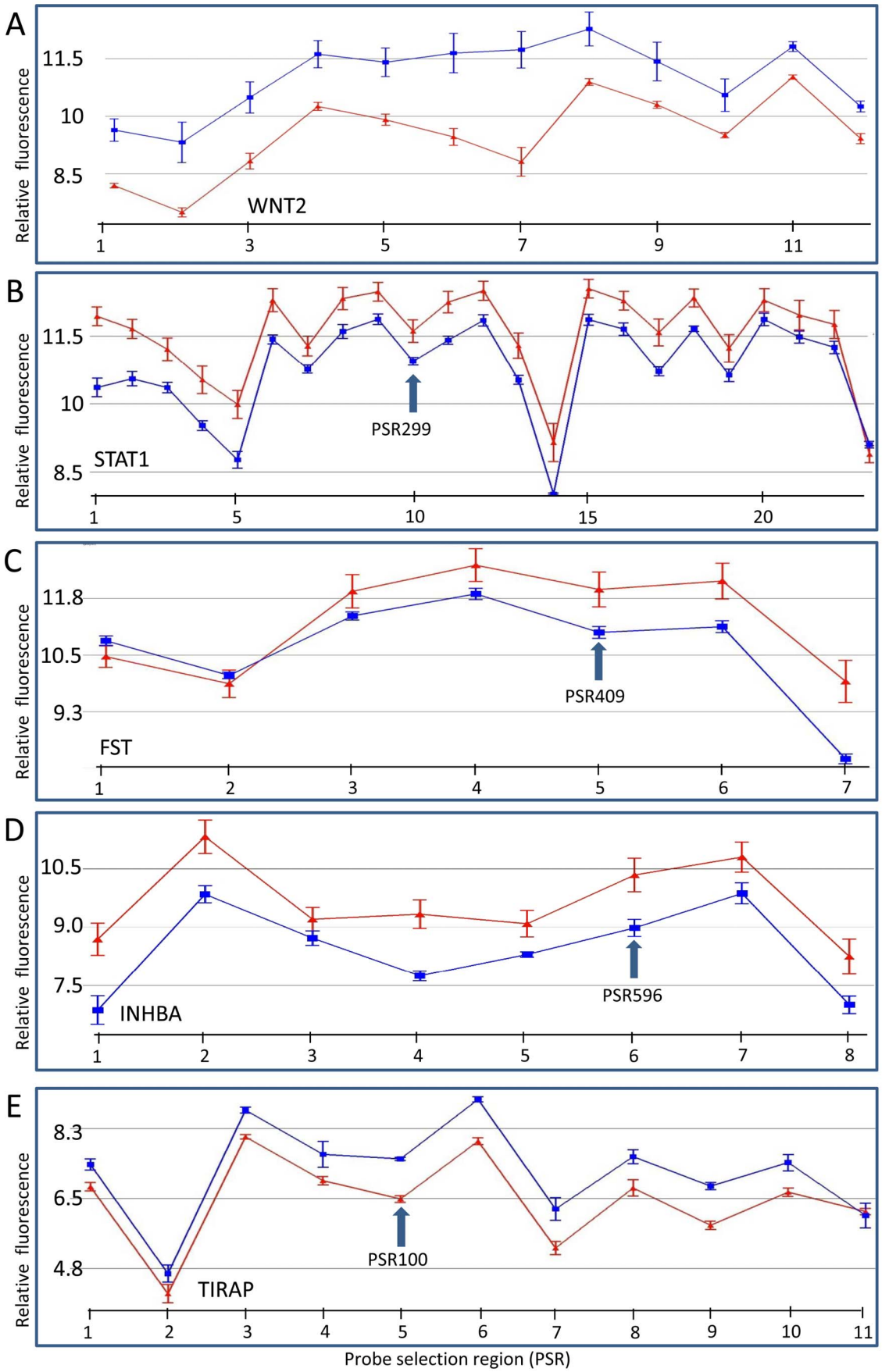
A
Relative fluorescence
11.5
10
8.5
WNT2
1
3
5
7
9
11
B
Relative fluorescence
11.5
10
8.5
PSR299
STAT1
1
5
10
15
20
C
Relative fluorescence
11.8
10.5
9.3
PSR409
FST
1
2
3
4
5
6
7
D
Relative fluorescence
10.5
9.0
7.5
PSR596
INHBA
1
2
3
4
5
6
7
8
E
Relative fluorescence
8.3
6.5
4.8
PSR100
TIRAP
1
2
3
4
5
6
7
8
9
10
11
Probe selection region (PSR)

Figure 5. The gene expression of genes that are modulated differently in DD patient fibroblasts compared to control fibroblasts including those involved in the inflammatory response and tissue remodelling. (A) *WNT2,* (B) *STAT1,* (C) *FST,* (D) *INHBA* and (E) *TIRAP*. Relative PSR fluorescence (y-axis) is plotted for each PSR (points along x-axis). Samples were either from DD fibroblast (blue) or skin fibroblasts from patients without DD (red). PSRs are oriented 5′ to 3′ across the gene from left to right on the x-axis. Relative expression levels are plotted on a $\log_2$ scale. Arrow represents a PSR region that was used for subsequent PCR validation. Four separate samples from different individuals were used for the DD cohort and six different individuals' samples for control fibroblasts. Error bars = SEM. Actual PSR numbers are shown in Figure S1.
doi:10.1371/journal.pone.0059056.g005

levels in DD compared to controls which is consistent with other studies that have investigated fibroblasts from DD patients [36,37]. This proteoglycan prevents protein deposition on to cartilage but its function in DD remains unclear.

Not all gene transcripts associated with the ECM showed higher levels in DD. For example, two fibronectin genes, fibronectin type III domain containing 3A (*FNDC3A*), and fibronectin leucine rich transmembrane protein (*FLRT2)* showed lower levels in DD fibroblasts. There was also a down-regulation of transcripts from laminin 4 alpha gene (*LAMA4*). Laminin 4 alpha is part of laminin 411 which is found in endothelial basal laminae and is believed to up-regulate insulin gene expression [57]. This gene may reflect the high incidence of diabetes in DD patients [58]. Another gene that has been associated with type II diabetes and shows higher gene transcript levels in DD, is angiopoietin-like 4 (*ANGPTL4*), a glycosylated, secreted protein with a fibrinogen C-terminal domain involved in glucose homeostasis, lipid metabolism and insulin sensitivity [59]. It inhibits proliferation, migration and tubule formation in endothelial cells and is induced and accumulates in the ECM in response to hypoxia.

Our data indicate an increase in cell-to-cell interaction and dysfunction in the regulation of cytoskeletal structure. Many transcripts from genes involved in cell adhesion are found at a higher level in DD. For example, the vascular cell adhesion protein, (*VCAM1*) cell adhesion molecule 1 (*CADM1*), chitinase 3 like 1 (*CHI3L1*), neuronal cell adhesion molecule (*NRCAM*), and thrombospondin 4 (*THBS4*). As vascular cell adhesion gene (*VCAM1*) has an important function in cell-cell recognition and thrombospondin 4 is an adhesive glycoprotein that can bind fibrogen, fibronectin, laminin and type V collagen, an increase in these proteins would increase the amount of adhesion between the cells as well as with the ECM. There are also lower transcription levels in DD of the podocalyxin-like gene (*PODXL*), a negative regulator of the cell adhesion. These finding suggest that genes promoting cell adhesion are increased in the development and progression of DD.

ADAMs proteins are active metalloproteinases with gelatinolytic and collagenolytic activity. They inhibit beta-1 integrin mediated cell adhesion and migration. The ADAMs suppress cell mobility, cleave E-cadherin in response to growth factor depletion and may be active in cartilage remodelling. We found gene transcripts of these proteins, which increase cell adhesion and decrease cell mobility, are increased in DD as in previous studies [34]. Integrins are also involved in cell adhesion and participate in cell-surface mediated signalling [60]. The integrins (ITG) gene transcripts were found to be both higher and lower in DD. For example, *ITGA11* transcripts were found at higher levels in DD whereas *ITGA2*, *ITGA6*, and *ITGA4* gene transcripts were lower in DD. Integrin alpha 11 cell surface adhesion receptor is involved in cell adhesion to the ECM and to other cells. The levels of this gene are increased in DD possibly increasing adhesion of cells and ECM in DD. Integrin alpha-2/beta-1 is a receptor for laminin, collagen, fibronectin and E-cadherin and is responsible for adhesion of cells to collagen, modulation of collagen and collagen gene expression, and organization of newly synthesized ECM. The levels of *ITGA2* transcript, which encodes for integrin alpha 2, are down in DD which may cause a disorganisation of collagen.

Many of the gene transcripts that are lower in DD are involved in cytoskeletal structures (cytoskeleton associated protein 2 (*CKAP2*)), microtubule-based movement (KIF family), spindle formation (e.g., TPX2), centromere proteins such as kinetochores (*NUF2*, *CENPF*), and chromosome condensing (*NCAPG*). Lower levels of transcripts in these genes may reflect differences in proliferation between the two sample groups, however, there is also a lower level of Rho-associated genes that are involved in cytoskeletal rearrangement and cell motility. This includes SEMA3A, a protein possibly involved in cytoskeletal organisation, and indicates a possible association between DD and cytoskeletal structure.

We were interested to determine if follistatin and activin were involved in DD disease. Follistatin has been shown to antagonise fibrosis by complexing with activin [61] and to modulate the proinflammatory and profibrotic actions of activin during wound healing, tumourigenesis [62,63] and in rats treated with bleomycin, an agent that causes DNA double-strand breaks [64]. When we analysed the differences in follistatin and activin subunit gene expression, we observed that levels of follistatin were much lower in the DD samples, which is consistent with the proposed anti-fibrotic actions of follistatin [61]. Our study found unexpectedly that the levels of *INHBA*, which codes for the βA subunit of activin and is known to be involved with fibrosis, were also down-regulated. In contrast, expression levels of *INHBB*, which encodes for the activin βB subunit, were elevated in DD fibroblasts when compare with controls. However, the levels of *INHBB* transcript varied greatly between individuals, for both DD and control patients. Further, there is little data on the role of activin B in the modulation of fibrosis as assays for this protein have only become available recently [65]. *In vitro* studies are required now to further explore the relationship between follistatin, activins and collagen synthesis in DD fibroblasts because of the potential for follistatin to be used as a novel treatment for DD.

Two fibroblast growth factor genes (*FGF9 and FGF11)* were significantly up-regulated in DD fibroblasts. The FGF family of genes encode for mitogens and proteins involved in cell survival and various cell processes. Up-regulation of these growth factors in DD fibroblasts links with the increase in fibroblast proliferation and fibromatosis in DD. The proteins encoded by these genes are members of the fibroblast growth factor (FGF) family and are implicated in the stimulation of cell growth and tissue repair. The protein encoded by *FGF9* was isolated as a secreted factor that stimulates growth in cultured glial cell but the exact functions of both *FGF9* and *FGF11* on fibroblasts, and particularly those from DD patients, have yet to be determined (http://www.ncbi.nlm.nih.gov/gene/2256). Platelet-derived growth factors have been recently implicated in DD [66,67] and have a specific effect on angiogenesis. However none of the three PDGF genes (*PDGFB, PDGFC, PDGFD*) examined in this study were up-regulated in DD fibroblasts suggesting that enhanced angiogenesis is not a critical factor in the establishment of DD.

Other genes up-regulated in DD are also involved in inflammatory diseases. For example, tumour necrosis factor,

alpha-induced protein 6 (*TNFAIP6*), which is found in the synovial fluid of patients with osteoarthritis and rheumatoid arthritis was up-regulated in DD. Vascular cell adhesion gene (*VCAM1*), which may play a role in atherosclerosis and rheumatoid arthritis, showed a 30-fold increase in expression in DD. VCAM1 also has an important function in cell-cell recognition. However another gene that codes for a protein involved in the innate immune response, STAT1, had a lower expression level in DD patients which may reflect the lack of inflammation observed in DD.

There is also up-regulation of a suite of keratin genes, particularly *KRT34*, in DD fibroblasts. Keratin is a protein usually involved in the formation stratified squamous epithelium and hair and is particularly associated with keratinocytes in the skin. Currently the nature of this relationship between up-regulated expression of *KRT* genes in DD fibroblast and DD is unclear.

Application of an alternative splicing algorithm to our exon array data revealed a number of gene isoforms that appear to have different levels between DD and control fibroblasts. These included *THBS4*, *KRT34*, *TIRAP*, *KIF14* and *KIF23*. There is approximately a 12 fold increase in the *THBS4* gene transcript in DD patients but only for part of the gene. The data suggests an increase in a transcript that codes for a protein that is missing approximately the first 92 aa of the N-terminus. As the N-terminus of this protein binds to heparin (possible binding site between aa 102 and 105) [68]; this protein may have an altered heparin binding capability but would probably still be involved in cell-matrix interactions. As there is an increase in KRT34 gene in all but the first PSR (first exon) in DD, the increased *KRT34* transcript codes for a protein missing approximately the first 43 aa of the N-terminus. The *TIRAP* transcript increased in DD patients is missing the 5′UTR of the gene. Although the resulting protein would be unchanged, the stability of the transcript may be altered. The expression profiles of both *KIF14* and *KIF23* indicate that the regions corresponding to exon 1 in both genes are unchanged, but all the following PSRs are decreased in DD fibroblasts. Transcripts in these unchanged regions may be protected from RNA degradation that is occurring in DD or premature termination of transcription is occurring at this point. A similar profile of decreased transcript expression with protection of the first exon was found 4 hours following 10 Gy ionizing radiation of fibroblasts in both *KIF14* and *KIF23* [69]. Recently published papers examining the response of fibroblasts to ionizing radiation found that a common general response mechanism to that stress is the use of alternative start sites [69,70]. The disease state in DD could reflect a defect in a stress response leading to alternative isoforms that have substantial effects on the normal production of the ECM. Alternatively, lower oxygen levels may be present in the zone of the affected region of the hand, which may induce alternative transcripts.

Recently, a large study that looked at SNPs in 1365 DD patient bloods identified a number of WNT gene SNPs as being associated with DD patients [41]. One of the SNPs was in *SFRP4*, a frizzle-related gene which was at the top of our list for genes that are more highly expressed in DD compared to normal samples. However, this SNP was more closely associated with the gene *EPDR1*, a gene involved in cell adhesion, which we found had an increased expression in DD. These results provide intriguing clues to the cause of DD disease.

An advantage of our study was the use of control samples from donors with no DD genetic background. This avoided the potential complication of associated genetics in control samples from DD-affected tissue donor which have been used as controls in some previous investigations. We also had the advantage that highly sensitive exon arrays were used to obtain quality results. In this study we have not only identified transcripts which are precursors to known fibrotic components, but also have identified a large number of potential DD treatment candidates, some of which have also been identified in other genomic studies. Some of our findings, however, also contrast with and contradict those of other studies and require further examination to discovery how they relate to the onset and progression of DD.

In conclusion, we have comprehensively characterized the transcription profile differences between DD and normal primary fibroblasts. Our data indicate that in DD there is an excess of collagen and other ECM that is not controlled due to a reduction in matrix metalloproteinases and other matrix remodelling proteins. A reduction in the fibrotic control protein, follistatin, may also contribute to DD. In addition, the fibroblasts lack expression of genes involved in cell movement and cytoskeletal organisation and an increase in genes involved in cell adhesion. These indicate a lack of organisation of both extra- and intra-cellular matrix as well as a lack of cellular movement in DD. Alternative transcripts have also been identified which are expressed at different levels in the DD patients compared to the controls and may reflect cell stress such as hypoxia. These conclusions will be the basis for future experimentation. Many of the identified genes are potential candidates for the treatment of DD. There was a close correlation between expression levels in some genes from our study and data from previous studies using DD tissue samples providing reason to pursue investigations into potential therapeutic development strategies using *in vitro* studies on DD fibroblasts. It is likely some of these candidate genes for treating DD will also be effective for fibrotic diseases in general, including injury-related and radiotherapy-induced fibrosis.

Supporting Information

Figure S1 Gene expression graphs across each exon for selected genes. Graphs are as depicted in figure 2.
(PDF)

Figure S2 αSMA staining of primary fibroblast cells. Two control primary fibroblast cell lines, Control 1 and control 2, and 5 primary fibroblasts from DD patients were stained with αSMA (green) and counterstained with chromatin staining Hoechst (blue). Bar in picture is 50 micrometers long.
(PDF)

Table S1 PCR primer sequences.
(XLSX)

Table S2 Genes that show higher gene expression in DD samples with a p-value of <0.05 and a fold change of >2.
(XLSX)

Table S3 Genes that show lower gene expression in DD samples with a p-value of <0.05 and a fold change of >2.
(XLSX)

Author Contributions

Conceived and designed the experiments: PTS DDK GS CNS. Performed the experiments: HBF PTS SH CNS. Analyzed the data: HBF PTS CNS. Contributed reagents/materials/analysis tools: PTS GS CNS. Wrote the paper: HBF PTS SH DDK GS CNS.

References

1. Niessen FB, Spauwen PH, Schalkwijk J, Kon M (1999) On the nature of hypertrophic scars and keloids: a review. Plast Reconstr Surg 104: 1435–1458.
2. Bowley E, O'Gorman DB, Gan BS (2007) Beta-catenin signaling in fibroproliferative disease. J Surg Res 138: 141–150.
3. Rayan GM (2007) Dupuytren disease: Anatomy, pathology, presentation, and treatment. J Bone Joint Surg Am 89: 189–198.
4. Desai SS, Hentz VR (2010) Collagenase clostridium histolyticum for Dupuytren's contracture. Expert Opin Biol Ther 10: 1395–1404.
5. Rayan GM (1999) Clinical presentation and types of Dupuytren's disease. Hand Clin 15: 87–96, vii.
6. Thurston AJ (2003) Dupuytren's disease. J Bone Joint Surg Br 85: 469–477.
7. Yi IS, Johnson G, Moneim MS (1999) Etiology of Dupuytren's disease. Hand Clin 15: 43–51, vi.
8. Murrell GA, Hueston JT (1990) Aetiology of Dupuytren's contracture. Aust N Z J Surg 60: 247–252.
9. Slattery D (2010) Review: Dupuytren's disease in Asia and the migration theory of Dupuytren's disease. ANZ J Surg 80: 495–499.
10. Burge P (1999) Genetics of Dupuytren's disease. Hand Clin 15: 63–71.
11. Gudmundsson KG, Arngrimsson R, Sigfusson N, Bjornsson A, Jonsson T (2000) Epidemiology of Dupuytren's disease: clinical, serological, and social assessment. The Reykjavik Study. J Clin Epidemiol 53: 291–296.
12. Ling RS (1963) The genetic factor in Dupuytren's disease. J Bone Joint Surg Br 45: 709–718.
13. Ross DC (1999) Epidemiology of Dupuytren's disease. Hand Clin 15: 53–62, vi.
14. Bocanegra TS, King P, Vasey FB, Germain BF, Espinoza LR (1981) Dupuytren's contracture: a genetically predisposed disorder? J Rheumatol 8: 1026–1027.
15. Anthony SG, Lozano-Calderon SA, Simmons BP, Jupiter JB (2008) Gender ratio of Dupuytren's disease in the modern U.S. population. Hand (N Y) 3: 87–90.
16. Al-Qattan MM (2006) Factors in the pathogenesis of Dupuytren's contracture. J Hand Surg Am 31: 1527–1534.
17. Townley WA, Baker R, Sheppard N, Grobbelaar AO (2006) Dupuytren's contracture unfolded. BMJ 332: 397–400.
18. Hueston JT (1963) Dupuytren's contnracture: Williams & Wilkins Co.
19. Hindocha S, McGrouther DA, Bayat A (2009) Epidemiological evaluation of Dupuytren's disease incidence and prevalence rates in relation to etiology. Hand (N Y) 4: 256–269.
20. van Rijssen AL, Gerbrandy FS, Ter Linden H, Klip H, Werker PM (2006) A comparison of the direct outcomes of percutaneous needle fasciotomy and limited fasciectomy for Dupuytren's disease: a 6-week follow-up study. J Hand Surg Am 31: 717–725.
21. van Rijssen AL, Werker PM (2006) Percutaneous needle fasciotomy in dupuytren's disease. J Hand Surg Br 31: 498–501.
22. Bainbridge C, Gerber RA, Szczypa PP, Smith T, Kushner H, et al. (2012) Efficacy of collagenase in patients who did and did not have previous hand surgery for Dupuytren's contracture. J Plast Surg Hand Surg.
23. Coleman S, Gilpin D, Tursi J, Kaufman G, Jones N, et al. (2012) Multiple concurrent collagenase clostridium histolyticum injections to dupuytren's cords: an exploratory study. BMC Musculoskelet Disord 13: 61.
24. Hurst LC, Badalamente MA, Hentz VR, Hotchkiss RN, Kaplan FT, et al. (2009) Injectable collagenase clostridium histolyticum for Dupuytren's contracture. N Engl J Med 361: 968–979.
25. Desai SS, Hentz VR (2011) The treatment of Dupuytren disease. J Hand Surg Am 36: 936–942.
26. Augoff K, Kula J, Gosk J, Rutowski R (2005) Epidermal growth factor in Dupuytren's disease. Plast Reconstr Surg 115: 128–133.
27. Bisson MA, McGrouther DA, Mudera V, Grobbelaar AO (2003) The different characteristics of Dupuytren's disease fibroblasts derived from either nodule or cord: expression of alpha-smooth muscle actin and the response to stimulation by TGF-beta1. J Hand Surg Br 28: 351–356.
28. Shih B, Watson S, Bayat A (2012) Whole genome and global expression profiling of Dupuytren's disease: systematic review of current findings and future perspectives. Ann Rheum Dis.
29. Qian A, Meals RA, Rajfer J, Gonzalez-Cadavid NF (2004) Comparison of gene expression profiles between Peyronie's disease and Dupuytren's contracture. Urology 64: 399–404.
30. Forsman M, Paakkonen V, Tjaderhane L, Vuoristo J, Kallioinen L, et al. (2008) The expression of myoglobin and ROR2 protein in Dupuytren's disease. J Surg Res 146: 271–275.
31. Rehman S, Salway F, Stanley JK, Ollier WE, Day P, et al. (2008) Molecular phenotypic descriptors of Dupuytren's disease defined using informatics analysis of the transcriptome. J Hand Surg Am 33: 359–372.
32. Zhang AY, Fong KD, Pham H, Nacamuli RP, Longaker MT, et al. (2008) Gene expression analysis of Dupuytren's disease: the role of TGF-beta2. J Hand Surg Eur Vol 33: 783–790.
33. Johnston P, Chojnowski AJ, Davidson RK, Riley GP, Donell ST, et al. (2007) A complete expression profile of matrix-degrading metalloproteinases in Dupuytren's disease. J Hand Surg Am 32: 343–351.
34. Johnston P, Larson D, Clark IM, Chojnowski AJ (2008) Metalloproteinase gene expression correlates with clinical outcome in Dupuytren's disease. J Hand Surg Am 33: 1160–1167.
35. Lee LC, Zhang AY, Chong AK, Pham H, Longaker MT, et al. (2006) Expression of a novel gene, MafB, in Dupuytren's disease. J Hand Surg Am 31: 211–218.
36. Shih B, Wijeratne D, Armstrong DJ, Lindau T, Day P, et al. (2009) Identification of biomarkers in Dupuytren's disease by comparative analysis of fibroblasts versus tissue biopsies in disease-specific phenotypes. J Hand Surg Am 34: 124–136.
37. Satish L, LaFramboise WA, O'Gorman DB, Johnson S, Janto B, et al. (2008) Identification of differentially expressed genes in fibroblasts derived from patients with Dupuytren's Contracture. BMC Med Genomics 1: 10.
38. Branton MH, Kopp JB (1999) TGF-beta and fibrosis. Microbes Infect 1: 1349–1365.
39. Krause C, Kloen P, Ten Dijke P (2011) Elevated transforming growth factor beta and mitogen-activated protein kinase pathways mediate fibrotic traits of Dupuytren's disease fibroblasts. Fibrogenesis Tissue Repair 4: 14.
40. Sgonc R, Wick G (2008) Pro- and anti-fibrotic effects of TGF-beta in scleroderma. Rheumatology (Oxford) 47 Suppl 5: v5–7.
41. Dolmans GH, Werker PM, Hennies HC, Furniss D, Festen EA, et al. (2011) Wnt signaling and Dupuytren's disease. N Engl J Med 365: 307–317.
42. O'Gorman DB, Wu Y, Seney S, Zhu RD, Gan BS (2006) Wnt expression is not correlated with beta-catenin dysregulation in Dupuytren's Disease. J Negat Results Biomed 5: 13.
43. Satish L, Gallo PH, Baratz ME, Johnson S, Kathju S (2011) Reversal of TGF-beta1 stimulation of alpha-smooth muscle actin and extracellular matrix components by cyclic AMP in Dupuytren's-derived fibroblasts. BMC Musculoskelet Disord 12: 113.
44. Gilpin D, Coleman S, Hall S, Houston A, Karrasch J, et al. (2010) Injectable collagenase Clostridium histolyticum: a new nonsurgical treatment for Dupuytren's disease. J Hand Surg Am 35: 2027–2038 e2021.
45. Sprung CN, Chao M, Leong T, McKay MJ (2005) Chromosomal radiosensitivity in two cell lineages derived from clinically radiosensitive cancer patients. Clin Cancer Res 11: 6352–6358.
46. Bengtsson H, Simpson K, Bullard J, Hansen K (2006) Aroma. affymetris: A generic framework in R for analyaing small to very large Affymetrix data sets in bounded memory.: University of California, Berkeley. 745 745.
47. Pan D, Watson HK, Swigart C, Thomson JG, Honig SC, et al. (2003) Microarray gene analysis and expression profiles of Dupuytren's contracture. Ann Plast Surg 50: 618–622.
48. Chammas M, Bousquet P, Renard E, Poirier JL, Jaffiol C, et al. (1995) Dupuytren's disease, carpal tunnel syndrome, trigger finger, and diabetes mellitus. J Hand Surg Am 20: 109–114.
49. Ratkaj I, Bujak M, Jurisic D, Baus Loncar M, Bendelja K, et al. (2012) Microarray Analysis of Dupuytren's Disease Cells: The Profibrogenic Role of the TGF-beta Inducible p38 MAPK Pathway. Cell Physiol Biochem 30: 927–942.
50. Rehman S, Xu Y, Dunn WB, Day PJ, Westerhoff HV, et al. (2012) Dupuytren's disease metabolite analyses reveals alterations following initial short-term fibroblast culturing. Mol Biosyst.
51. Chang HY, Chi JT, Dudoit S, Bondre C, van de Rijn M, et al. (2002) Diversity, topographic differentiation, and positional memory in human fibroblasts. Proc Natl Acad Sci U S A 99: 12877–12882.
52. Bazin S, Le Lous M, Duance VC, Sims TJ, Bailey AJ, et al. (1980) Biochemistry and histology of the connective tissue of Dupuytren's disease lesions. Eur J Clin Invest 10: 9–16.
53. Murrell GA, Francis MJ, Bromley L (1987) Free radicals and Dupuytren's contracture. Br Med J (Clin Res Ed) 295: 1373–1375.
54. Murphy G, Cockett MI, Stephens PE, Smith BJ, Docherty AJ (1987) Stromelysin is an activator of procollagenase. A study with natural and recombinant enzymes. Biochem J 248: 265–268.
55. Rozen WM, Edirisinghe Y, Crock J (2012) Late Complications of Clinical Clostridium Histolyticum Collagenase Use in Dupuytren's Disease. PLoS ONE 7: e43406.
56. Pegorier S, Campbell GA, Kay AB, Lloyd CM (2010) Bone morphogenetic protein (BMP)-4 and BMP-7 regulate differentially transforming growth factor (TGF)-beta1 in normal human lung fibroblasts (NHLF). Respir Res 11: 85.
57. Nikolova G, Jabs N, Konstantinova I, Domogatskaya A, Tryggvason K, et al. (2006) The vascular basement membrane: a niche for insulin gene expression and Beta cell proliferation. Dev Cell 10: 397–405.
58. Noble J, Heathcote JG, Cohen H (1984) Diabetes mellitus in the aetiology of Dupuytren's disease. J Bone Joint Surg Br 66: 322–325.
59. Grootaert C, Van de Wiele T, Verstraete W, Bracke M, Vanhoecke B (2012) Angiopoietin-like protein 4: health effects, modulating agents and structure-function relationships. Expert Rev Proteomics 9: 181–199.
60. Akiyama SK (1996) Integrins in cell adhesion and signaling. Hum Cell 9: 181–186.
61. Patella S, Phillips DJ, Tchongue J, de Kretser DM, Sievert W (2006) Follistatin attenuates early liver fibrosis: effects on hepatic stellate cell activation and hepatocyte apoptosis. Am J Physiol Gastrointest Liver Physiol 290: G137–144.

62. Antsiferova M, Huber M, Meyer M, Piwko-Czuchra A, Ramadan T, et al. (2011) Activin enhances skin tumourigenesis and malignant progression by inducing a pro-tumourigenic immune cell response. Nat Commun 2: 576.
63. Tsuchida K, Nakatani M, Hitachi K, Uezumi A, Sunada Y, et al. (2009) Activin signaling as an emerging target for therapeutic interventions. Cell Commun Signal 7: 15.
64. Aoki F, Kurabayashi M, Hasegawa Y, Kojima I (2005) Attenuation of bleomycin-induced pulmonary fibrosis by follistatin. Am J Respir Crit Care Med 172: 713–720.
65. Ludlow H, Phillips DJ, Myers M, McLachlan RI, de Kretser DM, et al. (2009) A new 'total' activin B enzyme-linked immunosorbent assay (ELISA): development and validation for human samples. Clin Endocrinol (Oxf) 71: 867–873.
66. Badalamente MA, Hurst LC, Grandia SK, Sampson SP (1992) Platelet-derived growth factor in Dupuytren's disease. J Hand Surg Am 17: 317–323.
67. Battegay EJ, Raines EW, Seifert RA, Bowen-Pope DF, Ross R (1990) TGF-beta induces bimodal proliferation of connective tissue cells via complex control of an autocrine PDGF loop. Cell 63: 515–524.
68. Lawler J, McHenry K, Duquette M, Derick L (1995) Characterization of human thrombospondin-4. J Biol Chem 270: 2809–2814.
69. Sprung CN, Li J, Hovan D, McKay MJ, Forrester HB (2011) Alternative transcript initiation and splicing as a response to DNA damage. PLoS ONE 6: e25758.
70. Forrester HB, Li J, Hovan D, Ivashkevich AN, Sprung CN (2012) DNA repair genes: alternative transcription and gene expression at the exon level in response to the DNA damaging agent, ionizing radiation. PLoS ONE 7: e53358.

Table S1. PCR primer sequences

Name*	PSR	Forward (5'-3')	Reverse (5'-3')	Annealing temp. (°C)
COL15A1	685-763	GGTGGAACCGCTTCGCCATGA	GGGATGCGGCTGTGCTCCTC	60
FGF9	910	AAGCACGTGGACACTGGAAGGC	TAGTCCCTTCTCTCGGGGTCCCA	60
FST	409	GTCTGTGCCAGTGACAATGC	GTCTTCCGAAATGGAGTTGC	60
INHBA	596	GGGCAAAGTCGGGGAGAACGG	CCTGGCTGTTCCTGACTCGGC	60
KIF14	403	ACCACCCATTGCTTCCCTGAGT	ACAAGTTTCCTGTTCCCAACACTTTGA	60
KIF23	839	GCAAGGCGTAGGCAGCAGGA	GGAACCACCTCCCTGCCTTCAGT	60
KRT34	912	TCCTGACCCAAGCAAAGACACACA	ACAGGCTCGACCCTCAACAGGA	60
MPP1	817	GTTGCAGCTCATGAACTCGGCCA	TCCTGAGCTAGCTGAACATCACCAC	60
PGK	reference gene	CTGGAGAACCTCCGCTTTCAT	TGGCTCGGCTTTAACCTTGTT	60
STAT1	299	CGTTACTGAAGAGCTTCACTCCCTT	TCGAGGTCAATTACCAAACCAGGC	60

* Gene names are followed by the last three digits of the PSR identification number. PSR: Probe Selection Region

Table S2. Genes that show higher gene expression in DD samples with a p-value of <0.05 and a fold change of >2

Gene Symbol	Gene ID (RefSeq)	p-value	Fold-Change(Control vs. DD)	Fold change direction
VCAM1	NM_001078	5.07E-11	-35.1342	CL down vs DD
COMP	NM_000095	8.61E-21	-34.3401	CL down vs DD
SFRP4	NM_003014	1.10E-02	-30.7416	CL down vs DD
CHI3L1	NM_001276	2.86E-16	-20.9531	CL down vs DD
DDIT4	NM_019058	7.80E-10	-17.4606	CL down vs DD
SCRG1	NM_007281	3.50E-19	-14.576	CL down vs DD
C10orf10	NM_007021	4.36E-04	-13.2329	CL down vs DD
FGF9	NM_002010	4.57E-03	-11.8243	CL down vs DD
FMOD	NM_002023	1.91E-03	-9.95692	CL down vs DD
KRT34	NM_021013	1.53E-06	-9.59421	CL down vs DD
CHAC1	NM_024111	7.00E-03	-9.54938	CL down vs DD
CADM1	NM_014333	2.71E-10	-9.35959	CL down vs DD
THBS4	NM_003248	1.40E-30	-8.74083	CL down vs DD
PTPRD	NM_002839	5.86E-29	-8.59582	CL down vs DD
CRLF1	NM_004750	1.98E-27	-8.46392	CL down vs DD
SPON1	NM_006108	4.48E-09	-7.64994	CL down vs DD
PAPPA2	NM_020318	1.11E-36	-7.16121	CL down vs DD
ANGPTL4	NM_139314	2.96E-11	-6.89301	CL down vs DD
PFKFB4	NM_004567	6.37E-23	-6.27251	CL down vs DD
DACT1	NM_016651	1.06E-15	-6.24109	CL down vs DD
C7orf68	NM_013332	9.42E-04	-5.78641	CL down vs DD
NRCAM	NM_001193582	6.68E-23	-5.72873	CL down vs DD
SLC2A5	NM_003039	1.97E-25	-5.64975	CL down vs DD
NDUFA4L2	NM_020142	2.48E-03	-5.64615	CL down vs DD
IL26	NM_018402	1.15E-04	-5.58784	CL down vs DD
CILP2	NM_153221	5.12E-24	-5.41481	CL down vs DD
ANKRD37	NM_181726	0.000196107	-5.39884	CL down vs DD
DAPK1	NM_004938	3.24E-09	-5.29651	CL down vs DD
CPA4	NM_016352	3.85E-02	-5.18093	CL down vs DD
RBP4	NM_006744	2.47E-04	-5.17563	CL down vs DD
LOXL3	NM_032603	2.70E-03	-5.08977	CL down vs DD
MOCOS	NM_017947	4.29E-08	-5.00414	CL down vs DD
ASPHD2	NM_020437	1.16E-06	-4.91587	CL down vs DD
UNC5B	NM_170744	1.68E-08	-4.90931	CL down vs DD
WNT2	NM_003391	1.39E-05	-4.82891	CL down vs DD
SPAG4	NM_003116	7.90E-23	-4.60329	CL down vs DD
RDH10	NM_172037	1.31E-02	-4.58245	CL down vs DD
TRIB3	NM_021158	3.67E-09	-4.46002	CL down vs DD
APLN	NM_017413	2.06E-08	-4.34215	CL down vs DD
MSC	NM_005098	5.40E-04	-4.33854	CL down vs DD
MTHFD2	NR_027405	2.00E-03	-4.3355	CL down vs DD
CPZ	NM_001014448	6.94E-11	-4.28206	CL down vs DD
COL15A1	NM_001855	1.18E-03	-4.26303	CL down vs DD
SLC7A5	NM_003486	2.08E-06	-4.25905	CL down vs DD
PDLIM3	NM_014476	4.79E-05	-4.22887	CL down vs DD
TFAP2B	NM_003221	3.30E-09	-4.17167	CL down vs DD
CXCL16	NM_022059	1.19E-07	-4.15755	CL down vs DD
PRG4	NM_005807	1.76E-10	-4.15362	CL down vs DD
SLC2A1	NM_006516	4.14E-09	-4.13188	CL down vs DD
CBS	NM_000071	1.10E-07	-4.1273	CL down vs DD
TPD52L1	NM_001003395	4.18E-02	-4.05934	CL down vs DD
MPP7	NM_173496	4.84E-05	-4.02996	CL down vs DD
PALM	NM_002579	5.82E-12	-4.02615	CL down vs DD
STAC	NM_003149	1.61E-03	-3.95684	CL down vs DD
VLDLR	NM_003383	2.66E-11	-3.94901	CL down vs DD
IER3	NM_003897	3.50E-08	-3.93968	CL down vs DD
KCTD15	NM_024076	2.49E-04	-3.93457	CL down vs DD
SLC6A9	NM_201649	1.06E-22	-3.88253	CL down vs DD
BOK	NM_032515	3.11E-02	-3.83128	CL down vs DD
ITGA11	NM_001004439	3.36E-15	-3.8181	CL down vs DD
GSC	NM_173849	5.42E-10	-3.76618	CL down vs DD
ABLIM1	NM_002313	4.20E-17	-3.76294	CL down vs DD
PCK2	NM_004563	4.62E-22	-3.74174	CL down vs DD
GALNTL4	NM_198516	2.43E-19	-3.7284	CL down vs DD
EYA4	NM_004100	3.07E-24	-3.68832	CL down vs DD
PFKFB3	NM_004566	1.17E-06	-3.66686	CL down vs DD
SERPINA3	NM_001085	1.61E-03	-3.64863	CL down vs DD
GPT2	NM_001142466	1.73E-08	-3.63693	CL down vs DD
SEL1L3	NM_015187	2.34E-07	-3.57735	CL down vs DD
COL5A1	NM_000093	8.24E-25	-3.57201	CL down vs DD
FLJ40536	AK097855	2.81E-05	-3.55258	CL down vs DD
SESN2	NM_031459	8.10E-11	-3.52325	CL down vs DD
KCNG1	NM_002237	2.75E-02	-3.47133	CL down vs DD
SORBS2	NM_021069	3.36E-18	-3.46938	CL down vs DD
ARHGAP28	NM_001010000	3.39E-05	-3.39836	CL down vs DD
SYNPO	NM_007286	4.20E-36	-3.36392	CL down vs DD
ABCB6	NM_005689	2.49E-19	-3.32978	CL down vs DD
PHGDH	NM_006623	1.73E-08	-3.30993	CL down vs DD
ELN	NM_000501	7.19E-11	-3.28479	CL down vs DD
SULF2	NM_018837	7.63E-08	-3.28351	CL down vs DD
PDK3	NM_001142386	1.98E-06	-3.28174	CL down vs DD
NDRG1	NM_001135242	3.73E-15	-3.25238	CL down vs DD
NUAK1	NM_014840	1.61E-02	-3.1817	CL down vs DD
SYBU	NM_001099744	1.20E-02	-3.17094	CL down vs DD
FKBP4	NM_002014	5.13E-06	-3.1628	CL down vs DD
MIF	NM_002415	0.0218613	-3.14781	CL down vs DD
HOXA13	NM_000522	3.70E-14	-3.14483	CL down vs DD

KCNH1	NM_172362	2.36E-02	-3.13922	CL down vs DD
HIST1H1C	NM_005319	1.15E-03	-3.10989	CL down vs DD
EIF4EBP1	NM_004095	4.82E-06	-3.07336	CL down vs DD
MKNK2	NM_199054	4.65E-10	-3.07208	CL down vs DD
KIAA1244	NM_020340	7.68E-19	-3.01181	CL down vs DD
WARS	NM_004184	3.84E-05	-2.94143	CL down vs DD
FGF11	NM_004112	3.99E-03	-2.93097	CL down vs DD
NEDD9	NM_001142393	1.01E-04	-2.91829	CL down vs DD
MAF	NM_001031804	1.76E-06	-2.9066	CL down vs DD
VWA5A	NM_001130142	2.11E-05	-2.89242	CL down vs DD
TXNIP	NM_006472	2.03E-02	-2.89179	CL down vs DD
SYT7	NM_004200	2.41E-04	-2.88232	CL down vs DD
NFKBIZ	NM_031419	2.03E-14	-2.86239	CL down vs DD
ALPL	NM_000478	2.89E-02	-2.85537	CL down vs DD
GALNT13	NM_052917	4.18E-09	-2.85467	CL down vs DD
LONP1	NM_004793	5.79E-17	-2.84375	CL down vs DD
ZNF395	NM_018660	6.75E-07	-2.83945	CL down vs DD
THBS3	NM_007112	4.62E-04	-2.81879	CL down vs DD
ARHGEF2	NM_001162383	1.65E-14	-2.81828	CL down vs DD
CSF2RB	NM_000395	1.82E-04	-2.79497	CL down vs DD
KCND3	NM_004980	8.00E-03	-2.78963	CL down vs DD
LSP1	NM_002339	6.11E-08	-2.78337	CL down vs DD
CYGB	NM_134268	3.49E-02	-2.78062	CL down vs DD
ADM2	NM_024866	4.32E-17	-2.77515	CL down vs DD
PVR	NM_006505	2.82E-02	-2.77403	CL down vs DD
KIAA1324L	NM_001142749	1.30E-03	-2.76669	CL down vs DD
LOXL2	NM_002318	5.91E-10	-2.76391	CL down vs DD
SERPINH1	NM_001235	5.98E-05	-2.74284	CL down vs DD
KCNT2	NM_198503	9.02E-04	-2.7415	CL down vs DD
KLHL35	NM_001039548	2.05E-02	-2.73809	CL down vs DD
TYMP	NM_001113756	9.23E-17	-2.70951	CL down vs DD
CECR5	NM_033070	1.81E-06	-2.68546	CL down vs DD
CYR61	NM_001554	7.12E-06	-2.66734	CL down vs DD
IL27RA	NM_004843	1.06E-04	-2.65751	CL down vs DD
COL4A4	NM_000092	1.90E-20	-2.65467	CL down vs DD
C1orf113	NM_001162530	9.41E-09	-2.65357	CL down vs DD
TP53I11	NM_001076787	2.22E-02	-2.64661	CL down vs DD
MAPK11	NM_002751	1.36E-07	-2.63789	CL down vs DD
NTRK3	NM_001007156	3.40E-06	-2.63731	CL down vs DD
PGM1	NM_002633	4.44E-12	-2.62812	CL down vs DD
CGREF1	NM_006569	5.00E-03	-2.61787	CL down vs DD
SNORD49A	NR_002744	5.80E-03	-2.60345	CL down vs DD
ITGB2	NM_000211	4.68E-09	-2.60311	CL down vs DD
FOSL2	NM_005253	1.20E-06	-2.59105	CL down vs DD
SOX4	NM_003107	1.31E-11	-2.5901	CL down vs DD
TM6SF1	NM_023003	1.09E-05	-2.56537	CL down vs DD
DBC1	NM_014618	3.79E-09	-2.56524	CL down vs DD
C21orf33	NM_004649	1.94E-03	-2.56517	CL down vs DD
ANKZF1	NM_018089	1.19E-10	-2.5617	CL down vs DD
CILP	NM_003613	9.55E-04	-2.5557	CL down vs DD
GYS1	NM_002103	1.76E-11	-2.54916	CL down vs DD
GATA6	NM_005257	2.85E-12	-2.54569	CL down vs DD
ADAMTS10	NM_030957	4.34E-21	-2.54557	CL down vs DD
SBNO2	NM_014963	1.28E-21	-2.54349	CL down vs DD
SMO	NM_005631	2.60E-09	-2.5308	CL down vs DD
ACSS1	NM_032501	1.93E-14	-2.52887	CL down vs DD
MAZ	NM_001042539	8.12E-03	-2.50309	CL down vs DD
CADM4	NM_145296	2.25E-03	-2.49898	CL down vs DD
ADAM15	NM_207196	2.06E-05	-2.49582	CL down vs DD
ADAMTS3	NM_014243	2.85E-02	-2.49419	CL down vs DD
PFKL	NR_024108	5.78E-11	-2.49014	CL down vs DD
CLMN	NM_024734	7.03E-06	-2.48375	CL down vs DD
JUB	NM_032876	2.81E-03	-2.46058	CL down vs DD
B4GALT2	NM_003780	5.15E-08	-2.45699	CL down vs DD
SBF1	NM_002972	9.09E-16	-2.45623	CL down vs DD
CHST6	NM_021615	1.36E-02	-2.45609	CL down vs DD
PPM1M	NM_144641	7.28E-03	-2.44893	CL down vs DD
MFSD10	NM_001146069	1.12E-07	-2.44819	CL down vs DD
DHRS13	NM_144683	5.10E-03	-2.44243	CL down vs DD
TIAM2	NM_012454	3.47E-06	-2.43994	CL down vs DD
MTFP1	NM_016498	1.17E-02	-2.4333	CL down vs DD
C13orf18	NM_025113	4.43E-02	-2.42893	CL down vs DD
ANK3	NM_020987	4.29E-05	-2.42411	CL down vs DD
CRIP2	NM_001312	2.89E-07	-2.42181	CL down vs DD
TLE2	NM_003260	1.38E-09	-2.42065	CL down vs DD
PKNOX2	NM_022062	3.64E-04	-2.42041	CL down vs DD
MFI2	NM_005929	9.87E-06	-2.41442	CL down vs DD
PTPN3	NM_002829	5.92E-06	-2.41185	CL down vs DD
RCC1	NR_030725	1.82E-10	-2.40364	CL down vs DD
PLOD2	NM_182943	2.20E-16	-2.40084	CL down vs DD
EPB41L4A	NM_022140	4.79E-03	-2.39677	CL down vs DD
RNF41	NM_194358	0.00258915	-2.39609	CL down vs DD
C6orf48	NM_001040437	2.16E-11	-2.36816	CL down vs DD
WDR18	NM_024100	8.08E-06	-2.3665	CL down vs DD
RCOR2	NM_173587	9.74E-04	-2.36525	CL down vs DD
PHB	NM_002634	5.01E-04	-2.3639	CL down vs DD
MARS	NM_004990	4.65E-20	-2.36018	CL down vs DD
EFNA3	NM_004952	3.86E-02	-2.36	CL down vs DD
COL5A2	NM_000393	0	-2.35919	CL down vs DD

NALCN	NM_052867	1.19E-02	-2.35485	CL down vs DD
KCNJ12	NM_021012	4.58E-06	-2.35451	CL down vs DD
GMDS	NM_001500	1.87E-03	-2.35011	CL down vs DD
TSC22D3	NM_198057	6.09E-08	-2.34979	CL down vs DD
SIK1	NM_173354	1.60E-07	-2.3489	CL down vs DD
COL4A2	NM_001846	2.17E-17	-2.34587	CL down vs DD
FAM174B	NM_207446	3.11E-07	-2.34506	CL down vs DD
GDPD5	NM_030792	0.00730335	-2.34454	CL down vs DD
KLK9	NM_012315	0.00425009	-2.34066	CL down vs DD
ADAMTS2	NM_014244	3.35E-12	-2.33958	CL down vs DD
RBCK1	NM_031229	2.85E-07	-2.33571	CL down vs DD
PTPRU	NM_005704	2.50E-02	-2.33346	CL down vs DD
PEX6	NM_000287	6.90E-03	-2.33345	CL down vs DD
RCC2	NM_018715	5.21E-07	-2.33193	CL down vs DD
ABCC3	NM_003786	2.53E-05	-2.32085	CL down vs DD
GTPBP2	NM_019096	1.33E-10	-2.30966	CL down vs DD
NLGN4X	NM_020742	7.64E-09	-2.30371	CL down vs DD
C2orf19	BC031945	4.31E-02	-2.30347	CL down vs DD
YBX2	NM_015982	1.44E-06	-2.29974	CL down vs DD
EFEMP1	NM_004105	9.84E-08	-2.29796	CL down vs DD
CD70	NM_001252	4.24E-03	-2.29613	CL down vs DD
TMEM134	NM_025124	1.36E-06	-2.29466	CL down vs DD
PTGES2	NM_025072	3.11E-07	-2.28741	CL down vs DD
CDR2L	NM_014603	1.76E-06	-2.28411	CL down vs DD
QSOX1	NM_002826	2.71E-12	-2.28206	CL down vs DD
SEMA3B	NM_004636	8.30E-06	-2.27769	CL down vs DD
NRG1	NM_013960	2.18E-09	-2.27667	CL down vs DD
KCNK7	NM_005714	9.12E-06	-2.26944	CL down vs DD
TPSD1	NM_012217	1.14E-03	-2.26653	CL down vs DD
COL4A1	NM_001845	1.97E-06	-2.26167	CL down vs DD
FZD1	NM_003505	2.05E-02	-2.26122	CL down vs DD
PHPT1	NM_001135861	5.23E-18	-2.25573	CL down vs DD
DCI	NM_001919	1.42E-03	-2.25251	CL down vs DD
CTU1	NM_145232	2.02E-02	-2.25034	CL down vs DD
FKBP10	NM_021939	6.32E-10	-2.23312	CL down vs DD
WDR54	NM_032118	4.41E-06	-2.23138	CL down vs DD
TUFM	NM_003321	3.35E-02	-2.21475	CL down vs DD
CTDSP1	NM_021198	1.75E-07	-2.20918	CL down vs DD
C1orf66	NM_015997	1.89E-08	-2.20568	CL down vs DD
GGT7	NM_178026	1.41E-02	-2.19297	CL down vs DD
ECSIT	NM_016581	7.38E-03	-2.18533	CL down vs DD
SORCS2	NM_020777	8.71E-03	-2.18482	CL down vs DD
RGL2	NM_004761	2.70E-05	-2.17615	CL down vs DD
ABTB1	NM_172027	3.01E-03	-2.17585	CL down vs DD
ARHGEF19	NM_153213	2.80E-08	-2.17363	CL down vs DD
FCN2	NM_004108	1.68E-02	-2.17063	CL down vs DD
GPI	NM_000175	3.09E-08	-2.16987	CL down vs DD
FBP1	NM_000507	2.98E-02	-2.16853	CL down vs DD
RSPO1	NM_001038633	1.91E-04	-2.16685	CL down vs DD
RNPEPL1	NM_018226	6.75E-10	-2.16672	CL down vs DD
C16orf58	NM_022744	6.58E-06	-2.16648	CL down vs DD
TMEM121	NM_025268	1.70E-04	-2.16539	CL down vs DD
MFSD3	NM_138431	0.000614593	-2.16164	CL down vs DD
NLRX1	NM_024618	0.000611263	-2.16134	CL down vs DD
ILVBL	NM_006844	5.94E-03	-2.15861	CL down vs DD
CACNG6	NM_145814	3.43E-02	-2.15662	CL down vs DD
TSPY26P	NR_002781	2.14E-02	-2.15521	CL down vs DD
FOXP1	NM_032682	2.82E-15	-2.15468	CL down vs DD
DGKD	NM_152879	3.55E-09	-2.15276	CL down vs DD
CMTM3	NM_144601	8.20E-22	-2.15103	CL down vs DD
ABCA3	NM_001089	3.26E-05	-2.14977	CL down vs DD
NTRK2	NM_006180	1.94E-03	-2.14439	CL down vs DD
KDM4B	NM_015015	1.77E-08	-2.14126	CL down vs DD
ST3GAL3	NM_174963	2.97E-08	-2.13971	CL down vs DD
C7orf62	BC028365	6.28E-04	-2.13915	CL down vs DD
METTL11A	NM_014064	2.59E-03	-2.13862	CL down vs DD
EXOSC5	NM_020158	2.53E-02	-2.13386	CL down vs DD
PPP1R1C	NM_001080545	3.32E-03	-2.13352	CL down vs DD
PTPRO	NM_030667	5.07E-06	-2.13151	CL down vs DD
IMMP2L	NM_032549	0.037824	-2.12903	CL down vs DD
PEX10	NM_153818	1.67E-05	-2.12862	CL down vs DD
IMPA2	NM_014214	6.97E-03	-2.12782	CL down vs DD
HIST1H4C	NM_003542	2.32E-02	-2.12778	CL down vs DD
MEIS3	NM_020160	2.03E-03	-2.12574	CL down vs DD
HEXDC	NM_173620	8.00E-05	-2.12374	CL down vs DD
ZNF581	NM_016535	4.78E-02	-2.12291	CL down vs DD
MRPL17	NM_022061	7.77E-11	-2.11845	CL down vs DD
MTA1	NM_004689	1.16E-17	-2.11742	CL down vs DD
NUBP2	NM_012225	0.000903581	-2.1138	CL down vs DD
AMOTL2	NM_016201	1.23E-10	-2.11362	CL down vs DD
LRRC23	NM_001135217	3.02E-03	-2.11011	CL down vs DD
SOCS3	NM_003955	7.07E-03	-2.09633	CL down vs DD
IMPDH2	NM_000884	1.04E-03	-2.09448	CL down vs DD
SSTR3	NM_001051	3.52E-02	-2.09261	CL down vs DD
TMEM132A	NM_017870	1.93E-06	-2.08819	CL down vs DD
VASH1	NM_014909	1.80E-03	-2.08759	CL down vs DD
TSPAN17	NM_012171	7.75E-08	-2.08677	CL down vs DD
EFNB3	NM_001406	0.0378684	-2.08461	CL down vs DD
NAALADL1	NM_005468	2.45E-06	-2.0795	CL down vs DD

HYOU1	NM_006389	2.35E-10	-2.07849	CL down vs DD
IER5L	NM_203434	5.82E-07	-2.07017	CL down vs DD
FPGS	NM_004957	1.59E-04	-2.06889	CL down vs DD
SLC13A3	NM_022829	6.50E-04	-2.06852	CL down vs DD
ITM2C	NM_030926	1.35E-03	-2.06467	CL down vs DD
PDK1	NM_002610	1.81E-06	-2.06407	CL down vs DD
CHP2	NM_022097	2.61E-03	-2.06243	CL down vs DD
ME3	NM_001161586	3.25E-02	-2.06115	CL down vs DD
STXBP2	NM_006949	4.70E-05	-2.05951	CL down vs DD
DPYSL4	NM_006426	1.19E-03	-2.05788	CL down vs DD
MLLT1	NM_005934	2.28E-03	-2.05372	CL down vs DD
LMBR1L	NM_018113	4.99E-02	-2.05192	CL down vs DD
TNIP1	NM_006058	1.57E-02	-2.05155	CL down vs DD
CRYBB3	NM_004076	1.28E-02	-2.05101	CL down vs DD
BSCL2	NM_001130702	3.92E-06	-2.05055	CL down vs DD
HIST1H1E	NM_005321	8.94E-04	-2.04984	CL down vs DD
GPR124	NM_032777	9.26E-15	-2.04796	CL down vs DD
IGSF8	NM_052868	5.35E-06	-2.04491	CL down vs DD
NOL3	NM_001185058	6.06E-07	-2.04458	CL down vs DD
SLC48A1	NM_017842	1.04E-03	-2.04159	CL down vs DD
TBL2	NM_012453	2.64E-07	-2.03717	CL down vs DD
CALCB	NM_000728	0.00859335	-2.03652	CL down vs DD
HIST4H4	NM_175054	6.62E-03	-2.03341	CL down vs DD
RCAN1	NM_004414	4.09E-07	-2.03317	CL down vs DD
PPP2R2B	NM_181674	0.00531692	-2.03193	CL down vs DD
NDUFS7	NM_024407	1.34E-02	-2.03055	CL down vs DD
SIAH2	NM_005067	5.62E-04	-2.02949	CL down vs DD
FASTK	NM_006712	1.26E-12	-2.02918	CL down vs DD
GPR176	NM_007223	8.96E-10	-2.02032	CL down vs DD
RNH1	NM_002939	2.33E-04	-2.01978	CL down vs DD
SMOC2	NM_022138	1.22E-08	-2.01814	CL down vs DD
ANKRD13B	NM_152345	3.22E-06	-2.0174	CL down vs DD
BAT5	NM_021160	2.95E-10	-2.01101	CL down vs DD
TRIB2	NM_021643	3.84E-02	-2.00884	CL down vs DD
NT5DC2	NM_022908	6.16E-09	-2.0084	CL down vs DD
STK32C	NM_173575	9.87E-07	-2.00764	CL down vs DD
MRPL12	NM_002949	1.51E-02	-2.00756	CL down vs DD
DDX51	NM_175066	5.21E-11	-2.00525	CL down vs DD
PROK2	NM_001126128	0.026788	-2.00489	CL down vs DD
GMEB2	NM_012384	9.05E-06	-2.00384	CL down vs DD
WAS	NM_000377	7.58E-08	-2.00349	CL down vs DD
APH1A	NM_016022	5.44E-03	-2.00253	CL down vs DD

Table S3. Genes that show lower gene expression in DD samples with a p-value of <0.05 and a fold change of >2

Gene Symbol	Gene ID (RefSeq)	p-value	Fold-Change(Control vs. DD)	Fold change direction
MMP1	NM_002421	8.63E-14	56.6277	CL up vs DD
SEMA3A	NM_006080	1.63E-24	32.9807	CL up vs DD
KIT	NM_000222	0	19.8159	CL up vs DD
MMP3	NM_002422	2.75E-14	18.5218	CL up vs DD
PBK	NM_018492	1.02E-04	14.2813	CL up vs DD
TFPI	NM_006287	1.47E-18	14.109	CL up vs DD
SERPINB2	NM_001143818	1.32E-08	14.0724	CL up vs DD
TFPI2	NM_006528	9.40E-04	13.4744	CL up vs DD
KIF11	NM_004523	2.38E-05	13.0349	CL up vs DD
TOP2A	NM_001067	4.95E-36	12.6288	CL up vs DD
CTSK	NM_000396	1.26E-07	12.4257	CL up vs DD
TRPC4	NM_016179	6.46E-05	11.8229	CL up vs DD
IL13RA2	NM_000640	1.40E-04	11.7517	CL up vs DD
ANLN	NM_018685	2.06E-23	11.0621	CL up vs DD
DLGAP5	NM_001146015	3.47E-23	10.8337	CL up vs DD
LPHN2	NM_012302	2.54E-38	10.8311	CL up vs DD
CENPF	NM_016343	1.35E-22	9.51298	CL up vs DD
EEA1	NM_003566	3.44E-16	9.30826	CL up vs DD
KIF20B	NM_016195	9.28E-30	9.06	CL up vs DD
SMC2	NM_001042550	4.04E-18	8.26822	CL up vs DD
HMCN1	NM_031935	0.00E+00	8.08127	CL up vs DD
ROCK1	NM_005406	4.43E-20	8.07519	CL up vs DD
NCAPG	NM_022346	9.35E-26	7.93099	CL up vs DD
KIF23	NM_138555	3.38E-27	7.87122	CL up vs DD
GALNT5	NM_014568	4.63E-02	7.74798	CL up vs DD
MKI67	NM_002417	7.71E-16	7.68071	CL up vs DD
CASC5	NM_170589	0.00E+00	7.52791	CL up vs DD
CKAP2	NM_018204	1.64E-30	7.5254	CL up vs DD
ASPM	NM_018136	0.00E+00	7.37628	CL up vs DD
KIF18A	NM_031217	9.13E-06	7.28334	CL up vs DD
SCIN	NM_001112706	2.34E-11	7.28039	CL up vs DD
MELK	NM_014791	2.78E-22	7.11972	CL up vs DD
VPS13C	NM_020821	0.00E+00	7.1057	CL up vs DD
TTK	NM_003318	2.62E-16	7.00696	CL up vs DD
CENPK	NM_022145	1.49E-08	6.94789	CL up vs DD
HELLS	NM_018063	2.60E-27	6.94526	CL up vs DD
SHCBP1	NM_024745	2.66E-21	6.74075	CL up vs DD
CEP55	NM_018131	5.33E-15	6.70633	CL up vs DD
KITLG	NM_000899	3.62E-03	6.60831	CL up vs DD
RECQL	NM_002907	1.09E-21	6.56328	CL up vs DD
PODXL	NM_001018111	1.32E-20	6.47796	CL up vs DD
HMMR	NM_001142556	9.34E-16	6.46258	CL up vs DD
CD109	NM_133493	2.08E-02	6.42551	CL up vs DD
ECT2	NM_018098	2.02E-16	6.42206	CL up vs DD
NUF2	NM_145697	3.60E-21	6.40957	CL up vs DD
KIF5B	NM_004521	2.43E-27	6.31599	CL up vs DD
ITGA2	NM_002203	1.59E-16	6.27779	CL up vs DD
GAS2L3	NM_174942	1.09E-09	6.27478	CL up vs DD
GGH	NM_003878	5.16E-04	6.25643	CL up vs DD
DST	NM_015548	0.00E+00	6.25435	CL up vs DD
FAM111B	NM_198947	3.78E-06	6.22711	CL up vs DD
SACS	NM_014363	6.75E-07	6.20277	CL up vs DD
MOXD1	NM_015529	1.28E-29	6.17493	CL up vs DD
TPX2	NM_012112	1.23E-14	5.96579	CL up vs DD
CCNE2	NM_057749	1.37E-15	5.95473	CL up vs DD
KIF14	NM_014875	3.56E-34	5.92298	CL up vs DD
FANCI	NM_001113378	7.35E-24	5.91775	CL up vs DD
WDHD1	NM_007086	7.51E-18	5.89357	CL up vs DD
AK5	NM_174858	2.36E-13	5.81968	CL up vs DD
NDC80	NM_006101	1.15E-06	5.80552	CL up vs DD
FANCI	NM_001113378	2.24E-03	5.79815	CL up vs DD
SDCCAG1	NM_004713	1.47E-29	5.79762	CL up vs DD
ENPP2	NM_006209	7.99E-07	5.79271	CL up vs DD
BRIP1	NM_032043	3.08E-09	5.78674	CL up vs DD
GNG11	NM_004126	1.65E-03	5.72626	CL up vs DD
CCDC88A	NM_001135597	0.00E+00	5.7261	CL up vs DD
KIAA1524	NM_020890	6.33E-19	5.70174	CL up vs DD
KTN1	NM_182926	9.14E-06	5.68394	CL up vs DD
SETDB2	NM_031915	5.17E-03	5.65075	CL up vs DD
PPIP5K2	NM_015216	5.27E-06	5.62992	CL up vs DD
DPP4	NM_001935	1.66E-02	5.60927	CL up vs DD
SMC4	NM_005496	0.00E+00	5.58937	CL up vs DD
ARHGAP18	NM_033515	1.25E-35	5.54417	CL up vs DD
LAMA4	NM_001105206	0.00E+00	5.5117	CL up vs DD
CENPE	NM_001813	0.00E+00	5.47133	CL up vs DD
TBK1	NM_013254	1.59E-08	5.45296	CL up vs DD
VIT	NM_053276	3.19E-10	5.41436	CL up vs DD

DIAPH3	NM_001042517	2.92E-13	5.40822	CL up vs DD
GOLGA4	NM_002078	8.31E-37	5.40775	CL up vs DD
SLC6A15	NM_182767	5.30E-04	5.39557	CL up vs DD
GPNMB	NM_001005340	1.76E-11	5.39506	CL up vs DD
PVRL3	NM_015480	1.43E-03	5.38217	CL up vs DD
MCM8	NM_032485	4.97E-12	5.34564	CL up vs DD
ATAD2	NM_014109	0.00E+00	5.33692	CL up vs DD
RPAP3	NM_024604	1.45E-02	5.28476	CL up vs DD
G2E3	NM_017769	2.16E-05	5.26008	CL up vs DD
SMC3	NM_005445	3.63E-20	5.23897	CL up vs DD
GRIA3	NM_007325	4.95E-14	5.22698	CL up vs DD
ZWILCH	NR_003105	1.44E-07	5.19662	CL up vs DD
ROCK2	NM_004850	6.90E-41	5.18801	CL up vs DD
NUSAP1	NM_016359	1.40E-05	5.16089	CL up vs DD
C14orf106	NM_018353	1.04E-19	5.16001	CL up vs DD
ESF1	NM_016649	2.60E-12	5.15027	CL up vs DD
TMTC3	NM_181783	7.11E-23	5.14067	CL up vs DD
MPHOSPH9	NM_022782	3.17E-07	5.12705	CL up vs DD
ETV1	NM_004956	2.94E-12	5.12656	CL up vs DD
ARHGAP12	NM_018287	1.53E-36	5.12294	CL up vs DD
OSBPL8	NM_020841	7.32E-36	5.09649	CL up vs DD
TTC37	NM_014639	3.81E-22	5.08268	CL up vs DD
FAP	NM_004460	2.16E-10	5.06304	CL up vs DD
RALGPS2	NM_152663	1.78E-16	5.04682	CL up vs DD
SKAP2	NM_003930	5.06E-21	5.04242	CL up vs DD
MARCH7	NM_022826	3.77E-06	5.00717	CL up vs DD
FGF5	NM_004464	5.20E-05	5.00416	CL up vs DD
REV3L	NM_002912	0.00E+00	5.0009	CL up vs DD
CENPI	NM_006733	5.87E-09	4.99907	CL up vs DD
ABCA6	NM_080284	7.33E-10	4.99088	CL up vs DD
COLEC12	NM_130386	8.25E-09	4.99047	CL up vs DD
SGIP1	NM_032291	0.00E+00	4.97805	CL up vs DD
DTL	NM_016448	4.05E-10	4.97688	CL up vs DD
SGOL2	NM_152524	2.51E-13	4.97102	CL up vs DD
JMJD1C	NM_032776	2.11E-08	4.96039	CL up vs DD
SMC6	NM_001142286	8.15E-23	4.95395	CL up vs DD
SLK	NM_014720	0.00E+00	4.93229	CL up vs DD
ZEB1	NM_030751	5.24E-10	4.92331	CL up vs DD
C10orf118	NM_018017	1.11E-08	4.91646	CL up vs DD
PIK3R1	NM_181523	5.02E-25	4.8926	CL up vs DD
DNAJC13	NM_015268	5.31E-04	4.858	CL up vs DD
MAP4K5	NM_198794	0.00E+00	4.84898	CL up vs DD
CCNA2	NM_001237	4.00E-10	4.81353	CL up vs DD
HERC4	NM_022079	0.00E+00	4.81063	CL up vs DD
PLK4	NM_014264	5.08E-17	4.79872	CL up vs DD
CLEC2B	NM_005127	6.24E-03	4.79756	CL up vs DD
PUS7L	NM_001098615	9.04E-14	4.76577	CL up vs DD
SNX2	NM_003100	1.18E-04	4.75214	CL up vs DD
PRC1	NM_003981	7.94E-16	4.74323	CL up vs DD
RANBP2	NM_006267	1.99E-33	4.73475	CL up vs DD
TRIP11	NM_004239	5.17E-10	4.71639	CL up vs DD
BUB1	NM_004336	2.62E-14	4.71177	CL up vs DD
BUB1B	NM_001211	4.92E-28	4.67039	CL up vs DD
APC	NM_001127511	1.41E-11	4.66966	CL up vs DD
LUC7L3	NM_016424	6.18E-14	4.65946	CL up vs DD
TGFBR3	NM_003243	4.03E-13	4.64352	CL up vs DD
BAZ1A	NM_013448	0.00E+00	4.62951	CL up vs DD
DOCK11	NM_144658	7.72E-08	4.62909	CL up vs DD
ATP6V1C1	NM_001695	8.56E-05	4.60917	CL up vs DD
HSD17B14	NM_016246	3.19E-14	4.60149	CL up vs DD
HMGCS1	NM_001098272	2.08E-06	4.59412	CL up vs DD
SCML1	NM_001037540	1.69E-08	4.59305	CL up vs DD
DCBLD2	NM_080927	0.00E+00	4.56306	CL up vs DD
OPA1	NM_130837	6.39E-31	4.5541	CL up vs DD
SUZ12	NM_015355	1.41E-05	4.48974	CL up vs DD
PPP1R12A	NM_002480	1.35E-26	4.48136	CL up vs DD
NAE1	NM_001018159	7.67E-25	4.47752	CL up vs DD
TPR	NM_003292	0.00E+00	4.47672	CL up vs DD
THOC2	NM_001081550	3.35E-17	4.47508	CL up vs DD
MPHOSPH6	NM_005792	3.86E-05	4.47095	CL up vs DD
EIF5B	NM_015904	1.53E-34	4.46208	CL up vs DD
KIAA1033	NM_015275	1.25E-02	4.46202	CL up vs DD
CD36	NM_001001548	2.34E-14	4.44826	CL up vs DD
ATP13A3	NM_024524	3.22E-07	4.4451	CL up vs DD
USP1	NM_003368	4.39E-18	4.41957	CL up vs DD
ITGA4	NM_000885	6.89E-38	4.3984	CL up vs DD
UPF2	NM_080599	4.98E-12	4.38588	CL up vs DD
STAG2	NM_001042750	6.14E-30	4.36998	CL up vs DD
ARID4A	NM_002892	1.36E-19	4.36447	CL up vs DD

CEP290	NM_025114	0.00E+00	4.35727	CL up vs DD
CHEK1	NM_001114122	2.37E-12	4.34776	CL up vs DD
POLK	NM_016218	1.75E-17	4.34473	CL up vs DD
ADAM10	NM_001110	1.70E-37	4.34271	CL up vs DD
CKAP2L	NM_152515	2.59E-06	4.33918	CL up vs DD
GCNT4	NM_016591	3.86E-02	4.31757	CL up vs DD
TFAP2C	NM_003222	3.96E-17	4.29001	CL up vs DD
RASA2	NM_006506	3.80E-14	4.28858	CL up vs DD
KCNQ5	NM_001160133	2.63E-16	4.27646	CL up vs DD
RND3	NM_005168	8.40E-08	4.276	CL up vs DD
ITGA6	NM_000210	4.30E-22	4.27503	CL up vs DD
SLTM	NM_024755	2.55E-06	4.27024	CL up vs DD
PCM1	NM_006197	1.47E-25	4.26146	CL up vs DD
ZNHIT6	NM_017953	3.48E-14	4.25363	CL up vs DD
KNTC1	NM_014708	7.63E-34	4.22375	CL up vs DD
C12orf48	NM_017915	8.54E-09	4.22238	CL up vs DD
CLSPN	NM_022111	2.80E-21	4.2182	CL up vs DD
FZD6	NM_003506	2.98E-39	4.18611	CL up vs DD
MMS22L	NM_198468	3.60E-18	4.18333	CL up vs DD
SGOL1	NM_001012410	3.05E-04	4.17794	CL up vs DD
STXBP3	NM_007269	4.09E-13	4.17377	CL up vs DD
GCC2	NM_181453	1.02E-17	4.17253	CL up vs DD
TOP2B	NM_001068	1.75E-14	4.16753	CL up vs DD
KIF4A	NM_012310	4.57E-03	4.16479	CL up vs DD
CDKN3	NM_005192	2.46E-06	4.16078	CL up vs DD
GLIPR1	NM_006851	2.49E-06	4.15643	CL up vs DD
SHOC2	NM_007373	3.02E-07	4.15138	CL up vs DD
XG	NM_001141919	6.83E-05	4.13891	CL up vs DD
ATAD5	NM_024857	6.33E-17	4.11977	CL up vs DD
AURKA	NM_198433	2.12E-08	4.11386	CL up vs DD
ADK	NM_006721	4.41E-13	4.11336	CL up vs DD
NEXN	NM_144573	2.12E-02	4.10913	CL up vs DD
CCNB2	NM_004701	8.12E-05	4.08661	CL up vs DD
MASTL	NM_001172303	1.39E-02	4.0658	CL up vs DD
STS	NM_000351	2.13E-37	4.04596	CL up vs DD
CCNB1	NM_031966	8.12E-16	4.04222	CL up vs DD
SELENBP1	NM_003944	4.26E-16	4.03869	CL up vs DD
MUDENG	NM_018229	1.31E-02	4.03652	CL up vs DD
SFRS18	NM_032870	7.60E-08	4.03064	CL up vs DD
C10orf12	BC024315	1.45E-03	4.02606	CL up vs DD
GEN1	NM_182625	1.37E-17	4.02442	CL up vs DD
RNF219	NM_024546	2.97E-03	4.01599	CL up vs DD
LGR4	NM_018490	3.45E-41	4.00826	CL up vs DD
PKN2	NM_006256	1.75E-10	4.00509	CL up vs DD
ATP11C	NM_173694	1.03E-17	3.98655	CL up vs DD
PCF11	NM_015885	2.28E-19	3.93257	CL up vs DD
TOPBP1	NM_007027	7.07E-16	3.92117	CL up vs DD
SRSF2IP	NM_004719	9.33E-05	3.91764	CL up vs DD
SAMD9L	NM_152703	4.47E-10	3.91486	CL up vs DD
DIS3	NM_014953	1.02E-07	3.91152	CL up vs DD
CP110	NM_014711	5.37E-09	3.89985	CL up vs DD
IL6ST	NM_002184	1.75E-04	3.89619	CL up vs DD
DZIP3	NM_014648	1.70E-06	3.89375	CL up vs DD
RMI1	NM_024945	4.31E-10	3.89301	CL up vs DD
USP47	NM_017944	2.18E-27	3.88641	CL up vs DD
SREK1	NM_139168	8.08E-18	3.8846	CL up vs DD
CCDC55	NM_032141	1.99E-02	3.88354	CL up vs DD
PRLR	NM_000949	3.26E-16	3.87438	CL up vs DD
ZFYVE16	NM_001105251	1.21E-16	3.87358	CL up vs DD
EPB41L3	NM_012307	0.00E+00	3.86747	CL up vs DD
C12orf75	NM_001145199	1.63E-12	3.86265	CL up vs DD
DNTTIP2	NM_014597	5.18E-06	3.85644	CL up vs DD
JAK2	NM_004972	1.79E-36	3.84984	CL up vs DD
MYO5A	NM_000259	5.69E-40	3.84959	CL up vs DD
C9orf102	NM_001010895	1.03E-06	3.84685	CL up vs DD
CLDN11	NM_005602	3.46E-08	3.84553	CL up vs DD
MAN2A1	NM_002372	0.00E+00	3.84552	CL up vs DD
CCDC82	NM_024725	1.54E-17	3.84018	CL up vs DD
CAB39L	NM_030925	4.72E-03	3.82051	CL up vs DD
C12orf4	NM_020374	6.71E-03	3.82029	CL up vs DD
NPAT	NM_002519	4.34E-06	3.81284	CL up vs DD
DMXL2	NM_001174116	0.00E+00	3.80965	CL up vs DD
C5orf42	BC144069	0.00E+00	3.78993	CL up vs DD
RFC3	NM_002915	9.89E-11	3.78829	CL up vs DD
RAB11FIP2	NM_014904	4.84E-09	3.78523	CL up vs DD
SAMD9	NM_017654	6.81E-08	3.77858	CL up vs DD
TRPM7	NM_017672	4.93E-39	3.77282	CL up vs DD
CCDC14	NM_022757	6.39E-10	3.77171	CL up vs DD
SSX2IP	NM_001166417	1.29E-36	3.7667	CL up vs DD

C11orf41	NM_012194	5.67E-03	3.76117	CL up vs DD
ZNF267	NM_003414	7.43E-04	3.75413	CL up vs DD
NAA15	NM_057175	6.55E-32	3.7489	CL up vs DD
DIAPH2	NM_007309	9.61E-26	3.74654	CL up vs DD
NAV3	NM_014903	9.88E-25	3.74125	CL up vs DD
USP16	NM_006447	1.06E-10	3.73759	CL up vs DD
BIRC2	NM_001166	1.83E-24	3.73735	CL up vs DD
MLF1IP	NM_024629	9.30E-17	3.71742	CL up vs DD
ZIC1	NM_003412	4.65E-05	3.70989	CL up vs DD
FANCM	NM_020937	6.49E-04	3.70943	CL up vs DD
KIAA0586	NM_014749	7.86E-34	3.69246	CL up vs DD
FAR1	NM_032228	5.59E-20	3.69106	CL up vs DD
CHD1	NM_001270	1.64E-16	3.6901	CL up vs DD
FAM177A1	NM_001079519	6.15E-06	3.68704	CL up vs DD
ASPN	NM_017680	1.51E-06	3.68702	CL up vs DD
EVI2B	NM_006495	3.58E-02	3.68488	CL up vs DD
ATP2B1	NM_001001323	1.01E-17	3.66077	CL up vs DD
PLEKHA5	NM_019012	2.89E-34	3.65825	CL up vs DD
CDK17	NM_001170464	1.16E-20	3.65242	CL up vs DD
DOCK10	NM_014689	5.92E-17	3.64965	CL up vs DD
NKTR	NM_005385	2.31E-21	3.64407	CL up vs DD
FAM111A	NM_001142520	7.94E-13	3.6423	CL up vs DD
HMGCR	NM_000859	1.90E-05	3.63318	CL up vs DD
SGK3	NM_013257	4.11E-17	3.63223	CL up vs DD
RBL1	NM_002895	7.28E-28	3.63217	CL up vs DD
CHD9	NM_025134	5.55E-39	3.62769	CL up vs DD
HAUS6	NM_017645	3.30E-02	3.62566	CL up vs DD
BBS7	NM_176824	1.15E-13	3.62317	CL up vs DD
CACNA2D1	NM_000722	4.81E-26	3.62253	CL up vs DD
ARFGEF1	NM_006421	0.00E+00	3.61924	CL up vs DD
GNG2	NM_053064	4.96E-02	3.61585	CL up vs DD
PHIP	NM_017934	2.76E-39	3.61291	CL up vs DD
CHN1	NM_001822	2.11E-21	3.61252	CL up vs DD
SNX16	NM_022133	6.10E-05	3.60717	CL up vs DD
DLD	NM_000108	2.02E-11	3.6067	CL up vs DD
BLZF1	NM_003666	3.12E-05	3.59914	CL up vs DD
FSD1L	NM_207647	5.87E-06	3.59774	CL up vs DD
NBEAL1	NM_001114132	2.54E-05	3.58928	CL up vs DD
NBN	NM_002485	1.04E-19	3.5878	CL up vs DD
CDCA2	NM_152562	1.21E-27	3.58298	CL up vs DD
RBM25	NM_021239	4.06E-09	3.5788	CL up vs DD
RFX8	NM_001145664	1.15E-10	3.57836	CL up vs DD
PIBF1	NM_006346	3.10E-07	3.56977	CL up vs DD
LRRC2	NM_024512	1.10E-04	3.56195	CL up vs DD
SKA3	NM_145061	8.30E-14	3.55727	CL up vs DD
DYNLT3	NM_006520	1.85E-02	3.55598	CL up vs DD
PRPF4B	NM_003913	1.23E-11	3.55588	CL up vs DD
TTC14	NM_001042601	3.20E-23	3.55549	CL up vs DD
CKAP5	NM_001008938	6.97E-27	3.54252	CL up vs DD
EXOC5	NM_006544	1.17E-10	3.53978	CL up vs DD
GNPTAB	NM_024312	1.05E-37	3.53373	CL up vs DD
PIK3R3	NM_003629	9.56E-06	3.53049	CL up vs DD
ZBTB41	NM_194314	1.24E-02	3.52811	CL up vs DD
CUL5	NM_003478	2.26E-24	3.52769	CL up vs DD
ECHDC1	NM_001002030	1.97E-02	3.52363	CL up vs DD
FAM164A	NM_016010	2.71E-03	3.51801	CL up vs DD
PHF3	NM_015153	6.35E-05	3.51351	CL up vs DD
NCEH1	NM_001146276	4.48E-14	3.51196	CL up vs DD
PLXNC1	NM_005761	5.13E-12	3.50427	CL up vs DD
KRR1	NM_007043	1.47E-03	3.49781	CL up vs DD
BDP1	NM_018429	1.51E-36	3.4959	CL up vs DD
FAM72D	AB096683	5.11E-11	3.49284	CL up vs DD
RB1	NM_000321	3.96E-18	3.49	CL up vs DD
OSBPL1A	NM_080597	0.00E+00	3.48595	CL up vs DD
ARHGAP24	NM_001025616	2.43E-13	3.48024	CL up vs DD
IFT74	NM_025103	2.17E-06	3.47017	CL up vs DD
TMOD2	NM_014548	5.69E-04	3.47011	CL up vs DD
BMPER	NM_133468	2.09E-24	3.46196	CL up vs DD
ANO4	NM_178826	2.10E-39	3.46174	CL up vs DD
MALAT1	NR_002819	1.15E-15	3.46111	CL up vs DD
RAD50	NM_005732	7.76E-28	3.46097	CL up vs DD
HEXB	NM_000521	4.15E-27	3.45776	CL up vs DD
TMEM135	NM_022918	1.10E-07	3.45218	CL up vs DD
MRE11A	NM_005591	1.28E-05	3.45029	CL up vs DD
ZFC3H1	NM_144982	1.55E-39	3.4437	CL up vs DD
GLCE	NM_015554	1.22E-08	3.43669	CL up vs DD
VRK2	NM_001130483	3.96E-21	3.43641	CL up vs DD
STIL	NM_001048166	2.15E-15	3.43618	CL up vs DD
LTN1	NM_015565	2.87E-30	3.43223	CL up vs DD

ZNF195	NM_001130520	8.91E-03	3.43188	CL up vs DD
PLCB4	NM_001172646	4.21E-07	3.42691	CL up vs DD
CEP97	NM_024548	2.68E-14	3.42669	CL up vs DD
NAA25	NM_024953	3.48E-15	3.42353	CL up vs DD
ASAH1	NM_177924	0.00E+00	3.41648	CL up vs DD
FBXO5	NM_012177	1.04E-04	3.41548	CL up vs DD
AGL	NM_000028	1.04E-39	3.41361	CL up vs DD
CCDC46	NM_145036	3.78E-12	3.411	CL up vs DD
PHLDA1	NM_007350	1.31E-21	3.40513	CL up vs DD
MIER1	NM_020948	8.24E-05	3.39812	CL up vs DD
GOLGB1	NM_004487	4.91E-26	3.39652	CL up vs DD
PRKG1	NM_001098512	2.30E-19	3.39512	CL up vs DD
BAALC	NM_024812	1.45E-13	3.38293	CL up vs DD
CENPJ	NM_018451	1.61E-08	3.36934	CL up vs DD
LIN7C	NM_018362	8.45E-04	3.35823	CL up vs DD
SLIT2	NM_004787	5.79E-16	3.35794	CL up vs DD
UCHL3	NM_006002	2.06E-05	3.35736	CL up vs DD
NLGN1	NM_014932	1.43E-07	3.35609	CL up vs DD
PCDH18	NM_019035	9.15E-10	3.35232	CL up vs DD
NEK1	NM_012224	1.93E-24	3.34979	CL up vs DD
ODF2L	NM_001184765	1.26E-10	3.3428	CL up vs DD
MALT1	NM_006785	0.00E+00	3.34213	CL up vs DD
BRCA2	NM_000059	5.72E-11	3.33183	CL up vs DD
BCAP29	NM_018844	1.10E-03	3.32814	CL up vs DD
ATM	NM_000051	5.68E-18	3.32722	CL up vs DD
ASAP1	NM_018482	1.08E-27	3.32594	CL up vs DD
RSRC1	NM_016625	1.12E-03	3.32396	CL up vs DD
FGD4	NM_139241	5.43E-16	3.31722	CL up vs DD
ANKRD12	NM_015208	0.00E+00	3.31686	CL up vs DD
ACADSB	NM_001609	8.35E-05	3.31398	CL up vs DD
C5orf51	NM_175921	1.28E-17	3.31025	CL up vs DD
VPS26A	NM_004896	2.59E-18	3.30914	CL up vs DD
DHX29	NM_019030	3.63E-12	3.30643	CL up vs DD
BOD1L	NM_148894	1.38E-14	3.3038	CL up vs DD
RIF1	NM_018151	1.87E-10	3.30194	CL up vs DD
ACSL3	NM_004457	1.48E-09	3.29628	CL up vs DD
NOL8	NR_024020	1.75E-08	3.28308	CL up vs DD
PEX3	NM_003630	5.49E-08	3.28003	CL up vs DD
THBD	NM_000361	1.19E-12	3.27789	CL up vs DD
IFT80	NM_001190241	1.50E-02	3.27739	CL up vs DD
VPS13B	NM_017890	0.00E+00	3.27721	CL up vs DD
SFRP1	NM_003012	2.18E-08	3.27397	CL up vs DD
ACAT1	NM_000019	1.46E-10	3.27226	CL up vs DD
UBL3	NM_007106	4.65E-03	3.2633	CL up vs DD
PGAP1	NM_024989	8.16E-16	3.2626	CL up vs DD
EIF3A	NM_003750	3.48E-39	3.25798	CL up vs DD
KIAA0020	NM_014878	4.12E-09	3.25108	CL up vs DD
EXOC1	NM_001024924	4.40E-19	3.23903	CL up vs DD
AKAP11	NM_016248	2.18E-13	3.22838	CL up vs DD
MYO6	NM_004999	4.40E-16	3.22815	CL up vs DD
SRSF11	NM_004768	5.51E-12	3.22614	CL up vs DD
SOAT1	NM_003101	1.42E-04	3.2241	CL up vs DD
SMARCAD1	NM_001128429	7.43E-15	3.22144	CL up vs DD
EHBP1	NM_015252	1.07E-08	3.21081	CL up vs DD
AHR	NM_001621	1.74E-17	3.21004	CL up vs DD
CCDC18	NM_206886	1.91E-04	3.20919	CL up vs DD
BBS10	NM_024685	2.44E-02	3.20635	CL up vs DD
ZNF83	NM_001105549	5.28E-03	3.20604	CL up vs DD
XRN1	NM_019001	1.41E-24	3.20175	CL up vs DD
RNF152	NM_173557	1.99E-05	3.20102	CL up vs DD
CHUK	NM_001278	5.15E-03	3.19957	CL up vs DD
GOLIM4	NM_014498	3.63E-12	3.19565	CL up vs DD
SMC5	NM_015110	3.45E-41	3.1934	CL up vs DD
MANEA	NM_024641	3.55E-04	3.19275	CL up vs DD
PAMR1	NM_015430	1.13E-23	3.19164	CL up vs DD
NIPBL	NM_015384	1.06E-36	3.19104	CL up vs DD
RPS6KA3	NM_004586	5.27E-07	3.19021	CL up vs DD
TWSG1	NM_020648	3.94E-06	3.18892	CL up vs DD
EPB41L2	NM_001431	3.50E-06	3.18781	CL up vs DD
ORC3	NM_181837	8.34E-04	3.18545	CL up vs DD
RABEP1	NM_004703	1.99E-28	3.18442	CL up vs DD
RASA1	NM_002890	6.80E-26	3.1771	CL up vs DD
CSE1L	NM_001316	7.38E-17	3.17263	CL up vs DD
MYO9A	NM_006901	1.06E-13	3.17245	CL up vs DD
KIAA1468	NM_020854	2.54E-03	3.16693	CL up vs DD
ZNF638	NM_014497	6.68E-39	3.15538	CL up vs DD
SCFD1	NM_016106	4.78E-09	3.15042	CL up vs DD
UTRN	NM_007124	0.00E+00	3.14949	CL up vs DD
USP8	NM_001128611	4.76E-13	3.14476	CL up vs DD

NEDD4	NM_006154	1.16E-08	3.13774	CL up vs DD
KIF3A	NM_007054	1.35E-04	3.1367	CL up vs DD
CLGN	NM_001130675	1.22E-06	3.12956	CL up vs DD
QPCT	NM_012413	8.52E-08	3.12869	CL up vs DD
NIN	NM_020921	0.00E+00	3.12821	CL up vs DD
C14orf135	NM_022495	2.20E-03	3.12247	CL up vs DD
KIAA0196	NM_014846	1.03E-20	3.1204	CL up vs DD
STK3	NM_006281	1.02E-06	3.12015	CL up vs DD
LIFR	NM_002310	5.30E-13	3.11853	CL up vs DD
TMF1	NM_007114	4.37E-03	3.11781	CL up vs DD
DMXL1	NM_005509	9.61E-20	3.11769	CL up vs DD
TLR3	NM_003265	4.64E-05	3.11703	CL up vs DD
RBM41	NM_018301	1.43E-06	3.11449	CL up vs DD
HAUS3	NM_024511	1.46E-17	3.11098	CL up vs DD
CDC27	NM_001114091	5.35E-04	3.10588	CL up vs DD
SOCS4	NM_199421	3.18E-07	3.10544	CL up vs DD
MAP4K3	NM_003618	1.08E-28	3.1048	CL up vs DD
SCYL2	NM_017988	7.41E-04	3.10397	CL up vs DD
CTSS	NM_004079	4.69E-14	3.1002	CL up vs DD
PAPOLA	NM_032632	1.35E-16	3.0988	CL up vs DD
UTP20	NM_014503	0.00E+00	3.09872	CL up vs DD
ZNF644	NM_201269	1.42E-10	3.09706	CL up vs DD
VRK1	NM_003384	1.03E-03	3.09545	CL up vs DD
SLC30A9	NM_006345	4.52E-15	3.08481	CL up vs DD
TRIM24	NM_015905	8.73E-35	3.08316	CL up vs DD
OSTF1	NM_012383	1.30E-02	3.08232	CL up vs DD
RICTOR	NM_152756	3.99E-24	3.08152	CL up vs DD
UBA6	NM_018227	2.89E-14	3.07441	CL up vs DD
DOCK7	NM_033407	1.89E-15	3.07431	CL up vs DD
VEZT	NM_017599	1.25E-05	3.07429	CL up vs DD
CYLD	NM_015247	9.56E-18	3.073	CL up vs DD
SLC7A8	NM_012244	6.47E-07	3.07291	CL up vs DD
CUL2	NM_003591	4.38E-16	3.07254	CL up vs DD
TPP2	NM_003291	0.00E+00	3.0718	CL up vs DD
KIAA1841	NM_001129993	7.74E-21	3.0697	CL up vs DD
CIT	NM_007174	0.00E+00	3.06837	CL up vs DD
PIK3CA	NM_006218	1.50E-05	3.06611	CL up vs DD
METAP2	NM_006838	3.03E-02	3.06102	CL up vs DD
GXYLT1	NM_173601	1.40E-11	3.0541	CL up vs DD
RCBTB1	NM_018191	2.32E-14	3.04266	CL up vs DD
EDNRA	NM_001957	7.81E-07	3.04044	CL up vs DD
CLK4	NM_020666	5.24E-05	3.03482	CL up vs DD
HERC3	NM_014606	2.90E-21	3.03377	CL up vs DD
SPAG9	NM_001130528	5.14E-35	3.03298	CL up vs DD
NUP107	NM_020401	9.26E-09	3.03201	CL up vs DD
POLE2	NM_002692	1.27E-10	3.03086	CL up vs DD
CTNNAL1	NM_003798	4.80E-23	3.02884	CL up vs DD
ATG2B	NM_018036	5.47E-19	3.02629	CL up vs DD
NT5E	NM_002526	1.46E-04	3.01939	CL up vs DD
PRTFDC1	NM_020200	1.19E-22	3.01863	CL up vs DD
ELK3	NM_005230	2.52E-04	3.01759	CL up vs DD
PLCB1	NM_182734	3.23E-20	3.01181	CL up vs DD
ERI1	NM_153332	3.40E-08	3.00858	CL up vs DD
PI4K2B	NM_018323	2.08E-23	3.00512	CL up vs DD
BIVM	NM_017693	2.91E-24	3.00309	CL up vs DD
LNPEP	NM_005575	1.38E-29	3.00135	CL up vs DD
SRSF5	NM_001039465	7.78E-17	3.00074	CL up vs DD
AHI1	NM_001134831	5.65E-28	2.99973	CL up vs DD
MEIS1	NM_002398	2.83E-12	2.99727	CL up vs DD
CCAR1	NM_018237	5.27E-21	2.99419	CL up vs DD
UTP15	NM_032175	8.93E-07	2.99228	CL up vs DD
USPL1	NM_005800	2.99E-06	2.98928	CL up vs DD
UBR3	NM_172070	5.57E-04	2.98902	CL up vs DD
ASCC3	NM_006828	1.23E-06	2.98661	CL up vs DD
SASS6	NM_194292	6.24E-07	2.98522	CL up vs DD
RNF182	NM_001165032	5.51E-07	2.98197	CL up vs DD
RBBP8	NM_002894	1.01E-10	2.97904	CL up vs DD
LAMP2	NM_002294	9.72E-13	2.97899	CL up vs DD
RASSF8	NM_007211	5.89E-03	2.97791	CL up vs DD
NCAPG2	NM_017760	2.94E-06	2.97657	CL up vs DD
BAT2L2	NM_015172	2.83E-28	2.97647	CL up vs DD
FAM13B	NM_016603	2.92E-24	2.9728	CL up vs DD
CTSL1	NM_001912	5.12E-09	2.97079	CL up vs DD
BAZ2B	NM_013450	6.94E-10	2.97037	CL up vs DD
MSH2	NM_000251	1.70E-13	2.96903	CL up vs DD
ERCC5	NM_000123	4.90E-17	2.96901	CL up vs DD
SENP7	NM_020654	2.13E-19	2.96721	CL up vs DD
MORC3	NM_015358	9.57E-17	2.96633	CL up vs DD
DOPEY1	NM_015018	5.25E-17	2.96143	CL up vs DD

XPO1	NM_003400	2.59E-14	2.95986	CL up vs DD
ELTD1	NM_022159	1.70E-02	2.95939	CL up vs DD
HMGN3	NM_004242	2.92E-08	2.957	CL up vs DD
PRPF18	NM_003675	3.08E-02	2.95446	CL up vs DD
AKAP9	NM_005751	0.00E+00	2.95258	CL up vs DD
SF3B1	NM_012433	1.75E-22	2.94837	CL up vs DD
BMP2K	NM_198892	2.73E-28	2.9455	CL up vs DD
FXR1	NM_001013439	2.75E-12	2.94032	CL up vs DD
SENP6	NM_015571	7.64E-13	2.94027	CL up vs DD
PDP1	NM_001161778	2.39E-12	2.93492	CL up vs DD
USP25	NM_013396	3.87E-26	2.93123	CL up vs DD
SETX	NM_015046	2.89E-33	2.9306	CL up vs DD
SNX13	NM_015132	3.17E-28	2.92702	CL up vs DD
SPAG5	NM_006461	4.76E-06	2.9265	CL up vs DD
CD2AP	NM_012120	4.90E-19	2.92284	CL up vs DD
RUFY2	NM_017987	5.68E-09	2.92279	CL up vs DD
ACAT2	NM_005891	5.09E-07	2.91895	CL up vs DD
MPP5	NM_022474	2.62E-04	2.91809	CL up vs DD
BRMS1L	NM_032352	2.78E-12	2.91552	CL up vs DD
LMNB1	NM_005573	5.39E-11	2.91459	CL up vs DD
UACA	NM_018003	1.49E-31	2.91288	CL up vs DD
FPGT	NM_003838	2.29E-07	2.91236	CL up vs DD
CWF19L2	NM_152434	8.20E-04	2.91163	CL up vs DD
PTPN13	NM_080683	0.00E+00	2.91095	CL up vs DD
FAM178A	NM_018121	1.85E-28	2.90947	CL up vs DD
EDEM3	NM_025191	9.44E-16	2.90947	CL up vs DD
SBNO1	NM_001167856	4.55E-14	2.90901	CL up vs DD
SOS2	NM_006939	6.81E-09	2.90783	CL up vs DD
ABCA5	NM_018672	7.75E-19	2.90739	CL up vs DD
C14orf145	NM_152446	2.55E-02	2.90351	CL up vs DD
ASPH	NM_004318	2.41E-15	2.90319	CL up vs DD
DDX58	NM_014314	6.02E-18	2.90232	CL up vs DD
SEC62	NM_003262	2.75E-17	2.90074	CL up vs DD
EXO1	NM_130398	6.90E-14	2.89936	CL up vs DD
IDI1	NM_004508	2.53E-20	2.89823	CL up vs DD
GNPDA2	NM_138335	4.28E-05	2.89738	CL up vs DD
LDLR	NM_000527	3.74E-28	2.89381	CL up vs DD
MTIF2	NM_002453	7.41E-15	2.8917	CL up vs DD
NPC2	NM_006432	1.35E-03	2.89168	CL up vs DD
KIF15	NM_020242	5.03E-06	2.89157	CL up vs DD
MET	NM_001127500	3.75E-20	2.89073	CL up vs DD
HLTF	NM_003071	6.70E-16	2.89019	CL up vs DD
TBC1D15	NM_022771	9.15E-15	2.88978	CL up vs DD
PTGER2	NM_000956	8.99E-07	2.8885	CL up vs DD
DENND4C	NM_017925	4.25E-03	2.88778	CL up vs DD
SC5DL	NM_006918	8.95E-03	2.8869	CL up vs DD
TTLL7	NM_024686	1.87E-22	2.88639	CL up vs DD
TRAPPC8	NM_014939	6.90E-41	2.88513	CL up vs DD
TRIP13	NM_004237	3.09E-08	2.88358	CL up vs DD
DHX36	NM_020865	4.10E-18	2.88069	CL up vs DD
USP34	NM_014709	6.84E-18	2.87753	CL up vs DD
CLK1	NR_027856	1.27E-05	2.8696	CL up vs DD
CFL2	NM_138638	5.85E-16	2.86258	CL up vs DD
GLMN	NM_053274	2.19E-04	2.86227	CL up vs DD
KIAA1598	NM_001127211	2.95E-32	2.85996	CL up vs DD
PLK1	NM_005030	6.40E-04	2.85955	CL up vs DD
PTBP2	NM_021190	2.09E-14	2.85867	CL up vs DD
SULF1	NM_001128205	3.40E-20	2.85643	CL up vs DD
RAB23	NM_016277	4.80E-07	2.855	CL up vs DD
TARDBP	NM_007375	1.90E-17	2.85452	CL up vs DD
MLL5	NM_182931	3.21E-36	2.85342	CL up vs DD
VBP1	NM_003372	4.52E-04	2.85327	CL up vs DD
VPS13A	NM_033305	1.59E-19	2.85312	CL up vs DD
ZNF280C	NM_017666	1.38E-07	2.84946	CL up vs DD
NR1D2	NM_005126	1.09E-02	2.84933	CL up vs DD
TXNDC9	NM_005783	1.99E-06	2.84536	CL up vs DD
CPEB2	NM_182485	2.54E-19	2.84522	CL up vs DD
GMFB	NM_004124	4.90E-05	2.84392	CL up vs DD
MTBP	NM_022045	9.44E-14	2.8437	CL up vs DD
METTL14	NM_020961	3.73E-13	2.83507	CL up vs DD
AIMP1	NM_004757	6.91E-04	2.82926	CL up vs DD
XPO4	NM_022459	1.09E-05	2.82896	CL up vs DD
C4orf21	NM_018392	1.73E-24	2.82798	CL up vs DD
C5orf30	BC009203	2.20E-02	2.82451	CL up vs DD
MAPK6	NM_002748	1.16E-12	2.82207	CL up vs DD
CCDC112	NM_001040440	1.59E-05	2.82163	CL up vs DD
DDX46	NM_014829	1.39E-33	2.82072	CL up vs DD
GPD2	NM_001083112	3.68E-22	2.81885	CL up vs DD
QSER1	NM_001076786	1.30E-19	2.81871	CL up vs DD

BPTF	NM_004459	1.84E-14	2.81296	CL up vs DD
TMEM171	NM_173490	5.27E-10	2.81278	CL up vs DD
RSRC2	NR_036435	1.68E-05	2.80992	CL up vs DD
CHM	NM_000390	2.12E-14	2.80833	CL up vs DD
MEF2C	NM_002397	1.30E-19	2.80648	CL up vs DD
MLLT10	NM_004641	1.78E-25	2.79539	CL up vs DD
DTWD1	NM_020234	5.34E-04	2.79398	CL up vs DD
FNDC3A	NM_001079673	9.43E-04	2.79284	CL up vs DD
SLMAP	NM_007159	4.13E-17	2.78956	CL up vs DD
PHF20L1	NM_016018	9.72E-25	2.7866	CL up vs DD
LYST	NM_000081	4.24E-31	2.78509	CL up vs DD
SP100	NM_003113	3.57E-17	2.78456	CL up vs DD
CPD	NM_001304	7.76E-39	2.78398	CL up vs DD
THOC1	NM_005131	1.57E-12	2.78349	CL up vs DD
KIF2C	NM_006845	2.69E-15	2.78308	CL up vs DD
OXTR	NM_000916	2.18E-12	2.78182	CL up vs DD
TIA1	NM_022173	1.25E-07	2.78136	CL up vs DD
ZNF449	NM_152695	7.15E-09	2.78108	CL up vs DD
EXOSC9	NM_001034194	5.19E-24	2.77795	CL up vs DD
TMEFF1	NM_003692	1.09E-13	2.77681	CL up vs DD
ABCE1	NM_002940	5.37E-06	2.77473	CL up vs DD
USP24	NM_015306	2.26E-08	2.77453	CL up vs DD
CHURC1	NM_145165	4.93E-03	2.7692	CL up vs DD
C1orf27	NM_017847	1.28E-03	2.76812	CL up vs DD
CNTLN	NM_017738	3.13E-07	2.76761	CL up vs DD
ZNF280D	NM_017661	1.35E-07	2.76669	CL up vs DD
PHTF2	NM_001127358	6.28E-19	2.76598	CL up vs DD
LRRCC1	NM_033402	4.66E-10	2.76514	CL up vs DD
NAV2	NM_182964	9.01E-28	2.76176	CL up vs DD
SGCD	NM_000337	1.08E-18	2.75428	CL up vs DD
ZNF300P1	NR_026867	2.37E-04	2.75159	CL up vs DD
PRKD3	NM_005813	1.35E-04	2.74993	CL up vs DD
ATG4C	NM_032852	2.81E-02	2.74791	CL up vs DD
OXCT1	NM_000436	4.86E-19	2.74364	CL up vs DD
AMD1	NM_001634	9.07E-04	2.7429	CL up vs DD
ARGLU1	NM_018011	7.07E-26	2.73657	CL up vs DD
UBR1	NM_174916	2.09E-19	2.73492	CL up vs DD
KDELC2	NM_153705	5.81E-12	2.73303	CL up vs DD
FBN2	NM_001999	1.34E-19	2.7328	CL up vs DD
DPM1	NM_003859	2.65E-03	2.73027	CL up vs DD
FOXN2	NM_002158	1.06E-04	2.72874	CL up vs DD
PCYOX1	NM_016297	1.14E-04	2.72871	CL up vs DD
TAOK3	NM_016281	3.96E-12	2.72801	CL up vs DD
SETD4	NM_017438	1.81E-08	2.72611	CL up vs DD
PPP1CC	NM_002710	3.76E-05	2.72571	CL up vs DD
WHSC1L1	NM_023034	5.56E-30	2.72465	CL up vs DD
MGST1	NM_145791	4.92E-06	2.7225	CL up vs DD
IKBIP	NM_153687	4.59E-05	2.71849	CL up vs DD
CAMSAP1L1	NM_203459	5.32E-10	2.7157	CL up vs DD
CSTF3	NM_001326	3.35E-06	2.71459	CL up vs DD
ITFG1	NM_030790	1.41E-08	2.71398	CL up vs DD
CDC73	NM_024529	2.55E-19	2.71365	CL up vs DD
SLC36A4	NM_152313	1.06E-09	2.70783	CL up vs DD
GALNT7	NM_017423	1.66E-16	2.70723	CL up vs DD
GBP1	NM_002053	2.51E-03	2.70328	CL up vs DD
SPG20	NM_001142295	1.19E-21	2.70311	CL up vs DD
ALKBH8	NM_138775	7.60E-05	2.70309	CL up vs DD
RAD21	NM_006265	5.52E-09	2.70282	CL up vs DD
SRBD1	NM_018079	8.49E-13	2.70111	CL up vs DD
APLP2	NM_001642	9.09E-35	2.70067	CL up vs DD
BMS1	NM_014753	3.13E-06	2.6998	CL up vs DD
GGNBP2	NM_024835	4.71E-15	2.69899	CL up vs DD
PRKAR2B	NM_002736	3.44E-26	2.69772	CL up vs DD
ZFP106	NM_022473	4.37E-04	2.6975	CL up vs DD
NDUFA5	NM_005000	4.24E-02	2.69527	CL up vs DD
INPP4B	NM_003866	7.13E-14	2.6928	CL up vs DD
ESCO1	NM_052911	1.05E-05	2.69264	CL up vs DD
TMEM38B	NM_018112	1.92E-09	2.68915	CL up vs DD
VPS41	NM_014396	1.12E-14	2.68831	CL up vs DD
ADD3	NM_016824	9.69E-08	2.68775	CL up vs DD
CTR9	NM_014633	1.04E-24	2.68741	CL up vs DD
PBX3	NM_006195	3.64E-12	2.68735	CL up vs DD
CPNE8	NM_153634	9.42E-13	2.68503	CL up vs DD
TYMS	NM_001071	2.71E-08	2.68402	CL up vs DD
C13orf34	NM_024808	6.58E-09	2.68022	CL up vs DD
BLM	NM_000057	1.92E-07	2.67965	CL up vs DD
ANKRD26	NM_014915	2.70E-14	2.67908	CL up vs DD
GPN3	NM_001164372	7.92E-03	2.67616	CL up vs DD
RB1CC1	NM_014781	5.96E-27	2.67555	CL up vs DD

C11orf82	NM_145018	1.08E-04	2.67514	CL up vs DD
NFAT5	NM_138714	1.95E-39	2.67508	CL up vs DD
KRIT1	NM_194455	6.20E-35	2.67254	CL up vs DD
CXorf23	NM_198279	3.43E-03	2.67225	CL up vs DD
SWAP70	NM_015055	1.28E-02	2.67217	CL up vs DD
GALNTL2	NM_054110	1.68E-07	2.66664	CL up vs DD
NCAPH	NM_015341	1.31E-05	2.66619	CL up vs DD
USP9X	NM_001039590	4.30E-27	2.65978	CL up vs DD
DDX1	NM_004939	9.77E-38	2.65885	CL up vs DD
ZNF385D	NM_024697	3.17E-11	2.65683	CL up vs DD
ZNF302	NM_018443	1.59E-08	2.655	CL up vs DD
NEIL3	NM_018248	1.08E-05	2.65341	CL up vs DD
LRPPRC	NM_133259	0.00E+00	2.65092	CL up vs DD
IQGAP1	NM_003870	0.00E+00	2.64916	CL up vs DD
DCN	NM_001920	1.09E-04	2.64546	CL up vs DD
ALPK2	NM_052947	2.22E-15	2.64217	CL up vs DD
RRAGC	NM_022157	7.05E-28	2.64112	CL up vs DD
ARSK	NM_198150	3.29E-11	2.63848	CL up vs DD
RFC1	NM_002913	2.64E-12	2.63844	CL up vs DD
PRPF38B	NM_018061	5.86E-30	2.63753	CL up vs DD
PIGK	NM_005482	5.33E-18	2.63656	CL up vs DD
FAM179B	NM_015091	2.63E-23	2.63646	CL up vs DD
ZZZ3	NM_015534	4.50E-11	2.63618	CL up vs DD
KAT2B	NM_003884	1.72E-11	2.63505	CL up vs DD
PON2	NM_000305	4.48E-19	2.63262	CL up vs DD
NAPB	NM_022080	2.32E-10	2.63176	CL up vs DD
NMD3	NM_015938	3.49E-08	2.63147	CL up vs DD
PRUNE2	NM_015225	1.67E-04	2.63137	CL up vs DD
FAM126A	NM_032581	5.22E-18	2.63059	CL up vs DD
CCDC41	NM_016122	8.91E-11	2.62982	CL up vs DD
SRFBP1	NM_152546	1.12E-11	2.62834	CL up vs DD
ITGA8	NM_003638	1.84E-09	2.62787	CL up vs DD
STARD5	NM_181900	2.10E-05	2.6276	CL up vs DD
ACER3	NM_018367	2.52E-02	2.62513	CL up vs DD
ZRANB2	NM_005455	1.62E-03	2.62485	CL up vs DD
CEP110	NM_007018	7.04E-18	2.62275	CL up vs DD
IFI30	NM_006332	1.88E-03	2.62266	CL up vs DD
RBBP6	NM_006910	3.23E-39	2.61829	CL up vs DD
HJURP	NM_018410	4.07E-07	2.6182	CL up vs DD
ACAD11	NM_032169	4.94E-09	2.61562	CL up vs DD
KIAA1009	NM_014895	8.53E-10	2.61329	CL up vs DD
C6orf155	NR_026807	3.51E-03	2.61275	CL up vs DD
STRBP	NM_001171137	4.47E-08	2.61198	CL up vs DD
DBF4	NM_006716	3.01E-06	2.60186	CL up vs DD
TM9SF3	NM_020123	2.20E-10	2.60002	CL up vs DD
MACF1	NM_012090	0.00E+00	2.59859	CL up vs DD
FAM171B	NM_177454	8.04E-20	2.59848	CL up vs DD
CLIP1	NM_002956	0.00E+00	2.59648	CL up vs DD
MPDZ	NM_003829	4.71E-27	2.59175	CL up vs DD
HAT1	NM_003642	6.66E-07	2.58905	CL up vs DD
ANXA4	NM_001153	5.83E-13	2.58869	CL up vs DD
HSDL2	NM_032303	2.08E-22	2.58783	CL up vs DD
ZNF451	NM_001031623	1.36E-33	2.5878	CL up vs DD
CEP57	NM_014679	1.16E-10	2.58725	CL up vs DD
RAD17	NM_133338	1.13E-12	2.58659	CL up vs DD
STRN3	NM_001083893	1.05E-12	2.58466	CL up vs DD
API5	NR_024625	4.44E-02	2.58338	CL up vs DD
CLCN3	NM_173872	3.32E-03	2.58177	CL up vs DD
ATR	NM_001184	3.64E-32	2.58096	CL up vs DD
GINS1	NM_021067	1.06E-09	2.58044	CL up vs DD
RAPGEF6	NM_001164386	0.00E+00	2.57938	CL up vs DD
STAG1	NM_005862	4.18E-25	2.5768	CL up vs DD
INA	NM_032727	1.65E-15	2.57667	CL up vs DD
UHRF1BP1L	NM_015054	8.56E-23	2.57186	CL up vs DD
PSMD14	NM_005805	2.39E-07	2.57186	CL up vs DD
LEO1	NM_138792	2.27E-05	2.57071	CL up vs DD
ZNF33A	NM_006954	8.17E-03	2.56988	CL up vs DD
PAG1	NM_018440	2.34E-12	2.56968	CL up vs DD
UBA5	NM_024818	1.79E-15	2.56964	CL up vs DD
CAMK2D	NM_001221	9.44E-19	2.5641	CL up vs DD
SYNJ1	NM_003895	0.00E+00	2.56399	CL up vs DD
IFNAR1	NM_000629	7.72E-23	2.56369	CL up vs DD
ACADM	NM_000016	2.97E-09	2.56166	CL up vs DD
MAGOH	NM_002370	8.09E-03	2.55837	CL up vs DD
NKIRAS1	NM_020345	2.96E-07	2.55743	CL up vs DD
YTHDC2	NM_022828	4.79E-18	2.55623	CL up vs DD
MDH1	NM_005917	1.65E-09	2.55546	CL up vs DD
ANP32E	NM_030920	6.86E-03	2.55529	CL up vs DD
EPM2AIP1	NM_014805	7.71E-03	2.5526	CL up vs DD

VPS35	NM_018206	7.84E-12	2.55191	CL up vs DD
OFD1	NM_003611	3.76E-10	2.55171	CL up vs DD
MFN1	NM_033540	3.70E-11	2.55092	CL up vs DD
DDX21	NM_004728	1.26E-17	2.54981	CL up vs DD
DMTF1	NR_024549	2.81E-20	2.54931	CL up vs DD
FAM175A	NM_139076	1.51E-04	2.5486	CL up vs DD
RNF6	NM_005977	1.34E-22	2.54598	CL up vs DD
CDC7	NM_001134420	1.88E-05	2.54593	CL up vs DD
POLA1	NM_016937	7.49E-16	2.54464	CL up vs DD
FBXL3	NM_012158	5.11E-34	2.54318	CL up vs DD
PGM2L1	NM_173582	1.74E-18	2.54117	CL up vs DD
STMN1	NM_203401	6.30E-12	2.54091	CL up vs DD
KPNA3	NM_002267	1.10E-02	2.53803	CL up vs DD
PDS5B	NM_015032	2.14E-39	2.53726	CL up vs DD
ZWINT	NM_032997	5.10E-10	2.53705	CL up vs DD
PIGB	NM_004855	2.66E-14	2.53637	CL up vs DD
ACAP2	NM_012287	2.26E-28	2.53507	CL up vs DD
ANKMY2	NM_020319	8.80E-12	2.53306	CL up vs DD
MIOS	NM_019005	2.75E-09	2.52972	CL up vs DD
ATAD1	NM_032810	5.83E-08	2.5295	CL up vs DD
PDS5A	NM_001100399	0.00E+00	2.52738	CL up vs DD
CEP350	NM_014810	0.00E+00	2.52646	CL up vs DD
SKA1	NM_001039535	2.14E-05	2.52645	CL up vs DD
TAF1B	NM_005680	8.00E-05	2.52619	CL up vs DD
GALNT6	NM_007210	3.33E-26	2.52605	CL up vs DD
FAM76B	NM_144664	3.63E-14	2.52544	CL up vs DD
HERC1	NM_003922	1.28E-33	2.52526	CL up vs DD
LIG4	NM_002312	3.37E-03	2.52408	CL up vs DD
ATF7IP	NM_018179	6.36E-17	2.52366	CL up vs DD
FLRT2	NM_013231	8.10E-05	2.52172	CL up vs DD
ATP1B3	NM_001679	3.30E-03	2.51927	CL up vs DD
MPHOSPH10	NM_005791	8.54E-18	2.51919	CL up vs DD
SMG1	NM_015092	8.83E-14	2.51905	CL up vs DD
TBC1D8B	NM_017752	2.94E-10	2.51733	CL up vs DD
YAF2	NR_034000	3.99E-07	2.5153	CL up vs DD
FBXO3	NM_033406	4.96E-04	2.5139	CL up vs DD
C12orf11	NM_018164	2.84E-02	2.51011	CL up vs DD
PROS1	NM_000313	1.19E-09	2.50861	CL up vs DD
DOCK5	NM_024940	0.00E+00	2.50426	CL up vs DD
PTPN11	NM_002834	1.32E-08	2.5025	CL up vs DD
TAX1BP1	NM_006024	2.04E-15	2.5014	CL up vs DD
ANKRD29	NM_173505	3.27E-04	2.50139	CL up vs DD
SH3BGRL	NM_003022	6.54E-03	2.50121	CL up vs DD
NHLRC2	NM_198514	3.02E-02	2.50114	CL up vs DD
SYAP1	NM_032796	9.96E-09	2.50079	CL up vs DD
UBR5	NM_015902	0.00E+00	2.50051	CL up vs DD
LRRFIP2	NM_006309	5.07E-22	2.49968	CL up vs DD
KIAA1826	NM_032424	2.60E-05	2.49744	CL up vs DD
PHKB	NM_001031835	8.95E-37	2.49671	CL up vs DD
PTPLA	NM_014241	3.54E-13	2.49428	CL up vs DD
SCLT1	NM_144643	1.34E-22	2.49313	CL up vs DD
USP32	NM_032582	3.65E-27	2.49265	CL up vs DD
LYAR	NM_017816	9.61E-03	2.49194	CL up vs DD
SSH2	NM_033389	1.06E-02	2.4917	CL up vs DD
TMOD3	NM_014547	2.07E-03	2.49021	CL up vs DD
HSPB8	NM_014365	2.84E-02	2.48753	CL up vs DD
DNAJC10	NM_018981	3.42E-10	2.48726	CL up vs DD
RSU1	NM_012425	1.66E-14	2.48702	CL up vs DD
THOC7	NM_025075	1.12E-02	2.48375	CL up vs DD
ZNF254	NM_203282	3.22E-02	2.48291	CL up vs DD
CEP135	NM_025009	1.88E-06	2.48265	CL up vs DD
WNK1	NM_018979	0.00E+00	2.48207	CL up vs DD
NCL	NM_005381	6.55E-06	2.48092	CL up vs DD
TAOK1	NM_020791	9.29E-21	2.48007	CL up vs DD
MOBKL1A	NM_173468	5.84E-08	2.47949	CL up vs DD
NCOA3	NM_181659	6.60E-06	2.47699	CL up vs DD
UBE2V2	NM_003350	9.59E-03	2.47545	CL up vs DD
ARID4B	NM_016374	4.58E-15	2.47392	CL up vs DD
IDE	NM_004969	3.06E-16	2.4731	CL up vs DD
EZH2	NM_004456	4.02E-18	2.47306	CL up vs DD
RRM2B	NM_015713	5.79E-06	2.47229	CL up vs DD
COQ10B	NM_025147	3.75E-10	2.47222	CL up vs DD
GRIK2	NM_175768	8.64E-04	2.47124	CL up vs DD
SREK1IP1	NM_173829	3.36E-05	2.47083	CL up vs DD
UEVLD	NM_001040697	1.06E-35	2.47061	CL up vs DD
ANXA1	NM_000700	5.93E-03	2.47025	CL up vs DD
PLA2R1	NM_007366	1.81E-11	2.47	CL up vs DD
MAP3K5	NM_005923	0.00E+00	2.46657	CL up vs DD
SAMHD1	NM_015474	2.97E-19	2.46529	CL up vs DD

SLC4A4	NM_001098484	1.97E-12	2.46462	CL up vs DD
CD46	NM_002389	1.42E-17	2.46412	CL up vs DD
CCND1	NM_053056	3.71E-13	2.46252	CL up vs DD
RPGR	NM_000328	7.11E-33	2.46108	CL up vs DD
SMARCA1	NM_003069	5.33E-30	2.45425	CL up vs DD
HDAC9	NM_178423	1.10E-23	2.45284	CL up vs DD
MOSPD1	NM_019556	4.79E-06	2.45077	CL up vs DD
DICER1	NM_177438	3.06E-25	2.45074	CL up vs DD
NRD1	NM_002525	8.56E-27	2.44685	CL up vs DD
VCAN	NM_004385	1.25E-03	2.4466	CL up vs DD
HECTD1	NM_015382	1.93E-34	2.44423	CL up vs DD
ZNF420	NM_144689	2.05E-08	2.44356	CL up vs DD
GUF1	NM_021927	9.55E-03	2.44211	CL up vs DD
ANPEP	NM_001150	3.27E-15	2.43983	CL up vs DD
SRPX	NM_006307	2.47E-12	2.43961	CL up vs DD
ZDHHC21	NM_178566	5.73E-03	2.43829	CL up vs DD
PPP4R4	NM_058237	9.05E-21	2.43757	CL up vs DD
YTHDC1	NM_001031732	1.50E-16	2.43625	CL up vs DD
CSPP1	NM_024790	4.15E-04	2.4361	CL up vs DD
ZCCHC6	NM_024617	3.24E-09	2.4353	CL up vs DD
PSME4	NM_014614	3.05E-20	2.43376	CL up vs DD
SLC25A46	NM_138773	7.70E-15	2.43359	CL up vs DD
HNRNPA2B1	NM_031243	9.51E-23	2.43323	CL up vs DD
WDR76	NM_024908	6.92E-08	2.43277	CL up vs DD
XRCC4	NM_022550	3.44E-10	2.43265	CL up vs DD
PPM1B	NM_177968	1.34E-16	2.43226	CL up vs DD
WAPAL	NM_015045	3.54E-24	2.43072	CL up vs DD
ATP2C1	NM_014382	0.00E+00	2.43057	CL up vs DD
CTHRC1	NM_138455	2.43E-06	2.42843	CL up vs DD
FAM98A	NM_015475	2.92E-21	2.42762	CL up vs DD
MYOF	NM_013451	8.04E-28	2.427	CL up vs DD
NAA50	NM_025146	5.03E-03	2.4266	CL up vs DD
PHF6	NM_032458	3.73E-16	2.42595	CL up vs DD
GPBP1	NM_022913	3.25E-03	2.42472	CL up vs DD
ITGA1	NM_181501	7.29E-29	2.42406	CL up vs DD
DNMBP	NM_015221	1.34E-14	2.42379	CL up vs DD
KIAA1586	NM_020931	5.25E-08	2.42301	CL up vs DD
B3GALNT1	NM_001038628	6.21E-19	2.4218	CL up vs DD
IFIT5	NM_012420	1.89E-04	2.42108	CL up vs DD
ATP2B4	NM_001001396	0.00E+00	2.41999	CL up vs DD
SPRED1	NM_152594	2.41E-16	2.41786	CL up vs DD
SOS1	NM_005633	1.63E-07	2.41739	CL up vs DD
SMC1A	NM_006306	2.23E-31	2.41618	CL up vs DD
TMEM30A	NM_018247	7.61E-04	2.41615	CL up vs DD
METTL4	NM_022840	2.81E-15	2.41538	CL up vs DD
FBXO11	NM_001190274	1.16E-16	2.41465	CL up vs DD
XPA	NR_027302	1.45E-10	2.412	CL up vs DD
ALCAM	NM_001627	4.33E-18	2.41188	CL up vs DD
PNPT1	NM_033109	1.17E-05	2.41168	CL up vs DD
MKLN1	NM_001145354	1.37E-21	2.40813	CL up vs DD
RPS6KB1	NM_003161	2.66E-03	2.40679	CL up vs DD
RAD18	NM_020165	4.51E-20	2.40495	CL up vs DD
MTM1	NM_000252	2.13E-05	2.40466	CL up vs DD
HSPH1	NM_006644	5.21E-14	2.40213	CL up vs DD
SLC12A2	NM_001046	0.00E+00	2.40158	CL up vs DD
DENND2C	NM_198459	0.00E+00	2.39949	CL up vs DD
NARG2	NM_024611	4.64E-08	2.39854	CL up vs DD
ERBB2IP	NM_018695	2.76E-12	2.39754	CL up vs DD
LNX1	NM_001126328	1.01E-04	2.39264	CL up vs DD
ACSL4	NM_022977	3.05E-14	2.39247	CL up vs DD
UCHL5	NM_015984	8.07E-23	2.39155	CL up vs DD
SCAPER	NM_020843	1.57E-08	2.39148	CL up vs DD
AHSA2	NM_152392	5.72E-05	2.39058	CL up vs DD
ZNF84	NM_003428	2.68E-08	2.38934	CL up vs DD
DCTN6	NM_006571	2.85E-05	2.38873	CL up vs DD
LAMB1	NM_002291	2.22E-35	2.38844	CL up vs DD
ATP8B1	NM_005603	3.08E-34	2.38379	CL up vs DD
MEIS2	NM_172316	8.97E-27	2.38377	CL up vs DD
WDR19	NM_025132	2.49E-14	2.38144	CL up vs DD
PPWD1	NM_015342	8.37E-03	2.3807	CL up vs DD
TOPORS	NM_005802	3.27E-19	2.38035	CL up vs DD
KIAA0528	BC143878	5.97E-18	2.37917	CL up vs DD
MMP16	NM_005941	2.09E-04	2.37759	CL up vs DD
SLC38A4	NM_018018	5.23E-06	2.37341	CL up vs DD
ERI2	NM_001142725	1.17E-16	2.37308	CL up vs DD
NRP1	NM_003873	2.72E-09	2.3727	CL up vs DD
PITPNC1	NM_181671	5.00E-07	2.37183	CL up vs DD
NEDD1	NM_152905	5.01E-07	2.37155	CL up vs DD
HERC6	NM_017912	2.38E-19	2.36991	CL up vs DD

ORMDL1	NM_016467	2.94E-03	2.36969	CL up vs DD
SNRNP48	NM_152551	3.91E-03	2.36668	CL up vs DD
PRKG2	NM_006259	8.44E-13	2.36489	CL up vs DD
UVRAG	NM_003369	4.27E-04	2.3644	CL up vs DD
PRKAA1	NM_206907	1.03E-17	2.36438	CL up vs DD
C13orf27	NM_138779	1.02E-03	2.36342	CL up vs DD
PPHLN1	NM_016488	2.22E-11	2.36338	CL up vs DD
DEK	NM_003472	2.49E-07	2.36241	CL up vs DD
STX7	NM_003569	6.88E-11	2.36131	CL up vs DD
CALD1	NM_033138	2.68E-22	2.36104	CL up vs DD
NCAPD3	NM_015261	1.91E-20	2.35887	CL up vs DD
POLR3F	NM_006466	4.11E-04	2.35879	CL up vs DD
POT1	NM_015450	1.05E-05	2.35726	CL up vs DD
BOD1L	NM_148894	2.43E-12	2.35696	CL up vs DD
CCDC15	NM_025004	3.12E-06	2.35451	CL up vs DD
NF1	NM_001042492	1.17E-27	2.35445	CL up vs DD
WWP1	NM_007013	1.43E-19	2.35388	CL up vs DD
PHF11	NM_001040443	9.67E-08	2.35315	CL up vs DD
CABLES1	NM_001100619	1.01E-02	2.35099	CL up vs DD
UHMK1	NM_175866	5.25E-10	2.3501	CL up vs DD
OBFC2A	NM_001031716	9.30E-17	2.34996	CL up vs DD
CCDC47	NM_020198	1.34E-02	2.34902	CL up vs DD
MIER3	NM_152622	1.11E-06	2.34769	CL up vs DD
SCRN3	NM_024583	1.70E-07	2.34737	CL up vs DD
SERINC1	NM_020755	1.37E-03	2.34726	CL up vs DD
CAMK2N1	NM_018584	5.28E-10	2.34608	CL up vs DD
ZC3H7A	NM_014153	1.82E-07	2.34504	CL up vs DD
CDK12	NM_016507	4.09E-11	2.34499	CL up vs DD
WDR47	NM_001142550	9.62E-08	2.34396	CL up vs DD
PRKDC	NM_006904	0.00E+00	2.34282	CL up vs DD
TRIM23	NM_001656	4.19E-07	2.34252	CL up vs DD
MAP1B	NM_005909	1.48E-29	2.34216	CL up vs DD
STK17A	NM_004760	7.10E-08	2.341	CL up vs DD
CCBE1	NM_133459	2.71E-15	2.33923	CL up vs DD
NTNG1	NM_001113226	7.93E-08	2.33864	CL up vs DD
HOOK3	NM_032410	1.84E-30	2.33854	CL up vs DD
TRIM37	NM_015294	1.32E-13	2.33815	CL up vs DD
ANKRD28	NM_001195098	5.66E-25	2.33654	CL up vs DD
FIGNL1	NM_001042762	9.89E-06	2.33642	CL up vs DD
HECTD2	NM_182765	3.62E-23	2.3363	CL up vs DD
IGF2BP3	NM_006547	1.69E-08	2.33606	CL up vs DD
TTF1	NM_007344	3.00E-07	2.33471	CL up vs DD
SLC9A9	NM_173653	8.30E-06	2.33415	CL up vs DD
NPR3	NM_000908	2.46E-04	2.33149	CL up vs DD
TOP1	NM_003286	1.44E-04	2.32897	CL up vs DD
USO1	NM_003715	1.91E-31	2.32879	CL up vs DD
FBXO30	NM_032145	1.17E-13	2.32645	CL up vs DD
TAF2	NM_003184	3.17E-15	2.32625	CL up vs DD
PAPD4	NM_001114394	1.26E-11	2.32434	CL up vs DD
GRK5	NM_005308	1.33E-07	2.32432	CL up vs DD
EPC2	NM_015630	2.00E-02	2.32354	CL up vs DD
CD59	NM_203330	1.33E-06	2.32242	CL up vs DD
RIOK1	NM_031480	5.59E-03	2.32072	CL up vs DD
CAPRIN2	NM_001002259	1.51E-11	2.31989	CL up vs DD
WDR75	NM_032168	1.52E-07	2.31956	CL up vs DD
AP3B1	NM_003664	5.26E-05	2.3191	CL up vs DD
EMX2	NM_004098	7.42E-15	2.3189	CL up vs DD
TCF12	NM_207036	6.28E-39	2.3183	CL up vs DD
PLEK2	NM_016445	3.55E-04	2.3183	CL up vs DD
VPS54	NM_016516	3.05E-14	2.31756	CL up vs DD
CXorf57	NM_018015	2.88E-07	2.31717	CL up vs DD
IPO8	NM_006390	2.07E-04	2.31543	CL up vs DD
TLK1	NM_012290	1.15E-24	2.31312	CL up vs DD
PDGFRA	NM_006206	0.00E+00	2.31199	CL up vs DD
HIVEP2	NM_006734	1.46E-03	2.31154	CL up vs DD
UBXN4	NM_014607	3.34E-12	2.31068	CL up vs DD
SLC25A24	NM_213651	1.07E-13	2.31062	CL up vs DD
FER	NM_005246	1.74E-03	2.31054	CL up vs DD
ZC3H13	NM_015070	2.67E-17	2.30969	CL up vs DD
CCDC77	NM_032358	2.90E-11	2.30795	CL up vs DD
SMARCA5	NM_003601	3.55E-37	2.30651	CL up vs DD
ARHGAP5	NM_001030055	1.63E-15	2.30484	CL up vs DD
KIF13A	NM_022113	0.00E+00	2.30335	CL up vs DD
APAF1	NM_181861	5.13E-19	2.30226	CL up vs DD
ATL2	NM_022374	6.34E-03	2.30099	CL up vs DD
PBRM1	NM_018165	7.08E-31	2.29779	CL up vs DD
TMEM144	NM_018342	1.23E-03	2.29775	CL up vs DD
GNA13	NM_006572	1.60E-09	2.29378	CL up vs DD
RFC4	NM_002916	2.48E-07	2.29372	CL up vs DD

UTP11L	NM_016037	1.74E-07	2.29349	CL up vs DD
ZMYM2	NM_003453	2.45E-04	2.29316	CL up vs DD
EIF2AK2	NM_002759	3.97E-02	2.28992	CL up vs DD
RAB31	NM_006868	1.31E-05	2.28912	CL up vs DD
COG6	NR_026745	6.12E-07	2.28585	CL up vs DD
FASTKD1	NM_024622	3.20E-14	2.28356	CL up vs DD
NIPAL2	NM_024759	1.40E-11	2.2834	CL up vs DD
MCM4	NM_005914	1.56E-34	2.28221	CL up vs DD
LPCAT2	NM_017839	8.79E-03	2.28093	CL up vs DD
C3orf64	NM_173654	6.90E-13	2.28006	CL up vs DD
SDCBP	NM_005625	1.58E-05	2.27767	CL up vs DD
E2F7	NM_203394	3.31E-19	2.2768	CL up vs DD
INHBA	NM_002192	1.48E-02	2.2765	CL up vs DD
PRR16	NM_016644	7.29E-03	2.27645	CL up vs DD
NCALD	NM_001040624	5.74E-09	2.27429	CL up vs DD
GOLGA5	NM_005113	2.45E-02	2.27312	CL up vs DD
ZC3H15	NM_018471	1.20E-08	2.27215	CL up vs DD
AGTPBP1	NM_015239	4.59E-10	2.27095	CL up vs DD
HPS3	NM_032383	4.53E-33	2.26942	CL up vs DD
TDP2	NM_016614	4.96E-03	2.26919	CL up vs DD
NPHP3	NM_153240	0.00E+00	2.26814	CL up vs DD
CUL3	NM_003590	2.00E-08	2.26691	CL up vs DD
EIF5	NM_183004	3.91E-08	2.26679	CL up vs DD
RG9MTD1	NM_017819	7.77E-03	2.26633	CL up vs DD
KLHL9	NM_018847	2.60E-07	2.26588	CL up vs DD
TBC1D8	NM_001102426	8.74E-16	2.2657	CL up vs DD
UGGT2	NM_020121	0.00E+00	2.26471	CL up vs DD
ZMPSTE24	NM_005857	4.48E-13	2.2647	CL up vs DD
YME1L1	NM_139312	3.03E-05	2.26195	CL up vs DD
UGP2	NM_001001521	3.43E-14	2.26032	CL up vs DD
WRN	NM_000553	9.42E-07	2.25973	CL up vs DD
THUMPD1	NM_017736	3.42E-10	2.25925	CL up vs DD
SKOR1	NM_001031807	2.66E-15	2.25879	CL up vs DD
COL4A3BP	NM_005713	7.04E-31	2.25772	CL up vs DD
CASP8AP2	NM_012115	4.93E-14	2.25715	CL up vs DD
RP2	NM_006915	3.44E-05	2.25668	CL up vs DD
BIRC6	NM_016252	0.00E+00	2.2565	CL up vs DD
XRCC2	NM_005431	3.82E-03	2.25346	CL up vs DD
C15orf41	NM_001130010	1.79E-11	2.25206	CL up vs DD
EML4	NM_019063	5.62E-33	2.25142	CL up vs DD
SUV39H2	NM_001193424	9.60E-06	2.25142	CL up vs DD
C5orf41	NM_153607	7.28E-10	2.25065	CL up vs DD
LTBP1	NM_206943	0.00E+00	2.24953	CL up vs DD
ARL1	NM_001177	2.15E-07	2.24857	CL up vs DD
COPB1	NM_016451	8.62E-41	2.24805	CL up vs DD
RACGAP1	NM_013277	7.29E-09	2.24724	CL up vs DD
ZFP1	NM_153688	1.35E-09	2.24556	CL up vs DD
FAM82A1	NM_001170792	4.55E-14	2.24425	CL up vs DD
HNRNPH3	NM_012207	1.24E-09	2.24392	CL up vs DD
EIF2C4	NM_017629	2.15E-11	2.24391	CL up vs DD
CREBZF	NM_001039618	1.96E-16	2.2432	CL up vs DD
RBM26	NM_022118	4.99E-12	2.24303	CL up vs DD
LARP4	NM_052879	1.18E-04	2.24188	CL up vs DD
ALG11	NM_001004127	1.71E-10	2.23722	CL up vs DD
SYF2	NM_015484	3.33E-06	2.23324	CL up vs DD
TFRC	NM_003234	1.78E-14	2.23241	CL up vs DD
LBR	NM_002296	2.43E-10	2.23198	CL up vs DD
ADSS	NM_001126	1.93E-10	2.23172	CL up vs DD
ZNF326	NM_182976	2.28E-12	2.2279	CL up vs DD
FAM48A	NM_001014286	3.49E-15	2.22631	CL up vs DD
TMPO	NM_001032283	5.21E-06	2.22582	CL up vs DD
NUCB2	NM_005013	3.02E-09	2.2253	CL up vs DD
CDK6	NM_001259	4.41E-18	2.22363	CL up vs DD
CLTC	NM_004859	0.00E+00	2.22256	CL up vs DD
AP1AR	NM_018569	2.19E-09	2.22252	CL up vs DD
DDX52	NM_152300	3.94E-06	2.22126	CL up vs DD
BMI1	NM_005180	4.69E-11	2.22099	CL up vs DD
INTS6	NM_012141	9.34E-15	2.22028	CL up vs DD
FASTKD2	NM_001136194	1.83E-04	2.22018	CL up vs DD
SLC4A8	NM_001039960	0.00E+00	2.2193	CL up vs DD
CEP192	NM_032142	3.49E-35	2.21925	CL up vs DD
SLFN5	NM_144975	1.84E-06	2.21822	CL up vs DD
RCN2	NM_002902	5.32E-08	2.21466	CL up vs DD
SHC3	NM_016848	1.78E-07	2.21036	CL up vs DD
DENND4A	NM_001144823	7.75E-23	2.20988	CL up vs DD
ATG3	NM_022488	5.96E-07	2.20796	CL up vs DD
RAB8B	NM_016530	7.00E-08	2.20669	CL up vs DD
PIGN	NM_176787	1.57E-08	2.20495	CL up vs DD
KLF4	NM_004235	6.69E-03	2.20435	CL up vs DD

LCORL	NM_153686	5.41E-11	2.2041	CL up vs DD
MTF2	NM_007358	6.28E-07	2.20366	CL up vs DD
APPBP2	NM_006380	4.72E-18	2.20351	CL up vs DD
CCDC55	NM_032141	2.10E-12	2.20348	CL up vs DD
FANCB	NM_001018113	2.28E-08	2.20347	CL up vs DD
SECISBP2L	NM_001193489	1.22E-23	2.20164	CL up vs DD
PER3	NM_016831	6.81E-37	2.20125	CL up vs DD
TGFBR2	NM_001024847	6.81E-17	2.20066	CL up vs DD
RCAN2	NM_005822	8.57E-16	2.20066	CL up vs DD
ZBTB2	NM_020861	7.29E-04	2.19827	CL up vs DD
IFT81	NM_014055	1.17E-26	2.19436	CL up vs DD
ORC6	NM_014321	2.23E-08	2.19416	CL up vs DD
GNAI3	NM_006496	7.28E-04	2.19397	CL up vs DD
ETNK1	NM_018638	2.72E-13	2.19275	CL up vs DD
TRIM2	NM_015271	1.01E-13	2.19224	CL up vs DD
SRSF2	NM_003016	9.32E-09	2.19171	CL up vs DD
MAPKSP1	NM_021970	6.59E-04	2.18717	CL up vs DD
ZNF569	NM_152484	6.48E-06	2.18569	CL up vs DD
OXR1	NM_001198533	2.05E-10	2.18487	CL up vs DD
MON2	NM_015026	2.45E-24	2.17998	CL up vs DD
MKL2	NM_014048	6.42E-07	2.17918	CL up vs DD
ARMCX3	NM_016607	2.75E-17	2.17878	CL up vs DD
STRN	NM_003162	1.48E-12	2.17824	CL up vs DD
LDB2	NM_001130834	5.28E-04	2.17789	CL up vs DD
KIN	NM_012311	2.65E-03	2.17728	CL up vs DD
DPP8	NM_197960	1.37E-18	2.17534	CL up vs DD
SNX7	NR_033716	7.00E-03	2.17494	CL up vs DD
TRIM33	NM_015906	0.00E+00	2.17382	CL up vs DD
SYNE2	NM_182914	0.00E+00	2.17368	CL up vs DD
FAM190B	NM_018999	2.39E-19	2.17336	CL up vs DD
STARD4	NM_139164	1.51E-10	2.17024	CL up vs DD
AQR	NM_014691	4.35E-33	2.1701	CL up vs DD
ZCCHC14	NM_015144	3.38E-04	2.16886	CL up vs DD
HIPK3	NM_005734	1.15E-16	2.16877	CL up vs DD
PPP2R3C	NM_017917	1.08E-07	2.16812	CL up vs DD
INTS2	NR_026641	1.82E-22	2.16799	CL up vs DD
LAMC1	NM_002293	9.05E-12	2.16581	CL up vs DD
TBC1D23	NM_018309	7.67E-20	2.1657	CL up vs DD
C9orf72	NM_018325	1.93E-07	2.16475	CL up vs DD
DNAJC24	NM_181706	3.26E-03	2.16386	CL up vs DD
TNRC6A	NM_014494	8.94E-18	2.16359	CL up vs DD
MREG	NM_018000	6.40E-08	2.1632	CL up vs DD
GTPBP10	NM_033107	1.66E-04	2.16299	CL up vs DD
SGTB	NM_019072	3.52E-07	2.16216	CL up vs DD
LARP1B	NM_018078	2.10E-02	2.16121	CL up vs DD
FAM126B	NM_173822	1.50E-02	2.16083	CL up vs DD
CCBL2	NM_001008661	1.81E-02	2.15952	CL up vs DD
ZNF330	NM_014487	1.39E-11	2.1586	CL up vs DD
ERLEC1	NM_015701	4.67E-10	2.15853	CL up vs DD
PAN3	NM_175854	3.40E-31	2.1583	CL up vs DD
GTF2A1	NM_015859	6.23E-08	2.15751	CL up vs DD
SPTBN1	NM_003128	2.97E-23	2.15593	CL up vs DD
OSTM1	NM_014028	7.02E-15	2.15552	CL up vs DD
SLC35F5	NM_025181	0.00E+00	2.15538	CL up vs DD
LGALS3	NR_003225	5.84E-12	2.1553	CL up vs DD
MFSD1	NM_022736	1.36E-14	2.15512	CL up vs DD
CPEB4	NM_030627	1.11E-05	2.15492	CL up vs DD
MAN1A2	NM_006699	6.22E-18	2.15304	CL up vs DD
EID1	NM_014335	5.46E-11	2.15271	CL up vs DD
SCYL3	ENST00000367772	2.83E-03	2.15224	CL up vs DD
ARMCX1	NM_016608	8.87E-07	2.15142	CL up vs DD
ABI1	NM_005470	1.48E-09	2.14991	CL up vs DD
BRWD1	NM_033656	6.59E-28	2.1486	CL up vs DD
C16orf45	NM_033201	6.41E-24	2.14822	CL up vs DD
ZMYM5	NM_001142684	1.91E-03	2.14745	CL up vs DD
SLFN12	NM_018042	4.30E-02	2.1465	CL up vs DD
SLMO2	NM_016045	4.28E-03	2.14396	CL up vs DD
B3GNT2	NM_006577	4.48E-04	2.14386	CL up vs DD
LRCH2	NM_020871	1.73E-11	2.14269	CL up vs DD
VTA1	NM_016485	1.81E-03	2.14248	CL up vs DD
ALMS1	NM_015120	4.82E-22	2.14214	CL up vs DD
DCK	NM_000788	4.06E-17	2.14114	CL up vs DD
AASS	NM_005763	2.91E-33	2.14106	CL up vs DD
RAB5A	NM_004162	4.02E-10	2.14104	CL up vs DD
LIN54	NM_194282	6.87E-11	2.14095	CL up vs DD
MND1	NM_032117	1.21E-09	2.13999	CL up vs DD
LOC100133106	AY358216	3.31E-03	2.13767	CL up vs DD
SYTL2	NM_206927	5.43E-27	2.13707	CL up vs DD
TOB1	NM_005749	2.87E-02	2.13587	CL up vs DD

DDX3X	NM_001356	5.67E-35	2.13344	CL up vs DD
MTMR6	NM_004685	1.44E-07	2.13066	CL up vs DD
ZEB2	NM_014795	8.62E-13	2.13026	CL up vs DD
SCPEP1	NM_021626	1.69E-14	2.12873	CL up vs DD
E2F8	NM_024680	3.39E-07	2.12433	CL up vs DD
USP33	NM_015017	3.60E-17	2.12325	CL up vs DD
VPS36	NM_016075	2.27E-02	2.12087	CL up vs DD
ZNF510	NM_014930	6.92E-07	2.12055	CL up vs DD
CAPZA2	NM_006136	9.42E-05	2.1202	CL up vs DD
SIRT1	NM_012238	8.79E-26	2.11934	CL up vs DD
BCCIP	NM_016567	6.86E-05	2.11913	CL up vs DD
TXLNG	NM_018360	1.76E-20	2.11769	CL up vs DD
SUCLG2	NM_003848	3.72E-02	2.11577	CL up vs DD
SLC25A12	NM_003705	1.52E-05	2.11537	CL up vs DD
NCK1	NM_006153	9.48E-07	2.11485	CL up vs DD
ARHGEF12	NM_015313	4.26E-12	2.11457	CL up vs DD
KIAA0922	NM_001131007	1.64E-29	2.1139	CL up vs DD
RGL1	NM_015149	2.20E-13	2.11323	CL up vs DD
YTHDF3	NM_152758	4.74E-03	2.11255	CL up vs DD
CAV2	NM_001233	3.25E-13	2.11252	CL up vs DD
BTAF1	NM_003972	1.06E-16	2.11224	CL up vs DD
RAB11A	NM_004663	3.69E-05	2.1113	CL up vs DD
EFHA1	NM_152726	4.13E-07	2.11096	CL up vs DD
C21orf45	NM_018944	1.19E-12	2.11028	CL up vs DD
C1orf9	NM_014283	7.34E-21	2.1095	CL up vs DD
OSBPL3	NM_015550	0.00E+00	2.10948	CL up vs DD
FAT4	NM_024582	1.54E-26	2.1093	CL up vs DD
PPAT	NM_002703	1.29E-11	2.10927	CL up vs DD
DSN1	NM_001145316	9.67E-20	2.10903	CL up vs DD
FRMD5	NM_032892	7.19E-11	2.10882	CL up vs DD
KRAS	NM_033360	1.76E-09	2.10845	CL up vs DD
ERCC6	NM_000124	1.17E-17	2.10843	CL up vs DD
NUP35	NM_138285	5.43E-06	2.10679	CL up vs DD
ZNF273	NR_003099	9.83E-03	2.10535	CL up vs DD
C6orf211	AK298490	5.97E-05	2.10437	CL up vs DD
PMPCB	NM_004279	4.46E-02	2.10434	CL up vs DD
BUB3	NM_004725	1.16E-06	2.10407	CL up vs DD
FGFR1OP2	NM_015633	5.38E-12	2.10245	CL up vs DD
TCERG1	NM_006706	5.63E-20	2.10222	CL up vs DD
BET1	NM_005868	3.41E-04	2.1016	CL up vs DD
RCBTB2	NM_001268	8.73E-06	2.0985	CL up vs DD
COL14A1	NM_021110	2.95E-07	2.0982	CL up vs DD
RNF19A	NM_183419	2.44E-17	2.0969	CL up vs DD
ACBD5	NM_145698	8.35E-15	2.09663	CL up vs DD
TMEM123	NM_052932	4.13E-18	2.09604	CL up vs DD
GTF2F2	NM_004128	6.15E-09	2.09548	CL up vs DD
TMEM55A	NM_018710	4.06E-03	2.09477	CL up vs DD
MTERFD3	NM_001033050	1.65E-08	2.09461	CL up vs DD
IRAK3	NM_007199	6.57E-04	2.09382	CL up vs DD
CCDC91	NM_018318	2.66E-06	2.09245	CL up vs DD
PLAT	NM_000930	1.01E-13	2.09205	CL up vs DD
ENY2	NR_036472	1.00E-04	2.0917	CL up vs DD
NEK3	NM_002498	2.63E-14	2.09142	CL up vs DD
WDR26	NM_025160	7.79E-05	2.08956	CL up vs DD
OSBPL11	NM_022776	1.98E-04	2.08781	CL up vs DD
SLC38A9	NM_173514	5.25E-10	2.0851	CL up vs DD
RAC2	NM_002872	7.46E-12	2.0849	CL up vs DD
TAB2	NM_015093	2.66E-08	2.08329	CL up vs DD
FOXM1	NM_202002	2.07E-09	2.08232	CL up vs DD
DDHD1	NM_001160148	4.53E-10	2.08224	CL up vs DD
EIF5A2	NM_020390	4.18E-02	2.08137	CL up vs DD
SNX14	NM_153816	5.49E-25	2.08121	CL up vs DD
IPO7	NM_006391	7.37E-03	2.08032	CL up vs DD
ANO3	NM_031418	6.60E-20	2.0798	CL up vs DD
CENPP	NM_001012267	5.72E-05	2.07876	CL up vs DD
HIVEP1	NM_002114	1.12E-16	2.07874	CL up vs DD
ZNF107	NM_016220	2.13E-03	2.07837	CL up vs DD
GABBR2	NM_005458	1.21E-33	2.07649	CL up vs DD
LRIG3	NM_153377	5.22E-11	2.07544	CL up vs DD
OTUD4	NM_001102653	4.55E-07	2.07516	CL up vs DD
RAD23B	NM_002874	4.14E-21	2.07508	CL up vs DD
TMEM97	NM_014573	2.71E-06	2.07412	CL up vs DD
RPP40	NM_006638	3.00E-02	2.07326	CL up vs DD
PSMA4	NM_002789	2.22E-03	2.07307	CL up vs DD
FUT8	NM_178155	2.51E-24	2.07215	CL up vs DD
RELN	NM_005045	4.55E-22	2.07055	CL up vs DD
CHMP2B	NM_014043	1.44E-10	2.0686	CL up vs DD
HELZ	NM_014877	1.91E-16	2.06829	CL up vs DD
GM2A	NM_000405	1.13E-04	2.06815	CL up vs DD

TIPIN	NM_017858	4.21E-03	2.0674	CL up vs DD
RCAN3	NM_013441	9.67E-12	2.06686	CL up vs DD
SCP2	NM_002979	1.76E-11	2.06585	CL up vs DD
LRP12	NM_013437	6.39E-10	2.06413	CL up vs DD
CCNL1	NM_020307	4.33E-35	2.06254	CL up vs DD
ARSJ	NM_024590	8.67E-16	2.06192	CL up vs DD
TIPARP	NM_015508	5.68E-12	2.06173	CL up vs DD
ATG4A	NM_052936	1.64E-08	2.06169	CL up vs DD
GMNN	NM_015895	2.90E-11	2.06166	CL up vs DD
WDFY1	NM_020830	3.86E-30	2.06011	CL up vs DD
COX11	NM_004375	1.29E-02	2.05934	CL up vs DD
KIF1B	NM_015074	6.07E-29	2.0588	CL up vs DD
SMAGP	NM_001033873	2.04E-07	2.05868	CL up vs DD
LPIN1	NM_145693	2.53E-11	2.05774	CL up vs DD
RNMT	NM_003799	5.08E-03	2.05771	CL up vs DD
CUL4B	NM_001079872	6.34E-22	2.0569	CL up vs DD
SLC44A1	NM_080546	7.86E-08	2.05641	CL up vs DD
RAD54B	NM_012415	6.91E-23	2.05635	CL up vs DD
C9orf41	BC034033	2.91E-18	2.0558	CL up vs DD
RABGAP1	NM_012197	2.80E-10	2.05393	CL up vs DD
SLC25A32	NM_030780	1.56E-16	2.0538	CL up vs DD
PSMC3IP	NM_016556	1.72E-09	2.05324	CL up vs DD
MCM10	NM_182751	2.30E-23	2.05305	CL up vs DD
UTP3	NM_020368	9.61E-04	2.05285	CL up vs DD
SETD2	NM_014159	1.61E-03	2.05209	CL up vs DD
ZNF776	NM_173632	9.64E-11	2.0508	CL up vs DD
HMGA2	NM_003483	1.62E-09	2.04937	CL up vs DD
N4BP2L2	NM_014887	3.15E-06	2.0489	CL up vs DD
CDC42BPA	NM_003607	6.55E-40	2.04852	CL up vs DD
SS18	NM_001007559	1.18E-06	2.04842	CL up vs DD
ABCD3	NM_002858	1.73E-21	2.04831	CL up vs DD
SVIL	NM_021738	4.52E-36	2.04794	CL up vs DD
SAAL1	NM_138421	3.03E-02	2.04617	CL up vs DD
C13orf1	NM_020456	1.08E-14	2.04596	CL up vs DD
CDC42EP3	NM_006449	1.89E-11	2.04559	CL up vs DD
MUT	NM_000255	4.24E-02	2.04553	CL up vs DD
PHYH	NM_006214	1.61E-06	2.04476	CL up vs DD
LRBA	NM_006726	1.28E-29	2.04365	CL up vs DD
LEPR	NM_002303	4.25E-13	2.04204	CL up vs DD
TMX3	NM_019022	6.72E-18	2.04186	CL up vs DD
TUBGCP5	NM_052903	1.38E-08	2.04154	CL up vs DD
RGMB	NM_001012761	1.27E-24	2.0414	CL up vs DD
KDM6A	NM_021140	1.39E-16	2.04134	CL up vs DD
PLRG1	NM_002669	9.32E-03	2.04132	CL up vs DD
RAB7A	NM_004637	1.73E-04	2.04084	CL up vs DD
EWSR1	NM_013986	2.39E-04	2.04055	CL up vs DD
FANCD2	NM_033084	5.03E-18	2.03818	CL up vs DD
PSMD1	NM_002807	5.49E-28	2.03693	CL up vs DD
NCAM2	NM_004540	8.99E-12	2.03634	CL up vs DD
MYST4	NM_012330	8.40E-06	2.03615	CL up vs DD
SLC38A6	NR_033344	2.19E-13	2.0355	CL up vs DD
PLDN	NM_012388	6.87E-11	2.035	CL up vs DD
GTF2H1	NM_001142307	7.14E-07	2.03496	CL up vs DD
PPP2R3A	NM_002718	3.45E-13	2.03327	CL up vs DD
ZNF350	NM_021632	1.94E-02	2.03216	CL up vs DD
RAB22A	NM_020673	6.17E-14	2.03152	CL up vs DD
KLF3	NM_016531	2.96E-06	2.02952	CL up vs DD
ITGB3	NM_000212	2.65E-04	2.02929	CL up vs DD
RAI14	NM_001145525	4.85E-15	2.0291	CL up vs DD
GIPC2	NM_017655	5.50E-13	2.02883	CL up vs DD
TMX1	NM_030755	6.41E-12	2.0282	CL up vs DD
ARIH1	NM_005744	1.53E-13	2.02804	CL up vs DD
FBLN5	NM_006329	1.81E-23	2.02752	CL up vs DD
ESD	NM_001984	5.45E-09	2.02712	CL up vs DD
CDC5L	NM_001253	3.85E-07	2.02666	CL up vs DD
IREB2	NM_004136	3.04E-10	2.02581	CL up vs DD
HIF1A	NM_001530	4.85E-09	2.0253	CL up vs DD
TNKS2	NM_025235	0.00E+00	2.02505	CL up vs DD
NCKAP1	NM_013436	2.47E-36	2.02459	CL up vs DD
SLC35E3	NM_018656	2.74E-08	2.02454	CL up vs DD
MDM1	NM_017440	2.73E-14	2.02326	CL up vs DD
MCCC1	NM_020166	3.31E-04	2.02124	CL up vs DD
RC3H2	NM_001100588	1.18E-10	2.02082	CL up vs DD
TCF19	NM_007109	9.84E-08	2.02045	CL up vs DD
FAM49B	BC017297	1.58E-11	2.02024	CL up vs DD
ZCRB1	NM_033114	1.24E-02	2.02001	CL up vs DD
PDCD10	NM_007217	1.59E-02	2.01819	CL up vs DD
UBR2	NM_015255	1.21E-03	2.01808	CL up vs DD
ASH1L	NM_018489	2.35E-16	2.01773	CL up vs DD

IFT88	NM_175605	5.44E-07	2.01771	CL up vs DD
EHHADH	NM_001966	1.21E-05	2.01656	CL up vs DD
QDPR	NM_000320	2.50E-07	2.01517	CL up vs DD
SLC20A1	NM_005415	1.38E-06	2.01507	CL up vs DD
POLQ	NM_199420	2.90E-30	2.01476	CL up vs DD
ANTXR2	NM_058172	3.62E-19	2.01468	CL up vs DD
ZDHHC13	NM_019028	8.03E-07	2.01439	CL up vs DD
VPS4B	NM_004869	2.74E-10	2.01342	CL up vs DD
CD44	NM_000610	2.50E-29	2.01327	CL up vs DD
UBE2W	NM_001001481	4.60E-03	2.01289	CL up vs DD
SUPT16H	NM_007192	9.90E-28	2.01277	CL up vs DD
MYNN	NM_001185118	2.51E-02	2.01182	CL up vs DD
ANGEL2	NM_144567	1.87E-06	2.0117	CL up vs DD
USP48	NM_032236	3.37E-15	2.01157	CL up vs DD
HMGXB4	NR_027780	1.29E-23	2.0103	CL up vs DD
SPG11	NM_025137	9.22E-29	2.00928	CL up vs DD
MPHOSPH8	NM_017520	4.18E-04	2.00801	CL up vs DD
KPNA4	NM_002268	2.73E-03	2.00677	CL up vs DD
TSNAX	NM_005999	1.75E-03	2.00583	CL up vs DD
C6orf174	NM_001012279	3.60E-02	2.00573	CL up vs DD
MLL3	NM_170606	0.00E+00	2.00449	CL up vs DD
NAA16	NM_024561	7.19E-11	2.00339	CL up vs DD
C2orf3	NM_003203	1.16E-17	2.00268	CL up vs DD
MYO1B	NM_001130158	4.87E-26	2.00237	CL up vs DD
GTSE1	NM_016426	7.09E-18	2.00167	CL up vs DD
ZNF354B	NM_058230	4.96E-07	2.0011	CL up vs DD