Article

Fibroblasts from the Human Skin Dermo-Hypodermal Junction are Distinct from Dermal Papillary and Reticular Fibroblasts and from Mesenchymal Stem Cells and Exhibit a Specific Molecular Profile Related to Extracellular Matrix Organization and Modeling

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Abstract: Human skin dermis contains fibroblast subpopulations in which characterization is crucial due to their roles in extracellular matrix (ECM) biology. This study investigates the properties of fibroblasts localized at the frontier of deep dermis and hypodermis, i.e., dermo-hypodermal junction fibroblasts (F-DHJ), which were compared to intermediate reticular dermis (Fr) and superficial papillary dermis (Fp) fibroblasts. F-DHJ differed from Fr and Fp cells in their wider potential for differentiation into mesodermal lineages and in their absence of contractility when integrated in a three-dimensional dermal equivalent. The transcriptomic profile of F-DHJ exhibited specificities in the expression of genes involved in ECM synthesis-processing and “tissue skeleton” organization. In accordance with transcriptome data, ECM proteins, notably Tenascin C, distributions differed between the reticular dermis and the dermo-hypodermal junction areas, which was documented in normal adult skin. Finally, genome-wide transcriptome profiling was used to evaluate the molecular proximity of F-DHJ with the two dermal fibroblast populations (Fp and Fr) and with the mesenchymal stem cells (MSCs) corresponding to five tissue origins (bone marrow, fat, amnion, chorion, and cord). This comparative analysis classified the three skin fibroblast types, including F-DHJ, as a clearly distinct group from the five MSC sample origins.

Keywords: human dermis; fibroblasts; extracellular matrix (ECM); dermo-hypodermal junction; papillary fibroblasts (Fp); reticular fibroblasts (Fr); Tenascin C (TNC); mesenchymal stem cells (MSCs)
1. Introduction

In human skin, interfollicular dermis is a heterogeneous tissue compartment, considering its fibroblast content and extracellular matrix (ECM) structure. Its segmentation into two biologically distinct territories (i.e., superficial papillary dermis and deeper reticular dermis) occurs during the embryonic development at 12 weeks of gestation in humans [1,2]. Major structural specificities of these dermal territories concern collagen reticulation and organization of the elastin network, which are dynamic characteristics in constant evolution during the intra-uterine and postnatal life (for review, see [3]).

Specificities of the different dermal territories also concern their fibroblast contents, in which characterization drives an increasing interest considering their widely expected functions in skin physiology. The existence of two dermal fibroblast populations, named papillary (Fp) and reticular (Fr) fibroblasts according to their dermal localization, was reported in human skin in the late seventies [4]. Since then, studies have been conducted to further explore their cellular properties [5] and molecular profiles [6,7]. Biological aspects that are attracting attention are the cellular and molecular changes that affect Fp and Fr cells through skin ageing [8,9].

Other fibroblast or fibroblast-like mesenchymal cell populations are present within the dermis, such as pericytes and telocytes. Pericytes appear in the fetal dermis at eight weeks of gestation in humans and acquire their mature characteristics at 21 weeks of gestation [10]. These cells contribute to the maintenance of capillary vessel integrity and may play a role in the maintenance of mesenchymal tissues in the contexts of homeostasis and/or wound healing [11]. In addition, pericytes may contribute to the niche that regulates the symmetrical versus asymmetrical division choice of epidermal keratinocyte precursors [12]. Telocytes possess an atypical fibroblast morphology characterized by long and slender moniliform cellular prolongations termed telopodes [13]. These cells serve as connecting devices, constructing homocellular junctions and connections with other cells types [14]. Telocytes are usually present at a low density (around 10 cells/mm²) [15]. These cells may participate in the stem cell niche, as shown in the intestine crypts [16]. Another described function of telocytes is the transmission of signals via atypical junctions [17] or extracellular vesicles [18], as reported in the heart. In the dermis, telocyte density augments with depth, together with the quantity of telopodes found in connection with endothelial cells, nerve endings, and hair follicle bulges [19]. Implications of telocytes in regeneration and wound healing is expected in skin but not fully demonstrated [19].

In the present study, we investigated the cellular and molecular properties of fibroblasts localized at the frontier of deep dermis and hypodermis, i.e., dermo-hypodermal junction fibroblasts (F-DHJ). Using parameters such as contractility, differentiation potential, and the supportive effect on epidermis reconstruction, we documented marked functional differences between F-DHJ and dermal (Fp and Fr) fibroblasts. At a molecular level, the study identified specific signatures in F-DHJ concerning the expression of genes involved in ECM synthesis-processing and “tissue skeleton” organization, which could explain structural properties of their tissue compartment. Finally, genome-wide transcriptome profiling was used to evaluate the molecular proximity of F-DHJ with the two dermal fibroblast populations (Fp and Fr) and the with mesenchymal stem cells (MSCs) corresponding to five tissue origins (bone marrow, fat, amnion, chorion, and cord). This approach identified skin fibroblasts and MSCs as distinct groups and will certainly contribute to the knowledge of the hierarchical clustering within the mesenchymal lineages.

2. Materials and Methods

2.1. Fibroblast Isolation and Culture

2.1.1. Human Skin Biopsy Collection

Full-thickness biopsies of human breasts and abdominal skin, collected from healthy subjects undergoing reconstructive or aesthetical surgery, were obtained from Icelltis (Toulouse, France);
Alphenyx (Marseille, France); and Biopredic (Saint-Grégoire, France) under the authorizations delivered by the French Ministry of Research with the approval of the French Ethical Committee. The written informed consent was obtained from all individuals. The tissue collection used in this study included 10 biopsies of breast skin (mammoplasties) with ages ranging between 18 and 65 years and 6 biopsies of abdominal skin (abdominoplasties) with ages between 42 and 51 years. A typical skin section showing the papillary, reticular, and dermo-hypodermal dermis regions is shown in Figure 1A.

F-DHJ hypodermis was gently removed from skin biopsies by dissection using clamps and scissors to preserve the junction between hypodermis and dermis. Then, the tissue area containing

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**Figure 1.** Skin localization and cellular morphology of papillary dermis fibroblasts (Fp), reticular dermis fibroblasts (Fr), and dermo-hypodermal junction (DHJ) fibroblasts. (A) Representation of the papillary dermis, reticular dermis, and dermo-hypodermal junction areas. A typical full-thickness skin section is shown, as well as schemes of the three areas of interest. (B) Photographs of skin pieces taken from the below side after fat tissue removal, showing the macroscopic aspect of the conjunctival junctions that connect the dermis to the hypodermis. (C) Cellular morphology of cultured Fp, Fr, and DHJ fibroblasts. In F-DHJ cultures, red arrows point to small tricuspid cells and white arrows to large cells with a visible trabecular cytoplasmic network.
the conjunctival junctions that connect the dermis to the hypodermis (Figure 1B) was harvested by dissection for extraction of fibroblasts from the demo-hypodermal junction (DHJ). Dissected pieces were checked under binocular loupe and selected according to the presence of both adipose tissue and conjunctival structures, validating their DHJ localization. F-DHJ were then extracted by tissue digestion with type II collagenase 0.2% (Gibco, France) for 2 h at 37 °C. Tissue dissociation was facilitated by 30 s of vortexing every 30 min.

2.1.2. Fp and Fr

After removing the epidermis by treatment with 2.4 U/mL dispase (Roche, Boulogne-Billancourt, France) for 16 h at 4°C and then mechanical dissection, papillary fibroblasts (Fp) were extracted by digestion of the tissue in type II collagenase 0.2% (Gibco, France) for 3 h at 37 °C. Tissue dissociation was facilitated by 30 s of vortexing every 30 min. Then, a second cut was performed on the noncut remaining part of the sample at a depth of 700 µm. This intermediate region of the dermis (depth between 300 and 700 µm) was not used for fibroblast extraction to avoid mixing papillary and reticular material. The deepest dermis slice (700 µm depth from skin surface and below) corresponded strictly to the reticular dermis and was used to extract the Fr fibroblast fraction by tissue digestion in type II collagenase 0.2% (Gibco, France) for 5 h at 37 °C. Tissue dissociation was facilitated by 30 s of vortexing every 30 min.

2.1.3. Bidimensional Mass Culture

Fp, Fr, and F-DHJ cells were cultured in similar conditions. Seeding density was 3800 cells/cm², and culture medium was composed of MEM supplemented with 10% FBS (PAN Biotech GmbH, Aidenbach, Germany); penicillin-streptomycin (20 U/mL) (Biochrom Ltd., Cambridge, UK); sodium pyruvate (Gibco, France); nonessential amino acids (Gibco, France); and glutamine (2 mM) (Invitrogen, Carlsbad, CA, USA). Cultures were incubated at 37 °C in a 90% humidified atmosphere containing 5% CO₂.

2.2. Mesenchymal Stem Cell (MSC) Isolation and Culture

All human samples were collected and handled in full respect of the Declaration of Helsinki.

2.2.1. BM-MSCs

Human bone marrow MSCs (BM-MSCs) were obtained from patients undergoing routine total hip replacement surgery in Percy Hospital (Clamart, France) after written informed consent. As previously reported [20], spongious bone fragments were mixed in phosphate-buffered saline (PBS, PAN-Dominique Dutcher, Issy-les-Moulineaux, France); 1 mM EDTA (Prolabo-VWR, Paris, France); ACD-A; and 0.5% human serum-albumin (HAS, LFB). After 20 min of settling, the supernatant was collected, centrifuged at 480 g for 10 min, and filtered (70 µm). Bone marrow mononuclear cells (BM-MNCs) were counted using an automated cell analyzer (Sysmex, Villepinte, France)

2.2.2. Ad-MSCs

Human adipose tissue MSCs (Ad-MSCs) were isolated from fat obtained after liposuction surgery in Percy Hospital (Clamart, France) after written informed consent. Fat was washed by an addition of PBS supplemented with 1 µg/mL ciprofloxacin (Panpharma, Luitré, France). After centrifugation at 815 g for 2 min, the washing solution (containing blood, lipids, and adrenalin added before surgery) was discarded. This operation was repeated until washing solution was clear. Fat tissue was then enzymatically digested in 0.075% type I collagenase (75 mg/100 mL fat) for 45 min at 37 °C with agitation each 15 min. Digested fat was then centrifuged at 200 g for 5 min. The supernatant that contained lipids and adipocytes was discarded. The pellet that contained the stoma-vascular fraction was washed three times with α-MEM (Cliniscience, Nanterre, France) and filtered (70 µm). Cell
numeration was performed after sample treatment with Zap Oglobin lytic reagent (Beckman Coulter, Villepinte, France).

2.2.3. Amnion, Chorion, and Umbilical Cord MSCs

Perinatal tissues were obtained from full-term deliveries after maternal written informed consent (Hôpital d’Instruction des Armées Bégin, Saint-Mande). As previously reported [20], samples of placental membranes (amnion and chorion) and umbilical cords were incubated in an antibiotic and antifungal solution for 90 min at room temperature and then cut into pieces. Amnion and chorion 2 cm² pieces were digested in PBS containing 0.1% type IV collagenase (Thermo-Fisher for Life Technologies, Waltham, MA, USA) and 2.4 U/mL grade II dispase (Roche, Boulogne-Billancourt, France) for 90 min at 37 °C and then in PBS containing 0.025% trypsin-EDTA (Thermo-Fisher for Life Technologies, Waltham, MA, USA) for 30 min at 37 °C. Umbilical cord 2 cm-long pieces were cut into smaller formats (around 1–2 mm³) for digestion in PBS containing 300 U/mL type I collagenase (Thermo-Fisher for Life Technologies, Waltham, MA, USA) and 1 mg/mL hyaluronidase (Calbiochem-Merck, Fontenay sous Bois, France) for 60 min at 37 °C and then in PBS containing 0.025% trypsin-EDTA (Thermo-Fisher for Life Technologies, Waltham, MA, USA) for 30 min at 37 °C. Cell samples were filtered through a 100 µm cell strainer (BD Biosciences, Le Pont de Claix, France) and then centrifuged at 200 × g for 10 min.

Cells were counted in a Malassez chamber using the trypan blue exclusion method.

2.2.4. Bidimensional Mass Cultures

Samples from the different tissue origins were cultured in the same conditions. Freshly-extracted cells were seeded at a density of 30000 cells/cm² in a medium composed of α-MEM (Clinisciences, Nanterre, France) supplemented with 0.01 mg/mL ciprofloxacin; 2 U/mL heparin (Choay-Sanofi Aventis); and 5% platelet lysate (obtained from a platelet apheresis collection performed at the ‘Centre de Transfusion Sanguine des Armées’, Clamart). The medium was renewed 3 times a week. Cultures were trypsinized when reaching the stage of 80% confluence (trypsin-EDTA, Thermo-Fisher for Life Technologies, Waltham, MA, USA). Then, MSC subcultures were initiated at a density of 4,000 cells/cm². For storage, MSC samples were frozen in α-MEM (Clinisciences, Nanterre, France) supplemented with 10% human serum-albumin and 10% DMSO (Sigma-Aldrich, St Louis, MO, USA).

2.3. Colony Assay

Cells were plated at low densities in 10 cm diameter culture-treated plastic petri dishes (400 cells/dish for Fp and 800 cells/dish for Fr and F-DHJ) and cultured during 3 weeks in a medium of similar composition to that used for mass cultures, which was renewed 3 times a week. Cultures were then fixed in 70% ethanol and stained with blue RAL. Colonies were counted manually.

2.4. Three-Dimensional Fibroblast Contractility Assay

Dermal equivalents (lattices) were produced by mixing 100000 fibroblasts in MEM containing 10% FBS and 26% (w/v) bovine type I collagen (Symatese, Chaponost, France) in a total volume of 5 mL (3.4 mm diameter petri dishes). Spontaneous collagen polymerization occurred within a few hours of culture. Lattices were then detached from the plastic surface of petri dishes 48 h after culture initiation, enabling a contraction process that led to progressive reduction of the lattice diameter. Kinetics of contraction was characterized by measurement of the lattice diameter (millimeter scale) after 1 h, 3 h, 6 h, and 24 h. Full description of the assay principle is provided in [8].

2.5. Three-Dimensional Skin Reconstruction

Reconstructed skins were prepared as previously described [21]. Briefly, fibroblasts (1 × 10⁶ cells per sample of reconstructed dermis) were embedded into a bovine type I collagen gel (Symatese, Chaponost, France). Thereafter, keratinocytes (50,000 cells per sample) were seeded onto the lattices.
and stuck to the bottom of 60 mm diameter petri dishes. The keratinocytes used in this study were frozen banked samples from a single donor amplified in a serum-containing medium in the presence of a feeder-layer of growth-arrested murine 3T3 fibroblasts [5] according to the principle described by Rheinwald and Green [22]. Developing skin reconstructs were maintained for 1 week immersed in a medium composed of MEM (Invitrogen, Carlsbad, CA, USA) supplemented with 10% FBS (Sigma, St Louis, MO, USA); epidermal growth factor (EGF) (10 ng/mL) (BD Biosciences, San Jose, CA, USA); hydrocortisone (0.4 mg/mL) (Sigma, St Louis, MO, USA); and cholera toxin (0.1 nM) (Biomol Int., Plymouth, PA, USA). Complete epidermal stratification and full differentiation was obtained 1 week after raising the system at the air-liquid interface. During the whole process of skin reconstruction, cultures were maintained at 37 °C in a fully humidified atmosphere containing 5% CO₂. Reconstructed skin samples were embedded in a paraffin and used to prepare hematoxylin eosin saffron-stained sections.

2.6. Neosynthetized ECM Samples

Protocol was adapted from [23]. Fibroblasts were seeded on glass slides and cultured till postconfluence. After an additional 48 h, slides were washed twice in PBS, and cells were then lysed using a solution containing 0.5% Triton X-100 and 20 mM of NH₄OH. Cell debris were washed in PBS. Slides coated with ECM components synthesized by fibroblasts were stored in PBS at 4 °C until characterization.

2.7. Mesodermal Differentiation Assays

2.7.1. Adipocyte Lineage

Fibroblasts were seeded at a density of 1400 cells/cm² and cultured in the medium used for mass expansion and colony assay till confluency. After an additional 48 h, the fibroblast cultures medium was substituted by an adipocyte differentiation medium composed of DMEM/20% fetal calf serum (PAN Biotech GmbH, Aidenbach, Germany); 60 µM indometacin (Dr. Ehrenstorfer GmbH, Germany); 0.5 mM 3-isobutyl-1-methylxanthine (IBMX) (Sigma, St Louis, MO, USA); and 10⁻⁶ M dexamethasone (Sigma, St Louis, MO, USA). After 3 weeks of cultures in the adipocyte differentiation medium, cultures were fixed in 4% paraformaldehyde. Cells differentiated into adipocytes were visualized and quantified under microscope according to the presence of refringent lipid droplets in the cytoplasm.

2.7.2. Osteoblast Lineage

As for adipocyte differentiation, the fibroblast culture medium was substituted 48 h postconfluence by an osteoblast differentiation medium composed of MEM/10% fetal calf serum (PAN Biotech GmbH, Aidenbach, Germany); 2 mM β-glycerophosphate (Sigma, St Louis, MO, USA); and 10⁻⁷ M dexamethasone (Sigma, St Louis, MO, USA). After 3 weeks of cultures in the osteoblast differentiation medium, cultures were fixed in 4% paraformaldehyde. Cells differentiated into osteoblasts were visualized and quantified after alizarin-red staining of the calcified extracellular matrix.

2.7.3. Chondrocyte Lineage

For each sample, 10⁵ cells were centrifuged and kept as pellets for 24 h to initiate formation of spheroid structures. The fibroblast culture medium was then substituted by a chondrocyte differentiation medium composed of MEM; 0.5 µg/mL insulin (Gibco, France); 0.5 µg/mL transferrin (Sigma, St Louis, MO, USA); 0.5 ng/mL sodium selenite (Gibco, France); 6.25 µg/mL linoleic acid (Gibco, France); 6.25 µg/mL oleic acid (Gibco, France); 1.25 mg/mL bovine serum-albumin (Sigma, St Louis, MO, USA); 1 mM of sodium pyruvate (Gibco, France); 0.17 mM ascorbic acid 2-phosphate (Sigma, St Louis, MO, USA); 0.1 µg/mL Insulin-like growth factor 1 (RnD System, France). After 3 weeks of cultures in the chondrocyte differentiation medium, spheroids were included in OCT for cryosectioning. Chondrocyte differentiation was revealed by
toluidine blue (Sigma, St Louis, MO, USA) and safranin O (Thermo-Fisher, France) staining and immunostaining of aggrecan (ACAN) and collagen XIα1 (ColXIα1).

2.8. Transcriptome Analysis

2.8.1. RNA Extraction

Total RNA was extracted using the RNeasy kit (QIAgen, Courtaboeuf, France), using cultured fibroblasts at the stage of 7 to 10 population doublings. To limit the impact of experimental variations on gene expression profiles, culture conditions were standardized as follows: RNA extraction was systematically performed at 80% culture confluency and 24 h after a full medium renewal. Extracted RNA samples were split into aliquots in the perspective of microarray and qRT-PCR analyses.

2.8.2. Microarray Transcriptome Profiling

Human full-genome Affymetrix GeneChip HG-U133 Plus 2.0 (PartnerChip, Evry, France) were used following the manufacturer’s recommendations. These microarrays contain 55000 probe sets (25 nucleotides per set) covering 30000 transcripts. Briefly, RNA quality and quantity were estimated using the Nanodrop (ND-1000) and BioAnalyzer 2100 systems (Agilent, Les Ulis, France). When too-high concentrations of salts or solvents were detected, RNA precipitation and washing were performed before sample processing. Quantification of array fluorescence signals was carried out using a GeneChip 3000 scanner. Then, array data were analyzed using the Affymetrix Command Console software. Quality control and statistical analyses were performed using the Affymetrix Expression Console and GeneSpring GX11 softwares.

2.8.3. qRT-PCR

RNA samples were reverse-transcribed using the random primer and Superscript II Reverse transcriptase system following the manufacturer’s instructions (Invitrogen, France). Amplifications were performed using a MyiQ™ LightCycler (Biorad, Marnes-la-Coquette, France). Real-time quantitative PCR was performed using a MyiQ™ LightCycler (Biorad, Marnes-la-Coquette, France) and analyzed using the iQ™ 5 software. Gene expression (primers listed in Table 1) was normalized according to GAPDH and TBP transcript levels.

Table 1. qRT-PCR primers. Primer list and references are provided.

| Gene Symbol | Supplier Reference |
|-------------|--------------------|
| ACAN | QT00001365 |
| CADM1 | QT00050001 |
| COL11A1 | QT00088711 |
| DIRAS3 | QT00040558 |
| EFHD1 | QT00086163 |
| EMCN | QT00025158 |
| FGF9 | QT00000091 |
| GAPDH | QT01192646 |
| KLF9 | QT00208537 |
| LIMCH1 | QT00038794 |
| MGST1 | QT00063357 |
| NPR3 | QT00047250 |
| RHOJ | QT00092078 |
| SFRP2 | QT00073220 |
| SOST | QT00219968 |
Table 1. Cont.

| Gene Symbol | Supplier Reference |
|-------------|--------------------|
| SOX11       | QT00221466         |
| TBP         | QT0000721          |
| TGFβ2       | QT02290316         |
| TOX         | QT00070063         |
| UCP2        | QT0014140          |
| VCAM1       | QT00018347         |

2.9. Immunofluorescence

2.9.1. Tissue Section Staining

Skin samples were fixed in neutral formalin and then embedded in a paraffin. Tissue sections of 5 µm thickness were prepared. For antibody staining, sections were permeabilized in 0.1% SDS after deparaffinization and epitope retrieval in a citrate buffer (pH = 6). To limit background signals, unspecific antibody fixation sites were saturated by sample incubation in 5% BSA. Sections were incubated with primary and secondary Alexa Fluor-coupled antibodies (see Table 2 for antibody references and working dilutions). Stained skin sections were mounted in ProLong Gold supplemented with DAPI (Thermo for Molecular Probes, Waltham, MA, USA, and images were acquired using a Leica microscope coupled with a QIMAGINE RETIGA 2000R Fast 1394 camera. Signal quantification was performed using ImageJ software. Quantification of cells positive for KLF9 expression was performed by visual counting on skin samples from 4 donors. Percentages of KLF9+ cells were determined in a total of 806 cells for Fr, 289 cells for Fr, and 246 cells for F-DHJ fibroblasts.

Table 2. Antibodies. Antibody references and working dilutions are provided.

| Protein name     | Supplier                        | Reference   | Dilution |
|------------------|---------------------------------|-------------|----------|
| alpha Sm actin   | Sigma (Saint-Quentin Falaviers—France) | A5228 | 1/200    |
| ACAN (Aggrecan)* | Abcam (Paris—France)             | ab3778 | 1/20     |
| Col XI a1        | Sigma (Saint-Quentin Falaviers—France) | SAB4500393 | 1/50 |
| Desmine (clone D33) | Dako—Agilent (France)        | M0760 | 1/50     |
| GAPDH            | Interchim for Meridian (France)   | H86504M | 1/2000   |
| KLF9             | Abcam (Paris—France)             | ab170980 | 1/100  (IHC)—1/1000  (WB) |
| Phalloidine Rhodamin | Invitrogen (France)              | R415 | 1/50     |
| TNC (Tenascin C) | Novus Biologicals (Abington—UK) | NB110-68136 | 1/50 |
| Vimentin         | TEBU (Le Perray-en-Yvelines—France) | MON3005 | 1/10    |
| Goat anti-Mouse Alexa 488 | Molecular Probes Invitrogen (France) | A21121 | 1/250    |
| Goat anti-Rabbit Alexa 555 | Molecular Probes Invitrogen (France) | A21428 | 1/250    |
| Zenon Alexa 488  | Molecular Probes Invitrogen (France) | Z25002 |         |
| Goat anti-Rabbit HRP | Thermo-Fisher, France           | 32460 | 1/2000   |

* Pre-processing: keratanase (0.1 U/mL) + chondroitinase (0.1 U/mL)—3 h—37 °C.
2.9.2. Cell Staining

Cultured cells were fixed in 4% paraformaldehyde, permeabilized in 0.1% SDS, and incubated in 5% BSA for saturation of unspecific antibody binding sites and then with primary and secondary Alexa Fluor-coupled antibodies (see Table 2). Labeled cells were mounted in ProLong Gold supplemented with DAPI (Thermo - Molecular Probes, Waltham, MA, USA). Immunofluorescence images were acquired using a Leica microscope coupled with a QIMAGINE RETIGA 2000R Fast 1394 camera (QImageing, Canada). Signal quantification was performed using ImageJ software.

2.9.3. ECM Staining

ECM slides were incubated in 5% BSA for saturation of unspecific antibody binding sites. Incubation with Alexa Fluor-coupled antibodies (Zenon technology – Thermo – Molecular Probes, Waltham, MA, USA) was performed during 30 min at room temperature (see Table 2). Immunofluorescence images were acquired using a Leica microscope coupled with a QIMAGINE RETIGA 2000R Fast 1394 camera (QImageing, Surrey, BC, Canada). Signal quantification was performed using ImageJ software.

2.10. Western Blot Analysis

Expression of KLF9 was assessed by western blot analysis on total protein extracts from cell cultures. Protein extracts were prepared using a radioimmunoprecipitation assay (RIPA) buffer. Proteins (40 µg) were separated by 15% sodium dodecyl sulphate-polyacrylamide gel electrophoresis (PAGE) and electrotransferred onto a 0.45 µm nitrocellulose membrane. The membrane was incubated with the primary antibody, washed, and probed with the peroxidase-labeled secondary antibody. Detection was achieved by enhanced chemiluminescence (West Femto HRP substrates, ThermoFisher Scientific, France). After dehybridization, control loading was achieved by anti-glyceraldehyde-3-phosphate dehydrogenase antibodies. Densitometric analyses were performed using ImageJ.

2.11. Statistics

Error bars represent SEM. The Wilcoxon-Mann-Whitney test and the Friedman test were applied to determine p-values. Data with $p < 0.05$ (*) or $p < 0.01$ (**) were considered as statistically significant.

3. Results

3.1. Cellular Characteristics and Growth Potential Distinguish F-DHJ from Fp and Fr

The cellular morphology of the three fibroblast populations were isolated based on their skin localization, i.e., papillary dermis fibroblasts (Fp), reticular dermis fibroblasts (Fr), and dermo-hypodermal junction fibroblasts (F-DHJ) were examined in cultures and compared (Figure 1C). As previously described [4], Fp cells exhibited a thin morphology, with bi or tricuspid shapes, whereas Fr had spread morphologies and stellate shapes. F-DHJ were more heterogeneous, from small tricuspids (red arrow) to larger cells with stellate shapes (white arrow) with visible trabecular networks.

Analysis of the four markers proposed in Gabbiani’s classification [24] (Figure 2A,B) confirmed the fibroblast statuses of the Fp, Fr, and F-DHJ cellular material, as all cell types expressed almost homogenously actin (ACT) and vimentin (VIM) but expressed neither desmin (DES) nor $\alpha$-smooth muscle actin ($\alpha$-SMA): $\text{ACT}^+ / \text{VIM}^+ / \text{DES}^- / \alpha$-SMA$^-$ phenotype. In each population, only a minority of cells exhibited the myofibroblast $\text{ACT}^+ / \text{VIM}^+ / \text{DES}^- / \alpha$-SMA$^+$ phenotype, probably due to the cultures’ environments. Few cells corresponding to the $\text{ACT}^+ / \text{VIM}^- / \text{DES}^+ / \alpha$-SMA$^+$ vascular smooth muscle cell phenotype were also detected. In addition, the Fr population contained few $\text{ACT}^+ / \text{VIM}^- / \text{DES}^- / \alpha$-SMA$^+$ cells, corresponding to smooth muscle cells probably originating from arrector pili muscles.
Taken together, these data show that Fp, Fr, and F-DHJ fibroblasts exhibit different cellular characteristics.

**Figure 2.** Phenotypic and functional properties of Fp, Fr, and F-DHJ fibroblasts. (A) Detection of actin (ACT) and vimentin (VIM), desmin (DES), and α-smooth muscle actin (α-SMA) by immunochemistry in cultured Fp, Fr, and F-DHJ fibroblasts in the perspective of scoring according to Gabbiani’s classification [24]. White arrow points to rare DES+ cells present within the Fr population. (B) Scoring of Fp, Fr, and F-DHJ fibroblasts according to ACT, VIM, DES, and α-SMA detection: (−) = not present, (+/−) = low representation, (+++) = frequent representation, and (++++) = major representation. (C) Long-term growth capacity of Fp, Fr, and F-DHJ cells. Maximal cumulative population doubling values obtained with samples from independent donors are shown. Means ± SEM are indicated (*p < 0.05, **p < 0.01; Wilcoxon test). (D) Colony-forming unit efficiency of Fp, Fr, and F-DHJ cells.
Fibroblast colony-forming unit (CFU-F) efficiency values (% of plated cells) obtained with samples from independent donors are shown. Means ± SEM are indicated (* p < 0.05, ** p < 0.01; Wilcoxon test).

(E) Contractile capacity of Fp, Fr, and F-DHJ cells in the 3D context of collagen lattices. Kinetics of lattice diameter evolutions. Means ± SEM are indicated (values obtained with samples from 9 independent donors) (* p < 0.05. Friedman’s test). (F) Efficiency of Fp, Fr, and F-DHJ cells in promoting epidermis organogenesis by keratinocytes in a 3D reconstructed skin model. Representative reconstructed skin sections are shown (3 independent donors, each fibroblast sample tested in triplicates). The black arrow points to the epidermal granular layer that was obtained only in the presence of Fp fibroblasts.

The proliferative capacity of Fp, Fr, and F-DHJ cells was assessed in mass long-term cultures (Figure 2C) and using a colony assay (Figure 2D) (cell samples from n = 9 individuals were studied). As previously described [4,5], the proliferative capacity of Fr was lower than that of Fp, according to both criteria. Indeed, the maximum population doublings (PD) reached by Fp was 54 ± 2 versus 37 ± 2 for Fr (p < 0.01), and colony-forming efficiency was 16.2% ± 1.7 for Fp and 6.1% ± 1.2 for Fr (p < 0.01). F-DHJ exhibited the lowest growth capacity of the three fibroblast types, with a maximum PD reaching only 29 ± 3 and colony-forming efficiency 3% ± 0.7 (p < 0.05, calculated versus Fr).

Taken together, these data show that Fp, Fr, and F-DHJ fibroblasts exhibit different cellular characteristics.

3.2. Behavior in 3D Tissue and Differentiation Potential Distinguish F-DHJ from Fp and Fr

A functional assay was designed to assess fibroblast contractile capacity in a three-dimensional environment based on a follow-up of collagen lattice contractions. Fp, Fr, and F-DHJ integrated in collagen lattices exhibited nonequivalent contraction behaviors (Figure 2E) (cell samples from n = 9 individuals were tested). Reduction of the lattice diameter was more rapid and marked with Fp than with Fr cells. In contrast, a more moderate lattice diameter reduction was observed with F-DHJ cells, indicating a lower contractile capacity for this fibroblast population. The three lattice contraction curves showed statistically significant differences (p < 0.05).

The next functional property of Fp, Fr, and F-DHJ that was investigated and compared was their efficiency in promoting epidermis organogenesis by keratinocytes in a model of in vitro three-dimensional skin reconstruction. Lattices containing either Fp, Fr, or F-DHJ cells were produced and used as dermal equivalents. On top of which, keratinocytes were then plated in order to obtain epidermis development (Figure 2F) (fibroblasts samples from n = 3 individuals were tested, in association with keratinocytes from a single donor). Fp cells were the most efficient fibroblast population for promoting the development of a correctly differentiated epidermis comprising a regular basal layer, as well as fully differentiated granular and horny layers. Epidermis reconstructs were of a lower quality with dermal lattices containing Fr fibroblasts; basal keratinocytes were of bigger sizes and less regular, and differentiation of the granular layer was incomplete. Dermal lattices populated with F-DHJ promoted poor epidermis stratification and differentiation.

Finally, Fp, Fr, and F-DHJ were studied for their differentiation capacity into three mesodermal cell lineages: adipocytes (presence of cytoplasmic lipid droplets); osteoblasts (alizarin-red staining); and chondrocytes (toluidine blue and safranin O staining, aggrecan (ACAN) and collagen XIα1 (ColXIα1) expression). This functionality was documented using cells obtained from skin biopsies corresponding to ages ranging between 20 and 31 years (Figure 3). Interestingly, F-DHJ exhibited a wider differentiation potential than that of Fp and Fr fibroblasts, as these cells efficiently responded to the three lineage-oriented differentiation conditions. Fp fibroblasts gave rise to fewer quantities of adipocytes and chondrocytes and did not differentiate into osteoblasts. Fr fibroblasts could give rise to differentiated cells of the three lineages but with a much lower efficiency than F-DHJ cells.
Figure 3. Differentiation capacities of Fp, Fr, and F-DHJ fibroblasts into mesodermal lineages. Samples from 5 independent “young” donors (20, 22, 25, 28, and 31 years old) were tested for their capacity to differentiate into chondrocytes (toluidine blue and safranin O staining, aggrecan (ACAN) and collagen XIα1 (ColXIα1) expression, white arrows); adipocytes (presence of cytoplasmic lipid droplets, black arrows); and osteoblasts (alizarin-red staining). Scoring of differentiation capabilities are presented: (−) = not present, (+/−) = low representation, (+++) = major representation.

Taken together, these data show that Fp, Fr, and F-DHJ fibroblasts exhibit different functional characteristics.
3.3. Molecular Profiles Distinguish the Fp, Fr, and F-DHJ Fibroblast Populations

The molecular profiles of Fp, Fr, and F-DHJ cells were characterized and compared by microarray genome-wide transcriptome profiling (Figures 4 and 5A). In the perspective of identifying molecular signatures distinguishing the Fp, Fr, and F-DHJ fibroblast populations whatever the donor’s age, the selected donor cohort covered both young and older ages: 22, 25, 28, 55, 61, and 65 y.o. As a first screen, a fold-change threshold value of three, together with a \(p\)-value of 0.05, were used to identify differential signals. According to these filters, a hierarchical clustering was built based on expression levels of 1078 transcripts, identifying signatures that validated at the transcriptome level of the distinct natures of Fp, Fr, and F-DHJ (Figure 4A). Next, transcriptome data were reanalyzed considering only the statistical significance threshold \(p\)-value < 0.05 independently of fold-change values (Figure 4B). This analysis identified 3420, 2073, and 2929 probe sets, which could be used to define signatures of Fp, Fr, and F-DHJ cells, respectively. Fr cells shared the highest level of commonalities with the other fibroblast populations, probably due to their intermediate tissue localization: 3270 probe sets in common with Fp (not detected in F-DHJ) and 2284 probe sets in common with F-DHJ (not detected in Fp).

F-DHJ were then compared more specifically with Fr cells, which are in spatial proximity in the tissue. A gene ontology (GO) term analysis was performed based on 2540 probe sets (1647 genes) exhibiting differential signals between the two populations (parameters: fold-change > 1.5 and \(p\)-value < 0.05) (Figure 4C). Notably, this analysis revealed marked differences between Fr and F-DHJ concerning the expression of transcripts related to the tissue skeleton (see [9]), as 26% of the transcripts differentially expressed were linked to the structuration of this network (Figure 4D and Table 3). In particular, differentially expressed probe sets were enriched in transcripts related to ECM components, cytoskeleton, and secreted factors.

For validation of our microarray data, 19 genes were selected from the signatures that distinguished Fp, Fr, and F-DHJ identities, and transcript levels were analyzed by qRT-PCR in cell samples from the six donors (Figure 5A,B). Validation of microarray data was obtained for the 19 selected transcripts. As an attempt to identify a biomarker of F-DHJ cells, a focus was made on KLF9, which the transcript was detected as overexpressed in F-DHJ versus Fr by both technics in the six tested donors. The transcription factor KLF9 regulates the early phases of adipocyte differentiation [25], and thus, attracted attention due to the proximity of F-DHJ cells with hypodermis adipose tissue. Expression of KLF9 was analyzed at the protein level by western blot in cultured cells from six donors (Figure 5C) and by immune-fluorescence in skin biopsies from four individuals (Figure 5D). As expected from transcriptome data, the KLF9 protein was expressed at a higher level in cultured F-DHJ than in cultured Fp and Fr \((p < 0.05)\). In skin sections, the percentage of cells expressing KLF9 was higher in F-DHJ than in Fp and Fr regions, respectively 18.8 ± 3.4% versus 9.2 ± 1.3% and 5.3 ± 1.9%.
Figure 4. Microarray analysis of the transcriptome profiles of Fp, Fr, and F-DHJ fibroblasts (donors’ ages: 22, 25, 28, 55, 61, and 65 y.o.). (A) Hierarchical clustering based on 1078 differentially expressed transcripts (fold-change cutoff at 3 and \( p < 0.05 \)). (B) Venn Diagrams summarizing Fp, Fr, and F-DHJ-enriched transcriptional signatures \( (p < 0.05) \). (C) List of the 20 most significant gene ontology (GO) terms differentiating F-DHJ from Fr cells, based on 2540 probe sets (1647 transcripts) exhibiting differential signals (fold-change >1.5 and \( p < 0.05 \)). (D) Signatures identifying Fr fibroblasts (black bars) and F-DHJ fibroblasts (grey bars) among transcripts related to the tissue skeleton biology (fold-change >1.5 and \( p < 0.05 \)).
Figure 5. Biomarker validations at mRNA and protein levels. (A) Selection of transcripts in which differential expression was confirmed by qRT-PCR in cell samples from 6 donors (donors’ ages: 22, 25, 28, 55, 61, and 65 y.o). (B) Detailed qRT-PCR comparative analysis of the KLF9 transcript in cells from the 6 donors (donors’ ages: 22, 25, 28, 55, 61, and 65 y.o). Means ± SEM are indicated (*p < 0.05, Wilcoxon test). (C) Western blot comparative analysis of the KLF9 protein in cells from the 5 donors (*p < 0.05, Wilcoxon test). A histogram detailing quantifications and a representative western blot gel is shown. (D) Immunofluorescence detection of the KLF9 protein in skin sections (breast). The percentage of KLF9+ cells was determined by observation under a fluorescence microscope of a total of 806 cells for Fp, 289 cells for Fr, and 246 cells for F-DHJ fibroblasts (skin sections from 4 donors were included in the analysis).
Table 3. Transcripts related to the tissue skeleton differentially expressed in reticular dermis fibroblasts (Fr) and dermo-hypodermal junction fibroblasts (F-DHJ). This transcript list was extracted from microarray data using a fold-change >1.5 and \( p < 0.05 \) as inclusion parameters. The transcript signature with predominant expression in Fr cells concerned 297 probe sets corresponding to transcripts directly involved in the tissue skeleton structure, comprising 33 transcripts related to the extracellular matrix (ECM), 125 focal adhesion point transcripts, 60 cytoskeleton transcripts, 1 LINC complex transcript, and 8 nucleoskeleton transcripts. The transcript signature with predominant expression in F-DHJ cells concerned 359 probe sets corresponding to transcripts directly involved in the tissue skeleton structure, comprising 94 transcripts related to ECM, 76 focal adhesion point transcripts, 50 cytoskeleton transcripts, 1 LINC complex transcript, and 7 nucleoskeleton transcripts. In addition, transcripts encoding soluble factors were found in both signatures, respectively 70 and 131 for Fr and F-DHJ cells.

| Probe Set ID | Gene Symbol | Gene Symbol | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Symbol | adj-pval | FC |
|--------------|-------------|-------------|----------|----|--------------|-------------|-------------|----------|----|
| 205941_s_at  | COL10A1     | collagen, type X, alpha 1 | 9.41 × 10^{-3} | 4.23 | 220518_at    | ABI3BP      | ABI family, member 3 (NESH) binding protein | 2.37 × 10^{-2} | 2.92 |
| 211343_s_at  | COL13A1     | collagen, type XIII, alpha 1 | 1.44 × 10^{-2} | 2.26 | 1559077_at   | ABI3BP      | ABI family, member 3 (NESH) binding protein | 7.43 × 10^{-2} | 2.49 |
| 211809_x_at  | COL13A1     | collagen, type XIII, alpha 1 | 2.74 × 10^{-2} | 1.74 | 222486_s_at  | ADAMTS1     | ADAM metallopeptidase with thrombospondin type 1 motif, 1 | 2.76 × 10^{-2} | 2.33 |
| 221900_at    | COL8A2      | collagen, type VIII, alpha 2 | 2.88 × 10^{-1} | 2.23 | 222162_s_at  | ADAMTS1     | ADAM metallopeptidase with thrombospondin type 1 motif, 1 | 4.36 × 10^{-2} | 1.91 |
| 226824_at    | CPXM2       | carboxypeptidase X (M14 family), member 2 | 2.01 × 10^{-1} | 1.88 | 226997_at    | ADAMTS12    | ADAM metallopeptidase with thrombospondin type 1 motif, 12 | 3.75 × 10^{-3} | 2.78 |
| 221541_at    | CRISPLD2    | cysteine-rich secretory protein LCCL domain containing 2 | 5.98 × 10^{-2} | 2.03 | 214913_at    | ADAMTS3     | ADAM metallopeptidase with thrombospondin type 1 motif, 3 | 1.94 × 10^{-2} | 1.94 |
| 206595_at    | CST6        | cystatin E/M | 2.34 × 10^{-2} | 3.12 | 237411_at    | ADAMTS6     | ADAM metallopeptidase with thrombospondin type 1 motif, 6 | 1.36 × 10^{-1} | 1.61 |
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                    | adj-pval   | FC  | Probe Set ID | Gene Symbol | Gene Title                                    | adj-pval   | FC  |
|--------------|-------------|-----------------------------------------------|------------|-----|--------------|-------------|-----------------------------------------------|------------|-----|
| 225681_at    | CTHRC1      | collagen triple helix repeat containing 1     | $1.31 \times 10^{-2}$ | 2.82 | 224396_s_at  | ASPN        | asporin                                       | $2.47 \times 10^{-2}$ | 4.48 |
| 202450_s_at  | CTSK        | cathepsin K                                   | $2.05 \times 10^{-1}$ | 1.76 | 219087_at    | ASPN        | asporin                                       | $1.32 \times 10^{-2}$ | 3.54 |
| 213068_at    | DPT         | dermatopontin                                 | $8.16 \times 10^{-2}$ | 3.67 | 203477_at    | COL15A1     | collagen, type XV, alpha 1                     | $2.18 \times 10^{-1}$ | 2.78 |
| 207977_s_at  | DPT         | dermatopontin                                 | $1.24 \times 10^{-1}$ | 2.85 | 209082_s_at  | COL18A1     | collagen, type XVIII, alpha 1                  | $6.56 \times 10^{-4}$ | 2.99 |
| 222885_at    | EMCN        | endomucin                                     | $6.59 \times 10^{-2}$ | 2.74 | 209081_s_at  | COL18A1     | collagen, type XVIII, alpha 1                  | $3.92 \times 10^{-3}$ | 2.83 |
| 227874_at    | EMCN        | endomucin                                     | $2.70 \times 10^{-1}$ | 1.81 | 208096_s_at  | COL21A1     | collagen, type XXI, alpha 1                    | $1.12 \times 10^{-2}$ | 6.88 |
| 219436_s_at  | EMCN        | endomucin                                     | $1.79 \times 10^{-1}$ | 1.77 | 232458_at    | COL3A1      | Collagen, type III, alpha 1                    | $6.64 \times 10^{-3}$ | 2.66 |
| 224374_s_at  | EMILIN2     | elastin microfibril interfacер 2             | $6.75 \times 10^{-2}$ | 1.68 | 211981_at    | COL4A1      | collagen, type IV, alpha 1                     | $2.12 \times 10^{-3}$ | 1.93 |
| 203088_at    | FBLN5       | fibulin 5                                     | $2.24 \times 10^{-2}$ | 1.88 | 211980_at    | COL4A1      | collagen, type IV, alpha 1                     | $1.66 \times 10^{-3}$ | 1.61 |
| 203638_s_at  | FGFR2       | fibroblast growth factor receptor 2          | $3.21 \times 10^{-3}$ | 4.52 | 222073_at    | COL4A3      | collagen, type IV, alpha 3 (Goodpasture antigen) | $2.28 \times 10^{-2}$ | 1.70 |
| 208228_s_at  | FGFR2       | fibroblast growth factor receptor 2          | $2.04 \times 10^{-2}$ | 2.52 | 229779_at    | COL4A4      | collagen, type IV, alpha 4                     | $2.85 \times 10^{-8}$ | 5.32 |
| 210187_at    | FKBPIA      | FK506 binding protein 1A, 12 kDa             | $8.48 \times 10^{-2}$ | 1.81 | 214602_at    | COL4A4      | collagen, type IV, alpha 4                     | $2.30 \times 10^{-5}$ | 4.16 |
| 226145_s_at  | FRAS1       | Fraser syndrome 1                             | $6.34 \times 10^{-2}$ | 2.31 | 213110_s_at  | COL4A5      | collagen, type IV, alpha 5                     | $1.05 \times 10^{-1}$ | 3.62 |
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 204983_s_at  | GPC4        | glypican 4 | $3.14 \times 10^{-2}$ | 2.07 | 52255_s_at   | COL5A3      | collagen, type V, alpha 3 | $2.47 \times 10^{-3}$ | 3.07 |
| 204984_at    | GPC4        | glypican 4 | $1.57 \times 10^{-2}$ | 2.02 | 218975_at    | COL5A3      | collagen, type V, alpha 3 | $2.83 \times 10^{-3}$ | 2.65 |
| 235944_at    | HMCN1       | hemicentin 1 | $3.52 \times 10^{-5}$ | 6.28 | 205832_at    | CPA4        | carboxypeptidase A4 | $2.37 \times 10^{-2}$ | 4.34 |
| 203417_at    | MFAP2       | microfibrillar-associated prot 2 | $8.08 \times 10^{-2}$ | 1.70 | 201116_s_at | CPE         | carboxypeptidase E    | $7.11 \times 10^{-3}$ | 2.37 |
| 204580_at    | MMP12       | matrix metalloproteinase 12 (macrophage elastase) | $2.58 \times 10^{-1}$ | 2.17 | 201117_s_at | CPE         | carboxypeptidase E    | $4.90 \times 10^{-3}$ | 2.10 |
| 205828_at    | MMP3        | matrix metalloproteinase 3 | $4.79 \times 10^{-3}$ | 7.70 | 227138_at    | CRTAP       | cartilage associated protein | $1.31 \times 10^{-2}$ | 1.63 |
| 209596_at    | MXRA5       | matrix-remodelling associated 5 | $2.09 \times 10^{-2}$ | 2.52 | 201360_at    | CST3        | cystatin C              | $6.11 \times 10^{-2}$ | 1.55 |
| 236088_at    | NTNG1       | netrin G1  | $2.16 \times 10^{-2}$ | 2.55 | 201487_at    | CTSC        | cathepsin C             | $6.11 \times 10^{-5}$ | 2.41 |
| 222722_at    | OGN         | osteoglycin| $1.91 \times 10^{-1}$ | 2.04 | 225646_at    | CTSC        | cathepsin C             | $1.80 \times 10^{-3}$ | 2.32 |
| 228186_s_at  | RSPO3       | R-spondin 3 homolog (X. laevis) | $1.35 \times 10^{-2}$ | 2.98 | 225647_s_at | CTSC        | cathepsin C             | $1.37 \times 10^{-3}$ | 2.25 |
| 218638_s_at  | SPON2       | spondin 2, extracellular matrix prot | $3.07 \times 10^{-2}$ | 2.84 | 231234_at    | CTSC        | cathepsin C             | $5.72 \times 10^{-3}$ | 2.03 |
| 216005_at    | TNC         | Tenascin C | $1.24 \times 10^{-2}$ | 2.61 | 202295_s_at  | CTSN        | cathepsin H             | $4.00 \times 10^{-2}$ | 1.85 |
| 201645_at    | TNC         | tenascin C | $4.34 \times 10^{-2}$ | 1.59 | 209335_at    | DCN         | decorin                  | $1.02 \times 10^{-1}$ | 2.05 |
Table 3. Cont.

| Extracellular Matrix Genes | UP in F-DHJ |
|----------------------------|-------------|
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|------------------|-------------|-------------|----------|----|----------------|-------------|-------------|----------|----|
| 211896_s_at      | DCN         | decorin     | 2.16 × 10⁻¹ | 1.69 |
| 211813_x_at      | DCN         | decorin     | 1.52 × 10⁻¹ | 1.68 |
| 201893_x_at      | DCN         | decorin     | 1.77 × 10⁻¹ | 1.56 |
| 1568779_a_at     | ECM2        | extracellular matrix protein 2 | 1.76 × 10⁻¹ | 1.71 |
| 206101_at        | ECM2        | extracellular matrix protein 2 | 2.50 × 10⁻¹ | 1.57 |
| 201843_s_at      | EFEMP1      | EGF-containing fibulin-like extracellular matrix protein 1 | 7.68 × 10⁻⁴ | 3.62 |
| 201842_s_at      | EFEMP1      | EGF-containing fibulin-like extracellular matrix protein 1 | 4.62 × 10⁻⁴ | 2.87 |
| 228421_s_at      | EFEMP1      | EGF-containing fibulin-like extracellular matrix protein 1 | 2.23 × 10⁻¹ | 1.61 |
| 226911_at        | EGFLAM      | EGF-like, fibronectin type III and laminin G domains | 3.95 × 10⁻³ | 4.36 |
| 204834_at        | FGL2        | fibrinogen-like 2 | 4.12 × 10⁻⁴ | 6.37 |
| 227265_at        | FGL2        | fibrinogen-like 2 | 4.28 × 10⁻³ | 3.56 |
| 202709_at        | FMOD        | fibromodulin | 1.12 × 10⁻³ | 2.96 |
| 205206_at        | KAL1        | Kallmann syndrome 1 sequence | 9.65 × 10⁻⁴ | 7.84 |
| 227048_at        | LAMA1       | laminin, alpha 1 | 2.82 × 10⁻¹ | 1.83 |
### Table 3. Cont.

| Probe Set ID | Gene Symbol (formerly) | Gene Symbol | Gene Title                                      | adj-pval  | FC   |
|--------------|------------------------|-------------|-------------------------------------------------|-----------|------|
| 216840_s_at  | LAMA2                  | LAMA2       | laminin, alpha 2                                | 5.17 × 10⁻³| 2.80 |
| 205116_at    | LAMA2                  | LAMA2       | laminin, alpha 2                                | 1.05 × 10⁻²| 2.67 |
| 213519_s_at  | LAMA2                  | LAMA2       | laminin, alpha 2                                | 1.10 × 10⁻²| 2.57 |
| 210150_s_at  | LAMA5                  | LAMA5       | laminin, alpha 5                                | 4.86 × 10⁻²| 1.57 |
| 211651_s_at  | LAMB1                  | LAMB1       | laminin, beta 1                                 | 8.27 × 10⁻²| 1.54 |
| 200770_s_at  | LAMC1                  | LAMC1       | laminin, gamma 1 (formerly LAMB2)               | 7.61 × 10⁻⁶| 1.91 |
| 200771_at    | LAMC1                  | LAMC1       | laminin, gamma 1 (formerly LAMB2)               | 7.75 × 10⁻⁷| 1.90 |
| 202267_at    | LAMC2                  | LAMC2       | laminin, gamma 2                                | 7.41 × 10⁻⁴| 10.0 |
| 200923_at    | LGALS3BP LOC100133842  |            | lectin, galactoside-binding, soluble, 3 binding protein similar to lectin, galactoside-binding, soluble, 3 binding protein | 1.02 × 10⁻²| 2.45 |
| 242767_at    | LMCD1                  | LMCD1       | LIM and cysteine-rich domains 1                  | 1.72 × 10⁻²| 2.01 |
| 202998_s_at  | LOXL2                  | LOXL2       | lysyl oxidase-like 2                            | 4.16 × 10⁻³| 1.59 |
| 227145_at    | LOXL4                  | LOXL4       | lysyl oxidase-like 4                            | 3.15 × 10⁻²| 2.43 |
| 219922_s_at  | LTBP3                  | LTBP3       | latent transforming growth factor beta binding protein 3 | 7.19 × 10⁻²| 1.64 |
| 227308_x_at  | LTBP3                  | LTBP3       | latent transforming growth factor beta binding protein 3 | 2.22 × 10⁻³| 1.53 |
| Probe Set ID  | Gene Symbol | Gene Title                        | adj-pval | FC     | Probe Set ID  | Gene Symbol | Gene Title                        | adj-pval | FC |
|--------------|-------------|-----------------------------------|----------|--------|--------------|-------------|-----------------------------------|----------|----|
| 213765_at    | MFAP5       | microfibrillar associated prot 5  | $3.51 \times 10^{-3}$ | 1.61   |              |             |                                   |          |    |
| 213764_s_at  | MFAP5       | microfibrillar associated prot 5  | $3.23 \times 10^{-3}$ | 1.53   |              |             |                                   |          |    |
| 210605_s_at  | MFGES       | milk fat globule-EGF factor 8 protein | $1.80 \times 10^{-1}$ | 1.75   |              |             |                                   |          |    |
| 202291_s_at  | MGP         | matrix Gla protein                | $3.10 \times 10^{-4}$ | 7.14   |              |             |                                   |          |    |
| 207847_s_at  | MUC1        | mucin 1, cell surface associated  | $1.58 \times 10^{-1}$ | 2.38   |              |             |                                   |          |    |
| 213693_s_at  | MUC1        | mucin 1, cell surface associated  | $2.03 \times 10^{-2}$ | 2.04   |              |             |                                   |          |    |
| 204114_at    | NID2        | nidogen 2 (osteonidogen)          | $2.32 \times 10^{-3}$ | 2.83   |              |             |                                   |          |    |
| 223315_at    | NTN4        | netrin 4                          | $1.76 \times 10^{-4}$ | 14.27  |              |             |                                   |          |    |
| 201860_s_at  | PLAT        | plasminogen activator, tissue     | $2.56 \times 10^{-2}$ | 2.15   |              |             |                                   |          |    |
| 211668_s_at  | PLAU        | plasminogen activator, urokinase  | $2.43 \times 10^{-1}$ | 1.99   |              |             |                                   |          |    |
| 228224_at    | PRELP       | proline/arginine-rich end leucine-rich repeat protein | $2.74 \times 10^{-2}$ | 3.46   |              |             |                                   |          |    |
| 204223_at    | PRELP       | proline/arginine-rich end leucine-rich repeat protein | $3.27 \times 10^{-2}$ | 3.27   |              |             |                                   |          |    |
| 205923_at    | RELN        | reelin                            | $3.58 \times 10^{-8}$ | 9.15   |              |             |                                   |          |    |
| Probe Set ID | Gene Symbol | Gene Title                                                                 | adj-pval | FC   | Probe Set ID | Gene Symbol | Gene Title                                                                 | adj-pval | FC   |
|--------------|-------------|------------------------------------------------------------------------------|----------|------|--------------|-------------|------------------------------------------------------------------------------|----------|------|
| 202376_at    | SERPINA3    | serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3 | $6.25 \times 10^{-2}$ | 2.05 | 204614_at    | SERPINB2    | serpin peptidase inhibitor, clade B (ovalbumin), member 2 | $9.41 \times 10^{-2}$ | 5.27 |
| 209723_at    | SERPINB9    | serpin peptidase inhibitor, clade B (ovalbumin), member 9 | $5.41 \times 10^{-3}$ | 2.25 | 200986_at    | SERPING1    | serpin peptidase inhibitor, clade G (C1 inhibitor), member 1 | $2.27 \times 10^{-1}$ | 1.72 |
| 205352_at    | SERPINI1    | serpin peptidase inhibitor, clade I (neuroserpin), member 1 | $1.54 \times 10^{-3}$ | 2.71 | 213493_at    | SNED1       | sushi, nidogen and EGF-like domains 1 | $3.24 \times 10^{-2}$ | 2.47 |
| 213488_at    | SNED1       | sushi, nidogen and EGF-like domains 1 | $2.30 \times 10^{-1}$ | 1.94 | 205236_x_at  | SOD3        | superoxide dismutase 3, extracellular | $1.15 \times 10^{-1}$ | 1.71 |
| 202363_at    | SPOCK1      | sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1 | $5.31 \times 10^{-3}$ | 2.13 | 201858_s_at  | SRGN        | serglycin | $3.34 \times 10^{-4}$ | 8.11 |
| Probe Set ID | Gene Symbol | Gene Title                                                      | adj-pval   | FC  | Probe Set ID | Gene Symbol | Gene Title                                                      | adj-pval   | FC  |
|--------------|-------------|----------------------------------------------------------------|------------|-----|--------------|-------------|----------------------------------------------------------------|------------|-----|
| 201859_at    | SRGN        | serglycin                                                       | $3.81 \times 10^{-4}$ | 4.87|              |             | serglycin                                                       |            |     |
| 219552_at    | SVEP1       | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | $1.07 \times 10^{-1}$ | 1.70|              |             | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | $1.07 \times 10^{-1}$ | 1.70|
| 213247_at    | SVEP1       | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | $6.04 \times 10^{-2}$ | 1.70|              |             | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | $6.04 \times 10^{-2}$ | 1.70|
| 226506_at    | THSD4       | thrombospondin, type I, domain containing 4                     | $6.68 \times 10^{-4}$ | 3.97|              |             | thrombospondin, type I, domain containing 4                     | $6.68 \times 10^{-4}$ | 3.97|
| 222835_at    | THSD4       | thrombospondin, type I, domain containing 4                     | $5.26 \times 10^{-5}$ | 3.43|              |             | thrombospondin, type I, domain containing 4                     | $5.26 \times 10^{-5}$ | 3.43|
| 219058_x_at  | TINAGL1     | tubulointerstitial nephritis antigen-like 1                     | $8.12 \times 10^{-3}$ | 2.50|              |             | tubulointerstitial nephritis antigen-like 1                     | $8.12 \times 10^{-3}$ | 2.50|
| 216333_x_at  | TNXA        | tenascin XA pseudogene tenascin XB                               | $7.97 \times 10^{-5}$ | 11.18|              |             | tenascin XA pseudogene tenascin XB                               | $7.97 \times 10^{-5}$ | 11.18|
| 206093_x_at  | TNXA        | tenascin XA pseudogene tenascin XB                               | $5.32 \times 10^{-5}$ | 10.76|              |             | tenascin XA pseudogene tenascin XB                               | $5.32 \times 10^{-5}$ | 10.76|
| 213451_x_at  | TNXA        | tenascin XA pseudogene tenascin XB                               | $1.65 \times 10^{-4}$ | 9.71|              |             | tenascin XA pseudogene tenascin XB                               | $1.65 \times 10^{-4}$ | 9.71|
| 208609_s_at  | TNXB        | tenascin XB                                                      | $7.07 \times 10^{-5}$ | 8.99|              |             | tenascin XB                                                      | $7.07 \times 10^{-5}$ | 8.99|
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                | adj-pval       | FC  | Probe Set ID | Gene Symbol | Gene Title                                | adj-pval       | FC  |
|--------------|-------------|-------------------------------------------|----------------|-----|-------------|-------------|-------------------------------------------|----------------|-----|
| 205730_s_at  | ABLIM3      | actin binding LIM protein family, member 3 | 1.06 × 10\(^{-1}\) | 1.53 | 200965_s_at | ABLIM1      | actin binding LIM protein 1               | 2.02 × 10\(^{-5}\) | 4.17|
| 213497_at    | ABTB2       | ankyrin repeat and BTB (POZ) domain containing 2 | 6.59 × 10\(^{-2}\) | 1.61 | 205882_x_at | ADD3        | adducin 3 (gamma)                         | 6.45 × 10\(^{-3}\) | 1.59|
| 205268_s_at  | ADD2        | adducin 2 (beta)                          | 8.16 × 10\(^{-4}\) | 7.50 | 201752_s_at | ADD3        | adducin 3 (gamma)                         | 9.71 × 10\(^{-3}\) | 1.56|
| 205771_s_at  | AKAP7       | A kinase (PRKA) anchor prot 7             | 1.03 × 10\(^{-1}\) | 1.58 | 227529_s_at | AKAP12      | A kinase (PRKA) anchor prot 12            | 6.81 × 10\(^{-3}\) | 8.03|
| 205257_s_at  | AMPH        | amphiphysin                               | 1.45 × 10\(^{-7}\) | 6.02 | 227530_at   | AKAP12      | A kinase (PRKA) anchor prot 12            | 4.43 × 10\(^{-3}\) | 6.10|
| 1552619_a_at | ANLN        | anillin, actin binding protein            | 3.48 × 10\(^{-2}\) | 2.47 | 210517_s_at | AKAP12      | A kinase (PRKA) anchor prot 12            | 6.53 × 10\(^{-3}\) | 4.66|
| 222608_s_at  | ANLN        | anillin, actin binding protein            | 4.60 × 10\(^{-2}\) | 2.25 | 202920_at   | ANK2        | ankyrin 2, neuronal                        | 8.40 × 10\(^{-3}\) | 2.34|
| 203526_s_at  | APC         | adenomatous polyposis coli                | 3.34 × 10\(^{-3}\) | 1.60 | 206385_s_at | ANK3        | ankyrin 3, node of Ranvier (ankyrin G)    | 3.69 × 10\(^{-3}\) | 3.16|
| 204492_at    | ARHGAP11A   | Rho GTPase activating protein 11A         | 3.11 × 10\(^{-2}\) | 2.12 | 227337_at   | ANKRD37     | ankyrin repeat domain 37                  | 4.35 × 10\(^{-6}\) | 6.04|
| 37577_at     | ARHGAP19    | Rho GTPase activating protein 19          | 9.72 × 10\(^{-4}\) | 1.72 | 204671_s_at | ANKRD6      | ankyrin repeat domain 6                   | 3.20 × 10\(^{-2}\) | 2.12|
| 206298_at    | ARHGAP22    | Rho GTPase activating protein 22          | 8.57 × 10\(^{-3}\) | 1.58 | 204672_s_at | ANKRD6      | ankyrin repeat domain 6                   | 5.69 × 10\(^{-2}\) | 1.96|
Table 3. Cont.

| Focal Adhesion Points | UP in Fr | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|-----------------------|----------|----------|----|--------------|-------------|------------|----------|----|
| 201288_at ARHGDIB    | Rho GDP dissociation inhibitor (GDI) beta | 3.85 × 10^{-2} | 1.54 | 228368_at ARHGAP20 | Rho GTPase activating prot 20 | 1.15 × 10^{-4} | 5.72 |
| 204092_s_at AURKA    | aurora kinase A | 2.07 × 10^{-2} | 2.88 | 227911_at ARHGAP28 | Rho GTPase activating prot 28 | 1.07 × 10^{-3} | 2.38 |
| 208079_s_at AURKA    | aurora kinase A | 3.80 × 10^{-2} | 2.45 | 206167_s_at ARHGAP6 | Rho GTPase activating prot 6 | 1.09 × 10^{-1} | 1.65 |
| 209464_at AURKB      | aurora kinase B | 1.04 × 10^{-2} | 2.92 | 205109_s_at ARHGEF4 | Rho guanine nucleotide exchange factor (GEF) 4 | 1.49 × 10^{-1} | 1.53 |
| 205294_at BAIAP2     | BAI1-associated protein 2 | 2.67 × 10^{-3} | 1.51 | 201615_x_at CALD1 | caldesmon 1 | 1.61 × 10^{-1} | 1.79 |
| 210334_x_at BIRC5    | baculoviral IAP repeat-containing 5 | 1.01 × 10^{-2} | 2.69 | 201616_s_at CALD1 | caldesmon 1 | 1.89 × 10^{-2} | 1.53 |
| 202094_at BIRC5      | baculoviral IAP repeat-containing 5 | 4.10 × 10^{-2} | 2.63 | 236473_at CC2D2A | coiled-coil and C2 domain containing 2A | 2.18 × 10^{-3} | 2.56 |
| 202095_s_at BIRC5    | baculoviral IAP repeat-containing 5 | 1.72 × 10^{-2} | 2.47 | 203139_at DAPK1 | death-associated protein kinase 1 | 2.66 × 10^{-2} | 3.97 |
| 220935_s_at CDK5RAP2 | CDK5 regulatory subunit associated protein 2 | 1.91 × 10^{-7} | 1.78 | 229800_at DCLK1 | Doublecortin-like kinase 1 | 1.78 × 10^{-1} | 1.99 |
| 204962_s_at CENPA    | centromere protein A | 3.83 × 10^{-2} | 2.88 | 217208_s_at DLG1 | discs, large homolog 1 (Drosophila) | 6.19 × 10^{-3} | 2.32 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|---------|----|--------------|-------------|------------|---------|----|
| 210821_x_at  | CENPA       | centromere protein A | $4.21 \times 10^{-3}$ | 1.98 | 202515_at    | DLG1        | discs, large homolog 1 (Drosophila) | $1.59 \times 10^{-3}$ | 1.72 |
| 205046_at    | CENPE       | centromere protein E, 312 kDa | $7.08 \times 10^{-2}$ | 2.65 | 202514_at    | DLG1        | discs, large homolog 1 (Drosophila) | $6.69 \times 10^{-3}$ | 1.72 |
| 209172_s_at  | CENPF       | centromere protein F, 350/400 ka (mitosin) | $1.33 \times 10^{-2}$ | 2.98 | 230229_at    | DLG1        | Discs, large homolog 1 (Drosophila) | $1.49 \times 10^{-1}$ | 1.63 |
| 207828_s_at  | CENPF       | centromere protein F, 350/400 ka (mitosin) | $2.29 \times 10^{-2}$ | 2.94 | 202516_s_at  | DLG1        | discs, large homolog 1 (Drosophila) | $5.92 \times 10^{-2}$ | 1.60 |
| 231772_x_at  | CENPH       | centromere protein H | $2.74 \times 10^{-2}$ | 1.82 | 203881_s_at  | DMD         | dystrophin | $1.06 \times 10^{-4}$ | 5.02 |
| 214804_at    | CENPI       | centromere protein I | $5.29 \times 10^{-2}$ | 1.96 | 208086_s_at  | DMD         | dystrophin | $2.36 \times 10^{-2}$ | 1.58 |
| 207900_s_at  | CENPI       | centromere protein I | $1.62 \times 10^{-2}$ | 1.88 | 227081_at    | DNALI1      | dynein, axonemal, light intermediate chain 1 | $2.64 \times 10^{-2}$ | 1.64 |
| 223513_at    | CENPJ       | centromere protein J | $2.83 \times 10^{-2}$ | 1.69 | 226875_at    | DOCK11      | dedicator of cytokinesis 11 | $4.24 \times 10^{-4}$ | 1.78 |
| 222848_at    | CENPK       | centromere protein K | $1.00 \times 10^{-1}$ | 1.94 | 1554863_s_at | DOK5        | docking protein 5 | $1.93 \times 10^{-2}$ | 1.59 |
| 1554271_a_at | CENPL       | centromere protein L | $1.69 \times 10^{-1}$ | 1.54 | 214844_s_at  | DOK5        | docking protein 5 | $2.98 \times 10^{-3}$ | 1.52 |
| 218741_at    | CENPM       | centromere protein M | $1.86 \times 10^{-2}$ | 2.36 | 220161_s_at  | EPB41L4B    | erythrocyte membrane protein band 4.1 like 4B | $5.64 \times 10^{-2}$ | 2.33 |
| 219555_s_at  | CENPN       | centromere protein N | $9.25 \times 10^{-3}$ | 1.89 | 209829_at    | FAM65B      | family with sequence similarity 65, member B | $3.97 \times 10^{-2}$ | 2.58 |
| Probe Set ID  | Gene Symbol | Gene Title       | adj-pval | FC  | Probe Set ID  | Gene Symbol | Gene Title                                                   | adj-pval | FC  |
|--------------|-------------|------------------|----------|-----|--------------|-------------|--------------------------------------------------------------|----------|-----|
| 222118_at    | CENPN       | centromere protein N | 1.24 x 10^{-1} | 1.84 | 206707_x_at  | FAM65B      | family with sequence similarity 65, member B               | 3.02 x 10^{-2} | 2.20 |
| 228559_at    | CENPN       | centromere protein N | 8.63 x 10^{-2} | 1.74 | 226129_at    | FAM83H      | family with sequence similarity 83, member H               | 2.04 x 10^{-2} | 1.75 |
| 226118_at    | CENPO       | centromere protein O | 6.22 x 10^{-2} | 1.78 | 227948_at    | FGD4        | FYVE, RhoGEF and PH domain containing 4                     | 9.89 x 10^{-4} | 3.94 |
| 219294_at    | CENPQ       | centromere protein Q | 5.50 x 10^{-2} | 1.56 | 230559_x_at  | FGD4        | FYVE, RhoGEF and PH domain containing 4                     | 3.65 x 10^{-3} | 2.66 |
| 205642_at    | CEP110      | centrosomal protein 110 kDa | 6.59 x 10^{-3} | 1.87 | 225167_at    | FRMD4A      | FERM domain containing 4A                                   | 1.45 x 10^{-2} | 2.04 |
| 239413_at    | CEP152      | centrosomal protein 152 kDa | 3.34 x 10^{-3} | 1.71 | 225163_at    | FRMD4A      | FERM domain containing 4A                                   | 8.39 x 10^{-3} | 1.98 |
| 218542_at    | CEP55       | centrosomal protein 55 kDa | 2.63 x 10^{-2} | 2.44 | 225168_at    | FRMD4A      | FERM domain containing 4A                                   | 2.22 x 10^{-2} | 1.76 |
| 206324_s_at  | DAPK2       | death-associated protein kinase 2 | 7.47 x 10^{-2} | 1.73 | 1560031_at   | FRMD4A      | FERM domain containing 4A                                   | 1.07 x 10^{-3} | 1.71 |
| 227666_at    | DCLK2       | doublecortin-like kinase 2 | 7.38 x 10^{-2} | 1.52 | 208476_s_at  | FRMD4A      | FERM domain containing 4A                                   | 7.85 x 10^{-3} | 1.69 |
| 207147_at    | DLX2        | distal-less homeobox 2 | 1.94 x 10^{-2} | 6.12 | 1554034_a_at | FRMD4A      | FERM domain containing 4A                                   | 2.32 x 10^{-1} | 1.57 |
| 215116_s_at  | DNM1        | dynamin 1          | 2.03 x 10^{-4} | 3.83 | 239290_at    | FRMD4       | FERM and PDZ domain containing 4                            | 1.74 x 10^{-1} | 1.56 |
| 219279_at    | DOCK10      | dedicator of cytokinesis 10 | 2.60 x 10^{-2} | 1.66 | 203037_s_at  | MTSS1       | metastasis suppressor 1                                     | 2.31 x 10^{-3} | 4.32 |
Table 3. Cont.

| Focal Adhesion Points | UP in Fr | | | UP in F-DHJ | | |
|-----------------------|----------|-------|----------------|----------------|
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
| 213160_at | DOCK2 | dedicator of cytokinesis 2 | $1.12 \times 10^{-4}$ | 1.76 | 212096_s_at | MTUS1 | mitochondrial tumor supp 1 | $1.02 \times 10^{-1}$ | 2.47 |
| 205003_at | DOCK4 | dedicator of cytokinesis 4 | $1.44 \times 10^{-1}$ | 1.54 | 212095_s_at | MTUS1 | mitochondrial tumor supp 1 | $1.08 \times 10^{-1}$ | 1.74 |
| 206710_s_at | EPB41L3 | erythrocyte membrane protein band 4.1-like 3 | $1.31 \times 10^{-2}$ | 3.52 | 228098_s_at | MYLIP | myosin regulatory light chain interacting protein | $5.16 \times 10^{-2}$ | 1.57 |
| 212681_at | EPB41L3 | erythrocyte membrane protein band 4.1-like 3 | $1.38 \times 10^{-2}$ | 3.22 | 220319_s_at | MYLIP | myosin regulatory light chain interacting protein | $4.55 \times 10^{-2}$ | 1.50 |
| 211776_s_at | EPB41L3 | erythrocyte membrane protein band 4.1-like 3 | $1.48 \times 10^{-2}$ | 3.20 | 237206_at | MYOCD | myocardin | $8.62 \times 10^{-3}$ | 3.85 |
| 218980_at | FHOD3 | formin homology 2 domain containing 3 | $7.93 \times 10^{-3}$ | 3.13 | 213782_s_at | MYOZ2 | myozeenin 2 | $8.68 \times 10^{-2}$ | 2.16 |
| 238621_at | FMN1 | formin 1 | $6.44 \times 10^{-3}$ | 2.47 | 207148_x_at | MYOZ2 | myozeenin 2 | $8.91 \times 10^{-2}$ | 2.07 |
| 1555471_a_at | FMN2 | formin 2 | $2.05 \times 10^{-2}$ | 1.85 | 219073_s_at | OSBPL10 | oxysterol binding protein-like 10 | $3.31 \times 10^{-2}$ | 2.11 |
| 223618_at | FMN2 | formin 2 | $2.05 \times 10^{-2}$ | 1.82 | 209621_s_at | PDLIM3 | PDZ and LIM domain 3 | $8.38 \times 10^{-2}$ | 3.31 |
| 215017_s_at | FNB1L | formin binding protein 1-like | $3.68 \times 10^{-3}$ | 1.52 | 213684_s_at | PDLIM5 | PDZ and LIM domain 5 | $6.28 \times 10^{-3}$ | 1.87 |
Table 3. Cont.

| Probe Set ID  | Gene Symbol | Gene Title                                | adj-pval | FC    | Probe Set ID  | Gene Symbol | Gene Title                                | adj-pval | FC    |
|---------------|-------------|-------------------------------------------|----------|-------|---------------|-------------|-------------------------------------------|----------|-------|
| 230645_at     | FRMD3       | FERM domain containing 3                   | 2.69 × 10^{-1} | 1.63  | 221994_at     | PDLIM5      | PDZ and LIM domain 5                       | 2.46 × 10^{-3} | 1.81  |
| 230831_at     | FRMD5       | FERM domain containing 5                   | 1.02 × 10^{-2} | 2.87  | 203242_s_at   | PDLIM5      | PDZ and LIM domain 5                       | 1.86 × 10^{-3} | 1.68  |
| 238756_at     | GAS2L3      | Growth arrest-specific 2 like 3            | 1.22 × 10^{-2} | 2.33  | 216804_s_at   | PDLIM5      | PDZ and LIM domain 5                       | 4.90 × 10^{-3} | 1.60  |
| 235709_at     | GAS2L3      | growth arrest-specific 2 like 3            | 2.92 × 10^{-2} | 1.81  | 207717_s_at   | PKP2        | plakophilin 2                             | 2.96 × 10^{-2} | 3.09  |
| 226308_at     | HAUS8       | HAUS augmin-like complex, subunit 8        | 3.75 × 10^{-2} | 1.71  | 201927_s_at   | PKP4        | plakophilin 4                             | 2.90 × 10^{-1} | 1.68  |
| 226364_at     | HIP1        | Huntingtin interacting protein 1           | 1.05 × 10^{-3} | 2.73  | 227148_at     | PLEKHH2     | pleckstrin homology domain containing, family H member 2 | 3.16 × 10^{-3} | 3.05  |
| 205425_at     | HIP1        | huntingtin interacting protein 1           | 9.54 × 10^{-3} | 2.66  | 203407_at     | PPL         | periplakin                                | 7.99 × 10^{-3} | 3.20  |
| 218934_s_at   | HSPB7       | heat shock 27 kDa protein family, member 7 | 7.51 × 10^{-2} | 2.16  | 226627_at     | SEPT8       | septin 8                                  | 1.20 × 10^{-1} | 1.74  |
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC   | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC       |
|--------------|-------------|------------|------------|------|--------------|-------------|------------|----------|----------|
| 227750_at    | KALRN       | kalirin, RhoGEF kinase | 8.61 x 10^-3 | 1.53 | 226438_at    | SNTB1       | syntrophin, beta 1 (dystrophin-associated protein A1, 59 kDa, basic component 1) | 1.03 x 10^-2 | 1.84     |
| 229125_at    | KANK4       | KN motif and ankyrin repeat domains 4 | 1.76 x 10^-2 | 3.51 | 214708_at    | SNTB1       | syntrophin, beta 1 (dystrophin-associated protein A1, 59 kDa, basic component 1) | 3.83 x 10^-2 | 1.53     |
| 204444_at    | KIF11       | kinesin family member 11 | 4.00 x 10^-2 | 2.43 | 227179_at    | STAU2       | staufen, RNA binding protein, homolog 2 (Drosophila) | 1.58 x 10^-2 | 1.89     |
| 236641_at    | KIF14       | kinesin family member 14 | 1.15 x 10^-2 | 3.50 | 212565_at    | STK38L      | serine/threonine kinase 38 like | 5.74 x 10^-5 | 1.94     |
| 206364_at    | KIF14       | kinesin family member 14 | 5.29 x 10^-2 | 2.87 | 212572_at    | STK38L      | serine/threonine kinase 38 like | 5.09 x 10^-3 | 1.53     |
| 219306_at    | KIF15       | kinesin family member 15 | 1.87 x 10^-2 | 2.65 | 202796_at    | SYNPO       | synaptopodin | 7.05 x 10^-2 | 2.18     |
| 221258_s_at  | KIF18A      | kinesin family member 18A | 1.25 x 10^-2 | 2.79 | 227662_at    | SYNPO2      | synaptopodin 2 | 1.29 x 10^-1 | 3.30     |
| 222039_at    | KIF18B      | kinesin family member 18B | 6.34 x 10^-2 | 2.25 | 213135_at    | TIAM1       | T-cell lymphoma invasion and metastasis 1 | 1.12 x 10^-1 | 1.65     |
| 218755_at    | KIF20A      | kinesin family member 20A | 1.17 x 10^-2 | 2.81 | 209904_at    | TNNC1       | troponin C type 1 (slow) | 6.34 x 10^-2 | 2.76     |
| 205235_s_at  | KIF20B      | kinesin family member 20B | 1.83 x 10^-2 | 1.95 | 215389_s_at  | TNNT2       | troponin T type 2 (cardiac) | 5.06 x 10^-2 | 3.22     |
| Probe Set ID | Gene Symbol | Gene Title                  | adj-pval   | FC   | Probe Set ID | Gene Symbol | Gene Title                                                                 | adj-pval   | FC   |
|-------------|-------------|-----------------------------|------------|------|-------------|-------------|----------------------------------------------------------------------------|------------|------|
| 216969_s_at | KIF22       | kinesin family member 22    | 9.75 × 10^{-2} | 1.92 | 210276_s_at | TRIOBP      | TRIO and F-actin binding prot                                            | 6.96 × 10^{-2} | 1.52 |
| 202183_s_at | KIF22       | kinesin family member 22    | 6.19 × 10^{-3} | 1.65 | 223279_s_at | UACA        | uveal autoantigen with coiled-coil domains and ankyrin repeats            | 6.84 × 10^{-3} | 1.79 |
| 204709_s_at | KIF23       | kinesin family member 23    | 3.68 × 10^{-2} | 2.55 | 238868_at   | UACA        | uveal autoantigen with coiled-coil domains and ankyrin repeats            | 1.37 × 10^{-1} | 1.66 |
| 244427_at  | KIF23       | Kinesin family member 23    | 2.68 × 10^{-3} | 1.76 |             |             |                                                                            |            |      |
| 209408_at  | KIF2C       | kinesin family member 2C    | 3.86 × 10^{-2} | 2.95 |             |             |                                                                            |            |      |
| 211519_s_at | KIF2C       | kinesin family member 2C    | 2.04 × 10^{-2} | 2.80 |             |             |                                                                            |            |      |
| 218355_at  | KIF4A       | kinesin family member 4A    | 3.29 × 10^{-2} | 2.60 |             |             |                                                                            |            |      |
| 209680_s_at | KIFC1       | kinesin family member C1    | 1.72 × 10^{-2} | 2.43 |             |             |                                                                            |            |      |
| 206316_s_at | KNTC1       | kinetochore associated 1     | 1.88 × 10^{-2} | 1.86 |             |             |                                                                            |            |      |
| 224823_at  | MYLK        | myosin light chain kinase   | 1.91 × 10^{-1} | 1.72 |             |             |                                                                            |            |      |
| 236718_at  | MYO10       | myosin X                    | 1.05 × 10^{-3} | 1.86 |             |             |                                                                            |            |      |
| 244350_at  | MYO10       | myosin X                    | 1.45 × 10^{-2} | 1.70 |             |             |                                                                            |            |      |
| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval  | FC | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval  | FC |
|--------------|-------------|-------------------------------------------------|-----------|----|--------------|-------------|-------------------------------------------------|-----------|----|
| 241966_at    | MYO5A       | myosin VA (heavy chain 12, myoxin)              | $2.21 \times 10^{-2}$ | 1.51 |              |             |                                                 |           |    |
| 201774_s_at  | NCAPD2      | non-SMC condensin I complex, subunit D2         | $1.30 \times 10^{-1}$ | 1.57 |              |             |                                                 |           |    |
| 212789_at    | NCAPD3      | non-SMC condensin II complex, subunit D3        | $5.55 \times 10^{-2}$ | 1.56 |              |             |                                                 |           |    |
| 218663_at    | NCAPG       | non-SMC condensin I complex, subunit G          | $1.03 \times 10^{-1}$ | 2.23 |              |             |                                                 |           |    |
| 218662_s_at  | NCAPG       | non-SMC condensin I complex, subunit G          | $8.24 \times 10^{-2}$ | 2.11 |              |             |                                                 |           |    |
| 219588_s_at  | NCAPG2      | non-SMC condensin II complex, subunit G2        | $2.03 \times 10^{-2}$ | 1.86 |              |             |                                                 |           |    |
| 212949_at    | NCAPH       | non-SMC condensin I complex, subunit H          | $3.01 \times 10^{-2}$ | 2.58 |              |             |                                                 |           |    |
| Probe Set ID  | Gene Symbol | Gene Title                                                                 | adj-pval      | FC   | Probe Set ID  | Gene Symbol | Gene Title                                                                 | adj-pval      | FC   |
|---------------|-------------|----------------------------------------------------------------------------|---------------|------|---------------|-------------|----------------------------------------------------------------------------|---------------|------|
| 204641_at     | NEK2        | NIMA (never in mitosis gene a)-related kinase 2                             | $2.34 \times 10^{-2}$ | 2.97 |              |             |                                                                           |               |      |
| 211080_s_at   | NEK2        | NIMA (never in mitosis gene a)-related kinase 2                             | $4.89 \times 10^{-3}$ | 2.64 |              |             |                                                                           |               |      |
| 223381_at     | NUF2        | NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae)           | $8.44 \times 10^{-2}$ | 2.67 |              |             |                                                                           |               |      |
| 219978_s_at   | NUSAP1      | nucleolar and spindle associated protein 1                                 | $1.39 \times 10^{-1}$ | 2.48 |              |             |                                                                           |               |      |
| 218039_at     | NUSAP1      | nucleolar and spindle associated protein 1                                 | $2.98 \times 10^{-2}$ | 2.42 |              |             |                                                                           |               |      |
| 204972_at     | OAS2        | 2'-5'-oligoadenylate synthetase 2, 69/71 kDa                               | $2.83 \times 10^{-1}$ | 1.68 |              |             |                                                                           |               |      |
| 209626_s_at   | OSBPL3      | oxysterol binding protein-like 3                                            | $5.77 \times 10^{-2}$ | 1.67 |              |             |                                                                           |               |      |
| 238575_at     | OSBPL6      | oxysterol binding protein-like 6                                            | $1.17 \times 10^{-2}$ | 2.13 |              |             |                                                                           |               |      |
| 223805_at     | OSBPL6      | oxysterol binding protein-like 6                                            | $9.15 \times 10^{-3}$ | 2.09 |              |             |                                                                           |               |      |
| Probe Set ID  | Gene Symbol | Gene Title                           | adj-pval   | FC  | Probe Set ID  | Gene Symbol | Gene Title                           | adj-pval   | FC  |
|--------------|-------------|--------------------------------------|------------|-----|--------------|-------------|--------------------------------------|------------|-----|
| 218644_at    | PLEK2       | pleckstrin 2                         | $4.94 \times 10^{-3}$ | 2.63 |              |             |                                      |            |     |
| 218009_s_at  | PRC1        | protein regulator of cytokinesis 1   | $2.03 \times 10^{-2}$ | 2.37 |              |             |                                      |            |     |
| 222077_s_at  | RACGAP1     | Rac GTPase activating protein 1      | $1.49 \times 10^{-2}$ | 1.99 |              |             |                                      |            |     |
| 219263_at    | RNF128      | ring finger protein 128              | $2.50 \times 10^{-2}$ | 3.03 |              |             |                                      |            |     |
| 230730_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | $2.17 \times 10^{-2}$ | 3.65 |              |             |                                      |            |     |
| 213543_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | $2.12 \times 10^{-2}$ | 3.57 |              |             |                                      |            |     |
| 228602_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | $6.41 \times 10^{-2}$ | 3.55 |              |             |                                      |            |     |
| 214492_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | $5.41 \times 10^{-3}$ | 3.18 |              |             |                                      |            |     |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval    | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval    | FC  |
|--------------|-------------|------------|-------------|-----|--------------|-------------|------------|-------------|-----|
| 210329_s_at  | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 8.64 x 10^-3 | 2.72 |              |             |            |             |     |
| 210330_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 3.47 x 10^-2 | 2.43 |              |             |            |             |     |
| 207302_at    | SGCG        | sarcoglycan, gamma (35 kDa dystrophin-associated glycoprotein) | 1.42 x 10^-1 | 3.09 |              |             |            |             |     |
| 217678_at    | SLC7A11     | solute carrier family 7, (cationic amino acid transporter, y+ system) member 11 | 7.43 x 10^-2 | 1.53 |              |             |            |             |     |
| 209921_at    | SLC7A11     | solute carrier family 7, (cationic amino acid transporter, y+ system) member 11 | 3.18 x 10^-2 | 1.53 |              |             |            |             |     |
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 1556583_a_at | SLC8A1      | solute carrier family 8 (sodium/calcium exchanger), member 1 | $1.96 \times 10^{-1}$ | 1.85 | | | | | |
| 241752_at    | SLC8A1      | solute carrier family 8 (sodium/calcium exchanger), member 1 | $2.94 \times 10^{-1}$ | 1.61 | | | | | |
| 200783_s_at  | STMN1       | stathmin 1 | $1.16 \times 10^{-2}$ | 2.14 | | | | | |
| 222557_at    | STMN3       | stathmin-like 3 | $1.48 \times 10^{-2}$ | 1.83 | | | | | |
| 212703_at    | TLN2        | talin 2    | $5.18 \times 10^{-4}$ | 1.84 | | | | | |
| 206117_at    | TPM1        | tropomyosin 1 (alpha) | $5.66 \times 10^{-3}$ | 2.26 | | | | | |
| 210052_s_at  | TPX2        | TPX2, microtubule-associated, homolog (Xenopus laevis) | $1.78 \times 10^{-2}$ | 2.56 | | | | | |
| 1555938_x_at | VIM         | vimentin   | $2.81 \times 10^{-2}$ | 2.00 | | | | | |
| 202663_at    | WIPF1       | WAS/WASL interacting protein family, member 1 | $6.39 \times 10^{-3}$ | 1.64 | | | | | |
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC |
|--------------|-------------|------------------------------------------------|--------------|----|--------------|-------------|------------------------------------------------|--------------|----|
| 202664_at    | WIPF1       | WAS/WASL interacting protein family, member 1  | $5.61 \times 10^{-4}$ | 1.58 |             |             |                                                |              |    |
| 202665_s_at  | WIPF1       | WAS/WASL interacting protein family, member 1  | $2.97 \times 10^{-3}$ | 1.51 |             |             |                                                |              |    |

**Cytoskeleton**

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC |
|--------------|-------------|------------------------------------------------|--------------|----|--------------|-------------|------------------------------------------------|--------------|----|
| 205132_at    | ACTC1       | actin, alpha, cardiac muscle 1                 | $1.80 \times 10^{-3}$ | 4.22 | 203563_at    | AFAP1       | actin filament associated protein 1             | $2.27 \times 10^{-3}$ | 1.90 |
| 230925_at    | APBB1IP     | amyloid beta (A4) precursor protein-binding, family B, member 1 interacting protein | $1.66 \times 10^{-2}$ | 2.50 | 206488_s_at  | CD36        | CD36 molecule (thrombospondin receptor)       | $1.46 \times 10^{-8}$ | 20.69 |
| 226292_at    | CAPN5       | calpain 5                                       | $2.20 \times 10^{-4}$ | 1.51 | 209555_s_at  | CD36        | CD36 molecule (thrombospondin receptor)       | $3.58 \times 10^{-8}$ | 19.05 |
| 217523_at    | CD44        | CD44 molecule (Indian blood group)              | $1.89 \times 10^{-2}$ | 1.64 | 228766_at    | CD36        | CD36 molecule (thrombospondin receptor)       | $2.97 \times 10^{-6}$ | 11.94 |
| 220115_s_at  | CDH10       | cadherin 10, type 2 (T2-cadherin)               | $1.94 \times 10^{-1}$ | 1.90 | 201005_at    | CD9         | CD9 molecule                                   | $7.82 \times 10^{-4}$ | 2.58 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 207030_s_at  | CSRP2       | cysteine and glycine-rich protein 2 | 1.93 × 10^{-2} | 1.74 | 201131_s_at  | CDH1        | cadherin 1, type 1, E-cadherin (epithelial) | 4.31 × 10^{-2} | 2.54 |
| 211126_s_at  | CSRP2       | cysteine and glycine-rich protein 2 | 2.34 × 10^{-2} | 1.71 | 204726_at    | CDH13       | cadherin 13, H-cadherin (heart) | 3.20 × 10^{-2} | 2.60 |
| 214724_at    | DIXDC1      | DIX domain containing 1 | 1.14 × 10^{-2} | 1.53 | 203256_at    | CDH3        | cadherin 3, type 1, P-cadherin (placental) | 3.21 × 10^{-2} | 1.84 |
| 202668_at    | EFNB2       | ephrin-B2   | 1.85 × 10^{-1} | 3.24 | 200621_at    | CSRP1       | cysteine and glycine-rich protein 1 | 1.70 × 10^{-2} | 1.56 |
| 205031_at    | EFNB3       | ephrin-B3   | 2.95 × 10^{-10} | 2.47 | 203716_s_at  | DPP4        | dipeptidyl-peptidase 4 | 4.05 × 10^{-2} | 1.93 |
| 1555480_a_at | FBLIM1      | filamin binding LIM protein 1 | 1.07 × 10^{-2} | 1.89 | 211478_s_at  | DPP4        | dipeptidyl-peptidase 4 | 2.67 × 10^{-1} | 1.80 |
| 1554795_a_at | FBLIM1      | filamin binding LIM protein 1 | 2.26 × 10^{-2} | 1.61 | 203717_at    | DPP4        | dipeptidyl-peptidase 4 | 1.08 × 10^{-1} | 1.67 |
| 225258_at    | FBLIM1      | filamin binding LIM protein 1 | 2.87 × 10^{-3} | 1.56 | 227955_s_at  | EFNA5       | ephrin-A5 | 4.68 × 10^{-2} | 1.94 |
| 204379_s_at  | FGFR3       | fibroblast growth factor receptor 3 | 9.77 × 10^{-2} | 2.01 | 214036_at    | EFNA5       | ephrin-A5 | 1.32 × 10^{-1} | 1.53 |
| 242592_at    | GPR137C     | G protein-coupled receptor 137C | 1.50 × 10^{-2} | 2.18 | 201983_s_at  | EGFR        | epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian) | 1.75 × 10^{-3} | 1.82 |
| 235961_at    | GPR161      | G protein-coupled receptor 161 | 4.34 × 10^{-4} | 1.56 | 201809_s_at  | ENG         | endoglin | 2.31 × 10^{-3} | 2.06 |
### Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 230369_at    | GPR161      | G protein-coupled receptor 161 | $3.44 \times 10^{-2}$ | 1.53 | 201539_s_at  | FHL1        | four and a half LIM domains 1 | $8.39 \times 10^{-3}$ | 6.09 |
| 229055_at    | GPR68       | G protein-coupled receptor 68   | $7.83 \times 10^{-3}$ | 1.70 | 214505_s_at  | FHL1        | four and a half LIM domains 1 | $6.48 \times 10^{-3}$ | 5.76 |
| 234303_s_at  | GPR85       | G protein-coupled receptor 85   | $7.25 \times 10^{-2}$ | 2.04 | 210299_s_at  | FHL1        | four and a half LIM domains 1 | $1.55 \times 10^{-3}$ | 5.39 |
| 203632_s_at  | GPRC5B      | G protein-coupled receptor, family C, group 5, member B | $1.76 \times 10^{-1}$ | 1.92 | 210298_x_at  | FHL1        | four and a half LIM domains 1 | $6.70 \times 10^{-3}$ | 5.18 |
| 222899_at    | ITGA11      | integrin, alpha 11             | $1.21 \times 10^{-2}$ | 1.59 | 201540_at    | FHL1        | four and a half LIM domains 1 | $4.21 \times 10^{-4}$ | 3.20 |
| 227314_at    | ITGA2       | integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) | $5.68 \times 10^{-2}$ | 2.53 | 222853_at    | FLRT3       | fibronectin leucine rich transmembrane protein 3 | $7.40 \times 10^{-4}$ | 3.36 |
| 205032_at    | ITGA2       | integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) | $3.78 \times 10^{-2}$ | 2.41 | 219250_s_at  | FLRT3       | fibronectin leucine rich transmembrane protein 3 | $4.52 \times 10^{-2}$ | 2.12 |
| 228080_at    | LAYN        | layilin                          | $4.84 \times 10^{-3}$ | 2.59 | 212950_at    | GPR116      | G protein-coupled receptor 116 | $1.98 \times 10^{-1}$ | 3.52 |
| 216250_s_at  | LPXN        | leupaxin                         | $2.03 \times 10^{-5}$ | 3.08 | 213094_at    | GPR126      | G protein-coupled receptor 126 | $9.65 \times 10^{-4}$ | 5.14 |
| 210869_s_at  | MCAM        | melanoma cell adhesion molecule  | $1.03 \times 10^{-6}$ | 7.67 | 232267_at    | GPR133      | G protein-coupled receptor 133 | $1.46 \times 10^{-2}$ | 2.44 |
Table 3. Cont.

| Probe Set ID   | Gene Symbol | Gene Title                                      | adj-pval    | FC  | Probe Set ID   | Gene Symbol     | Gene Title                                      | adj-pval    | FC  |
|----------------|-------------|------------------------------------------------|-------------|-----|----------------|----------------|------------------------------------------------|-------------|-----|
| 209087_x_at    | MCAM        | melanoma cell adhesion molecule                 | 1.08 × 10^{-6} | 7.38| 228949_at      | GPR177         | G protein-coupled receptor 177                 | 3.16 × 10^{-4} | 2.71|
| 211340_s_at    | MCAM        | melanoma cell adhesion molecule                 | 1.07 × 10^{-6} | 6.81| 228950_s_at    | GPR177         | G protein-coupled receptor 177                 | 3.49 × 10^{-3} | 2.63|
| 209086_x_at    | MCAM        | melanoma cell adhesion molecule                 | 2.85 × 10^{-8} | 5.09| 221958_s_at    | GPR177         | G protein-coupled receptor 177                 | 1.52 × 10^{-3} | 2.50|
| 203062_s_at    | MDC1        | mediator of DNA damage checkpoint 1             | 3.87 × 10^{-3} | 1.58| 229105_at      | GPR39          | G protein-coupled receptor 39                  | 2.66 × 10^{-2} | 1.90|
| 212843_at      | NCAM1       | neural cell adhesion molecule 1                 | 8.99 × 10^{-7} | 4.58| 212070_at      | GPR56          | G protein-coupled receptor 56                  | 2.12 × 10^{-2} | 1.78|
| 227394_at      | NCAM1       | neural cell adhesion molecule 1                 | 1.26 × 10^{-6} | 3.16| 203108_at      | GPRC5A         | G protein-coupled receptor, family C, group 5, member A | 2.08 × 10^{-3} | 8.54|
| 213438_at      | NFASC       | neurofascin homolog (chicken)                   | 3.12 × 10^{-2} | 2.57| 202638_s_at    | ICAM1          | intercellular adhesion molecule 1             | 1.31 × 10^{-1} | 2.21|
| 230242_at      | NFASC       | neurofascin homolog (chicken)                   | 5.17 × 10^{-3} | 2.19| 202637_s_at    | ICAM1          | intercellular adhesion molecule 1             | 7.04 × 10^{-2} | 1.70|
| 243645_at      | NFASC       | neurofascin homolog (chicken)                   | 2.12 × 10^{-3} | 2.03| 205885_s_at    | ITGA4          | integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor) | 2.52 × 10^{-1} | 1.71|
| Probe Set ID | Gene Symbol | Gene Title               | adj-pval   | FC  | Probe Set ID | Gene Symbol | Gene Title               | adj-pval   | FC  |
|--------------|-------------|--------------------------|------------|-----|--------------|-------------|--------------------------|------------|-----|
| 219773_at    | NOX4        | NADPH oxidase 4           | 8.60 × 10⁻²| 1.80| 216331_at    | ITGA7       | integrin, alpha 7         | 1.01 × 10⁻²| 3.76|
| 37966_at     | PARVB       | parvin, beta             | 4.78 × 10⁻¹₀| 2.88| 209663_s_at  | ITGA7       | integrin, alpha 7         | 4.49 × 10⁻²| 3.70|
| 204629_at    | PARVB       | parvin, beta             | 2.58 × 10⁻⁸| 2.28| 204990_s_at  | ITGB4       | integrin, beta 4          | 8.14 × 10⁻²| 1.67|
| 37965_at     | PARVB       | parvin, beta             | 7.26 × 10⁻⁵| 1.98| 226189_at    | ITGB8       | integrin, beta 8          | 2.19 × 10⁻²| 1.69|
| 216253_s_at  | PARVB       | parvin, beta             | 4.90 × 10⁻³| 1.80| 220765_s_at  | LIMS2       | LIM and senescent cell    | 1.80 × 10⁻²| 1.80|
| 225977_at    | PCDH18      | protocadherin 18         | 4.98 × 10⁻³| 2.18| 226974_at    | NEDD4L      | neural precursor cell      | 4.84 × 10⁻²| 2.02|
| 225975_at    | PCDH18      | protocadherin 18         | 1.29 × 10⁻²| 1.76| 212448_at    | NEDD4L      | neural precursor cell      | 9.48 × 10⁻²| 1.78|
| 207011_s_at  | PTK7        | PTK7 protein tyrosine kinase 7 | 3.74 × 10⁻³| 2.23| 212445_s_at  | NEDD4L      | neural precursor cell      | 1.04 × 10⁻¹| 1.76|
| 1555324_at   | PTK7        | PTK7 protein tyrosine kinase 7 | 5.32 × 10⁻³| 1.78| 202150_s_at  | NEDD9       | neural precursor cell      | 3.21 × 10⁻³| 1.97|
| Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC  |
|--------------|-------------|------------|-----------|-----|--------------|-------------|------------|-----------|-----|
| 207419_s_at  | RAC2        | ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2) | $1.39 \times 10^{-2}$ | 2.37 | 202149_at    | NEDD9       | neural precursor cell expressed, developmentally down-regulated 9 | $3.93 \times 10^{-4}$ | 1.90 |
| 223168_at    | RHOU        | ras homolog gene family, member U | $1.13 \times 10^{-5}$ | 3.13 | 223435_s_at  | PCDH10      | protocadherin 10 | $2.55 \times 10^{-3}$ | 3.91 |
| 201286_at    | SDC1        | syndecan 1 | $7.78 \times 10^{-3}$ | 3.11 | 202565_s_at  | SVIL        | supervillin | $5.25 \times 10^{-3}$ | 3.45 |
| 201287_s_at  | SDC1        | syndecan 1 | $3.47 \times 10^{-3}$ | 3.04 | 202566_s_at  | SVIL        | supervillin | $5.31 \times 10^{-2}$ | 2.32 |
Table 3. Cont.

| Probe Set ID | Gene Symbol | Gene Title                  | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title                  | adj-pval | FC  |
|--------------|-------------|------------------------------|----------|----|--------------|-------------|------------------------------|----------|-----|
| 202898_at    | SDC3        | syndecan 3                   | $2.98 \times 10^{-2}$ | 1.66 | 206702_at    | TEK         | TEK tyrosine kinase, endothelial | $4.91 \times 10^{-4}$ | 3.67 |
| 21087_s_at   | SORBS1      | sorbin and SH3 domain containing 1 | $1.05 \times 10^{-2}$ | 4.48 |
| 222513_s_at  | SORBS1      | sorbin and SH3 domain containing 1 | $3.04 \times 10^{-2}$ | 2.95 |
| 208850_s_at  | THY1        | Thy-1 cell surface antigen   | $2.80 \times 10^{-1}$ | 1.91 |
| 213869_x_at  | THY1        | Thy-1 cell surface antigen   | $1.38 \times 10^{-1}$ | 1.77 |
| 208851_s_at  | THY1        | Thy-1 cell surface antigen   | $2.50 \times 10^{-1}$ | 1.70 |
| 217853_at    | TNS3        | tensin 3                     | $5.51 \times 10^{-5}$ | 2.61 |
| 217979_at    | TSPAN13     | tetraspanin 13               | $1.08 \times 10^{-4}$ | 4.67 |
| 227307_at    | TSPAN18     | Tetraspanin 18               | $2.78 \times 10^{-4}$ | 3.95 |
| 227236_at    | TSPAN2      | tetraspanin 2                | $1.85 \times 10^{-1}$ | 2.19 |
| 214606_at    | TSPAN2      | tetraspanin 2                | $1.19 \times 10^{-1}$ | 1.83 |

LINC Complexes

| Probe Set ID | Gene Symbol | Gene Title                  | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title                  | adj-pval | FC  |
|--------------|-------------|------------------------------|----------|----|--------------|-------------|------------------------------|----------|-----|
| 203145_at    | SPAG5       | sperm associated antigen 5   | $2.63 \times 10^{-2}$ | 2.48 | 219888_at    | SPAG4       | sperm associated antigen 4   | $8.03 \times 10^{-2}$ | 1.87 |
Table 3. Cont.

| Nucleoskeleton | UP in Fr | Secreted Factors | UP in F-DHJ |
|----------------|----------|------------------|-------------|
| **Probe Set ID** | **Gene Symbol** | **Gene Title** | **adj-pval** | **FC** | **Probe Set ID** | **Gene Symbol** | **Gene Title** | **adj-pval** | **FC** |
| 205436_s_at | H2AFX | H2A histone family, member X | 1.88 × 10^{-2} | 1.71 | 215071_s_at | HIST1H2AC | histone cluster 1, H2ac | 2.13 × 10^{-2} | 1.70 |
| 214463_x_at | HIST1H4J | histone cluster 1, H4j | 1.24 × 10^{-2} | 1.53 | 214455_at | HIST1H2BC | histone cluster 1, H2bc | 1.34 × 10^{-2} | 1.71 |
| 201795_at | LBR | lamin B receptor | 8.68 × 10^{-4} | 1.88 | 236193_at | HIST1H2BC | histone cluster 1, H2bc | 1.57 × 10^{-2} | 1.60 |
| 203276_at | LMNB1 | lamin B1 | 8.33 × 10^{-2} | 2.42 | 209911_x_at | HIST1H2BD | histone cluster 1, H2bd | 1.63 × 10^{-2} | 1.63 |
| 209753_s_at | TMPO | thymopoietin | 5.06 × 10^{-3} | 1.98 | 208527_x_at | HIST1H2BE | histone cluster 1, H2be | 4.22 × 10^{-3} | 1.54 |
| 224944_at | TMPO | thymopoietin | 5.13 × 10^{-3} | 1.84 | 232035_at | HIST1H4B | Histone cluster 1, H4b | 5.60 × 10^{-3} | 1.96 |
| 209754_s_at | TMPO | thymopoietin | 2.51 × 10^{-2} | 1.83 | 208180_s_at | HIST1H4B | Histone cluster 1, H4b | 1.34 × 10^{-1} | 1.59 |
| 203432_at | TMPO | thymopoietin | 1.02 × 10^{-1} | 1.64 | | | | | |
| **Probe Set ID** | **Gene Symbol** | **Gene Title** | **adj-pval** | **FC** | **Probe Set ID** | **Gene Symbol** | **Gene Title** | **adj-pval** | **FC** |
| 205608_s_at | ANGPT1 | angiopoietin 1 | 1.27 × 10^{-4} | 3.04 | 231773_at | ANGPTL1 | angiopoietin-like 1 | 3.01 × 10^{-2} | 2.12 |
| 205609_at | ANGPT1 | angiopoietin 1 | 7.38 × 10^{-6} | 2.97 | 224339_s_at | ANGPTL1 | angiopoietin-like 1 | 7.59 × 10^{-2} | 1.71 |
| 213001_at | ANGPTL2 | angiopoietin-like 2 | 1.03 × 10^{-1} | 1.50 | 239183_at | ANGPTL1 | angiopoietin-like 1 | 8.51 × 10^{-2} | 1.50 |
| 220988_s_at | C1QTNF3 | C1q and tumor necrosis factor related protein 3 | 9.99 × 10^{-2} | 1.78 | 221009_s_at | ANGPTL4 | angiopoietin-like 4 | 6.59 × 10^{-3} | 2.88 |
| 1405_i_at | CCL5 | chemokine (C-C motif) ligand 5 | 1.12 × 10^{-1} | 1.56 | 223333_s_at | ANGPTL4 | angiopoietin-like 4 | 1.80 × 10^{-1} | 2.11 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 203666_at    | CXCL12      | chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) | $6.11 \times 10^{-3}$ | 2.98 | 209546_s_at  | APOL1       | apolipoprotein L, 1 | $1.42 \times 10^{-1}$ | 1.78 |
| 209687_at    | CXCL12      | chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) | $1.99 \times 10^{-2}$ | 2.24 | 221087_s_at  | APOL3       | apolipoprotein L, 3 | $6.19 \times 10^{-2}$ | 1.83 |
| 222484_s_at  | CXCL14      | chemokine (C-X-C motif) ligand 14 | $5.41 \times 10^{-4}$ | 7.47 | 205239_at    | AREG        | amphiregulin          | $1.14 \times 10^{-1}$ | 1.75 |
| 218002_s_at  | CXCL14      | chemokine (C-X-C motif) ligand 14 | $1.22 \times 10^{-3}$ | 6.46 | 202701_at    | BMP1        | bone morphogenetic protein 1 | $5.22 \times 10^{-2}$ | 1.54 |
| 204602_at    | DKK1        | dickkopf homolog 1 (Xenopus laevis) | $2.42 \times 10^{-2}$ | 2.04 | 205289_at    | BMP2        | bone morphogenetic protein 2 | $2.65 \times 10^{-2}$ | 2.54 |
| 219908_at    | DKK2        | dickkopf homolog 2 (Xenopus laevis) | $7.38 \times 10^{-4}$ | 4.54 | 205290_s_at  | BMP2        | bone morphogenetic protein 2 | $8.44 \times 10^{-2}$ | 2.25 |
| 228952_at    | ENPP1       | ectonucleotide pyrophosphatase/phosphodiesterase 1 | $5.77 \times 10^{-7}$ | 4.95 | 211518_s_at  | BMP4        | bone morphogenetic protein 4 | $1.68 \times 10^{-2}$ | 4.03 |
| 229088_at    | ENPP1       | ectonucleotide pyrophosphatase/phosphodiesterase 1 | $5.38 \times 10^{-7}$ | 4.83 | 206176_at    | BMP6        | bone morphogenetic protein 6 | $2.52 \times 10^{-2}$ | 2.33 |
| Secreted Factors | UP in Fr | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|-----------------|----------|----------|----|-------------|-------------|------------|----------|----|-------------|-------------|------------|----------|----|
| 205066_s_at     | ENPP1    | ectonucleotide pyrophosphatase/phosphodiesterase 1 | 3.10 × 10^{-5} | 4.76 | 239349_at  | C1QTNF7    | C1q and tumor necrosis factor related protein 7 | 2.49 × 10^{-1} | 1.53 |
| 205065_at       | ENPP1    | ectonucleotide pyrophosphatase/phosphodiesterase 1 | 3.78 × 10^{-7} | 3.82 | 202357_s_at | C2 CFB     | complement component 2 complement factor B | 3.16 × 10^{-3} | 3.85 |
| 205110_s_at     | FGF13    | fibroblast growth factor 13 | 3.58 × 10^{-8} | 4.73 | 217767_at  | C3         | complement component 3 | 2.71 × 10^{-1} | 2.42 |
| 214240_at       | GAL      | galanin prepropeptide | 9.61 × 10^{-2} | 1.59 | 208451_s_at | C4A C4B    | complement component 4A (Rodgers blood group) complement component 4B (Chido blood group) | 1.98 × 10^{-1} | 1.83 |
| 205505_at       | GCNT1    | glucosaminyl (N-acetyl) transferase 1, core 2 (beta-1,6-N-acetylglicosaminyl transferase) | 1.70 × 10^{-5} | 1.66 | 206407_s_at | CCL13      | chemokine (C-C motif) ligand 13 | 8.28 × 10^{-2} | 3.52 |
| 240509_s_at     | GREM2    | gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis) | 2.66 × 10^{-3} | 3.23 | 216598_s_at | CCL2       | chemokine (C-C motif) ligand 2 | 5.37 × 10^{-4} | 8.18 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  |
|--------------|-------------|------------|---------|-----|--------------|-------------|------------|---------|-----|
| 235504_at    | GREM2       | gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis) | $9.10 \times 10^{-2}$ | 3.11 | CD70         | CD70 molecule | $1.14 \times 10^{-1}$ | 2.44 |
| 220794_at    | GREM2       | gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis) | $2.06 \times 10^{-2}$ | 2.76 | CFH          | complement factor H | $8.63 \times 10^{-5}$ | 6.48 |
| 206326_at    | GRP         | gastrin-releasing peptide | $3.05 \times 10^{-2}$ | 1.59 | CFHR1        | complement factor H related 1 | $4.95 \times 10^{-6}$ | 10.91 |
| 203821_at    | HBEGF       | heparin-binding EGF-like growth factor | $1.31 \times 10^{-1}$ | 1.64 | CFHR2        | complement factor H related 2 | $8.81 \times 10^{-3}$ | 1.60 |
| 203819_s_at  | IGF2BP3     | insulin-like growth factor 2 mRNA binding protein 3 | $4.18 \times 10^{-2}$ | 2.51 | CHI3L1       | chitinase 3-like 1 (cartilage glycoprotein-39) | $1.10 \times 10^{-2}$ | 4.08 |
| 203820_s_at  | IGF2BP3     | insulin-like growth factor 2 mRNA binding protein 3 | $6.30 \times 10^{-2}$ | 2.13 | CHI3L1       | chitinase 3-like 1 (cartilage glycoprotein-39) | $4.55 \times 10^{-2}$ | 1.94 |
| 212143_s_at  | IGFBP3      | insulin-like growth factor binding protein 3 | $1.26 \times 10^{-2}$ | 1.54 | CRLF1        | cytokine receptor-like factor 1 | $8.40 \times 10^{-3}$ | 3.23 |
Table 3. Cont.

| Secreted Factors | UP in Fr | | Secreted Factors | UP in F-DHJ | |
|------------------|----------|---|------------------|-------------|---|
| Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
| 227760_at        | IGFBPL1   | insulin-like growth factor binding protein-like 1 | $3.76 \times 10^{-3}$ | 1.94 | 209774_x_at | CXCL2 | chemokine (C-X-C motif) ligand 2 | $1.37 \times 10^{-1}$ | 3.03 |
| 204773_at        | IL11RA    | interleukin 11 receptor, alpha | $1.36 \times 10^{-3}$ | 1.97 | 207850_at | CXCL3 | chemokine (C-X-C motif) ligand 3 | $2.50 \times 10^{-1}$ | 2.07 |
| 206172_at        | IL13RA2   | interleukin 13 receptor, alpha 2 | $8.39 \times 10^{-2}$ | 3.56 | 219837_s_at | CYTL1 | cytokine-like 1 | $1.99 \times 10^{-1}$ | 2.02 |
| 227997_at        | IL17RD    | interleukin 17 receptor D | $9.70 \times 10^{-2}$ | 1.70 | 219501_at | ENOX1 | v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian) | $1.84 \times 10^{-2}$ | 2.35 |
| 222062_at        | IL27RA    | interleukin 27 receptor, alpha | $4.50 \times 10^{-4}$ | 3.73 | 226213_at | ERBB3 | fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor) | $2.56 \times 10^{-1}$ | 1.70 |
| 205926_at        | IL27RA    | interleukin 27 receptor, alpha | $5.58 \times 10^{-4}$ | 1.67 | 205738_s_at | FABP3 | fatty acid binding protein 4, adipocyte | $5.11 \times 10^{-2}$ | 2.16 |
| 226218_at        | IL7R      | interleukin 7 receptor | $9.41 \times 10^{-2}$ | 1.71 | 203980_at | FABP4 | fibroblast growth factor 1 (acidic) | $8.61 \times 10^{-3}$ | 2.95 |
| 205798_at        | IL7R      | interleukin 7 receptor | $1.78 \times 10^{-1}$ | 1.59 | 205117_at | FGF1 | fibroblast growth factor 1 (acidic) | $1.47 \times 10^{-2}$ | 2.71 |
| 231798_at        | NOG       | noggin | $6.76 \times 10^{-5}$ | 3.98 | 1552721_a_at | FGF1 | fibroblast growth factor 1 (acidic) | $9.05 \times 10^{-2}$ | 1.73 |
| 206343_s_at      | NRG1      | neuregulin 1 | $6.34 \times 10^{-3}$ | 2.68 | 208240_s_at | FGF1 | fibroblast growth factor 1 (acidic) | $1.71 \times 10^{-1}$ | 2.09 |
| Secreted Factors | UP in Fr | adj-pval | FC | Secreted Factors | UP in F-DHJ | adj-pval | FC |
|------------------|----------|----------|----|------------------|-------------|----------|----|
| Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC |
| 208230_s_at      | NRG1      | neuregulin 1 | 1.20×10^{-2} | 1.90 | 211029_x_at      | FGF18       | fibroblast growth factor 18 | 2.54×10^{-1} | 1.64 |
| 204766_s_at      | NUDT1     | nudix (nucleoside diphosphate linked moiety X)-type motif 1 | 2.22×10^{-5} | 1.59 | 221577_x_at      | GDF15       | growth differentiation factor 15 | 3.41×10^{-2} | 2.03 |
| 213131_at        | OLFM1     | olfactomedin 1 | 1.82×10^{-1} | 1.71 | 206614_at        | GDF5        | growth differentiation factor 5 | 4.96×10^{-2} | 2.01 |
| 213125_at        | OLFML2B   | olfactomedin-like 2B | 2.17×10^{-1} | 1.93 | 201348_at        | GPX3        | glutathione peroxidase 3 (plasma) | 2.15×10^{-2} | 3.24 |
| 218162_at        | OLFML3    | olfactomedin-like 3 | 3.28×10^{-2} | 1.72 | 214091_s_at      | GPX3        | glutathione peroxidase 3 (plasma) | 7.64×10^{-2} | 1.99 |
| 222719_s_at      | PDGFC     | platelet derived growth factor C | 2.01×10^{-3} | 1.61 | 209960_at        | HGF         | hepatocyte growth factor (hepapoietin A; scatter factor) | 7.99×10^{-2} | 3.24 |
| 201578_at        | PODXL     | podocalyxin-like | 1.11×10^{-2} | 5.15 | 210997_at        | HGF         | hepatocyte growth factor (hepapoietin A; scatter factor) | 2.26×10^{-2} | 2.96 |
| 210195_s_at      | PSG1      | pregnancy specific beta-1-glycoprotein 1 | 2.14×10^{-1} | 1.82 | 210998_s_at      | HGF         | hepatocyte growth factor (hepapoietin A; scatter factor) | 3.94×10^{-2} | 1.80 |
| 208134_x_at      | PSG2      | pregnancy specific beta-1-glycoprotein 2 | 1.56×10^{-3} | 3.17 | 210619_s_at      | HYAL1       | hyaluronoglucosaminidase 1 | 1.86×10^{-3} | 3.19 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  |
|--------------|-------------|------------|----------|-----|--------------|-------------|------------|----------|-----|
| 203399_x_at  | PSG3        | pregnancy specific beta-1-glycoprotein 3 | $8.06 \times 10^{-3}$ | 3.33 | 209540_at    | IGF1        | insulin-like growth factor 1 (somatomedin C) | $2.78 \times 10^{-1}$ | 1.97 |
| 215821_x_at  | PSG3        | pregnancy specific beta-1-glycoprotein 3 | $2.08 \times 10^{-2}$ | 2.47 | 209542_x_at  | IGF1        | insulin-like growth factor 1 (somatomedin C) | $2.03 \times 10^{-1}$ | 1.57 |
| 211741_x_at  | PSG3        | pregnancy specific beta-1-glycoprotein 3 | $1.76 \times 10^{-2}$ | 2.22 | 202718_at    | IGFBP2      | insulin-like growth factor binding protein 2, 36 kDa | $8.69 \times 10^{-2}$ | 3.80 |
| 204830_x_at  | PSG5        | pregnancy specific beta-1-glycoprotein 5 | $8.14 \times 10^{-3}$ | 3.53 | 201508_at    | IGFBP4      | insulin-like growth factor binding protein 4 | $1.12 \times 10^{-1}$ | 1.68 |
| 209738_x_at  | PSG6        | pregnancy specific beta-1-glycoprotein 6 | $7.00 \times 10^{-3}$ | 3.35 | 203426_s_at  | IGFBP5      | insulin-like growth factor binding protein 5 | $2.55 \times 10^{-2}$ | 3.31 |
| 208106_x_at  | PSG6        | pregnancy specific beta-1-glycoprotein 6 | $4.99 \times 10^{-3}$ | 3.26 | 211958_at    | IGFBP5      | insulin-like growth factor binding protein 5 | $2.16 \times 10^{-1}$ | 2.76 |
| 209594_x_at  | PSG9        | pregnancy specific beta-1-glycoprotein 9 | $5.91 \times 10^{-3}$ | 3.49 | 1555997_s_at | IGFBP5      | insulin-like growth factor binding protein 5 | $1.64 \times 10^{-1}$ | 2.46 |
Table 3. Cont.

| Secreted Factors | UP in Fr | adj-pval | FC | Secreted Factors | UP in F-DHJ | adj-pval | FC |
|------------------|----------|----------|----|------------------|--------------|----------|----|
| Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC |
| 207733_x_at      | PSG9      | pregnancy specific beta-1-glycoprotein 9 | $1.20 \times 10^{-2}$ | 3.03 | 203425_s_at      | IGFBP5    | insulin-like growth factor binding protein 5 | $1.58 \times 10^{-1}$ | 1.80 |
| 212187_x_at      | PTGDS     | prostaglandin D2 synthase 21 kDa (brain) | $5.94 \times 10^{-3}$ | 1.91 | 206295_at        | IL18       | interleukin 18 (interferon-gamma-inducing factor) | $3.70 \times 10^{-2}$ | 3.75 |
| 211748_x_at      | PTGDS     | prostaglandin D2 synthase 21 kDa (brain) | $2.12 \times 10^{-3}$ | 1.69 | 207526_s_at      | IL1RL1    | interleukin 1 receptor-like 1 | $1.32 \times 10^{-1}$ | 2.07 |
| 206631_at        | PTGER2    | prostaglandin E receptor 2 (subtype EP2), 53 kDa | $4.68 \times 10^{-2}$ | 1.71 | 242809_at        | IL1RL1    | Interleukin 1 receptor-like 1 | $2.38 \times 10^{-1}$ | 1.60 |
| 211737_x_at      | PTN       | pleiotrophin | $7.25 \times 10^{-2}$ | 3.28 | 221111_at        | IL26       | interleukin 26 | $4.68 \times 10^{-2}$ | 3.44 |
| 209465_x_at      | PTN       | pleiotrophin | $4.83 \times 10^{-2}$ | 3.24 | 209821_at        | IL33       | interleukin 33 | $1.79 \times 10^{-1}$ | 1.50 |
| 209466_x_at      | PTN       | pleiotrophin | $1.03 \times 10^{-1}$ | 2.42 | 205207_at        | IL6        | interleukin 6 (interferon, beta 2) | $2.42 \times 10^{-4}$ | 3.20 |
| 209897_s_at      | SLIT2     | slit homolog 2 (Drosophila) | $1.55 \times 10^{-2}$ | 1.98 | 204863_s_at      | IL6ST      | interleukin 6 signal transducer (gp130, oncostatin M receptor) | $1.97 \times 10^{-2}$ | 1.99 |
| 205016_at        | TGFA      | transforming growth factor, alpha | $4.19 \times 10^{-2}$ | 3.27 | 211000_s_at      | IL6ST      | interleukin 6 signal transducer (gp130, oncostatin M receptor) | $1.21 \times 10^{-2}$ | 1.88 |
| 203085_s_at      | TGFBI     | transforming growth factor, beta 1 | $7.50 \times 10^{-3}$ | 1.60 | 204926_at        | INHBA      | inhibin, beta A | $1.44 \times 10^{-2}$ | 2.47 |
| Secreted Factors | UP in Fr | adj-pval | FC | UP in F-DHJ | adj-pval | FC |
|------------------|----------|----------|----|-------------|----------|----|
| Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
| 236561_at        | TGFBR1   | Transforming growth factor, beta receptor 1 | $4.05 \times 10^{-2}$ | 1.71 | 210511_s_at | INHBA | inhibin, beta A | $4.64 \times 10^{-3}$ | 2.42 |
| 203887_s_at      | THBD     | thrombomodulin | $2.94 \times 10^{-1}$ | 2.27 | 205266_at | LIF | leukemia inhibitory factor (cholinergic differentiation factor) | $7.91 \times 10^{-2}$ | 2.44 |
| 239336_at        | THBS1    | Thrombospondin 1 | $1.84 \times 10^{-1}$ | 1.58 | 219181_at | LIPG | lipase, endothelial | $3.51 \times 10^{-2}$ | 2.89 |
| 227420_at        | TNFAIP8L1 | tumor necrosis factor, alpha-induced protein 8-like 1 | $3.38 \times 10^{-3}$ | 1.71 | 205381_at | LRRC17 | leucine rich repeat containing 17 | $2.67 \times 10^{-4}$ | 18.57 |
| 219478_at        | WFDC1    | WAP four-disulfide core domain 1 | $3.17 \times 10^{-2}$ | 5.38 | 216320_x_at | MST1 | macrophage stimulating 1 (hepatocyte growth factor-like) | $1.05 \times 10^{-1}$ | 1.53 |
| 221029_s_at      | WNT5B    | wingless-type MMTV integration site family, member 5B | $5.20 \times 10^{-4}$ | 2.39 | 231361_at | NLGN1 | Neuroligin 1 | $4.86 \times 10^{-2}$ | 3.33 |
| 223337_s_at      | WNT5B    | wingless-type MMTV integration site family, member 5B | $2.99 \times 10^{-2}$ | 1.65 | 205893_at | NLGN1 | neuroligin 1 | $7.72 \times 10^{-2}$ | 3.23 |
| 204501_at        | NOV      | nephroblastoma overexpressed gene | $2.01 \times 10^{-2}$ | 2.95 |
| 214321_at        | NOV      | nephroblastoma overexpressed gene | $1.69 \times 10^{-2}$ | 2.60 |
Table 3. Cont.

| Secreted Factors | UP in Fr | UP in F-DHJ |
|------------------|----------|-------------|
| Probe Set ID     | Gene Symbol | adj-pval | FC  | Gene Symbol | adj-pval | FC  |
| 217525_at        | OLFML1   | 5.70 × 10^{-2} | 3.66 |
| 213075_at        | OLFML2A  | 1.64 × 10^{-2} | 2.12 |
| 205729_at        | OSMR     | 6.53 × 10^{-2} | 1.71 |
| 224942_at        | PAPPA    | 2.20 × 10^{-2} | 1.88 |
| 1559400_s_at     | PAPPA    | 3.28 × 10^{-2} | 1.84 |
| 201981_at        | PAPPA    | 3.78 × 10^{-2} | 1.74 |
| 224940_s_at      | PAPPA    | 1.72 × 10^{-2} | 1.73 |
| 224941_at        | PAPPA    | 1.36 × 10^{-2} | 1.69 |
| 228128_x_at      | PAPPA    | 2.13 × 10^{-2} | 1.64 |
| 205560_at        | PCSK5    | 2.21 × 10^{-3} | 2.70 |
| 213652_at        | PCSK5    | 5.18 × 10^{-4} | 2.66 |
### Table 3. Cont.

| Secreted Factors | | |
|------------------|------------------|
| **UP in Fr** | **UP in F-DHJ** |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | | Gene Symbol | Gene Title | adj-pval | FC |
| 205559_s_at | PCSK5 | proprotein convertase subtilisin/kexin type 5 | $1.23 \times 10^{-3}$ | 2.52 |
| 227759_at | PCSK9 | proprotein convertase subtilisin/kexin type 9 | $2.34 \times 10^{-2}$ | 1.97 |
| 216867_s_at | PDGFA | platelet-derived growth factor alpha polypeptide | $2.46 \times 10^{-2}$ | 1.97 |
| 222860_s_at | PDGFD | platelet derived growth factor D | $1.50 \times 10^{-1}$ | 1.57 |
| 1555778_a_at | POSTN | periostin, osteoblast specific factor | $4.41 \times 10^{-3}$ | 4.30 |
| 214981_at | POSTN | periostin, osteoblast specific factor | $2.20 \times 10^{-3}$ | 2.96 |
| 210809_s_at | POSTN | periostin, osteoblast specific factor | $8.30 \times 10^{-3}$ | 2.47 |
| 207808_s_at | PROS1 | protein S (alpha) | $3.88 \times 10^{-3}$ | 1.51 |
| 213421_x_at | PRSS3 | protease, serine, 3 | $2.41 \times 10^{-2}$ | 2.68 |
| 210367_s_at | PTGES | prostaglandin E synthase | $3.17 \times 10^{-4}$ | 4.21 |
| 207388_s_at | PTGES | prostaglandin E synthase | $4.23 \times 10^{-2}$ | 2.51 |
| 224950_at | PTGFRN | prostaglandin F2 receptor negative regulator | $4.86 \times 10^{-2}$ | 1.78 |
| 211892_s_at | PTGIS | prostaglandin I2 (prostacyclin) synthase | $4.91 \times 10^{-2}$ | 2.06 |
| 210702_s_at | PTGIS | prostaglandin I2 (prostacyclin) synthase | $1.13 \times 10^{-1}$ | 1.70 |
| Probe Set ID | Gene Symbol | Gene Title                                               | adj-pval   | FC   | Probe Set ID | Gene Symbol | Gene Title                                               | adj-pval   | FC   |
|--------------|-------------|----------------------------------------------------------|------------|------|--------------|-------------|----------------------------------------------------------|------------|------|
| 208131_s_at  | PTGIS       | prostaglandin I2 (prostacyclin) synthase                  | 2.43 × 10⁻²| 1.67 |              |              |                                                          |            |      |
| 211756_at    | PTHLH       | parathyroid hormone-like hormone                          | 6.78 × 10⁻²| 3.45 |              |              |                                                          |            |      |
| 206300_s_at  | PTHLH       | parathyroid hormone-like hormone                          | 7.08 × 10⁻²| 2.86 |              |              |                                                          |            |      |
| 210355_at    | PTHLH       | parathyroid hormone-like hormone                          | 1.70 × 10⁻¹| 2.21 |              |              |                                                          |            |      |
| 206157_at    | PTX3        | pentraxin-related gene, rapidly induced by IL-1 beta      | 1.47 × 10⁻⁴| 2.21 |              |              |                                                          |            |      |
| 201482_at    | QSOX1       | quiescin Q6 sulphhydryl oxidase 1                          | 2.19 × 10⁻³| 1.68 |              |              |                                                          |            |      |
| 223824_at    | RNLS        | renalase, FAD-dependent amine oxidase                     | 5.18 × 10⁻⁴| 1.74 |              |              |                                                          |            |      |
| 204035_at    | SCG2        | secretogranin II (chromogranin C)                         | 2.66 × 10⁻²| 2.56 |              |              |                                                          |            |      |
| 205475_at    | SCRG1       | scrapie responsive protein 1                              | 6.88 × 10⁻⁷| 7.73 |              |              |                                                          |            |      |
| 213716_s_at  | SECTM1      | secreted and transmembrane 1                              | 3.32 × 10⁻²| 3.29 |              |              |                                                          |            |      |
| 203071_at    | SEMA3B      | sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B | 6.35 × 10⁻²| 2.54 |              |              |                                                          |            |      |
Table 3. Cont.

| Secreted Factors | Probe Set ID | Gene Symbol | adj-pval | FC   | Probe Set ID | Gene Symbol | adj-pval | FC |
|------------------|--------------|-------------|----------|------|--------------|-------------|----------|----|
| SEMA3C           | 203788_s_at  | SEMA3C      |          |      | 203789_s_at  | SEMA3C      |          |    |
| sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) | 203788_s_at  | SEMA3C      |          |      | 203789_s_at  | SEMA3C      |          |    |
| 3C               | 203788_s_at  | SEMA3C      |          |      | 203789_s_at  | SEMA3C      |          |    |
| stratifin        | 33323_r_at   | SFN         |          |      | 223122_s_at  | SFRP2       |          |    |
| secreted frizzled-related prot 2 | 223122_s_at  | SFRP2       |          |      | 223122_s_at  | SFRP2       |          |    |
| secreted frizzled-related prot 4 | 223122_s_at  | SFRP2       |          |      | 223122_s_at  | SFRP2       |          |    |
| secreted frizzled-related prot 4 | 223122_s_at  | SFRP2       |          |      | 223122_s_at  | SFRP2       |          |    |
| tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) | 210665_at  | TFPI        |          |      | 210664_s_at  | TFPI        |          |    |
| 3C               | 203788_s_at  | SEMA3C      |          |      | 203789_s_at  | SEMA3C      |          |    |
| tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) | 210665_at  | TFPI        |          |      | 210664_s_at  | TFPI        |          |    |
Table 3. Cont.

| Secreted Factors | Secreted Factors |
|------------------|------------------|
| Probe Set ID     | Gene Symbol      | Gene Title                                                      | adj-pval   | FC  |
|                  |                  | tissue factor pathway inhibitor                                  |            |     |
|                  |                  | (lipoprotein-associated coagulation inhibitor)                   |            |     |
| 209676_at        | TFPI             | tissue factor pathway inhibitor                                  | $2.96 \times 10^{-2}$ | 3.35 |
|                  |                  | (lipoprotein-associated coagulation inhibitor)                   |            |     |
| 213258_at        | TFPI             | tissue factor pathway inhibitor                                  | $2.61 \times 10^{-2}$ | 3.24 |
|                  |                  | (lipoprotein-associated coagulation inhibitor)                   |            |     |
| 228121_at        | TGFB2            | transforming growth factor, beta 2                               | $1.08 \times 10^{-6}$ | 5.13 |
| 209909_s_at      | TGFB2            | transforming growth factor, beta 2                               | $5.47 \times 10^{-5}$ | 3.64 |
| 204731_at        | TGFBR3           | transforming growth factor, beta receptor III                    | $2.06 \times 10^{-1}$ | 1.70 |
| 203083_at        | THBS2            | thrombospondin 2                                                 | $4.84 \times 10^{-6}$ | 2.83 |
| 202644_s_at      | TNFAIP3          | tumor necrosis factor, alpha-induced protein 3                   | $1.61 \times 10^{-3}$ | 3.88 |
| 202643_s_at      | TNFAIP3          | tumor necrosis factor, alpha-induced protein 3                   | $4.35 \times 10^{-3}$ | 3.52 |
| 206025_s_at      | TNFAIP6          | tumor necrosis factor, alpha-induced protein 6                   | $1.57 \times 10^{-2}$ | 2.29 |
| 206026_s_at      | TNFAIP6          | tumor necrosis factor, alpha-induced protein 6                   | $3.57 \times 10^{-2}$ | 2.15 |
| 210260_s_at      | TNFAIP8          | tumor necrosis factor, alpha-induced protein 8                   | $5.99 \times 10^{-4}$ | 2.01 |
| Secreted Factors | UP in Fr | UP in F-DHJ |
|------------------|----------|-------------|
| Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC  | Probe Set ID     | Gene Symbol | Gene Title | adj-pval | FC  |
| 208296_x_at      | TNFAIP8   | tumor necrosis factor, alpha-induced protein 8 | $1.11 \times 10^{-3}$ | 1.94 |
| 235737_at        | TSLP      | thymic stromal lymphopoietin | $1.72 \times 10^{-1}$ | 2.02 |
| 210513_s_at      | VEGFA     | vascular endothelial growth factor A | $9.18 \times 10^{-2}$ | 1.57 |
| 205648_at        | WNT2      | wingless-type MMTV integration site family member 2 | $2.83 \times 10^{-1}$ | 2.08 |
| 202643_s_at      | TNFAIP3   | tumor necrosis factor, alpha-induced protein 3 | $4.35 \times 10^{-3}$ | 3.52 |
| 206025_s_at      | TNFAIP6   | tumor necrosis factor, alpha-induced protein 6 | $1.57 \times 10^{-2}$ | 2.29 |
| 206026_s_at      | TNFAIP6   | tumor necrosis factor, alpha-induced protein 6 | $3.57 \times 10^{-2}$ | 2.15 |
| 210260_s_at      | TNFAIP8   | tumor necrosis factor, alpha-induced protein 8 | $5.99 \times 10^{-4}$ | 2.01 |
| 208296_x_at      | TNFAIP8   | tumor necrosis factor, alpha-induced protein 8 | $1.11 \times 10^{-3}$ | 1.94 |
| 235737_at        | TSLP      | thymic stromal lymphopoietin | $1.72 \times 10^{-1}$ | 2.02 |
| 210513_s_at      | VEGFA     | vascular endothelial growth factor A | $9.18 \times 10^{-2}$ | 1.57 |
| 205648_at        | WNT2      | wingless-type MMTV integration site family member 2 | $2.83 \times 10^{-1}$ | 2.08 |
3.4. The Dermo-Hypodermal Junction and Reticular Dermis Differ in Their Matrix Architectural Meshwork

From the lists of transcripts differentially expressed between F-DHJ and Fr, our attention was attracted by tenascin C (TNC), considering its major role in the organization of collagen fibril anchoring points. Indeed, TNC forms a typical disulfide-linked hexamer, called the hexabrachion, in which six flexible arms emanate from a central globular particle, which possibly catches and stabilizes a bifurcation of the ECM fibrils composed of FN1 and type I collagen to underlie the extracellular meshwork architecture (for review, see [26]). Our transcriptome analysis indicated a 2.61-fold lower expression of TNC in F-DHJ versus Fr cells (Table 3). To explore this property at the protein level, immunostaining of TNC was performed on samples of ECM synthesized by F-DHJ and Fr cells in vitro (Figure 6A,B) (cells from n = 3 individuals were tested). Notably, reticulation of TNC was more marked in ECM samples synthesized by Fr than in ECM secreted by F-DHJ (Figure 6A). Moreover, signal quantification indicated TNC levels lower in ECM produced by F-DHJ versus Fr (p < 0.01) (Figure 6B).

Architectural differences between the DHJ and reticular areas were confirmed in skin sections (Figure 6C–E). In the reticular area, TNC protein-staining revealed a thin mesh structuration around collagen bundles in agreement with the alveolar organization of this dermal territory, whereas this structuration was not present in the DHJ area (Figure 6C,D). In addition, quantification of the TNC immunostaining signals performed in sections of mammary skin (biopsies from seven individuals) and abdominal skin (six individuals) indicated a higher level of TNC in the reticular dermis area than in the HDJ area for both skin anatomical origins (p < 0.05) (Figure 6E).
Figure 6. Architecture of the tenascin C (TNC) meshwork produced in vitro by Fr and F-DHJ fibroblasts in skin sections. (A) Immunostaining pictures of the TNC meshwork produced by Fr and F-DHJ cells in 2D cultures. (B) Quantification of TNC secreted in 2D cultures. Cell samples from 3 donors were used. Values corresponding to 10 replicate analyses for each cell sample are shown. Means ± SEM are indicated (** p < 0.01, Wilcoxon test) A.U. for arbitrary units. (C) Photographs of TNC immunostaining in skin sections, illustrating the structural differences between reticular dermis and the dermo-hypodermal junction area (representative from 13 analyzed donors). (D) Image reconstitution of TNC meshwork architectures based on the immunostaining photographs shown in panel (C). (E) Quantification of TNC in the skin reticular and dermo-hypodermal areas. Values
in skin sections, illustrating the structural differences between reticular dermis and the dermo-hypodermal junction area (representative from 13 analyzed donors). (D) Image reconstitution of TNC meshwork architectures based on the immunostaining photographs shown in panel (C). (E) Quantification of TNC in the skin reticular and dermo-hypodermal areas. Values obtained from the analysis of skin samples from 13 donors are shown. Samples from two anatomical localizations: breast skin (7 donors of ages between 18 and 65 years) and abdominal skin (6 donors of ages between 42 and 51 years). No age-related changes in TNC synthesis/meshwork were observed. Means ± SEM are indicated (* $p < 0.05$, Wilcoxon test) A.U. for arbitrary units.

3.5. F-DHJ Fibroblasts and Adipose-Derived MSCs Exhibit Distinct Transcriptome Profiles

Given the anatomical proximity between F-DHJ and MSCs derived from hypodermal adipose tissues, their molecular characteristics were explored at the level of the global transcriptome to determine whether these two cell populations have a distinct identity or not. To widen this question, the three fibroblast types (Fp, Fr, and F-DHJ) were analyzed together with MSC samples corresponding to five sources (bone marrow aspirates, adipose tissue, amnion, chorion, and umbilical cord jelly) (Figure 7). A hierarchical clustering based on 380 discriminant probe sets revealed a clear segmentation between the “fibroblast” group and the “MSC” group (Figure 7A), which confirmed the distinct identities of F-DHJ and adipose MSCs. Within the “fibroblast” group, F-DHJ appeared more similar with Fr than they were with Fp cells. Within the “MSC” group, cells from the three fetal origins (amnion, chorion, and cord) were more similar to each other than they were with the two adult origins (marrow and adipose). This clustering was confirmed when a full transcriptome analysis was considered (Pearson correlation coefficients) (Figure 7B). To document biological characteristics distinguishing the fibroblast and MSC groups, a gene ontology (GO) term analysis was performed based on 2974 probe sets (1984 genes) distinguishing the two sample groups (parameters: fold-change $> 2$ and $p$-value $< 0.05$). Among the twenty most significant GO terms, transcripts related to structuration of the tissue skeleton were largely represented, including numerous ECM, focal adhesion, cytoskeleton, LINC complexes, nucleoskeleton, and secreted factor transcripts, in which their levels distinguish fibroblasts from MSCs (Figure 7C,D and Table 4). In particular, a signature of 42 transcripts directly related to ECM structure and composition was identified (Figure 7E), constituting a pool of candidates to further explore the biological differences between F-DHJ and adipose MSCs.
Figure 7. Comparative microarray transcriptome profiling of the three fibroblasts populations (Fp, Fr, and F-DHJ) and mesenchymal stem cell (MSC) samples corresponding to five sources (bone marrow aspirates, adipose tissue, amnion, chorion, and umbilical cord jelly). (A) Hierarchical clustering of fibroblast and MSC samples based on the 380 most discriminant probe sets showing a marked distinction between the “fibroblast” and “MSC” groups. (B) Pearson correlation coefficients evaluating sample-to-sample proximity based on comparisons of global transcriptome profiles. Notably, this analysis showed the low proximity between F-DHJ with adipose tissue MSCs (93.83% similarity) and high proximity with Fr fibroblasts (96.89% similarity). (C) List of the 20 most significant gene ontology (GO) terms differentiating the “fibroblast” and “MSC” groups based on 2974 probe sets (1984 transcripts) exhibiting differential signals (fold-change > 2 and p < 0.05). (D) Signatures identifying the “fibroblast” group (black bars) and the “MSC” group (grey bars) among transcripts related to the tissue skeleton biology (fold-change >2 and p < 0.05). (E) Focus on 42 transcripts directly involved in the structuration and composition of the ECM network and identified within the signature that distinguishes the “fibroblast” and “MSC” groups. Values were obtained by GCRMA microarray signals and corresponded to an indication of transcript levels (arbitrary units) in F-DHJ and adipose MSCs.
Table 4. Transcripts related to the tissue skeleton, in which differential expressions distinguish the “fibroblast” and mesenchymal stem cell or “MSC” groups. This transcript list was extracted from microarray data using fold-change >2 and \( p < 0.05 \) as inclusion parameters. The transcript signature with predominant expression in the “fibroblast” group concerned 424 probe sets corresponding to transcripts directly involved in the tissue skeleton structure, comprising 145 transcripts related to ECM, 63 focal adhesion point transcripts, 68 cytoskeleton transcripts, 4 LINC complex transcripts, and 12 nucleoskeleton transcripts. The transcript signature with predominant expression in the “MSC” group concerned 241 probe sets corresponding to transcripts directly involved in the tissue skeleton structure, comprising 53 transcripts related to ECM, 63 focal adhesion point transcripts, 52 cytoskeleton transcripts, 2 LINC complex transcripts, and 7 nucleoskeleton transcripts. In addition, transcripts encoding soluble factors were found in both signatures, respectively 132 and 79 for the “fibroblast” and “MSC” groups.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  |
|--------------|-------------|------------|----------|-----|--------------|-------------|------------|----------|-----|
| 205679_x_at  | ACAN        | aggrecan   | \(8.39 \times 10^{-22}\) | 25.41 | 209765_at    | ADAM19      | ADAM metallopeptidase domain 19 (meltrin beta) | \(7.41 \times 10^{-28}\) | 8.60 |
| 207692_s_at  | ACAN        | aggrecan   | \(7.55 \times 10^{-21}\) | 23.23 | 226997_at    | ADAMTS12    | ADAM metallopeptidase with thrombospondin type 1 motif, 12 | \(9.13 \times 10^{-13}\) | 4.00 |
| 217161_x_at  | ACAN        | aggrecan   | \(1.14 \times 10^{-20}\) | 20.79 | 214913_at    | ADAMTS3     | ADAM metallopeptidase with thrombospondin type 1 motif, 3 | \(1.26 \times 10^{-10}\) | 4.41 |
| 232570_s_at  | ADAM33      | ADAM metallopeptidase domain 33 | \(2.07 \times 10^{-9}\) | 4.20 | 1570351_at   | ADAMTS6     | ADAM metallopeptidase with thrombospondin type 1 motif, 6 | \(3.98 \times 10^{-15}\) | 2.31 |
| 233868_x_at  | ADAM33      | ADAM metallopeptidase domain 33 | \(3.16 \times 10^{-8}\) | 2.98 | 222043_at    | CLU         | clusterin | \(5.59 \times 10^{-4}\) | 2.05 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 214454_at    | ADAMTS2     | ADAM metalloproteinase with thrombospondin type 1 motif, 2 | 4.55 x 10^{-14} | 2.74 | 225288_at    | COL27A1     | collagen, type XXVII, alpha 1 | 3.75 x 10^{-9} | 2.35 |
| 229357_at    | ADAMTS5     | ADAM metalloproteinase with thrombospondin type 1 motif, 5 | 1.26 x 10^{-16} | 22.33 | 213110_s_at  | COL4A5      | collagen, type IV, alpha 5 | 2.61 x 10^{-3} | 3.17 |
| 219935_at    | ADAMTS5     | ADAM metalloproteinase with thrombospondin type 1 motif, 5 | 6.18 x 10^{-16} | 21.71 | 204136_at    | COL7A1      | collagen, type VII, alpha 1 | 5.86 x 10^{-5} | 2.46 |
| 235368_at    | ADAMTS5     | ADAM metalloproteinase with thrombospondin type 1 motif, 5 | 1.86 x 10^{-15} | 11.70 | 223475_at    | CRISPLD1    | cysteine-rich secretory protein LCCL domain containing 1 | 2.40 x 10^{-5} | 2.02 |
| 219087_at    | ASPN        | asporin    | 3.78 x 10^{-15} | 18.79 | 201487_at    | CTSC        | cathepsin C | 2.84 x 10^{-13} | 3.90 |
| 224396.s_at  | ASPN        | asporin    | 6.26 x 10^{-6}  | 3.63  | 225646.at    | CTSC        | cathepsin C | 1.77 x 10^{-7}  | 2.77 |
| 201262.s_at  | BGN         | biglycan   | 4.64 x 10^{-10} | 3.10  | 225647.s_at  | CTSC        | cathepsin C | 4.24 x 10^{-7}  | 2.64 |
| 213905.x_at  | BGN         | biglycan   | 5.80 x 10^{-7}  | 2.15  | 231234_at    | CTSC        | cathepsin C | 7.29 x 10^{-8}  | 2.40 |
| 201261.x_at  | BGN         | biglycan   | 1.53 x 10^{-6}  | 2.00  | 229115.at    | DYNC1H1     | dynein, cytoplasmic 1, heavy chain 1 | 8.64 x 10^{-5} | 2.02 |
| 241986_at    | BMPER       | BMP binding endothelial regulator | 1.17 x 10^{-9} | 2.75  | 207379_at    | EDIL3       | EGF-like repeats and discoidin I-like domains 3 | 2.94 x 10^{-4} | 2.09 |
| Probe Set ID  | Gene Symbol | Gene Title                          | adj-pval  | FC  | Probe Set ID  | Gene Symbol | Gene Title                          | adj-pval  | FC  |
|--------------|-------------|-------------------------------------|-----------|-----|--------------|-------------|-------------------------------------|-----------|-----|
| 227526_at    | CDON        | Cdon homolog (mouse)                | $1.16 \times 10^{-6}$ | 2.34 | 226911_at    | EGFLAM      | EGF-like, fibronectin type III and laminin G domains | $5.99 \times 10^{-5}$ | 3.25 |
| 209732_at    | CLEC2B      | C-type lectin domain family 2, member B | $9.58 \times 10^{-18}$ | 66.68 | 203184_at    | FBN2        | fibrillin 2                         | $5.58 \times 10^{-5}$ | 6.34 |
| 1556209_at   | CLEC2B      | C-type lectin domain family 2, member B | $4.34 \times 10^{-6}$ | 4.46 | 236028_at    | IBSP        | integrin-binding sialoprotein       | $1.83 \times 10^{-3}$ | 2.85 |
| 205200_at    | CLEC3B      | C-type lectin domain family 3, member B | $1.76 \times 10^{-12}$ | 17.53 | 223689_at    | IGF2BP1     | insulin-like growth factor 2 mRNA binding protein 1 | $1.37 \times 10^{-17}$ | 5.58 |
| 217428_s_at  | COL10A1     | collagen, type X, alpha 1           | $3.42 \times 10^{-4}$ | 3.59 | 203819_s_at  | IGF2BP3     | insulin-like growth factor 2 mRNA binding protein 3 | $1.72 \times 10^{-28}$ | 39.96 |
| 205941_s_at  | COL10A1     | collagen, type X, alpha 1           | $5.32 \times 10^{-4}$ | 3.30 | 203820_s_at  | IGF2BP3     | insulin-like growth factor 2 mRNA binding protein 3 | $1.52 \times 10^{-29}$ | 30.51 |
| 231879_at    | COL12A1     | collagen, type XII, alpha 1         | $7.44 \times 10^{-15}$ | 5.04 | 216493_s_at  | IGF2BP3     | insulin-like growth factor 2 mRNA binding protein 3 | $2.04 \times 10^{-22}$ | 6.25 |
| 234951_s_at  | COL12A1     | collagen, type XII, alpha 1         | $3.01 \times 10^{-8}$ | 3.71 | 205206_at    | KAL1        | Kallmann syndrome 1 sequence          | $8.59 \times 10^{-6}$ | 5.25 |
| 225664_at    | COL12A1     | collagen, type XII, alpha 1         | $5.13 \times 10^{-11}$ | 2.60 | 202728_s_at  | LTBP1       | latent transforming growth factor beta binding protein 1 | $3.50 \times 10^{-12}$ | 4.74 |
| 231766_s_at  | COL12A1     | collagen, type XII, alpha 1         | $1.68 \times 10^{-6}$ | 2.34 | 202729_s_at  | LTBP1       | latent transforming growth factor beta binding protein 1 | $2.67 \times 10^{-12}$ | 3.43 |
### Table 4. Cont.

|                                | **UP in Dermal Fibroblasts** | **Extracellular Matrix Genes** | **UP in MSCs** |
|--------------------------------|-----------------------------|-------------------------------|---------------|
| **Probe Set ID**               | **Gene Symbol**             | **Gene Title**                | **adj-pval**  | **Gene Symbol**              | **Gene Title**                  | **adj-pval**  | **FC** |
| 203477_at                      | COL15A1                     | collagen, type XV, alpha 1    | 2.08 × 10⁻¹¹  | 223614_at                   | MMP16 matrix metallopeptidase 16 (membrane-inserted) | 7.85 × 10⁻¹¹  | 3.87   |
| 211966_at                      | COL4A2                      | collagen, type IV, alpha 2    | 2.64 × 10⁻⁴   | 207012_at                   | MMP16 matrix metallopeptidase 16 (membrane-inserted) | 4.43 × 10⁻¹³  | 3.63   |
| 226277_at                      | COL4A3BP                    | collagen, type IV, alpha 3 (Goodpasture antigen) binding protein | 6.82 × 10⁻³⁴  | 229346_at                   | NES nestin                         | 6.51 × 10⁻¹⁸  | 6.19   |
| 229779_at                      | COL4A4                      | collagen, type IV, alpha 4    | 2.16 × 10⁻⁶   | 218678_at                   | NES nestin                         | 3.67 × 10⁻⁹   | 3.84   |
| 221900_at                      | COL8A2                      | collagen, type VIII, alpha 2  | 1.22 × 10⁻⁷   | 201860_s_at                 | PLAT plasminogen activator, tissue | 3.31 × 10⁻¹⁶  | 6.86   |
| 52651_at                       | COL8A2                      | collagen, type VIII, alpha 2  | 3.02 × 10⁻⁸   | 205479_s_at                 | PLAU plasminogen activator, urokinase | 4.34 × 10⁻²⁸  | 22.23  |
| 205713_s_at                    | COMP                        | cartilage oligomeric matrix protein | 1.03 × 10⁻²⁶  | 211668_s_at                 | PLAU plasminogen activator, urokinase | 2.42 × 10⁻²⁰  | 12.30  |
| 226824_at                      | CPXM2                       | carboxypeptidase X (M14 family), member 2 | 1.74 × 10⁻⁸   | 211924_s_at                 | PLUR plasminogen activator, urokinase receptor | 7.22 × 10⁻¹⁷  | 2.73   |
| 208978_at                      | CRIP2                       | cysteine-rich protein 2       | 6.66 × 10⁻¹⁴  | 210845_s_at                 | PLUR plasminogen activator, urokinase receptor | 2.18 × 10⁻²²  | 2.69   |
| 221541_at                      | CRISPLD2                    | cysteine-rich secretory protein LCCL domain containing 2 | 1.80 × 10⁻⁵   | 206007_at                   | PRG4 proteoglycan 4                | 1.12 × 10⁻⁶   | 2.17   |
### Table 4. Cont.

| Probe Set ID   | Gene Symbol | Gene Title                                      | adj-pval  | FC  | Probe Set ID   | Gene Symbol | Gene Title                                      | adj-pval   | FC  |
|----------------|-------------|-------------------------------------------------|-----------|-----|----------------|-------------|-------------------------------------------------|------------|-----|
| 204971_at      | CSTA        | cystatin A (stefin A)                            | 9.43 × 10^{-5} | 3.43 | 221872_at      | RARRES1     | retinoic acid receptor responder (tazarotene induced) 1 | 5.43 × 10^{-19} | 6.46 |
| 209101_at      | CTGF        | connective tissue growth factor                  | 5.63 × 10^{-10} | 2.09 | 206392_s_at    | RARRES1     | retinoic acid receptor responder (tazarotene induced) 1 | 1.34 × 10^{-16} | 4.46 |
| 200661_at      | CTSA        | cathepsin A                                     | 5.53 × 10^{-17} | 2.18 | 222784_at      | SMOC1       | SPARC related modular calcium binding 1            | 4.56 × 10^{-4}  | 2.10 |
| 200766_at      | CTSD        | cathepsin D                                     | 5.83 × 10^{-18} | 2.96 | 201858_s_at    | SRGN        | serglycin                                       | 1.63 × 10^{-6}  | 6.82 |
| 203657_s_at    | CTSF        | cathepsin F                                     | 1.31 × 10^{-37} | 7.43 | 201859_at      | SRGN        | serglycin                                       | 3.48 × 10^{-7}  | 4.90 |
| 202295_s_at    | CTSH        | cathepsin H                                     | 8.10 × 10^{-5}  | 2.03 | 209277_at      | TFPI2       | tissue factor pathway inhibitor 2                 | 3.21 × 10^{-13} | 10.83 |
| 203758_at      | CTSO        | cathepsin O                                     | 5.40 × 10^{-11} | 2.37 | 209278_s_at    | TFPI2       | tissue factor pathway inhibitor 2                 | 4.82 × 10^{-12} | 6.13 |
| 210042_s_at    | CTSZ        | cathepsin Z                                     | 4.41 × 10^{-13} | 2.63 | 209909_s_at    | TGFB2       | transforming growth factor, beta 2               | 1.36 × 10^{-9}  | 7.65 |
| 209335_at      | DCN         | decorin                                         | 2.15 × 10^{-17} | 5.05 | 228121_at      | TGFB2       | transforming growth factor, beta 2               | 2.09 × 10^{-7}  | 5.04 |
| 211896_s_at    | DCN         | decorin                                         | 2.64 × 10^{-17} | 4.08 | 220407_s_at    | TGFB2       | transforming growth factor, beta 2               | 2.05 × 10^{-9}  | 3.60 |
| 211813_x_at    | DCN         | decorin                                         | 1.62 × 10^{-16} | 3.47 | 201042_at      | TGM2        | transglutaminase 2                               | 7.33 × 10^{-12} | 8.42 |
| 201893_x_at    | DCN         | decorin                                         | 1.32 × 10^{-16} | 3.17 | 211573_x_at    | TGM2        | transglutaminase 2                               | 6.53 × 10^{-25} | 4.14 |
| 213068_at      | DPT         | dermatopontin                                   | 2.61 × 10^{-22} | 47.71 | 211003_x_at    | TGM2        | transglutaminase 2                               | 6.51 × 10^{-23} | 3.00 |
| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC   | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC   |
|--------------|-------------|-------------------------------------------------|--------------|------|--------------|-------------|-------------------------------------------------|--------------|------|
| 207977_s_at  | DPT         | dermatopontin                                   | $1.64 \times 10^{-19}$ | 20.11| 222835_at    | THSD4       | thrombospondin, type I, domain containing 4       | $2.65 \times 10^{-9}$ | 4.10 |
| 213071_at    | DPT         | dermatopontin                                   | $2.41 \times 10^{-18}$ | 14.09| 226506_at    | THSD4       | thrombospondin, type I, domain containing 4       | $3.76 \times 10^{-7}$ | 3.35 |
| 209365_s_at  | ECM1        | extracellular matrix protein 1                  | $1.55 \times 10^{-26}$ | 3.53 | 202643_s_at  | TNFAIP3     | tumor necrosis factor, alpha-induced protein 3   | $1.91 \times 10^{-9}$ | 4.48 |
| 206101_at    | ECM2        | extracellular matrix protein 2, female organ and adipocyte specific | $6.39 \times 10^{-13}$ | 10.63| 202644_s_at  | TNFAIP3     | tumor necrosis factor, alpha-induced protein 3   | $2.35 \times 10^{-8}$ | 3.98 |
| 201843_s_at  | EFEMP1      | EGF-containing fibulin-like extracellular matrix protein 1 | $4.72 \times 10^{-3}$ | 2.04 | 206025_s_at  | TNFAIP6     | tumor necrosis factor, alpha-induced protein 6   | $4.06 \times 10^{-5}$ | 2.04 |
| 209356_x_at  | EFEMP2      | EGF-containing fibulin-like extracellular matrix protein 2 | $2.39 \times 10^{-21}$ | 3.14 |              |             |                                                  |              |      |
| 212670_at    | ELN         | elastin                                         | $0.00 \times 10^{+00}$ | 34.17|              |             |                                                  |              |      |
| 222885_at    | EMCN        | endomucin                                       | $6.61 \times 10^{-8}$ | 4.14 |              |             |                                                  |              |      |
| 227874_at    | EMCN        | endomucin                                       | $6.01 \times 10^{-6}$ | 2.25 |              |             |                                                  |              |      |
| 204363_at    | F3          | coagulation factor III (thromboplastin, tissue factor) | $2.04 \times 10^{-6}$ | 5.30 |              |             |                                                  |              |      |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                        | adj-pval  | FC  | Probe Set ID | Gene Symbol | Gene Title                        | adj-pval  | FC  |
|--------------|-------------|-----------------------------------|-----------|-----|--------------|-------------|-----------------------------------|-----------|-----|
| 202995_s_at  | FBLN1       | fibulin 1                          | 4.84 × 10^{-8} | 2.48| 203886_s_at  | FBLN2       | fibulin 2                          | 7.69 × 10^{-21} | 18.44|
| 203088_at    | FBLN5       | fibulin 5                          | 7.88 × 10^{-28} | 10.14|              |             |                                   |           |     |
| 203638_s_at  | FGFR2       | fibroblast growth factor receptor 2| 1.16 × 10^{-11} | 6.98| 227265_at    | FGL2        | fibrinogen-like 2                  | 1.58 × 10^{-5} | 6.33 |
| 204834_at    | FGL2        | fibrinogen-like 2                  | 2.20 × 10^{-7}  | 5.59| 202709_at    | FMOD        | fibromodulin                       | 4.30 × 10^{-22} | 8.88 |
| 226930_at    | FNDC1       | fibronectin type III domain containing 1 | 2.46 × 10^{-19} | 47.43|              |             |                                   |           |     |
| 226145_s_at  | FRAS1       | Fraser syndrome 1                  | 0.00 × 10^{+00} | 76.26| 202755_s_at  | GPC1        | glypican 1                         | 3.75 × 10^{-15} | 2.10 |
| 204984_at    | GPC4        | glypican 4                         | 5.19 × 10^{-15} | 9.94| 204983_s_at  | GPC4        | glypican 4                         | 8.43 × 10^{-12} | 5.40 |
| 230204_at    | HAPLN1      | hyaluronan and proteoglycan link protein 1 | 2.18 × 10^{-7}  | 7.98| 205523_at    | HAPLN1      | hyaluronan and proteoglycan link protein 1 | 5.24 × 10^{-7}  | 7.86 |
| 205524_s_at  | HAPLN1      | hyaluronan and proteoglycan link protein 1 | 5.34 × 10^{-8}  | 7.86|              |             |                                   |           |     |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval   | FC  | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval   | FC  |
|--------------|-------------|-------------------------------------------------|------------|-----|--------------|-------------|-------------------------------------------------|------------|-----|
| 230895_at    | HAPLN1      | hyaluronan and proteoglycan link protein 1       | 6.93 × 10^{-7} | 7.40|              |             |                                                 |            |     |
| 227262_at    | HAPLN3      | hyaluronan and proteoglycan link protein 3       | 5.18 × 10^{-16} | 4.01|              |             |                                                 |            |     |
| 235944_at    | HMCN1       | hemicentin 1                                     | 5.33 × 10^{-8} | 4.24|              |             |                                                 |            |     |
| 201185_at    | HTRA1       | HtrA serine peptidase 1                          | 3.62 × 10^{-10} | 3.08|              |             |                                                 |            |     |
| 209541_at    | IGF1        | insulin-like growth factor 1 (somatomedin C)     | 4.41 × 10^{-6} | 2.51|              |             |                                                 |            |     |
| 202718_at    | IGFBP2      | insulin-like growth factor binding protein 2, 36 kDa | 1.20 × 10^{-2} | 2.37|              |             |                                                 |            |     |
| 212143_s_at  | IGFBP3      | insulin-like growth factor binding protein 3     | 1.20 × 10^{-23} | 28.32|              |             |                                                 |            |     |
| 210095_s_at  | IGFBP3      | insulin-like growth factor binding protein 3     | 5.39 × 10^{-19} | 9.31|              |             |                                                 |            |     |
| 211959_at    | IGFBP5      | insulin-like growth factor binding protein 5     | 2.35 × 10^{-11} | 5.19|              |             |                                                 |            |     |
| 203424_s_at  | IGFBP5      | insulin-like growth factor binding protein 5     | 7.05 × 10^{-7} | 4.65|              |             |                                                 |            |     |
Table 4. Cont.

| Probe Set ID  | Gene Symbol | Gene Title                                      | adj-pval   | FC  | Probe Set ID  | Gene Symbol | Gene Title                                      | adj-pval   | FC  |
|---------------|-------------|------------------------------------------------|------------|-----|---------------|-------------|------------------------------------------------|------------|-----|
| 211958_at     | IGFBP5      | insulin-like growth factor binding protein 5    | $1.68 \times 10^{-7}$ | 3.69 |               |             |                                                 |            |     |
| 1555997_s_at  | IGFBP5      | insulin-like growth factor binding protein 5    | $9.64 \times 10^{-6}$ | 2.41 |               |             |                                                 |            |     |
| 203426_s_at   | IGFBP5      | insulin-like growth factor binding protein 5    | $2.17 \times 10^{-4}$ | 2.08 |               |             |                                                 |            |     |
| 203851_at     | IGFBP6      | insulin-like growth factor binding protein 6    | $2.87 \times 10^{-7}$ | 2.03 |               |             |                                                 |            |     |
| 227760_at     | IGFBPL1     | insulin-like growth factor binding protein-like 1 | $6.32 \times 10^{-20}$ | 2.75 |               |             |                                                 |            |     |
| 218574_s_at   | LMCD1       | LIM and cysteine-rich domains 1                 | $1.08 \times 10^{-20}$ | 5.35 |               |             |                                                 |            |     |
| 242767_at     | LMCD1       | LIM and cysteine-rich domains 1                 | $2.61 \times 10^{-5}$ | 2.23 |               |             |                                                 |            |     |
| 201744_s_at   | LUM         | lumican                                         | $3.33 \times 10^{-9}$ | 2.53 |               |             |                                                 |            |     |
| 212713_at     | MFAP4       | microfibrillar-associated prot 4                | $5.47 \times 10^{-25}$ | 11.79 |               |             |                                                 |            |     |
| 209758_s_at   | MFAP5       | microfibrillar associated prot 5                | $8.86 \times 10^{-9}$ | 9.84  |               |             |                                                 |            |     |
| 213765_at     | MFAP5       | microfibrillar associated prot 5                | $1.07 \times 10^{-7}$ | 9.67  |               |             |                                                 |            |     |
Table 4. Cont.

| Probe Set ID   | Gene Symbol | Gene Title                               | adj-pval   | FC  | Probe Set ID   | Gene Symbol | Gene Title                               | adj-pval   | FC  |
|----------------|-------------|------------------------------------------|------------|-----|----------------|-------------|------------------------------------------|------------|-----|
| 213764_s_at    | MFAP5       | microfibrillar associated prot 5         | 8.21 × 10⁻⁸ | 8.97|                |             |                                          |            |     |
| 210605_s_at    | MFGE8       | milk fat globule-EGF factor 8 protein    | 2.85 × 10⁻⁸ | 3.58|                |             |                                          |            |     |
| 202291_s_at    | MGP         | matrix Gla protein                       | 5.61 × 10⁻⁵ | 5.61|                |             |                                          |            |     |
| 204475_at      | MMP1        | matrix metallopeptidase 1 (interstitial collagenase) | 3.34 × 10⁻⁴ | 3.31|                |             |                                          |            |     |
| 204580_at      | MMP12       | matrix metallopeptidase 12 (macrophage elastase) | 8.73 × 10⁻⁴ | 2.60|                |             |                                          |            |     |
| 205828_at      | MMP3        | matrix metallopeptidase 3 (stromelysin 1, progelatinase) | 5.32 × 10⁻⁸ | 16.81|                |             |                                          |            |     |
| 213693_s_at    | MUC1        | mucin 1, cell surface associated         | 2.96 × 10⁻¹⁸ | 3.90|                |             |                                          |            |     |
| 207847_s_at    | MUC1        | mucin 1, cell surface associated         | 3.37 × 10⁻¹¹ | 3.78|                |             |                                          |            |     |
| 209596_at      | MXRA5       | matrix-remodelling associated 5          | 6.87 × 10⁻²⁶ | 30.61|                |             |                                          |            |     |
| 235836_at      | MXRA7       | matrix-remodelling associated 7          | 7.77 × 10⁻¹⁰ | 2.16|                |             |                                          |            |     |
| 213422_s_at    | MXRA8       | matrix-remodelling associated 8          | 9.88 × 10⁻³⁰ | 2.13|                |             |                                          |            |     |
| Probe Set ID   | Gene Symbol | Gene Title                                      | adj-pval  | FC  | Probe Set ID   | Gene Symbol | Gene Title                                      | adj-pval  | FC  |
|---------------|-------------|------------------------------------------------|-----------|-----|---------------|-------------|------------------------------------------------|-----------|-----|
| 214321_at     | NOV         | nephroblastoma overexpressed gene               | $6.98 \times 10^{-20}$ | 10.34 |               |             |                                                 |           |     |
| 204501_at     | NOV         | nephroblastoma overexpressed gene               | $4.71 \times 10^{-9}$ | 2.90  |               |             |                                                 |           |     |
| 1564494_s_at  | P4HB        | prolyl 4-hydroxylase, beta polypeptide          | $7.83 \times 10^{-23}$ | 3.48  |               |             |                                                 |           |     |
| 219295_s_at   | PCOLCE2     | procollagen C-endopeptidase enhancer 2          | $3.15 \times 10^{-6}$ | 7.20  |               |             |                                                 |           |     |
| 226522_at     | PODN        | podocan                                        | $3.74 \times 10^{-12}$ | 3.16  |               |             |                                                 |           |     |
| 1555778_a_at  | POSTN       | periostin, osteoblast specific factor           | $1.43 \times 10^{-3}$ | 2.70  |               |             |                                                 |           |     |
| 210809_s_at   | POSTN       | periostin, osteoblast specific factor           | $3.60 \times 10^{-4}$ | 2.31  |               |             |                                                 |           |     |
| 228224_at     | PRELP       | proline/arginine-rich end leucine-rich repeat protein | $1.49 \times 10^{-13}$ | 6.34  |               |             |                                                 |           |     |
| 204223_at     | PRELP       | proline/arginine-rich end leucine-rich repeat protein | $3.05 \times 10^{-10}$ | 4.16  |               |             |                                                 |           |     |
| 209496_at     | RARRES2     | retinoic acid receptor responder (tazarotene induced) 2 | $5.58 \times 10^{-9}$ | 4.86  |               |             |                                                 |           |     |
| 205923_at     | RELN        | reelin                                         | $8.98 \times 10^{-4}$ | 2.09  |               |             |                                                 |           |     |
| 228186_s_at   | RSPO3       | R-spondin 3 homolog (Xenopus laevis)            | $5.88 \times 10^{-14}$ | 5.81  |               |             |                                                 |           |     |
Table 4. Cont.

| Probe Set ID  | Gene Symbol | Gene Title                                             | adj-pval  | FC  | Probe Set ID  | Gene Symbol | Gene Title                                             | adj-pval  | FC  |
|---------------|-------------|--------------------------------------------------------|-----------|-----|---------------|-------------|--------------------------------------------------------|-----------|-----|
| 202037_s_at   | SFRP1       | secreted frizzled-related prot 1                       | 1.60 × 10^{-4} | 2.53 | 202035_s_at   | SFRP1       | secreted frizzled-related prot 1                       | 2.84 × 10^{-3} | 2.35 |
| 202036_s_at   | SFRP1       | secreted frizzled-related prot 1                       | 3.39 × 10^{-3} | 2.18 | 223122_s_at   | SFRP2       | secreted frizzled-related prot 2                       | 1.65 × 10^{-29} | 54.89 |
| 223121_s_at   | SFRP2       | secreted frizzled-related prot 2                       | 5.66 × 10^{-18} | 13.22 | 203813_s_at   | SLIT3       | slit homolog 3 (Drosophila)                            | 1.22 × 10^{-21} | 10.53 |
| 223869_at     | SOST        | sclerosteosis                                          | 1.85 × 10^{-7} | 4.21 |               |             |                                                        |           |     |
| 213247_at     | SVEP1       | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | 5.98 × 10^{-13} | 5.61 |               |             |                                                        |           |     |
| 219552_at     | SVEP1       | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 | 8.40 × 10^{-11} | 2.87 |               |             |                                                        |           |     |
| 205016_at     | TGFA        | transforming growth factor, alpha                      | 9.81 × 10^{-19} | 9.55 |               |             |                                                        |           |     |
| 203085_s_at   | TGFB1       | transforming growth factor beta 1                      | 9.57 × 10^{-14} | 2.17 |               |             |                                                        |           |     |
| 239336_at     | THBS1       | Thrombospondin 1                                       | 7.00 × 10^{-26} | 7.23 |               |             |                                                        |           |     |
Table 4. Cont.

| Probe Set ID  | Gene Symbol | Gene Title                  | adj-pval     | FC  | Probe ID   | Gene Symbol | Gene Title                  | adj-pval     | FC  |
|---------------|-------------|-----------------------------|--------------|-----|------------|-------------|-----------------------------|--------------|-----|
| 201107_s_at   | THBS1       | thrombospondin 1            | 7.00 × 10⁻²⁶ | 6.92|            |             |                             |              |     |
| 201108_s_at   | THBS1       | thrombospondin 1            | 5.67 × 10⁻²⁸ | 4.10|            |             |                             |              |     |
| 235086_at     | THBS1       | Thrombospondin 1            | 1.09 × 10⁻¹⁶ | 3.35|            |             |                             |              |     |
| 215775_at     | THBS1       | Thrombospondin 1            | 5.62 × 10⁻¹⁸ | 2.96|            |             |                             |              |     |
| 201109_s_at   | THBS1       | thrombospondin 1            | 7.70 × 10⁻²³ | 2.47|            |             |                             |              |     |
| 201150_s_at   | TIMP3       | TIMP metalloproteinase 3    | 2.68 × 10⁻⁹  | 2.06|            |             |                             |              |     |
| 201149_s_at   | TIMP3       | TIMP metalloproteinase 3    | 2.03 × 10⁻⁵  | 2.02|            |             |                             |              |     |
| 201645_at     | TNC         | Tenascin C                  | 6.48 × 10⁻⁷  | 2.67|            |             |                             |              |     |
| 216005_at     | TNC         | Tenascin C                  | 1.97 × 10⁻³  | 2.27|            |             |                             |              |     |
| 213451_x_at   | TNXA / TNXB | tenascin XA pseudogene XA   | 7.61 × 10⁻⁹  | 7.23|            |             |                             |              |     |
| 206093_x_at   | TNXA / TNXB | tenascin XA pseudogene XA   | 3.25 × 10⁻⁸  | 6.27|            |             |                             |              |     |
| 216333_x_at   | TNXA / TNXB | tenascin XA pseudogene XA   | 1.07 × 10⁻⁷  | 6.23|            |             |                             |              |     |
| 208609_s_at   | TNXB        | Tenascin XB                 | 2.48 × 10⁻⁵  | 3.26|            |             |                             |              |     |
| 235616_at     | TSHZ2       | teashirt zinc finger homebox 2 | 8.68 × 10⁻⁸ | 2.28|            |             |                             |              |     |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                          | adj-pval | FC   | Probe Set ID | Gene Symbol | Gene Title                          | adj-pval | FC   |
|--------------|-------------|-------------------------------------|----------|------|--------------|-------------|-------------------------------------|----------|------|
| 227899_at    | VIT         | vitrin                              | $6.33 \times 10^{-10}$ | 3.99 |              |             |                                     |          |      |
| 210102_at    | VWA5A       | von Willebrand factor A domain containing 5A | $9.24 \times 10^{-6}$ | 2.64 |              |             |                                     |          |      |
| Probe Set ID | Gene Symbol | Gene Title                          | adj-pval | FC   | Probe Set ID | Gene Symbol | Gene Title                          | adj-pval | FC   |
|--------------|-------------|-------------------------------------|----------|------|--------------|-------------|-------------------------------------|----------|------|
| 200965_s_at  | ABLIM1      | actin binding LIM protein 1         | $5.19 \times 10^{-5}$ | 2.74 | 206385_s_at  | ANK3        | ankyrin 3, node of Ranvier (ankyrin G) | $4.82 \times 10^{-8}$ | 3.98 |
| 205268_s_at  | ADD2        | adducin 2 (beta)                    | $6.03 \times 10^{-7}$ | 3.71 | 218950_at    | ARAP3       | ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 3 | $3.65 \times 10^{-15}$ | 2.95 |
| 202022_at    | ALDOC       | aldolase C, fructose-bisphosphate   | $6.50 \times 10^{-21}$ | 6.09 | 227911_at    | ARHGAP28    | Rho GTPase activating protein 28    | $2.26 \times 10^{-11}$ | 3.59 |
| 202920_at    | ANK2        | ankyrin 2, neuronal                  | $7.80 \times 10^{-8}$ | 3.58 | 206167_s_at  | ARHGAP6     | Rho GTPase activating protein 6     | $1.68 \times 10^{-8}$ | 2.90 |
| 213606_s_at  | ARHGDIA     | Rho GDP dissociation inhibitor (GDI) alpha | $2.12 \times 10^{-15}$ | 2.88 | 1555812_a_at | ARHGDI     | Rho GDP dissociation inhibitor (GDI) beta | $4.29 \times 10^{-5}$ | 2.17 |
| 201167_x_at  | ARHGDIA     | Rho GDP dissociation inhibitor (GDI) alpha | $2.10 \times 10^{-14}$ | 2.36 | 218501_at    | ARHGEF3     | Rho guanine nucleotide exchange factor (GEF) 3 | $1.16 \times 10^{-15}$ | 3.82 |
| 222696_at    | AXIN2       | axin 2                              | $3.23 \times 10^{-6}$ | 2.37 | 227372_s_at  | BAIAP2L1    | BAI1-associated protein 2-like 1    | $6.04 \times 10^{-14}$ | 2.08 |
| 227850_x_at  | CDC42EP5    | CDC42 effector protein (Rho GTPase binding) 5 | $3.62 \times 10^{-8}$ | 2.20 | 213373_s_at  | CASP8       | caspase 8, apoptosis-related cysteine peptidase | $7.10 \times 10^{-17}$ | 2.15 |
Table 4. Cont.

| Focal Adhesion Points | UP in Dermal Fibroblasts | UP in MSCs |
|-----------------------|--------------------------|------------|
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
| 228739_at | CYS1 | cystin 1 | $4.46 \times 10^{-26}$ | 5.02 | 234936_s_at | CC2D2A | coiled-coil and C2 domain containing 2A | $3.92 \times 10^{-26}$ | 3.10 |
| 220559_at | EN1 | engrailed homeobox 1 | $2.00 \times 10^{-19}$ | 15.83 | 203881_s_at | DMD | dystrophin | $8.99 \times 10^{-5}$ | 2.84 |
| 206710_s_at | EPB41L3 | erythrocyte membrane protein band 4.1-like 3 | $4.86 \times 10^{-4}$ | 3.86 | 242283_at | DNAH14 | dynein, axonemal, heavy chain 14 | $4.14 \times 10^{-18}$ | 2.72 |
| 212681_at | EPB41L3 | erythrocyte membrane protein band 4.1-like 3 | $4.79 \times 10^{-4}$ | 3.39 | 205186_at | DNALI1 | dynein, axonemal, light intermediate chain 1 | $3.02 \times 10^{-12}$ | 2.71 |
| 211776_s_at | EPB41L3 | erythrocyte membrane protein band 4.1-like 3 | $5.45 \times 10^{-4}$ | 3.26 | 227081_at | DNALI1 | dynein, axonemal, light intermediate chain 1 | $1.38 \times 10^{-6}$ | 2.00 |
| 226129_at | FAM83H | family with sequence similarity 83, member H | $1.37 \times 10^{-9}$ | 2.03 | 212838_at | DNMBP | dynamin binding protein | $2.88 \times 10^{-16}$ | 2.05 |
| 212288_at | FNBP1 | formin binding protein 1 | $9.29 \times 10^{-19}$ | 2.31 | 228674_s_at | EML4 | echinoderm microtubule associated protein like 4 | $1.66 \times 10^{-19}$ | 2.39 |
| 230389_at | FNBP1 | formin binding protein 1 | $2.64 \times 10^{-11}$ | 2.19 | 220386_s_at | EML4 | echinoderm microtubule associated protein like 4 | $1.34 \times 10^{-16}$ | 2.32 |
| Probe Set ID | Gene Symbol | Gene Title                     | adj-pval   | FC  | Gene Symbol | Gene Title                     | adj-pval   | FC  |
|--------------|-------------|--------------------------------|------------|-----|-------------|--------------------------------|------------|-----|
| 230645_at    | FRMD3       | FERM domain containing 3       | $8.23 \times 10^{-12}$ | 3.10 | 223068_at   | EML4 echinoderm microtubule    | $3.04 \times 10^{-22}$ | 2.18 |
|              |             |                                |            |     |             | associated protein like 4      |            |     |
| 229893_at    | FRMD3       | FERM domain containing 3       | $1.74 \times 10^{-10}$ | 2.18 | 201340_s_at | ENC1 ectodermal-neural cortex  | $4.58 \times 10^{-7}$ | 2.76 |
|              |             |                                |            |     |             | (with BTB-like domain)          |            |     |
| 226364_at    | HIP1        | Huntingtin interacting prot 1  | $2.94 \times 10^{-7}$ | 2.09 | 1555137_a_at| FGD6 FYVE, RhoGEF and PH       | $2.15 \times 10^{-8}$ | 2.23 |
|              |             |                                |            |     |             | domain containing 6            |            |     |
| 209558_s_at  | HIP1R       | huntingtin interacting prot 1  | $3.28 \times 10^{-15}$ | 2.09 | 219901_at   | FGD6 FYVE, RhoGEF and PH       | $1.02 \times 10^{-8}$ | 2.22 |
|              |             | related                        |            |     |             | domain containing 6            |            |     |
| 226352_at    | JMY         | junction mediating and regulatory protein, p53 cofactor | $1.44 \times 10^{-15}$ | 5.56 | 225167_at   | FRMD4A FERM domain containing 4A | $2.68 \times 10^{-19}$ | 4.09 |
| 241985_at    | JMY         | junction mediating and regulatory protein, p53 cofactor | $1.04 \times 10^{-16}$ | 2.12 | 208476_s_at | FRMD4A FERM domain containing 4A | $3.98 \times 10^{-15}$ | 3.51 |
| 226534_at    | KITLG       | KIT ligand                     | $1.06 \times 10^{-5}$ | 2.21 | 225163_at   | FRMD4A FERM domain containing 4A | $3.05 \times 10^{-17}$ | 3.31 |
| 213371_at    | LDB3        | LIM domain binding 3           | $1.66 \times 10^{-2}$ | 2.05 | 225168_at   | FRMD4A FERM domain containing 4A | $9.69 \times 10^{-17}$ | 2.99 |
| 227219_x_at  | MAP1LC3A    | microtubule-associated protein 1 light chain 3 alpha | $1.93 \times 10^{-18}$ | 2.79 | 1560031_at  | FRMD4A FERM domain containing 4A | $2.08 \times 10^{-13}$ | 2.76 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|--------------|-------------|------------|----------|----|--------------|-------------|------------|----------|----|
| 224378_s_at  | MAP1LC3A    | microtubule-associated protein 1 light chain 3 alpha | $2.64 \times 10^{-14}$ | 2.72 | 230831_at     | FRMD5       | FERM domain containing 5 | $1.24 \times 10^{-19}$ | 6.37 |
| 232011_s_at  | MAP1LC3A    | microtubule-associated protein 1 light chain 3 alpha | $1.07 \times 10^{-13}$ | 2.60 | 220773_s_at  | GPHN        | gephyrin | $9.51 \times 10^{-19}$ | 2.13 |
| 208786_s_at  | MAP1LC3B    | microtubule-associated protein 1 light chain 3 beta | $5.66 \times 10^{-32}$ | 2.26 | 223319_at     | GPHN        | gephyrin | $7.91 \times 10^{-18}$ | 2.06 |
| 205442_at    | MFAP3L      | microfibrillar-associated protein 3-like | $6.52 \times 10^{-14}$ | 6.61 | 202962_at     | KIF13B      | kinesin family member 13B | $1.09 \times 10^{-19}$ | 2.74 |
| 204631_at    | MYH2        | myosin, heavy chain 2, skeletal muscle, adult | $7.89 \times 10^{-8}$ | 6.38 | 226003_at     | KIF21A      | kinesin family member 21A | $2.27 \times 10^{-25}$ | 2.33 |
| 201058_s_at  | MYL9        | myosin, light chain 9, regulatory | $1.46 \times 10^{-7}$ | 2.00 | 231875_at     | KIF21A      | kinesin family member 21A | $1.40 \times 10^{-16}$ | 2.21 |
| 228098_s_at  | MYLIP       | myosin regulatory light chain interacting protein | $5.37 \times 10^{-27}$ | 7.57 | 225613_at     | MAST4       | Microtubule associated serine/threonine kinase family member 4 | $2.87 \times 10^{-16}$ | 3.50 |
| 223130_s_at  | MYLIP       | myosin regulatory light chain interacting protein | $1.59 \times 10^{-28}$ | 7.13 | 225611_at     | MAST4       | Microtubule associated serine/threonine kinase family member 4 | $6.91 \times 10^{-15}$ | 2.95 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC  | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval     | FC  |
|--------------|-------------|------------------------------------------------|--------------|-----|--------------|-------------|------------------------------------------------|--------------|-----|
| 220319_s_at  | MYLIP       | myosin regulatory light chain interacting protein | $7.00 \times 10^{-16}$ | 2.93| 40016_g_at  | MAST4       | microtubule associated serine/threonine kinase family member 4 | $5.49 \times 10^{-15}$ | 2.43|
| 223129_x_at  | MYLIP       | myosin regulatory light chain interacting protein | $1.25 \times 10^{-14}$ | 2.03| 213511_s_at  | MTMR1       | myotubularin related protein 1                        | $2.10 \times 10^{-20}$ | 2.23|
| 202555_s_at  | MYLK        | myosin light chain kinase                        | $2.64 \times 10^{-5}$  | 2.37| 216095_x_at  | MTMR1       | myotubularin related protein 1                        | $4.13 \times 10^{-21}$ | 2.09|
| 224823_at    | MYLK        | myosin light chain kinase                        | $3.68 \times 10^{-5}$  | 2.11| 237206_at    | MYOCD       | myocardin                                           | $7.88 \times 10^{-3}$   | 2.36|
| 212338_at    | MYO1D       | myosin ID                                       | $3.13 \times 10^{-14}$ | 8.06| 219073_s_at  | OSBPL10     | oxysterol binding protein-like 10                   | $5.46 \times 10^{-8}$   | 2.27|
| 223464_at    | OSBPL5      | oxysterol binding protein-like 5                | $1.87 \times 10^{-17}$ | 2.26| 219938_s_at  | PSTPIP2     | proline-serine-threonine phosphatase interacting protein 2 | $9.14 \times 10^{-13}$ | 2.08|
| 209019_s_at  | PINK1       | PTEN induced putative kinase 1                  | $2.23 \times 10^{-26}$ | 2.64| 223471_at    | RAB3IP      | RAB3A interacting protein (rabin3)                   | $4.80 \times 10^{-24}$ | 4.06|
| 209018_s_at  | PINK1       | PTEN induced putative kinase 1                  | $8.46 \times 10^{-26}$ | 2.62| 219045_at    | RHOF        | ras homolog gene family, member F (in filopodia)     | $3.42 \times 10^{-18}$ | 3.29|
| 226627_at    | SEPT8       | septin 8                                        | $1.33 \times 10^{-9}$  | 2.22| 219263_at    | RNF128      | ring finger protein 128                              | $3.33 \times 10^{-3}$   | 2.11|
| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval | FC    | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval | FC    |
|--------------|-------------|------------------------------------------------|----------|-------|--------------|-------------|------------------------------------------------|----------|-------|
| 230730_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 3.81 × 10^{-13} | 10.01 | 204967_at    | SHROOM2     | shroom family member 2                          | 2.29 × 10^{-14} | 15.26 |
| 213543_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 4.91 × 10^{-13} | 8.70  | 213109_at    | TNIK        | TRAF2 and NCK interacting kinase                | 8.89 × 10^{-6}  | 2.75  |
| 228602_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 1.66 × 10^{-8}  | 5.55  | 213107_at    | TNIK        | TRAF2 and NCK interacting kinase                | 1.18 × 10^{-4}  | 2.51  |
| 210330_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 1.25 × 10^{-12} | 4.80  | 216251_s_at  | TTLL12      | tubulin tyrosine ligase-like family member 12   | 1.63 × 10^{-17} | 2.07  |
| 210329_s_at  | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 1.01 × 10^{-10} | 3.87  | 1552257_a_at | TTLL12      | tubulin tyrosine ligase-like family member 12   | 1.20 × 10^{-18} | 2.00  |
| 214492_at    | SGCD        | sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein) | 3.87 × 10^{-7}  | 2.93  | 203702_s_at  | TTLL4       | tubulin tyrosine ligase-like family member 4    | 3.28 × 10^{-17} | 2.24  |
| 207302_at    | SGCG        | sarcoglycan, gamma (35 kDa dystrophin-associated glycoprotein) | 6.41 × 10^{-28} | 38.26 |               |             |                                                 |          |       |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval  | FC   | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval  | FC   |
|--------------|-------------|-------------------------------------------------|-----------|------|--------------|-------------|-------------------------------------------------|-----------|------|
| 228400_at    | SHROOM3     | shroom family member 3                          | $1.15 \times 10^{-24}$ | 15.85 |              |             |                                                 |           |      |
| 225548_at    | SHROOM3     | shroom family member 3                          | $2.47 \times 10^{-24}$ | 11.91 |              |             |                                                 |           |      |
| 217678_at    | SLC7A11     | solute carrier family 7, (cationic amino acid transporter, y+ system) member 11 | $1.52 \times 10^{-7}$ | 2.36  |              |             |                                                 |           |      |
| 203516_at    | SNTA1       | syntrophin, alpha 1 (dystrophin-associated protein A1, 59 kDa, acidic component) | $1.56 \times 10^{-19}$ | 2.89  |              |             |                                                 |           |      |
| 201061_s_at  | STOM        | stomatin                                        | $2.06 \times 10^{-23}$ | 2.38  |              |             |                                                 |           |      |
| 209306_s_at  | SWAP70      | SWAP-70 protein                                 | $3.61 \times 10^{-37}$ | 2.22  |              |             |                                                 |           |      |
| 209904_at    | TNNC1       | troponin C type 1 (slow)                        | $6.23 \times 10^{-5}$  | 2.12  |              |             |                                                 |           |      |
| 238688_at    | TPM1        | Tropomyosin 1 (alpha)                           | $1.82 \times 10^{-9}$  | 2.70  |              |             |                                                 |           |      |
| 206117_at    | TPM1        | tropomyosin 1 (alpha)                           | $6.69 \times 10^{-11}$ | 2.33  |              |             |                                                 |           |      |
| 202479_s_at  | TRIB2       | tribbles homolog 2 (Drosophila)                 | $1.37 \times 10^{-11}$ | 2.20  |              |             |                                                 |           |      |
| 202478_at    | TRIB2       | tribbles homolog 2 (Drosophila)                 | $3.53 \times 10^{-10}$ | 2.09  |              |             |                                                 |           |      |
Table 4. Cont.

| Table 4. Cont. | Table 4. Cont. |
|----------------|----------------|
| **UP in Dermal Fibroblasts** | **UP in MSCs** |
| **Focal Adhesion Points** | **Focal Adhesion Points** |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|---------------|-------------|-------------|-----------|----|---------------|-------------|-------------|-----------|----|
| 213908_at | WHAMM1L1 | WAS protein homolog associated with actin, golgi membranes and microtubules-like 1/2 | $4.06 \times 10^{-21}$ | 3.52 | | | | | |
| 1557261_at | WHAMM1L1 | WAS protein homolog associated with actin, golgi membranes and microtubules-like 1/2 | $2.06 \times 10^{-15}$ | 3.26 | | | | | |
| **Cytoskeleton** | **Cytoskeleton** |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|---------------|-------------|-------------|-----------|----|---------------|-------------|-------------|-----------|----|
| 205132_at | ACTC1 | actin, alpha, cardiac muscle 1 | $1.23 \times 10^{-34}$ | 78.69 | 202274_at | ACTG2 | actin, gamma 2, smooth muscle, enteric | $6.12 \times 10^{-10}$ | 13.98 |
| 220115_s_at | CDH10 | cadherin 10, type 2 (T2-cadherin) | $1.12 \times 10^{-7}$ | 3.11 | 210517_s_at | AKAP12 | A kinase (PRKA) anchor protein 12 | $6.41 \times 10^{-6}$ | 3.58 |
| 205532_s_at | CDH6 | cadherin 6, type 2, K-cadherin (fetal kidney) | $1.02 \times 10^{-2}$ | 2.36 | 227529_s_at | AKAP12 | A kinase (PRKA) anchor protein 12 | $1.17 \times 10^{-2}$ | 2.42 |
| 232898_at | DAB2 | disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila) | $8.32 \times 10^{-10}$ | 3.32 | 227530_at | AKAP12 | A kinase (PRKA) anchor protein 12 | $6.85 \times 10^{-3}$ | 2.41 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                           | adj-pval     | FC  | Probe Set ID | Gene Symbol | Gene Title                                           | adj-pval     | FC  |
|--------------|-------------|------------------------------------------------------|--------------|-----|--------------|-------------|------------------------------------------------------|--------------|-----|
| 201279_s_at  | DAB2        | disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila) | $1.60 \times 10^{-18}$ | 2.30 | 206298_at    | ARHGAP22    | Rho GTPase activating protein 22                      | $4.33 \times 10^{-30}$ | 4.16 |
| 201280_s_at  | DAB2        | disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila) | $3.78 \times 10^{-21}$ | 2.28 | 201005_at    | CD9         | CD9 molecule                                         | $7.48 \times 10^{-6}$ | 2.96 |
| 201278_at    | DAB2        | disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila) | $1.77 \times 10^{-23}$ | 2.26 | 214297_at    | CSPG4       | chondroitin sulfate proteoglycan 4                   | $8.70 \times 10^{-5}$ | 2.37 |
| 210757_x_at  | DAB2        | disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila) | $4.14 \times 10^{-18}$ | 2.17 | 220512_at    | DLC1        | deleted in liver cancer 1                            | $2.59 \times 10^{-15}$ | 3.03 |
| 240873_x_at  | DAB2        | disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila) | $1.06 \times 10^{-13}$ | 2.08 | 211478_s_at  | DPP4        | dipeptidyl-peptidase 4                               | $2.91 \times 10^{-19}$ | 11.71 |
| 214724_at    | DIXDC1      | DIX domain containing 1                              | $1.31 \times 10^{-9}$ | 2.20 | 203716_s_at  | DPP4        | dipeptidyl-peptidase 4                               | $2.07 \times 10^{-21}$ | 10.11 |
| 224814_at    | DPP7        | dipeptidyl-peptidase 7                               | $1.13 \times 10^{-21}$ | 2.61 | 203717_at    | DPP4        | dipeptidyl-peptidase 4                               | $9.35 \times 10^{-19}$ | 6.79 |
| 205031_at    | EFNB3       | ephrin-B3                                            | $1.05 \times 10^{-9}$ | 2.43 | 217901_at    | DSG2        | desmoglein 2                                         | $1.05 \times 10^{-10}$ | 19.57 |
| 208228_s_at  | FGFR2       | fibroblast growth factor receptor 2                  | $9.30 \times 10^{-10}$ | 3.71 | 1553105_s_at | DSG2        | desmoglein 2                                         | $4.29 \times 10^{-9}$ | 7.96 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC  |
|-------------|-------------|------------|-----------|-----|-------------|-------------|------------|-----------|-----|
| 204379_s_at | FGFR3       | fibroblast growth factor receptor 3 | 1.66 × 10^{-19} | 4.70 | 227955_s_at | EFNA5       | ephrin-A5  | 1.28 × 10^{-10} | 4.10 |
| 201539_s_at | FHL1        | four and a half LIM domains 1 | 2.10 × 10^{-4} | 2.76 | 214036_at    | EFNA5       | ephrin-A5  | 1.68 × 10^{-7}  | 2.33 |
| 214505_s_at | FHL1        | four and a half LIM domains 1 | 6.14 × 10^{-4} | 2.37 | 202669_s_at  | EFNB2       | ephrin-B2  | 2.57 × 10^{-2}  | 2.16 |
| 210299_s_at | FHL1        | four and a half LIM domains 1 | 2.65 × 10^{-4} | 2.29 | 201983_s_at  | EGFR        | epidermal growth factor receptor | 3.46 × 10^{-10} | 2.10 |
| 210298_x_at | FHL1        | four and a half LIM domains 1 | 6.34 × 10^{-4} | 2.27 | 218796_at    | FERMT1      | fermitin family homolog 1 (Drosophila) | 2.45 × 10^{-12} | 4.17 |
| 208748_s_at | FLOT1       | flotillin 1 | 5.72 × 10^{-7} | 3.13 | 60474_at     | FERMT1      | fermitin family homolog 1 (Drosophila) | 9.46 × 10^{-13} | 3.84 |
| 222899_at  | ITGA11      | integrin, alpha 11 | 1.08 × 10^{-21} | 26.89 | 242422_at    | G3BP1       | GTPase activating protein (SH3 domain) binding protein 1 | 3.82 × 10^{-5}  | 2.28 |
| 215177_s_at | ITGA6       | integrin, alpha 6 | 9.34 × 10^{-11} | 6.34 | 206383_s_at  | G3BP2       | GTPase activating protein (SH3 domain) binding protein 2 | 1.94 × 10^{-17} | 2.17 |
| 201656_at  | ITGA6       | integrin, alpha 6 | 5.30 × 10^{-11} | 4.58 | 206074_s_at  | HMGA1       | high mobility group AT-hook 1 | 8.66 × 10^{-22} | 2.89 |
| 214265_at  | ITGA8       | integrin, alpha 8 | 7.06 × 10^{-7}  | 4.79 | 208025_s_at  | HMGA2       | high mobility group AT-hook 2 | 5.89 × 10^{-29} | 22.82 |
| 227297_at  | ITGA9       | integrin, alpha 9 | 6.70 × 10^{-8}  | 2.35 | 1567224_at   | HMGA2       | high mobility group AT-hook 2 | 2.78 × 10^{-21} | 4.79 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC  |
|--------------|-------------|------------|----------|-----|--------------|-------------|------------|----------|-----|
| 202803_s_at  | ITGB2       | integrin, beta 2 (complement component 3 receptor 3 and 4 subunit) | $9.97 \times 10^{-9}$ | 2.63 | 1558683_a_at | HMGA2       | high mobility group AT-hook 2 | $3.31 \times 10^{-25}$ | 4.32 |
| 226189_at    | ITGB8       | integrin, beta 8 | $8.02 \times 10^{-14}$ | 6.70 | 1561633_at   | HMGA2       | high mobility group AT-hook 2 | $4.45 \times 10^{-22}$ | 3.95 |
| 205422_s_at  | ITGBL1      | integrin, beta-like 1 (with EGF-like repeat domains) | $2.20 \times 10^{-16}$ | 12.03 | 1558682_at   | HMGA2       | high mobility group AT-hook 2 | $3.32 \times 10^{-22}$ | 2.27 |
| 231993_at    | ITGBL1      | integrin, beta-like 1 (with EGF-like repeat domains) | $1.41 \times 10^{-15}$ | 10.90 | 202638_s_at  | ICAM1       | intercellular adhesion molecule 1 | $3.48 \times 10^{-5}$ | 2.74 |
| 214927_at    | ITGBL1      | integrin, beta-like 1 (with EGF-like repeat domains) | $2.34 \times 10^{-13}$ | 8.91  | 202637_s_at  | ICAM1       | intercellular adhesion molecule 1 | $6.68 \times 10^{-8}$ | 2.33 |
| 1557080_s_at | ITGBL1      | integrin, beta-like 1 (with EGF-like repeat domains) | $1.48 \times 10^{-12}$ | 8.22  | 213620_s_at  | ICAM2       | intercellular adhesion molecule 2 | $3.73 \times 10^{-13}$ | 2.64 |
| 1557079_at   | ITGBL1      | integrin, beta-like 1 (with EGF-like repeat domains) | $3.54 \times 10^{-16}$ | 7.56  | 213446_s_at  | IQGAP1      | IQ motif containing GTPase activating protein 1 | $1.13 \times 10^{-6}$ | 2.08 |
| 228080_at    | LAYN        | layilin    | $8.17 \times 10^{-10}$ | 2.89  | 206766_at    | ITGA10      | integrin, alpha 10 | $2.50 \times 10^{-6}$ | 4.61 |
| 220765_s_at  | LIMS2       | LIM and senescent cell antigen-like domains 2 | $1.13 \times 10^{-10}$ | 2.99  | 227314_at    | ITGA2       | integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) | $6.15 \times 10^{-8}$ | 3.59 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
|---------------|-------------|------------|----------|----|---------------|-------------|------------|----------|----|
| 202674_s_at   | LMO7        | LIM domain 7 | $4.31 \times 10^{-14}$ | 2.85 | 205032_at | ITGA2 | integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) | $4.90 \times 10^{-7}$ | 2.82 |
| 242722_at     | LMO7        | LIM domain 7 | $4.41 \times 10^{-10}$ | 2.49 | 204627_s_at | ITGB3 | integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61) | $9.77 \times 10^{-9}$ | 2.61 |
| 213490_s_at   | MAP2K2      | mitogen-activated protein kinase kinase 2 | $7.78 \times 10^{-5}$ | 2.09 | 223800_s_at | LIMS3 | LIM and senescent cell antigen-like domains 3 | $4.73 \times 10^{-19}$ | 4.89 |
| 213438_at     | NFASC       | neurofascin homolog (chicken) | $1.78 \times 10^{-16}$ | 16.35 | 209615_s_at | PAK1 | p21 protein (Cdc42/Rac)-activated kinase 1 | $3.17 \times 10^{-15}$ | 2.06 |
| 230242_at     | NFASC       | neurofascin homolog (chicken) | $2.51 \times 10^{-12}$ | 3.55 | 228635_at | PCDH10 | protocadherin 10 | $2.29 \times 10^{-11}$ | 16.71 |
| 243645_at     | NFASC       | neurofascin homolog (chicken) | $6.86 \times 10^{-15}$ | 2.84 | 205534_at | PCDH7 | protocadherin 7 | $2.49 \times 10^{-4}$ | 3.81 |
| 222455_s_at   | PARVA       | parvin, alpha | $5.02 \times 10^{-28}$ | 2.01 | 228640_at | PCDH7 | protocadherin 7 | $7.79 \times 10^{-3}$ | 2.84 |
| 37965_at      | PARVB       | parvin, beta | $8.71 \times 10^{-9}$ | 2.05 | 205535_s_at | PCDH7 | protocadherin 7 | $6.91 \times 10^{-5}$ | 2.57 |
| 225977_at     | PCDH18      | protocadherin 18 | $2.01 \times 10^{-24}$ | 7.05 | 219737_s_at | PCDH9 | protocadherin 9 | $2.28 \times 10^{-3}$ | 2.60 |
| 225975_at     | PCDH18      | protocadherin 18 | $5.95 \times 10^{-23}$ | 5.41 | 238419_at | PHLDB2 | pleckstrin homology-like domain, family B, member 2 | $1.23 \times 10^{-8}$ | 3.41 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval (Dermal Fibroblasts) | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval (MSCs) | FC |
|--------------|-------------|------------|-------------------------------|----|--------------|-------------|------------|----------------|----|
| 223854_at    | PCDHB10     | protocadherin beta 10 | $2.58 \times 10^{-11}$ | 2.37 | 214374_s_at | PPFIBP1 | PTPRF interacting protein, binding protein 1 (liprin beta 1) | $5.08 \times 10^{-8}$ | 2.07 |
| 232099_at    | PCDHB16     | protocadherin beta 16 | $7.07 \times 10^{-15}$ | 3.65 | 203650_at | PROCR | protein C receptor, endothelial (EPCR) | $1.20 \times 10^{-14}$ | 2.89 |
| 231725_at    | PCDHB2      | protocadherin beta 2  | $1.82 \times 10^{-30}$ | 10.23 | 216915_s_at | PTPN12 | protein tyrosine phosphatase, non-receptor type 12 | $2.10 \times 10^{-8}$ | 2.00 |
| 212841_s_at  | PPFIBP2     | PTPRF interacting protein, binding protein 2 (liprin beta 2) | $9.85 \times 10^{-32}$ | 4.48 | 202565_s_at | SVIL | supervillin | $3.65 \times 10^{-6}$ | 2.95 |
| 207011_s_at  | PTK7        | PTK7 protein tyrosine kinase 7 | $1.50 \times 10^{-6}$ | 2.06 | 206702_at | TEK | TEK tyrosine kinase, endothelial | $3.34 \times 10^{-15}$ | 13.28 |
| 227557_at    | SCARF2      | scavenger receptor class F, member 2 | $1.76 \times 10^{-18}$ | 2.42 | 223314_at | TSPAN14 | tetraspanin 14 | $1.52 \times 10^{-15}$ | 2.71 |
| 212154_at    | SDC2        | syndecan 2  | $1.02 \times 10^{-14}$ | 2.45 | 221002_s_at | TSPAN14 | tetraspanin 14 | $2.48 \times 10^{-15}$ | 2.01 |
| 212157_at    | SDC2        | syndecan 2  | $3.60 \times 10^{-12}$ | 2.16 | 209890_at | TSPAN5  | tetraspanin 5  | $5.39 \times 10^{-26}$ | 2.00 |
| 212158_at    | SDC2        | syndecan 2  | $7.05 \times 10^{-13}$ | 2.10 | 203868_s_at | VCAM1 | vascular cell adhesion molecule 1 | $2.90 \times 10^{-4}$ | 4.10 |
| 202898_at    | SDC3        | syndecan 3  | $2.33 \times 10^{-9}$ | 2.98 | 209890_at | TSPAN5  | tetraspanin 5  | $5.39 \times 10^{-26}$ | 2.00 |
| 226438_at    | SNTB1       | syntrophin, beta 1 (dystrophin-associated protein A1, 59 kDa, basic component 1) | $2.90 \times 10^{-4}$ | 2.11 |
| Probe Set ID | Gene Symbol | Gene Title                          | adj-pval   | FC  | Probe Set ID | Gene Symbol | Gene Title                          | adj-pval   | FC  |
|-------------|-------------|-------------------------------------|------------|-----|-------------|-------------|-------------------------------------|------------|-----|
| 218087_s_at | SORBS1      | sorbin and SH3 domain containing 1 | 2.49 × 10^{-4} | 3.11 |             |             |                                     |            |     |
| 222513_s_at | SORBS1      | sorbin and SH3 domain containing 1 | 4.61 × 10^{-3} | 2.00 |             |             |                                     |            |     |
| 225728_at   | SORBS2      | sorbin and SH3 domain containing 2 | 9.66 × 10^{-4} | 2.52 |             |             |                                     |            |     |
| 204288_s_at | SORBS2      | sorbin and SH3 domain containing 2 | 1.01 × 10^{-3} | 2.10 |             |             |                                     |            |     |
| 202796_at   | SYNPO       | synaptopodin                        | 8.58 × 10^{-4} | 2.06 |             |             |                                     |            |     |
| 225720_at   | SYNPO2      | synaptopodin 2                      | 8.30 × 10^{-16} | 15.40 |             |             |                                     |            |     |
| 225895_at   | SYNPO2      | synaptopodin 2                      | 6.69 × 10^{-16} | 9.94  |             |             |                                     |            |     |
| 225721_at   | SYNPO2      | synaptopodin 2                      | 2.22 × 10^{-16} | 9.02  |             |             |                                     |            |     |
| 225894_at   | SYNPO2      | synaptopodin 2                      | 4.14 × 10^{-15} | 4.97  |             |             |                                     |            |     |
| 40837_at    | TLE2        | transducin-like enhancer of split 2 (E(sp1) homolog, Drosophila) | 1.54 × 10^{-15} | 3.71  |             |             |                                     |            |     |
| 221747_at   | TNS1        | tensin 1                            | 4.25 × 10^{-10} | 2.00  |             |             |                                     |            |     |
| 227307_at   | TSPAN18     | Tetraspanin 18                      | 2.81 × 10^{-9}  | 4.58  |             |             |                                     |            |     |
| 227236_at   | TSPAN2      | tetraspanin 2                       | 4.44 × 10^{-6}  | 3.18  |             |             |                                     |            |     |
| 209264_s_at | TSPAN4      | tetraspanin 4                       | 3.72 × 10^{-11} | 2.46  |             |             |                                     |            |     |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC   | Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC   |
|-------------|-------------|------------|------------|------|-------------|-------------|------------|------------|------|
| 209230_s_at | NUPR1       | nuclear protein 1 | 2.43 × 10^{-15} | 12.15 | 206550_s_at | NUP155      | nucleoparin 155 kDa | 1.03 × 10^{-15} | 2.04 |
| 219888_at  | SPAG4       | sperm associated antigen 4 | 1.16 × 10^{-9} | 3.27  | 225470_at  | NUP35       | nucleoparin 35 kDa   | 1.38 × 10^{-21} | 2.06 |
| 232027_at  | SYNE1       | Spectrin repeat containing, nuclear envelope 1 | 1.61 × 10^{-17} | 6.92  |             |             |            |            |      |
| 209447_at  | SYNE1       | spectrin repeat containing, nuclear envelope 1 | 5.46 × 10^{-12} | 2.25  |             |             |            |            |      |
|             |             |            |            |      |             |             |            |            |      |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC   | Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC   |
|-------------|-------------|------------|------------|------|-------------|-------------|------------|------------|------|
| 215071_s_at | HIST1H2AC   | histone cluster 1, H2ac | 8.12 × 10^{-9} | 2.61  | 227048_at  | LAMA1       | laminin, alpha 1 | 7.19 × 10^{-11} | 4.99 |
| 209911_x_at | HIST1H2BD   | histone cluster 1, H2bd | 1.44 × 10^{-7} | 2.08  | 211651_s_at | LAMB1       | laminin, beta 1  | 2.68 × 10^{-21} | 2.83 |
| 214290_s_at | HIST2H2AA3  | histone cluster 2, H2aa3 | 1.07 × 10^{-10} | 2.38  | 201505_at  | LAMB1       | laminin, beta 1  | 6.03 × 10^{-20} | 2.43 |
|             | HIST2H2AA4  | histone cluster 2, H2aa4 |            |      |             |             |            |            |      |
| 218280_x_at | HIST2H2AA3  | histone cluster 2, H2aa3 | 8.30 × 10^{-11} | 2.22  | 242918_at  | NASP        | Nuclear autoantigenic sperm protein (histone-binding) | 1.21 × 10^{-4} | 2.15 |
|             | HIST2H2AA4  | histone cluster 2, H2aa4 |            |      |             |             |            |            |      |
| 202708_s_at | HIST2H2BE   | histone cluster 2, H2be | 1.53 × 10^{-8} | 2.20  | 201970_s_at | NASP        | nuclear autoantigenic sperm protein (histone-binding) | 2.90 × 10^{-16} | 2.04 |
| 221582_at  | HIST3H2A    | histone cluster 3, H2a | 1.51 × 10^{-19} | 2.39  | 209754_s_at | TMPO        | thymopoietin    | 7.79 × 10^{-15} | 2.99 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval    | FC | Probe Set ID | Gene Symbol | Gene Title       | adj-pval    | FC  |
|--------------|-------------|-------------------------------------------------|-------------|----|--------------|-------------|------------------|-------------|-----|
| 205116_at    | LAMA2       | laminin, alpha 2                                | $1.03 \times 10^{-10}$ | 4.64 | 209753_s_at  | TMPO        | thymopoietin     | $3.32 \times 10^{-8}$ | 2.02 |
| 216840_s_at  | LAMA2       | laminin, alpha 2                                | $4.12 \times 10^{-10}$ | 4.36 |
| 213519_s_at  | LAMA2       | laminin, alpha 2                                | $1.78 \times 10^{-10}$ | 3.97 |
| 202202_s_at  | LAMA4       | laminin, alpha 4                                | $7.35 \times 10^{-6}$  | 5.39 |
| 210089_s_at  | LAMA4       | laminin, alpha 4                                | $1.39 \times 10^{-7}$  | 3.10 |
| 216264_s_at  | LAMB2       | laminin, beta 2 (laminin S)                     | $1.72 \times 10^{-26}$ | 2.94 |

Nucleoskeleton

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval    | FC | Probe Set ID | Gene Symbol | Gene Title       | adj-pval    | FC  |
|--------------|-------------|-------------------------------------------------|-------------|----|--------------|-------------|------------------|-------------|-----|
| 229819_at    | A1BG        | alpha-1-B glycoprotein                          | $1.21 \times 10^{-14}$ | 2.11 | 204694_at    | AFP         | alpha-fetoprotein | $2.77 \times 10^{-12}$ | 2.11 |
| 202912_at    | ADM         | adrenomedullin                                  | $9.27 \times 10^{-10}$ | 2.59 | 221009_s_at  | ANGPTL4     | angiopoietin-like 4 | $4.26 \times 10^{-25}$ | 21.5 |
| 205141_at    | ANG         | angiogenin, ribonuclease, RNase A family, 5     | $7.82 \times 10^{-13}$ | 2.35 | 223333_s_at  | ANGPTL4     | angiopoietin-like 4 | $1.89 \times 10^{-21}$ | 11.7 |
| 213001_at    | ANGPTL2     | angiopoietin-like 2                             | $5.71 \times 10^{-23}$ | 7.43 | 205239_at    | AREG        | amphiregulin      | $9.14 \times 10^{-7}$  | 2.28 |
| 213004_at    | ANGPTL2     | angiopoietin-like 2                             | $9.64 \times 10^{-26}$ | 4.96 | 211518_s_at  | BMP4        | bone morphogenetic protein 4 | $6.50 \times 10^{-3}$  | 2.09 |
| 219514_at    | ANGPTL2     | angiopoietin-like 2                             | $4.12 \times 10^{-22}$ | 2.90 | 209301_at    | CA2         | carbonic anhydrase II | $1.60 \times 10^{-6}$  | 8.34 |
| 238987_at    | B4GALT1     | UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1 | $1.32 \times 10^{-8}$ | 2.15 | 216598_s_at  | CCL2        | chemokine (C-C motif) ligand 2 | $7.24 \times 10^{-8}$  | 6.16 |

Secreted Factors
Table 4. Cont.

| Secreted Factors | UP in Dermal Fibroblasts | UP in MSCs |
|------------------|--------------------------|------------|
| Probe Set ID     | Gene Symbol              | Gene Title                        | adj-pval | FC | Probe Set ID | Gene Symbol      | Gene Title                        | adj-pval | FC |
| 206176_at        | BMP6                     | bone morphogenetic protein 6      | 9.19 x 10^{-5} | 2.75 | 205476_at    | CCL20            | chemokine (C-C motif) ligand 20   | 2.08 x 10^{-6} | 2.24 |
| 220988_s_at      | C1QTNF3                  | C1q and tumor necrosis factor related protein 3 | 7.54 x 10^{-9} | 2.28 | 208075_s_at  | CCL7             | chemokine (C-C motif) ligand 7    | 2.99 x 10^{-9} | 2.30 |
| 223499_at        | C1QTNF5/MFRP             | C1q and tumor necrosis factor related protein 5/membrane frizzled-related protein | 2.40 x 10^{-25} | 8.01 | 215388_s_at  | CFH/CFHR1        | complement factor H complement factor H-related 1 | 1.27 x 10^{-3} | 2.82 |
| 235221_at        | CBLN3                    | cerebellin 3 precursor            | 5.03 x 10^{-12} | 2.22 | 209395_at    | CHI3L1           | chitinase 3-like 1 (cartilage glycoprotein-39) | 9.49 x 10^{-5} | 5.50 |
| 209616_s_at      | CES1                     | carboxylesterase 1 (monocyte/macrophage serine esterase 1) | 1.15 x 10^{-4} | 2.88 | 209396_s_at  | CHI3L1           | chitinase 3-like 1 (cartilage glycoprotein-39) | 3.39 x 10^{-4} | 3.69 |
| 205382_s_at      | CFD                      | complement factor D (adipsin)     | 2.42 x 10^{-18} | 5.81 | 235099_at    | CMTM8            | CKLF-like MARVEL transmembrane domain containing 8 | 7.13 x 10^{-5} | 2.02 |
| 200884_at        | CKB                      | creatine kinase, brain            | 2.07 x 10^{-31} | 6.59 | 205832_at    | CPA4             | carboxypeptidase A4             | 5.82 x 10^{-3} | 2.61 |
| 201117_s_at      | CPE                      | carboxypeptidase E                | 3.74 x 10^{-32} | 34.67 | 204470_at    | CXCL1            | chemokine (C-X-C motif) ligand 1   | 2.10 x 10^{-8} | 9.57 |
| 201116_s_at      | CPE                      | carboxypeptidase E                | 9.98 x 10^{-32} | 26.80 | 209774_x_at  | CXCL2            | chemokine (C-X-C motif) ligand 2   | 1.84 x 10^{-13} | 14.5 |
| 206100_at        | CPM                      | carboxypeptidase M                | 7.56 x 10^{-6}  | 2.80  | 207850_at    | CXCL3            | chemokine (C-X-C motif) ligand 3   | 3.30 x 10^{-17} | 15.1 |
Table 4. Cont.

| Secreted Factors | UP in Dermal Fibroblasts | UP in MSCs |
|------------------|--------------------------|------------|
| Probe Set ID     | Gene Symbol              | Gene Title                          | adj-pval | FC    | Probe Set ID | Gene Symbol        | Gene Title                          | adj-pval | FC    |
| 201200_at        | CREG1                    | cellular repressor of E1A-stimulated genes 1 | 1.40 × 10^{-10} | 2.97  | 214974_x_at | CXCL5                  | chemokine (C-X-C motif) ligand 5 | 5.88 × 10^{-11} | 12.1  |
| 201360_at        | CST3                     | cystatin C                           | 6.04 × 10^{-15} | 2.23  | 215101_s_at | CXCL5                  | chemokine (C-X-C motif) ligand 5 | 5.26 × 10^{-10} | 8.60  |
| 206595_at        | CST6                     | cystatin E/M                         | 6.70 × 10^{-13} | 7.45  | 206336_at  | CXCL6                  | chemokine (C-X-C motif) ligand 6 (granulocyte chemotactic protein 2) | 2.59 × 10^{-4} | 5.46  |
| 209687_at        | CXCL12                   | chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) | 2.68 × 10^{-10} | 8.12  | 213092_x_at | DNAJC9                 | DnaJ (Hsp40) homolog, subfamily C, member 9 | 5.56 × 10^{-13} | 2.08  |
| 203666_at        | CXCL12                   | chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) | 1.08 × 10^{-7} | 6.47  | 201430_s_at | DPYSL3                | dihydropyrimidinase-like 3 | 3.53 × 10^{-11} | 2.69  |
| 222484_s_at      | CXCL14                   | chemokine (C-X-C motif) ligand 14     | 2.55 × 10^{-14} | 8.48  | 201431_s_at | DPYSL3                | dihydropyrimidinase-like 3 | 1.07 × 10^{-11} | 2.61  |
| 218002_s_at      | CXCL14                   | chemokine (C-X-C motif) ligand 14     | 1.02 × 10^{-13} | 7.50  | 206254_at  | EGF                    | epidermal growth factor (beta-urogastrone) | 1.25 × 10^{-7} | 2.37  |
| 212977_at        | CXCR7                    | chemokine (C-X-C motif) receptor 7    | 2.78 × 10^{-13} | 17.10 | 1559072_a_at | ELFN2                  | extracellular leucine-rich repeat and fibronectin type III domain containing 2 | 2.43 × 10^{-8} | 2.17  |
Table 4. Cont.

| Secreted Factors | UP in Dermal Fibroblasts | UP in MSCs |
|------------------|-------------------------|------------|
| Probe Set ID     | Gene Symbol             | Gene Title             | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title             | adj-pval | FC |
| 232746_at        | CXCR7                   | Chemokine (C-X-C motif) receptor 7 | $4.11 \times 10^{-6}$ | 2.28 | 205767_at  | EREG        | epiregulin              | $1.96 \times 10^{-10}$ | 5.08 |
| 222996_s_at      | CXXC5                   | CXXC finger 5            | $1.25 \times 10^{-9}$ | 2.33 | 208378_x_at | FGF5        | fibroblast growth factor 5 | $2.27 \times 10^{-12}$ | 2.17 |
| 233955_x_at      | CXXC5                   | CXXC finger 5            | $2.25 \times 10^{-9}$ | 2.29 | 210310_s_at | FGF5        | fibroblast growth factor 5 | $5.16 \times 10^{-11}$ | 2.13 |
| 224516_s_at      | CXXC5                   | CXXC finger 5            | $1.17 \times 10^{-8}$ | 2.19 | 206614_at  | GDF5        | growth differentiation factor 5 | $1.17 \times 10^{-17}$ | 6.75 |
| 207169_x_at      | DDR1                    | discoidin domain receptor tyrosine kinase 1 | $2.84 \times 10^{-10}$ | 2.06 | 38037_at    | HBEGF       | heparin-binding EGF-like growth factor | $1.51 \times 10^{-9}$ | 3.17 |
| 204602_at        | DKK1                    | dickkopf homolog 1 (Xenopus laevis) | $9.91 \times 10^{-7}$ | 2.54 | 203821_at  | HBEGF       | heparin-binding EGF-like growth factor | $2.98 \times 10^{-9}$ | 3.15 |
| 202196_s_at      | DKK3                    | dickkopf homolog 3 (Xenopus laevis) | $8.90 \times 10^{-10}$ | 4.17 | 209960_at  | HGF         | hepatocyte growth factor (hepapoietin A; scatter factor) | $6.82 \times 10^{-10}$ | 8.20 |
| 221127_s_at      | DKK3                    | dickkopf homolog 3 (Xenopus laevis) | $2.77 \times 10^{-11}$ | 3.45 | 210997_at  | HGF         | hepatocyte growth factor (hepapoietin A; scatter factor) | $2.11 \times 10^{-6}$ | 4.34 |
| 214247_s_at      | DKK3                    | dickkopf homolog 3 (Xenopus laevis) | $1.33 \times 10^{-8}$ | 2.71 | 210998_s_at | HGF         | hepatocyte growth factor (hepapoietin A; scatter factor) | $1.82 \times 10^{-4}$ | 2.28 |
| 230508_at        | DKK3                    | dickkopf homolog 3 (Xenopus laevis) | $8.73 \times 10^{-5}$ | 2.07 | 206924_at  | IL11        | interleukin 11              | $6.19 \times 10^{-6}$ | 2.45 |
| 222802_at        | EDN1                    | endothelin 1              | $8.74 \times 10^{-7}$ | 4.31 | 210118_s_at | IL1A        | interleukin 1, alpha         | $4.81 \times 10^{-4}$ | 2.87 |
### Table 4. Cont.

| Secreted Factors | UP in Dermal Fibroblasts | UP in MSCs |
|------------------|--------------------------|------------|
| Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval | FC |
| 218995_s_at | EDN1 | endothelin 1 | 3.17 × 10⁻⁶ | 4.06 | 205067_at | IL1B | interleukin 1, beta | 1.25 × 10⁻⁵ | 5.09 |
| 227708_at | EEF1A1 | eukaryotic translation elongation factor 1 alpha 1 | 1.54 × 10⁻¹⁴ | 2.03 | 39402_at | IL1B | interleukin 1, beta | 4.60 × 10⁻⁵ | 4.09 |
| 201313_at | ENO2 | enolase 2 (gamma, neuronal) | 2.61 × 10⁻⁸ | 2.11 | 209821_at | IL33 | interleukin 33 | 5.24 × 10⁻⁵ | 2.71 |
| 210839_s_at | ENPP2 | ectonucleotide pyrophosphatase/phosphodiesterase 2 | 9.19 × 10⁻¹⁰ | 12.01 | 204863_s_at | IL6ST | interleukin 6 signal transducer (gp130, oncostatin M receptor) | 1.19 × 10⁻⁸ | 2.33 |
| 209392_at | ENPP2 | ectonucleotide pyrophosphatase/phosphodiesterase 2 | 2.29 × 10⁻¹⁰ | 10.40 | 211000_s_at | IL6ST | interleukin 6 signal transducer (gp130, oncostatin M receptor) | 3.36 × 10⁻⁸ | 2.17 |
| 205756_s_at | F8 | coagulation factor VIII, procoagulant component | 2.18 × 10⁻⁸ | 2.13 | 202859_x_at | IL8 | interleukin 8 | 4.66 × 10⁻⁸ | 8.46 |
| 226722_at | FAM20C | family with sequence similarity 20, member C | 3.87 × 10⁻⁷ | 2.58 | 211506_s_at | IL8 | interleukin 8 | 2.57 × 10⁻⁶ | 5.63 |
| 205110_s_at | FGF13 | fibroblast growth factor 13 | 7.54 × 10⁻⁹ | 3.02 | 204926_at | INHBA | inhibin, beta A | 1.82 × 10⁻¹⁴ | 4.83 |
| 204222_s_at | FGF2 | fibroblast growth factor 2 (basic) | 6.77 × 10⁻¹⁹ | 2.29 | 210511_s_at | INHBA | inhibin, beta A | 6.98 × 10⁻⁸ | 4.63 |
| Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC | Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC   |
|--------------|-------------|------------|------------|----|--------------|-------------|------------|------------|------|
| 205782_at    | FGF7        | fibroblast growth factor 7 (keratinocyte growth factor) | $1.37 \times 10^{-11}$ | 10.94 | 205266_at    | LIF         | leukemia inhibitory factor (cholinergic differentiation factor) | $4.28 \times 10^{-10}$ | 6.74 |
| 1554741_s_at | FGF7        | fibroblast growth factor 7 (keratinocyte growth factor) | $6.50 \times 10^{-11}$ | 7.49  | 205381_at    | LRRC17      | leucine rich repeat containing 17 | $5.79 \times 10^{-13}$ | 42.4 |
| 206404_at    | FGF9        | fibroblast growth factor 9 (glia-activating factor) | $1.50 \times 10^{-5}$  | 2.74  | 207703_at    | NLGN4Y      | neureolin 4, Y-linked | $6.00 \times 10^{-9}$  | 5.96 |
| 209093_s_at  | GBA         | glucosidase, beta; acid (includes glucosylceramidase) | $1.35 \times 10^{-18}$ | 2.01  | 229838_at    | NUCB2       | nucleobindin 2 | $4.07 \times 10^{-22}$ | 2.21 |
| 205498_at    | GHR         | growth hormone receptor | $5.70 \times 10^{-6}$  | 2.11  | 216867_s_at  | PDGFA       | platelet-derived growth factor alpha polypeptide | $4.78 \times 10^{-10}$ | 3.93 |
| 220794_at    | GREM2       | gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis) | $1.54 \times 10^{-29}$ | 52.50 | 205463_s_at  | PDGFA       | platelet-derived growth factor alpha polypeptide | $3.82 \times 10^{-10}$ | 3.83 |
| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval | FC  | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval | FC  |
|-------------|-------------|------------------------------------------------|----------|-----|-------------|-------------|------------------------------------------------|----------|-----|
| 240509_s_at| GREM2       | gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis) | 3.80 × 10^{-33} | 45.90 | 221898_at   | PDPN        | podoplanin                                      | 2.45 × 10^{-8} | 3.21 |
| 235504_at  | GREM2       | gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis) | 2.59 × 10^{-33} | 37.93 | 204879_at   | PDPN        | podoplanin                                      | 8.06 × 10^{-7} | 2.10 |
| 216041_x_at| GRN         | granulin                                       | 4.12 × 10^{-26} | 2.77 | 218454_at   | PLBD1       | phospholipase B domain containing 1             | 7.38 × 10^{-7} | 2.70 |
| 200678_x_at| GRN         | granulin                                       | 8.63 × 10^{-27} | 2.60 | 213449_at   | POP1        | processing of precursor 1, ribonuclease P/MPR subunit (S. cerevisiae) | 6.40 × 10^{-12} | 2.14 |
| 211284_s_at| GRN         | granulin                                       | 1.04 × 10^{-26} | 2.45 | 213421_x_at| PRSS3       | protease, serine, 3                             | 9.97 × 10^{-4} | 2.31 |
| 206326_at  | GRP         | gastrin-releasing peptide                      | 1.71 × 10^{-5}  | 2.37 | 207463_x_at| PRSS3       | protease, serine, 3                             | 2.59 × 10^{-3} | 2.17 |
| 204773_at  | IL11RA      | interleukin 11 receptor, alpha                 | 9.87 × 10^{-12} | 2.32 | 206631_at   | PTGER2      | prostaglandin E receptor 2 (subtype EP2), 53 kDa | 2.43 × 10^{-9} | 2.96 |
| 206295_at  | IL18        | interleukin 18 (interferon-gamma-inducing factor) | 6.66 × 10^{-3}  | 2.15 | 204897_at   | PTGER4      | prostaglandin E receptor 4 (subtype EP4)         | 1.62 × 10^{-5} | 4.35 |
| 202948_at  | IL1R1       | interleukin 1 receptor, type I                 | 2.88 × 10^{-10} | 2.33 | 227146_at   | QSOX2       | quiescin Q6 sulfhydryl oxidase 2                 | 1.21 × 10^{-23} | 2.14 |
| Probe Set ID | Gene Symbol | Gene Title                  | adj-pval | FC | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval | FC    |
|--------------|-------------|-----------------------------|----------|----|--------------|-------------|------------------------------------------------|----------|-------|
| 228575_at    | IL20RB      | interleukin 20 receptor beta | $3.21 \times 10^{-33}$ | 20.03 | 204916_at   | RAMP1       | receptor (G protein-coupled) activity modifying protein 1 | $5.83 \times 10^{-5}$ | 2.06 |
| 221658_s_at  | IL21R       | interleukin 21 receptor      | $5.81 \times 10^{-10}$ | 2.67 | 219140_s_at | RBP4        | retinol binding protein 4, plasma                                  | $1.87 \times 10^{-4}$ | 2.28 |
| 226333_at    | IL6R        | interleukin 6 receptor       | $1.33 \times 10^{-9}$  | 2.61 | 206805_at   | SEMA3A      | sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A | $1.29 \times 10^{-5}$ | 2.54 |
| 206693_at    | IL7         | interleukin 7                | $7.42 \times 10^{-8}$  | 2.00 | 244163_at   | SEMA3A      | sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A | $4.25 \times 10^{-7}$ | 2.02 |
| 226218_at    | IL7R        | interleukin 7 receptor       | $4.57 \times 10^{-14}$ | 12.12 | 230345_at   | SEMA7A      | semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group) | $5.22 \times 10^{-8}$ | 2.70 |
| 205798_at    | IL7R        | interleukin 7 receptor       | $5.98 \times 10^{-15}$ | 10.35 | 209723_at   | SERPINB9    | serpin peptidase inhibitor, clade B (ovalbumin), member 9                     | $1.23 \times 10^{-7}$ | 4.73 |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval   | FC | Probe Set ID | Gene Symbol | Gene Title                                      | adj-pval   | FC          |
|--------------|-------------|-------------------------------------------------|------------|----|--------------|-------------|-------------------------------------------------|------------|-------------|
| 205258_at    | INHBB       | inhibin, beta B                                 | 4.04 × 10⁻⁷ | 6.33 | 205576_at    | SERPIND1    | serpin peptidase inhibitor, clade D (heparin cofactor), member 1 | 1.39 × 10⁻⁶ | 2.04        |
| 20051_s_at   | KIT         | v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog | 1.65 × 10⁻¹³ | 6.91 | 213600_at    | SIPA1L3     | signal-induced proliferation-associated 1 like 3 | 4.01 × 10⁻²³ | 2.39        |
| 207092_at    | LEP         | leptin                                          | 4.09 × 10⁻⁵ | 2.83 | 37831_at     | SIPA1L3     | signal-induced proliferation-associated 1 like 3 | 3.40 × 10⁻²⁵ | 2.07        |
| 206684_at    | LY96        | lymphocyte antigen 96                           | 1.50 × 10⁻¹⁹ | 2.46 | 204466_s_at  | SNCA        | synuclein, alpha (non A4 component of amyloid precursor) | 8.83 × 10⁻⁶ | 3.50        |
| 232224_at    | MASP1       | mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor) | 4.44 × 10⁻⁷ | 5.65 | 201562_s_at  | SORD        | sorbitol dehydrogenase                           | 4.85 × 10⁻¹⁵ | 2.16        |
| 201621_at    | NBL1        | neuroblastoma, suppression of tumorigenicity 1 | 2.11 × 10⁻⁹ | 2.66 | 242408_at    | STYX        | serine/threonine/tyrosine interacting protein     | 3.00 × 10⁻⁸ | 2.02        |
| 37005_at     | NBL1        | neuroblastoma, suppression of tumorigenicity 1 | 1.16 × 10⁻⁸ | 2.33 | 209676_at    | TFPI        | tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) | 4.68 × 10⁻⁵ | 2.43        |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC    |
|--------------|-------------|------------|-----------|-----|--------------|-------------|------------|-----------|-------|
| 205893_at    | NLGN1       | neurophin 1| $7.98 \times 10^{-3}$ | 2.09| 213258_at    | TFPI        | tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) | $3.07 \times 10^{-5}$ | 2.34 |
| 231361_at    | NLGN1       | Neuroligin 1| $4.26 \times 10^{-3}$ | 2.02| 210664_s_at  | TFPI        | tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) | $1.32 \times 10^{-4}$ | 2.22 |
| 231798_at    | NOG         | noggin     | $2.87 \times 10^{-11}$ | 97.99| 235737_at    | TSLP        | thymic stromal lymphopoietin | $5.21 \times 10^{-14}$ | 6.10 |
| 206343_s_at  | NRG1        | neuregulin 1| $4.21 \times 10^{-4}$ | 2.02| 213425_at    | WNT5A       | wingless-type MMTV integration site family, member 5A | $1.06 \times 10^{-13}$ | 4.23 |
| 218625_at    | NRN1        | neuritin 1  | $3.68 \times 10^{-15}$ | 29.54| 205990_s_at  | WNT5A       | wingless-type MMTV integration site family, member 5A | $6.42 \times 10^{-14}$ | 3.76 |
| 200649_at    | NUCB1       | nucleobindin 1 | $7.18 \times 10^{-12}$ | 2.05| 238105_x_at  | WNT7B       | wingless-type MMTV integration site family, member 7B | $1.17 \times 10^{-11}$ | 2.58 |
| 213131_at    | OLFM1       | olfactomedin 1 | $5.16 \times 10^{-35}$ | 18.89|               |             |             |           |       |
| 205591_at    | OLFM1       | olfactomedin 1 | $0.00 \times 10^{+00}$ | 15.89|               |             |             |           |       |
| 214620_x_at  | PAM         | peptidylglycine alpha-amidating monoxygenase | $8.58 \times 10^{-23}$ | 2.25|               |             |             |           |       |
| 202336_s_at  | PAM         | peptidylglycine alpha-amidating monoxygenase | $1.74 \times 10^{-22}$ | 2.25|               |             |             |           |       |
| Probe Set ID | Gene Symbol | Gene Title                                    | adj-pval  | FC  | Probe Set ID | Gene Symbol | Gene Title                                    | adj-pval  | FC  |
|-------------|-------------|-----------------------------------------------|-----------|-----|-------------|-------------|-----------------------------------------------|-----------|-----|
| 212958_x_at | PAM         | peptidylglycine alpha-amidating monoxygenase   | 1.18 × 10^{-21} | 2.09 |             |             |                                               |           |     |
| 219304_s_at | PDGFD       | platelet derived growth factor D               | 1.83 × 10^{-15} | 9.33 |             |             |                                               |           |     |
| 209652_s_at | PGF         | placental growth factor                       | 1.69 × 10^{-6}  | 2.11 |             |             |                                               |           |     |
| 201578_at   | PODXL       | podocalyxin-like                              | 7.00 × 10^{-20}  | 20.38 |             |             |                                               |           |     |
| 207808_s_at | PROS1       | protein S (alpha)                             | 8.76 × 10^{-9}   | 3.01 |             |             |                                               |           |     |
| 200866_s_at | PSAP        | prosaposin                                    | 2.12 × 10^{-13}  | 2.29 |             |             |                                               |           |     |
| 208257_x_at | PSG1        | pregnancy specific beta-1-glycoprotein 1      | 7.51 × 10^{-7}   | 6.45 |             |             |                                               |           |     |
| 210195_s_at | PSG1        | pregnancy specific beta-1-glycoprotein 1      | 1.76 × 10^{-8}   | 3.21 |             |             |                                               |           |     |
| 210196_s_at | PSG1        | pregnancy specific beta-1-glycoprotein 1      | 3.24 × 10^{-5}   | 2.18 |             |             |                                               |           |     |
| 208134_x_at | PSG2        | pregnancy specific beta-1-glycoprotein 2      | 4.46 × 10^{-19}  | 5.98 |             |             |                                               |           |     |
| 211741_x_at | PSG3        | pregnancy specific beta-1-glycoprotein 3      | 3.72 × 10^{-27}  | 28.52 |             |             |                                               |           |     |
| 203399_x_at | PSG3        | pregnancy specific beta-1-glycoprotein 3      | 4.42 × 10^{-30}  | 25.95 |             |             |                                               |           |     |
| 215821_x_at | PSG3        | pregnancy specific beta-1-glycoprotein 3      | 1.34 × 10^{-22}  | 7.87 |             |             |                                               |           |     |
| 208191_x_at | PSG4        | pregnancy specific beta-1-glycoprotein 4      | 6.32 × 10^{-6}   | 8.81 |             |             |                                               |           |     |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC    | Probe Set ID | Gene Symbol | Gene Title | adj-pval  | FC    |
|--------------|-------------|------------|----------|-------|--------------|-------------|------------|----------|-------|
| 204830_x_at  | PSG5        | pregnancy specific beta-1-glycoprotein 5 | $9.42 \times 10^{-29}$ | 200.65 |
| 209738_x_at  | PSG6        | pregnancy specific beta-1-glycoprotein 6 | $4.68 \times 10^{-29}$ | 78.75  |
| 208106_x_at  | PSG6        | pregnancy specific beta-1-glycoprotein 6 | $2.35 \times 10^{-28}$ | 51.80  |
| 205602_x_at  | PSG7        | pregnancy specific beta-1-glycoprotein 7 | $1.27 \times 10^{-5}$  | 4.78   |
| 209594_x_at  | PSG9        | pregnancy specific beta-1-glycoprotein 9 | $1.83 \times 10^{-29}$ | 89.31  |
| 207733_x_at  | PSG9        | pregnancy specific beta-1-glycoprotein 9 | $5.66 \times 10^{-26}$ | 12.06  |
| 212187_x_at  | PTGDS       | prostaglandin D2 synthase 21 kDa (brain) | $1.76 \times 10^{-5}$  | 3.89   |
| 211748_x_at  | PTGDS       | prostaglandin D2 synthase 21 kDa (brain) | $6.16 \times 10^{-6}$  | 3.30   |
| 211663_x_at  | PTGDS       | prostaglandin D2 synthase 21 kDa (brain) | $7.37 \times 10^{-4}$  | 2.32   |
| 213933_at    | PTGER3      | prostaglandin E receptor 3 (subtype EP3) | $3.46 \times 10^{-7}$  | 3.51   |
| 1555097_a_at | PTGFR       | prostaglandin F receptor (FP) | $5.53 \times 10^{-8}$  | 2.27   |
Table 4. Cont.

| Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC  | Probe Set ID | Gene Symbol | Gene Title | adj-pval   | FC  |
|--------------|-------------|------------|------------|-----|--------------|-------------|------------|------------|-----|
| 207177_at    | PTGFR       | prostaglandin F receptor (FP) | 1.00 × 10^{-7} | 2.21 |              |             |            |            |     |
| 206187_at    | PTGIR       | prostaglandin I2 (prostacyclin) receptor (IP) | 1.11 × 10^{-13} | 2.31 |              |             |            |            |     |
| 208131_s_at  | PTGIS       | prostaglandin I2 (prostacyclin) synthase | 2.20 × 10^{-16} | 42.66 |              |             |            |            |     |
| 211892_s_at  | PTGIS       | prostaglandin I2 (prostacyclin) synthase | 2.07 × 10^{-8} | 3.10 |              |             |            |            |     |
| 210702_s_at  | PTGIS       | prostaglandin I2 (prostacyclin) synthase | 7.89 × 10^{-9} | 2.99 |              |             |            |            |     |
| 211756_at    | PTHLH       | parathyroid hormone-like hormone | 8.63 × 10^{-3} | 2.07 |              |             |            |            |     |
| 215253_s_at  | RCAN1       | regulator of calcineurin 1 | 1.52 × 10^{-6} | 2.47 |              |             |            |            |     |
| 203498_at    | RCAN2       | regulator of calcineurin 2 | 1.23 × 10^{-39} | 49.77 |              |             |            |            |     |
| 226272_at    | RCAN3       | RCAN family member 3 | 1.16 × 10^{-12} | 2.59 |              |             |            |            |     |
| 213716_s_at  | SECTM1      | secreted and transmembrane 1 | 1.48 × 10^{-4} | 2.14 |              |             |            |            |     |
Table 4. Cont.

| Secreted Factors | UP in Dermal Fibroblasts | UP in MSCs |
|------------------|--------------------------|------------|
| **Probe Set ID** | **Gene Symbol** | **Gene Title** | **adj-pval** | **FC** | **Probe Set ID** | **Gene Symbol** | **Gene Title** | **adj-pval** | **FC** |
| 226492_at | SEMA6D | sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D | $1.30 \times 10^{-4}$ | 2.71 |
| 200986_at | SERPING1 | serpin peptidase inhibitor, clade G (C1 inhibitor), member 1 | $2.81 \times 10^{-20}$ | 13.38 |
| 204596_s_at | STC1 | stanniocalcin 1 | $1.03 \times 10^{-4}$ | 2.89 |
| 204595_s_at | STC1 | stanniocalcin 1 | $3.40 \times 10^{-5}$ | 2.12 |
| 203438_at | STC2 | stanniocalcin 2 | $1.40 \times 10^{-6}$ | 2.84 |
| 203439_s_at | STC2 | stanniocalcin 2 | $9.48 \times 10^{-5}$ | 2.27 |
| 212344_at | SULF1 | sulfatase 1 | $4.55 \times 10^{-12}$ | 9.94 |
| 212353_at | SULF1 | sulfatase 1 | $5.41 \times 10^{-10}$ | 8.59 |
| 212354_at | SULF1 | sulfatase 1 | $6.12 \times 10^{-11}$ | 8.19 |
| 224724_at | SULF2 | sulfatase 2 | $2.31 \times 10^{-10}$ | 3.82 |
| 207426_s_at | TNFSF4 | tumor necrosis factor (ligand) superfamily, member 4 | $1.47 \times 10^{-2}$ | 2.59 |
| 206907_at | TNFSF9 | tumor necrosis factor (ligand) superfamily, member 9 | $2.10 \times 10^{-16}$ | 4.73 |
| 219478_at | WFDC1 | WAP four-disulfide core domain 1 | $2.78 \times 10^{-15}$ | 35.49 |
| 205792_at | WISP2 | WNT1 inducible signaling pathway protein 2 | $3.53 \times 10^{-4}$ | 2.90 |
3.6. Differentiation Capacity is Reduced in F-DHJ from Aged Skin

Finally, the capacity for differentiation into the adipocyte, osteoblast, and chondrocyte lineages was compared in F-DHJ samples from “young” (between 20 and 31 years, n = five donors) and “older” (between 55 and 65 years, n = four donors) ages (Figure 8). The three-lineage mesenchymal differentiation potential of F-DHJ described in Figure 3 appeared altered in cell samples from older skin biopsies (Figure 8A–D). Although chondrocyte differentiation was maintained (Figure 8A–D), the capacity for differentiation into osteoblasts was reduced (Figure 8B,D) and differentiation into the adipocyte lineage was almost lost (Figure 8C,D). A comparative analysis of the differentiation potential of Fp, Fr, and F-DHJ from old donors indicated functional differences (data not shown). The capacity for differentiation into adipocytes persisted with a low efficiency in old Fp and Fr, although it was lost with age in F-DHJ. In contrast, differentiation into osteoblasts was not obtained with old Fp or Fr, whereas this capacity was present in old F-DHJ. Finally, we observed that the capacity for differentiation into chondrocytes was increased with age in the three cell types but remained more efficient in F-DHJ, as compared with Fp and Fr cells. In addition to these age-related changes in the F-DHJ differentiation potential, the extracellular deposition of ColXIα1 and ACAN were respectively 3.6-fold and 2.5-fold higher in skin biopsies from the older than in the young donor group (p < 0.05) (Figure 8E,F). These observations pinpoint the interest of considering F-DHJ cells in future studies on skin ageing.
Figure 8. Different characteristics of DHJ components in skin from “young” and “old” donors. The “young” group comprised 5 donors (20, 22, 25, 28, and 31 years old) (same donors as in Figure 3), and the “old” group comprised 4 donors (55, 61, 65, and 65 years old). (A–C) Capacity of “young” and “old” F-DHJ cells to differentiate in vitro into three mesenchymal lineages: (A) chondrocytes (toluidine blue and safranin O staining, aggrecan (ACAN) and collagen XIα1 (ColXIα1) expression); (B) adipocytes (presence of cytoplasmic lipid droplets, black arrows); and (C) osteoblasts (alizarin-red staining). For panels (A–C), representative photographs are shown. (D) Summary of the differentiation capacity into chondrocytes, adipocytes, and osteoblasts of F-DHJ from “young” and “old” skin. Scoring (-) = not present, (+) = low representation, (++) = frequent representation, and (+++) = major representation. (E,F) Immunofluorescence detection of ColXIα1 (E) and ACAN (F) in skin biopsies from “young” and “old” donors.
of differentiation capabilities are presented: (−) = not present, (+) = low representation, (++) = frequent representation, and (+++) = major representation. (E,F) Immunofluorescence detection of ColXla1 (E) and ACAN (F) in skin biopsies from “young” and “old” donors. Representative photographs are shown, in association with quantification values corresponding to a total of 12 (E) and 15 (F) regions of interest (ROI) for the 3 analyzed “young” donors (20, 22, and 28 years old) and a total of 14 (E) and 15 (F) ROI for the 3 analyzed “old” donors (57, 61, and 65 years old). Means ± SEM are indicated (* p < 0.05, Wilcoxon test).

4. Discussion

The present work investigates the properties of a fibroblast compartment localized within the conjunctival junctions that connects the dermis to the hypodermis, i.e., dermo-hypodermal junction fibroblasts (F-DHJ), which were compared to intermediate reticular dermis (Fr) and superficial papillary dermis (Fp) fibroblasts. Cellular functional assays, combined with transcriptome profiling, indicated that F-DHJ had distinct characteristics from those of Fp and Fr cells. F-DHJ had the lowest proliferation and clonogenic capacity of the three fibroblast populations in bidimensional culture conditions. Moreover, when integrated within the dermal component of an in vitro three-dimensional reconstructed skin model, F-DHJ showed a low capacity for collagen lattice contractions and had a poor capacity for promoting epidermis organogenesis by keratinocytes. Inefficient dialog with keratinocytes observed here in vitro is in agreement with F-DHJ natural deep localizations, which are not in proximity with the epidermis, unlike the superficial Fp population. The lattice contraction assay provided the opportunity to assess the contractile capacity of specific cell types in a three-dimensional matrix environment. The contraction of the lattice is proportional to the force exerted by the cells in the matrix. Parameters that impact lattice contractions include characteristics of cell matrix anchoring structures, cytoskeleton organization, and the capacity of cells to coordinate and exert unidirectional forces. These parameters are governed by components of the “tissue skeleton” network [8,9] and may participate in vivo to confer specific biophysical characteristics to the different dermal tissue compartments. Extrapolation of the in vitro observations to the specific in vivo functions of Fp, Fr, and F-DHJ will require further studies, considering the high matrix complexity of the dermis.

We observed that F-DHJ exhibited an efficient capacity for three-lineage mesenchymal differentiation (i.e., adipocyte, osteoblast, and chondrocyte lineages), which could be interpreted as an MSC-like cellular identity, considering their anatomical proximity with the hypodermis, a tissue that contains adipose MSCs. Interestingly, the hierarchical clustering built on the basis of the transcriptome profiles of the three skin fibroblast populations (Fp, Fr, and F-DHJ) and five MSC origins (bone marrow, adipose, amnion, chorion, and cord) indicated a clear “fibroblast” molecular identity of F-DHJ, which did not segregate together with the MSC group.

The molecular signature that identified F-DHJ cells comprised transcripts involved in the stabilization of monomeric proteoglycan aggregates associated with hyaluronic acid molecules, such as HAPLN1 and HAPLN3 [27], which were found overexpressed in F-DHJ in comparison with all MSC types. Transcripts overexpressed in F-DHJ also included ACAN, which is involved in conferring tissue biomechanical resistance [28]. In addition, the overexpressed F-DHJ signature also comprised transcripts related to the collagen meshwork, such as FMOD and TNX, which are involved in collagen processing [29]; transcripts related to collagen fibril anchorage points, such as POSTN and FNDCT [26]; and transcripts related to the elastic network, such as ELN; DCN; MFAP4 and 5; FBN2; and FBLN1, 2, and 5 [30]. On the contrary, the comparison of F-DHJ and Fr molecular profiles identified a signature of transcripts underexpressed in the F-DHJ population, which could be interpreted in accordance with the reduced ECM mesh structuration within the DHJ area, in comparison with the reticular dermis. Notably, this character was documented by lower levels of the TNC transcript in F-DHJ than in Fr cells, which is associated with a lower accumulation of the TNC protein and loss of the TNC network in the DHJ area. Thus, the molecular specificities that distinguish F-DHJ and Fr cells may contribute to the different ECM characteristics of the reticular dermis and DHJ areas.
The existence of a fibroblast population exhibiting adipocyte-like molecular characteristics within the deep reticular dermis has been reported both in mouse [31,32] and human skin [33,34]. In human skin, the capacity for adipocyte differentiation was reported to be low for FAP+/CD90− papillary fibroblasts, intermediate for FAP+/CD90+ fibroblasts from the superior reticular dermis, and high for FAP+/CD90+ deep reticular dermis fibroblasts [33]. This gradation is consistent with the data shown in the present study, showing a correlation between the capacity for adipocyte differentiation and the depth of fibroblast dermal localization. The study by Korosec et al., which used cells from skin donors of ages ranging between 26 and 61 years, did not report an age-related reduction of the adipocyte differentiation capacity [33], as documented here for F-DHJ cells, although this phenomenon has been previously described for dermal fibroblast cells [35]. In the present study, “F-DHJ” is used to name the fibroblast population that we isolated according to its junctional localization between the deep reticular dermis and the hypodermis. This terminology distinguishes the deepest dermal part from the reticular dermis compartment, which is in agreement with their particular molecular and functional characteristics that may be critical for modeling their local ECM environment.

Interestingly, data were obtained pointing to age-related changes in the DHJ region characteristics, such as augmented levels of the ECM proteins ColXIα1 and ACAN and a reduced adipocyte differentiation potential of F-DHJ in old skin. Data from the literature concerning the evolution of the dermal fibroblast capacity for differentiation into adipocytes can appear contradictory, with regard to our observation of a decreased adipogenic potential. Indeed, a study performed on mice has, on the contrary, reported the acquisition of proadipogenic traits in dermal fibroblasts from aged animals [32], in which the difference may result from physiological species-related specificities. In a recent study, a single-cell RNA-sequencing analysis of 15,000 dermal fibroblasts isolated from human skin samples from young and old donors did not detect an up-modulation of adipogenic genes associated with ageing [36]. Of note, in humans, subcutaneous fat tissue masses tend to reduce with ageing, in particular in the face (for review, see [37]).

As we performed here using collagen lattices as a dermal matrix model, human fibroblasts isolated from the deep dermis were used to populate acellular dead desepidermized dermis (DED) pieces and analyzed for their capacity to support epidermis reconstruction by keratinocytes [34]. The two studies converged to show that fibroblasts from the deep dermis do not promote the formation of a correctly differentiated multilayered epithelium, which is consistent with their distant skin localization. Interestingly, deep dermis fibroblasts spontaneously populated the deepest part of the DED [34], in which homing may be due to the recognition of specific ECM characteristics.

Fibroblast-ECM interrelations are crucial for the maintenance of dermal integrity. In a mouse model, dermal fibroblasts were studied by intravital time-lapse, which revealed active membrane dynamics characterized by protrusions that rapidly grow and shrink from a more stable cell body [38]. By this process, fibroblasts may dialog with their cellular and ECM neighbors, and thus, adapt their behaviors and fate. Accordingly, the development of membrane extensions in living cells has been proposed to compensate for the appearance of cell-free volumes due to fibroblast deaths in the dermis of aged skin [38]. These observations may be explored at a molecular level considering genes related to the network termed as “tissue skeleton” that connects the cells with their tissue environment (comprising the nucleoskeleton, the cytoskeleton, linker complexes, ECM components, and focal adhesion points), in which their expressions differ in fibroblasts according to their dermal localization and evolve with ageing (present study and [8,9]. Disruption of this multiparametric network of interactions may result in changes that affect aged dermis, including the loss of contact surfaces between fibroblasts and their surrounding ECM [39] and modification of the deposition of ECM components, such as ColXIα1 and ACAN, as shown here.
5. Patent

V.H. and D.A. are the inventors on the filed patent application numbered 1759023 (28th September 2017) entitled “Molecular signatures of aging of 3 subpopulations of dermal fibroblasts (papillary, reticular, dermo-hypodermic junction) and dermal equivalents comprising aged fibroblasts”.

V.H is the inventor on the filed patent application numbered 1855987 (June 29th 2018) entitled “Modèle de peau comprenant des fibroblastes de la jonction dermo-hypodermique pour l’identification d’actif pro-différenciant vers des lignages adipocytaire, chondroblastique et ostéoblastique”.

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