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(54) **Title**: METHOD AND KIT FOR THE CLASSIFICATION AND PROGNOSIS OF WOUNDS

(57) **Abstract**: Method and Kit for the classification and prognosis of wounds The invention relates to methods of diagnosis or prognosis of a nonhealing or chronic wound tissue or a wound tissue developing an abnormal scar, such as a fibrosis, a hyperthrophic scar or a keloid, comprising the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein different genes or miRNA markers are studied.

Method and Kit for the classification and prognosis of wounds

Field of the invention

The present invention relates to a method and kit for the classification and prognosis of wounds of mammalian, in particular in human. The method defines a molecular signature that enables one to characterize a pathological wound healing such as chronic or non-healing wound or abnormal scar, such as fibrosis (hypertrophic scars or keloids).

Background of the invention

The natural wound healing is divided into three sequential phases; each phase is characterized by specific cellular activities: the inflammatory phase, the proliferative phase and the remodeling phase.

The first phase, called the inflammatory phase, begins minutes after injury. The blood vessels rupture induces the clot formation, composed mainly of fibrin and fibronectin. The clot fills partially the lesion and allows the migration of the inflammatory cells within the lesion. The inflammatory cells are recruited to debride the wound. Platelets secrete factors, such as growth factors or cytokines, which induce the recruitment of cells implicated in the wound healing (inflammatory cells such as neutrophils and macrophages, fibroblasts and endothelial cells).

The second phase is called the proliferative phase and corresponds to the development of the granulation tissue. Fibroblasts migrate into the wound area, proliferate and form a new provisional extracellular matrix by secreting extracellular matrix (ECM) proteins. Then endothelial cells migrate to promote the neovascularization or angiogenesis of the lesion. Inside the granulation tissue, fibroblasts activate and differentiate into myofibroblasts, presenting contractile properties thanks to their expression of alpha-smooth muscle actin (similar to that in smooth muscle cells). Myofibroblasts have a key role in wound healing as they provide the contraction of the wound. Finally, keratinocytes migrate from the wound edge, proliferate and differentiate to reconstitute the epidermis.

The last phase of the wound healing process appears after the wound closure. It corresponds to the remodeling of the granulation tissue. The granulation tissue is reorganized, type III collagen is replaced by type I collagen, as normal dermis is principally composed of type I collagen. During this phase, myofibroblasts in excess are eliminated by apoptosis. The last phase of the wound healing is long. One year after injury, the scar is remodeled; it gets less red and thinner.

However, this process is not only complex but fragile; it is susceptible to interruption or failure leading to the formation of chronic or non-healing wounds or formation of abnormal scars. Factors which may contribute to this include diseases (such as diabetes, venous or arterial disease), age, infection or tissue localization.

Chronic or non-healing wounds

Chronic wounds are a worldwide health problem, in part due to a lack of adequate methods of treatment. In 2010, more than 7 million people worldwide suffered from chronic wounds, and the projected annual increase is at least 10 percent.

Chronic wounds are sometimes non-healing wounds. Common types of chronic wounds include, but are not limited to, venous leg ulcers, diabetic foot ulcers, decubitus ulcers, arterial leg ulcers, those of mixed etiology (venous and arterial) or those with no known etiology. We can also find acute wounds that become chronic as they do not heal correctly.

Non-healing wounds or chronic wounds are a challenge for the patient, the health care professional, and the health care system. They significantly impair the quality of life for millions of people and impart burden on society in terms of lost productivity and health care money.

Wound healing is a dynamic pathway that leads to the restoration of tissue integrity and functions. A chronic wound or non-healing wound develops when the normal reparative process is disturbed. By understanding the biology of wound healing, the physician can optimize the wound healing by choosing the adequate treatment.

In chronic or non-healing wounds, the natural healing process is altered, and thus healing is prolonged, incomplete and sometimes wounds never close. A chronic wound occurs when some factor causes the disruption of the normal inflammatory and proliferative phases. Thus, there is a need for a reliable method for diagnosing a non-healing or chronic wound in order to adapt the best treatment to provide the wound closure and healing. There is also a need for a better care of the wound and for the reduction of the deadline of said care.

Fibrosis, hypertrophic scars and keloids

Hypertrophic, keloid or fibrous scars result from abnormal wound healing. These scars are characterized by an excessive deposit of ECM proteins, especially collagen. In these abnormal wounds, granulation tissue is hyper proliferative, due to an excess of myofibroblasts (Armour A, Scott PG, Tredget EE. Wound Repair Regen. 2007 Sep-Oct;15 Suppl 1:S6-17. Review. Erratum in: Wound Repair Regen. 2008 Jul-Aug;16(4):582).

In normal wound healing, fibroblasts get activated, and then differentiate into myofibroblasts presenting contractile properties thanks to their expression of alpha-smooth muscle actin (αSMA). Myofibroblasts are responsible for the deposit of extra cellular matrix and for the wound closure by moving closer the wound edges. In hypertrophic scar, keloid or fibrous wound healing, the activity of myofibroblasts persists and leads to tissue deformation, which is particularly evident, for example, in hypertrophic scars developed after burn injury.

Hypertrophic and keloid scars are characterized by deposit of excessive amounts of collagen leading to a raised scar (more intense in keloids than in hypertrophic scars). They are formed most often at the sites of pimples, body piercings, cuts and burns.

Some hypertrophic scars are non-functional scars as they limit the function of the skin where they developed. They generate a loss of mobility of the scar zone and the neighboring zones, which can completely limit the movements (for example, elbow and mobility of the arm). They are mostly the result of burns of specific anatomical zones.

In some pathological diseases or specific anatomic localizations, early diagnosis of the potential onset of a wound may help to prevent the development of a wound. In the situation where a wound has already developed, knowledge of the diagnosis or prognosis of a wound may enable patients to receive maximum benefit from therapy. Thus, the treatment of the wound is especially adapted to the wound in its early stage if it presents a risk of developing an abnormal scar or failing to heal correctly.

It would be beneficial to know which patients are susceptible to develop chronic or non-healing wounds and furthermore, if a chronic wound does develop, how likely the patient is to respond to a specific therapy. Thus a critical objective is to identify a diagnostic or prognostic method for chronic or non-healing wounds, so as to provide earlier and improved choices of treatment.

Although some common clinical/pathological factors may assist in pre-judging if a wound may be "healing" or "non-healing", or if an acute wound may become chronic, there is no specific laboratory test(s) to distinguish among wound types. Woundcheck status® commercialized by Systagenix enables one to measure proteases activity but is not specific enough to distinguish between the chronic wounds that could heal quicker and better than other chronic wounds that could not heal.

For example, present techniques, such as wound clinical observation, fail to predict chronic or non-healing wound development and are insufficient to categorize patients with the healing outcome of the wound. If patients at risk of developing a chronic or non-healing wound could be identified, suitable preventive measures or treatments could be used in a targeted program of potentially great effectiveness.

For fibrosis, hypertrophic scars or keloids, there are no techniques available for the prediction of these skin disorders. It is known that some phototypes or tissue localization, such as joints, are more likely to develop keloids or hypertrophic scars, but no reliable prognosis or diagnosis method is known.

WO 2011/033249 discloses a method and kit for the classification and prognosis of wounds based on molecular markers or genes.

However, there remains a need in the art for a method for the early diagnosis or prognosis of wound fate. In particular, there is a need for a sensitive and reliable method of diagnosing or prognosing of chronic or non-healing wounds such as, but not limited to, venous leg ulcers, diabetic foot ulcers, decubitus ulcers, and arterial leg ulcers, non-healing acute wounds, or the development of fibrosis, hypertrophic scars or keloids.

It is therefore an object of the present invention to provide a method of diagnosis or prognosis of the outcome of the wound.

In a first aspect of the invention, a method of diagnosis or prognosis of a non-healing or chronic wound tissue is provided, said method comprising the step of determining the levels of expression of genes encoding different molecular markers in the wound from a mammalian, wherein said genes are defined as follows:

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, ADAMTS7, CFB, COMP, ECM2, EDIL3, EFHD1, FOLR1, ITGA11, KIT, LBH, LGR5, MFAP5, NR4A3, OMD, PALM, PHACTR3, PI16, PPARG, PTH1R, PTX3, RCAN2, RSPO1, SPON2, TAGLN, TMEM37, TMSB4Y, TXNIP and WFDC1,

- or at least the following miRNA show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

AC084368.1,

- or at least one of the following genes shows a normal expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CNN1 and KRT16,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

AMIGO2, CCL11, CDC45L, CSF2, CSF3, FOXS1, GOS2, IF44L, INHBA, KPRP, LCP1, LPAR3, MICAL2, MT1F, MT1M, POLQ, POU2F2, RRM2, SERPINA9, SOX9, STC1, TFIP2 and UCN2,

- or at least one of the following miRNA show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

MIR147B and MIR1181.

In a preferred embodiment of the invention, the method of diagnosis or prognosis of a non-healing or chronic wound tissue also comprises the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein said genes are defined as follows:

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, ADAMTS7, COMP, ECM2, EDIL3, EFHD1, FOLR1, ITGA11, LBH, LGR5, MFAP5, OMD, PALM, PHACTR3, PI16, PTH1R, RSPO1, SPON2, TAGLN, TMEM37, TMSB4Y, TXNIP and WFDC1,

- or at least the following miRNA show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

AC084368.1,

- or at least one of the following genes shows a normal expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CNN1 and KRT16,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CCL11, CDC45L, CSF2, CSF3, GOS2, IF44L, KPRP, LCP1, LPAR3, MT1F, MT1M, POLQ, RRM2, SERPINA9, STC1 and TFIP2,

- or at least one of the following miRNA show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

MIR147B and MIR1181.

In a specific embodiment of the invention, the method of diagnosis or prognosis of a non-healing or chronic wound tissue furthermore comprises another step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein said genes are defined as follows:

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTA2, APOD, FGF9, ID4, POSTN and SMAD3,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CXCL1, CXCL5, CXCL6, MMP10, MMP3, SERPINB2, SPHK1, HALPN1 and CTGF.

In another specific embodiment of the invention, the method of diagnosis or prognosis of a non-healing or chronic wound tissue furthermore comprises another step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein said genes are defined as follows:

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTA2, FGF9, ID4 and POSTN,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CXCL1, CXCL5, CXCL6, MMP10, MMP3 and SERPINB2.

By "chronic wound" or "chronic wound tissue" or "non-healing wound", it is meant, for example, a disorder chosen from venous leg ulcers, diabetic foot ulcers, decubitus ulcers and arterial leg ulcers or non-healing acute wounds or non-healing wounds.

In a second aspect of the invention, a method of diagnosis or prognosis of a wound tissue developing an abnormal scar, such as a fibrosis, a hypertrophic scar or a keloid is provided, said method comprising the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein said genes are defined as follows:

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

APOD, CFB, CXCL1, KIT, NR4A3, PPARG, PTX3, RCAN2, STC1 and TFPI2,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, AMIGO2, CNN1, COMP, CTGF, EDIL3, EFHD1, FOXS1, HAPLN1, INHBA, ITGA11, KRT16, MICAL2, PI16, POSTN, POU2F2, SOX9, SPHK1, TAGLN and UCN2.

In a preferred embodiment of the invention, a method of diagnosis or prognosis of a wound tissue developing an abnormal scar, such as a fibrosis, a hypertrophic scar or a keloid is provided, said method comprising the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein said genes are defined as follows:

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CXCL1, STC1 and TFPI2,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, CNN1, COMP, EDIL3, EFHD1, ITGA11, KRT16, PI16, POSTN and TAGLN.

The full identity of the genes according to the invention is available on the NCBI database (http://www.ncbi.nlm.nih.gov/), or is well known to those skilled in the art.

In a preferred aspect of the invention, the wound tissue is a human tissue, and the normal dermal fibroblasts are Normal Human Dermal Fibroblasts (NHDF).

In a preferred aspect of the invention, the normal dermal fibroblasts arise from the healthy skin of the said mammalian, and preferably the normal dermal fibroblasts arise from the healthy skin of the same animal or individual.

The term "determining the levels of expression of genes" as used above means qualitative and/or quantitative detection (measuring levels) with reference to a control. Typically the determination of the levels of expression of genes may be measured for example by RT-PCR performed on the sample or in situ hybridization or high-throughput sequencing, such as Lynx Therapeutics' Massively Parallel Signature Sequencing (MPSS), Polony sequencing, 454 pyrosequencing, Illumina (Solexa) sequencing, SOLiD sequencing, Ion semiconductor sequencing, DNA nanoball sequencing, Helioscope® single molecule sequencing, Single Molecule real time (RNAP), Single Molecule SMRT® sequencing, Nanopore DNA sequencing, VisiGen Biotechnologies approach.

Typically, said determination comprises contacting the sample with selective reagents such as probes, primers or ligands, and thereby detecting the presence, or measuring the amount of nucleic acids of interest originally present in the sample. Contacting may be performed in any suitable device, such as a plate, microtiter dish, test tube, well, glass or column. In specific embodiments, the contacting is performed on a substrate coated with the reagent, such as a nucleic acid array or a specific ligand array. The substrate may be a solid or semi-solid substrate such as any suitable support comprising glass, plastic, nylon, paper, metal, polymers and the like. The substrate may be of various forms and sizes, such as a slide, a membrane, a bead, a column or a gel. The contacting may be made under any condition suitable for a detectable complex, such as a nucleic acid hybrid, to be formed between the reagent and the nucleic acids of the sample.

In a particular embodiment, the determination of the levels of expression of genes may be determined by quantifying the RNA of said genes. Said RNA are preferably chosen from mRNA and miRNA. Preferably, said RNA are mRNA.

Methods for measuring the quantity of mRNA are well known in the art. For example the nucleic acid contained in the samples (e.g., cell or tissue prepared from the patient) is first extracted according to standard methods, for example using lytic enzymes or chemical solutions or extracted by nucleic-acid-binding resins following the manufacturer's instructions. The extracted mRNA may be then detected by hybridization (e. g., Northern blot analysis).

Alternatively, the extracted mRNA may be subjected to coupled reverse transcription and amplification, such as reverse transcription and amplification by polymerase chain reaction (RT-PCR), using specific oligonucleotide primers that enable amplification of a region in the target gene. Preferably quantitative or semi-quantitative RT-PCR is used. Real-time quantitative or semi-quantitative RT-PCR is particularly advantageous. Extracted mRNA may be reverse-transcripted and amplified, after which amplified sequences may be detected by hybridization with a suitable probe or by direct sequencing, or high-throughput sequencing or any other appropriate method known in the art.

Other methods of amplification include ligase chain reaction (LCR), transcription-mediated amplification (TMA), strand displacement amplification (SDA) and nucleic acid sequence based amplification (NASBA).

Nucleic acids having at least 10 nucleotides and exhibiting sequence complementarity or homology to the RNA of interest herein find utility as hybridization probes or amplification primers. It is understood that such nucleic acids need not be identical, but are typically at least about 80% identical to the homologous region of comparable size, more preferably at least 85% identical and even more preferably at least 90%, preferably at least 95% identical. In certain embodiments, it will be advantageous to use nucleic acids in combination with appropriate means, such as a detectable label, for detecting hybridization. A wide variety of appropriate indicators are known in the art including, fluorescent, radioactive, enzymatic or other ligands (e. g. avidin/biotin).

Probes typically comprise single-stranded nucleic acids of between 10 to 1000 nucleotides in length, for instance of between 10 and 800, more preferably of

between 15 and 700, typically of between 20 and 500. Primers typically are shorter single-stranded nucleic acids, of between 10 to 25 nucleotides in length, designed to perfectly or almost perfectly match a nucleic acid of interest, to be amplified. The probes and primers are "specific" to the nucleic acids they hybridize to, i.e. they preferably hybridize under high stringency hybridization conditions (corresponding to the highest melting temperature Tm, e.g., 50 % formamide, 3x, 5x or 6x SCC. SCC is a 0.15 M NaCl, 0.015 M Na-citrate).

In the method of the invention, the presence of RNA, preferably total RNA, and more preferably the amount of mRNA, is assayed in the examined samples of wound tissue. All the techniques available for measuring RNA content can be used. Said techniques may include Northern blot, quantitative polymerase chain reaction, NanoString Technologies, microarray technology, or Serial Analysis of Gene expression (SAGE). In the present invention, high-throughput sequencing, such as Lynx Therapeutics' Massively Parallel Signature Sequencing (MPSS), Polony sequencing, 454 pyrosequencing, Illumina (Solexa) sequencing, SOLiD sequencing, Ion semiconductor sequencing, DNA nanoball sequencing, Helioscope® single molecule sequencing, Single Molecule real time (RNAP), Single Molecule SMRT® sequencing, Nanopore DNA sequencing, VisiGen Biotechnologies approach can also be used.

In an alternative embodiment of the invention, the determination of the levels of expression of genes in the sample may also be performed by quantifying the corresponding encoded proteins, except for the miRNA expression. All the techniques available for measuring protein content can be used. This may be made by using antibodies.

Such methods comprise contacting a sample with a binding partner capable of selectively interacting with the target protein present in the sample. The binding partner is generally an antibody that may be polyclonal or monoclonal, preferably monoclonal.

The presence of the protein can be detected using standard electrophoretic and immunodiagnostic techniques, including immunoassays such as competition, direct reaction, or sandwich type assays. Such assays include, but are not limited to, Western blots; agglutination tests; enzyme-labeled and mediated immunoassays, such as ELISAs; biotin/avidin type assays; radioimmunoassays; immunoelectrophoresis; immunoprecipitation, etc. The reactions generally include revealing labels such as fluorescent, chemiluminescent, radioactive, enzymatic labels or dye molecules, or other methods for detecting the formation of a complex between the antigen and the antibody or antibodies reacted therewith.

The aforementioned assays generally involve separation of unbound protein in a liquid phase from a solid phase support to which antigen-antibody complexes are bound. Solid supports which can be used in the practice of the invention include substrates such as nitrocellulose (e. g., in membrane or microtiter well form); polyvinylchloride (e. g., sheets or microtiter wells); polystyrene latex (e.g., beads or microtiter plates); polyvinylidine fluoride; diazotized paper; nylon membranes; activated beads, magnetically responsive beads, and the like.

More particularly, an ELISA method can be used, wherein the wells of a microtiter plate are coated with a set of antibodies against the proteins to be tested. A sample containing or suspected of containing the marker protein is then added to the coated wells. After a period of incubation sufficient to allow the formation of antibody-antigen complexes, the plate(s) can be washed to remove unbound moieties and a detectably labelled secondary binding molecule is added. The secondary binding molecule is allowed to react with any captured sample marker protein, the plate is washed and the presence of the secondary binding molecule is detected using methods well known in the art.

In an another aspect of the invention, there is provided a kit for performing any one or more of the aforementioned methods, wherein said kit comprises probes to detect and quantify the expression level of at least one target gene.

By "probes", it is meant single-stranded nucleic acids of between 10 to 1000 nucleotides in length, for instance of between 10 and 800, more preferably of

between 15 and 700, typically of between 20 and 500, which hybridize with the target gene under high stringency hybridization conditions (corresponding to the highest melting temperature Tm, e.g., 50 % formamide, 3x, 5x or 6x SCC. SCC is a 0.15 M NaCl, 0.015 M Na-citrate).

According to a further aspect of the invention, there is provided a kit for performing any one of the aforementioned methods wherein said kit comprises:

(1) A plurality of probes for detecting and quantifying the expression level of all the genes specified in table 1,
(2) Optionally, reagents and instructions pertaining to the use of said probes.

In yet a further preferred aspect of the invention there is provided a kit for determining the prognosis of mammalian wound tissue which comprises:

(1) A plurality of probes for detecting and quantifying the expression level of at least one RNA or protein of each one of the genes of table 1,
(2) Optionally, reagents and instructions pertaining to the use of said probes.

Ideally, the instructions describe how to determine the expression level of each of said genes.

According to a further aspect of the invention there is provided a microarray comprising or consisting of any one or more of the aforementioned sets of probes. The kit according to the invention may use an apparatus such as the Ion Proton Sequencer of Life Technologies.

In another aspect of the invention, there is provided a kit for determining wound type in a patient, said kit comprising at least two microarrays, each comprising a plurality of probes for detecting and quantifying the expression level of all the genes specified in one of the above methods.

In a further aspect of the invention, there is provided a method for treating a wound which comprises the step of performing any one or more of the aforementioned methods for determining the classification or prognosis of wound tissue in order to identify whether said wound tissue is chronic or non-healing or said wound tissue will

develop a fibrosis or become a hypertrophic scar or a keloid or not and selecting an appropriate treatment based on the classification or prognosis of the wound tissue.

In another aspect of the invention, there is provided a therapy consisting in increasing the expression of PI16 in chronic or non-healing wound condition or in decreasing the expression of PI16 in fibrosis, hypertrophic scar or keloid.

Role of fibroblasts in wound healing

Fibroblasts are implicated in the process of wound healing, this involves several steps of differentiation from a quiescent fibroblast to a mobilized fibroblast that will transform into a myofibroblast and finally enter apoptosis. In chronic or non-healing wounds, this process is misregulated and fibroblasts fail to undertake the myofibroblast differentiation and are found in the wound as unfunctional fibroblasts, called pseudo senescent fibroblasts (Telgenhoff D, Shroot B (2005) Cellular senescence mechanisms in chronic wound healing. Cell Death Differ 12: 695-698). The aim of the present invention is to map, at the whole genome scale, the different genes that will be activated or deactivated during this process, and thus providing a molecular signature of chronic or non-healing wounds.

Human fibroblasts have the ability to enter into a physiological process named senescence, which permits a limited replicative cell cycle and thus avoids loss of genetic information. It usually occurs when a cell has already conducted several rounds of replication (called replicative senescence and dependent from telomere length), but can also occur in response to environmental stress (Muller M (2009) Cellular senescence: molecular mechanisms, in vivo significance, and redox considerations. *Antioxid Redox Signal* 11: 59-98). Senescence cells are arrested in cell cycle but maintain metabolic activity (Telgenhoff D, Shroot B (2005) Cellular senescence mechanisms in chronic wound healing. *Cell Death Differ* 12: 695-698).

Fibroblasts of chronic wounds lose some of their functionalities, and more particularly, they lose part or all of their replicative function (Telgenhoff D, Shroot B (2005) Cellular senescence mechanisms in chronic wound healing. *Cell Death Differ*

12: 695-698). In a wound, human fibroblasts are also associated with an up-regulation of APA-1, a protein which induces matrix remodeling, demonstrating that pseudo-senescence fibroblast phenotype was not induced by telomere attrition (Benanti JA, Williams DK, Robinson KL, Ozer HL, Galloway DA (2002) Induction of extracellular matrix-remodeling genes by the senescence-associated protein APA-1. *Mol Cell Biol* 22: 7385-7397). Thus, senescent fibroblasts in chronic wounds would appear more particularly due to a chronic inflammation than to a telomere shortening (Telgenhoff D, Shroot B (2005) Cellular senescence mechanisms in chronic wound healing. *Cell Death Differ* 12: 695-698).

Some biological markers, such as TAGLN, are described in the prior art (Thweatt R, Lumpkin CK, Jr., Goldstein S (1992) A novel gene encoding a smooth muscle protein is overexpressed in senescent human fibroblasts. *Biochem Biophys Res Commun* 187: 1-7). In this publication, gene expression is increased in senescent cells whereas in the chronic or non-healing wound model used by the inventors, the gene expression of TAGLN is decreased when compared with normal fibroblast gene expression.

In (Yoon IK, Kim HK, Kim YK, Song IH, Kim W, Kim S, Baek SH, Kim JH, Kim JR (2004) Exploration of replicative senescence-associated genes in human dermal fibroblasts by cDNA microarray technology. *Exp Gerontol* 39: 1369-1378), GOS2 is described as being overexpressed in prepuce fibroblast senescent cells. However, in this article, the fibroblasts are in replicative senescence, obtained after more than twenty doubling population whereas in the present invention, as the inventors work on a chronic or non-healing wound model, the fibroblasts are pseudo-senescent and not in replicative senescence.

Dermal fibroblast is a good experimental material since human cells can be obtained from different donors. By the way fibroblasts represent the key cells in wound healing, as they secrete the ECM proteins and differentiate in myofibroblasts that lead to the wound contraction.

Some biological markers are already described on fibroblasts from different tissues: for example, CCL11 in lung (Puxeddu I, Bader R, Piliponsky AM, Reich R, Levi-

Schaffer F, Berkman N (2006), The CC chemokine eotaxin/CCL11 has a selective profibrogenic effect on human lung fibroblasts, J Allergy Clin Immunol 117: 103-110) or TFIP2 in synovial fibroblasts (Scaife S, Brown R, Kellie S, Filer A, Martin S, Thomas AM, Bradfield PF, Amft N, Salmon M, Buckley CD (2004) Detection of differentially expressed genes in synovial fibroblasts by restriction fragment differential display. *Rheumatology* (Oxford) 43: 1346-1352).

Fibroblasts are the main cells of connective (or mesenchymal) tissues, in which cells are surrounded by extracellular matrix (contrary to epithelium where they are jointed together). Connective tissues represent a wide variety of physical structures and different functions: tendons, cartilage, bone, dermis, cornea, etc... As organs and tissues have specific functions (for example, skin functions are protection, sensation and heat regulation), connective tissues constituting these tissues and organs have also precise functions provided by specific cell types. In many types of connective tissues, the matrix-secreting cells are called fibroblasts. Each connective tissue has its own type of fibroblasts, as they secreted specific ECM proteins and fibers composing the connective tissue. For example, fibroblasts of papillar or reticular dermis secrete collagen I, III and V, XIV, elastic fibers, perlecan or SPARC. On the contrary, types III, IX, X collagens are found associated with aggregan and dermatan sulfate in tendons. It is thus impossible to compare dermal fibroblasts to other fibroblasts, such as lung or cardiac fibroblasts, as they present specific characteristics and functions.

The legends of the figures are the following:

Figure 1: Schematic representation of the experiments performed with Human Normal Dermal Fibroblasts

Figure 2: levels of αSMA mRNA determined by quantitative RT-PCR in the different experiments

Figure 3: αSMA and tubulin expression determined by Western-Blot in the different experiments

Figure 4: Definition of the Lists I, II, III

Table 1: List of genes encoding the molecular markers of the present invention

Table 2: Gene signature list for the non-healing or chronic wounds

Table 3: Gene signature list for the fibrosis, hypertrophic or keloid

Table 4: List of all genes transcripts identified in all the experiments performed (lists I, II and III).

Example

In response to a lesion, fibroblasts migrate into the wound where they differentiate into contractile myofibroblasts that will finally enter into apoptosis during the remodelling phase. This differentiation process can be studied ex-vivo in environmentally controlled tissue culture conditions, and therefore the timely controlled succession of different gene expression patterns can be addressed.

Materials and methods

Establishment of an *ex vivo* model of chronic wounds

An ex vivo model of chronic or non-healing wounds was established by adding exudates from chronic wounds on cultured fibroblasts in order to reproduce the pathological state. Then, the gene expression was studied to define a molecular signature of chronic or non-healing wounds.

NHDF, isolated from human explants, were purchased from Promocell. NHDF were cultivated in DMEM-F12 (Invitrogen), supplemented with 10% FCS (Invitrogen, 5µg/mL of insulin and 1ng/mL of b-FGF (PromoKine)).

To collect exudates, four patients with mixed ulcers were recruited (mean age, 76 years; range 57-88 years). For patient selection, it was decided to exclude any other comorbidity factor potentially involved in wound etiology: diabetes, peripheral arterial diseases, malnutrition. Exudates were collected from negative pressure therapy. All the exudates were centrifuged at 1,500 x g for 3 minutes to remove cell debris. The

supernatant was filtered and store at -80°C until use. Aliquots were used to determine protein concentration according to BCA method (Sigma).

For experiments, cells were deprived of insulin and b-FGF during 48 hours. Then, the cells were cultivated on collagen coated culture plates in DMEM-F12, supplemented with 10% FCS, 10ng/mL of TGF-β1 (Promocell) for 4 days. Four points were tested in order to appreciate the effect of exudate on fibroblast differentiation: untreated cells (T-E-), fibroblasts treated with TGF-β1 (T+E-), cells treated with exudate (T-E+) and finally fibroblasts treated with TGF-β1 and exudate at the same time (T+E+).

Establishment of an ex vivo model for fibrosis or hypertrophic scar

Myofibroblasts represent the key players in the physiological reconstruction of skin after injury and in generating the pathological tissue deformations that characterize fibrosis such as hypertrophic scars (Desmouliere A, Chaponnier C, Gabbiani G (2005) Tissue repair, contraction, and the myofibroblast. Wound Repair Regen 13: 7-12).

To study the myofibroblasts involved in generating hypertrophic or keloid scars, NHDF were cultivated on collagen coated culture plates in DMEM-F12 (Invitrogen), supplemented with 10% FCS (Invitrogen), 5µg/mL of insulin and 1ng/mL of b-FGF (PromoKine) and 10 ng/mL of TGF-β1 (Promocell), as TGF-β1 is known to induce the expression of αSMA in fibroblasts (Desmouliere A, Geinoz A, Gabbiani F, Gabbiani G (1993) Transforming growth factor-beta 1 induces alpha-smooth muscle actin expression in granulation tissue myofibroblasts and in quiescent and growing cultured fibroblasts. *J Cell Biol,* 1993 jul, 122(1): 103-111).

The efficiency of fibroblast differentiation was estimated by analyzing the expression of the myofibroblast marker alpha smooth muscle actin (αSMA).

This αSMA expression was assessed by RT-qPCR (mRNA levels) and by Western Blot (protein).

Western Blotting assay

Total proteins were extracted by scratching the cells with lysis buffer (TRIS, NaCl, NP40, EDTA, IMDTT) and incubated 30 min in ice. To remove cell debris, the samples were centrifuged at 13,000 x g for 10 min at 4°C and store at -20°C until use. Protein concentration was determined according to BCA method (Sigma). Equal amounts of total protein (20µg) were loaded to NuPAGE 10% BIS-Tris gel (Invitrogen), separated by migration at 150 V, and transferred to nitrocellulose membrane (Whatman) 1 hour at 30 V. Then, membranes were stained for α-SMA (Abcam) and tubulin (Abcam). Incubations were followed by secondary antibodies goat anti-rabbit IgG and goat anti-mouse IgG, respectively, conjugated with horseradish-peroxidase (HRP) (Promega). Signals were detected by ECL chemiluminescence using UptiLight HS WB Substrate (Uptima, Interchim). Bands were digitized with a scanner and the ratio between all bands density of the same blot was calculated by software (ImageJ 1.43u, 64-bit). Relative α-SMA expression was normalized to the respective value for tubulin.

Total RNA Sample Preparation

After four days of experiment, treated fibroblasts were detached with TRIzol Reagent (Invitrogen) and stored at -80°C. Then RNA was purified using chloroform and precipitated by isopropanol. Total RNA was quantified on the NanoDrop 2000c Spectrophotometer (Thermo Scientific). Reverse transcription of 500 ng total RNA to cDNA was done with oligot dT (Invitrogen) using SuperScript III RT (Invitrogen) and RNAse OUT (Invitrogen). The cDNA was store at -20°C.

Quantitative real-time RT-PCR

Quantitative real-time PCR (RT-qPCR) was done using 5µL of 1:20 diluted cDNA on the LightCycler480 system (Roche) using Maxima SYBR Green qPCR Master Mix (Fermentas). Forward and reverse primers were designed by Eurofins (MWG, αSMA forward: CTGTTTTCCCATCCATTGTG (SEQ ID NO:1), αSMA reverse: CCATGTTCTATCGGGTACTT (SEQ ID NO:2)) and a 100µM stock was stored at -20°C. Forward and reverse primer pairs were used for each RT-qPCR reaction. The cycling conditions were as follows : an initial 95°C for 10 minutes, followed by 45 cycles of 95°C for 15 sec, 58°C for 30 sec, 72°C for 20 sec. LightCycler 480 SW 1.5 was used

to evaluate the TM curves, to determine the Cp and to approximate the relative concentration for each amplification reaction.

Results

For the chronic or non-healing wound model, chronic wound exudates were added to cell cultures (500µg/mL of total proteins of exudate). The experiments that were performed are depicted in Figure 1: cells were either not treated (T-E-), either treated with TGF-β alone (T+E-), exudate alone (T-E+) or TGF-β and exudate (T+E+) for 4 days. The assays described previously were used to assess the level of differentiation. Chronic wound exudates decrease the expression of αSMA (mRNA and protein, figures 2 and 3). This indicated that chronic wound exudates clearly inhibit fibroblast differentiation. This is correlated to the fact that in chronic wounds, we can find unfunctional fibroblasts, also called pseudo-senescent fibroblasts.

In order to analyze the genes expressed upon different treatments of the fibroblasts in a chronic or non-healing wound model or fibrosis, hypertrophic scar model, mRNA deep sequencing was realized.

Total RNA was extracted by TRIzol Equal amounts of total RNA of the different treated cells (5 to 6 µg) were precipitated by absolute ethanol, supplemented by sodium acetate for RNA sequencing.

The mRNA sequencing was performed by Fasteris SA (Switzerland). RNA was sent as total RNA, after two rounds of polyA purification, the Reverse transcription and the cDNA libraries were done. The sequencing was performed on a HiSeq2000 (Illumina).

One gene can contain different isoforms, and some isoforms can have one or more exons in common. Unfortunately, when the number of reads present in each isoforms is counted and fused in gene entities, sometimes the same reads may be counted several times and thus biases the analyses for genes with numerous isoforms. To solve this problem, it was decided to create a fictive transcript for each gene corresponding to the maximal portion of exon coverage, and to count the

number of reads present in these entities. After the normalization and analysis of differential expression steps, only genes showing a differential expression associated with an adjusted p-value of 1.10^{-3} or less were retained. A supplementary filter on the logFC (Fold Change) to study complete lists (the absolute value of logFC has to be superior or equal to 2) was applied.

Pathologic wound healing analysis: chronic or non-healing wounds or fibrosis/hypertrophic scar/keloid

The aim of the invention was to know if genes are differentially expressed between two conditions, in order to determine if the wound is a chronic or non-healing wound or not, or if the wound will turn into fibrosis/hypertrophic scar or keloid.

The abundance of gene transcripts between two conditions was compared, the T-E- point (normal dermal fibroblasts) being the reference. 3 lists (as defined in Figure 4) were considered: List I compared between T+E- and T-E-, List II compared T-E+ and T-E- and List III compared T+E+ and T-E-. The comparison of the lists II and III with normal dermal fibroblasts provides the list of genes affected by chronic exudate during the process of differentiation, in fact genes affected in the pathological situation found in chronic wound healing. Thus, lists II and III represent the chronic or non-healing wound situation. List I represents the fibrosis or hypertrophic scar situation.

With the p value adjusted and the Log FC filters determined, 171 genes were identified as differentially expressed in list I, 409 genes in list II and 1006 genes in list III.

Some genes, thanks to their high increased or decreased expression, are of particular interest. For example, the expression of PI16 is largely decreased in non-healing or chronic wounds and increased in fibrosis/hypertrophic scar or keloid model. Thus, PI16 is a favorite candidate for therapy. The present invention also directed to a therapy consisting in increasing its expression in chronic or non-healing wound condition or in decreasing its expression in fibrosis, hypertrophic scar or keloid.

Table 1

ACTA2	HAPLN	PI16
AC084368.1	ID4	POLQ
ACTC1	IF44L	POSTN
ADAMTS7	INHBA	POU2F2
AMIGO2	ITGA1	PPARG
APOD	KIT	PTH1R
CCL11	KPRP	PTX3
CDC45L	KRT16	RCAN2
CFB	LBH	RRM2
CNN1	LCP1	RSPO1
COMP	LGR5	SERPINA9
CSF2	LPAR3	SERPINB2
CSF3	MFAP5	SMAD3
CTGF	MICAL2	SOX9
CXCL1	MIR147B	SPHK1
CXCL5	MIR1181	SPON2
CXCL6	MMP10	STC1
ECM2	MMP3	TAGLN
EDIL3	MT1F	TFIP2
EFHD1	MT1M	TMEM37
FGF9	NR4A3	TMSB4Y
FOLR1	OMD	TXNIP
FOXS1	PALM	UCN2
GOS2	PHACTR3	WFDC1

Table 2:

AC084368.1	Decrease in non-healing or chronic wounds
ACTA2	Decrease in non-healing or chronic wounds
ACTC1	Decrease in non-healing or chronic wounds
ADAMTS7	Decrease in non-healing or chronic wounds
AMIGO2	Increase in non-healing or chronic wounds
APOD	Decrease in non-healing or chronic wounds
CCL11	Increase in non-healing or chronic wounds
CDC45L	Increase in non-healing or chronic wounds
CFB	Decrease in non-healing or chronic wounds
CNN1	Normal in non-healing or chronic wounds
COMP	Decrease in non-healing or chronic wounds
CSF2	Increase in non-healing or chronic wounds
CSF3	Increase in non-healing or chronic wounds
CTGF	Increase in non-healing or chronic wounds
CXCL1	Increase in non-healing or chronic wounds
CXCL5	Increase in non-healing or chronic wounds
CXCL6	Increase in non-healing or chronic wounds
ECM2	Decrease in non-healing or chronic wounds
EDIL3	Decrease in non-healing or chronic wounds
EFHD1	Decrease in non-healing or chronic wounds
FGF9	Decrease in non-healing or chronic wounds
FOLR1	Decrease in non-healing or chronic wounds
FOXS1	Increase in non-healing or chronic wounds
GOS2	Increase in non-healing or chronic wounds

HAPLN	Increase in non-healing or chronic wounds
ID4	Decrease in non-healing or chronic wounds
IF44L	Increase in non-healing or chronic wounds
INHBA	Increase in non-healing or chronic wounds
ITGA1	Decrease in non-healing or chronic wounds
KIT	Decrease in non-healing or chronic wounds
KPRP	Increase in non-healing or chronic wounds
KRT16	Normal in non-healing or chronic wounds
LBH	Decrease in non-healing or chronic wounds
LCP1	Increase in non-healing or chronic wounds
LGR5	Decrease in non-healing or chronic wounds
LPAR3	Increase in non-healing or chronic wounds
MFAP5	Decrease in non-healing or chronic wounds
MICAL2	Increase in non-healing or chronic wounds
MIR147B	Increase in non-healing or chronic wounds
MIR1181	Increase in non-healing or chronic wounds
MMP10	Increase in non-healing or chronic wounds
MMP3	Increase in non-healing or chronic wounds
MT1F	Increase in non-healing or chronic wounds
MT1M	Increase in non-healing or chronic wounds
NR4A3	Decrease in non-healing or chronic wounds
OMD	Decrease in non-healing or chronic wounds
PALM	Decrease in non-healing or chronic wounds
PHACTR3	Decrease in non-healing or chronic wounds
PI16	Decrease in non-healing or chronic wounds
POLQ	Increase in non-healing or chronic wounds
POSTN	Decrease in non-healing or chronic wounds

POU2F2	Increase in non-healing or chronic wounds
PPARG	Decrease in non-healing or chronic wounds
PTH1R	Decrease in non-healing or chronic wounds
PTX3	Decrease in non-healing or chronic wounds
RCAN2	Decrease in non-healing or chronic wounds
RRM2	Increase in non-healing or chronic wounds
RSPO1	Decrease in non-healing or chronic wounds
SERPINA9	Increase in non-healing or chronic wounds
SERPINB2	Increase in non-healing or chronic wounds
SMAD3	Decrease in non-healing or chronic wounds
SOX9	Increase in non-healing or chronic wounds
SPHK1	Increase in non-healing or chronic wounds
SPON2	Decrease in non-healing or chronic wounds
STC1	Increase in non-healing or chronic wounds
TAGLN	Decrease in non-healing or chronic wounds
TFIP2	Increase in non-healing or chronic wounds
TMEM37	Decrease in non-healing or chronic wounds
TMSB4Y	Decrease in non-healing or chronic wounds
TXNIP	Decrease in non-healing or chronic wounds
UCN2	Increase in non-healing or chronic wounds
WFDC1	Decrease in non-healing or chronic wounds

Table 3:

ACTA2	Increase in fibrosis/hypertrophic scar or keloid
ACTC1	Increase in fibrosis/hypertrophic scar or keloid
AMIGO2	Increase in fibrosis/hypertrophic scar or keloid
APOD	Decrease in fibrosis/hypertrophic scar or keloid
CFB	Decrease in fibrosis/hypertrophic scar or keloid
CNN1	Increase in fibrosis/hypertrophic scar or keloid
COMP	Increase in fibrosis/hypertrophic scar or keloid
CXCL1	Decrease in fibrosis/hypertrophic scar or keloid
EDIL3	Increase in fibrosis/hypertrophic scar or keloid
EFHD1	Increase in fibrosis/hypertrophic scar or keloid
FOXS1	Increase in fibrosis/hypertrophic scar or keloid
HAPLN1	Increase in fibrosis/hypertrophic scar or keloid
INHBA	Increase in fibrosis/hypertrophic scar or keloid
ITGA11	Increase in fibrosis/hypertrophic scar or keloid
KIT	Decrease in fibrosis/hypertrophic scar or keloid
KRT16	Increase in fibrosis/hypertrophic scar or keloid
MICAL2	Increase in fibrosis/hypertrophic scar or keloid
NR4A3	Decrease in fibrosis/hypertrophic scar or keloid
PI16	Increase in fibrosis/hypertrophic scar or keloid
POSTN	Increase in fibrosis/hypertrophic scar or keloid
POU2F2	Increase in fibrosis/hypertrophic scar or keloid
PPARG	Decrease in fibrosis/hypertrophic scar or keloid

PTX3	Decrease in fibrosis/hypertrophic scar or keloid
RCAN2	Decrease in fibrosis/hypertrophic scar or keloid
SMAD3	Decrease in fibrosis/hypertrophic scar or keloid
SOX9	Increase in fibrosis/hypertrophic scar or keloid
SPHK1	Increase in fibrosis/hypertrophic scar or keloid
STC1	Decrease in fibrosis/hypertrophic scar or keloid
TAGLN	Increase in fibrosis/hypertrophic scar or keloid
TFPI2	Decrease in fibrosis/hypertrophic scar or keloid
UCN2	Increase in fibrosis/hypertrophic scar or keloid

Table 4:

	RPKM	List III		List I		List II	
name	T-E-	Log FC	Padj	Log FC	Padj	Log FC	Padj
J01415.1	285,08	10,75	2,87E-78	0,14	1,00E+00	10,27	1,92E-76
MEOX1	0,08	9,35	1,50E-51	3,21	5,87E-01	4,09	2,98E-02
J01415.4	249,69	8,55	6,48E-96	-0,21	9,95E-01	8,57	2,40E-83
SOX9	0,02	8,55	2,78E-26	7,61	1,80E-15	3,69	2,85E-03
KRT81	0,09	8,22	9,80E-39	5,42	1,91E-07	1,09	9,07E-01
KIF18B	0,09	8,21	9,69E-17	4,19	7,03E-01	6,89	7,31E-06
CSF3	0,00	8,13	2,80E-23	ND	ND	8,65	7,91E-25
COL10A1	0,14	7,75	3,38E-54	5,51	1,30E-20	3,70	2,63E-06
PRR15	0,03	7,73	5,00E-12	7,31	3,86E-08	4,21	2,49E-01
MT1F	0,50	7,29	2,67E-43	0,95	9,95E-01	8,00	1,89E-47
RP13-463N16.6	0,13	7,22	2,77E-12	4,59	3,51E-01	3,91	4,65E-01
HIST1H1B	0,09	7,15	5,29E-10	4,11	8,68E-01	6,47	6,65E-05
CHRNA9	4,68E-03	7,14	1,11E-09	7,30	2,46E-07	0,04	1,00E+00
MT1G	6,89	7,14	2,34E-75	2,62	5,23E-05	6,80	2,26E-64
CXCL3	0,11	7,11	4,56E-31	-2,33	9,95E-01	10,11	1,63E-60
IL8	0,46	7,08	1,65E-61	-3,26	5,82E-01	8,38	2,61E-70
RP11-180C1.1	0,01	7,04	5,76E-12	3,51	8,05E-01	-1,14	1,00E+00
MT2A	82,15	6,85	2,66E-96	2,55	3,88E-08	5,82	9,24E-84
ESM1	0,21	6,83	2,45E-47	1,04	9,95E-01	1,09	7,70E-01
IL1B	0,02	6,83	3,05E-13	1,29	9,94E-01	7,71	3,44E-16
DCLK3	0,01	6,52	1,26E-09	1,52	9,12E-01	3,31	2,59E-02
KISS1	0,92	6,50	2,73E-46	3,92	8,30E-04	-0,43	9,99E-01
MT1M	2,70	6,41	1,27E-58	0,79	9,69E-01	6,38	7,48E-52

AL121963.1	0,00	6,36	2,67E-06	2,62	3,09E-01	1,64	6,81E-01
SLCO4A1	0,04	6,28	6,26E-10	-1,35	1,00E+00	5,70	2,14E-03
DACT1	0,19	5,97	8,33E-48	6,52	1,13E-44	-0,64	9,98E-01
KPRP	0,04	5,95	1,07E-09	-1,24	1,00E+00	5,36	4,85E-04
AC005358.1	0,05	5,95	5,32E-10	3,20	5,05E-01	3,79	2,14E-02
DNER	0,03	5,79	5,93E-06	3,46	5,52E-01	4,85	6,31E-03
CSF2	0,02	5,74	2,23E-08	0,00	1,00E+00	7,46	4,74E-16
ETV4	0,72	5,71	2,78E-36	1,95	1,45E-01	3,73	9,08E-15
MMP10	0,03	5,68	9,57E-10	-1,14	1,00E+00	6,80	7,90E-16
MT1X	9,93	5,68	3,25E-39	1,71	2,73E-02	5,29	5,77E-03
CLDN14	0,01	5,60	3,05E-05	3,67	7,30E-01	1,30	9,87E-01
FNDC1	0,14	5,55	7,62E-52	5,51	3,97E-45	0,62	8,64E-01
PKP1	0,01	5,38	1,67E-17	4,10	3,97E-03	-1,01	9,27E-01
NT5DC4	0,03	5,34	1,21E-04	0,00	1,00E+00	3,61	5,68E-03
G0S2	1,56	5,28	2,47E-41	1,31	9,93E-01	5,52	1,27E-41
GPR126	0,02	5,27	3,61E-08	3,26	3,29E-01	1,76	7,07E-01
BTBD11	0,01	5,24	4,92E-07	1,91	9,95E-01	0,67	1,00E+00
PTPRR	0,04	5,24	6,84E-05	3,16	4,65E-02	3,29	3,08E-02
AP000695.4	0,00	5,20	1,15E-04	4,16	1,13E-03	ND	ND
POU2F2	3,29	5,17	9,68E-81	2,59	3,20E-04	3,57	9,13E-15
ANXA8L1	6,88E-03	5,16	2,34E-04	4,63	3,68E-05	0,00	1,00E+00
FOXS1	0,07	5,15	7,78E-06	6,67	1,80E-11	-0,78	9,60E-01
LIF	0,20	5,10	5,70E-28	3,09	2,40E-03	4,52	3,15E-12
PRR11	0,49	5,09	1,79E-32	0,72	9,95E-01	3,93	4,40E-15
PTPRB	0,04	5,06	9,46E-12	3,22	1,99E-01	2,92	5,83E-02

CXCL1	15,47	5,05	1,67E-30	-3,01	9,48E-04	7,17	2,36E-06
MT1E	15,38	5,05	2,02E-47	0,68	7,20E-01	4,69	4,22E-33
HIST1H3J	0,27	5,03	3,09E-06	2,20	8,78E-01	3,78	1,69E-02
SERPINA9	0,00	5,01	4,85E-04	ND	ND	ND	ND
XYLT1	0,26	4,98	6,81E-38	3,98	6,27E-07	1,96	1,98E-01
IFI44L	0,13	4,97	1,64E-28	-0,02	1,00E+00	5,46	6,68E-36
RP4-620F22.2	0,41	4,92	3,38E-06	0,79	1,00E+00	4,81	3,21E-04
RP11-229P13.23	0,10	4,90	3,28E-04	2,52	3,52E-01	2,80	1,17E-01
CKAP2L	0,33	4,89	2,94E-31	0,85	9,69E-01	4,14	7,49E-11
NRG1	0,44	4,87	1,35E-50	5,14	2,69E-19	1,79	7,94E-02
RP11-69I8.3	0,75	4,82	3,15E-10	3,30	8,30E-02	0,06	9,28E-01
LCP1	0,03	4,78	7,00E-04	1,61	9,95E-01	1,68	8,83E-01
J01415.9	8071,60	4,78	3,47E-14	-0,42	9,69E-01	4,56	1,58E-13
ITGB3	0,09	4,77	5,39E-12	3,66	6,42E-04	2,42	5,85E-02
CXCL5	0,27	4,76	2,85E-20	-2,06	9,69E-01	7,75	4,06E-64
PPAPDC1A	0,15	4,75	3,11E-12	5,42	1,28E-11	-2,73	7,52E-01
MT1H	0,71	4,72	4,11E-16	2,45	1,01E-01	4,78	6,91E-13
RP11-435D7.3	0,17	4,72	1,20E-05	3,23	2,77E-01	4,47	1,41E-03
SP6	0,05	4,70	1,43E-05	1,71	9,69E-01	2,57	4,59E-01
HIST1H4C	1,22	4,65	8,51E-10	2,29	7,04E-01	3,34	5,25E-03
AC093677.1	0,08	4,65	1,24E-05	-1,92	9,95E-01	6,84	7,07E-22
CDH4	0,11	4,64	1,81E-12	3,20	3,17E-02	2,60	1,26E-01
P2RY6	0,17	4,57	1,81E-10	1,99	8,85E-01	-0,16	1,00E+00
CDH2	0,49	4,56	4,24E-50	4,75	9,33E-24	-0,31	9,76E-01
LPAR3	0,05	4,53	6,59E-06	-1,88	9,95E-01	5,49	1,86E-10

AC015933.2	0,20	4,51	5,80E-05	5,20	4,98E-05	0,94	8,70E-01
AC099057.8	1,01	4,51	4,87E-14	0,57	1,00E+00	3,75	1,18E-04
KRTAP2-1	0,85	4,46	4,87E-23	0,77	9,95E-01	2,26	5,29E-02
J01415.6	497,79	4,45	1,90E-84	-0,42	1,00E+00	5,48	2,33E-85
MPP4	0,04	4,41	1,47E-10	1,74	9,69E-01	1,66	7,30E-01
IGFBP3	63,76	4,40	9,45E-94	3,78	9,49E-21	-1,84	7,37E-02
PTPRN	0,05	4,40	7,81E-10	3,55	3,21E-04	2,81	2,56E-02
HIST1H1E	0,42	4,34	7,68E-12	1,92	5,62E-01	3,77	1,09E-05
AC112205.1	0,18	4,32	3,43E-06	-1,00	1,00E+00	3,66	3,71E-03
CNIH3	0,24	4,32	6,44E-40	-0,32	1,00E+00	3,57	2,83E-14
CLSPN	1,71	4,32	4,15E-24	0,98	9,55E-01	3,75	9,12E-17
RP11-889L3.3	0,02	4,31	3,12E-04	0,74	1,00E+00	2,35	7,07E-01
RP11-400N13.3	0,32	4,29	3,23E-08	6,31	1,32E-22	-1,16	9,07E-01
SMCHD1	0,09	4,25	1,64E-05	1,89	9,54E-01	2,99	8,76E-02
CXCL6	1,09	4,24	3,37E-19	-3,58	6,02E-02	8,65	2,14E-81
FBXO43	0,06	4,22	5,86E-04	1,29	9,95E-01	3,68	3,87E-02
GPR68	0,47	4,21	1,70E-18	0,39	1,00E+00	2,59	2,04E-03
C6orf105	0,13	4,21	6,39E-15	0,71	1,00E+00	-0,81	7,87E-01
ORC1L	0,16	4,21	3,55E-10	0,65	9,95E-01	3,11	3,28E-03
IER3	15,53	4,21	1,96E-80	3,44	2,57E-21	2,59	2,48E-09
NTSR1	0,04	4,21	9,14E-06	-3,46	9,95E-01	2,96	3,00E-01
ROBO4	0,12	4,19	5,42E-10	0,70	1,00E+00	2,86	2,32E-02
HIST2H2BF	0,73	4,17	1,16E-11	0,68	1,00E+00	3,13	4,44E-05
GBP5	0,09	4,13	1,90E-16	0,89	9,74E-01	4,38	1,01E-27
HIST1H2AM	0,34	4,12	1,27E-04	1,37	9,95E-01	3,05	6,64E-02

SKA3	1,57	4,12	1,80E-24	0,86	9,69E-01	2,81	2,69E-07
PAPPA2	0,02	4,09	3,18E-04	2,99	3,72E-01	2,61	2,56E-01
AL161907.1	0,26	4,06	4,46E-06	2,31	9,55E-01	1,82	6,50E-01
FAM196B	0,08	4,05	1,87E-07	0,37	1,00E+00	2,96	1,75E-02
DTL	0,63	4,02	2,70E-42	0,42	1,00E+00	3,20	1,79E-08
C9orf140	0,23	4,01	1,35E-15	1,74	8,47E-01	2,14	1,91E-01
AC015936.1	0,72	4,00	1,03E-19	1,22	9,95E-01	2,82	5,35E-03
AC090673.2	0,29	3,99	2,46E-05	1,70	9,95E-01	3,34	1,84E-02
CDT1	1,85	3,96	8,64E-22	0,78	9,95E-01	2,55	1,37E-04
CDC20	7,78	3,96	1,47E-28	1,32	1,83E-01	2,31	1,32E-06
HIST1H2AE	0,68	3,95	2,57E-04	1,81	9,95E-01	2,45	4,37E-01
IL11	0,61	3,95	3,09E-28	1,33	8,85E-01	1,71	1,42E-01
CDC45L	0,84	3,93	4,39E-22	0,87	9,55E-01	3,19	3,42E-09
MKI67	2,39	3,93	4,62E-41	1,00	4,07E-01	3,19	1,85E-34
KCTD4	0,90	3,93	1,29E-18	1,71	6,20E-01	2,83	1,61E-04
HHIP	0,02	3,92	2,39E-04	3,09	4,19E-01	0,84	9,96E-01
CDCP1	0,75	3,92	4,11E-22	-0,29	9,95E-01	3,60	1,90E-11
NCAPH	1,05	3,91	1,63E-40	1,20	7,03E-01	2,60	2,06E-05
SPC25	0,52	3,90	7,21E-20	0,97	9,95E-01	2,85	1,50E-03
CALB2	0,22	3,90	2,48E-12	4,57	2,85E-12	-1,36	8,19E-01
PKMYT1	4,57	3,88	1,00E-26	1,16	4,56E-01	2,39	4,25E-06
PTPRE	0,01	3,88	7,58E-04	1,31	9,95E-01	2,70	1,85E-01
GTSE1	0,65	3,88	2,39E-41	0,52	1,00E+00	2,72	6,57E-05
WDR62	0,67	3,87	4,23E-23	1,65	4,91E-01	2,87	8,07E-05
CD274	0,25	3,86	8,89E-16	1,40	9,04E-01	2,28	1,26E-02

KIF4B	0,09	3,85	9,00E-07	1,12	9,95E-01	2,64	7,68E-02
MCM10	0,24	3,84	2,47E-11	0,00	1,00E+00	3,35	8,45E-06
PLK4	0,29	3,84	6,05E-11	0,52	1,00E+00	2,91	1,54E-03
MYOCD	0,43	3,84	2,91E-34	1,52	6,05E-01	2,28	1,32E-04
SLAMF8	0,13	3,83	4,27E-05	2,10	9,24E-01	2,73	1,56E-01
BLM	0,23	3,82	1,94E-11	1,01	9,95E-01	2,55	4,20E-03
CDC25C	0,79	3,82	1,40E-32	0,74	9,95E-01	2,80	1,52E-05
EXO1	0,32	3,82	4,10E-11	0,65	9,95E-01	3,21	8,47E-05
HIST1H2BM	0,67	3,82	4,10E-07	0,72	1,00E+00	2,48	8,16E-02
HAPLN1	0,48	3,80	2,39E-31	5,21	1,69E-25	-0,82	7,72E-01
CXCL2	0,46	3,80	7,42E-18	-2,88	5,49E-01	6,92	4,17E-56
GAS2L3	0,41	3,78	4,19E-15	0,57	9,95E-01	3,26	2,73E-05
HJURP	1,95	3,76	3,14E-22	0,95	9,69E-01	2,77	1,30E-08
MYBL2	4,16	3,76	3,72E-28	1,39	9,47E-02	2,62	6,59E-09
HMMR	0,77	3,75	1,82E-29	0,84	9,82E-01	3,14	2,57E-08
ASF1B	2,31	3,73	3,77E-20	1,12	8,47E-01	2,69	8,53E-07
HIST1H2BO	0,92	3,73	5,13E-08	0,54	1,00E+00	2,22	1,14E-01
SGOL1	0,56	3,73	3,05E-13	0,19	1,00E+00	2,94	3,57E-05
UCN2	0,79	3,71	7,54E-17	3,35	5,10E-05	1,64	3,99E-01
HIST1H2BL	0,20	3,71	8,82E-04	1,69	9,69E-01	2,66	2,27E-01
C15orf48	0,63	3,71	1,94E-07	-1,78	9,55E-01	5,28	4,62E-25
TROAP	1,87	3,70	4,39E-27	1,22	7,03E-01	2,48	1,55E-05
P4HA3	0,58	3,70	8,07E-14	4,46	4,60E-16	-1,54	5,64E-01
SPRY4	0,28	3,69	1,32E-13	0,68	9,95E-01	2,54	5,01E-03
AURKB	6,15	3,68	5,35E-46	1,53	9,32E-02	2,40	2,96E-07

MYO7B	0,11	3,68	1,91E-12	2,43	6,23E-02	-0,77	9,06E-01	
AC116914.1	0,24	3,66	1,59E-07	0,66	1,00E+00	2,75	2,28E-02	
GPR3	0,20	3,66	1,14E-07	0,02	1,00E+00	2,60	4,15E-02	
CDCA2	0,46	3,66	7,81E-11	0,42	1,00E+00	3,34	6,11E-06	
RHEBL1	0,40	3,65	1,40E-05	1,82	9,54E-01	2,63	5,38E-02	
CDCA5	1,71	3,65	9,67E-25	1,29	6,29E-01	2,57	5,14E-06	
AC090673.1	0,35	3,64	3,28E-13	2,51	4,20E-02	3,11	8,75E-05	
EPHB2	0,05	3,63	1,14E-07	2,01	8,12E-01	-0,09	1,00E+00	
FAM83D	1,18	3,63	1,39E-31	1,41	9,36E-01	2,50	1,84E-03	
HMGA2	1,59	3,62	4,80E-23	0,14	1,00E+00	2,64	1,95E-07	
GINS4	0,39	3,61	1,62E-10	0,61	1,00E+00	3,03	2,86E-04	
MCM4	1,79	3,60	4,72E-17	0,45	1,00E+00	2,49	3,92E-05	
FERMT1	0,09	3,59	6,60E-06	0,41	1,00E+00	2,75	6,03E-02	
SKA1	0,24	3,59	4,86E-10	0,99	9,95E-01	2,56	9,98E-03	
MMP3	13,04	3,57	4,17E-29	-1,76	4,50E-02	4,90	2,32E-25	
PMEPA1	5,18	3,57	1,45E-24	2,84	1,92E-09	-1,74	4,31E-03	
KIFC1	1,91	3,56	9,04E-20	1,34	4,11E-01	2,39	7,04E-06	
PODXL	0,86	3,55	8,69E-21	0,43	1,00E+00	-0,12	9,96E-01	
POLQ	0,14	3,54	5,20E-11	0,49	1,00E+00	3,30	3,66E-06	
J01415.14	376,66	3,53	1,11E-28	-0,43	9,98E-01	4,20	1,17E-77	
CITED4	1,45	3,53	2,66E-13	1,48	5,98E-01	2,57	1,60E-03	
NUF2	1,11	3,52	2,23E-13	-0,01	1,00E+00	2,79	2,57E-05	
INHBA	3,33	3,52	2,75E-18	3,09	9,23E-09	1,33	1,09E-01	
MICAL2	3,76	3,51	3,98E-24	3,41	1,18E-12	0,92	2,92E-01	
TNFRSF6B	7,91	3,50	3,29E-21	-0,17	1,00E+00	2,55	4,49E-06	

AC016399.1	0,33	3,49	1,32E-06	1,87	8,57E-01	1,26	6,68E-01
ESPL1	0,51	3,49	1,13E-28	0,75	9,95E-01	2,72	8,40E-05
E2F1	2,24	3,49	3,76E-20	0,98	8,85E-01	2,69	3,14E-08
PAQR4	3,39	3,48	4,79E-31	0,99	6,48E-01	2,05	2,57E-04
C9orf167	0,30	3,48	1,85E-08	1,23	9,69E-01	2,43	7,68E-02
IQGAP3	1,37	3,47	1,22E-52	1,10	5,04E-01	2,62	5,93E-09
HMGA1	54,29	3,46	4,30E-24	0,48	9,95E-01	2,14	9,65E-06
POLE2	0,64	3,46	1,48E-11	0,59	9,95E-01	2,39	1,99E-02
CENPF	1,74	3,46	1,27E-34	0,77	9,46E-01	2,81	5,07E-11
C11orf41	0,43	3,45	1,46E-23	0,90	9,95E-01	2,08	3,95E-03
KIF2C	2,05	3,44	6,55E-21	0,92	9,24E-01	2,32	3,35E-05
E2F7	0,20	3,44	3,48E-17	0,96	9,69E-01	2,30	8,24E-03
UBE2C	7,53	3,43	6,98E-30	0,75	9,24E-01	2,53	1,82E-07
ERCC6L	0,27	3,42	3,12E-08	0,36	1,00E+00	2,60	2,29E-02
PLK1	7,94	3,41	5,57E-64	1,13	3,00E-01	2,04	2,59E-05
AC005631.1	1,28	3,41	1,16E-08	1,49	9,24E-01	2,43	2,17E-02
FABP5L3	1,07	3,41	1,16E-08	1,49	9,24E-01	2,43	2,17E-02
MND1	0,69	3,40	1,44E-07	0,84	9,95E-01	3,06	2,36E-04
MIR147B	2,78	3,40	6,10E-04	-2,50	9,69E-01	4,90	3,53E-11
RRM2	4,33	3,40	3,05E-31	0,41	1,00E+00	3,00	1,59E-16
SPC24	0,75	3,39	2,92E-18	1,10	8,18E-01	1,37	1,81E-01
E2F8	0,20	3,37	5,13E-06	-0,60	1,00E+00	2,44	7,28E-02
SPAG5	1,25	3,37	2,63E-15	0,93	9,69E-01	2,73	6,80E-07
SIPA1L3	0,75	3,37	7,36E-32	0,47	9,95E-01	1,85	3,48E-03
FANCB	0,13	3,36	7,01E-05	1,82	8,85E-01	2,88	1,66E-02

HIST1H4H	1,74	3,36	6,24E-13	1,28	9,69E-01	2,70	2,11E-04
KIF4A	0,79	3,35	1,99E-15	0,68	9,95E-01	2,23	5,31E-04
CDC6	1,26	3,34	1,12E-15	0,85	9,69E-01	2,72	4,70E-07
SHCBP1	0,66	3,33	7,00E-14	1,06	9,69E-01	2,77	3,30E-05
ADAMTS6	0,79	3,32	4,13E-17	2,29	1,77E-03	2,48	1,11E-06
ELK3	1,82	3,30	5,13E-15	-0,06	1,00E+00	2,42	1,61E-04
LRRN3	0,22	3,30	1,09E-06	1,57	8,85E-01	2,81	2,44E-03
SCARNA9L	3,71	3,28	6,81E-05	-0,73	9,95E-01	1,90	4,38E-01
TPX2	4,60	3,28	2,41E-20	0,90	8,47E-01	2,11	2,73E-05
RRAD	4,09	3,28	1,94E-21	0,72	9,95E-01	3,03	1,62E-10
MCM5	3,56	3,28	1,44E-27	1,40	1,58E-01	2,06	1,14E-04
OPCML	2,10	3,28	5,96E-19	2,43	2,86E-05	1,41	3,64E-02
ODZ4	0,09	3,28	7,96E-12	1,97	5,76E-01	-0,18	8,91E-01
CDA	1,02	3,27	1,96E-07	2,91	4,31E-03	2,37	1,56E-02
CENPI	0,27	3,27	4,47E-07	1,65	7,66E-01	2,29	3,55E-02
KIF14	0,28	3,25	5,43E-10	0,83	9,69E-01	2,86	3,92E-05
BIRC5	8,11	3,24	1,46E-45	0,79	8,55E-01	2,14	6,32E-06
Z99716.2	5,20	3,24	3,16E-07	1,13	9,69E-01	1,73	2,50E-01
AP001610.5	1,50	3,24	4,51E-10	-2,01	9,69E-01	4,06	3,22E-10
TOP2A	6,98	3,23	1,38E-18	0,31	1,00E+00	3,05	9,31E-15
CHAF1B	0,93	3,23	5,36E-12	0,76	9,78E-01	2,22	3,31E-03
SPHK1	9,80	3,22	1,10E-26	2,67	5,09E-07	0,94	4,54E-01
DLGAP5	1,00	3,22	1,78E-12	0,72	9,88E-01	3,03	2,37E-08
RAD51AP1	0,83	3,21	1,22E-09	0,66	9,95E-01	3,16	4,39E-06
LMNB1	1,95	3,19	3,62E-24	-0,01	1,00E+00	2,44	5,41E-07

C11orf82	0,42	3,19	9,44E-08	-0,11	1,00E+00	2,38	2,49E-02
FAM64A	3,89	3,19	9,09E-17	0,89	8,85E-01	2,03	1,19E-03
DEPDC1	0,25	3,18	3,64E-10	0,11	1,00E+00	2,73	5,66E-05
KIF20B	1,35	3,18	6,37E-15	0,06	1,00E+00	2,75	1,36E-07
CTGF	66,82	3,18	1,80E-20	4,05	6,06E-44	-1,61	3,57E-03
CEP55	2,93	3,17	1,96E-16	0,34	9,95E-01	2,19	2,92E-05
CHTF18	0,57	3,17	1,08E-19	1,35	7,01E-01	1,56	1,59E-01
DEPDC1B	0,13	3,17	1,21E-04	-1,70	9,95E-01	2,89	1,31E-02
WNK4	0,06	3,16	5,81E-05	-1,20	9,95E-01	0,08	1,00E+00
PLEK2	2,33	3,16	7,79E-25	1,79	1,34E-01	-0,82	6,77E-01
GINS2	2,18	3,15	2,61E-22	0,65	9,95E-01	2,03	1,01E-03
TRIP13	1,73	3,14	2,07E-24	0,45	9,95E-01	2,17	1,06E-04
SERPINE1	111,64	3,11	3,59E-20	2,14	4,47E-04	0,61	5,03E-01
KCNJ15	0,21	3,11	3,11E-10	1,99	1,12E-01	1,74	6,75E-02
CDCA8	1,80	3,11	1,39E-17	0,88	9,95E-01	2,30	1,05E-03
RECQL4	1,19	3,11	5,60E-17	1,04	8,85E-01	1,74	2,41E-02
IGF2BP1	0,13	3,11	2,08E-06	2,49	5,69E-02	0,98	7,52E-01
CENPM	2,16	3,10	3,07E-12	1,22	7,40E-01	2,08	7,14E-03
SUV39H1	0,66	3,10	1,05E-14	1,32	8,51E-01	1,78	7,26E-02
MT1P2	2,72	3,10	5,72E-09	2,41	7,01E-03	2,78	8,48E-05
TRAIP	0,14	3,10	7,10E-05	1,34	9,55E-01	2,05	2,73E-01
CCDC99	2,21	3,09	1,36E-23	2,30	3,13E-05	1,23	8,98E-02
SLC35F2	1,18	3,09	8,93E-14	1,48	3,11E-01	1,11	3,80E-01
PSD4	0,44	3,08	1,15E-15	1,85	1,49E-01	1,18	5,47E-01
BRCA1	0,52	3,08	1,67E-13	0,12	1,00E+00	2,83	7,44E-07

CCNB2	6,05	3,08	2,09E-16	1,31	3,43E-01	2,27	1,54E-05
ENC1	2,61	3,08	5,36E-16	1,47	1,82E-01	2,51	7,88E-09
DGKI	0,06	3,06	5,67E-04	2,12	6,30E-01	0,51	9,83E-01
KIF18A	0,26	3,06	2,04E-05	0,24	1,00E+00	2,34	6,65E-02
SCG5	1,85	3,05	4,85E-21	1,07	8,85E-01	0,68	6,57E-01
MMP1	22,88	3,04	8,36E-16	-2,21	3,20E-02	4,76	6,99E-82
BUB1	0,77	3,04	5,63E-15	0,09	1,00E+00	2,52	1,29E-05
OAS3	0,73	3,04	2,66E-23	-1,09	9,54E-01	3,48	1,30E-39
PRIM1	1,07	3,03	1,52E-06	0,40	1,00E+00	2,12	6,35E-02
CYTSB	0,11	3,02	8,37E-09	3,45	5,09E-08	0,19	9,47E-01
ASPM	0,86	3,02	4,12E-16	0,04	1,00E+00	2,49	1,44E-07
PRC1	7,49	3,02	5,52E-49	1,27	2,22E-01	2,07	1,26E-05
KCNG1	0,67	3,02	1,83E-11	2,63	2,51E-03	0,28	9,81E-01
RAD54B	0,25	3,02	9,02E-06	1,37	9,54E-01	2,44	1,46E-02
BUB1B	0,88	3,01	9,39E-13	0,56	9,95E-01	2,33	2,14E-04
ANKRD1	1,09	3,01	9,83E-13	1,18	8,85E-01	0,15	8,69E-01
C17orf53	0,64	3,01	1,54E-09	0,31	1,00E+00	2,06	7,88E-02
C16orf75	1,66	3,01	2,42E-09	0,72	9,95E-01	2,72	6,71E-05
TK1	25,22	3,00	7,81E-24	1,21	1,21E-01	1,76	3,95E-04
RP5-955M13.3	0,65	3,00	8,67E-12	2,59	4,15E-03	0,25	9,84E-01
UHRF1	1,49	2,99	1,18E-13	0,43	1,00E+00	1,94	4,80E-03
FOSL1	25,88	2,99	5,51E-35	0,54	9,69E-01	2,16	1,17E-06
MCM2	2,21	2,98	2,74E-16	0,85	8,38E-01	2,21	7,89E-06
ARNTL2	0,71	2,98	1,34E-05	1,19	9,95E-01	1,99	1,15E-01
CCDC15	0,40	2,98	3,02E-06	-0,12	1,00E+00	1,95	1,19E-01

CENPE	1,55	2,97	9,02E-15	0,55	1,00E+00	2,70	1,20E-07
XRCC3	0,95	2,96	1,52E-12	0,91	9,69E-01	2,24	7,60E-03
PLEKHN1	0,32	2,96	3,98E-06	1,36	9,54E-01	1,92	1,87E-01
FZD8	0,94	2,95	2,66E-13	3,06	4,62E-08	0,36	8,89E-01
FOXD2	0,40	2,95	2,88E-10	1,43	5,02E-01	0,19	9,68E-01
SGOL2	0,93	2,95	1,60E-12	-0,04	1,00E+00	2,65	7,12E-06
PTTG3P	10,50	2,95	2,40E-24	0,24	9,95E-01	1,52	1,42E-02
ZNF367	0,40	2,94	5,03E-07	-0,58	9,95E-01	3,09	3,88E-05
KIF11	1,46	2,94	7,89E-20	0,24	1,00E+00	2,19	8,47E-05
HPDL	0,25	2,94	1,09E-04	-0,38	1,00E+00	1,19	7,52E-01
KIF23	2,61	2,93	6,99E-16	0,90	6,70E-01	2,15	5,35E-06
HIST1H2BN	0,36	2,93	1,67E-04	1,12	9,95E-01	2,10	1,40E-01
MT1A	1,64	2,93	1,21E-08	1,65	4,83E-01	2,50	5,36E-03
CENPK	0,20	2,93	9,66E-07	-0,10	9,96E-01	2,58	2,31E-03
NEK2	0,64	2,92	1,31E-09	0,56	9,95E-01	2,26	3,49E-03
WNT16	0,38	2,92	2,57E-06	1,26	8,85E-01	4,06	8,63E-30
CASC5	0,24	2,91	2,62E-07	-0,39	1,00E+00	2,48	9,97E-04
FABP5	4,13	2,91	1,57E-15	0,93	9,69E-01	2,10	5,78E-04
ITGA2	0,23	2,91	1,23E-11	-0,01	1,00E+00	1,88	1,46E-02
RELT	0,39	2,91	4,47E-08	2,24	3,93E-02	1,63	1,96E-01
CCNB1	8,07	2,91	1,44E-21	0,87	8,54E-01	2,06	1,70E-05
ARHGAP22	2,71	2,91	1,84E-23	1,47	1,34E-01	0,64	7,30E-01
PTTG1	21,31	2,90	1,18E-29	0,50	9,95E-01	1,91	9,50E-05
PNP	8,72	2,90	8,53E-19	1,22	3,44E-01	1,16	1,03E-01
APOBEC3B	2,43	2,89	1,28E-12	-0,22	1,00E+00	2,32	1,37E-04

OASL	0,87	2,88	1,86E-11	-1,60	9,24E-01	4,45	2,16E-17
CCNF	0,80	2,88	3,11E-12	0,61	9,69E-01	1,69	4,04E-02
PBK	4,04	2,87	8,27E-15	0,00	1,00E+00	2,50	2,32E-06
WDR76	0,51	2,87	6,04E-09	-0,17	1,00E+00	2,23	1,89E-03
CDK1	2,14	2,87	7,95E-19	0,01	1,00E+00	2,45	5,58E-07
THBD	0,18	2,87	1,28E-04	-1,35	9,95E-01	3,55	2,60E-07
TCF19	3,02	2,86	1,14E-14	0,60	9,95E-01	1,65	5,26E-03
CDCA3	8,17	2,86	4,48E-20	0,81	9,24E-01	2,06	8,40E-05
ZWINT	2,99	2,85	4,26E-13	0,46	1,00E+00	2,13	6,97E-04
KIF15	0,40	2,85	3,84E-08	0,83	9,95E-01	2,55	7,66E-04
CALR3	0,27	2,85	1,71E-04	0,82	9,95E-01	1,99	1,37E-01
RAD51	1,62	2,85	5,10E-16	0,91	9,69E-01	1,91	4,89E-03
TTK	0,42	2,82	2,35E-09	-0,29	1,00E+00	2,28	4,09E-04
PCDH19	0,09	2,82	9,81E-05	0,65	1,00E+00	-2,38	5,62E-02
ARHGAP11B	1,16	2,82	8,56E-09	0,41	1,00E+00	2,13	3,04E-03
INPP4B	0,18	2,80	1,79E-12	2,37	1,60E-03	2,63	1,74E-06
FN1	100,20	2,79	1,50E-10	2,83	2,55E-08	0,51	7,14E-01
RP5-907D15.2	0,30	2,79	1,74E-07	1,36	9,69E-01	0,22	9,62E-01
SLC1A3	0,29	2,79	1,45E-10	-1,15	9,69E-01	2,25	1,18E-03
ANLN	2,30	2,78	1,93E-16	0,00	1,00E+00	2,46	8,49E-09
TBX3	1,07	2,78	3,58E-11	-0,51	9,95E-01	1,60	1,09E-01
ESCO2	0,19	2,77	1,20E-04	-0,40	1,00E+00	2,44	1,02E-02
SIGLEC11	0,15	2,77	8,66E-04	0,17	1,00E+00	2,00	1,60E-01
AL049651.1	0,21	2,77	4,78E-04	-1,39	9,95E-01	3,36	4,14E-06
COL7A1	2,60	2,76	2,50E-21	2,46	1,92E-06	0,76	5,03E-01

KCNN4	0,46	2,75	3,99E-05	2,32	1,43E-01	0,33	9,06E-01
J01415.18	11748,44	2,75	2,57E-04	-0,15	1,00E+00	2,38	1,42E-03
MX1	6,60	2,75	1,01E-44	-1,80	1,38E-02	3,63	1,59E-16
HELLS	0,27	2,74	3,57E-08	-0,14	1,00E+00	2,57	8,07E-05
CMPK2	0,33	2,73	1,03E-11	-2,24	8,43E-01	4,44	1,11E-15
C16orf59	0,95	2,73	7,79E-06	0,73	1,00E+00	1,57	5,46E-01
E2F2	0,28	2,71	1,50E-05	0,07	1,00E+00	2,44	5,58E-03
FANCD2	0,27	2,71	5,68E-08	0,53	9,95E-01	2,03	6,09E-03
TACC3	2,80	2,70	4,53E-16	0,83	8,85E-01	1,95	1,31E-04
CHAF1A	2,78	2,70	2,67E-15	0,30	1,00E+00	1,86	2,68E-03
ARHGDIB	2,55	2,69	3,89E-08	1,07	9,95E-01	0,22	9,55E-01
CTA-150C2.16	2,54	2,69	1,50E-06	-0,20	1,00E+00	2,10	2,01E-02
BRCA2	0,11	2,69	6,46E-05	0,04	1,00E+00	3,05	1,67E-06
MCM7	9,67	2,69	2,09E-17	0,88	7,55E-01	1,55	4,70E-03
RFC3	0,47	2,68	1,96E-04	0,00	1,00E+00	1,75	3,36E-01
RTTN	0,34	2,67	1,31E-08	1,77	1,38E-01	1,55	1,05E-01
EPHB1	0,21	2,67	1,06E-05	0,14	1,00E+00	0,23	9,41E-01
C21orf58	0,28	2,66	1,15E-04	0,27	1,00E+00	1,42	5,09E-01
AC013418.2	0,63	2,66	1,50E-07	0,34	9,95E-01	1,77	3,41E-02
LRRC15	10,12	2,66	2,67E-25	2,35	5,84E-09	-1,01	4,76E-01
WDR51A	2,56	2,65	3,39E-13	0,86	9,85E-01	1,70	1,93E-02
NCAPG	1,88	2,65	1,79E-12	0,42	1,00E+00	2,17	4,41E-05
NDC80	1,79	2,65	4,50E-09	0,39	1,00E+00	2,27	1,76E-04
TMEM51	0,56	2,64	1,39E-05	-0,63	9,95E-01	1,23	4,98E-01
MFSD2A	0,22	2,64	7,57E-04	0,46	1,00E+00	3,18	1,18E-04

STIL	0,25	2,63	1,65E-06	-0,15	1,00E+00	1,81	7,43E-02
BDKRB1	0,67	2,63	4,18E-04	0,42	1,00E+00	2,45	2,37E-02
LRRC8C	0,35	2,62	1,97E-10	-0,16	1,00E+00	1,84	1,47E-02
J01415.21	361,74	2,62	5,12E-11	0,30	1,00E+00	2,92	2,54E-14
ARHGAP11A	1,65	2,62	4,96E-16	0,55	9,69E-01	2,04	4,76E-05
CENPA	1,48	2,61	1,38E-09	0,41	9,95E-01	2,14	7,46E-04
SAA1	2,45	2,61	2,23E-07	0,39	9,95E-01	3,11	1,57E-10
RTEL1	1,83	2,61	2,23E-16	0,07	1,00E+00	1,72	6,59E-03
APCDD1L	3,23	2,60	6,76E-19	1,27	8,47E-01	0,63	7,52E-01
EPHA2	0,95	2,60	1,53E-10	2,13	1,53E-02	1,13	3,63E-01
TSPAN13	0,74	2,59	1,41E-05	1,97	3,20E-02	-0,67	8,69E-01
MCM3	2,70	2,57	1,11E-13	0,57	9,95E-01	1,70	1,25E-02
RP11-15B17.1	4,94	2,57	9,18E-12	1,00	8,85E-01	1,61	1,93E-02
BHLHE40	1,54	2,55	1,79E-13	2,15	9,29E-04	-1,52	2,73E-01
C1orf170	0,62	2,55	1,18E-06	0,37	1,00E+00	1,26	5,32E-01
WDFY2	1,02	2,55	2,71E-05	0,83	9,95E-01	2,19	3,58E-03
RP4-539M6.11	1,28	2,54	3,36E-07	1,69	3,00E-01	0,89	7,39E-01
KIF20A	3,73	2,53	7,05E-15	0,40	9,95E-01	1,68	1,72E-03
NUSAP1	5,38	2,53	6,73E-15	0,19	9,95E-01	2,04	2,26E-05
LIG1	2,07	2,52	3,56E-12	0,41	1,00E+00	1,34	1,68E-01
C6orf173	5,81	2,52	6,89E-10	0,58	1,00E+00	1,62	5,41E-02
ANGPTL4	8,24	2,51	2,70E-15	-3,05	1,57E-03	1,62	1,33E-02
NET1	1,91	2,51	1,02E-12	1,42	2,74E-01	1,67	8,34E-03
ABLIM3	2,18	2,51	5,05E-15	1,14	6,99E-01	1,11	2,14E-01
MCM8	0,59	2,51	1,41E-05	0,10	1,00E+00	1,86	6,60E-02

INCENP	0,64	2,51	1,49E-08	0,74	9,69E-01	1,84	1,54E-02
ELTD1	0,46	2,51	4,29E-05	0,90	9,69E-01	1,06	6,55E-01
CCND1	52,06	2,50	6,01E-16	0,68	9,55E-01	1,28	1,78E-02
DDX12	0,75	2,50	3,96E-06	0,41	1,00E+00	1,38	4,31E-01
MFSD2B	2,96	2,50	1,89E-20	0,48	9,95E-01	1,50	1,51E-02
AURKA	5,33	2,49	4,05E-14	0,27	9,95E-01	2,20	4,25E-06
DBF4B	0,15	2,48	7,56E-04	0,68	1,00E+00	1,40	5,22E-01
CIT	1,08	2,48	7,93E-14	0,13	1,00E+00	2,24	7,12E-06
KIAA1524	0,88	2,48	4,96E-06	0,26	1,00E+00	2,35	8,31E-04
HAS2AS	4,22	2,48	1,74E-08	-0,32	1,00E+00	2,74	1,11E-07
MAD2L1	1,95	2,47	1,88E-08	-0,06	1,00E+00	2,10	4,65E-03
CDC25A	0,55	2,47	3,21E-07	0,02	1,00E+00	2,05	8,19E-03
FEN1	5,38	2,46	7,71E-13	0,30	1,00E+00	1,73	5,67E-03
C18orf56	1,60	2,46	3,54E-04	0,46	1,00E+00	1,86	4,30E-01
ATAD5	0,34	2,46	9,36E-04	-0,24	1,00E+00	2,19	1,62E-02
UBE2T	4,74	2,46	2,07E-09	0,70	9,95E-01	1,85	9,42E-03
FOXM1	9,20	2,46	5,13E-15	0,94	4,92E-01	1,49	3,50E-03
FAM54A	0,58	2,44	5,28E-04	-0,01	1,00E+00	1,70	2,78E-01
SAA2	0,40	2,42	6,31E-04	-0,57	1,00E+00	2,40	1,52E-03
DDIT4L	0,23	2,40	1,15E-04	-1,82	9,69E-01	1,47	4,73E-01
POLD1	1,96	2,39	3,46E-10	0,55	9,95E-01	1,27	3,07E-01
PFKFB4	0,55	2,39	1,11E-09	1,46	2,46E-01	0,48	8,55E-01
WDHD1	0,44	2,39	3,17E-06	0,40	1,00E+00	2,10	3,23E-03
HBEGF	0,49	2,38	1,80E-05	1,22	7,72E-01	1,51	1,12E-01
C1orf135	0,60	2,38	8,49E-04	-0,28	1,00E+00	1,61	2,73E-01

RFC2	2,59	2,38	4,74E-09	0,51	9,95E-01	1,31	1,65E-01
HS3ST3A1	2,31	2,38	8,97E-10	0,73	9,95E-01	1,55	6,57E-02
PDPN	1,34	2,35	1,56E-08	0,52	9,54E-01	2,80	2,14E-10
HMGB1L1	13,30	2,35	1,33E-10	0,28	1,00E+00	1,14	2,34E-01
RACGAP1	3,68	2,35	1,29E-13	0,40	9,95E-01	1,52	2,06E-02
CDCA7	1,05	2,35	1,68E-07	-0,19	1,00E+00	1,86	7,56E-03
ETV5	1,52	2,35	2,31E-10	0,69	9,69E-01	2,11	2,55E-04
CENPH	0,73	2,33	2,09E-04	0,00	1,00E+00	1,77	8,08E-02
CENPN	2,76	2,33	9,00E-11	0,38	9,95E-01	1,57	5,62E-03
PDCD1LG2	3,61	2,32	4,86E-10	1,20	8,85E-01	1,67	1,57E-02
KIAA0101	3,56	2,31	1,90E-08	0,65	9,54E-01	2,64	1,11E-07
DOCK2	0,63	2,31	4,59E-08	2,91	8,19E-07	0,11	9,43E-01
CEP152	0,35	2,31	2,78E-04	0,68	9,95E-01	1,87	4,60E-02
UBE2S	55,48	2,30	2,49E-14	0,56	9,67E-01	1,10	1,34E-01
ZC3H12A	2,92	2,30	1,35E-15	0,55	9,69E-01	2,37	1,37E-07
NETO2	0,72	2,30	5,11E-04	1,08	9,93E-01	1,58	4,16E-01
J01415.22	387,08	2,30	1,57E-06	-0,10	1,00E+00	2,72	3,15E-12
TYMS	19,11	2,30	7,48E-13	-0,18	1,00E+00	1,92	1,73E-04
ORAOV1	33,95	2,30	2,99E-15	0,95	7,72E-01	1,11	7,06E-02
PMCH	1,06	2,30	5,04E-04	-0,98	1,00E+00	1,93	5,62E-02
WWC1	1,18	2,30	3,08E-08	0,13	1,00E+00	2,41	6,82E-05
KIF22	9,67	2,29	3,84E-13	0,77	9,24E-01	1,16	1,11E-01
OAS2	1,48	2,28	1,85E-25	-1,40	6,94E-01	3,10	2,90E-13
RSAD2	0,29	2,27	1,38E-06	-2,60	4,54E-01	4,43	3,07E-38
AMIGO2	3,56	2,27	1,30E-07	3,37	1,06E-11	-2,72	2,09E-07

PTPRF	2,25	2,27	3,70E-11	1,12	6,60E-01	0,55	8,19E-01
LHFPL5	0,59	2,27	6,92E-04	0,37	1,00E+00	1,42	4,17E-01
LMNB2	13,80	2,26	2,18E-13	0,19	1,00E+00	1,22	7,24E-02
ADAM12	4,66	2,26	3,08E-09	2,97	4,08E-11	0,50	8,59E-01
MLF1IP	2,32	2,26	3,08E-08	0,17	1,00E+00	2,11	8,48E-05
KRT7	43,68	2,25	1,11E-10	3,95	1,54E-37	-1,65	1,44E-02
TIMELESS	2,11	2,24	1,08E-09	-0,03	1,00E+00	1,37	8,20E-02
MLXIP	2,32	2,24	4,17E-09	1,07	8,77E-01	0,95	5,95E-01
NAMPTL	2,26	2,23	7,73E-06	-0,47	9,96E-01	3,48	3,36E-13
POLA2	2,68	2,22	1,83E-08	0,43	1,00E+00	1,27	2,27E-01
CSMD2	0,16	2,22	1,26E-05	1,53	3,94E-01	1,34	1,93E-01
OSBPL6	0,52	2,22	8,07E-06	1,31	8,11E-01	1,91	1,22E-02
CKS1B	3,78	2,21	4,17E-09	0,60	9,95E-01	1,25	1,67E-01
FJX1	5,21	2,21	3,38E-14	0,96	4,22E-01	1,53	8,61E-03
H2AFX	36,37	2,21	1,28E-12	0,47	9,94E-01	1,19	9,01E-02
STX1A	1,60	2,21	4,88E-09	1,05	5,94E-01	0,76	5,97E-01
SLC2A1	3,32	2,21	6,28E-13	2,32	1,99E-04	0,81	5,08E-01
J01415.2	523,66	2,20	4,45E-06	0,14	1,00E+00	2,62	1,86E-09
LRP8	0,44	2,19	4,88E-05	-0,02	1,00E+00	1,88	1,56E-02
SLC38A5	3,94	2,19	4,30E-12	2,31	2,02E-05	0,37	8,19E-01
PLK3	1,30	2,19	7,58E-07	1,26	6,70E-01	0,86	7,52E-01
C21orf45	2,91	2,18	7,80E-06	0,03	1,00E+00	1,36	1,82E-01
SMC2	2,41	2,17	3,41E-08	0,18	1,00E+00	1,62	2,49E-02
MELK	2,40	2,17	1,12E-07	0,30	1,00E+00	1,59	2,00E-02
FAM60A	0,66	2,17	5,91E-04	1,14	9,50E-01	1,25	4,85E-01

KNTC1	0,52	2,15	1,68E-06	0,21	1,00E+00	1,84	2,76E-03
PSMD2	24,55	2,15	2,89E-14	0,70	9,28E-01	0,18	9,23E-01
ATAD2	1,27	2,15	7,20E-07	0,00	1,00E+00	1,72	5,82E-03
TM4SF1	1,28	2,15	3,89E-04	-2,44	1,38E-01	2,00	2,09E-03
C19orf48	13,87	2,14	9,23E-11	0,66	9,87E-01	1,34	8,59E-02
DHFR	1,05	2,14	3,83E-06	0,14	1,00E+00	2,03	1,90E-03
CTPS	4,20	2,14	7,70E-09	2,08	1,84E-03	1,09	1,77E-01
MGLL	17,36	2,13	9,02E-15	0,86	9,54E-01	1,95	5,38E-04
PSRC1	2,39	2,13	2,57E-08	0,59	9,95E-01	1,48	3,62E-02
RNASEH2A	16,97	2,12	3,58E-11	0,83	9,24E-01	1,49	1,26E-02
RFX8	1,25	2,12	2,02E-05	-0,63	1,00E+00	1,85	8,17E-03
SLC29A1	2,62	2,11	5,74E-12	1,75	3,17E-02	-0,13	9,05E-01
MX2	0,45	2,11	6,66E-17	-1,50	6,06E-01	3,36	3,84E-14
SMAD7	1,86	2,10	3,00E-08	1,46	1,07E-01	-0,12	1,00E+00
GINS3	1,28	2,10	2,04E-05	-0,24	1,00E+00	1,38	2,04E-01
FANCG	1,76	2,10	6,47E-07	0,64	9,95E-01	0,92	6,32E-01
NFKBIL2	0,55	2,10	3,34E-06	0,34	1,00E+00	1,01	6,68E-01
DUSP6	1,41	2,10	7,90E-08	-1,01	9,95E-01	2,91	2,85E-11
SMURF2	6,12	2,10	2,54E-10	-0,55	9,95E-01	1,72	1,18E-03
SLC25A10	3,65	2,09	7,46E-07	0,33	1,00E+00	0,94	7,30E-01
DNMT1	4,83	2,09	7,41E-10	0,31	1,00E+00	1,54	1,28E-02
MLPH	0,46	2,08	1,49E-05	-0,46	9,95E-01	0,74	7,54E-01
ZNF185	2,94	2,08	5,96E-10	1,15	5,76E-01	-0,07	1,00E+00
GPRIN1	0,84	2,07	7,35E-05	0,73	9,95E-01	1,31	3,73E-01
RP4-539M6.19	2,35	2,07	1,70E-05	1,47	4,02E-01	0,53	8,55E-01

RAP1GAP2	0,54	2,06	5,85E-07	0,77	9,69E-01	1,04	3,59E-01
CCNA2	8,55	2,06	1,97E-09	0,54	9,69E-01	1,26	3,27E-02
GMNN	3,07	2,06	5,20E-08	0,31	9,95E-01	1,19	1,02E-01
TMEM158	5,70	2,05	1,69E-07	-0,31	9,95E-01	2,21	1,38E-03
CSRNP1	1,98	2,04	6,47E-09	1,68	3,93E-02	0,21	9,12E-01
HIVEP3	0,23	2,04	3,07E-06	0,62	9,95E-01	0,81	7,22E-01
SMTN	5,94	2,04	1,52E-11	0,80	8,29E-01	0,58	6,89E-01
PLAUR	7,13	2,03	2,81E-12	0,51	9,95E-01	0,56	6,74E-01
RFC4	2,90	2,02	3,70E-07	0,24	1,00E+00	1,34	5,27E-02
AC114772.2	0,82	2,02	5,25E-04	0,20	1,00E+00	1,94	9,26E-03
EZH2	1,76	2,02	1,70E-06	0,45	9,95E-01	1,47	4,02E-02
CDCA4	5,00	2,02	3,59E-08	0,49	9,95E-01	0,88	5,52E-01
PDGFC	2,57	2,01	1,03E-06	1,10	5,98E-01	0,12	9,94E-01
BGN	82,98	2,01	2,29E-09	2,70	2,96E-09	-1,69	7,42E-03
TRIB2	1,35	2,01	5,61E-06	2,78	5,14E-08	-0,83	7,52E-01
CDKN3	11,82	2,01	6,61E-09	0,33	9,95E-01	1,48	1,06E-02
TWIST1	58,90	-2,00	2,11E-22	-1,20	7,54E-01	-0,72	6,41E-01
PLAC9	44,12	-2,00	2,20E-15	-0,41	1,00E+00	-1,49	1,10E-02
GSTA4	14,55	-2,00	3,09E-12	-0,58	9,79E-01	-0,96	2,79E-01
AP003117.1	21,73	-2,01	4,80E-13	-0,54	9,95E-01	-1,26	9,10E-02
ADAMTS14	1,73	-2,02	1,69E-06	-1,73	6,76E-01	0,31	8,83E-01
ID2	78,31	-2,02	4,53E-71	-0,51	9,95E-01	-2,16	2,32E-06
MEGF6	12,34	-2,02	4,25E-16	1,08	4,37E-01	-2,81	2,18E-10
AKAP12	28,92	-2,02	2,44E-20	-1,82	4,21E-02	-0,60	7,44E-01
THRB	2,21	-2,03	1,63E-15	-1,40	3,51E-01	-0,29	8,19E-01

GHR	0,75	-2,03	6,67E-05	-1,44	8,47E-01	-0,65	7,21E-01	
C5orf4	3,81	-2,04	1,68E-08	-0,78	9,69E-01	-1,50	3,77E-02	
FRY	0,69	-2,04	9,00E-07	-1,30	6,77E-01	0,39	8,83E-01	
N4BP2L1	1,50	-2,04	1,04E-06	-0,66	9,94E-01	-0,99	3,46E-01	
NAALADL2	0,74	-2,04	4,93E-05	-1,30	8,85E-01	-0,31	9,10E-01	
CYP2U1	3,28	-2,05	5,32E-10	-1,03	9,50E-01	-1,18	1,40E-01	
MMP11	1,76	-2,05	3,14E-05	-0,25	1,00E+00	-2,10	1,00E-03	
PIR	5,16	-2,05	1,05E-07	-0,86	8,85E-01	-0,90	5,23E-01	
TRAPPC6A	18,61	-2,05	6,70E-09	-0,02	1,00E+00	-1,05	2,95E-01	
AHR	2,72	-2,05	1,04E-10	-1,56	8,01E-01	-0,11	9,82E-01	
FAM46A	14,15	-2,06	6,82E-17	-0,76	6,49E-01	-0,80	2,43E-01	
RP11-69E11.4	1,70	-2,06	1,10E-04	-0,93	9,69E-01	-0,77	7,30E-01	
ZNF385D	1,63	-2,06	5,19E-08	-2,05	4,61E-02	-1,56	2,66E-02	
AL365277.3	2,32	-2,07	9,50E-05	-0,93	9,69E-01	-0,78	7,30E-01	
PLD1	1,39	-2,07	8,62E-09	-1,95	5,65E-02	0,16	9,38E-01	
KITLG	5,47	-2,07	1,73E-12	-1,78	2,89E-01	0,28	8,77E-01	
TLE1	3,56	-2,07	6,13E-10	-1,89	1,21E-01	-0,23	9,47E-01	
FUCA1	5,52	-2,08	1,95E-06	-0,36	9,95E-01	-1,25	2,88E-01	
NUDT14	28,34	-2,08	5,88E-10	-0,57	9,95E-01	-1,15	1,35E-01	
LAMA2	4,10	-2,08	1,95E-16	-0,38	9,69E-01	-1,79	4,48E-04	
STRBP	2,18	-2,08	2,43E-08	-1,14	7,69E-01	-1,22	1,72E-01	
RP11-417E7.1	14,28	-2,09	2,85E-06	0,05	1,00E+00	-2,16	3,15E-04	
DTX4	0,58	-2,09	1,10E-04	0,05	1,00E+00	-1,20	3,52E-01	
ADAM33	20,67	-2,09	2,84E-16	-0,82	9,73E-01	-0,67	6,83E-01	
AC013283.2	14,07	-2,09	7,41E-05	0,17	9,95E-01	-2,13	2,42E-02	

PSG8	3,70	-2,09	4,71E-11	-1,57	3,42E-01	-1,21	2,03E-01
GABARAPL1	64,05	-2,10	1,57E-17	-0,87	7,84E-01	-1,05	1,17E-01
PSG2	15,92	-2,10	5,32E-10	-1,16	6,03E-01	-0,46	7,86E-01
GPR133	7,65	-2,10	2,53E-12	-1,60	4,29E-01	0,25	7,90E-01
AL671972.2	55,32	-2,10	7,08E-21	-1,23	7,69E-01	-0,70	7,30E-01
MAN1A1	3,14	-2,10	3,27E-16	-1,84	1,76E-01	0,22	9,83E-01
CAPS	5,41	-2,10	1,36E-10	-0,88	9,69E-01	-1,13	1,52E-01
CRLF1	7,36	-2,11	2,24E-06	1,30	2,15E-01	-4,47	8,29E-24
ADAMTS2	16,26	-2,11	2,19E-27	-0,04	1,00E+00	-1,76	2,06E-04
CCRL1	14,24	-2,11	3,14E-24	-1,67	4,07E-01	1,27	5,85E-02
EMX2	36,18	-2,11	1,01E-25	-0,84	8,85E-01	-1,47	4,52E-03
RP11-69D4.3	36,58	-2,11	4,13E-08	-2,04	6,49E-02	-0,88	3,56E-01
MYLIP	2,63	-2,12	1,29E-06	-1,49	5,48E-01	0,16	1,00E+00
J01415.16	3694,65	-2,12	2,43E-20	-0,32	1,00E+00	-2,09	1,13E-04
FBLN2	42,56	-2,12	1,04E-17	-0,46	9,95E-01	-1,77	1,65E-04
AC093734.11	0,51	-2,13	8,33E-04	-0,85	9,95E-01	-1,54	2,03E-01
RNASET2	3,70	-2,13	1,65E-11	-1,13	8,85E-01	-1,15	2,06E-01
FAM19A5	24,81	-2,13	5,09E-11	0,20	1,00E+00	-2,17	7,81E-05
GALNT5	4,27	-2,13	4,52E-12	-1,08	5,98E-01	-0,73	6,30E-01
EFNA5	4,88	-2,13	2,65E-13	-3,45	1,19E-04	0,36	8,19E-01
SH2D4A	56,15	-2,14	9,39E-19	-1,52	9,11E-02	-0,92	2,25E-01
PRICKLE1	3,86	-2,14	1,55E-17	-0,81	9,69E-01	-0,91	4,42E-01
LMOD1	19,94	-2,15	5,66E-17	1,12	6,88E-01	-1,68	4,64E-03
SLC1A1	1,54	-2,15	9,47E-05	-1,10	9,54E-01	0,02	9,68E-01
RP11-361F15.2	3,70	-2,15	1,69E-04	-1,14	9,55E-01	-0,69	7,52E-01

VGLL3	13,29	-2,15	6,63E-19	-0,99	9,69E-01	-0,19	1,00E+00
TRNP1	43,90	-2,16	3,71E-19	-0,78	9,69E-01	-0,64	6,72E-01
C1R	277,25	-2,17	2,46E-17	-1,24	3,37E-01	-0,52	7,52E-01
RP1-166H1.1	181,53	-2,17	4,98E-15	0,28	9,69E-01	-1,99	2,94E-03
APOL3	3,59	-2,17	1,81E-08	-1,64	2,25E-01	0,12	8,99E-01
RNF112	2,20	-2,17	1,77E-05	-0,92	9,69E-01	-1,72	3,97E-02
TCN2	3,55	-2,17	6,39E-07	-0,80	9,02E-01	-1,27	1,36E-01
SYNPO2	3,00	-2,18	1,09E-27	1,13	3,11E-01	-1,19	1,80E-01
VSTM2L	2,01	-2,18	8,17E-04	0,97	8,85E-01	-1,50	1,41E-01
SEMA3A	3,98	-2,19	3,33E-10	-2,94	1,30E-03	0,55	7,14E-01
RP11-69D4.5	19,89	-2,19	9,55E-06	-2,13	1,38E-01	-0,29	8,10E-01
BMP8A	1,53	-2,19	3,17E-04	-1,23	9,54E-01	-0,85	7,36E-01
MID1	12,38	-2,20	4,65E-20	-1,88	1,77E-02	-0,29	7,69E-01
C17orf103	2,69	-2,20	2,99E-11	-0,17	1,00E+00	-1,98	1,05E-03
ADSSL1	2,03	-2,21	1,42E-04	-1,16	9,54E-01	-1,31	4,66E-01
AC103810.1	3,22	-2,21	4,12E-09	-0,74	9,69E-01	-1,42	8,10E-02
TMEM35	2,11	-2,22	9,11E-05	-2,54	2,13E-01	-1,26	3,54E-01
FAM171B	1,97	-2,22	4,20E-12	-0,72	9,71E-01	-0,93	4,34E-01
CRABP2	207,10	-2,22	2,41E-39	-0,77	9,78E-01	-0,03	1,00E+00
SULF2	3,94	-2,22	1,27E-13	-0,62	9,69E-01	-1,96	7,40E-04
CCDC152	7,38	-2,22	7,51E-14	-2,42	1,15E-02	-0,67	5,09E-01
FAM46B	7,01	-2,23	3,81E-08	0,06	1,00E+00	-1,16	2,71E-01
AC012349.1	17,25	-2,23	2,39E-17	-1,60	1,48E-01	1,07	2,03E-01
PGF	18,85	-2,24	3,34E-12	-2,31	4,58E-02	1,68	1,06E-03
TMEM47	39,33	-2,24	7,34E-19	-0,95	9,54E-01	0,17	8,69E-01

TMEM119	129,20	-2,24	1,14E-19	0,03	1,00E+00	-0,90	3,35E-01
RP11-48O20.4	25,31	-2,24	1,69E-13	0,37	1,00E+00	-2,14	2,17E-04
B3GALT4	5,30	-2,24	5,10E-08	-0,57	9,95E-01	-1,90	9,28E-03
DAPK2	9,28	-2,24	1,17E-14	-0,56	9,95E-01	-0,32	8,97E-01
FAT4	1,45	-2,25	2,61E-16	-0,18	1,00E+00	0,35	8,69E-01
AKR1C2	23,51	-2,26	6,50E-22	-2,25	2,14E-03	-0,98	6,64E-02
ABCA1	2,17	-2,26	5,86E-15	-0,88	9,55E-01	-0,62	6,79E-01
LYPD6	1,26	-2,26	3,82E-06	-1,41	9,36E-01	-2,17	5,19E-02
BMP2K	11,52	-2,26	1,46E-23	-2,23	1,79E-02	-0,24	9,22E-01
CYB5A	83,33	-2,26	1,84E-18	-1,70	1,56E-01	-0,61	6,68E-01
L1CAM	7,77	-2,26	1,05E-11	-1,67	4,20E-02	0,04	1,00E+00
FBLN1	84,14	-2,27	8,96E-23	-1,92	1,32E-02	-1,03	9,50E-02
LMCD1	64,43	-2,27	2,59E-21	0,35	9,95E-01	-1,34	3,94E-02
HNMT	1,31	-2,28	3,11E-08	-1,14	9,55E-01	0,35	9,06E-01
ACSS1	1,43	-2,28	4,09E-08	-1,31	5,87E-01	-1,23	2,14E-01
ANKRD6	0,98	-2,29	6,24E-07	-0,06	1,00E+00	-1,70	7,59E-02
ADHFE1	0,88	-2,29	3,54E-04	-1,27	9,24E-01	-1,25	3,95E-01
NTN4	5,77	-2,29	9,82E-11	-0,81	9,69E-01	-0,03	1,00E+00
MFAP5	41,41	-2,29	4,77E-23	1,38	5,80E-02	-3,70	3,62E-59
LPCAT3	3,33	-2,30	1,41E-04	-1,32	8,85E-01	-2,24	2,43E-02
CDON	1,25	-2,30	2,21E-07	-2,01	1,84E-01	0,59	7,70E-01
AL132716.1	7,19	-2,30	3,47E-10	-1,91	1,31E-01	0,82	7,30E-01
TOX	2,48	-2,30	1,24E-06	-0,94	9,95E-01	-2,55	1,30E-03
C1S	97,74	-2,31	9,60E-21	-0,90	7,13E-01	-0,61	6,55E-01
CCDC148	1,42	-2,31	2,15E-06	-0,86	9,24E-01	-1,20	2,62E-01

AL132716.2	7,00	-2,31	3,37E-10	-1,91	1,34E-01	0,83	7,14E-01
NOVA1	3,78	-2,32	1,41E-12	-2,09	6,27E-02	0,92	5,62E-01
ARHGAP20	0,99	-2,32	7,53E-06	-2,20	2,48E-01	-2,08	5,73E-03
PAQR3	7,11	-2,32	7,87E-53	-2,16	3,63E-02	-0,37	8,69E-01
S100A10	729,00	-2,32	1,32E-22	-1,69	1,02E-01	-0,61	7,52E-01
PROS1	3,71	-2,32	1,73E-17	-0,93	8,94E-01	-1,25	7,83E-02
IL6R	3,35	-2,32	1,24E-14	-2,00	4,10E-02	-0,18	8,19E-01
NTN1	4,47	-2,33	5,21E-29	-2,25	8,60E-02	0,30	7,74E-01
PSG4	101,75	-2,33	8,96E-16	-1,05	9,47E-02	-1,13	5,01E-02
EPAS1	28,57	-2,33	8,59E-37	-1,50	2,08E-01	0,25	9,07E-01
SLC39A10	2,97	-2,33	4,78E-15	-0,94	9,69E-01	-2,33	1,06E-04
OLFML1	6,61	-2,33	2,41E-12	-2,16	2,56E-02	-0,93	2,96E-01
PRUNE2	1,33	-2,33	2,71E-23	0,41	9,95E-01	-0,89	5,28E-01
ADAMTS7	14,18	-2,34	1,28E-22	-0,22	1,00E+00	-2,28	7,17E-07
RP11-481K16.2	6,18	-2,34	5,33E-04	0,25	9,74E-01	-3,08	2,58E-03
COL3A1	141,40	-2,34	6,99E-32	-0,28	9,95E-01	-0,84	1,20E-01
NOTCH3	3,45	-2,35	3,25E-14	-1,45	5,02E-01	-1,45	4,15E-02
IL15	3,04	-2,36	1,30E-13	-0,85	9,37E-01	-0,37	7,97E-01
SHC2	0,88	-2,38	6,11E-04	-1,13	9,74E-01	-0,49	7,95E-01
GPRC5A	1,66	-2,39	1,56E-04	-1,33	9,36E-01	-1,36	5,11E-01
DCN	291,49	-2,39	1,40E-63	-1,87	4,44E-02	-0,31	8,69E-01
PMP22	65,70	-2,39	3,58E-22	-0,24	1,00E+00	-1,85	1,29E-04
RP11-350N15.1	3,87	-2,40	4,32E-07	0,18	9,95E-01	-1,39	5,93E-01
STK32B	3,09	-2,40	3,85E-12	-0,80	9,95E-01	-1,20	2,91E-01
GPNMB	36,16	-2,41	7,88E-32	-1,37	1,34E-01	-1,03	1,44E-01

AC008074.1	0,91	-2,41	8,63E-05	-0,22	1,00E+00	-0,33	9,75E-01
ARL4C	29,28	-2,41	5,13E-20	-1,50	5,73E-02	-0,76	2,30E-01
ASAP3	6,16	-2,41	2,59E-27	-0,23	1,00E+00	-1,37	3,08E-02
LDB2	1,70	-2,41	4,49E-10	-2,42	2,86E-02	-1,10	1,67E-01
SRGN	18,65	-2,42	4,05E-10	-2,26	3,02E-03	0,47	8,02E-01
ACE	1,84	-2,42	2,14E-08	-1,41	9,24E-01	-1,37	2,28E-01
IL11RA	24,80	-2,43	1,77E-23	-0,73	9,55E-01	-2,35	2,83E-07
GRASP	2,53	-2,43	7,62E-05	-0,28	1,00E+00	-2,10	1,26E-02
C11orf52	3,10	-2,44	5,93E-05	-0,73	9,95E-01	-1,57	2,30E-01
CYBRD1	43,50	-2,45	6,74E-32	-1,49	1,68E-01	-1,39	1,07E-02
SLC9A9	1,78	-2,45	1,08E-07	-1,72	2,45E-01	-0,29	8,69E-01
RNF141	16,22	-2,45	1,11E-19	-1,07	7,15E-01	-1,04	2,06E-01
GAS1	19,74	-2,45	1,04E-16	-2,68	8,96E-03	0,70	4,76E-01
GSTM3	11,64	-2,47	2,08E-32	-0,59	1,00E+00	-1,09	2,36E-01
RNF144B	3,35	-2,47	2,42E-18	-1,07	9,53E-01	-0,09	9,98E-01
NR4A3	2,11	-2,48	3,20E-11	6,24	8,83E-14	0,56	7,70E-01
GSTM5	6,90	-2,49	2,64E-21	-0,65	9,95E-01	-1,38	4,26E-02
AC087698.2	2,55	-2,50	5,76E-06	-0,54	1,00E+00	-1,83	1,59E-01
BCAM	1,43	-2,51	9,32E-04	-1,38	9,54E-01	-1,74	1,17E-01
MBL1P1	0,94	-2,51	1,29E-04	-1,65	9,54E-01	-2,14	3,65E-02
SVEP1	9,20	-2,51	4,73E-26	-1,12	5,79E-01	-0,32	8,83E-01
AC016734.3	14,88	-2,53	1,57E-15	0,54	5,12E-01	-3,09	1,43E-07
HR	2,68	-2,54	2,36E-12	-0,08	1,00E+00	-1,87	4,15E-03
LYNX1	4,82	-2,54	7,36E-32	-1,08	9,69E-01	-1,25	1,01E-01
ANXA3	1,15	-2,55	2,15E-08	-1,68	3,32E-01	-1,24	2,34E-01

NLGN1	1,36	-2,55	2,96E-11	-2,36	2,12E-02	-1,07	2,63E-01
RP11-514O12.4	8,24	-2,55	8,44E-08	-1,03	9,88E-01	-1,50	1,25E-01
AC112217.2	1,43	-2,55	3,73E-07	-1,38	8,55E-01	-0,29	8,05E-01
SNED1	6,50	-2,57	7,36E-32	-2,27	4,26E-03	-1,47	4,37E-03
ARRDC3	12,27	-2,58	1,05E-25	-1,68	3,37E-01	-0,62	7,52E-01
HAPLN3	11,23	-2,58	2,21E-16	-0,66	1,00E+00	-3,80	2,39E-21
SDPR	1,65	-2,58	2,45E-06	-1,87	4,62E-01	-0,30	9,14E-01
SMAD3	9,22	-2,59	1,18E-28	-2,73	4,72E-04	-0,17	9,59E-01
LRRN4CL	20,39	-2,59	1,05E-20	-2,30	2,23E-02	-0,37	7,52E-01
ADCY4	13,19	-2,59	3,66E-20	-0,56	9,86E-01	-0,38	8,69E-01
FGD4	0,26	-2,60	1,26E-06	-2,80	1,38E-01	-0,45	8,71E-01
J01415.29	1773,52	-2,60	1,74E-52	-0,62	1,00E+00	-2,15	5,11E-04
J01415.20	8297,29	-2,60	3,20E-17	0,29	9,95E-01	-2,51	1,79E-05
CYP1B1	28,40	-2,62	9,47E-74	-1,77	4,17E-02	0,59	7,52E-01
FMOD	27,92	-2,63	1,15E-34	-1,57	1,00E-01	-0,75	5,32E-01
GCHFR	8,25	-2,63	2,59E-08	-1,89	5,91E-01	-1,57	4,56E-02
RGMA	1,64	-2,64	1,80E-05	-1,00	9,69E-01	-0,83	6,13E-01
ABCA5	2,50	-2,64	1,84E-22	-1,43	1,90E-01	-0,64	6,30E-01
AL589182.5	1,06	-2,64	3,65E-05	1,34	5,12E-02	-3,40	1,37E-04
DPT	69,74	-2,64	2,03E-24	-0,10	9,95E-01	-2,83	4,34E-17
ANKRD29	6,74	-2,65	2,71E-15	-1,85	9,09E-02	-0,75	4,88E-01
KCNK15	6,09	-2,65	6,89E-09	0,06	1,00E+00	-0,11	9,18E-01
KIAA1683	0,89	-2,66	1,16E-12	-1,03	9,36E-01	-1,62	7,28E-02
J01415.8	8298,87	-2,66	1,15E-10	0,25	1,00E+00	-2,56	1,07E-05
PARD3B	7,51	-2,66	1,63E-23	-1,29	2,71E-01	-0,22	8,83E-01

PCDH7	0,65	-2,67	6,52E-08	-0,78	9,07E-01	-3,91	4,85E-09
IGF2	27,00	-2,68	3,30E-21	-1,16	7,32E-01	-3,08	4,50E-16
SEMA3F	9,97	-2,69	2,56E-51	-1,76	1,63E-01	-1,87	6,20E-04
RGS7	2,68	-2,70	6,73E-06	-1,53	9,24E-01	-0,66	8,83E-01
F10	19,24	-2,70	1,44E-16	-0,91	7,86E-01	-1,59	1,06E-02
PALM	1,73	-2,70	2,94E-05	1,98	1,15E-02	-4,24	1,13E-08
HSD17B6	1,78	-2,70	3,91E-04	-0,92	9,69E-01	-3,88	5,42E-05
AXIN2	1,91	-2,71	7,31E-09	-1,47	8,85E-01	-1,35	2,60E-01
TGFBR3	13,14	-2,71	1,85E-31	-2,34	1,57E-03	0,04	9,77E-01
METTL7B	6,29	-2,72	5,33E-11	-0,45	1,00E+00	-0,55	7,96E-01
RP4-735C1.4	21,12	-2,72	2,81E-19	-0,51	1,00E+00	-1,00	3,33E-01
HSD17B14	14,20	-2,72	4,86E-24	-0,56	9,95E-01	-2,36	3,00E-05
PNMAL2	1,03	-2,73	2,04E-04	-1,03	9,95E-01	-1,74	7,70E-02
AC084368.1	186,01	-2,74	3,70E-17	0,60	8,75E-01	-1,84	2,31E-02
BAMBI	6,53	-2,74	5,78E-10	-0,29	1,00E+00	-2,67	9,35E-05
RAB11FIP2	11,86	-2,74	3,55E-64	-1,32	2,45E-01	-1,36	1,24E-02
CPE	7,44	-2,75	2,11E-43	-0,51	9,95E-01	-1,01	1,70E-01
SYTL2	1,37	-2,75	2,42E-13	0,64	9,54E-01	-2,15	3,67E-03
THBS4	5,73	-2,76	3,71E-21	-1,48	7,81E-02	0,02	8,83E-01
CDHR3	0,38	-2,78	1,17E-05	-3,43	4,34E-02	-0,71	6,79E-01
RPS2P45	3,37	-2,79	1,75E-10	0,80	3,37E-01	-2,68	4,72E-03
HLA-J	11,23	-2,79	7,91E-16	-0,90	1,00E+00	-2,14	9,13E-03
MEOX2	4,23	-2,79	2,51E-17	-2,30	1,56E-01	-2,41	7,81E-04
PPARG	2,51	-2,80	1,69E-14	-4,12	9,23E-06	0,55	8,42E-01
KIAA1324L	1,77	-2,80	9,67E-25	-1,69	9,51E-01	-2,60	1,67E-04

STS	13,22	-2,81	1,48E-63	-2,66	1,30E-03	-0,95	3,24E-01
FAM20A	0,98	-2,82	2,17E-08	-2,15	2,19E-01	0,66	8,45E-01
CFD	38,76	-2,82	3,05E-52	-1,86	4,07E-02	-1,85	8,12E-06
CHST2	37,05	-2,83	3,32E-25	-3,06	2,63E-04	-2,03	3,00E-05
AQP1	24,17	-2,83	1,41E-40	0,66	6,82E-01	-1,01	4,66E-01
ANGPTL1	1,11	-2,84	3,09E-07	-1,24	8,85E-01	-0,65	8,19E-01
PDE5A	1,13	-2,84	2,04E-17	-1,38	8,47E-01	-2,08	3,41E-03
KCNJ2	1,33	-2,84	7,00E-09	-2,87	3,33E-02	1,79	7,32E-04
RHOBTB3	23,44	-2,85	2,94E-37	-2,08	3,17E-02	-0,90	2,69E-01
J01415.17	8772,49	-2,85	6,13E-21	0,67	9,69E-01	-2,72	7,70E-07
PTGIS	3,05	-2,86	4,21E-09	-1,35	3,51E-01	0,42	9,86E-01
PCTK3	0,77	-2,87	1,18E-05	-1,50	7,71E-01	-1,28	5,29E-01
FAIM2	0,55	-2,87	3,68E-05	-1,24	9,95E-01	-1,94	8,48E-02
CNKSR2	1,08	-2,87	5,48E-12	-2,99	1,17E-02	-1,48	1,07E-01
CTD-2201I18.1	1,84	-2,88	1,31E-09	-1,08	8,47E-01	0,09	9,26E-01
KCNE4	1,35	-2,88	2,06E-07	1,75	1,77E-02	-1,69	1,27E-01
C10orf54	16,95	-2,89	1,49E-62	-1,29	2,82E-01	-1,10	1,23E-01
LBH	13,26	-2,90	2,38E-33	0,60	7,41E-01	-2,87	2,07E-11
PSG7	13,30	-2,90	8,53E-19	-1,16	2,81E-01	-1,20	7,24E-02
AC007385.1	2,67	-2,92	6,23E-04	-2,16	8,85E-01	0,10	9,01E-01
FBN2	14,19	-2,92	3,43E-43	-1,62	7,03E-01	-1,16	2,68E-01
AC134043.1	0,61	-2,92	3,50E-04	-0,14	1,00E+00	-0,83	7,52E-01
GALNTL1	5,01	-2,93	4,33E-14	-0,53	9,95E-01	-1,19	8,56E-02
SOCS2	8,61	-2,94	5,56E-20	-2,50	1,44E-02	-0,22	9,26E-01
C4orf18	1,22	-2,94	7,74E-23	-0,60	1,00E+00	-0,81	4,59E-01

DKK2	3,85	-2,94	9,01E-31	-3,17	7,01E-03	-0,50	7,87E-01
GSG1	3,36	-2,94	1,38E-11	-2,64	3,17E-02	0,21	1,00E+00
OLFML2A	0,90	-2,96	5,95E-10	-2,00	5,49E-01	0,50	7,52E-01
LRRC32	3,49	-2,96	3,57E-15	0,56	9,95E-01	-0,66	6,57E-01
C10orf72	8,60	-2,96	7,74E-23	-1,77	1,43E-01	-1,27	6,39E-02
CEACAMP10	3,72	-2,96	9,67E-10	-2,13	1,31E-01	-1,40	1,90E-01
CXCL14	6,77	-2,96	2,88E-17	-3,24	1,31E-03	-2,17	3,17E-04
MN1	11,56	-2,97	2,67E-61	-0,96	9,54E-01	-2,14	2,45E-05
SECTM1	41,48	-2,98	4,96E-24	-2,65	2,49E-03	-0,89	2,33E-01
PCDH18	12,63	-2,99	1,04E-59	-0,71	9,95E-01	-1,08	2,10E-01
HRSP12	48,38	-3,00	3,57E-35	-2,67	4,72E-03	-0,55	7,55E-01
ID4	16,18	-3,00	1,84E-48	-0,85	9,93E-01	-5,44	5,52E-35
ADM	1049,41	-3,00	5,16E-91	-2,17	1,65E-02	-0,32	9,07E-01
PPAP2B	39,08	-3,00	2,28E-62	-1,56	4,98E-01	-0,69	6,68E-01
SELENBP1	22,20	-3,01	2,03E-26	-2,19	2,72E-02	-1,07	1,47E-01
LRIG3	4,92	-3,01	5,77E-18	-1,90	5,23E-02	-1,91	3,97E-04
LYPD6B	4,48	-3,01	1,73E-13	-0,39	1,00E+00	-2,01	5,84E-02
NPR3	1,26	-3,02	2,40E-10	-1,16	9,69E-01	0,26	9,57E-01
C4orf31	1,47	-3,04	1,52E-09	-2,05	3,98E-01	-0,70	8,19E-01
ITGA7	16,82	-3,04	1,34E-30	-0,38	1,00E+00	-0,68	6,68E-01
ALX4	2,35	-3,04	1,83E-32	-1,03	8,51E-01	-3,27	3,22E-12
C8orf34	0,23	-3,06	1,02E-06	-0,14	1,00E+00	-0,84	7,52E-01
RND2	1,00	-3,06	4,80E-08	-1,13	9,69E-01	-1,52	1,99E-01
AP001496.1	8,71	-3,06	7,90E-06	0,91	3,34E-01	-4,56	3,52E-08
MAP2	1,35	-3,07	4,34E-18	-2,42	2,08E-02	-1,67	1,46E-02

TXNIP	23,61	-3,07	4,16E-55	-0,04	1,00E+00	-5,07	4,04E-58	
NPTX1	0,85	-3,07	9,27E-17	-2,69	5,02E-02	0,59	9,98E-01	
C4orf49	26,13	-3,08	3,88E-24	-0,24	1,00E+00	-0,59	7,30E-01	
C1QTNF5	110,76	-3,08	6,44E-71	0,18	1,00E+00	-2,25	9,53E-07	
C13orf15	8,80	-3,09	8,33E-16	-3,65	3,70E-04	2,14	2,74E-04	
PTCH2	0,54	-3,09	2,56E-06	-2,24	5,45E-01	-1,42	4,21E-01	
AKR1C4	3,35	-3,09	2,43E-09	-2,09	2,21E-01	-1,47	1,18E-01	
GUCY1B3	1,30	-3,10	1,17E-09	-3,20	1,41E-02	-1,48	1,21E-01	
WFDC1	5,54	-3,10	5,99E-23	1,18	1,79E-01	-4,03	2,71E-11	
AC132217.4	211,13	-3,11	2,73E-25	-1,37	7,06E-01	-3,93	3,46E-51	
FGF13	0,52	-3,11	2,60E-07	-1,25	9,54E-01	0,34	1,00E+00	
ITGB8	0,35	-3,12	9,88E-09	-3,32	1,32E-02	2,05	1,56E-04	
INHBB	2,83	-3,13	6,87E-11	-2,16	1,59E-01	-0,68	7,80E-01	
TDRD10	0,24	-3,13	5,91E-04	-0,47	1,00E+00	-4,02	2,17E-02	
FRAS1	0,80	-3,14	1,89E-23	-1,52	2,04E-01	-1,29	3,14E-02	
AP006565.1	0,48	-3,14	6,47E-06	-0,10	1,00E+00	-1,61	3,68E-01	
JAG1	5,06	-3,14	4,28E-39	-0,93	8,85E-01	-1,56	2,63E-02	
AFF3	0,47	-3,15	5,07E-16	0,83	8,85E-01	-3,36	7,74E-06	
CYTL1	3,80	-3,15	1,32E-09	-2,52	1,59E-01	-2,17	2,92E-02	
AC138472.5	6,82	-3,16	1,43E-10	-4,60	2,80E-04	-0,49	9,06E-01	
APOD	4,76	-3,17	1,29E-29	-3,79	1,95E-04	-0,64	3,65E-01	
RP11-258C19.5	7,29	-3,18	9,79E-12	0,71	3,44E-01	-3,68	1,05E-07	
FANK1	1,54	-3,19	2,90E-13	-0,78	9,29E-01	-2,07	5,17E-03	
MORN3	1,04	-3,19	2,62E-04	-1,35	8,85E-01	-0,79	7,52E-01	
JAM2	11,11	-3,20	5,67E-62	-1,35	2,83E-01	-1,78	9,37E-04	

TNNC1	3,48	-3,21	4,30E-08	0,40	1,00E+00	-2,34	1,02E-02
LUM	29,42	-3,21	2,82E-34	-0,82	9,69E-01	-1,13	2,62E-01
AL512662.2	2,13	-3,22	8,37E-06	-1,88	9,23E-01	-2,96	4,31E-03
RP3-445N2.1	6,21	-3,22	4,37E-07	-1,13	1,00E+00	-2,09	1,07E-01
FMO4	0,59	-3,22	5,23E-04	-1,49	9,69E-01	-1,01	7,52E-01
PPARGC1A	0,14	-3,23	4,20E-04	-4,86	2,95E-03	-0,58	8,00E-01
ABCA10	0,69	-3,23	7,38E-14	-1,92	2,82E-01	-1,26	2,38E-01
SESN3	2,56	-3,24	2,21E-10	-1,62	7,01E-01	-0,88	7,52E-01
EMX2OS	21,66	-3,25	4,98E-48	-1,06	5,48E-01	-1,88	4,17E-04
C1orf183	3,04	-3,26	4,87E-27	-0,28	1,00E+00	-1,47	9,57E-02
KCNS2	1,43	-3,26	9,13E-14	-2,68	7,89E-02	-0,41	8,83E-01
IGFBP5	103,83	-3,27	2,55E-89	-1,69	4,70E-02	-1,10	1,85E-01
SBSN	5,86	-3,27	8,88E-07	-3,09	1,24E-01	-0,99	4,39E-01
PSG1	36,09	-3,28	4,48E-70	-2,42	3,75E-03	-1,18	7,36E-02
TINAGL1	1,21	-3,28	1,44E-14	-2,62	1,28E-01	-2,01	1,64E-02
SLC2A12	1,27	-3,28	6,15E-09	-3,15	2,38E-02	-2,02	1,92E-02
COL4A5	3,30	-3,28	4,55E-42	-1,41	4,16E-01	-0,88	4,59E-01
RSPO1	44,80	-3,29	3,48E-37	0,84	3,37E-01	-3,13	6,88E-13
RAB27B	0,23	-3,29	9,04E-06	-4,86	5,52E-03	-0,87	6,68E-01
LIN7A	3,57	-3,30	6,81E-11	-0,72	9,95E-01	-1,54	1,78E-01
GDF5	0,95	-3,31	1,68E-04	-2,81	3,61E-01	1,24	3,86E-01
EXOSC7	59,88	-3,31	5,05E-37	-1,96	3,38E-02	-2,72	3,25E-11
SPTLC3	0,40	-3,31	3,73E-07	-1,28	8,47E-01	-0,08	9,87E-01
NOV	27,55	-3,31	2,34E-57	-3,11	2,65E-04	-2,25	2,12E-05
ECM2	5,35	-3,31	2,23E-27	-0,08	1,00E+00	-2,49	3,85E-07

RP11-792D21.2	1,30	-3,31	2,13E-12	-2,05	2,71E-01	-0,68	7,25E-01
C5orf23	7,16	-3,32	5,37E-27	-1,36	8,57E-01	0,06	1,00E+00
RCAN2	11,26	-3,33	9,18E-53	-2,63	8,63E-04	-0,90	2,88E-01
SDK1	0,79	-3,34	1,74E-25	-2,59	5,00E-02	-0,16	9,97E-01
TMEM37	6,55	-3,34	1,44E-15	-0,17	1,00E+00	-5,21	5,69E-21
RARRES3	20,08	-3,34	1,47E-18	-3,06	5,28E-04	-0,40	8,83E-01
IGFBP4	1565,81	-3,35	4,66E-51	-2,31	7,94E-03	-0,91	4,18E-01
SEPP1	4,23	-3,37	1,01E-42	-3,15	5,31E-04	-1,13	3,62E-02
NRK	0,30	-3,39	4,32E-05	-2,92	1,76E-01	-1,06	7,47E-01
ADAMTS9	0,70	-3,40	4,15E-23	-0,87	9,69E-01	-0,96	4,66E-01
THBS2	55,06	-3,40	7,63E-52	-0,39	9,95E-01	-1,68	5,81E-04
GCNT4	0,85	-3,41	7,64E-07	-0,85	9,69E-01	-1,60	3,00E-01
ENPP2	128,64	-3,42	2,99E-59	-2,89	1,74E-05	-0,17	9,20E-01
SLC44A3	0,75	-3,42	1,92E-06	-1,12	9,54E-01	-0,69	8,13E-01
C6orf97	0,81	-3,43	2,23E-16	-2,48	1,08E-01	-1,56	4,24E-02
SERAC1	8,29	-3,43	3,12E-45	-0,40	1,00E+00	-1,31	1,34E-01
PDE1A	0,48	-3,43	3,28E-09	-1,54	6,70E-01	-2,31	1,26E-02
MT-CO2	11543,24	-3,46	1,05E-95	0,38	9,95E-01	-3,48	1,69E-14
BX470102.1	14,81	-3,47	3,65E-35	-0,16	9,95E-01	-2,68	6,27E-05
TPRG1	0,10	-3,47	3,00E-04	-5,92	2,44E-02	-2,32	2,01E-01
LGR5	0,48	-3,49	4,49E-04	1,10	6,60E-01	-5,59	6,33E-06
CD74	2,80	-3,50	4,24E-10	-3,60	3,87E-03	-1,21	3,96E-01
TNNC2	1,34	-3,52	3,00E-05	-2,80	1,80E-01	-2,14	3,62E-02
C1orf167	0,54	-3,52	4,25E-07	-1,26	8,85E-01	-2,97	1,60E-03
C21orf81	0,31	-3,52	4,08E-05	0,34	1,00E+00	-1,57	4,34E-01

TMTC1	13,74	-3,53	7,48E-67	-1,97	6,44E-02	-0,93	3,14E-01
MBP	0,95	-3,53	1,54E-17	-1,42	4,50E-01	-0,98	3,58E-01
RP3-370M22.8	3,98	-3,53	3,50E-12	-0,17	1,00E+00	-3,17	2,52E-04
PRELP	27,09	-3,53	1,01E-65	-0,75	9,69E-01	-2,15	2,12E-05
ALDH3A1	1,00	-3,53	1,92E-10	-3,32	9,84E-03	-0,70	5,09E-01
AKR1C3	52,10	-3,56	3,38E-69	-1,66	9,38E-02	-1,74	2,47E-04
SFRP4	0,32	-3,57	1,23E-04	1,09	9,37E-01	-3,12	1,93E-02
RP11-175P19.2	3,00	-3,58	3,00E-08	0,75	7,03E-01	-2,76	2,12E-02
NAP1L2	1,02	-3,59	2,85E-07	-2,34	2,88E-01	-1,35	3,18E-01
ADAMTS5	20,92	-3,60	5,39E-54	-2,70	1,99E-04	-1,24	4,31E-02
ANK1	1,69	-3,60	2,12E-23	-1,58	3,53E-01	-0,48	8,19E-01
CFB	8,93	-3,61	3,43E-62	-2,87	4,03E-05	0,67	5,75E-01
PTH1R	1,29	-3,61	3,53E-10	-0,76	9,95E-01	-3,66	1,15E-06
MAOB	0,51	-3,61	2,53E-08	-1,94	9,49E-01	1,27	3,98E-01
AC079776.2	2,86	-3,61	2,62E-05	-1,40	9,69E-01	-0,94	6,85E-01
PDE1C	1,83	-3,62	1,13E-19	-0,12	9,95E-01	-0,85	4,68E-01
XXbac-BPG116M5.17	14,35	-3,66	4,68E-62	-2,90	2,90E-05	0,65	6,01E-01
FABP3	17,76	-3,68	4,75E-34	-0,97	9,74E-01	-1,09	3,50E-01
CYP19A1	0,79	-3,69	9,07E-19	-4,18	5,25E-04	0,43	7,61E-01
PCSK9	0,60	-3,70	1,68E-11	-0,83	9,95E-01	-2,94	1,00E-03
RABGAP1	34,17	-3,73	3,19E-79	-2,05	2,19E-02	-2,33	3,80E-07
GPC3	2,13	-3,74	4,97E-15	-3,94	4,85E-03	-1,16	4,43E-01
TNXB	13,01	-3,74	4,48E-70	-1,26	3,22E-01	-1,17	5,35E-02
SEMA3B	12,30	-3,75	2,88E-57	-1,46	1,59E-01	-1,61	2,47E-03
J01415.23	64,30	-3,75	1,85E-15	-0,52	1,00E+00	-3,59	5,31E-07

PI16	6,29	-3,76	7,65E-23	5,43	2,09E-31	8,42	4,95E-23	
ASPN	6,59	-3,77	1,79E-41	1,47	3,27E-01	-5,45	2,66E-34	
OSR2	86,64	-3,77	1,38E-67	-2,18	3,85E-02	-1,34	3,53E-02	
RAMP1	2,91	-3,79	2,00E-12	-2,10	3,52E-01	-3,37	3,64E-05	
PTPRQ	0,35	-3,82	5,77E-12	-4,05	4,41E-03	-1,42	5,12E-01	
RTN4RL1	0,77	-3,82	2,12E-06	-3,68	7,96E-02	-1,59	4,76E-01	
MAP2K6	1,18	-3,82	7,60E-10	-0,87	9,95E-01	-1,72	1,17E-01	
RP11-696N14.1	1,00	-3,83	9,51E-22	-1,86	3,37E-01	-0,54	8,02E-01	
C2	1,32	-3,85	9,99E-22	-2,03	1,62E-01	-0,98	4,20E-01	
AP005117.2	0,49	-3,86	3,37E-05	-1,67	9,69E-01	-0,47	1,00E+00	
IGFBP2	280,78	-3,88	4,09E-88	-2,31	1,82E-02	-1,18	2,03E-01	
ADAMTS3	0,85	-3,88	7,35E-15	-3,19	2,11E-02	-1,45	7,45E-02	
DCLK1	0,53	-3,89	2,97E-21	-3,38	1,68E-03	-1,25	4,26E-02	
BMP4	3,32	-3,90	1,77E-17	-3,73	1,86E-03	-2,86	2,36E-05	
FHL1	91,71	-3,90	4,23E-81	-2,40	2,19E-03	-2,12	2,89E-06	
SOD3	246,65	-3,90	3,69E-74	-2,88	5,38E-04	-2,24	5,46E-07	
DIO2	7,02	-3,91	3,66E-50	-3,32	1,76E-04	-3,49	7,32E-18	
TNFRSF19	4,28	-3,92	2,11E-36	-1,86	1,84E-01	-1,21	1,81E-01	
CYP21A2	26,06	-3,94	5,90E-57	-1,28	2,71E-01	-1,28	2,14E-02	
ITIH5	2,15	-3,94	5,40E-33	-1,29	8,29E-01	-0,54	8,69E-01	
CACNB4	0,48	-3,95	3,90E-16	-0,50	9,95E-01	-1,62	7,16E-02	
UPK1A	0,82	-3,95	2,70E-04	-1,90	8,29E-01	-4,53	1,75E-03	
DMKN	1,17	-3,96	4,62E-22	-2,57	1,07E-01	-1,08	5,73E-01	
XPNPEP2	1,31	-3,96	1,64E-16	-2,58	2,23E-02	-1,77	3,12E-02	
RP11-523O18.1	7,98	-3,96	8,28E-12	-1,47	7,34E-01	-1,38	2,21E-01	

CHRDL1	1,21	-3,97	1,87E-17	-2,07	1,19E-01	-1,73	2,31E-02
C1orf95	0,11	-3,97	5,61E-04	-4,17	2,01E-03	-0,05	1,00E+00
RP11-558F24.4	1,83	-4,00	2,87E-05	0,18	1,00E+00	-2,41	6,48E-02
NTRK2	0,12	-4,00	1,15E-09	-1,90	5,06E-01	-5,24	2,69E-07
RP11-315J22.5	1,40	-4,00	2,66E-07	0,94	6,04E-01	-3,37	6,70E-03
MASP1	6,12	-4,01	6,04E-60	-3,18	2,74E-04	-0,86	3,13E-01
MATN2	5,07	-4,01	4,98E-42	-3,41	9,56E-07	-2,07	1,61E-04
C8orf47	1,69	-4,02	1,66E-07	-0,97	9,78E-01	-0,68	8,37E-01
STMN2	12,93	-4,03	1,48E-34	-0,98	2,39E-01	-2,70	4,71E-10
MAOA	9,26	-4,06	2,74E-47	-2,81	2,37E-03	-0,72	6,68E-01
GJA5	0,73	-4,08	7,09E-05	-1,48	9,17E-01	-0,59	8,99E-01
DAPK1	3,09	-4,09	7,39E-35	-1,77	1,16E-01	-1,39	4,60E-02
WNT4	0,68	-4,10	4,90E-05	2,45	4,45E-03	-4,24	1,26E-03
CYP21A1P	4,13	-4,10	2,98E-19	-1,48	4,32E-01	-1,20	1,49E-01
SPON2	42,18	-4,11	1,42E-73	-0,15	1,00E+00	-4,21	1,89E-68
RIMS4	0,77	-4,11	2,86E-13	-0,23	1,00E+00	-0,95	5,65E-01
IL31RA	1,79	-4,12	5,46E-27	-3,10	3,40E-03	-0,48	6,46E-01
PHACTR3	0,32	-4,16	2,61E-07	0,72	9,69E-01	-3,86	4,02E-04
RP4-781B1.2	3,54	-4,20	3,03E-05	-0,01	1,00E+00	-0,43	8,83E-01
CYP11A1	1,68	-4,23	1,22E-17	-0,02	9,95E-01	-3,78	1,75E-06
ASPA	0,19	-4,26	5,34E-05	-3,96	3,93E-01	0,57	8,47E-01
EXPH5	1,45	-4,31	1,01E-31	-4,02	1,52E-05	-1,60	3,22E-02
RTN1	0,31	-4,32	5,56E-12	-1,71	9,95E-01	-5,43	2,32E-06
RDH10	27,29	-4,33	1,06E-60	-0,83	9,06E-01	-1,34	2,06E-02
LEP	1,77	-4,33	8,51E-17	-1,28	8,85E-01	-1,92	3,14E-02

PPL	8,61	-4,34	4,28E-49	-1,56	1,32E-01	-0,32	7,52E-01
LSAMP	1,04	-4,34	4,77E-17	-2,04	1,67E-01	-2,52	1,79E-03
MRVI1	2,02	-4,34	2,37E-27	0,44	1,00E+00	-2,78	9,49E-06
WNT11	6,12	-4,36	5,62E-27	-2,48	1,01E-01	-2,20	2,05E-04
IRX6	2,12	-4,39	4,72E-17	-2,78	4,70E-02	-0,18	9,79E-01
SHE	0,17	-4,39	1,61E-06	-1,19	9,95E-01	-2,21	2,56E-01
HSPB3	20,54	-4,41	1,74E-29	-1,46	2,45E-01	0,09	1,00E+00
RP11-379K17.4	0,49	-4,45	7,15E-11	-2,99	2,04E-01	-3,09	1,49E-03
KIAA1199	111,97	-4,45	5,65E-87	-2,50	2,48E-03	-0,58	7,87E-01
TRPC6	3,63	-4,45	9,50E-34	-2,82	1,59E-02	-0,38	8,69E-01
NID2	25,81	-4,46	2,60E-73	-3,39	6,64E-08	-1,90	1,79E-05
PDE3A	0,43	-4,47	3,60E-07	-2,37	6,35E-01	-1,73	3,02E-01
ITIH3	0,18	-4,47	1,42E-04	-1,66	9,54E-01	-1,51	5,14E-01
DBC1	0,54	-4,51	1,45E-09	-2,81	1,07E-01	-1,15	4,60E-01
CTD-2090I13.1	2,87	-4,53	2,58E-35	0,22	9,54E-01	-5,45	4,33E-18
FXYD1	7,45	-4,53	3,38E-16	-1,38	7,72E-01	-2,48	9,04E-04
GGT5	0,49	-4,55	1,41E-06	-5,01	6,33E-02	-0,37	9,82E-01
TRPV6	0,06	-4,56	9,74E-05	-3,10	6,95E-01	-0,71	7,52E-01
ADRA2A	4,98	-4,59	4,77E-38	-3,61	2,81E-06	-7,16	1,01E-27
EFEMP1	240,95	-4,60	1,70E-91	-1,21	4,42E-01	-2,18	2,25E-05
AC015724.1	0,67	-4,60	3,35E-04	-3,89	3,96E-03	-1,83	3,11E-01
OLR1	0,31	-4,60	6,62E-05	-2,83	7,94E-01	-2,54	2,15E-01
PODN	52,97	-4,62	1,25E-71	-0,23	1,00E+00	-2,82	4,52E-12
EPHB6	7,83	-4,62	6,24E-51	-2,02	2,61E-02	-0,70	4,65E-01
C10orf107	1,79	-4,63	1,12E-17	-2,48	2,02E-01	-1,26	6,41E-01

QPRT	2,34	-4,64	4,04E-14	-1,75	5,11E-01	-2,45	6,08E-03
RP11-1042B17.2	11,60	-4,65	5,35E-18	0,45	8,05E-01	-4,93	1,59E-16
TRPM3	0,18	-4,66	2,16E-10	-3,81	4,49E-02	-2,26	3,17E-02
ROBO2	3,96	-4,67	9,71E-54	-1,67	2,47E-01	-1,10	4,02E-01
IGF2AS	0,26	-4,69	9,55E-05	-0,89	9,95E-01	-4,09	2,94E-04
MAF	5,68	-4,69	2,57E-51	-2,50	9,51E-03	-1,70	2,43E-03
COL14A1	0,28	-4,75	2,56E-12	-2,74	3,28E-01	-2,45	1,03E-02
FAM38B	1,89	-4,75	3,10E-18	-2,46	1,30E-01	-1,94	6,07E-02
PADI2	0,59	-4,75	8,88E-10	1,98	3,12E-02	-4,52	3,55E-06
AGT	0,60	-4,76	1,70E-09	-1,13	9,95E-01	-2,66	2,81E-02
COL5A3	8,48	-4,78	1,87E-49	-2,11	6,33E-02	-1,53	3,83E-02
SLC40A1	1,72	-4,80	1,57E-26	-4,08	2,03E-05	-4,02	9,18E-23
COL4A6	0,30	-4,81	8,89E-10	-2,75	1,62E-01	-0,76	8,69E-01
RSPO3	5,27	-4,82	2,47E-32	-4,73	1,17E-07	0,97	3,70E-01
RAP1GAP	0,31	-4,87	6,79E-07	-3,25	1,12E-01	-2,62	5,87E-02
CD79B	0,76	-4,88	2,70E-06	-4,41	8,30E-02	-1,69	4,15E-01
RP11-282K6.3	0,35	-4,89	4,93E-05	-0,61	1,00E+00	-0,88	8,47E-01
PRRT4	0,22	-4,93	1,44E-04	-1,27	9,95E-01	-1,83	3,75E-01
PTGDS	15,60	-5,00	1,44E-93	-1,59	2,48E-01	-1,82	1,47E-03
MYRIP	0,28	-5,01	3,57E-10	-4,06	1,08E-01	-0,51	8,91E-01
CPZ	18,77	-5,02	7,36E-115	-2,60	1,06E-02	-1,39	9,22E-03
GPR78	7,84	-5,02	9,77E-115	-2,59	1,11E-02	-1,40	8,34E-03
MSTN	0,45	-5,07	1,86E-05	-3,27	3,62E-01	-0,55	9,07E-01
RP11-334A14.5	262,98	-5,10	1,22E-144	-0,60	9,95E-01	-3,17	2,56E-13
RP11-334A14.8	1,17	-5,11	5,76E-11	-1,43	8,85E-01	-4,61	2,69E-07

AC106028.1	10,21	-5,13	1,16E-31	0,46	8,05E-01	-4,63	2,01E-09
C1orf88	0,46	-5,15	2,20E-12	-1,84	8,69E-01	-2,03	1,25E-01
LCNL1	0,50	-5,16	4,61E-13	-1,90	8,55E-01	-2,32	1,14E-02
CDH6	6,79	-5,17	2,61E-62	-1,80	9,26E-02	-3,80	3,07E-17
RP4-788L13.1	0,39	-5,22	2,01E-09	-5,44	9,83E-08	0,02	9,98E-01
OLFM2	37,33	-5,29	9,42E-112	-2,49	1,57E-02	-3,88	1,43E-49
SIX2	6,31	-5,34	3,22E-30	-2,48	1,41E-02	-6,63	1,47E-26
AC002115.7	1,83	-5,35	2,43E-09	-4,19	1,63E-02	-5,45	3,76E-07
SAMD5	1,04	-5,42	2,20E-22	-2,03	1,71E-01	-0,99	1,12E-01
FGFR2	0,21	-5,44	2,96E-08	0,26	1,00E+00	-2,71	3,10E-02
VIT	4,83	-5,45	1,99E-38	-2,27	3,11E-03	-2,68	1,79E-08
RSPO2	0,27	-5,45	5,90E-07	-3,43	8,02E-02	-5,07	1,76E-04
VCAM1	1,33	-5,45	4,25E-23	-3,68	1,39E-02	-3,85	6,13E-06
TPD52L1	15,81	-5,46	2,08E-101	-1,53	1,42E-01	-5,31	2,30E-48
SIPA1L2	5,72	-5,47	2,62E-91	-2,40	7,69E-03	-1,88	2,02E-03
MAN1C1	0,82	-5,50	2,62E-31	-2,36	1,38E-01	-3,32	1,14E-07
ERMN	0,24	-5,52	4,06E-08	-2,87	4,50E-01	-2,06	3,31E-01
AL109918.1	3,87	-5,52	1,21E-07	0,52	9,94E-01	-5,63	1,11E-04
RP11-88H9.2	0,63	-5,58	1,04E-04	0,43	9,95E-01	-4,53	3,08E-03
REM1	4,49	-5,60	3,97E-21	-3,33	3,06E-02	-1,92	4,19E-02
OMD	1,16	-5,60	7,35E-17	-1,50	6,49E-01	-4,36	4,91E-08
AP002004.1	0,81	-5,61	2,10E-10	-1,91	4,95E-01	-1,11	7,03E-01
P2RY14	0,46	-5,72	2,60E-11	-4,84	3,86E-05	-4,87	1,30E-06
HLA-DRA	1,14	-5,74	1,84E-11	-6,29	3,02E-03	-2,76	1,40E-02
GLDN	3,11	-5,82	2,42E-72	-6,98	2,32E-16	-0,75	4,00E-01

MEST	1,61	-5,86	4,62E-34	-2,56	5,21E-02	-2,80	2,12E-05
FGF9	0,43	-5,92	4,19E-12	0,15	1,00E+00	-6,65	1,23E-08
KCNB1	0,31	-5,94	1,52E-12	-2,57	1,74E-01	-2,21	2,97E-02
WISP2	29,39	-5,97	1,93E-149	-0,12	1,00E+00	-1,43	3,01E-03
ACAN	2,77	-5,97	2,47E-72	-2,62	3,75E-02	-9,92	6,95E-35
KCND3	7,96	-5,99	4,82E-118	-0,80	9,95E-01	-2,83	1,96E-09
C11orf87	0,46	-6,00	1,80E-06	-3,42	5,30E-01	-4,84	1,93E-03
TMEM26	0,47	-6,02	5,68E-16	-3,61	4,47E-02	-2,06	9,97E-02
ELANE	1,97	-6,03	2,79E-12	-3,47	3,11E-01	-4,75	2,33E-06
SEMA3D	3,20	-6,12	9,68E-75	-2,74	4,68E-04	-4,40	8,05E-40
IL34	4,35	-6,12	9,31E-27	-3,70	1,61E-03	0,21	1,00E+00
SLC1A7	1,56	-6,13	1,43E-21	-0,20	1,00E+00	-2,71	1,06E-04
TM4SF20	6,02	-6,13	4,29E-55	-0,02	9,95E-01	-2,18	9,60E-05
STEAP4	0,36	-6,17	1,46E-23	-4,97	5,31E-04	-0,03	1,00E+00
SCARA5	0,66	-6,17	3,87E-16	-6,58	7,53E-04	0,90	4,76E-01
ARHGAP28	0,29	-6,21	7,14E-18	-0,23	1,00E+00	-1,61	4,15E-02
FOLR1	0,90	-6,21	4,68E-11	0,82	9,82E-01	-4,45	1,94E-05
CPA4	0,99	-6,43	2,29E-19	-2,87	3,71E-02	-2,12	4,97E-02
COL21A1	1,02	-6,49	2,98E-34	-4,08	6,05E-05	-4,16	4,32E-20
PTX3	281,69	-6,58	6,99E-193	-5,33	1,71E-16	0,55	5,95E-01
KIT	4,11	-6,67	1,39E-66	-5,38	7,73E-09	-1,13	6,56E-01
PALMD	1,30	-6,70	1,06E-29	-2,47	1,19E-01	-0,83	6,46E-01
CLEC3B	271,39	-6,76	1,11E-175	-2,90	1,10E-04	-4,39	4,64E-70
EGFL6	2,70	-6,97	7,10E-32	-3,39	1,79E-03	-0,99	4,15E-01
IGSF10	6,85	-7,14	2,40E-174	-5,53	4,02E-16	-3,47	5,03E-59

PDGFD	5,13	-7,18	3,26E-68	-3,82	5,51E-05	-2,94	5,30E-09
THSD7B	0,45	-7,19	4,20E-18	-4,73	9,48E-04	-3,71	2,12E-05
FGF18	8,00	-7,28	1,56E-53	-2,80	3,20E-03	-5,36	2,59E-30
RP11-88H9.1	0,76	-7,39	7,60E-16	-0,07	1,00E+00	-5,75	8,89E-11
ADH1A	4,57	-7,70	4,51E-38	-8,11	1,55E-12	-1,14	1,37E-01
MED12L	3,92	-7,86	8,09E-111	-5,23	6,15E-13	-4,08	4,48E-31
TMSB4Y	4,96	-8,64	2,53E-41	0,45	7,20E-01	-8,31	2,22E-21
ADH1B	37,18	-11,15	7,44E-174	-9,24	3,50E-32	-0,98	4,89E-02

Claims

1. A method of diagnosis or prognosis of a non-healing or chronic wound tissue comprising the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein:

- at least one of the following genes shows decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, ADAMTS7, CFB, COMP, ECM2, EDIL3, EFHD1, FOLR1, ITGA11, KIT, LBH, LGR5, MFAP5, NR4A3, OMD, PALM, PHACTR3, PI16, PPARG, PTH1R, PTX3, RCAN2, RSPO1, SPON2, TAGLN, TMEM37, TMSB4Y, TXNIP and WFDC1,

- or at least the following miRNA shows decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

AC084368.1,

- or at least one of the following genes shows a normal expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CNN1 and KRT16,

- or at least one of the following genes shows increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

AMIGO2, CCL11, CDC45L, CSF2, CSF3, FOXS1, GOS2, IF44L, INHBA, KPRP, LCP1, LPAR3, MICAL2, MT1F, MT1M, POLQ, POU2F2, RRM2, SERPINA9, SOX9, STC1, TFIP2 and UCN2,

- or at least one of the following miRNA shows increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
MIR147B and MIR1181.

2. A method of diagnosis or prognosis of a non-healing or chronic wound tissue according to claim 1 comprising the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein:
- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
ACTC1, ADAMTS7, COMP, ECM2, EDIL3, EFHD1, FOLR1, ITGA11, LBH, LGR5, MFAP5, OMD, PALM, PHACTR3, PI16, PTH1R, RSPO1, SPON2, TAGLN, TMEM37, TMSB4Y, TXNIP and WFDC1,

- or at least the following miRNA show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
AC084368.1,

- or at least one of the following genes shows a normal expression when compared to the expression in normal dermal fibroblasts of said mammalian:
CNN1 and KRT16,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
CCL11, CDC45L, CSF2, CSF3, GOS2, IF44L, KPRP, LCP1, LPAR3, MT1F, MT1M, POLQ, RRM2, SERPINA9, STC1 and TFIP2,

- or at least one of the following miRNA show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
MIR147B and MIR1181.

3. A method according to claim 1 or 2, furthermore comprising another step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein:
- at least one of the following genes shows decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
ACTA2, APOD, FGF9, ID4, POSTN and SMAD3,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
CXCL1, CXCL5, CXCL6, MMP10, MMP3, SERPINB2, SPHK1, HALPN1 and CTGF.

4. A method according to any one of the preceding claims, furthermore comprising another step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein:
- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
ACTA2, FGF9, ID4 and POSTN,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:
CXCL1, CXCL5, CXCL6, MMP10, MMP3 and SERPINB2.

5. A method of diagnosis or prognosis of a wound tissue developing an abnormal scar, such as a fibrosis, a hypertrophic scar or a keloid, comprising the step of determining the levels of expression of genes encoding different molecular markers in a sample of a wound from a mammalian, wherein said genes are defined as follows :

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

APOD, CFB, CXCL1, KIT, NR4A3, PPARG, PTX3, RCAN2, STC1 and TFPI2,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, AMIGO2, CNN1, COMP, CTGF, EDIL3, EFHD1, FOXS1, HAPLN1, INHBA, ITGA11, KRT16, MICAL2, PI16, POSTN, POU2F2, SOX9, SPHK1, TAGLN and UCN2.

6. A method of diagnosis or prognosis according to claim 5 wherein said genes are defined as follows :

- at least one of the following genes show decreased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

CXCL1, STC1 and TFPI2,

- or at least one of the following genes show increased expression when compared with the expression in normal dermal fibroblasts of said mammalian:

ACTC1, CNN1, COMP, EDIL3, EFHD1, ITGA11, KRT16, PI16, POSTN and TAGLN.

7. A method according to any preceding claims, wherein said wound tissue is human wound tissue, and normal dermal fibroblasts are Normal Human Dermal Fibroblasts (NHDF).

8. A method according to any preceding claims, wherein the normal dermal fibroblasts arise from the healthy skin of the said mammalian and more preferably the wound tissue and the normal dermal fibroblasts arise from the same animal or individual.

9. A method according to any preceding claims, wherein the said levels of expression of genes are determined by quantifying the corresponding RNA.

10. A method according to claim 9, wherein said RNA is chosen from mRNA and miRNA.

11. A method according to any one of claims 1-8, wherein the said levels of expression of genes are determined by quantifying the corresponding encoded proteins, except for the miRNA expression.

12. A method according to claim 11, wherein said proteins are measured by using antibodies.

13. A kit for performing any one or more of the aforementioned methods according to any one of claims 1-12, wherein said kit comprises:
(1) A plurality of probes for detecting and quantifying the expression levels of all the genes specified in table 1,
(2) Optionally, reagents and instructions pertaining to the use of said probes.

14. A kit for determining the prognosis of mammalian wound which comprises:
(1) A plurality of probes for detecting and quantifying the expression level of at least one RNA or protein of each one of the genes of table 1,

(2) Optionally, reagents and instructions pertaining to the use of said probes.

15. A microarray consisting of any one or more of the sets of probes in claims 13-14.

16. A kit for determining a wound type in a patient, comprising:

at least two microarrays comprising a plurality of probes for detecting and quantifying the expression levels of all the genes specified in any one of claims 1 to 12.

17. A method for treating a wound which comprises the step of performing any one or more of the methods according to claim 1-12 for determining the classification or prognosis of wound tissue in order to identify whether said wound tissue is chronic or non-healing or will become an abnormal scar, such as a fibrosis, a hypertrophic scar or a keloid or not and selecting an appropriate treatment based on the classification or prognosis of the wound tissue.

18. A therapy consisting in increasing the expression of PI16 in chronic or non-healing wound condition or in decreasing the expression of PI16 in fibrosis, hypertrophic scar or keloid.

FIGURE 1

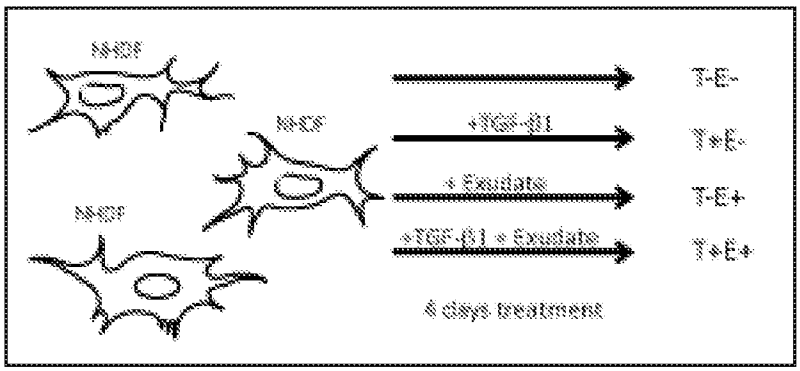


FIGURE 2

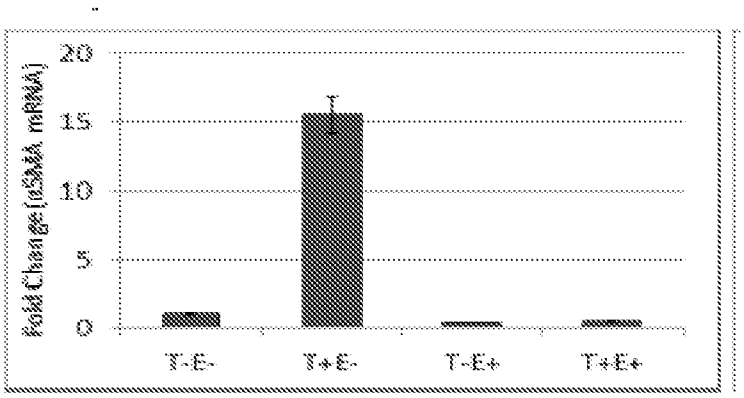


FIGURE 3

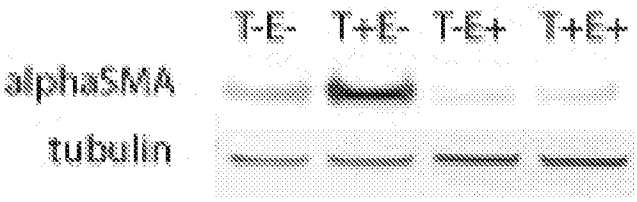
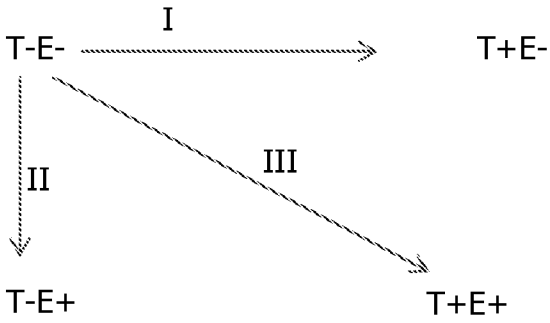


FIGURE 4



INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/000906

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	"GeneChip Human Genome U133 Set", INTERNET CITATION, 26 February 2003 (2003-02-26), XP002232760, Retrieved from the Internet: URL:http://www.affymetrix.com/support/technical/datasheets/hgu133_datasheet.pdf [retrieved on 2003-02-26]	13-16
A	the whole document	1-12,17, 18

Y	WO 2011/033249 A1 (UNIV CARDIFF [GB]; JIANG WENGUO [US]; HARDING KEITH GORDON [GB]) 24 March 2011 (2011-03-24) cited in the application	1-4,7-18
A	the whole document p. 4, ll. 10-32, p. 7, ll. 25-29, p. 14, ll. 19-27, claims 1-2, 20-24	5,6

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 February 2013	08/03/2013

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sauer, Tincuta

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/000906

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SABiosciences: "Human wound healing PCR array", , 19 December 2010 (2010-12-19), pages 1-5, XP002687677, Retrieved from the Internet: URL:http://web.archive.org/web/20101219235107/http://sabiosciences.com/rt_pcr_product/HTML/PAHS-121A.html [retrieved on 2012-11-20] the whole document p. 1	1-18
Y	CHEN LIN ET AL: "Positional differences in the wound transcriptome of skin and oral mucosa.", BMC GENOMICS 2010, vol. 11, 2010, page 471, XP0021072768, ISSN: 1471-2164 the whole document abstract, p. 8, col. 2, para. 1	1-18
Y	COOPER LISA ET AL: "Wound healing and inflammation genes revealed by array analysis of 'macrophageless' PU.1 null mice", GENOME BIOLOGY, BIOMED CENTRAL LTD., LONDON, GB, vol. 6, no. 1, 23 December 2004 (2004-12-23), page R5, XP021012937, ISSN: 1465-6906, DOI: 10.1186/GB-2004-6-1-R5 the whole document Fig. 3a, p. 5, col. 1	1-18
Y	SMITH JOAN C ET AL: "Gene profiling of keloid fibroblasts shows altered expression in multiple fibrosis-associated pathways.", THE JOURNAL OF INVESTIGATIVE DERMATOLOGY MAY 2008, vol. 128, no. 5, May 2008 (2008-05), pages 1298-1310, XP002687679, ISSN: 1523-1747	5-18
A	the whole document p. 1299, col. 1-2	1-4

-/--

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CHA ET AL: "Fibroblasts from non-healing human chronic wounds show decreased expression of betaig-h3, a TGF-beta inducible protein", JOURNAL OF DERMATOLOGICAL SCIENCE, ELSEVIER SCIENCE PUBLISHERS, SHANNON, IE, vol. 50, no. 1, 19 December 2007 (2007-12-19), pages 15-23, XP0022487263, ISSN: 0923-1811, DOI: 10.1016/J.JDERMSCI.2007.10.010 the whole document ----	1-18
Y	BYUNG-CHUL KIM ET AL: "Fibroblasts from chronic wounds show altered TGF-?-signaling and decreased TGF-? Type II Receptor expression", JOURNAL OF CELLULAR PHYSIOLOGY, vol. 195, no. 3, 1 June 2003 (2003-06-01), pages 331-336, XP055045109, ISSN: 0021-9541, DOI: 10.1002/jcp.10301 the whole document ----	1-18
Y	SHIH BARBARA ET AL: "Identification of novel keloid biomarkers through profiling of tissue biopsies versus cell cultures in keloid margin specimens compared to adjacent normal skin.", EPLASTY 2010, vol. 10, 2010, page e24, XP002687680, ISSN: 1937-5719 the whole document ----	1-18
T	BRIAN C. WULFF ET AL: "Novel differences in the expression of inflammation-associated genes between mid- and late-gestational dermal fibroblasts", WOUND REPAIR AND REGENERATION, 5 November 2012 (2012-11-05), pages 1-10, XP055045115, ISSN: 1067-1927, DOI: 10.1111/j.1524-475X.2012.00860.x the whole document Table 2, Fig. 2 ----	
Y	US 2009/305279 A1 (FERGUSON MARK WILLIAM JAMES [GB] ET AL) 10 December 2009 (2009-12-10) the whole document para. 24, Table 1 ----	1-18

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/000906

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TSOU RAYMOND ET AL: "Analysis of hypertrophic and normal scar gene expression with cDNA microarrays", JOURNAL OF BURN CARE AND REHABILITATION, MOSBY- YEARBOOK INC, US, vol. 21, no. 6, 1 November 2000 (2000-11-01), pages 541-550, XP009131413, ISSN: 0273-8481, DOI: 10.1097/00004630-200021060-00012 the whole document tables 5-7	1-18
Y	WO 2008/110356 A2 (FROST ROBERT [DE]; ENGELHARDT STEFAN [DE]) 18 September 2008 (2008-09-18) the whole document p. 13-14	1-18
Y	WO 2011/006214 A1 (PETER MACCALLUM CANCER INST [AU]; SPRUNG CARL N [AU]; MCKAY MICHAEL J) 20 January 2011 (2011-01-20) the whole document p. 8, l. 11 - p. 9, l. 7, p. 27, l. 25 - p. 28, l. 10	1-18
A	US 2009/220488 A1 (GARDNER HUMPHREY [US]) 3 September 2009 (2009-09-03) the whole document para. 2, 106	1-4,7-17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2012/000906

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

18(completely); 1-17(partially)

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17(partially)

methods and kit for classification of wounds(non-healing or chronic wounds, or abnormal scar) comprising determining the levels of expression of genes, wherein at least one gene is ACTC1;

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2. claims: 1-17(partially)

methods and kit for classification of wounds(non-healing or chronic wounds, or abnormal scar) comprising determining the levels of expression of genes, wherein at least one gene is ADAMTS7;

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3. claims: 18(completely); 1-17(partially)

methods and kit for classification of wounds(non-healing or chronic wounds, or abnormal scar) comprising determining the levels of expression of genes, wherein at least one gene is PI16;

4-57. claims: 1-17(partially)

methods and kit for classification of wounds(non-healing or chronic wounds, or abnormal scar) comprising determining the levels of expression of genes, wherein at least one gene is each further gene listed in claim 1.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2012/000906

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011033249 A1	24-03-2011	EP 2478374 A1	25-07-2012
		US 2012172250 A1	05-07-2012
		WO 2011033249 A1	24-03-2011
US 2009305279 A1	10-12-2009	AU 2007291074 A1	06-03-2008
		CA 2661699 A1	06-03-2008
		EP 2059611 A2	20-05-2009
		JP 2010502177 A	28-01-2010
		US 2009305279 A1	10-12-2009
		WO 2008025961 A2	06-03-2008
		ZA 200900638 A	28-04-2010
WO 2008110356 A2	18-09-2008	NONE	
WO 2011006214 A1	20-01-2011	NONE	
US 2009220488 A1	03-09-2009	US 2009220488 A1	03-09-2009
		WO 2007027509 A2	08-03-2007