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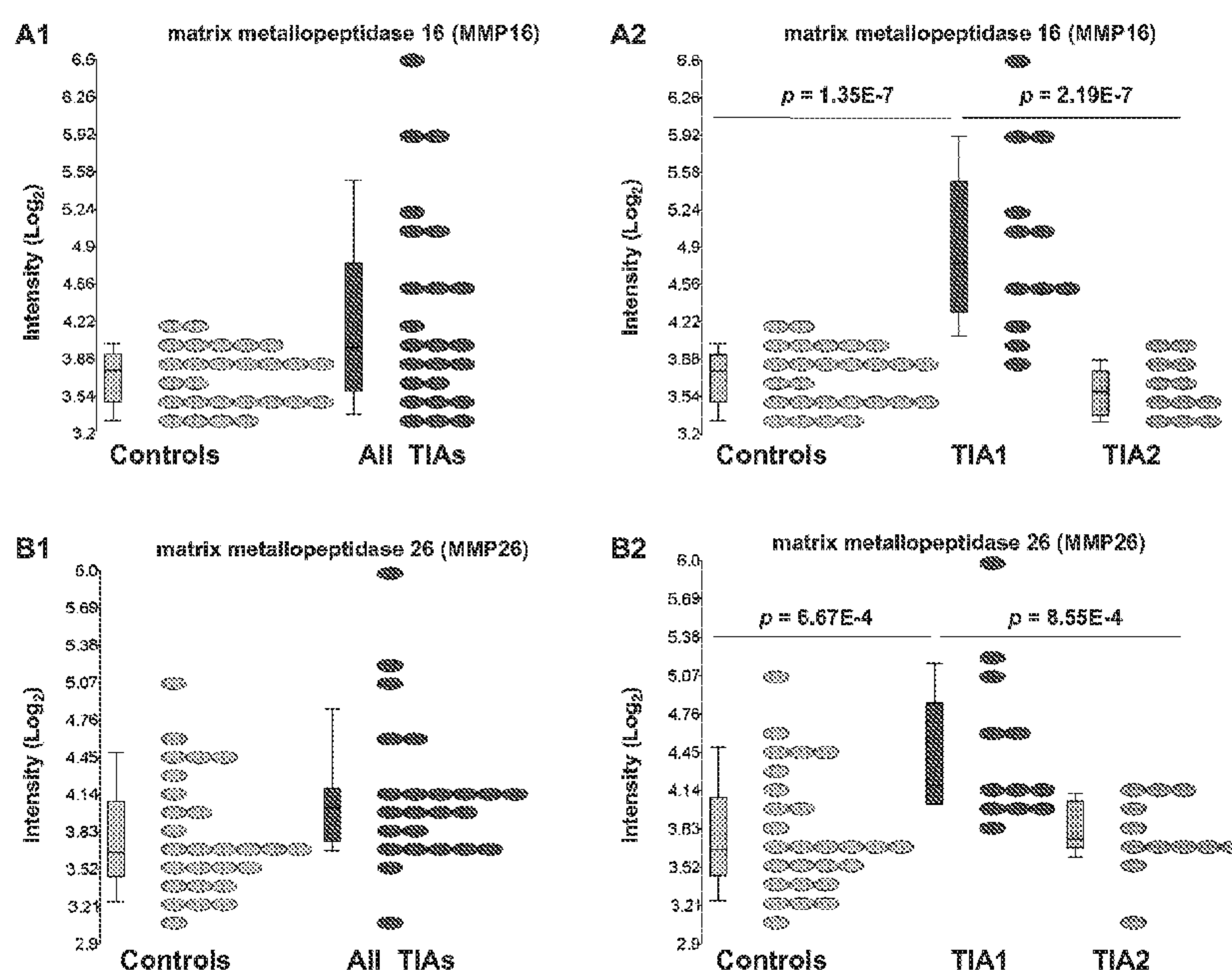


Figure 4

(57) Abrégé/Abstract:

The present invention provides methods and compositions for diagnosing and predicting the risk and cause of transient ischemic attacks (TIA).



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(54) Title: BIOMARKERS FOR DIAGNOSIS OF TRANSIENT ISCHEMIC ATTACKS

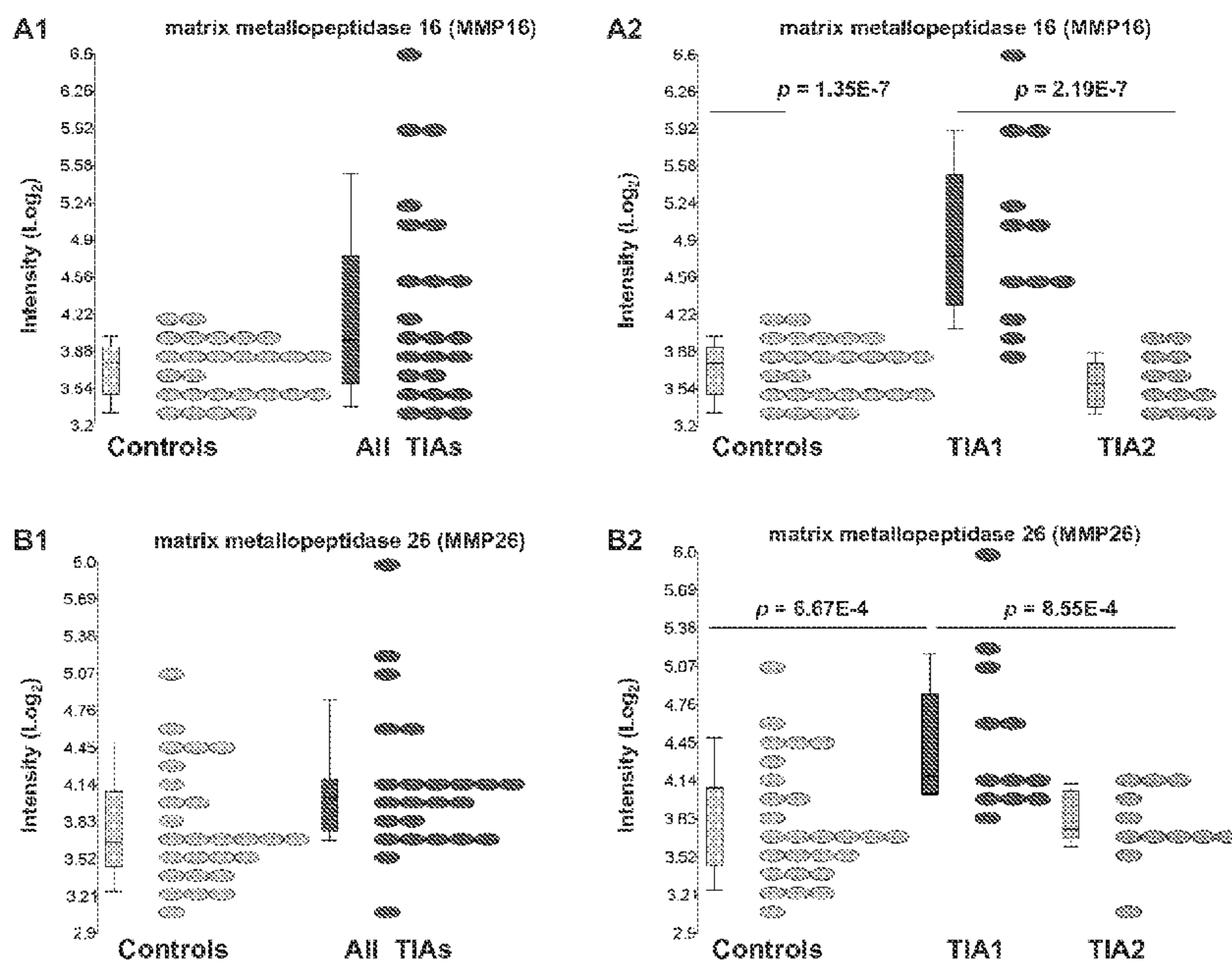


Figure 4

(57) Abstract: The present invention provides methods and compositions for diagnosing and predicting the risk and cause of transient ischemic attacks (TIA).

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BIOMARKERS FOR DIAGNOSIS OF TRANSIENT ISCHEMIC ATTACKS

CROSS-REFERENCE TO RELATED APPLICATIONS

5 [0001] This application claims the benefit of U.S. Provisional Application No. 61/364,334, filed on July 14, 2010, the entire disclosure of which is hereby incorporated herein by reference for all purposes.

STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY SPONSORED RESEARCH AND DEVELOPMENT

10 [0002] This invention was made with Government support under Grant No. NS056302, awarded by the National Institutes of Health. The government has certain rights in this invention.

FIELD OF THE INVENTION

[0003] The present invention provides methods and compositions for diagnosing
15 and predicting the risk and cause of transient ischemic attacks (TIA).

BACKGROUND OF THE INVENTION

[0004] Transient ischemic attacks (TIAs) are common, affecting over 300,000 persons per year in the United States alone. Though TIA symptoms resolve by definition, TIAs are far from benign. As many as 25% of TIA patients have recurrent
20 ischemic vascular events that occur within days to weeks following a TIA (1-3). Despite the high incidence and clinical importance, the development of therapies specifically targeted toward TIA has been limited by the paucity of knowledge regarding the underlying biology. Furthermore, the clinical diagnosis of TIA is imperfect and extensive evaluation in those incorrectly diagnosed with TIA is costly
25 (4).

[0005] We have previously demonstrated that blood gene expression profiles in rats change following experimental ischemic strokes and TIAs (5). Very brief focal ischemia in rats, simulating human TIA, elicits a dramatic change in brain tissue

characterized by increased Heat Shock Protein (HSP70) expression, microglial activation and macrophage infiltration (6). This change in brain cellular function and inflammation alters blood immune cells, a process that can be detected using whole genome expression analysis (5). Furthermore, the genes and associated functional pathways differ markedly between very brief focal ischemia and ischemic stroke (5).

[0006] Human TIAs have also been associated with alterations in systemic inflammation. TIA patients tend to have elevated C-reactive protein (CRP) (7), IL-6, VCAM-1 and cytokine levels, as well as elevated leukocyte counts (8-10). Lp-PLA2, a marker of unstable atherosclerotic plaque, is also associated with TIA (11-12) as are fibrinogen (13-14) and D-Dimer (15). Whether such biological differences represent a cause or consequence of TIA remains unclear. However, better understanding of the pathophysiology represented by such differences will facilitate development of treatments targeted to TIA.

[0007] Gene expression has been useful for identifying differences between patients with ischemic stroke and controls (16-18), but such studies have not been applied to TIA. The present invention is based, in part, on gene expression profiles that provide insight into the immunological differences that exist in patients with TIAs.

BRIEF SUMMARY OF THE INVENTION

[0008] The present invention provides compositions and methods for determining the occurrence, predicting the risk of occurrence and predicting the cause of transient ischemic attacks.

[0009] Accordingly, in one aspect, the invention provides methods for diagnosing a transient ischemic attack (TIA) or a predisposition for experiencing TIA, the method comprising: determining a level of expression of a plurality of TIA-associated biomarkers in a biological sample from a patient, wherein an increase or decrease of the level of expression compared to a control indicates that the patient has suffered or is at risk of experiencing TIA, wherein the plurality of TIA-associated biomarkers is selected from the biomarkers set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and 9.

[0010] In some embodiments, the methods further comprise obtaining a biological sample from the patient. In some embodiments, the biological sample is blood, serum or plasma.

[0011] In some embodiments, the determining step is performed at 3 or fewer hours after a suspected ischemic event. In some embodiments, the determining step is performed at 3 or more hours after a suspected ischemic event, for example, at about 6, 12, 24, 36, 48 or more hours after a suspected ischemic event. In some
 5 embodiments, the determining step is performed at least 24 hours after a suspected ischemic event.

[0012] In some embodiments, an increased expression level of one or more or all TIA-associated biomarkers selected from the group consisting of DKFZP434B061, FAM55D, FLJ30375, IGFBP5, LTBR and SCN2A indicates that the patient has
 10 suffered or is at risk of experiencing TIA. In some embodiments, an increased expression level of one or more or all TIA-associated biomarkers selected from the group consisting of GABRB2, ELAVL3, TWIST1, DPPA4, DKFZP434P211, DLX6, ZNF479, ASTN2, SNX31, ALS2CR11, LOC440345 indicates that the patient has suffered or is at risk of experiencing TIA.

[0013] In some embodiments, an increased expression level of one or more or all TIA-associated biomarkers selected from the group consisting of GABRB2, ELAVL3, COL1A1, SHOX2, GABRB2, TWIST1, DPPA4, DKFZP434P211, WIT1, SOX9, DLX6, ANXA3, EPHA3, SOX11, SLC26A8, CCRL1, FREM2, STOX2, ZNF479, LOC338862, ASTN2, FOLH1, SNX31, KREMEN1, ZNF479, ALS2CR11,
 15 FIGN, RORB, LOC732096, GYPA, ALPL, LHX2, GALNT5, SRD5A2L2, GALNT14, OVOL2, BMPR1B, UNC5B, ODZ2, ALPL, RASAL2, SHOX, C19orf59, ZNF114, SRGAP1, ELAVL2, NCRNA00032, LOC440345, FLJ30375, TFPI, PTGR1, ROBO1, NR2F2, GRM5, LUM, FLJ39051, COL1A2, CASP5, OPCML, TTC6, TFAP2B, CRISP2, SOX11, ANKRD30B, FLJ39051, SCN2A, MYNN,
 20 FOXA2, DKFZP434B061, LOC645323, SNIP, LOC645323, LOC374491, ADAM30, SIX3, FLJ36144, CARD8, KREMEN1, RP1-127L4.6, FAM149A, B3GAT2, SPOCK3, G30, ITGBL1, IQGAP3, C7orf45, ZNF608, LOC375010, LRP2, TGFB2, SHOX2, HOXC4 /// HOXC6, ELTD1, FAM182B /// RP13-401N8.2, PRO0478, LIFR, FOLH1, EHF, NDST3, BRUNOL5, LOC728460, PDE1A, POU2AF1, FAT1,
 25 PCDH11X /// PCDH11Y, FLJ37786, SLC22A4, DHRS13, EHF, MEG3, PIWIL1, LOC203274, LOC100133920 /// LOC286297, DMRT1, ADM, VWA3B, GAFA3, HESX1, ADAMDEC1, CAV1, LAMB4, TPTE, PPP1R1C, HPSE, AIM2, RUNDC3B, CARD16, FAM124A, MGC39584, OSM, RFX2, MYBPC1, LTBR,

C18orf2, SNRPN, FLJ36031, IL1B, TRPM1, OSTCL, MAPK14, KCNJ15 ///
 LOC100131955, FIGN, HNT, S100A12, CHIT1, C7orf53, FAM13A1, GNAO1,
 MAPK14, FAM55D, PRKD2, LIMK2, C18orf54, IGFBP5, EVI1, PLSCR1, FOXC1,
 LOC646627, ZNF462, CNTLN, ZNF438, DEFB105A /// DEFB105B, LOC340017,
 5 C1orf67, ACSL1, ADH1B, SLC2A14 /// SLC2A3, IL1B, ST3GAL4, UBE2J1,
 PNPLA3 and PAPP A indicates that the patient has suffered or is at risk of
 experiencing TIA.

[0014] In some embodiments, a decreased expression level of one or more or all
 TIA-associated biomarkers selected from the group consisting of ATG9B, DIP2C,
 10 EDAR, GSTM1, GUSBL2, SMURF2, ZNF512B indicates that the patient has
 suffered or is at risk of experiencing TIA.

[0015] In some embodiments, a decreased expression level of one or more or all
 TIA-associated biomarkers selected from the group consisting of NBPF10 /// RP11-
 94I2.2, SFXN1, SPIN3, UNC84A, OLFM2, PPM1K, P2RY10, ZNF512B,
 15 MORF4L2, GIGYF2, ERAP2, SLFN13, LOC401431, MED6, BAIAP2L1 ///
 LOC100128461, LNPEP, MBNL1, NOS3, MCF2L, KIAA1659, SCAMP5,
 LOC648921, ANAPC5, SPON1, FUS, GPR22, GAL3ST4, METTL3,
 LOC100131096, FAAH2, SMURF2, SNRPN, FBLN7, GLS, G3BP1, RCAN3,
 EPHX2, DIP2C, CCDC141, CLTC, FOSB, CACNA1I, UNQ6228, ATG9B, AK5,
 20 SPIN3, RBM14, SNRPN, MAN1C1, HELLS, EDAR, SLC3A1, ZNF519,
 LOC100130070 /// LOC100130775 /// LOC100131787 /// LOC100131905 ///
 LOC100132291 /// LOC100132488 /// RPS27, ZC3H12B, IQGAP2, SOX8,
 WHDC1L2, TNPO1, TNFRSF21, TSHZ2, DMRTC1 /// DMRTC1B, GSTM1,
 GSTM2, PNMA6A, CAND1, CCND3, GSTM1, GUSBL2 indicates that the patient
 25 has suffered or is at risk of experiencing TIA.

[0016] In some embodiments, an increased expression level of 2, 3, 4, 5, 6, 7, or
 more or all, TIA-associated biomarkers selected from the group consisting of
 FLJ30375, SCN2A, DKFZP434B061, LTBR, FAM55D, and IGFBP5 and a decreased
 expression level of 2, 3, 4, 5, 6, 7, or more or all, TIA-associated biomarkers selected
 30 from the group consisting of GUSBL2, GSTM1, EDAR, ATG9B, DIP2C, SMURF2,
 and ZNF512B indicates that the patient has suffered or is at risk of experiencing TIA.

[0017] In some embodiments, the methods further comprise determining the level of expression of one or biomarkers selected from the group consisting of CNTN4, TLR5, GPR84, BCL6, NELL2, APBA2 and MLL. In some embodiments, detection of an increased level of expression of a biomarker selected from CNTN4, TLR5, 5 GPR84 and BCL6 indicates that the patient has suffered or is at risk of experiencing TIA. In some embodiments, detection of a decreased level of expression of a biomarker selected from NELL2, APBA2 and MLL indicates that the patient suffered or is at risk of experiencing TIA.

[0018] In some embodiments, the methods further comprises the step of 10 determining the cause of stroke. In some embodiments, the patient overexpresses a plurality of genes listed in Table 7, indicative of a chronic inflammatory state. In some embodiments, the level of expression of one or more or all genes selected from the group consisting of MMP16, MMP19, MMP26, COL1A1, COL1A2, COL3A1, COL10A1, COL11A1, COL25A1, COL27A1, FGFs and EGFR is increased in 15 comparison to the control, and the patient is determined to have atherosclerosis.

[0019] In some embodiments, the patient is exhibiting symptoms of TIA. In some embodiments, the patient is asymptomatic.

[0020] In some embodiments, the methods further comprise the step of providing an appropriate treatment or prevention regime for TIA to the patient.

20 [0021] In some embodiments, the level of expression of the biomarker is determined at the transcriptional level. For example, RNA levels of the biomarker can be determined. The RNA can be mRNA, rRNA, tRNA or microRNA (miRNA). In some embodiments, the level of RNA expression is determined using a microarray.

25 [0022] In some embodiments, the level of expression is determined by detecting hybridization of an TIA-associated gene probe to gene transcripts of the biomarkers in the biological sample.

[0023] In some embodiments, the hybridization step is performed on a nucleic acid microarray chip. In some embodiments, the hybridization step is performed in a microfluidics assay plate.

[0024] In some embodiments, the level of expression is determined by amplification of gene transcripts of the biomarkers. In some embodiments, the amplification reaction is a polymerase chain reaction (PCR).

[0025] In some embodiments, the level of expression of the biomarker is
5 determined at the protein level.

[0026] In some embodiments, the level of expression of at least 15 biomarkers is determined. In some embodiments, the level of expression of about 15-85, 20-70, 30-60 or 40-50 biomarkers are determined. In some embodiments, about 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more, biomarkers are
10 determined. The levels of expression of the plurality of biomarkers can be concurrently or sequentially determined.

[0027] In some embodiments, the control is the expression level of a plurality of expressed endogenous reference biomarkers. In some embodiments, the one or more or all endogenous reference biomarkers are listed in Table 3. In some embodiments,
15 the TIA-associated biomarkers are overexpressed or underexpressed at least about 1.2-fold, 1.3-fold, 1.4-fold, 1.5-fold, 1.6-fold, 1.7-fold, 1.8-fold, 1.9-fold, 2.0-fold, 2.1 fold, 2.2-fold, 2.3-fold, 2.4-fold, 2.5-fold, 2.6-fold, 2.7-fold, 2.8-fold, 2.9-fold, 3.0-fold, 3.1-fold, 3.2-fold, 3.3-fold, 3.4-fold or 3.5-fold, or more, in comparison to the expression levels of a plurality of stably expressed endogenous reference biomarkers,
20 e.g., those listed in Table 3. In some embodiments, the expression levels of 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, or all, the endogenous reference biomarkers selected from the group consisting of USP7, MAPRE2, CSNK1G2, SAFB2, PRKAR2A, PI4KB, CRTC1, HADHA, MAP1LC3B, KAT5, CDC2L1 /// CDC2L2, GTSE1, CDC2L1 /// CDC2L2, TCF25, CHP, LRRC40, hCG_2003956 /// LYPLA2 ///
25 LYPLA2P1, DAXX, UBE2NL, EIF1, KCMF1, PRKRIP1, CHMP4A, TMEM184C, TINF2, PODNL1, FBXO42, LOC441258, RRP1, C10orf104, ZDHHC5, C9orf23, LRRC45, NACC1, LOC100133445 /// LOC115110, PEX16 are determined as a control.

[0028] In some embodiments, the control is the expression level of the same
30 biomarker in a healthy individual. In some embodiments, the control is the expression level of the same biomarker in an individual who has not experienced a vascular event (e.g., TIA, ischemic stroke, myocardial infarction, peripheral vascular

disease, or venous thromboembolism). In some embodiments, the control is a threshold level of expression, *e.g.*, of the same TIA-associated biomarker, optionally normalized to the expression level of a stably expressed endogenous reference biomarker, representative of a population of healthy individuals.

5 [0029] In a related aspect, the invention provides a solid support comprising a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9, wherein the nucleic acids are attached to the solid support. In some embodiments, the solid support comprises a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Tables 1 and 2. The solid
10 support can further comprise a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 3. The solid support can be attached to at least about 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 75, 80, 85, 90, 95 or 100, or more, genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8, 9 and/or 3. The solid support can be a microarray.

[0030] In one embodiment, the solid support comprises 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,
15 12, 13, 14, or more or all, nucleic acids that hybridize to a plurality of the genes selected from the group consisting of GUSBL2, GSTM1, FLJ30375, SCN2A, DKFZP434B061, EDAR, ATG9B, DIP2C, LTBR, SMURF2, FAM55D, IGFBP5, and ZNF512B.

DEFINITIONS

20 [0031] Unless defined otherwise, all technical and scientific terms used herein generally have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Generally, the nomenclature used herein and the laboratory procedures in cell culture, molecular genetics, organic chemistry and nucleic acid chemistry and hybridization described below are those well known and
25 commonly employed in the art. Standard techniques are used for nucleic acid and peptide synthesis. Generally, enzymatic reactions and purification steps are performed according to the manufacturer's specifications. The techniques and procedures are generally performed according to conventional methods in the art and various general references (*see generally*, Sambrook et al. MOLECULAR
30 CLONING: A LABORATORY MANUAL, 3rd ed. (2001) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. and Ausubel, *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, 1990-2008, Wiley Interscience), which

are provided throughout this document. The nomenclature used herein and the laboratory procedures in analytical chemistry, and organic synthetic described below are those well known and commonly employed in the art. Standard techniques, or modifications thereof, are used for chemical syntheses and chemical analyses.

5 [0032] “Ischemia” or “ischemic event” as used herein refers to diseases and disorders characterized by inadequate blood supply (*i.e.*, circulation) to a local area due to blockage of the blood vessels to the area. Ischemia includes for example, strokes and transient ischemic attacks. Strokes include, *e.g.*, ischemic stroke (including, but not limited to, cardioembolic strokes, atheroembolic or
10 atherothrombotic strokes, *i.e.*, strokes caused by atherosclerosis in the carotid, aorta, heart, and brain, small vessel strokes (*i.e.*, lacunar strokes), strokes caused by diseases of the vessel wall, *i.e.*, vasculitis, strokes caused by infection, strokes caused by hematological disorders, strokes caused by migraines, and strokes caused by medications such as hormone therapy), hemorrhagic ischemic stroke, intracerebral
15 hemorrhage, and subarachnoid hemorrhage.

[0033] The term “transient ischemic attack,” “TIA,” or “mini-stroke” interchangeably refer to a change in the blood supply to a particular area of the brain, resulting in brief neurologic dysfunction that persists, by definition, for less than 24 hours. By definition, a TIA resolves within 24 hours, but most TIA symptoms resolve
20 within a few minutes. If symptoms persist longer, then it is categorized as a stroke. Symptoms include temporary loss of vision (typically amaurosis fugax); difficulty speaking (aphasia); weakness on one side of the body (hemiparesis); numbness or tingling (paresthesia), usually on one side of the body, and dizziness, lack of coordination or poor balance. The symptoms of a TIA usually last a few seconds to a
25 few minutes and most symptoms disappear within 60 minutes.

[0034] “TIA reference expression profile” refers to the pattern of expression of a set of genes (*e.g.*, a plurality of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9 differentially expressed (*i.e.*, overexpressed or underexpressed) in an individual who has suffered or is at risk of experiencing TIA relative to the expression
30 in a control (*e.g.*, the expression level in an individual free of an ischemic event or the expression level of a stably expressed endogenous reference biomarker). A gene from Tables 1, 5B, 5C, 5D, 7, 8 and/or 9 that is expressed at a level that is at least about

1.5-, 1.6-, 1.7-, 1.8-, 1.9-, 2.0-, 2.1-, 2.2-, 2.3-, 2.4-, 2.5-, 2.6-, 2.7-, 2.8-, 2.9-, 3.0-, 3.1-, 3.2-, 3.3-, 3.4- or 3.5-fold higher than the level in a control is a gene overexpressed in TIA and a gene from Tables 2, 5A, 5C, 5D, 7, 8 and/or 9 that is expressed at a level that is at least about 1.5-, 1.6-, 1.7-, 1.8-, 1.9-, 2.0-, 2.1-, 2.2-, 2.3-, 2.4-, 2.5-, 2.6-, 2.7-, 2.8-, 2.9-, 3.0-, 3.1-, 3.2-, 3.3-, 3.4- or 3.5-fold lower than the level in a control is a gene underexpressed in TIA. Alternately, genes that are expressed at a level that is at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% higher than the level in a control is a gene overexpressed in TIA and a gene that is expressed at a level that is at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% lower than the level in a control is a gene underexpressed in TIA.

[0035] A “plurality” refers to two or more, for example, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or more (*e.g.*, genes). In some embodiments, a plurality refers to concurrent determination of expression levels about 15-85, 20-60 or 40-50 genes, for example, about 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more, genes. In some embodiments, “plurality” refers to all genes listed in one or more or all tables, *e.g.*, all genes listed in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9.

[0036] The terms “patient,” “subject” or “individual” interchangeably refers to a mammal, for example, a human or a non-human mammal, including primates (*e.g.*, macaque, pan troglodyte, pongo), a domesticated mammal (*e.g.*, felines, canines), an agricultural mammal (*e.g.*, bovine, ovine, porcine, equine) and a laboratory mammal or rodent (*e.g.*, rattus, murine, lagomorpha, hamster, guinea pig).

[0037] “Sample” or “biological sample” includes sections of tissues such as biopsy and autopsy samples, and frozen sections taken for histologic purposes. Such samples include blood, sputum, tissue, lysed cells, brain biopsy, cultured cells, *e.g.*, primary cultures, explants, and transformed cells, stool, urine, etc. A biological sample is typically obtained from a eukaryotic organism, most preferably a mammal such as a primate, *e.g.*, chimpanzee or human; cow; dog; cat; a rodent, *e.g.*, guinea pig, rat, mouse; rabbit; or a bird; reptile; or fish.

[0038] “Array” as used herein refers to a solid support comprising attached nucleic acid or peptide probes. Arrays typically comprise a plurality of different nucleic acid

or peptide probes that are coupled to a surface of a substrate in different, known locations. These arrays, also described as “microarrays” or colloquially “chips” have been generally described in the art, for example, U.S. Patent Nos. 5,143,854, 5,445,934, 5,744,305, 5,677,195, 6,040,193, 5,424,186 and Fodor *et al.*, *Science*,
5 251:767-777 (1991). These arrays may generally be produced using mechanical synthesis methods or light directed synthesis methods which incorporate a combination of photolithographic methods and solid phase synthesis methods. Techniques for the synthesis of these arrays using mechanical synthesis methods are described in, *e.g.*, U.S. Patent No. 5,384,261. Arrays may comprise a planar surface
10 or may be nucleic acids or peptides on beads, gels, polymeric surfaces, fibers such as fiber optics, glass or any other appropriate substrate as described in, *e.g.*, U.S. Patent No. 5,770,358, 5,789,162, 5,708,153, 6,040,193 and 5,800,992. Arrays may be packaged in such a manner as to allow for diagnostics or other manipulation of an all inclusive device, as described in, *e.g.*, U.S. Patent Nos. 5,856,174 and 5,922,591.

15 [0039] The term “gene” means the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding region (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons).

[0040] The terms “nucleic acid” and “polynucleotide” are used interchangeably
20 herein to refer to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. The term encompasses nucleic acids containing known nucleotide analogs or modified backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in
25 a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides, peptide-nucleic acids (PNAs).

[0041] Unless otherwise indicated, a particular nucleic acid sequence also
30 encompasses conservatively modified variants thereof (*e.g.*, degenerate codon substitutions) and complementary sequences, as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by

generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzner *et al.*, *Nucleic Acid Res.* 19:5081 (1991); Ohtsuka *et al.*, *J. Biol. Chem.* 260:2605-2608 (1985); Rossolini *et al.*, *Mol. Cell. Probes* 8:91-98 (1994)). The term nucleic acid is
5 used interchangeably with gene, cDNA, mRNA, oligonucleotide, and polynucleotide.

[0042] The phrase “stringent hybridization conditions” refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acid, but to no other sequences. Stringent hybridization conditions are sequence-dependent and will be different in different circumstances. Longer
10 sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, *Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Probes*, “Overview of principles of hybridization and the strategy of nucleic acid assays” (1993). Generally, stringent hybridization conditions are selected to be about 5-10°C lower than the thermal
15 melting point for the specific sequence at a defined ionic strength Ph . The T_m is the temperature (under defined ionic strength, Ph , and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m , 50% of the probes are occupied at equilibrium). Stringent hybridization conditions will be those in
20 which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at Ph 7.0 to 8.3 and the temperature is at least about 30°C for short probes (*e.g.*, 10 to 50 nucleotides) and at least about 60°C for long probes (*e.g.*, greater than 50 nucleotides). Stringent hybridization conditions may also be achieved with the addition of destabilizing agents such as
25 formamide. For selective or specific hybridization, a positive signal is at least two times background, optionally 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C.

30 [0043] Nucleic acids that do not hybridize to each other under stringent hybridization conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, for example, when a copy of a nucleic

acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary “moderately stringent hybridization conditions” include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 1X SSC at 45°C. A positive hybridization is at least twice background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency.

[0044] The terms “isolated,” “purified,” or “biologically pure” refer to material that is substantially or essentially free from components that normally accompany it as found in its native state. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein that is the predominant species present in a preparation is substantially purified. The term “purified” denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Particularly, it means that the nucleic acid or protein is at least 85% pure, more preferably at least 95% pure, and most preferably at least 99% pure.

[0045] The term “heterologous” when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not found in the same relationship to each other in nature. For instance, the nucleic acid is typically recombinantly produced, having two or more sequences from unrelated genes arranged to make a new functional nucleic acid, *e.g.*, a promoter from one source and a coding region from another source. Similarly, a heterologous protein indicates that the protein comprises two or more subsequences that are not found in the same relationship to each other in nature (*e.g.*, a fusion protein).

[0046] An “expression vector” is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

[0047] The terms “polypeptide,” “peptide” and “protein” are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of

a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer.

[0048] The term “amino acid” refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner similar to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, *e.g.*, hydroxyproline, α -carboxyglutamate, and O-phosphoserine. “Amino acid analogs” refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, *i.e.*, an α carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, *e.g.*, homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups (*e.g.*, norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. “Amino acid mimetics” refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions in a manner similar to a naturally occurring amino acid.

[0049] Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

[0050] “Conservatively modified variants” applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given protein. For instance, the codons GCA, GCC, GCG and GCU all encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to any of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are “silent variations,” which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes every possible silent variation of

the nucleic acid. One of skill will recognize that each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, each silent variation of a nucleic acid which
 5 encodes a polypeptide is implicit in each described sequence.

[0051] As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a “conservatively modified variant” where the
 10 alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitution tables providing functionally similar amino acids are well known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention.

[0052] The following eight groups each contain amino acids that are conservative
 15 substitutions for one another:

- 1) Alanine (A), Glycine (G);
 - 2) Aspartic acid (D), Glutamic acid (E);
 - 3) Asparagine (N), Glutamine (Q);
 - 4) Arginine I, Lysine (K);
 - 20 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V);
 - 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W);
 - 7) Serine (S), Threonine (T); and
 - 8) Cysteine (C), Methionine (M)
- (see, e.g., Creighton, *Proteins* (1984)).

25 [0053] The terms “identical” or percent “identity,” in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (*i.e.*, 60% identity, preferably 65%, 70%, 75%, 80%, 85%, 90%, or 95% identity over a specified region of a TIA-associated gene (*e.g.*, a
 30 gene set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9), when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by

manual alignment and visual inspection. Such sequences are then said to be “substantially identical.” This definition also refers to the compliment of a test sequence. Preferably, the identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

[0054] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters. For sequence comparison of nucleic acids and proteins to TIA-associated nucleic acids and proteins, the BLAST and BLAST 2.0 algorithms and the default parameters discussed below are used.

[0055] A “comparison window”, as used herein, includes reference to a segment of any one of the number of contiguous positions selected from the group consisting of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, *e.g.*, by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat’l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (see, *e.g.*, Current Protocols in Molecular Biology (Ausubel *et al.*, eds. 1995 supplement)).

[0056] A preferred example of algorithm that is suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.*, *Nuc. Acids Res.* 25:3389-3402 (1997) and

Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990), respectively. BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a word length (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a word length of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

[0057] The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, *e.g.*, Karlin & Altschul, *Proc. Nat'l. Acad. Sci. USA* 90:5873-5787 (1993)). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference

nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001.

[0058] An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second polypeptide, for example, where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequence.

[0059] The phrase “selectively (or specifically) hybridizes to” refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (e.g., total cellular or library DNA or RNA).

[0060] By “host cell” is meant a cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be, for example, prokaryotic cells such as *E. coli* or eukaryotic cells such as yeast cells or mammalian cells such as CHO cells.

[0061] “Inhibitors,” “activators,” and “modulators” of expression or of activity are used to refer to inhibitory, activating, or modulating molecules, respectively, identified using *in vitro* and *in vivo* assays for expression or activity, e.g., ligands, agonists, antagonists, and their homologs and mimetics. The term “modulator” includes inhibitors and activators. Inhibitors are agents that, e.g., inhibit expression of a polypeptide or polynucleotide of the invention or bind to, partially or totally block stimulation or enzymatic activity, decrease, prevent, delay activation, inactivate, desensitize, or down regulate the activity of a polypeptide or polynucleotide of the invention, e.g., antagonists. Activators are agents that, e.g., induce or activate the expression of a polypeptide or polynucleotide of the invention or bind to, stimulate, increase, open, activate, facilitate, enhance activation or enzymatic activity, sensitize or up regulate the activity of a polypeptide or polynucleotide of the invention, e.g.,

agonists. Modulators include naturally occurring and synthetic ligands, antagonists, agonists, small chemical molecules and the like. Assays to identify inhibitors and activators include, e.g., applying putative modulator compounds to cells, in the presence or absence of a polypeptide or polynucleotide of the invention and then
5 determining the functional effects on a polypeptide or polynucleotide of the invention activity. Samples or assays comprising a polypeptide or polynucleotide of the invention that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of effect. Control samples (untreated with modulators) are assigned a
10 relative activity value of 100%. Inhibition is achieved when the activity value of a polypeptide or polynucleotide of the invention relative to the control is about 80%, optionally 50% or 25-1%. Activation is achieved when the activity value of a polypeptide or polynucleotide of the invention relative to the control is 110%, optionally 150%, optionally 200-500%, or 1000-3000% higher.

15 [0062] The term “test compound” or “drug candidate” or “modulator” or grammatical equivalents as used herein describes any molecule, either naturally occurring or synthetic, e.g., protein, oligopeptide (e.g., from about 5 to about 25 amino acids in length, preferably from about 10 to 20 or 12 to 18 amino acids in length, preferably 12, 15, or 18 amino acids in length), small organic molecule,
20 polysaccharide, lipid, fatty acid, polynucleotide, RNAi, oligonucleotide, etc. The test compound can be in the form of a library of test compounds, such as a combinatorial or randomized library that provides a sufficient range of diversity. Test compounds are optionally linked to a fusion partner, e.g., targeting compounds, rescue compounds, dimerization compounds, stabilizing compounds, addressable
25 compounds, and other functional moieties. Conventionally, new chemical entities with useful properties are generated by identifying a test compound (called a “lead compound”) with some desirable property or activity, e.g., inhibiting activity, creating variants of the lead compound, and evaluating the property and activity of those variant compounds. Often, high throughput screening (HTS) methods are employed
30 for such an analysis.

[0063] A “small organic molecule” refers to an organic molecule, either naturally occurring or synthetic, that has a molecular weight of more than about 50 Daltons and less than about 2500 Daltons, preferably less than about 2000 Daltons, preferably

between about 100 to about 1000 Daltons, more preferably between about 200 to about 500 Daltons.

BRIEF DESCRIPTION OF THE DRAWINGS

[0064] **Figures 1A-B.** Heat map of 460 genes/probes differentially expressed in blood between Transient Ischemic Attack (TIA) patients and controls ($FDR \leq 0.05$, absolute fold change >1.5). Each column on the X axis represents 1 patient, with 24 TIA patients (blue) and 27 controls (pink). Each row on the Y axis represents individual genes. TIAs cluster separately from controls as indicated by the green arrow (top). Within TIA subjects, at least two clusters are apparent as indicated by the red arrow. These two TIA clusters are labeled TIA1 and TIA2. Two TIA patients (ID: 57 and 90) clustered with controls. Three controls (ID: 42, 68, and 74) clustered with TIAs. Red = up regulation. Green = down regulation. ID = subjects ID. Diagnosis = blue (TIA) and pink (Controls).

[0065] **Figure 2.** Cross-validation results for the 34 out of 460 TIA regulated genes that distinguish TIA patients from control subjects. The probability of predicted diagnosis is shown on the Y axis, and subjects are shown on the X axis. TIA patients are shown on the right, and Control subjects on the left. The predicted probability of TIA is shown in red, and the predicted probability of being control is shown in blue. TIA patients were distinguished from controls with 87.5% sensitivity and 96.3% specificity using a 10-fold cross-validation.

[0066] **Figure 3.** Cross-validation results for the 26 up-regulated genes identified by PAM to distinguish the TIA1 from TIA2 groups. The probability of the predicted diagnosis is shown on the Y axis, and subjects are shown on the X axis. TIA1 subjects are shown on the left, and TIA2 subjects on the right. The predicted probability of TIA2 is shown in red, and the predicted probability of TIA1 is shown in blue. TIA1 could be distinguished from TIA2 patients with 100% sensitivity and 100% specificity.

[0067] **Figures 4A-B.** MMP16 (A) and MMP26 (B) transcript expression in TIA patients (blue) and control subjects (pink). **A.** MMP16. There was no difference in MMP16 expression for all control subjects compared to all TIA patients (A1). There was a significant increase in expression of MMP16 in the TIA1 patients compared to

both control ($p=1.35 \times 10^{-7}$) and TIA2 groups ($p=2.19 \times 10^{-7}$) and no difference in MMP16 expression between control subjects and TIA2 patients (A2). **B. MMP26.** There was no difference in MMP26 expression for all control subjects compared to all TIA patients (B1). There was a significant increase in expression of MMP26 in the TIA1 group compared to both control ($p=6.67 \times 10^{-4}$) and TIA2 groups ($p=8.55 \times 10^{-4}$) and no difference in MMP26 expression between control subjects and TIA2 patients (B2). The X axis shows categories of subjects. The Y axis shows the log 2-intensity/RNA expression. Pink = controls. Dark blue = All TIA or TIA1. Light blue = TIA2.

10

DETAILED DESCRIPTION

1. Introduction

[0068] Although transient ischemic attacks (TIAs) are common, the underlying biology remains poorly understood. The present invention is based, in part, on the discovery that TIAs differentially regulate gene expression in blood. The differentially regulated genes indicative of the occurrence or risk of occurrence of TIAs find use in the diagnosis, treatment and prevention of TIAs in patients. Patients with recent TIAs can be differentiated from controls without previous vascular events using gene expression profiles in blood. In addition, human patients appear to develop different immune response subtypes following transient ischemic attacks.

2. Individuals Who Can Benefit from the Present Methods

[0069] Individuals who will benefit from the present methods may be exhibiting symptoms of TIA or stroke. Alternatively, the subject may be suspected of having experienced TIA. In some embodiments, the subject has not experienced and/or is not at risk of having an intracerebral hemorrhage. In some embodiments, the subject has not experienced and/or is not at risk of having an intracerebral hemorrhage or hemorrhagic stroke. In some embodiments, the subject has been diagnosed as having not experienced and/or not at risk of having an intracerebral hemorrhage or hemorrhagic stroke.

[0070] In some embodiments, the levels of expression of the panel of biomarkers is determined within 3 hours of a suspected ischemic event. In some embodiments, the levels of expression of the panel of biomarkers are determined at 3 or more hours

after a suspected ischemic event. In some embodiments, the levels of expression of the panel of biomarkers are determined within 6, 12, 18, 24, 36, 48 hours of a suspected ischemic event.

[0071] In some cases, the subject is asymptomatic, but may have a risk or predisposition to experiencing TIA, *e.g.*, based on genetics, a related disease condition, environment or lifestyle. For example, in some embodiments, the patient suffers from a chronic inflammatory condition, *e.g.*, has an autoimmune disease (*e.g.*, rheumatoid arthritis, Crohn's disease inflammatory bowel disease), atherosclerosis, hypertension, or diabetes. In some embodiments, the patient has high LDL-cholesterol levels or suffers from a cardiovascular disease (*e.g.*, atherosclerosis, coronary artery disease). In some embodiments, the patient has an endocrine system disorder, a neurodegenerative disorder, a connective tissue disorder, or a skeletal and muscular disorder. Exemplary disorders associated with, related to, or causative of TIA are provided in Table 7.

[0072] In some embodiments, the patient may have a neurological disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADH1B, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, BMPR1B, CASP5, CAV1, CNTN4, DIP2C, ELAVL2, EPHX2, ERAP2, FAM124A, FAM13A, FAM149A, FAT1, FOLH1, FOXC1, GABRB2, GIGYF2, GNAO1, GRM5, GSTM1, HESX1, HOXC6, IGFBP5, IL1B, IQGAP2, ITGBL1, LAMB4, LIFR, LTBR, MECOM, NBPF10, NDST3, NELL2, NOS3, NTM, ODZ2, OLFM2, OPCML, PDE1A, RFX2, ROBO1, S100A12, SCN2A, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SOX9, SPOCK3, SPON1, TGFB2, TLR5, TNFRSF21, TRPM1, TSHZ2, TTC6 (includes EG:115669), UNC5B, UNC84A and ZNF608.

[0073] In some embodiments, the patient may have a skeletal or muscular disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, BMPR1B, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, ELAVL2, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GIGYF2, GNAO1, HOXC6, IL1B, KCNJ15, LAMB4, LIFR, LTBR, LUM, MAPK14, MYBPC1, NOS3, ODZ2, OSM, PAPP, PDE1A,

ROBO1, RUNDC3B, S100A12, SCN2A, SHOX, SLC22A4 (includes EG:6583), SOX9, SPOCK3, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B and ZNF438.

[0074] In some embodiments, the patient may have an inflammatory disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CAV1, CCND3, CCRL1, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, ERAP2, FAM124A, FBLN7, FOSB, FREM2, GABRB2, GRM5, IL1B, KCNJ15, LAMB4, LHX2, LNPEP, LRP2, LTBR, LUM, MAPK14, MECOM, MYBPC1, NOS3, ODZ2, OPCML, OSM, PAPP, PDE1A, PPP1R1C, ROBO1, RUNDC3B, S100A12, SCN2A, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SMURF2, SNRPN, SPON1, TGFB2, TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B and ZNF438.

[0075] In some embodiments, the patient may have a cardiovascular disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ALPL, ASTN2 (includes EG:23245), BCL6, BMPR1B, C18ORF54, CACNA11, CARD16, CAV1, CNTN4, DMRT1, DNAH14, EDAR, EPHX2, ERAP2, FAM13A, FOLH1, FOSB, FREM2, GABRB2, GRM5, GSTM1, IL1B, IQGAP2, LIFR, LTBR, MAN1C1, MAPK14, MBNL1, MCF2L, MECOM, MYBPC1, NOS3, NTM, ODZ2, OLFM2, OPCML, PAPP, PDE1A, ROBO1, RORB, S100A12, SMURF2, SNRPN, SOX9, SPOCK3, SPON1, TFPI, TRPM1, UNC84A and VWA3B.

[0076] In some embodiments, the patient may have an immunological disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ANXA3, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CCRL1, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FAT1, FOSB, GABRB2, GOLGA6L2, GSTM1, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14, MYBPC1, NELL2, NOS3, NTM, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583),

SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0077] In some embodiments, the patient may have a metabolic disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, EPHX2, FAT1, FOXA2, GABRB2, GUSBL2, IGFBP5, IL1B, IQGAP2, ITGBL1, LRP2, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

[0078] In some embodiments, the patient may have an endocrine system disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LRP2, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SHOX, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

[0079] In some embodiments, the patient may have an autoimmune disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14, MYBPC1, NELL2, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0080] In some embodiments, the patient may have diabetes and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL,

ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes
 5 EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

[0081] In some embodiments, the patient may have a connective tissue disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2
 10 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SHOX, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

15 [0082] In some embodiments, the patient may have rheumatic disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15,
 20 LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0083] In some embodiments, the patient may have arthritis and have increased or decreased expression relative to a control level of expression of a plurality of
 25 biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes
 30 EG:115669), VWA3B, ZNF438.

[0084] In some embodiments, the patient may have atherosclerosis and have increased or decreased expression relative to a control level of expression of a

plurality of biomarkers selected from the group consisting of ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FOSB, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN,
 5 SPOCK3, SPON1, TRPM1, UNC84A and VWA3B.

[0085] In some embodiments, the patient may have inflammatory bowel disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14, ERAP2, FBLN7, FREM2,
 10 GRM5, IL1B, LHX2, LNPEP, LTBR, MECOM, NOS3, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B and ZNF438.

[0086] In some embodiments, the patient may have non-insulin-dependent diabetes mellitus and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of
 15 ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), CARD8, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, EPHA3, FAT1, FOXA2, GABRB2, IL1B, IQGAP2, ITGBL1, MBNL1, NOS3, NTM, ODZ2, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SPON1, SRGAP1, TLR5, UNC84A and
 20 VWA3B.

[0087] In some embodiments, the patient may have rheumatoid arthritis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CLTC, CNTN4, DIP2C, DNAH14, EDAR,
 25 EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0088] In some embodiments, the patient may have coronary artery disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM,
 30

NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A and VWA3B.

[0089] In some embodiments, the patient may have Crohn's disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14, ERAP2, FBLN7, FREM2, GRM5, LHX2, LNPEP, MECOM, ODZ2, OPCML, PAPP A, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B and ZNF438.

[0090] In some embodiments, the patient may have a neurodegenerative disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SCN2A, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2 and ZNF608.

[0091] In some embodiments, the patient may have Alzheimer's disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2 and ZNF608.

3. Biomarkers Indicative of the Occurrence or Risk of TIA

[0092] Overexpressed biomarkers indicative of the occurrence of TIA or useful to predict the risk of experiencing TIA are listed in Table 1. In practicing the present methods, the expression levels of a plurality of biomarkers from Table 1 are determined, optionally in combination with other TIA-associated biomarkers described herein (*e.g.*, in Tables 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9) and known in the art.

[0093] Preferably, the expression levels of a plurality in the range of about 15-85 total biomarkers are determined, for example, about 20-70, 30-60 or 40-50 biomarkers. The expression levels of the biomarkers can be concurrently or

sequentially determined. In some embodiments, the expression levels of at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 45, 50, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more, biomarkers listed in Table 1 are determined, optionally in combination with other TIA-associated biomarkers described herein (*e.g.*, in Tables 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9) and known in the art.

[0094] In patients who have experienced TIA or who are at risk of developing TIA, the biomarkers of Table 1 are overexpressed in comparison to a control level of expression. A control level of expression can refer to the level of expression of the same biomarker in an individual who has not had and is not at risk for a vascular event or the level of expression of a stably expressed endogenous control gene. In patients who have experienced TIA or who are at risk of developing TIA, the biomarkers of Table 1 are overexpressed at least 1.5-fold, *e.g.*, at least 1.6-fold, 1.7-fold, 1.8-fold, 1.9-fold, 2.0-fold, 2.1-fold, 2.2-fold, 2.3-fold, 2.4-fold, 2.5-fold, 2.6-fold, 2.7-fold, 2.8-fold, 2.9-fold, 3.0-fold, 3.1-fold, 3.2-fold, 3.3-fold, 3.4-fold or 3.5-fold, or more, in comparison to a control level of expression.

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
1557122_s_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	NM_000813 /// NM_021911	3.49668	TIA up vs Control
227612_at	ELAVL3	ELAV (embryonic lethal, abnormal vision, <i>Drosophila</i>)-like 3 (Hu antigen C)	NM_001420 /// NM_032281	3.23425	TIA up vs Control
1556499_s_at	COL1A1	collagen, type I, alpha 1	NM_000088	2.87107	TIA up vs Control
210135_s_at	SHOX2	short stature homeobox 2	NM_003030 /// NM_006884	2.86893	TIA up vs Control
242344_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	NM_000813 /// NM_021911	2.72458	TIA up vs Control
213943_at	TWIST1	twist homolog 1 (<i>Drosophila</i>)	NM_000474	2.72279	TIA up vs Control
241199_x_at	DPPA4	developmental	NM_018189	2.68174	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
		pluripotency associated 4			
222253_s_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	NR_003714	2.61011	TIA up vs Control
206954_at	WIT1	Wilms tumor upstream neighbor 1	NM_015855 /// NR_023920	2.58643	TIA up vs Control
202935_s_at	SOX9	SRY (sex determining region Y)-box 9	NM_000346	2.45928	TIA up vs Control
239309_at	DLX6	distal-less homeobox 6	NM_005222	2.4523	TIA up vs Control
209369_at	ANXA3	annexin A3	NM_005139	2.41095	TIA up vs Control
211164_at	EPHA3	EPH receptor A3	NM_005233 /// NM_182644	2.39314	TIA up vs Control
204913_s_at	SOX11	SRY (sex determining region Y)-box 11	NM_003108	2.34727	TIA up vs Control
237340_at	SLC26A8	solute carrier family 26, member 8	NM_052961 /// NM_138718	2.32491	TIA up vs Control
220351_at	CCRL1	chemokine (C-C motif) receptor-like 1	NM_016557 /// NM_178445	2.32444	TIA up vs Control
230964_at	FREM2	FRAS1 related extracellular matrix protein 2	NM_207361	2.30984	TIA up vs Control
231969_at	STOX2	storkhead box 2	NM_020225	2.2552	TIA up vs Control
1555367_at	ZNF479	zinc finger protein 479	NM_033273 /// XM_001714591 /// XM_001719979	2.25193	TIA up vs Control
1557717_at	LOC338862	hypothetical protein LOC338862	---	2.22946	TIA up vs Control
1554816_at	ASTN2	astrotactin 2	NM_014010 /// NM_198186 /// NM_198187 /// NM_198188	2.22748	TIA up vs Control
217487_x_at	FOLH1	folate hydrolase (prostate-specific membrane	NM_001014986 /// NM_004476	2.19987	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
		antigen) 1			
241987_x_at	SNX31	sorting nexin 31	NM_152628	2.19167	TIA up vs Control
227250_at	KREMEN1	kringle containing transmembrane protein 1	NM_001039570 /// NM_001039571	2.16406	TIA up vs Control
1555368_x_at	ZNF479	zinc finger protein 479	NM_033273 /// XM_001714591 /// XM_001719979	2.16203	TIA up vs Control
1563673_a_at	ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	NM_152525	2.15177	TIA up vs Control
239710_at	FIGN	fidgetin	NM_018086	2.14096	TIA up vs Control
242385_at	RORB	RAR-related orphan receptor B	NM_006914	2.14023	TIA up vs Control
1570009_at	LOC732096	similar to hCG2040240	XM_001720784 /// XM_001725388 /// XR_016064	2.13184	TIA up vs Control
1559520_at	GYPA	Glycophorin A	NM_002099	2.12904	TIA up vs Control
215783_s_at	ALPL	alkaline phosphatase, liver/bone/kidney	NM_000478 /// NM_001127501	2.1006	TIA up vs Control
206140_at	LHX2	LIM homeobox 2	NM_004789	2.0959	TIA up vs Control
240390_at	GALNT5	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	NM_014568	2.09257	TIA up vs Control
241961_at	SRD5A2L2	steroid 5 alpha-reductase 2-like 2	NM_001010874	2.08494	TIA up vs Control
219271_at	GALNT14	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	NM_024572	2.07605	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
206048_at	OVOL2	ovo-like 2 (Drosophila)	NM_021220	2.06333	TIA up vs Control
242579_at	BMPR1B	bone morphogenetic protein receptor, type IB	NM_001203	2.05687	TIA up vs Control
226899_at	UNC5B	unc-5 homolog B (C. elegans)	NM_170744	2.04351	TIA up vs Control
231867_at	ODZ2	odz, odd Oz/ten-m homolog 2 (Drosophila)	NM_001080428 /// NM_001122679	2.03143	TIA up vs Control
1557924_s_at	ALPL	alkaline phosphatase, liver/bone/kidney	NM_000478 /// NM_001127501	2.02022	TIA up vs Control
217194_at	RASAL2	RAS protein activator like 2	NM_004841 /// NM_170692	2.00632	TIA up vs Control
207570_at	SHOX	short stature homeobox	NM_000451 /// NM_006883	2.00103	TIA up vs Control
235568_at	C19orf59	chromosome 19 open reading frame 59	NM_174918	1.99789	TIA up vs Control
1552946_at	ZNF114	zinc finger protein 114	NM_153608	1.99445	TIA up vs Control
1554473_at	SRGAP1	SLIT-ROBO Rho GTPase activating protein 1	NM_020762	1.99203	TIA up vs Control
228260_at	ELAVL2	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B)	NM_004432	1.9905	TIA up vs Control
1559292_s_at	NCRNA00032	Clone IMAGE:2275835 C9orf14 mRNA, partial sequence; alternatively spliced	XM_376821 /// XM_938938	1.98554	TIA up vs Control
214984_at	LOC440345	hypothetical protein LOC440345	XR_015786	1.98536	TIA up vs Control
1557155_a_at	FLJ30375	CDNA clone IMAGE:5301781	XM_001724993 /// XM_001725199 /// XM_001725628	1.97451	TIA up vs Control
215447_at	TFPI	Tissue factor pathway inhibitor (lipoprotein-	NM_001032281 /// NM_006287	1.96509	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
		associated coagulation inhibitor),			
228825_at	PTGR1	prostaglandin reductase 1	NM_012212	1.95262	TIA up vs Control
213194_at	ROBO1	roundabout, axon guidance receptor, homolog 1 (Drosophila)	NM_002941 /// NM_133631	1.95207	TIA up vs Control
209119_x_at	NR2F2	nuclear receptor subfamily 2, group F, member 2	NM_021005	1.94377	TIA up vs Control
206819_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	NR_003714	1.93567	TIA up vs Control
207235_s_at	GRM5	glutamate receptor, metabotropic 5	NM_000842 /// NM_001143831	1.93451	TIA up vs Control
201744_s_at	LUM	lumican	NM_002345	1.93131	TIA up vs Control
230999_at	FLJ39051	CDNA FLJ39051 fis, clone NT2RP7011452	---	1.92605	TIA up vs Control
229218_at	COL1A2	collagen, type I, alpha 2	NM_000089	1.92067	TIA up vs Control
207500_at	CASP5	caspase 5, apoptosis-related cysteine peptidase	NM_001136109 /// NM_001136110 /// NM_001136111 /// NM_001136112 /// NM_004347 //	1.91798	TIA up vs Control
214111_at	OPCML	opioid binding protein/cell adhesion molecule-like	NM_001012393 /// NM_002545	1.91158	TIA up vs Control
1556666_a_at	TTC6	tetratricopeptide repeat domain 6	NM_001007795	1.91015	TIA up vs Control
214451_at	TFAP2B	transcription factor AP-2 beta (activating enhancer binding protein 2 beta)	NM_003221	1.89347	TIA up vs Control
210262_at	CRISP2	cysteine-rich secretory protein 2	NM_001142407 /// NM_001142408 /// NM_001142417 /// NM_001142435 ///	1.88349	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
			NM_003296		
204914_s_at	SOX11	SRY (sex determining region Y)-box 11	NM_003108	1.88201	TIA up vs Control
1562292_at	ANKRD30B	ankyrin repeat domain 30B	XM_001716904 /// XM_001717561 /// XM_001717810	1.86641	TIA up vs Control
227925_at	FLJ39051	CDNA FLJ39051 fs, clone NT2RP7011452	---	1.86433	TIA up vs Control
229057_at	SCN2A	sodium channel, voltage-gated, type II, alpha subunit	NM_001040142 /// NM_001040143 /// NM_021007	1.85129	TIA up vs Control
237510_at	MYNN	Myoneurin, mRNA (cDNA clone IMAGE:4721583)	NM_018657	1.85041	TIA up vs Control
40284_at	FOXA2	forkhead box A2	NM_021784 /// NM_153675	1.8498	TIA up vs Control
233092_s_at	DKFZP434B061	DKFZP434B061 protein	XR_015528 /// XR_040812	1.84946	TIA up vs Control
230902_at	LOC645323	CDNA clone IMAGE:5260726	NR_015436 /// NR_024383 /// NR_024384 /// XR_041118 /// XR_041119 /// XR_041120	1.84336	TIA up vs Control
232547_at	SNIP	SNAP25-interacting protein	NM_025248	1.83841	TIA up vs Control
238850_at	LOC645323	hypothetical LOC645323	NR_015436 /// NR_024383 /// NR_024384 /// XR_041118 /// XR_041119 /// XR_041120	1.81503	TIA up vs Control
233879_at	LOC374491	TPTE and PTEN	NR_002815	1.81019	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
		homologous inositol lipid phosphatase pseudogene			
243520_x_at	ADAM30	ADAM metallopeptidase domain 30	NM_021794	1.80193	TIA up vs Control
206634_at	SIX3	SIX homeobox 3	NM_005413	1.78989	TIA up vs Control
1560790_at	FLJ36144	hypothetical protein FLJ36144	XR_040632 /// XR_040633 /// XR_040634	1.78391	TIA up vs Control
232969_at	CARD8	caspase recruitment domain family, member 8	NM_014959	1.78265	TIA up vs Control
235370_at	KREMEN1	kringle containing transmembrane protein 1	NM_001039570 /// NM_001039571	1.77475	TIA up vs Control
1555990_at	RP1-127L4.6	hypothetical protein LOC150297	NM_001010859	1.76603	TIA up vs Control
222291_at	FAM149A	family with sequence similarity 149, member A	NM_001006655 /// NM_015398	1.75785	TIA up vs Control
239144_at	B3GAT2	beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S)	NM_080742	1.75721	TIA up vs Control
235342_at	SPOCK3	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 3	NM_001040159 /// NM_016950	1.75314	TIA up vs Control
1553024_at	G30	protein LG30-like	---	1.75094	TIA up vs Control
214927_at	ITGBL1	integrin, beta-like 1 (with EGF-like repeat domains)	NM_004791	1.73813	TIA up vs Control
229538_s_at	IQGAP3	IQ motif containing GTPase activating protein 3	NM_178229	1.73797	TIA up vs Control
1553329_at	C7orf45	chromosome 7 open reading frame 45	NM_145268	1.72974	TIA up vs Control
232303_at	ZNF608	zinc finger protein 608	NM_020747	1.72629	TIA up vs Control
1558982_at	LOC375010	hypothetical LOC375010	XR_041271	1.72485	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
230863_at	LRP2	low density lipoprotein-related protein 2	NM_004525	1.71146	TIA up vs Control
228121_at	TGFB2	transforming growth factor, beta 2	NM_001135599 /// NM_003238	1.70904	TIA up vs Control
208443_x_at	SHOX2	short stature homeobox 2	NM_003030 /// NM_006884	1.70616	TIA up vs Control
206858_s_at	HOXC4 /// HOXC6	homeobox C4 /// homeobox C6	NM_004503 /// NM_014620 /// NM_153633 /// NM_153693	1.70414	TIA up vs Control
219134_at	ELTD1	EGF, latrophilin and seven transmembrane domain containing 1	NM_022159	1.70282	TIA up vs Control
222205_x_at	FAM182B /// RP13-401N8.2	family with sequence similarity 182, member B /// hypothetical gene supported by	XM_001132551 /// XM_001133521 /// XM_001718365 /// XM_933752	1.70042	TIA up vs Control
220696_at	PRO0478	PRO0478 protein	---	1.69169	TIA up vs Control
225571_at	LIFR	leukemia inhibitory factor receptor alpha	NM_001127671 /// NM_002310	1.69168	TIA up vs Control
217483_at	FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	NM_001014986 /// NM_004476	1.68955	TIA up vs Control
232360_at	EHF	ets homologous factor	NM_012153	1.68951	TIA up vs Control
220429_at	NDST3	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 3	NM_004784	1.68889	TIA up vs Control
232416_at	BRUNOL5	bruno-like 5, RNA binding protein (Drosophila)	NM_021938	1.68747	TIA up vs Control
231434_at	LOC728460	similar to FLJ32921 protein	XM_001128581 /// XM_001129498 /// XM_001723364	1.68733	TIA up vs Control
208396_s_at	PDE1A	phosphodiesterase 1A,	NM_001003683 ///	1.68453	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
		calmodulin-dependent	NM_005019		
1569675_at	POU2AF1	POU class 2 associating factor 1, mRNA (cDNA clone MGC:45211 IMAGE:5554134)	NM_006235	1.67876	TIA up vs Control
201579_at	FAT1	FAT tumor suppressor homolog 1 (Drosophila)	NM_005245	1.67288	TIA up vs Control
210292_s_at	PCDH11X /// PCDH11Y	protocadherin 11 X-linked /// protocadherin 11 Y-linked	NM_014522 /// NM_032967 /// NM_032968 /// NM_032969 /// NM_032971 /// NM_032972	1.6605	TIA up vs Control
1558579_at	FLJ37786	hypothetical LOC642691	XR_041472 /// XR_041473	1.66029	TIA up vs Control
205896_at	SLC22A4	solute carrier family 22 (organic cation/ergothioneine transporter), member 4	NM_003059	1.65918	TIA up vs Control
226121_at	DHRS13	dehydrogenase/reductase (SDR family) member 13	NM_144683	1.65414	TIA up vs Control
219850_s_at	EHF	ets homologous factor	NM_012153	1.64412	TIA up vs Control
235077_at	MEG3	maternally expressed 3 (non-protein coding)	NR_002766 /// NR_003530 /// NR_003531	1.6384	TIA up vs Control
214868_at	PIWIL1	piwi-like 1 (Drosophila)	NM_004764	1.63171	TIA up vs Control
232034_at	LOC203274	CDNA FLJ31544 fis, clone NT2RI2000865	---	1.63147	TIA up vs Control
1556704_s_at	LOC100133920 /// LOC286297	hypothetical protein LOC100133920 /// hypothetical protein LOC286297	NR_024443 /// XM_001714612 /// XM_372109 /// XM_933054 /// XM_933058	1.63034	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
220493_at	DMRT1	doublesex and mab-3 related transcription factor 1	NM_021951	1.61917	TIA up vs Control
202912_at	ADM	adrenomedullin	NM_001124	1.61874	TIA up vs Control
1561200_at	VWA3B	von Willebrand factor A domain containing 3B	NM_144992	1.61802	TIA up vs Control
1555726_at	GAFA3	FGF-2 activity-associated protein 3	XM_001715321 /// XM_001722922 /// XM_001723636	1.61768	TIA up vs Control
211267_at	HESX1	HESX homeobox 1	NM_003865	1.61355	TIA up vs Control
206134_at	ADAMDEC1	ADAM-like, decysin 1	NM_014479	1.61274	TIA up vs Control
203065_s_at	CAV1	caveolin 1, caveolae protein, 22kDa	NM_001753	1.60773	TIA up vs Control
215516_at	LAMB4	laminin, beta 4	NM_007356	1.60646	TIA up vs Control
220205_at	TPTE	transmembrane phosphatase with tensin homology	NM_199259 /// NM_199260 /// NM_199261	1.60547	TIA up vs Control
1555462_at	PPP1R1C	protein phosphatase 1, regulatory (inhibitor) subunit 1C	NM_001080545	1.60542	TIA up vs Control
219403_s_at	HPSE	heparanase	NM_001098540 /// NM_006665	1.60481	TIA up vs Control
206513_at	AIM2	absent in melanoma 2	NM_004833	1.60396	TIA up vs Control
215321_at	RUNDC3B	RUN domain containing 3B	NM_001134405 /// NM_001134406 /// NM_138290	1.60322	TIA up vs Control
1552701_a_at	CARD16	caspase recruitment domain family, member 16	NM_001017534 /// NM_052889	1.59587	TIA up vs Control
230519_at	FAM124A	family with sequence similarity 124A	NM_145019	1.59499	TIA up vs Control
240814_at	MGC39584	hypothetical gene supported by BC029568	XR_017735 /// XR_017787 /// XR_041937	1.59341	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
230170_at	OSM	oncostatin M	NM_020530	1.58899	TIA up vs Control
226872_at	RFX2	regulatory factor X, 2 (influences HLA class II expression)	NM_000635 /// NM_134433	1.58786	TIA up vs Control
214087_s_at	MYBPC1	myosin binding protein C, slow type	NM_002465 /// NM_206819 /// NM_206820 /// NM_206821	1.58609	TIA up vs Control
203005_at	LTBR	lymphotoxin beta receptor (TNFR superfamily, member 3)	NM_002342	1.58399	TIA up vs Control
223977_s_at	C18orf2	chromosome 18 open reading frame 2	NM_031416 /// NR_023925 /// NR_023926 /// NR_023927 /// NR_023928	1.58384	TIA up vs Control
240204_at	SNRPN	small nuclear ribonucleoprotein polypeptide N	NM_003097 /// NM_022805 /// NM_022806 /// NM_022807 /// NM_022808 /// NR_001289	1.58295	TIA up vs Control
229521_at	FLJ36031	hypothetical protein FLJ36031	NM_175884	1.58141	TIA up vs Control
205067_at	IL1B	interleukin 1, beta	NM_000576	1.57884	TIA up vs Control
206479_at	TRPM1	transient receptor potential cation channel, subfamily M, member 1	NM_002420	1.57541	TIA up vs Control
1553931_at	OSTCL	oligosaccharyltransferase complex subunit-like	NM_145303	1.57501	TIA up vs Control
210449_x_at	MAPK14	mitogen-activated protein kinase 14	NM_001315 /// NM_139012 /// NM_139013 ///	1.57327	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold- Change (TIA vs. Control)	Fold- Change(TIA vs. Control) (Description)
			NM_139014		
238428_at	KCNJ15 /// LOC100131955	potassium inwardly- rectifying channel, subfamily J, member 15 /// similar to pot	NM_002243 /// NM_170736 /// NM_170737 /// XM_001713900 /// XM_001715532 /// XM_0	1.56965	TIA up vs Control
238964_at	FIGN	fidgetin	NM_018086	1.56796	TIA up vs Control
227566_at	HNT	neurotrimin	NM_001048209 /// NM_016522	1.56554	TIA up vs Control
205863_at	S100A12	S100 calcium binding protein A12	NM_005621	1.5633	TIA up vs Control
208168_s_at	CHIT1	chitinase 1 (chitotriosidase)	NM_003465	1.56138	TIA up vs Control
239203_at	C7orf53	chromosome 7 open reading frame 53	NM_001134468 /// NM_182597	1.55912	TIA up vs Control
1569025_s_at	FAM13A1	family with sequence similarity 13, member A1	NM_001015045 /// NM_014883	1.55876	TIA up vs Control
204763_s_at	GNAO1	guanine nucleotide binding protein (G protein), alpha activating activity polype	NM_020988 /// NM_138736	1.5542	TIA up vs Control
211561_x_at	MAPK14	mitogen-activated protein kinase 14	NM_001315 /// NM_139012 /// NM_139013 /// NM_139014	1.55337	TIA up vs Control
220645_at	FAM55D	family with sequence similarity 55, member D	NM_001077639 /// NM_017678	1.55166	TIA up vs Control
241669_x_at	PRKD2	protein kinase D2	NM_001079880 /// NM_001079881 /// NM_001079882 /// NM_016457	1.55139	TIA up vs Control
210582_s_at	LIMK2	LIM domain kinase 2	NM_001031801 /// NM_005569 ///	1.5485	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
			NM_016733		
1553652_a_at	C18orf54	chromosome 18 open reading frame 54	NM_173529	1.54796	TIA up vs Control
211959_at	IGFBP5	insulin-like growth factor binding protein 5	NM_000599	1.54545	TIA up vs Control
243277_x_at	EVI1	ecotropic viral integration site 1	NM_001105077 /// NM_001105078 /// NM_005241	1.5445	TIA up vs Control
202446_s_at	PLSCR1	phospholipid scramblase 1	NM_021105	1.54059	TIA up vs Control
1553613_s_at	FOXC1	forkhead box C1	NM_001453	1.53964	TIA up vs Control
1568933_at	LOC646627	phospholipase inhibitor	NM_001085474	1.53874	TIA up vs Control
244007_at	ZNF462	zinc finger protein 462	NM_021224	1.53545	TIA up vs Control
239989_at	CNTLN	centlein, centrosomal protein	NM_001114395 /// NM_017738	1.53478	TIA up vs Control
229743_at	ZNF438	zinc finger protein 438	NM_001143766 /// NM_001143767 /// NM_001143768 /// NM_001143769 /// NM_001143770	1.53049	TIA up vs Control
1553002_at	DEFB105A /// DEFB105B	defensin, beta 105A /// defensin, beta 105B	NM_001040703 /// NM_152250	1.52948	TIA up vs Control
1560823_at	LOC340017	hypothetical protein LOC340017	---	1.51946	TIA up vs Control
1554540_at	C1orf67	chromosome 1 open reading frame 67	NM_144989	1.51941	TIA up vs Control
207275_s_at	ACSL1	acyl-CoA synthetase long-chain family member 1	NM_001995	1.51866	TIA up vs Control
209614_at	ADH1B	alcohol dehydrogenase 1B (class I), beta polypeptide	NM_000668	1.51397	TIA up vs Control
216236_s_at	SLC2A14 /// SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 14 /// solute	NM_006931 /// NM_153449	1.51356	TIA up vs Control

Table 1 – TIA-associated biomarkers that are upregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
39402_at	IL1B	interleukin 1, beta	NM_000576	1.51316	TIA up vs Control
203759_at	ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	NM_006278 /// XM_001714343 /// XM_001726541 /// XM_001726562	1.51002	TIA up vs Control
222435_s_at	UBE2J1	ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	NM_016021	1.50758	TIA up vs Control
233030_at	PNPLA3	patatin-like phospholipase domain containing 3	NM_025225	1.50269	TIA up vs Control
1559400_s_at	PAPPA	pregnancy-associated plasma protein A, pappalysin 1	NM_002581	1.50009	TIA up vs Control

[0095] Underexpressed biomarkers indicative of the occurrence of TIA or useful to predict the risk of experiencing TIA are listed in Table 2. In practicing the present methods, the expression levels of a plurality of biomarkers from Table 2 are
5 determined, optionally in combination with other TIA-associated biomarkers described herein (*e.g.*, in Tables 1, 5A, 5B, 5C, 5D, 7, 8 and/or 9) and known in the art. In some embodiments, the expression levels of at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 45, 50, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more, biomarkers listed in Table 2 are determined, optionally in combination with other TIA-associated
10 biomarkers described herein (*e.g.*, in Tables 1, 5A, 5B, 5C, 5D, 7, 8 and/or 9) and known in the art.

[0096] In patients who have experienced TIA or who are at risk of developing TIA, the biomarkers of Table 2 are underexpressed in comparison to a control level of expression. A control level of expression can refer to the level of expression of the
15 same biomarker in an individual who has not had and is not at risk for a vascular event or the level of expression of a stably expressed endogenous control gene. In patients who have experienced TIA or who are at risk of developing TIA, the

biomarkers of Table 2 are underexpressed at least 1.5-fold, *e.g.*, at least 1.6-fold, 1.7-fold, 1.8-fold, 1.9-fold, 2.0-fold, 2.1-fold, 2.2-fold, 2.3-fold, 2.4-fold, 2.5-fold, 2.6-fold, 2.7-fold, 2.8-fold, 2.9-fold, 3.0-fold, 3.1-fold, 3.2-fold, 3.3-fold, 3.4-fold or 3.5-fold, or more, in comparison to a control level of expression.

5

Table 2 – TIA-associated biomarkers that are downregulated					
Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
242191_at	NBPF10 /// RP11-9412.2	neuroblastoma breakpoint family, member 10 /// hypothetical protein LOC200030	NM_001039703 /// NM_183372 /// XM_001722184	-1.50043	TIA down vs Control
232055_at	SFXN1	sideroflexin 1	NM_022754	-1.50117	TIA down vs Control
1555883_s_at	SPIN3	spindlin family, member 3	NM_001010862	-1.50348	TIA down vs Control
206487_at	UNC84A	unc-84 homolog A (C. elegans)	NM_001130965 /// NM_025154	-1.50376	TIA down vs Control
223601_at	OLFM2	olfactomedin 2	NM_058164	-1.5119	TIA down vs Control
244011_at	PPM1K	protein phosphatase 1K (PP2C domain containing)	NM_152542	-1.51501	TIA down vs Control
214615_at	P2RY10	purinergic receptor P2Y, G-protein coupled, 10	NM_014499 /// NM_198333	-1.51779	TIA down vs Control
55872_at	ZNF512B	zinc finger protein 512B	NM_020713	-1.52158	TIA down vs Control
243857_at	MORF4L2	Mrgx mRNA for MRGX	NM_001142418 /// NM_001142419 /// NM_001142420 /// NM_001142421 /// NM_001142422	-1.52328	TIA down vs Control
1560133_at	GIGYF2	GRB10 interacting GYF protein 2	NM_001103146 /// NM_001103147 /// NM_001103148 /// NM_015575	-1.52626	TIA down vs Control

Table 2 – TIA-associated biomarkers that are downregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold- Change (TIA vs. Control)	Fold- Change(TIA vs. Control) (Description)
1554273_a_at	ERAP2	endoplasmic reticulum aminopeptidase 2	NM_001130140 /// NM_022350	-1.52883	TIA down vs Control
1553423_a_at	SLFN13	schlafen family member 13	NM_144682	-1.53028	TIA down vs Control
229094_at	LOC401431	hypothetical gene LOC401431	XR_040272 /// XR_040273 /// XR_040274 /// XR_040275	-1.53069	TIA down vs Control
207078_at	MED6	mediator complex subunit 6	NM_005466	-1.53192	TIA down vs Control
227372_s_at	BAIAP2L1 /// LOC100128461	BAI1-associated protein 2- like 1 /// hypothetical protein LOC100128461	NM_018842 /// XM_001722656 /// XM_001724217 /// XM_001724858	-1.53271	TIA down vs Control
236728_at	LNPEP	leucyl/cystinyl aminopeptidase	NM_005575 /// NM_175920	-1.53387	TIA down vs Control
215663_at	MBNL1	muscleblind-like (Drosophila)	NM_021038 /// NM_207292 /// NM_207293 /// NM_207294 /// NM_207295 /// NM_207296	-1.53726	TIA down vs Control
229093_at	NOS3	nitric oxide synthase 3 (endothelial cell)	NM_000603	-1.53818	TIA down vs Control
212935_at	MCF2L	MCF.2 cell line derived transforming sequence-like	NM_001112732 /// NM_024979	-1.53863	TIA down vs Control
215750_at	KIAA1659	KIAA1659 protein	XM_001723799 /// XM_001725435 /// XM_001726785	-1.54646	TIA down vs Control
212699_at	SCAMP5	secretory carrier membrane protein 5	NM_138967	-1.54948	TIA down vs Control
1565911_at	LOC648921	MRNA full length insert cDNA clone	XM_001715629 /// XM_001720571 ///	-1.54981	TIA down vs Control

Table 2 – TIA-associated biomarkers that are downregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold- Change (TIA vs. Control)	Fold- Change(TIA vs. Control) (Description)
		EUROIMAGE 209544	XR_018520		
239651_at	ANAPC5	anaphase promoting complex subunit 5	NM_001137559 /// NM_016237	-1.55844	TIA down vs Control
213993_at	SPON1	spondin 1, extracellular matrix protein	NM_006108	-1.55928	TIA down vs Control
231108_at	FUS	fusion (involved in t(12;16) in malignant liposarcoma)	NM_004960	-1.56277	TIA down vs Control
221288_at	GPR22	G protein-coupled receptor 22	NM_005295	-1.56303	TIA down vs Control
219815_at	GAL3ST4	galactose-3-O- sulfotransferase 4	NM_024637	-1.5674	TIA down vs Control
242111_at	METTL3	methyltransferase like 3	NM_019852	-1.56742	TIA down vs Control
239062_at	LOC100131096	hypothetical LOC100131096	XM_001720907 /// XM_001726205 /// XM_001726705	-1.57675	TIA down vs Control
230792_at	FAAH2	fatty acid amide hydrolase 2	NM_174912	-1.57807	TIA down vs Control
232020_at	SMURF2	SMAD specific E3 ubiquitin protein ligase 2	NM_022739	-1.57992	TIA down vs Control
226587_at	SNRPN	small nuclear ribonucleoprotein polypeptide N	NM_003097 /// NM_022805 /// NM_022806 /// NM_022807 /// NM_022808 /// NR_001289	-1.58006	TIA down vs Control
229247_at	FBLN7	fibulin 7	NM_001128165 /// NM_153214	-1.58734	TIA down vs Control
223080_at	GLS	Glutaminase, mRNA (cDNA clone MGC:33744 IMAGE:5263220)	NM_014905	-1.59404	TIA down vs Control
1557350_at	G3BP1	GTPase activating protein	NM_005754 ///	-1.6194	TIA down vs

Table 2 – TIA-associated biomarkers that are downregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold- Change (TIA vs. Control)	Fold- Change(TIA vs. Control) (Description)
		(SH3 domain) binding protein 1	NM_198395		Control
219864_s_at	RCAN3	RCAN family member 3	NM_013441	-1.61977	TIA down vs Control
209368_at	EPHX2	epoxide hydrolase 2, cytoplasmic	NM_001979	-1.62474	TIA down vs Control
212504_at	DIP2C	DIP2 disco-interacting protein 2 homolog C (Drosophila)	NM_014974	-1.62614	TIA down vs Control
1553645_at	CCDC141	coiled-coil domain containing 141	NM_173648	-1.62867	TIA down vs Control
239871_at	CLTC	Clathrin, heavy chain (Hc), mRNA (cDNA clone IMAGE:4812912)	NM_004859	-1.63031	TIA down vs Control
202768_at	FOSB	FBJ murine osteosarcoma viral oncogene homolog B	NM_001114171 /// NM_006732	-1.63049	TIA down vs Control
221631_at	CACNA1I	calcium channel, voltage- dependent, T type, alpha 1I subunit	NM_001003406 /// NM_021096	-1.63297	TIA down vs Control
1558569_at	UNQ6228	MRNA; cDNA DKFZp667K1619 (from clone DKFZp667K1619)	XM_001725293 /// XM_001725359 /// XM_001726164	-1.63796	TIA down vs Control
229252_at	ATG9B	ATG9 autophagy related 9 homolog B (S. cerevisiae)	NM_173681	-1.64694	TIA down vs Control
222862_s_at	AK5	adenylate kinase 5	NM_012093 /// NM_174858	-1.64741	TIA down vs Control
155882_at	SPIN3	spindlin family, member 3	NM_001010862	-1.65127	TIA down vs Control
239635_at	RBM14	RNA binding motif protein 14	NM_006328	-1.65349	TIA down vs Control
1560741_at	SNRPN	small nuclear ribonucleoprotein polypeptide N	NM_003097 /// NM_022805 /// NM_022806 ///	-1.65945	TIA down vs Control

Table 2 – TIA-associated biomarkers that are downregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold- Change (TIA vs. Control)	Fold- Change(TIA vs. Control) (Description)
			NM_022807 /// NM_022808 /// NR_001289		
214180_at	MAN1C1	mannosidase, alpha, class 1C, member 1	NM_020379	-1.66631	TIA down vs Control
220085_at	HELLS	helicase, lymphoid- specific	NM_018063	-1.67692	TIA down vs Control
220048_at	EDAR	ectodysplasin A receptor	NM_022336	-1.69385	TIA down vs Control
239667_at	SLC3A1	solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, a	NM_000341	-1.69708	TIA down vs Control
1568873_at	ZNF519	zinc finger protein 519	NM_145287	-1.70283	TIA down vs Control
236621_at	LOC100130070 /// LOC100130775 /// LOC100131787 /// LOC100131905 /// LOC100132291 /// LOC100132488 /// RPS27	similar to metallopanstimulin /// similar to rCG63653 /// similar to metallopan	NM_001030 /// XM_001721002 /// XM_001722161 /// XM_001722965 /// XM_001723889 //	-1.70558	TIA down vs Control
229234_at	ZC3H12B	zinc finger CCCH-type containing 12B	NM_001010888	-1.72127	TIA down vs Control
241723_at	IQGAP2	IQ motif containing GTPase activating protein 2	NM_006633	-1.73571	TIA down vs Control
226913_s_at	SOX8	SRY (sex determining region Y)-box 8	NM_014587	-1.73755	TIA down vs Control
1557450_s_at	WHDC1L2	WAS protein homology region 2 domain containing 1-like 2	XM_926785	-1.75555	TIA down vs Control
1556116_s_at	TNPO1	Transportin 1, mRNA (cDNA clone MGC:17116	NM_002270 /// NM_153188	-1.7577	TIA down vs Control

Table 2 – TIA-associated biomarkers that are downregulated

Probeset ID	Gene Symbol	Gene Title	RefSeq Transcript ID	Fold-Change (TIA vs. Control)	Fold-Change(TIA vs. Control) (Description)
		IMAGE:4178989)			
218856_at	TNFRSF21	tumor necrosis factor receptor superfamily, member 21	NM_014452	-1.77712	TIA down vs Control
244521_at	TSHZ2	Cell growth-inhibiting protein 7	NM_173485	-1.86192	TIA down vs Control
1553998_at	DMRTC1 /// DMRTC1B	DMRT-like family C1 /// DMRT-like family C1B	NM_001080851 /// NM_033053	-1.86704	TIA down vs Control
204550_x_at	GSTM1	glutathione S-transferase mu 1	NM_000561 /// NM_146421	-1.95136	TIA down vs Control
219308_s_at	AK5	adenylate kinase 5	NM_012093 /// NM_174858	-1.95614	TIA down vs Control
204418_x_at	GSTM2	glutathione S-transferase mu 2 (muscle)	NM_000848 /// NM_001142368	-1.95729	TIA down vs Control
235758_at	PNMA6A	paraneoplastic antigen like 6A	NM_032882	-1.95731	TIA down vs Control
239771_at	CAND1	cullin-associated and neddylation-dissociated 1	NM_018448	-1.97531	TIA down vs Control
1562028_at	CCND3	Cyclin D3 (CCND3), transcript variant 3, mRNA	NM_001136017 /// NM_001136125 /// NM_001136126 /// NM_001760	-2.00377	TIA down vs Control
215333_x_at	GSTM1	glutathione S-transferase mu 1	NM_000561 /// NM_146421	-2.03103	TIA down vs Control
232207_at	GUSBL2	glucuronidase, beta-like 2	NR_003660 /// XR_042150 /// XR_042151	-2.10621	TIA down vs Control

4. Comparison to a Control Level of Expression

[0097] The expression of the TIA-associated biomarkers are compared to a control level of expression. As appropriate, the control level of expression can be the expression level of the same TIA-associated biomarker in an otherwise healthy individual (*e.g.*, in an individual who has not experienced and/or is not at risk of experiencing TIA). In some embodiments, the control level of expression is the expression level of a plurality of stably expressed endogenous reference biomarkers, as described herein or known in the art. In some embodiments, the control level of expression is a predetermined threshold level of expression of the same TIA-associated biomarker, *e.g.*, based on the expression level of the biomarker in a population of otherwise healthy individuals. In some embodiments, the expression level of the TIA-associated biomarker and the TIA-associated biomarker in an otherwise healthy individual are normalized to (*i.e.*, divided by), *e.g.*, the expression levels of a plurality of stably expressed endogenous reference biomarkers.

[0098] In some embodiments, the overexpression or underexpression of a TIA-associated biomarker is determined with reference to the expression of the same TIA-associated biomarker in an otherwise healthy individual. For example, a healthy or normal control individual has not experienced and/or is not at risk of experiencing TIA. The healthy or normal control individual generally has not experienced a vascular event (*e.g.*, TIA, ischemic stroke, myocardial infarction, peripheral vascular disease, or venous thromboembolism). The healthy or normal control individual generally does not have one or more vascular risk factors (*e.g.*, hypertension, diabetes mellitus, hyperlipidemia, or tobacco smoking). As appropriate, the expression levels of the target TIA-associated biomarker in the healthy or normal control individual can be normalized (*i.e.*, divided by) the expression levels of a plurality of stably expressed endogenous reference biomarkers.

[0099] In some embodiments, the overexpression or underexpression of a TIA-associated biomarker is determined with reference to one or more stably expressed endogenous reference biomarkers. Internal control biomarkers or endogenous reference biomarkers are expressed at the same or nearly the same expression levels in the blood of patients with stroke or TIAs as compared to control patients. Target biomarkers are expressed at higher or lower levels in the blood of the stroke or TIA

patients. The expression levels of the target biomarker to the reference biomarker are normalized by dividing the expression level of the target biomarker to the expression levels of a plurality of endogenous reference biomarkers. The normalized expression level of a target biomarker can be used to predict the occurrence or lack thereof of stroke or TIA, and/or the cause of stroke or TIA.

[0100] In some embodiments, the expression level of the TIA-associated biomarker from a patient suspected of having or experiencing TIA and from a control patient are normalized with respect to the expression levels of a plurality of stably expressed endogenous. The expression levels of the normalized expression of the TIA-associated biomarker is compared to the expression levels of the normalized expression of the same TIA-associated biomarker in a control patient. The determined fold change in expression = normalized expression of target biomarker in TIA patient/ normalized expression of target biomarker in control patient. Overexpression or underexpression of the normalized TIA-associated biomarker in the TIA patient by at least about 1.2-fold, 1.3-fold, 1.4-fold, 1.5-fold, 1.6-fold, 1.7-fold, 1.8-fold, 1.9-fold, 2.0-fold, 2.1 fold, 2.2-fold, 2.3-fold, 2.4-fold, 2.5-fold, 2.6-fold, 2.7-fold, 2.8-fold, 2.9-fold, 3.0-fold, 3.1-fold, 3.2-fold, 3.3-fold, 3.4-fold or 3.5-fold, or more, in comparison to the expression levels of the normalized TIA-associated biomarker in a healthy control patient indicates that the TIA patient has experienced or is at risk of experiencing TIA.

[0101] In some embodiments, the control level of expression is a predetermined threshold level. The threshold level can correspond to the level of expression of the same TIA-associated biomarker in an otherwise healthy individual or a population of otherwise healthy individuals, optionally normalized to the expression levels of a plurality of endogenous reference biomarkers. After expression levels and normalized expression levels of the TIA-associated biomarkers are determined in a representative number of otherwise healthy individuals and individuals predisposed to experiencing TIA, normal and TIA expression levels of the TIA-associated biomarkers can be maintained in a database, allowing for determination of threshold expression levels indicative of the presence or absence of risk to experience TIA or the occurrence of TIA. If the predetermined threshold level of expression is with respect to a population of normal control patients, then overexpression or underexpression of the TIA-associated biomarker (usually normalized) in the TIA

patient by at least about 1.2-fold, 1.3-fold, 1.4-fold, 1.5-fold, 1.6-fold, 1.7-fold, 1.8-fold, 1.9-fold, 2.0-fold, 2.1 fold, 2.2-fold, 2.3-fold, 2.4-fold, 2.5-fold, 2.6-fold, 2.7-fold, 2.8-fold, 2.9-fold, 3.0-fold, 3.1-fold, 3.2-fold, 3.3-fold, 3.4-fold or 3.5-fold, or more, in comparison to the threshold level indicates that the TIA patient has

5 experienced or is at risk of experiencing TIA. If the predetermined threshold level of expression is with respect to a population of patients known to have experienced TIA or known to be at risk for experiencing TIA, then an expression level in the patient suspected of experiencing TIA that is approximately equal to the threshold level (or overexpressed or underexpressed greater than the threshold level of expression),

10 indicates that the TIA patient has experienced or is at risk of experiencing TIA.

[0102] With respect to the endogenous reference biomarkers used for comparison, preferably, the endogenous reference biomarkers are stably expressed in blood. Exemplary endogenous reference biomarkers that find use are listed in Table 3, below. Further suitable endogenous reference biomarkers are published, *e.g.*, in

15 Stamova, *et al.*, *BMC Medical Genomics* (2009) 2:49. In some embodiments, the expression levels of a plurality of endogenous reference biomarkers are determined as a control. In some embodiments, the expression levels of at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, or more, endogenous reference biomarkers, *e.g.*, as listed in Table 3 or known in the art, are determined as a control.

20 [0103] In some embodiments, the expression levels of the endogenous reference biomarkers GAPDH, ACTB, B2M, HMBS and PPIB are determined as a control. In some embodiments, the expression levels of 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, or more, endogenous reference biomarkers selected from the group consisting of USP7, MAPRE2, CSNK1G2, SAFB2, PRKAR2A, PI4KB, CRTIC1, HADHA, MAP1LC3B,

25 KAT5, CDC2L1 /// CDC2L2, GTSE1, CDC2L1 /// CDC2L2, TCF25, CHP, LRRC40, hCG_2003956 /// LYPLA2 /// LYPLA2P1, DAXX, UBE2NL, EIF1, KCMF1, PRKRIP1, CHMP4A, TMEM184C, TINF2, PODNL1, FBXO42, LOC441258, RRP1, C10orf104, ZDHHC5, C9orf23, LRRC45, NACC1, LOC100133445 /// LOC115110, PEX16 are determined as a control.

30

[0104] **Table 3.** The 38 endogenous reference biomarkers stably expressed in blood for use in normalization and as control levels.

Table 3 – Stably Expressed Endogenous Reference Biomarkers						
Probe Set ID	Gene Symbol	Gene Title	GenBank ID	UniGene ID	RefSeq Transcript ID	RefSeq Protein ID
201499_s_at	USP7	ubiquitin specific peptidase 7 (herpes virus-associated)	NM_003470.1	Hs.706830	NM_003470	NP_003461
202501_at	MAPRE2	microtubule-associated protein, RP/EB family, member 2	NM_014268.1	Hs.532824	NM_001143826 /// NM_001143827 /// NM_014268 /// NR_026570	NP_001137298 /// NP_001137299 /// NP_055083
202573_at	CSNK1G2	casein kinase 1, gamma 2	AL530441	Hs.651905	NM_001319	NP_001310
203280_at	SAFB2	scaffold attachment factor B2	NM_014649.1	Hs.655392	NM_014649	NP_055464
204842_x_at	PRKAR2A	protein kinase, cAMP-dependent, regulatory, type II, alpha	BC002763.1	Hs.631923	NM_004157	NP_004148
206138_s_at	PI4KB	phosphatidylinositol 4-kinase, catalytic, beta	NM_002651.1	Hs.632465	NM_002651	NP_002642
207159_x_at	CRTC1	CREB regulated transcription coactivator 1	NM_025021.1	Hs.371096	NM_001098482 /// NM_015321	NP_001091952 /// NP_056136
208630_at	HADHA	hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), alpha subunit	A1972144	Hs.516032	NM_000182	NP_000173
208786_s_at	MAP1LC3B	microtubule-associated protein 1 light chain 3 beta	AF183417.1	Hs.356061	NM_022818	NP_073729
209192_x_at	KAT5	K(lysine) acetyltransferase 5	BC000166.2	Hs.397010	NM_006388 /// NM_182709 /// NM_182710	NP_006379 /// NP_874368 /// NP_874369
210474_s_at	CDC2L1 /// CDC2L2	cell division cycle 2-like 1 (PITSLRE proteins) /// cell division cycle 2-like 2 (PITSLRE proteins)	U04619.1	Hs.651226	NM_024011 /// NM_033486 /// NM_033487 /// NM_033488 /// NM_033489 /// NM_033492 /// NM_033493 /// NM_033529	NP_076916 /// NP_277021 /// NP_277022 /// NP_277023 /// NP_277024 /// NP_277027 /// NP_277028 /// NP_277071
211040_x_at	GTSE1	G-2 and S-phase expressed 1	BC006325.1	Hs.386189	NM_016426	NP_057510
211289_x_at	CDC2L1 /// CDC2L2	cell division cycle 2-like 1 (PITSLRE proteins) /// cell division cycle 2-like 2 (PITSLRE proteins)	AF067524.1	Hs.651228	NM_024011 /// NM_033486 /// NM_033487 /// NM_033488 /// NM_033489 /// NM_033492 /// NM_033493 /// NM_033529	NP_076916 /// NP_277021 /// NP_277022 /// NP_277023 /// NP_277024 /// NP_277027 /// NP_277028 /// NP_277071
213311_s_at	TCF25	transcription factor 25 (basic helix-loop-helix)	BF000251	Hs.415342	NM_014972	NP_055787
214665_s_at	CHP	calcium binding protein P22	AK000095.1	Hs.406234	NM_007236	NP_009167
215063_x_at	LRRC40	leucine rich repeat	AL390149.1	Hs.147836	NM_017768	NP_060238

Table 3 -- Stably Expressed Endogenous Reference Biomarkers

Probe Set ID	Gene Symbol	Gene Title	GenBank ID	UniGene ID	RefSeq Transcript ID	RefSeq Protein ID
		containing 40				
215200_x_at	---	---	AK022362.1	Hs.663419	---	---
215568_x_at	hCG_2003956 /// LYPLA2 /// LYPLA2P1	hCG2003956 /// lysophospholipase II /// lysophospholipase II pseudogene 1	AL031295	Hs.533479	NM_007260 /// NR_001444	NP_009191
216038_x_at	DAXX	death-domain associated protein	BE965715	Hs.336916	NM_001141969 /// NM_001141970 /// NM_001350 /// NR_024517	NP_001135441 /// NP_001135442 /// NP_001341
217393_x_at	UBE2NL	ubiquitin-conjugating enzyme E2N-like	AL109622	Hs.585177	NM_001012989	NP_001013007
217549_at	---	---	AW574933	Hs.527860	---	---
217672_x_at	EIF1	eukaryotic translation initiation factor 1	BF114906	Hs.150580	NM_005801	NP_005792
217938_s_at	KCMF1	potassium channel modulatory factor 1	NM_020122.1	Hs.654968	NM_020122	NP_064507
218378_s_at	PRKRIP1	PRKR interacting protein 1 (IL11 inducible)	NM_024653.1	Hs.406395	NM_024653	NP_078929
218571_s_at	CHMP4A	chromatin modifying protein 4A	NM_014169.1	Hs.279761	NM_014169	NP_054888
219074_at	TMEM184C	transmembrane protein 184C	NM_018241.1	Hs.203896	NM_018241	NP_060711
220052_s_at	TINF2	TERF1 (TRF1)-interacting nuclear factor 2	NM_012461.1	Hs.496191	NM_001099274 /// NM_012461	NP_001092744 /// NP_036593
220411_x_at	PODNL1	podocan-like 1	NM_024825.1	Hs.448497	NM_001146254 /// NM_001146255 /// NM_024825	NP_001139726 /// NP_001139727 /// NP_079101
221813_at	FBXO42	F-box protein 42	AI129395	Hs.522384	NM_018994	NP_061867
222207_x_at	LOC441258	Williams Beuren syndrome chromosome region 19 pseudogene	AK024602.1	Hs.711232	---	---
222733_x_at	RRP1	ribosomal RNA processing 1 homolog (S. cerevisiae)	BC000380.1	Hs.110757	NM_003683	NP_003674
224667_x_at	C10orf104	chromosome 10 open reading frame 104	AK023981.1	Hs.426296	NM_173473	NP_775744
224858_at	ZDHHC5	zinc finger, DHHC-type containing 5	AK023130.1	Hs.27239	NM_015457	NP_056272
225403_at	C9orf23	chromosome 9 open reading frame 23	AL528391	Hs.15961	NM_148178 /// NM_148179	NP_680544 /// NP_680545
226253_at	LRRC45	leucine rich repeat containing 45	BE965418	Hs.143774	NM_144999	NP_659436
227651_at	NACC1	nucleus accumbens associated 1, BEN and BTB (POZ) domain containing	AI498126	Hs.531614	NM_052876	NP_443108
232190_x_at	LOC100133445 /// LOC115110	hypothetical LOC100133445 /// hypothetical protein LOC115110	AI393958	Hs.132272	NR_026927 /// XR_036887 /// XR_038144	---
49678_at	PEX16	peroxisomal biogenesis factor 16	AA523441	Hs.100915	NM_004813 /// NM_057174	NP_004804 /// NP_476515

5. Methods of Determining the Cause of TIA

[0105] Subsets of the TIA-associated biomarkers described herein further find use in predicting or determining the cause of TIA.

5 [0106] For example, patients that overexpress genes involved in extracellular matrix remodeling including one or more or all genes selected from MMP16, MMP19, MMP26, COL1A1, COL1A2, COL3A1, COL10A1, COL11A1, COL25A1, COL27A1, FGFs and EGFR may have atherosclerosis.

10 [0107] Individuals can have a risk or predisposition to experiencing TIA, *e.g.*, based on genetics, a related disease condition, environment or lifestyle. For example, in some embodiments, the patient suffers from a chronic inflammatory condition, *e.g.*, has an autoimmune disease (*e.g.*, rheumatoid arthritis, Crohn's disease inflammatory bowel disease), atherosclerosis, hypertension, or diabetes. In some embodiments, the patient has high LDL-cholesterol levels or suffers from a cardiovascular disease (*e.g.*,
15 atherosclerosis, coronary artery disease). In some embodiments, the patient has an endocrine system disorder, a neurodegenerative disorder, a connective tissue disorder, or a skeletal and muscular disorder. Exemplary disorders associated with, related to, or causative of TIA are provided in Table 7.

[0108] In some embodiments, the patient may have a neurological disorder and
20 have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADH1B, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, BMPR1B, CASP5, CAV1, CNTN4, DIP2C, ELAVL2, EPHX2, ERAP2, FAM124A, FAM13A, FAM149A, FAT1, FOLH1, FOXC1, GABRB2, GIGYF2, GNAO1, GRM5, GSTM1, HESX1,
25 HOXC6, IGFBP5, IL1B, IQGAP2, ITGBL1, LAMB4, LIFR, LTBR, MECOM, NBPF10, NDST3, NELL2, NOS3, NTM, ODZ2, OLFM2, OPCML, PDE1A, RFX2, ROBO1, S100A12, SCN2A, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SOX9, SPOCK3, SPON1, TGFB2, TLR5, TNFRSF21, TRPM1, TSHZ2, TTC6 (includes EG:115669), UNC5B, UNC84A and ZNF608.

30 [0109] In some embodiments, the patient may have a skeletal or muscular disorder and have increased or decreased expression relative to a control level of expression of

a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, BMPR1B, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, ELAVL2, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GIGYF2, GNAO1, HOXC6, IL1B, KCNJ15, LAMB4, LIFR, LTBR, LUM, MAPK14, MYBPC1, NOS3, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SCN2A, SHOX, SLC22A4 (includes EG:6583), SOX9, SPOCK3, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B and ZNF438.

[0110] In some embodiments, the patient may have an inflammatory disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CAV1, CCND3, CCRL1, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, ERAP2, FAM124A, FBLN7, FOSB, FREM2, GABRB2, GRM5, IL1B, KCNJ15, LAMB4, LHX2, LNPEP, LRP2, LTBR, LUM, MAPK14, MECOM, MYBPC1, NOS3, ODZ2, OPCML, OSM, PAPP, PDE1A, PPP1R1C, ROBO1, RUNDC3B, S100A12, SCN2A, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SMURF2, SNRPN, SPON1, TGFB2, TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B and ZNF438.

[0111] In some embodiments, the patient may have a cardiovascular disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ALPL, ASTN2 (includes EG:23245), BCL6, BMPR1B, C18ORF54, CACNA1I, CARD16, CAV1, CNTN4, DMRT1, DNAH14, EDAR, EPHX2, ERAP2, FAM13A, FOLH1, FOSB, FREM2, GABRB2, GRM5, GSTM1, IL1B, IQGAP2, LIFR, LTBR, MAN1C1, MAPK14, MBNL1, MCF2L, MECOM, MYBPC1, NOS3, NTM, ODZ2, OLFM2, OPCML, PAPP, PDE1A, ROBO1, RORB, S100A12, SMURF2, SNRPN, SOX9, SPOCK3, SPON1, TFPI, TRPM1, UNC84A and VWA3B.

[0112] In some embodiments, the patient may have an immunological disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ANXA3, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CCRL1,

CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FAT1, FOSB, GABRB2, GOLGA6L2, GSTM1, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14, MYBPC1, NELL2, NOS3, NTM, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583),
 5 SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0113] In some embodiments, the patient may have a metabolic disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30,
 10 AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, EPHX2, FAT1, FOXA2, GABRB2, GUSBL2, IGFBP5, IL1B, IQGAP2, ITGBL1, LRP2, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SMURF2,
 15 SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

[0114] In some embodiments, the patient may have an endocrine system disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5,
 20 CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LRP2, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SHOX, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

[0115] In some embodiments, the patient may have an autoimmune disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2,
 30 GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14, MYBPC1, NELL2, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4

(includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0116] In some embodiments, the patient may have diabetes and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

[0117] In some embodiments, the patient may have a connective tissue disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SHOX, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0118] In some embodiments, the patient may have rheumatic disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0119] In some embodiments, the patient may have arthritis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4,

LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438.

[0120] In some embodiments, the patient may have atherosclerosis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FOSB, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A and VWA3B.

[0121] In some embodiments, the patient may have inflammatory bowel disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14, ERAP2, FBLN7, FREM2, GRM5, IL1B, LHX2, LNPEP, LTBR, MECOM, NOS3, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B and ZNF438.

[0122] In some embodiments, the patient may have non-insulin-dependent diabetes mellitus and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), CARD8, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, EPHA3, FAT1, FOXA2, GABRB2, IL1B, IQGAP2, ITGBL1, MBNL1, NOS3, NTM, ODZ2, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SPON1, SRGAP1, TLR5, UNC84A and VWA3B.

[0123] In some embodiments, the patient may have rheumatoid arthritis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

[0124] In some embodiments, the patient may have coronary artery disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, 5 FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A and VWA3B.

[0125] In some embodiments, the patient may have Crohn's disease and have increased or decreased expression relative to a control level of expression of a 10 plurality of biomarkers selected from the group consisting of ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14, ERAP2, FBLN7, FREM2, GRM5, LHX2, LNPEP, MECOM, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B and ZNF438.

15 [0126] In some embodiments, the patient may have a neurodegenerative disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SCN2A, SLC22A4 (includes EG:6583), 20 SLC2A3, SLC3A1, SPON1, TSHZ2 and ZNF608.

[0127] In some embodiments, the patient may have Alzheimer's disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, 25 MECOM, NDST3, NOS3, OPCML, RFX2, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2 and ZNF608.

6. Methods of Detecting Biomarkers associated with TIA

[0128] Gene expression may be measured using any method known in the art. One of skill in the art will appreciate that the means of measuring gene expression is not a 30 critical aspect of the invention. The expression levels of the biomarkers can be detected at the transcriptional or translational (*i.e.*, protein) level.

[0129] In some embodiments, the expression levels of the biomarkers are detected at the transcriptional level. A variety of methods of specific DNA and RNA measurement using nucleic acid hybridization techniques are known to those of skill in the art (*see*, Sambrook, *supra* and Ausubel, *supra*) and may be used to detect the expression of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9. Some methods involve an electrophoretic separation (e.g., Southern blot for detecting DNA, Northern blot for detecting RNA, RNase protection assays), but measurement of DNA and RNA can also be carried out in the absence of electrophoretic separation (e.g., by dot blot). Southern blot of genomic DNA (e.g., from a human) can be used for screening for restriction fragment length polymorphism (RFLP) to detect the presence of a genetic disorder affecting a polypeptide of the invention. All forms of RNA can be detected, including, *e.g.*, message RNA (mRNA), microRNA (miRNA), ribosomal RNA (rRNA) and transfer RNA (tRNA).

[0130] The selection of a nucleic acid hybridization format is not critical. A variety of nucleic acid hybridization formats are known to those skilled in the art. For example, common formats include sandwich assays and competition or displacement assays. Hybridization techniques are generally described in Hames and Higgins *Nucleic Acid Hybridization, A Practical Approach*, IRL Press (1985); Gall and Pardue, *Proc. Natl. Acad. Sci. U.S.A.*, 63:378-383 (1969); and John *et al. Nature*, 223:582-587 (1969).

[0131] Detection of a hybridization complex may require the binding of a signal-generating complex to a duplex of target and probe polynucleotides or nucleic acids. Typically, such binding occurs through ligand and anti-ligand interactions as between a ligand-conjugated probe and an anti-ligand conjugated with a signal. The binding of the signal generation complex is also readily amenable to accelerations by exposure to ultrasonic energy.

[0132] The label may also allow indirect detection of the hybridization complex. For example, where the label is a hapten or antigen, the sample can be detected by using antibodies. In these systems, a signal is generated by attaching fluorescent or enzyme molecules to the antibodies or in some cases, by attachment to a radioactive label (*see, e.g.*, Tijssen, "*Practice and Theory of Enzyme Immunoassays*," Laboratory

Techniques in Biochemistry and Molecular Biology, Burdon and van Knippenberg Eds., Elsevier (1985), pp. 9-20).

[0133] The probes are typically labeled either directly, as with isotopes, chromophores, lumiphores, chromogens, or indirectly, such as with biotin, to which a streptavidin complex may later bind. Thus, the detectable labels used in the assays of the present invention can be primary labels (where the label comprises an element that is detected directly or that produces a directly detectable element) or secondary labels (where the detected label binds to a primary label, e.g., as is common in immunological labeling). Typically, labeled signal nucleic acids are used to detect hybridization. Complementary nucleic acids or signal nucleic acids may be labeled by any one of several methods typically used to detect the presence of hybridized polynucleotides. The most common method of detection is the use of autoradiography with ^3H , ^{125}I , ^{35}S , ^{14}C , or ^{32}P -labeled probes or the like.

[0134] Other labels include, e.g., ligands that bind to labeled antibodies, fluorophores, chemiluminescent agents, enzymes, and antibodies which can serve as specific binding pair members for a labeled ligand. An introduction to labels, labeling procedures and detection of labels is found in Polak and Van Noorden *Introduction to Immunocytochemistry*, 2nd ed., Springer Verlag, NY (1997); and in Haugland *Handbook of Fluorescent Probes and Research Chemicals*, a combined handbook and catalogue Published by Molecular Probes, Inc. (1996).

[0135] In general, a detector which monitors a particular probe or probe combination is used to detect the detection reagent label. Typical detectors include spectrophotometers, phototubes and photodiodes, microscopes, scintillation counters, cameras, film and the like, as well as combinations thereof. Examples of suitable detectors are widely available from a variety of commercial sources known to persons of skill in the art. Commonly, an optical image of a substrate comprising bound labeling moieties is digitized for subsequent computer analysis.

[0136] Most typically, the amount of RNA is measured by quantifying the amount of label fixed to the solid support by binding of the detection reagent. Typically, the presence of a modulator during incubation will increase or decrease the amount of label fixed to the solid support relative to a control incubation which does not comprise the modulator, or as compared to a baseline established for a particular

reaction type. Means of detecting and quantifying labels are well known to those of skill in the art.

[0137] In preferred embodiments, the target nucleic acid or the probe is immobilized on a solid support. Solid supports suitable for use in the assays of the invention are known to those of skill in the art. As used herein, a solid support is a matrix of material in a substantially fixed arrangement.

[0138] For example, in one embodiment of the invention, microarrays are used to detect the pattern of gene expression. Microarrays provide one method for the simultaneous measurement of the expression levels of large numbers of genes. Each array consists of a reproducible pattern of a plurality of nucleic acids (e.g., a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9) attached to a solid support. Labeled RNA or DNA is hybridized to complementary probes on the array and then detected by laser scanning. Hybridization intensities for each probe on the array are determined and converted to a quantitative read-out of relative gene expression levels in transient ischemic attacks.

[0139] In some embodiments, a sample is obtained from a subject, total mRNA is isolated from the sample and is converted to labeled cRNA and then hybridized to an array. Relative transcript levels are calculated by reference to appropriate controls present on the array and in the sample. *See*, Mahadevappa and Warrington, *Nat. Biotechnol.* 17, 1134-1136 (1999).

[0140] A variety of automated solid-phase assay techniques are also appropriate. For instance, very large scale immobilized polymer arrays (VLSIPS™), available from Affymetrix, Inc. (Santa Clara, CA) can be used to detect changes in expression levels of a plurality of genes involved in the same regulatory pathways simultaneously. *See*, Tijssen, *supra.*, Fodor *et al.* (1991) *Science*, 251: 767- 777; Sheldon *et al.* (1993) *Clinical Chemistry* 39(4): 718-719, and Kozal *et al.* (1996) *Nature Medicine* 2(7): 753-759. Integrated microfluidic systems and other point-of-care diagnostic devices available in the art also find use. *See*, e.g., Liu and Mathies, *Trends Biotechnol.* (2009) 27(10):572-81 and Tothill, *Semin Cell Dev Biol* (2009) 20(1):55-62. Microfluidics systems for use in detecting levels of expression of a plurality of nucleic acids are available, e.g., from NanoString Technologies, on the internet at nanostring.com.

- [0141] Detection can be accomplished, for example, by using a labeled detection moiety that binds specifically to duplex nucleic acids (e.g., an antibody that is specific for RNA-DNA duplexes). One preferred example uses an antibody that recognizes DNA-RNA heteroduplexes in which the antibody is linked to an enzyme (typically by recombinant or covalent chemical bonding). The antibody is detected when the enzyme reacts with its substrate, producing a detectable product. Coutlee *et al.* (1989) *Analytical Biochemistry* 181:153-162; Bogulavski (1986) *et al. J. Immunol. Methods* 89:123-130; Prooijen-Knegt (1982) *Exp. Cell Res.* 141:397-407; Rudkin (1976) *Nature* 265:472-473, Stollar (1970) *Proc. Nat'l Acad. Sci. USA* 65:993-1000; Ballard (1982) *Mol. Immunol.* 19:793-799; Pisetsky and Caster (1982) *Mol. Immunol.* 19:645-650; Viscidi *et al.* (1988) *J. Clin. Microbial.* 41:199-209; and Kinney *et al.* (1989) *J. Clin. Microbiol.* 27:6-12 describe antibodies to RNA duplexes, including homo and heteroduplexes. Kits comprising antibodies specific for DNA:RNA hybrids are available, e.g., from Digene Diagnostics, Inc. (Beltsville, MD).
- [0142] In addition to available antibodies, one of skill in the art can easily make antibodies specific for nucleic acid duplexes using existing techniques, or modify those antibodies that are commercially or publicly available. In addition to the art referenced above, general methods for producing polyclonal and monoclonal antibodies are known to those of skill in the art (*see, e.g.,* Paul (3rd ed.) *Fundamental Immunology* Raven Press, Ltd., NY (1993); Coligan, *et al., Current Protocols in Immunology*, Wiley Interscience (1991-2008); Harlow and Lane, *Antibodies: A Laboratory Manual* Cold Spring Harbor Press, NY (1988); Harlow and Lane, *Using Antibodies*, Cold Spring Harbor Press, NY (1999); Stites *et al.* (eds.) *Basic and Clinical Immunology* (4th ed.) Lange Medical Publications, Los Altos, CA, and references cited therein; Goding *Monoclonal Antibodies: Principles and Practice* (2d ed.) Academic Press, New York, NY, (1986); and Kohler and Milstein *Nature* 256: 495-497 (1975)). Other suitable techniques for antibody preparation include selection of libraries of recombinant antibodies in phage or similar vectors (*see, Huse et al. Science* 246:1275-1281 (1989); and Ward *et al. Nature* 341:544-546 (1989)).
- Specific monoclonal and polyclonal antibodies and antisera will usually bind with a K_D of at least about 0.1 μM , preferably at least about 0.01 μM or better, and most typically and preferably, 0.001 μM or better.

[0143] The nucleic acids used in this invention can be either positive or negative probes. Positive probes bind to their targets and the presence of duplex formation is evidence of the presence of the target. Negative probes fail to bind to the suspect target and the absence of duplex formation is evidence of the presence of the target.

5 For example, the use of a wild type specific nucleic acid probe or PCR primers may serve as a negative probe in an assay sample where only the nucleotide sequence of interest is present.

[0144] The sensitivity of the hybridization assays may be enhanced through use of a nucleic acid amplification system that multiplies the target nucleic acid being
10 detected. Examples of such systems include the polymerase chain reaction (PCR) system, in particular RT-PCR, multiplex PCR, quantitative PCR or real time PCR, and the ligase chain reaction (LCR) system. Other methods recently described in the art are the nucleic acid sequence based amplification (NASBA, Cangene, Mississauga, Ontario) and Q Beta Replicase systems. These systems can be used to
15 directly identify mutants where the PCR or LCR primers are designed to be extended or ligated only when a selected sequence is present. Alternatively, the selected sequences can be generally amplified using, for example, nonspecific PCR primers and the amplified target region later probed for a specific sequence indicative of a mutation. High throughput multiplex nucleic acid sequencing or "deep sequencing"
20 to detect captured expressed biomarker genes also finds use. High throughput sequencing techniques are known in the art (*e.g.*, 454 Sequencing on the internet at 454.com).

[0145] An alternative means for determining the level of expression of the nucleic acids of the present invention is *in situ* hybridization. *In situ* hybridization assays are
25 well known and are generally described in Angerer *et al.*, *Methods Enzymol.* 152:649-660 (1987). In an *in situ* hybridization assay, cells, preferentially human cells, *e.g.*, blood cells, are fixed to a solid support, typically a glass slide. If DNA is to be probed, the cells are denatured with heat or alkali. The cells are then contacted with a hybridization solution at a moderate temperature to permit annealing of specific
30 probes that are labeled. The probes are preferably labeled with radioisotopes or fluorescent reporters.

[0146] In other embodiments, quantitative RT-PCR is used to detect the expression of a plurality of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9. A general overview of the applicable technology can be found, for example, in *A-Z of Quantitative PCR*, Bustin, ed., 2004, International University Line; *Quantitative PCR Protocols*, Kochanowski and Reischl, eds., 1999, Humana Press; *Clinical Applications of PCR*, Lo, ed., 2006, Humana Press; *PCR Protocols: A Guide to Methods and Applications* (Innis *et al.* eds. (1990)) and *PCR Technology: Principles and Applications for DNA Amplification* (Erlich, ed. (1992)). In addition, amplification technology is described in U.S. Patent Nos. 4,683,195 and 4,683,202.

5

10 Methods for multiplex PCR, known in the art, are applicable to the present invention.

[0147] Accordingly, in one embodiment of the invention provides a reaction mixture comprising a plurality of polynucleotides which specifically hybridize (*e.g.*, primers) to a plurality of nucleic acid sequences of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9. In some embodiments, the reaction mixture is a PCR mixture, for example, a multiplex PCR mixture.

15

[0148] This invention relies on routine techniques in the field of recombinant genetics. Generally, the nomenclature and the laboratory procedures in recombinant DNA technology described below are those well known and commonly employed in the art. Standard techniques are used for cloning, DNA and RNA isolation, amplification and purification. Generally enzymatic reactions involving DNA ligase, DNA polymerase, restriction endonucleases and the like are performed according to the manufacturer's specifications. Basic texts disclosing the general methods of use in this invention include Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (3rd ed. 2001); Kriegler, *Gene Transfer and Expression: A Laboratory Manual* (1990); and

20

25 Current Protocols in Molecular Biology (Ausubel *et al.*, eds., 1994-2008, Wiley Interscience)).

[0149] For nucleic acids, sizes are given in either kilobases (kb) or base pairs (bp). These are estimates derived from agarose or acrylamide gel electrophoresis, from sequenced nucleic acids, or from published DNA sequences. For proteins, sizes are given in kilodaltons (kDa) or amino acid residue numbers. Proteins sizes are estimated from gel electrophoresis, from sequenced proteins, from derived amino acid sequences, or from published protein sequences.

30

[0150] Oligonucleotides that are not commercially available can be chemically synthesized according to the solid phase phosphoramidite triester method first described by Beaucage & Caruthers, *Tetrahedron Letts.* 22:1859-1862 (1981), using an automated synthesizer, as described in Van Devanter *et. al.*, *Nucleic Acids Res.* 12:6159-6168 (1984). Purification of oligonucleotides is by either native acrylamide gel electrophoresis or by anion-exchange HPLC as described in Pearson & Reanier, *J. Chrom.* 255:137-149 (1983).

[0151] In some embodiments, the expression level of the biomarkers described herein are detected at the translational or protein level. Detection of proteins is well known in the art, and methods for protein detection known in the art find use. Exemplary assays for determining the expression levels of a plurality of proteins include, *e.g.*, ELISA, flow cytometry, mass spectrometry (*e.g.*, MALDI or SELDI), surface plasmon resonance (*e.g.*, BiaCore), microfluidics and other biosensor technologies. *See, e.g.*, Tothill, *Semin Cell Dev Biol* (2009) 20(1):55-62.

15 7. TIA Reference Profiles

[0152] The invention also provides ischemia reference profiles. The TIA reference profiles comprise information correlating the expression levels of a plurality of TIA-associated genes (*i.e.*, a plurality of the genes set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9) to the occurrence or risk of TIA. The profiles can conveniently be used to diagnose, monitor and prognose ischemia.

[0153] The reference profiles can be entered into a database, *e.g.*, a relational database comprising data fitted into predefined categories. Each table, or relation, contains one or more data categories in columns. Each row contains a unique instance of data for the categories defined by the columns. For example, a typical database for the invention would include a table that describes a sample with columns for age, gender, reproductive status, expression profile and so forth. Another table would describe a disease: symptoms, level, sample identification, expression profile and so forth. In one embodiment, the invention matches the experimental sample to a database of reference samples. The database is assembled with a plurality of different samples to be used as reference samples. An individual reference sample in one embodiment will be obtained from a patient during a visit to a medical professional. Information about the physiological, disease and/or pharmacological status of the

sample will also be obtained through any method available. This may include, but is not limited to, expression profile analysis, clinical analysis, medical history and/or patient interview. For example, the patient could be interviewed to determine age, sex, ethnic origin, symptoms or past diagnosis of disease, and the identity of any therapies the patient is currently undergoing. A plurality of these reference samples will be taken. A single individual may contribute a single reference sample or more than one sample over time. One skilled in the art will recognize that confidence levels in predictions based on comparison to a database increase as the number of reference samples in the database increases.

10 [0154] The database is organized into groups of reference samples. Each reference sample contains information about physiological, pharmacological and/or disease status. In one aspect the database is a relational database with data organized in three data tables, one where the samples are grouped primarily by physiological status, one where the samples are grouped primarily by disease status and one where the samples are grouped primarily by pharmacological status. Within each table the samples can be further grouped according to the two remaining categories. For example the physiological status table could be further categorized according to disease and pharmacological status.

[0155] As will be appreciated by one of skill in the art, the present invention may be embodied as a method, data processing system or program products. Accordingly, the present invention may take the form of data analysis systems, methods, analysis software, etc. Software written according to the present invention is to be stored in some form of computer readable medium, such as memory, hard-drive, DVD ROM or CD ROM, or transmitted over a network, and executed by a processor. The present invention also provides a computer system for analyzing physiological states, levels of disease states and/or therapeutic efficacy. The computer system comprises a processor, and memory coupled to said processor which encodes one or more programs. The programs encoded in memory cause the processor to perform the steps of the above methods wherein the expression profiles and information about physiological, pharmacological and disease states are received by the computer system as input. Computer systems may be used to execute the software of an embodiment of the invention (see, *e.g.*, U.S. Patent No. 5,733,729).

8. Providing Appropriate Treatment and Prevention Regimes to Patient

[0156] In some embodiments, the methods further comprise the step of prescribing and providing appropriate treatment and/or prevention regimes to a patient diagnosed as having TIA or at risk of the occurrence of TIA or stroke. For example, medications and life-style adjustments (*e.g.*, diet, exercise, stress) to minimize risk factors can be recommended, including reducing blood pressure and cholesterol levels, and controlling diabetes.

[0157] In additions, several medications to decrease the likelihood of a stroke after a transient ischemic attack. The medication selected will depend on the location, cause, severity and type of TIA, if TIA has occurred.

[0158] In some embodiments, the patient may be prescribed a regime of an anti-platelet drug. The most frequently used anti-platelet medication is aspirin. An alternative to aspirin is the anti-platelet drug clopidogrel (Plavix). Some studies indicate that aspirin is most effective in combination with another anti-platelet drug. In some embodiments, the patient is prescribed a combination of low-dose aspirin and the anti-platelet drug dipyridamole (Aggrenox), to reduce blood clotting. Ticlopidine (Ticlid) is another anti-platelet medication that finds use to prevent or reduce the risk of stroke in patients who have experienced TIA.

[0159] In some embodiments, the patient may be prescribed a regime of an anticoagulant. Exemplary anticoagulants include aspirin, heparin, warfarin, and dabigatran.

[0160] Patients having a moderately or severely narrowed neck (carotid) artery, may require or benefit from carotid endarterectomy. This preventive surgery clears carotid arteries of fatty deposits (atherosclerotic plaques) before another TIA or stroke can occur. In some embodiments, the patient may require or benefit from carotid angioplasty, or stenting. Carotid angioplasty involves using a balloon-like device to open a clogged artery and placing a small wire tube (stent) into the artery to keep it open.

9. Solid Supports and Kits

[0161] The invention further provides a solid supports comprising a plurality of nucleic acid probes that hybridize to a plurality (*e.g.*, two or more, or all) of the genes

set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9, and optionally Table 3. For example, the solid support can be a microarray attached to a plurality of nucleic acid probes that hybridize to a plurality (e.g., two or more, or all) of the genes set forth in Table 1, and optionally Table 3. In various embodiments, the solid support can be a
5 microarray attached to a plurality of nucleic acid probes that hybridize to a plurality (e.g., two or more, or all) of the genes set forth in Tables 5A, 5B, 5C, and 5D, and optionally Table 3. In various embodiments, the solid support can be a microarray attached to a plurality of nucleic acid probes that hybridize to a plurality (e.g., two or more, or all) of the genes set forth in Table 7, and optionally Table 3. In various, the
10 solid support can be a microarray attached to a plurality of nucleic acid probes that hybridize to a plurality (e.g., two or more, or all) of the genes set forth in Table 8, and optionally Table 3. In various, the solid support can be a microarray attached to a plurality of nucleic acid probes that hybridize to a plurality (e.g., two or more, or all) of the genes set forth in Table 9, and optionally Table 3.

15 [0162] In various embodiments, the solid supports are configured to exclude genes not associated with or useful to the diagnosis, prediction or confirmation of a stroke or the causes of stroke. For example, genes which are overexpressed or underexpressed less than 1.5-fold in subjects having or suspected of having TIA, in comparison to a control level of expression can be excluded from the present solid supports. In some
20 embodiments, genes that are overexpressed or underexpressed less than 1.2-fold in subjects with ischemic stroke, including cardioembolic stroke, atherothrombotic stroke, and stroke subsequent to atrial fibrillation, in comparison to a control level of expression can be excluded from the present solid supports. The solid support can comprise a plurality of nucleic acid probes that hybridize to a plurality (e.g., two or
25 more, or all) of the genes useful for the diagnosis of ischemic stroke, cardioembolic stroke, carotid stenosis, and/or atrial fibrillation, as described herein. As appropriate, nucleic acid probes that hybridize to a plurality (e.g., two or more, or all) of the genes useful for the diagnosis of ischemic stroke, cardioembolic stroke, carotid stenosis, and/or atrial fibrillation can be arranged in a predetermined array on the solid support.
30 In various embodiments, nucleic acids not specifically identified and/or not relating to the diagnosis of and/or not associated with the diagnosis of TIA are not attached to the solid support. In various embodiments, nucleic acids not specifically identified and/or not relating to the diagnosis of and/or not associated with the diagnosis of

ischemic stroke, cardioembolic stroke, carotid stenosis, and/or atrial fibrillation are not attached to the solid support. The solid support may be a component in a kit.

[0163] The invention also provides kits for diagnosing TIA or a predisposition for developing TIA. For example, the invention provides kits that include one or more
5 reaction vessels that have aliquots of some or all of the reaction components of the invention in them. Aliquots can be in liquid or dried form. Reaction vessels can include sample processing cartridges or other vessels that allow for the containment, processing and/or amplification of samples in the same vessel. The kits can comprise a plurality of nucleic acid probes that hybridize to a plurality the genes set forth in
10 Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9. The probes may be immobilized on a microarray as described herein.

[0164] In addition, the kit can comprise appropriate buffers, salts and other reagents to facilitate amplification and/or detection reactions (*e.g.*, primers, labels) for determining the expression levels of a plurality of the biomarkers set forth in Tables
15 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9. The kits can also include written instructions for the use of the kit.

[0165] In one embodiment, the kits comprise a plurality of antibodies that bind to a plurality of the biomarkers set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and/or 9. The antibodies may or may not be immobilized on a solid support, *e.g.*, an ELISA plate.

EXAMPLES

[0166] The following examples are offered to illustrate, but not to limit the claimed invention.

Example 1:

5 **Materials and Methods**

Subjects

[0167] TIA and control patients were recruited from the University of California Davis Medical Center, University of California San Francisco Medical Center and Wake Forest University Health Sciences. Institutional Review Boards at each
10 institution approved the study, and written informed consent was obtained from all patients.

[0168] A total of 27 control patients were compared to 24 TIA patients studied within 3 to 69 hours (average = 29.2 hours) of symptoms onset. The diagnosis of TIA was made by two independent board certified neurologists with access to all clinical
15 data. TIA was defined as an acute loss of focal cerebral or ocular function lasting <12 hours with a presumed ischemic etiology. To be recruited into the study TIA patients were required to have an ABCD² score ≥ 4 to further support the diagnosis of TIA. This ensured that TIA patients at higher risk for recurrent vascular events were studied (4, 19). The controls were recruited from the spouses or family members of
20 TIA patients or people from the community. They were subjects free of vascular events such as TIA, ischemic stroke, myocardial infarction, peripheral vascular disease, or venous thromboembolism. Control subjects with hypertension and/ or diabetes were also excluded in order to reduce the possibility of controls having silent TIA or other vascular events. Hypertension and diabetes both increase the probability
25 of TIA, as shown by the ABCD² score (4, 20).

RNA Isolation

[0169] A venous blood sample was collected into PAXgene vacutainers (PreAnalytiX, Hilden, Germany). Total RNA was isolated according to the manufacturer's protocol.

Microarray Hybridization

[0170] Biotin-labeled cDNA was synthesized from 50 ng of total RNA using the Ovation Whole Blood Solution (Nugen) kit according to protocol. Each RNA sample was processed on Affymetrix Human Genome HG-U133-Plus-2.0 microarrays as
5 previously described (18).

Statistical Analysis

[0171] Microarray probeset-level data were log transformed and normalized using Robust Multichip Average (RMA). Analysis of Covariance (ANCOVA) was conducted in Partek Genomics Suite 6.5 (Partek Inc., St. Louis, MI, USA) to identify
10 genes/probes significantly different between TIA and control subjects with adjustment for microarray batch effect and age. Genes/probes were considered significant with a p-value ≤ 0.05 after Benjamini-Hochberg multiple-comparison correction, and an absolute fold change > 1.5 . To exclude genes associated with hypertension, a second comparison was performed for 33 controls with hypertension to controls without
15 hypertension. The Identified “hypertension” genes that overlapped with the TIA gene lists were excluded from further analysis.

[0172] All data are presented as mean $\pm$ SE. Differences in demographic data between groups were analyzed using Chi-square test or t-test as appropriate. Prediction analysis was performed using 10-fold leave-one-out cross-validation in
20 Prediction Analysis of Microarrays (PAM). Functional and pathway analyses were performed using Ingenuity Pathways Analysis (IPA).

Results

Subjects

[0173] The demographic information for TIA and control subjects showed that age
25 was significantly different between TIA and controls (Table 4). Thus, age was adjusted for in the ANCOVA model.

Table 4.

Demographic summary of Transient Ischemic Attack (TIA) patients and control subjects

	Controls	TIA	p value
	(n=27)	(n=24)	
Age (yrs $\pm$ SE)	55.7 $\pm$ 0.8	70.2 $\pm$ 2.5	< 0.001
Gender Female: n (%)	19 (70.4)	14 (58.3)	0.39
Race			
Caucasian: n (%)	18 (66.6)	16 (66.6)	1.00
Non-Caucasian: n (%)	9 (33.3)	8 (33.3)	1.00

5 TIA Genomic Profiles

[0174] A total of 460 genes were differentially expressed between TIA patients and controls ($FDR \leq 0.05$; fold change ≥ 1.5) (Tables 5A-D). 135 genes were down-regulated (Table 2 and Table 5A) and 325 were up-regulated (Table 1 and Table 5B) in TIA compared to controls. A Hierarchical cluster analysis of the 460 genes showed that they separated TIAs from controls (Figure 1) except that two TIA patients (ID numbers: 57 and 90) clustered in the control group, and three control patients (ID numbers: 42, 68 and 74) clustered in the TIA group (Figure 1). The hierarchical cluster analysis also suggested the presence of two distinct TIA groups. Most of the up-regulated genes in the TIA1 group separated it from the TIA2 group and from controls (Figure 1).

Prediction Analysis

[0175] Cross-correlation performed with PAM using the 34 (Table 5C) out of 460 TIA associated genes distinguished TIA patients from controls with 87.5% sensitivity (21 out of 24 TIAs correctly classified) and 96.3% specificity (26 out of 27 controls correctly classified) (Figure 2).

TIA Specific Up-regulated Genes

[0176] The 325 up-regulated genes that distinguished TIA1 from TIA2 patients were input into PAM to derive the minimum number (n=26) of genes that differentiated the two groups. The 26 genes (Table 5D) distinguished TIA1 from TIA2 patients with 100% sensitivity and specificity (Figure 3). No clinical factors were identified that were significantly different between TIA1 and TIA2 including age, time after TIA, hypertension, diabetes, ABCD² score (Table 6) and medications. Notably, Metalloproteinase 16 and Metalloproteinase 26 were up-regulated in the TIA1 group but not in the TIA2 group (Figure 4).

10 **Table 6.** Demographic Summary of TIA subgroups

	TIA1 (n=12)	TIA2 (n=12)	P value
Age (yrs ± SE)	64.8 ± 3.7	63.7 ± 8.8	0.91
Gender Female (%)	5 (42)	5 (42)	1.00
Race			
Caucasian n (%)	7 (58)	9 (75)	0.18
Non-Caucasian n (%)	5 (42)	3 (25)	0.18
Vascular risk factor			
Hypertension n (%)	10 (83)	10 (83)	1.00
Diabetes n (%)	4 (33)	4 (33)	1.00
Hyperlipidemia n (%)	6 (50)	7 (58)	0.56
Smoke n (%)	6 (50)	4 (33)	0.22
Hours since TIA (± SE)	28.7 ± 4.4	29.7 ± 4.3	0.87
History of stroke n (%)	3 (25)	4 (33)	0.54
CVD n (%)	3 (25)	4 (33)	0.54
AF n (%)	1 (8)	2 (16)	0.43
LVD n (%)	1 (8)	2 (16)	0.43
ABCD ² score (± SE)	5.42 ± 0.29	5.25 ± 0.28	0.68

15 CVD: Cardiovascular Disorder; AF: Atrial Fibrillation; LVD: Large Vessel Disease. There was no any significant difference among two groups analyzed using t-test or Chi-square test. The factors contributed to the differences in RNA expression between TIA1 and TIA2 remained unclear.

Function Analysis of TIA Specific Genes

20 [0177] Functional analysis of the TIA specific genes (460 genes derived from TIA vs control) using IPA demonstrated that they were significantly associated with immune functions. Amongst the TIA specific genes, a number have been associated with autoimmune disease, diabetes, arthritis, rheumatoid arthritis, atherosclerosis, coronary artery disease and Crohn's disease (Table 7). The significantly regulated

genes for the TIA1 group compared to the TIA2 group ($\text{FDR} \leq 0.05$; fold change ≥ 1.5) are shown in Table 8 along with the most significant pathways (Table 9; see discussion below).

Table 7-TIA specific gene-functions

Category	Function	p-value	Molecules
Genetic Disorder	genetic disorder	2.29E-03	ACSL1, ADAM30, ADAMDEC1, ADH1B, AK5, ALPL, ALS2CR11, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, BMPR1B, CACNA1I, CARD8, CARD16, CASP5, CAV1, CCND3, CCRL1, CHIT1, CLTC, CNTN4, CNTN4, COL1A1, COL1A2, DIP2C, DMRT1, DNAH14, EDAR, ELAVL2, EPHA3, EPHX2, ERAP2, FAM124A, FAM13A, FAM149A, FAT1, FBLN7, FOLH1, FOXA2, FOXC1, FREM2, GABRB2, GIGYF2, GNAO1, GRM5, GSTM1, GYPA, HESX1, HOXC6, IGFBP5, IL1B, IQGAP2, ITGBL1, LAMB4, LHX2, LIFR, LNPEP, LRP2, LTBR, MAN1C1, MBNL1, MCF2L, MECOM, MLL, NBP10, NDST3, NELL2, NOS3, NTM, ODZ2, OLFM2, OPCML, OSM, PAPP, PDE1A, PLSCR1, PPP1R1C, RFX2, ROBO1, RORB, S100A12, SCN2A, SFXN1, SHOX, SIX3, SLC22A4 (includes EG:6583), SLC26A8, SLC2A3, SLC3A1, SMURF2, SNRPN, SOX9, SPOCK3, SPON1, SRGAP1, TFAP2B, TGFB2, TLR5, TRPM1, TSHZ2, TTC6 (includes EG:115669), TWIST1, UNC5B, UNC84A, VWA3B, ZNF438, ZNF608
Neurological Disease	neurological disorder	1.99E-02	ACSL1, ADH1B, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, BMPR1B, CASP5, CAV1, CNTN4, DIP2C, ELAVL2, EPHX2, ERAP2, FAM124A, FAM13A, FAM149A, FAT1, FOLH1, FOXC1, GABRB2, GIGYF2, GNAO1, GRM5, GSTM1, HESX1, HOXC6, IGFBP5, IL1B, IQGAP2, ITGBL1, LAMB4, LIFR, LTBR, MECOM, NBP10, NDST3, NELL2, NOS3, NTM, ODZ2, OLFM2, OPCML, PDE1A, RFX2, ROBO1, S100A12, SCN2A, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SOX9, SPOCK3, SPON1, TGFB2, TLR5, TNFRSF21, TRPM1, TSHZ2, TTC6 (includes EG:115669), UNC5B, UNC84A, ZNF608
Inflammatory Disease	inflammatory disorder	8.17E-06	ACSL1, ADM, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CAV1, CCND3, CCRL1, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, ERAP2, FAM124A, FBLN7, FOSB, FREM2, GABRB2, GRM5, IL1B, KCNJ15, LAMB4, LHX2, LNPEP, LRP2, LTBR, LUM, MAPK14, MECOM, MYBPC1, NOS3, ODZ2, OPCML, OSM, PAPP, PDE1A, PPP1R1C, ROBO1, RUNCDC3B, S100A12, SCN2A, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SMURF2, SNRPN, SPON1, TGFB2, TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B, ZNF438
Skeletal and Muscular Disorders	skeletal and muscular disorder	2.32E-03	ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, BMPR1B, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, ELAVL2, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GIGYF2, GNAO1, HOXC6, IL1B, KCNJ15, LAMB4, LIFR, LTBR, LUM, MAPK14, MYBPC1, NOS3, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNCDC3B, S100A12, SCN2A, SHOX, SLC22A4 (includes EG:6583), SOX9, SPOCK3, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B, ZNF438
Cardiovascular Disease	cardiovascular disorder	3.05E-05	ACSL1, ADM, AK5, ALPL, ASTN2 (includes EG:23245), BCL6, BMPR1B, C18ORF54, CACNA1I, CARD16, CAV1, CNTN4, DMRT1, DNAH14, EDAR, EPHA3, EPHX2, FAM13A, FOLH1, FOSB, FREM2, GABRB2, GRM5, GSTM1, IL1B, IQGAP2, LIFR, LTBR, MAN1C1, MAPK14, MBNL1, MCF2L, MECOM, MYBPC1, NOS3, NTM, ODZ2, OLFM2, OPCML, PAPP, PDE1A, ROBO1, RORB, S100A12, SMURF2, SNRPN, SOX9, SPOCK3, SPON1, TFPI, TRPM1, UNC84A, VWA3B
Immunological Disease	immunological disorder	2.11E-04	ACSL1, ADM, AK5, ANXA3, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CCRL1, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FAT1, FOSB, GABRB2, GOLGA6L2, GSTM1, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14,

Category	Function	p-value	Molecules
Metabolic Disease	metabolic disorder	1.03E-02	MYBPC1, NELL2, NOS3, NTM, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B, ZNF438
			ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, EPHX2, FAT1, FOXA2, GABRB2, GUSBL2, IQGAP2, ITGBL1, LRP2, LTR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A, VWA3B
Endocrine System Disorders	endocrine system disorder	3.00E-03	ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LRP2, LTR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SHOX, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A, VWA3B
			ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTR, MAPK14, MYBPC1, NELL2, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B, ZNF438
Immunological Disease	autoimmune disease	3.60E-04	ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTR, MAPK14, MYBPC1, NELL2, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B, ZNF438
			ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LTR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A, VWA3B
Connective Tissue Disorders	connective tissue disorder	2.72E-04	ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SHOX, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438
			ADM, AIM2, BCL6, BMPR1B, CARD8, CASP5, CAV1, CCND3, EDAR, FOSB, FOXA2, FUS, GALNT5, GNAO1, GRM5, HOXC6, IQGAP2, IL1B, IQGAP2, LTR, MAPK14, MCF2L, MECOM, MLL, NOS3, OSM, PIWIL1, PLSCR1, POU2AF1, SCN2A, SHOX, SLC2A3, SOX9, TFAP2B, TGFB2, TNFRSF21, TWIST1, UNC5B
Cell Death	apoptosis	1.65E-02	ADM, AIM2, BCL6, BMPR1B, CARD8, CASP5, CAV1, CCND3, EDAR, FOSB, FOXA2, FUS, GALNT5, GNAO1, GRM5, HOXC6, IQGAP2, IL1B, IQGAP2, LTR, MAPK14, MCF2L, MECOM, MLL, NOS3, OSM, PIWIL1, PLSCR1, POU2AF1, SCN2A, SHOX, SLC2A3, SOX9, TFAP2B, TGFB2, TNFRSF21, TWIST1, UNC5B
			BCL6, BMPR1B, CAV1, CCND3, EHF, ELAVL2, FOSB, FOXA2, FOXC1, FUS, GRM5, HELLS, HOXC6, IL1B, LTR, MAPK14, MECOM, MED6, MEG3 (includes EG:55384), MLL, NR2F2, OSM, OVOL2, POU2AF1, REM14, RORB, SHOX, SHOX2, SIK3, SLC3A1, SMURF2, SOX8, SOX9, SOX11, TFAP2B, TGFB2, TWIST1, ZNF462
Gene Expression	transcription	4.26E-04	BCL6, BMPR1B, CAV1, CCND3, EHF, ELAVL2, FOSB, FOXA2, FOXC1, FUS, GRM5, HELLS, HOXC6, IL1B, LTR, MAPK14, MECOM, MED6, MEG3 (includes EG:55384), MLL, NR2F2, OSM, OVOL2, POU2AF1, REM14, RORB, SHOX, SHOX2, SIK3, SLC3A1, SMURF2, SOX8, SOX9, SOX11, TFAP2B, TGFB2, TWIST1, ZNF462
			ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438
Inflammatory Disease	rheumatic disease	8.49E-04	ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438
			ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438
Inflammatory Disease	arthritis	7.29E-04	ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438
			ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438

Category	Function	p-value	Molecules
Cellular Growth and Proliferation	proliferation	5.91E-03	MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUND3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115668), VWA3B, ZNF438
			ADM, AIM2, BCL6, BMPR1B, CAV1, CCND3, CLTC, COL1A1, DLX6, DPPA4, FOSB, FOXA2, FUS, GRM5, GSTM1, HOXC6, IGFBP5, IL1B, LIFR, MAPK14, MECOM, MEG3 (includes EG:55384), MLL, NOS3, OSM, PAPP, PIWIL1, PLSCR1, SHOX2, SOX9, TFPI, TGFB2, TLR5, TNFRSF21
Cardiovascular Disease	atherosclerosis	1.22E-04	ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FOSB, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A, VWA3B
			ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14, ERAP2, FBLN7, FREM2, GRM5, IL1B, LHX2, LNPEP, LTBR, MECOM, NOS3, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B, ZNF438
Inflammatory Disease	inflammatory bowel disease	5.07E-05	ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCN15, LAMB4, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUND3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115668), VWA3B, ZNF438
			ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A, VWA3B
Endocrine System Disorders	non-insulin-dependent diabetes mellitus	4.48E-04	ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), CARD8, CCRL1, CNTN, CNTN4, COL1A2, DIP2C, DMRT1, EPHA3, FAT1, FOXA2, GABRB2, IL1B, IQGAP2, ITGBL1, MBNL1, NOS3, NTM, ODZ2, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SPON1, SRCAP1, TLR5, UNC84A, VWA3B
			ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCN15, LAMB4, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUND3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115668), VWA3B, ZNF438
Cardiovascular Disease	coronary artery disease	6.94E-05	ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A, VWA3B
			ADM, AIM2, BCL6, CARD8, CAV1, CCND3, DPPA4, FOSB, FOXA2, FUS, GALNT5, GNAO1, GSTM1, HOXC6, IGFBP5, IL1B, LTBR, MAPK14, MLL, NOS3, PIWIL1, PLSCR1, SHOX, SOX9, TFAP2B, TGFB2, TNFRSF21, TWIST1, UNC5B
Inflammatory Disease	Crohn's disease	2.08E-04	ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14, ERAP2, FBLN7, FREM2, GRM5, LHX2, LNPEP, MECOM, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B, ZNF438
			ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SCN2A, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2, ZNF608
Neurological Disease	Alzheimer's disease	1.72E-02	ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2, ZNF608
			ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2, ZNF608

Discussion

[0178] TIA is a harbinger of stroke and other vascular events. The present biomarker panels find use for intervention in TIA to prevent future vascular events. Prior to the present invention, there was limited knowledge regarding human TIA biology, and the development of specific TIA therapies has been limited. The present biomarker panels provide information to better understand the immune response in blood that occurs in patients with TIA. By examining the whole genome, unique TIA gene expression profiles showing two TIA subtypes were identified. These findings provide unique insight into TIA pathophysiology, and are consistent with the conclusion that there are specific immune responses that occur following transient focal cerebral ischemia in humans. They also suggest diagnostic tests to confirm a TIA diagnosis can be developed.

Systemic Inflammation and TIA

[0179] TIA patients appear to have unique patterns of inflammation associated with their vascular events. Indeed, compared to controls, TIA patients tend to have increased leukocyte activation and a systemic inflammatory response (8-9). Transient ischemic attacks have also been associated with a number of systemic inflammatory markers such as CRP (7), and inflammatory conditions such as inflammatory bowel disease (21-24). Alterations in immune function in TIAs are further implicated by an association between TIA and systemic infection, as well as TIA and periodontal disease (25-29). In this study, 63 genes involved in inflammation were differentially expressed in TIA compared to controls (Table 7). These genes show patterns of inflammation similar to that of inflammatory bowel disease (32 genes), rheumatoid arthritis (32 genes), and Crohn's disease (29 genes), suggesting that different, but related patterns of inflammation are associated with TIA. If the expression of these genes changed in a time-dependent manner after TIA onset, the inflammation could be a consequence of TIA. Otherwise, there might be some pre-existing inflammation that did not change with time that might promote the development of TIA. Therefore, a time-dependent analysis on the gene expression in the acute phase (blood draw within 24h of TIA onset; n = 11) and the sub acute phase (blood draw between 24h to 72h of TIA onset; n = 13) of TIA was performed. The results showed that the large

majority of the genes expressed in the acute phase were similar to those expressed in the sub acute phase (>90% similar). Thus, there may be a chronic inflammatory state prior to TIA and this could contribute to causing TIAs.

Anti-Oxidant Capacity

5 [0180] GSTM1 and GSTM2 encode cytosolic glutathione S-transferases (GSTs) that belong to the mu class. GST enzymes function in the detoxification of electrophilic compounds, such products of oxidative stress by conjugation with glutathione (30). GSTM1 and GSTM2 were both down-regulated in TIA patients, suggesting a decreased anti-oxidant capacity may exist in patients with TIAs. The
10 resultant enhanced oxidative stress may in turn promote ischemic vascular disease such as TIA. This result is consistent with our previous animal study that showed a specific GST family member (GSTT1) regulated following 10 minutes of brief focal ischemia simulating human TIAs (5).

Extracellular Matrix Remodeling

15 [0181] Our data suggest the presence of two subgroups of TIA patients. No measured clinical factor was significantly different between each group. The notion of subtypes of TIA is not new. For example, TIA subtypes exist based on MRI DWI status, ABCD² score, or the presence of large vessel disease or atrial fibrillation. In our study, two molecular subtypes of TIA were evident based on gene expression
20 profiles. Functional analysis of these two groups suggested over representation of genes involved in extracellular matrix remodeling in TIA1 compared to TIA2 including: MMP16, MMP19, MMP26, COL1A1, COL1A2, COL3A1, COL10A1, COL11A1, COL25A1, COL27A1, FGFs and EGFR. TIA1 patients may be more prone to extracellular matrix breakdown at the blood brain barrier and/or in
25 atherosclerotic plaque.

Limitations of the Study

[0182] The sample size is small. A control group at very low risk of TIA and other vascular events was chosen so that the controls would be very unlikely to have silent ischemic events that would complicate comparison to TIA. By doing so, differences
30 due to vascular risk factors are inevitably introduced. These factors were adjusted for by including age in the ANCOVA model, and excluding genes associated with

hypertension and diabetes. The advantage of comparing TIA to the controls in this study, therefore, is that the gene expression differences between TIA and controls were maximized, and allowed for the search for TIA subgroups. However, future studies will need to compare TIA patients to other controls to identify “TIA specific gene markers”. These controls should include patients with similar vascular risk factors and “TIA mimic” patients with migraine or seizures.

[0183] Group heterogeneity is another limitation in the study of TIA. Though stringent criteria were used to ensure subjects with TIA were indeed true transient ischemic events, it is possible that a few TIA patients were in fact TIA mimics. Similarly, though a comparison group at low risk for having silent ischemic vascular events was used, it is possible some patients in the control group had silent vascular events.

[0184] This is a discovery type study and thus there is no previous study to compare to. Though FDR correction was applied, the only way to account for multiple comparisons is to perform a future replication study. PCR verification was not performed since most changes on Affymetrix arrays have correlated extremely well with PCR in previous studies. In addition, PCR would only be needed once this study has been replicated and the PCR confirmed genes were to be used to develop clinical tests.

[0185] In summary, patients with recent TIAs can be differentiated from controls without previous vascular events using gene expression profiles in blood. In addition, there may be different immune response subtypes following transient ischemic attacks in humans.

REFERENCES

1. Johnston SC, Nguyen-Huynh MN, Schwarz ME et al. National Stroke Association guidelines for the management of transient ischemic attacks. *Ann Neurol.* 2006;60:301-313
2. Rothwell PM, Buchan A, Johnston SC. Recent advances in management of transient ischaemic attacks and minor ischaemic strokes. *Lancet Neurol.* 2006;5:323-331
3. Easton JD, Saver JL, Albers GW et al. Definition and Evaluation of Transient Ischemic Attack A Scientific Statement for Healthcare Professionals From

the American Heart Association/American Stroke Association Stroke Council;
 Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular
 Radiology and Intervention; Council on Cardiovascular Nursing; and the
 Interdisciplinary Council on Peripheral Vascular Disease The American Academy of
 5 Neurology affirms the value of this statement as an educational tool for neurologists.
Stroke. 2009;40:2276-2293

4. Josephson SA, Sidney S, Pham TN et al. Higher ABCD2 score predicts
 patients most likely to have true transient ischemic attack. *Stroke*. 2008;39:3096-3098

5. Zhan X, Ander BP, Jickling G et al. Brief focal cerebral ischemia that
 10 simulates transient ischemic attacks in humans regulates gene expression in rat
 peripheral blood. *J Cereb Blood Flow Metab*. 2010;30:110-118

6. Zhan X, Kim C, Sharp FR. Very brief focal ischemia simulating
 transient ischemic attacks (TIAs) can injure brain and induce Hsp70 protein. *Brain*
Res. 2008;1234:183-197

7. Arenillas JF, Alvarez-Sabin J, Molina CA et al. C-reactive protein
 15 predicts further ischemic events in first-ever transient ischemic attack or stroke
 patients with intracranial large-artery occlusive disease. *Stroke*. 2003;34:2463-2468

8. Elneihoum AM, Falke P, Axelsson L et al. Leukocyte activation
 detected by increased plasma levels of inflammatory mediators in patients with
 20 ischemic cerebrovascular diseases. *Stroke*. 1996;27:1734-1738

9. Ross AM, Hurn P, Perrin N et al. Evidence of the peripheral
 inflammatory response in patients with transient ischemic attack. *J Stroke*
Cerebrovasc Dis. 2007;16:203-207

10. Castillo J, Alvarez-Sabin J, Martinez-Vila E et al. Inflammation
 25 markers and prediction of post-stroke vascular disease recurrence: the MITICO study.
J Neurol. 2009;256:217-224

11. Nambi V, Hoogeveen RC, Chambless L et al. Lipoprotein-associated
 phospholipase A2 and high-sensitivity C-reactive protein improve the stratification of
 ischemic stroke risk in the Atherosclerosis Risk in Communities (ARIC) study.
 30 *Stroke*. 2009;40:376-381

12. Cucchiara BL, Messe SR, Sansing L et al. Lipoprotein-associated
 phospholipase A2 and C-reactive protein for risk-stratification of patients with TIA.
Stroke. 2009;40:2332-2336

13. Rothwell PM, Howard SC, Power DA et al. Fibrinogen concentration and risk of ischemic stroke and acute coronary events in 5113 patients with transient ischemic attack and minor ischemic stroke. *Stroke*. 2004;35:2300-2305
14. Woodward M, Lowe GD, Campbell DJ et al. Associations of
5 inflammatory and hemostatic variables with the risk of recurrent stroke. *Stroke*. 2005;36:2143-2147
15. Kang DW, Yoo SH, Chun S et al. Inflammatory and hemostatic biomarkers associated with early recurrent ischemic lesions in acute ischemic stroke. *Stroke*. 2009;40:1653-1658
- 10 16. Moore DF, Li H, Jeffries N et al. Using peripheral blood mononuclear cells to determine a gene expression profile of acute ischemic stroke: a pilot investigation. *Circulation*. 2005;111:212-221
17. Tang Y, Xu H, Du X et al. Gene expression in blood changes rapidly in neutrophils and monocytes after ischemic stroke in humans: a microarray study. *J Cereb Blood Flow Metab*. 2006;26:1089-1102
- 15 18. Xu H, Tang Y, Liu DZ et al. Gene expression in peripheral blood differs after cardioembolic compared with large-vessel atherosclerotic stroke: biomarkers for the etiology of ischemic stroke. *J Cereb Blood Flow Metab*. 2008;28:1320-1328
- 20 19. Giles MF, Rothwell PM. Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 transient ischemic attack risk scores. *Stroke*. 2010;41:667-673
20. Cucchiara BL, Messe SR, Sansing L et al. D-dimer, magnetic resonance imaging diffusion-weighted imaging, and ABCD2 score for transient
25 ischemic attack risk stratification. *J Stroke Cerebrovasc Dis*. 2009;18:367-373
21. Andersohn F, Waring M, Garbe E. Risk of ischemic stroke in patients with Crohn's disease: A population-based nested case-control study. *Inflamm Bowel Dis*. 2009
22. Freilinger T, Riedel E, Holtmannspotter M et al. Ischemic stroke and
30 peripheral arterial thromboembolism in a patient with Crohn's disease: a case presentation. *J Neurol Sci*. 2008;266:177-179
23. Karacostas D, Mavromatis J, Artemis K, Milonas I. Hemorrhagic cerebral infarct and ulcerative colitis. A case report. *Funct Neurol*. 1991;6:181-184

24. Schneiderman JH, Sharpe JA, Sutton DM. Cerebral and retinal vascular complications of inflammatory bowel disease. *Ann Neurol.* 1979;5:331-337
25. Beck JD, Offenbacher S. Systemic effects of periodontitis: epidemiology of periodontal disease and cardiovascular disease. *J Periodontol.* 2005;76:2089-2100
26. Beck J, Garcia R, Heiss G et al. Periodontal disease and cardiovascular disease. *J Periodontol.* 1996;67:1123-1137
27. Elter JR, Offenbacher S, Toole JF, Beck JD. Relationship of periodontal disease and edentulism to stroke/TIA. *J Dent Res.* 2003;82:998-1001
28. Grau AJ, Becher H, Ziegler CM et al. Periodontal disease as a risk factor for ischemic stroke. *Stroke.* 2004;35:496-501
29. Grau AJ. Infection, inflammation, and cerebrovascular ischemia. *Neurology.* 1997;49:S47-51
30. Dourado DF, Fernandes PA, Ramos MJ. Mammalian cytosolic glutathione transferases. *Curr Protein Pept Sci.* 2008;9:325-337

It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. All publications, sequence accession numbers, patents, and patent applications cited herein are hereby incorporated by reference in their entirety for all purposes.

Table 5. TIA associated gene lists (FDR ≤ 0.05 , absolute fold change ≥ 1.5 compared with control).

Table 5A. 135 Downregulated Genes

5

TABLE 5A			
AFFY ID	Gene Symbol	Gene Title	Fold-Change
233034_at	---	---	-2.44997
237597_at	---	---	-2.4398
1558409_at	---	---	-2.26242
1566485_at	---	---	-2.22393
1556932_at	---	---	-2.11785
242874_at	---	---	-2.03355
1561166_a_at	---	---	-1.9781
217671_at	---	---	-1.9453
1557733_a_at	---	---	-1.91008
1557580_at	---	---	-1.85725
1558410_s_at	---	---	-1.7902
242710_at	---	---	-1.76712
215314_at	---	---	-1.75283
229654_at	---	---	-1.74432
1560861_at	---	---	-1.74348
243512_x_at	---	---	-1.73922
238812_at	---	---	-1.70108
232943_at	---	---	-1.69925
233677_at	---	---	-1.68615
244226_s_at	---	---	-1.68579
233614_at	---	---	-1.68298
1557581_x_at	---	---	-1.67676
244860_at	---	---	-1.67397
239588_s_at	---	---	-1.667
244665_at	---	---	-1.65812
243107_at	---	---	-1.65279
1557519_at	---	---	-1.64084
242564_at	---	---	-1.63967
1557551_at	---	---	-1.63028
238281_at	---	---	-1.62416
1558710_at	---	---	-1.62037
239646_at	---	---	-1.60914
1568781_at	---	---	-1.60862
234148_at	---	---	-1.60079
233302_at	---	---	-1.59557
233862_at	---	---	-1.58604
1570329_at	---	---	-1.56927
241638_at	---	---	-1.56143
232834_at	---	---	-1.559
236524_at	---	---	-1.55759
1559723_s_at	---	---	-1.55744
1559401_a_at	---	---	-1.55691
236558_at	---	---	-1.55664
237803_x_at	---	---	-1.55619
231069_at	---	---	-1.5535
1557477_at	---	---	-1.54943

TABLE 5A

AFFY ID	Gene Symbol	Gene Title	Fold-Change
237953_at	---	---	-1.54815
243641_at	---	---	-1.547
1555194_at	---	---	-1.54304
217060_at	---	---	-1.54232
239449_at	---	---	-1.54082
237334_at	---	---	-1.53953
242074_at	---	---	-1.53917
1570106_at	---	---	-1.53564
244674_at	---	---	-1.53173
232372_at	---	---	-1.52446
238744_at	---	---	-1.52032
233127_at	---	---	-1.5089
243310_at	---	---	-1.50605
214309_s_at	---	---	-1.50383
244290_at	---	---	-1.50381
1562013_a_at	---	---	-1.50343
219308_s_at	AK5	adenylate kinase 5	-1.95614
222862_s_at	AK5	adenylate kinase 5	-1.64741
239651_at	ANAPC5	anaphase promoting complex subunit 5	-1.55844
209871_s_at	APBA2	amyloid beta (A4) precursor protein-binding, family A, member 2	-1.56895
229252_at	ATG9B	ATG9 autophagy related 9 homolog B (S. cerevisiae)	-1.64694
227372_s_at	BAIAP2L1 /// LOC100128461	BAI1-associated protein 2-like 1 /// hypothetical protein LOC100128461	-1.53271
221631_at	CACNA1I	calcium channel, voltage-dependent, T type, alpha 1I subunit	-1.63297
239771_at	CAND1	cullin-associated and neddylation-dissociated 1	-1.97531
1553645_at	CCDC141	coiled-coil domain containing 141	-1.62867
1562028_at	CCND3	Cyclin D3 (CCND3), transcript variant 3, mRNA	-2.00377
239871_at	CLTC	Clathrin, heavy chain (Hc), mRNA (cDNA clone IMAGE:4812912)	-1.63031
212504_at	DIP2C	DIP2 disco-interacting protein 2 homolog C (Drosophila)	-1.62614
1553998_at	DMRTC1 /// DMRTC1B	DMRT-like family C1 /// DMRT-like family C1B	-1.86704
220048_at	EDAR	ectodysplasin A receptor	-1.69385
209368_at	EPHX2	epoxide hydrolase 2, cytoplasmic	-1.62474
1554273_a_at	ERAP2	endoplasmic reticulum aminopeptidase 2	-1.52883
230792_at	FAAH2	fatty acid amide hydrolase 2	-1.57807
229247_at	FBLN7	fibulin 7	-1.58734
202768_at	FOXB	FBX murine osteosarcoma viral oncogene homolog B	-1.63049
231108_at	FUS	fusion (involved in t(12;16) in malignant liposarcoma)	-1.56277
1557350_at	G3BP1	GTPase activating protein (SH3 domain) binding protein 1	-1.6194
219815_at	GAL3ST4	galactose-3-O-sulfotransferase 4	-1.5674
1560133_at	GIGYF2	GRB10 interacting GYF protein 2	-1.52626
223080_at	GLS	Glutaminase, mRNA (cDNA clone MGC:33744 IMAGE:5263220)	-1.59404
221288_at	GPR22	G protein-coupled receptor 22	-1.56303
215333_x_at	GSTM1	glutathione S-transferase mu 1	-2.03103
204550_x_at	GSTM1	glutathione S-transferase mu 1	-1.95136
204418_x_at	GSTM2	glutathione S-transferase mu 2 (muscle)	-1.95729
232207_at	GUSBL2	glucuronidase, beta-like 2	-2.10621

TABLE 5A

AFFY_ID	Gene Symbol	Gene Title	Fold-Change
220085_at	HELLS	helicase, lymphoid-specific	-1.67692
241723_at	IQGAP2	IQ motif containing GTPase activating protein 2	-1.73571
215750_at	KIAA1659	KIAA1659 protein	-1.54646
236728_at	LNPEP	leucyl/cystinyl aminopeptidase	-1.53387
236621_at	LOC100130070 /// LOC100130775 /// LOC100131787 /// LOC100131905 /// LOC100132291 /// LOC100132488 /// RPS27	similar to metallopanstimulin /// similar to rCG63653 /// similar to metallopan similar to metallopan similar to metallopan similar to metallopan similar to metallopan similar to metallopan RPS27	-1.70558
239062_at	LOC100131096	hypothetical LOC100131096	-1.57675
229094_at	LOC401431	hypothetical gene LOC401431	-1.53069
1565911_at	LOC648921	MRNA full length insert cDNA clone EUROIMAGE 209544	-1.54981
214180_at	MAN1C1	mannosidase, alpha, class 1C, member 1	-1.66631
215663_at	MBNL1	muscleblind-like (Drosophila)	-1.53726
212935_at	MCF2L	MCF.2 cell line derived transforming sequence-like	-1.53863
207078_at	MED6	mediator complex subunit 6	-1.53192
242111_at	METTLL3	methyltransferase like 3	-1.56742
1559856_s_at	MLL	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila)	-1.59219
243857_at	MORF4L2	Mrgx mRNA for MRGX	-1.52328
242191_at	NBPF10 /// RP11- 94I2.2	neuroblastoma breakpoint family, member 10 /// hypothetical protein LOC200030	-1.50043
203413_at	NELL2	NEL-like 2 (chicken)	-1.5281
229093_at	NOS3	nitric oxide synthase 3 (endothelial cell)	-1.53818
223601_at	OLFM2	olfactomedin 2	-1.5119
214615_at	P2RY10	purinergic receptor P2Y, G-protein coupled, 10	-1.51779
235758_at	PNMA6A	paraneoplastic antigen like 6A	-1.95731
244011_at	PPM1K	protein phosphatase 1K (PP2C domain containing)	-1.51501
239635_at	RBM14	RNA binding motif protein 14	-1.65349
219864_s_at	RCAN3	RCAN family member 3	-1.61977
212699_at	SCAMP5	secretory carrier membrane protein 5	-1.54948
232055_at	SFXN1	sideroflexin 1	-1.50117
239667_at	SLC3A1	solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, a	-1.69708
1553423_a_at	SLEFN13	schlafen family member 13	-1.53028
232020_at	SMURF2	SMAD specific E3 ubiquitin protein ligase 2	-1.57992
1560741_at	SNRPN	small nuclear ribonucleoprotein polypeptide N	-1.65945
226587_at	SNRPN	small nuclear ribonucleoprotein polypeptide N	-1.58006
226913_s_at	SOX8	SRY (sex determining region Y)-box 8	-1.73755
1555882_at	SPIN3	spindlin family, member 3	-1.65127
1555883_s_at	SPIN3	spindlin family, member 3	-1.50348
213993_at	SPON1	spondin 1, extracellular matrix protein	-1.55928
218856_at	TNFRSF21	tumor necrosis factor receptor superfamily, member 21	-1.77712
1556116_s_at	TNPO1	Transportin 1, mRNA (cDNA clone MGC:17116 IMAGE:4178989)	-1.7577
244521_at	TSHZ2	Cell growth-inhibiting protein 7	-1.86192
206487_at	UNC84A	unc-84 homolog A (C. elegans)	-1.50376
1558569_at	UNQ6228	MRNA, cDNA DKFZp667K1619 (from clone DKFZp667K1619)	-1.63796
1557450_s_at	WHDC1L2	WAS protein homology region 2 domain containing 1-	-1.75555

TABLE 5A

AFFY ID	Gene Symbol	Gene Title	Fold-Change
		like 2	
239234_at	ZC3H12B	zinc finger CCCH-type containing 12B	-1.72127
55872_at	ZNF512B	zinc finger protein 512B	-1.52158
1568873_at	ZNF519	zinc finger protein 519	-1.70283

Table 5B. 325 Upregulated Genes

TABLE 5B			
AFFY ID	Gene Symbol	Gene Title	Fold-Change
1563546_at	---	---	3.50048
1559696_at	---	---	3.23854
1563033_x_at	---	---	3.18355
1563032_at	---	---	2.97375
1558496_at	---	---	2.87094
241566_at	---	---	2.82164
1568589_at	---	---	2.7205
215448_at	---	---	2.69149
237479_at	---	---	2.68144
234235_at	---	---	2.64462
231074_at	---	---	2.63519
1560905_at	---	---	2.63286
237871_x_at	---	---	2.55976
237937_x_at	---	---	2.541
207731_at	---	---	2.52426
240988_x_at	---	---	2.46734
243398_at	---	---	2.43872
241675_s_at	---	---	2.39854
241674_s_at	---	---	2.38362
228827_at	---	---	2.3697
233944_at	---	---	2.36679
227952_at	---	---	2.31481
1554225_a_at	---	---	2.30748
1560049_at	---	---	2.29877
215962_at	---	---	2.28524
1564306_at	---	---	2.20443
1557762_at	---	---	2.18276
231091_x_at	---	---	2.17817
1566862_at	---	---	2.1529
1560760_s_at	---	---	2.1184
230959_at	---	---	2.10492
238103_at	---	---	2.08283
242802_x_at	---	---	2.06924
234502_at	---	---	2.05567
241636_x_at	---	---	2.0384
236038_at	---	---	2.0344
216406_at	---	---	2.02612
1566805_at	---	---	2.00292
239464_at	---	---	2.00073
233875_at	---	---	1.99361
1561713_at	---	---	1.9693
1562480_at	---	---	1.94431
1556983_a_at	---	---	1.93605
1570191_at	---	---	1.93494
243902_at	---	---	1.93045
207744_at	---	---	1.92381
237233_at	---	---	1.90496
1561199_at	---	---	1.89756
1561902_at	---	---	1.89021
243273_at	---	---	1.88315

TABLE 5B

AFFY ID	Gene Symbol	Gene Title	Fold-Change
238368_at	---	---	1.88178
243666_at	---	---	1.87601
1556989_at	---	---	1.86984
238358_x_at	---	---	1.86726
229635_at	---	---	1.8637
238361_s_at	---	---	1.84576
231503_at	---	---	1.84378
229490_s_at	---	---	1.84229
1569344_a_at	---	---	1.83229
234083_at	---	---	1.83201
243183_at	---	---	1.83176
238405_at	---	---	1.82494
1559336_at	---	---	1.82388
1563568_at	---	---	1.81339
237983_at	---	---	1.81139
1563881_at	---	---	1.801
242198_at	---	---	1.79799
1562613_at	---	---	1.78841
1560086_at	---	---	1.78528
237893_at	---	---	1.77856
1562992_at	---	---	1.75888
240112_at	---	---	1.75583
1569810_at	---	---	1.75522
1566609_at	---	---	1.75501
243533_x_at	---	---	1.74919
1570152_at	---	---	1.74489
1561112_at	---	---	1.74035
231040_at	---	---	1.73604
1559695_a_at	---	---	1.7325
1560296_at	---	---	1.72689
1561473_at	---	---	1.72375
241654_at	---	---	1.71535
1557645_at	---	---	1.70892
1566498_at	---	---	1.70831
237399_at	---	---	1.70373
1562811_at	---	---	1.70357
1561448_at	---	---	1.68957
237933_at	---	---	1.68559
241457_at	---	---	1.67974
242420_at	---	---	1.67555
222342_at	---	---	1.6753
1556021_at	---	---	1.67385
239984_at	---	---	1.67188
244216_at	---	---	1.67082
234794_at	---	---	1.66748
215290_at	---	---	1.65929
243279_at	---	---	1.65749
1570268_at	---	---	1.65328
244384_at	---	---	1.65237
238571_at	---	---	1.64715
237552_at	---	---	1.64653

TABLE 5B

AFFY ID	Gene Symbol	Gene Title	Fold-Change
241461_at	---	---	1.63938
242718_at	---	---	1.63417
238392_at	---	---	1.62252
238354_x_at	---	---	1.62228
1560453_at	---	---	1.62059
215976_at	---	---	1.62035
1564840_at	---	---	1.6194
1561767_at	---	---	1.61738
1553275_s_at	---	---	1.61253
1563087_at	---	---	1.61106
1566597_at	---	---	1.59925
244668_at	---	---	1.59371
216518_at	---	---	1.5937
1563561_at	---	---	1.59351
236571_at	---	---	1.5893
216214_at	---	---	1.58555
240904_at	---	---	1.58293
235494_at	---	---	1.57849
240067_at	---	---	1.57319
237071_at	---	---	1.57301
233306_at	---	---	1.56521
216463_at	---	---	1.56326
237192_at	---	---	1.56114
1560517_s_at	---	---	1.55983
1555263_at	---	---	1.556
1566968_at	---	---	1.55262
241173_at	---	---	1.54723
1561351_at	---	---	1.54685
1559629_at	---	---	1.54679
238395_at	---	---	1.54457
1563026_at	---	---	1.54135
1562610_at	---	---	1.53899
1570506_at	---	---	1.53071
231546_at	---	---	1.52352
240714_at	---	---	1.52183
242495_at	---	---	1.51926
1561642_at	---	---	1.51919
234825_at	---	---	1.51483
241247_at	---	---	1.51115
236276_at	---	---	1.50976
238386_x_at	---	---	1.50861
241569_at	---	---	1.50674
1564851_at	---	---	1.50551
1556185_a_at	---	---	1.50406
243424_at	---	---	1.50374
238274_at	---	---	1.50237
207275_s_at	ACSL1	acyl-CoA synthetase long-chain family member 1	1.51866
243520_x_at	ADAM30	ADAM metallopeptidase domain 30	1.80193
206134_at	ADAMDEC1	ADAM-like, decysin 1	1.61274
209614_at	ADH1B	alcohol dehydrogenase 1B (class I), beta polypeptide	1.51397
202912_at	ADM	adrenomedullin	1.61874

TABLE 5B

AFFY ID	Gene Symbol	Gene Title	Fold-Change
206513_at	AIM2	absent in melanoma 2	1.60396
215783_s_at	ALPL	alkaline phosphatase, liver/bone/kidney	2.1006
1557924_s_at	ALPL	alkaline phosphatase, liver/bone/kidney	2.02022
1563673_a_at	ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	2.15177
1562292_at	ANKRD30B	ankyrin repeat domain 30B	1.86641
209369_at	ANXA3	annexin A3	2.41095
1554816_at	ASTN2	astrotactin 2	2.22748
239144_at	B3GAT2	beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S)	1.75721
228758_at	BCL6	Zinc finger protein	1.69127
215990_s_at	BCL6	B-cell CLL/lymphoma 6	1.59315
242579_at	BMPRII	bone morphogenetic protein receptor, type II	2.05687
232416_at	BRUNOL5	bruno-like 5, RNA binding protein (Drosophila)	1.68747
223977_s_at	C18orf2	chromosome 18 open reading frame 2	1.58384
1553652_a_at	C18orf54	chromosome 18 open reading frame 54	1.54796
235568_at	C19orf59	chromosome 19 open reading frame 59	1.99789
1554540_at	C1orf67	chromosome 1 open reading frame 67	1.51941
1553329_at	C7orf45	chromosome 7 open reading frame 45	1.72974
239203_at	C7orf53	chromosome 7 open reading frame 53	1.55912
1552701_a_at	CARD16	caspase recruitment domain family, member 16	1.59587
232969_at	CARD8	caspase recruitment domain family, member 8	1.78265
207500_at	CASP5	caspase 5, apoptosis-related cysteine peptidase	1.91798
203065_s_at	CAV1	caveolin 1, caveolae protein, 22kDa	1.60773
220351_at	CCRL1	chemokine (C-C motif) receptor-like 1	2.32444
208168_s_at	CHIT1	chitinase 1 (chitotriosidase)	1.56138
239989_at	CNTLN	centlein, centrosomal protein	1.53478
229084_at	CNTN4	contactin 4	1.7244
1556499_s_at	COL1A1	collagen, type I, alpha 1	2.87107
229218_at	COL1A2	collagen, type I, alpha 2	1.92067
210262_at	CRISP2	cysteine-rich secretory protein 2	1.88349
1553002_at	DEFB105A /// DEFB105B	defensin, beta 105A /// defensin, beta 105B	1.52948
226121_at	DHRS13	dehydrogenase/reductase (SDR family) member 13	1.65414
233092_s_at	DKFZP434B061	DKFZP434B061 protein	1.84946
222253_s_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	2.61011
206819_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	1.93567
239309_at	DLX6	distal-less homeobox 6	2.4523
220493_at	DMRT1	doublesex and mab-3 related transcription factor 1	1.61917
241199_x_at	DPPA4	developmental pluripotency associated 4	2.68174
232360_at	EHF	ets homologous factor	1.68951
219850_s_at	EHF	ets homologous factor	1.64412
228260_at	ELAVL2	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B)	1.9905
227612_at	ELAVL3	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 3 (Hu antigen C)	3.23425
219134_at	ELTD1	EGF, latrophilin and seven transmembrane domain containing 1	1.70282
211164_at	EPHA3	EPH receptor A3	2.39314
243277_x_at	EVII	ecotropic viral integration site 1	1.5445
230519_at	FAM124A	family with sequence similarity 124A	1.59499
1569025_s_at	FAM13A1	family with sequence similarity 13, member A1	1.55876

TABLE 5B

AFFY ID	Gene Symbol	Gene Title	Fold-Change
222291_at	FAM149A	family with sequence similarity 149, member A	1.75785
222205_x_at	FAM182B /// RP13-401N8.2	family with sequence similarity 182, member B /// hypothetical gene supported by	1.70042
220645_at	FAM55D	family with sequence similarity 55, member D	1.55166
201579_at	FAT1	FAT tumor suppressor homolog 1 (Drosophila)	1.67288
239710_at	FIGN	fidgetin	2.14096
238964_at	FIGN	fidgetin	1.56796
1557155_a_at	FLJ30375	CDNA clone IMAGE:5301781	1.97451
229521_at	FLJ36031	hypothetical protein FLJ36031	1.58141
1560790_at	FLJ36144	hypothetical protein FLJ36144	1.78391
1558579_at	FLJ37786	hypothetical LOC642691	1.66029
230999_at	FLJ39051	CDNA FLJ39051 fis, clone NT2RP7011452	1.92605
227925_at	FLJ39051	CDNA FLJ39051 fis, clone NT2RP7011452	1.86433
217487_x_at	FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	2.19987
217483_at	FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	1.68955
40284_at	FOXA2	forkhead box A2	1.8498
1553613_s_at	FOXC1	forkhead box C1	1.53964
230964_at	FREM2	FRAS1 related extracellular matrix protein 2	2.30984
1553024_at	G30	protein LG30-like	1.75094
1557122_s_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	3.49668
242344_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	2.72458
1555726_at	GAF3	FGF-2 activity-associated protein 3	1.61768
219271_at	GALNT14	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	2.07605
240390_at	GALNT5	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	2.09257
204763_s_at	GNAO1	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide	1.5542
223767_at	GPR84	G protein-coupled receptor 84	1.76044
207235_s_at	GRM5	glutamate receptor, metabotropic 5	1.93451
1559520_at	GYPA	Glycophorin A	2.12904
211267_at	HESX1	HESX homeobox 1	1.61355
227566_at	HNT	neurotrimin	1.56554
206858_s_at	HOXC4 /// HOXC6	homeobox C4 /// homeobox C6	1.70414
219403_s_at	HPSE	heparanase	1.60481
211959_at	IGFBP5	insulin-like growth factor binding protein 5	1.54545
205067_at	IL1B	interleukin 1, beta	1.57884
39402_at	IL1B	interleukin 1, beta	1.51316
229538_s_at	IQGAP3	IQ motif containing GTPase activating protein 3	1.73797
214927_at	ITGBL1	integrin, beta-like 1 (with EGF-like repeat domains)	1.73813
238428_at	KCNJ15 /// LOC100131955	potassium inwardly-rectifying channel, subfamily J, member 15 /// similar to pot	1.56965
227250_at	KREMEN1	kringle containing transmembrane protein 1	2.16406
235370_at	KREMEN1	kringle containing transmembrane protein 1	1.77475
215516_at	LAMB4	laminin, beta 4	1.60646
206140_at	LHX2	LIM homeobox 2	2.0959
225571_at	LIFR	leukemia inhibitory factor receptor alpha	1.69168
210582_s_at	LIMK2	LIM domain kinase 2	1.5485
1556704_s_at	LOC100133920 /// LOC286297	hypothetical protein LOC100133920 /// hypothetical protein LOC286297	1.63034
232034_at	LOC203274	CDNA FLJ31544 fis, clone NT2RI2000865	1.63147
1557717_at	LOC338862	hypothetical protein LOC338862	2.22946

TABLE 5B

AFFY ID	Gene Symbol	Gene Title	Fold-Change
1560823_at	LOC340017	hypothetical protein LOC340017	1.51946
233879_at	LOC374491	TPTE and PTEN homologous inositol lipid phosphatase pseudogene	1.81019
1558982_at	LOC375010	hypothetical LOC375010	1.72485
214984_at	LOC440345	hypothetical protein LOC440345	1.98536
230902_at	LOC645323	CDNA clone IMAGE:5260726	1.84336
238850_at	LOC645323	hypothetical LOC645323	1.81503
1568933_at	LOC646627	phospholipase inhibitor	1.53874
231434_at	LOC728460	similar to FLJ32921 protein	1.68733
1570009_at	LOC732096	similar to hCG2040240	2.13184
230863_at	LRP2	low density lipoprotein-related protein 2	1.71146
203005_at	LTBR	lymphotxin beta receptor (TNFR superfamily, member 3)	1.58399
201744_s_at	LUM	lumican	1.93131
210449_x_at	MAPK14	mitogen-activated protein kinase 14	1.57327
211561_x_at	MAPK14	mitogen-activated protein kinase 14	1.55337
235077_at	MEG3	maternally expressed 3 (non-protein coding)	1.6384
240814_at	MGC39584	hypothetical gene supported by BC029568	1.59341
214087_s_at	MYBPC1	myosin binding protein C, slow type	1.58609
237510_at	MYNN	Myoneurin, mRNA (cDNA clone IMAGE:4721583)	1.85041
1559292_s_at	NCRNA00032	Clone IMAGE:2275835 C9orf14 mRNA, partial sequence; alternatively spliced	1.98554
220429_at	NDST3	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 3	1.68889
209119_x_at	NR2F2	nuclear receptor subfamily 2, group F, member 2	1.94377
231867_at	ODZ2	odz, odd Oz/ten-m homolog 2 (Drosophila)	2.03143
214111_at	OPCML	opioid binding protein/cell adhesion molecule-like	1.91158
230170_at	OSM	oncostatin M	1.58899
1553931_at	OSTCL	oligosaccharyltransferase complex subunit-like	1.57501
206048_at	OVOL2	ovo-like 2 (Drosophila)	2.06333
1559400_s_at	PAPPA	pregnancy-associated plasma protein A, pappalysin 1	1.50009
210292_s_at	PCDH11X /// PCDH11Y	protocadherin 11 X-linked /// protocadherin 11 Y-linked	1.6605
208396_s_at	PDE1A	phosphodiesterase 1A, calmodulin-dependent	1.68453
214868_at	PIWIL1	piwi-like 1 (Drosophila)	1.63171
202446_s_at	PLSCR1	phospholipid scramblase 1	1.54059
233030_at	PNPLA3	patatin-like phospholipase domain containing 3	1.50269
1569675_at	POU2AF1	POU class 2 associating factor 1, mRNA (cDNA clone MGC:45211 IMAGE:5554134)	1.67876
1555462_at	PPP1R1C	protein phosphatase 1, regulatory (inhibitor) subunit 1C	1.60542
241669_x_at	PRKD2	protein kinase D2	1.55139
220696_at	PRO0478	PRO0478 protein	1.69169
228825_at	PTGR1	prostaglandin reductase 1	1.95262
217194_at	RASAL2	RAS protein activator like 2	2.00632
226872_at	RFX2	regulatory factor X, 2 (influences HLA class II expression)	1.58786
213194_at	ROBO1	roundabout, axon guidance receptor, homolog 1 (Drosophila)	1.95207
242385_at	RORB	RAR-related orphan receptor B	2.14023
1555990_at	RP1-127L4.6	hypothetical protein LOC150297	1.76603
215321_at	RUNDC3B	RUN domain containing 3B	1.60322
205863_at	S100A12	S100 calcium binding protein A12	1.5633
229057_at	SCN2A	sodium channel, voltage-gated, type II, alpha subunit	1.85129

TABLE 5B

AFFY ID	Gene Symbol	Gene Title	Fold-Change
207570_at	SHOX	short stature homeobox	2.00103
210135_s_at	SHOX2	short stature homeobox 2	2.86893
208443_x_at	SHOX2	short stature homeobox 2	1.70616
206634_at	SIX3	SIX homeobox 3	1.78989
205896_at	SLC22A4	solute carrier family 22 (organic cation/ergothioneine transporter), member 4	1.65918
237340_at	SLC26A8	solute carrier family 26, member 8	2.32491
216236_s_at	SLC2A14 /// SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 14 /// solute	1.51356
232547_at	SNIP	SNAP25-interacting protein	1.83841
240204_at	SNRPN	small nuclear ribonucleoprotein polypeptide N	1.58295
241987_x_at	SNX31	sorting nexin 31	2.19167
204913_s_at	SOX11	SRY (sex determining region Y)-box 11	2.34727
204914_s_at	SOX11	SRY (sex determining region Y)-box 11	1.88201
202935_s_at	SOX9	SRY (sex determining region Y)-box 9	2.45928
235342_at	SPOCK3	spare/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 3	1.75314
241961_at	SRD5A2L2	steroid 5 alpha-reductase 2-like 2	2.08494
1554473_at	SRGAP1	SLIT-ROBO Rho GTPase activating protein 1	1.99203
203759_at	ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	1.51002
231969_at	STOX2	storkhead box 2	2.2552
214451_at	TFAP2B	transcription factor AP-2 beta (activating enhancer binding protein 2 beta)	1.89347
215447_at	TFPI	Tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor),	1.96509
228121_at	TGFB2	transforming growth factor, beta 2	1.70904
210166_at	TLR5	toll-like receptor 5	1.9168
220205_at	TPTE	transmembrane phosphatase with tensin homology	1.60547
206479_at	TRPM1	transient receptor potential cation channel, subfamily M, member 1	1.57541
1556666_a_at	TTC6	tetratricopeptide repeat domain 6	1.91015
213943_at	TWIST1	twist homolog 1 (Drosophila)	2.72279
222435_s_at	UBE2J1	ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	1.50758
226899_at	UNC5B	unc-5 homolog B (C. elegans)	2.04351
1561200_at	VWA3B	von Willebrand factor A domain containing 3B	1.61802
206954_at	WIT1	Wilms tumor upstream neighbor 1	2.58643
1552946_at	ZNF114	zinc finger protein 114	1.99445
229743_at	ZNF438	zinc finger protein 438	1.53049
244007_at	ZNF462	zinc finger protein 462	1.53545
1555367_at	ZNF479	zinc finger protein 479	2.25193
1555368_x_at	ZNF479	zinc finger protein 479	2.16203
232303_at	ZNF608	zinc finger protein 608	1.72629

Table 5C. 34 Genes that differentiate TIA from Control

AFFY ID	Gene Symbol	Gene Title	Fold-Change
1557580_at	---	---	-1.85725
1559695_a_at	---	---	1.7325
1561767_at	---	---	1.61738
1563026_at	---	---	1.54135
1563568_at	---	---	1.81339
1568589_at	---	---	2.7205
1568781_at	---	---	-1.60862
216406_at	---	---	2.02612
229654_at	---	---	-1.74432
231040_at	---	---	1.73604
231069_at	---	---	-1.5535
231546_at	---	---	1.52352
233306_at	---	---	1.56521
236571_at	---	---	1.5893
237597_at	---	---	-2.4398
237953_at	---	---	-1.54815
242495_at	---	---	1.51926
242564_at	---	---	-1.63967
242710_at	---	---	-1.76712
244226_s_at	---	---	-1.68579
244665_at	---	---	-1.65812
229252_at	ATG9B	ATG9 autophagy related 9 homolog B (S. cerevisiae)	-1.64694
212504_at	DIP2C	DIP2 disco-interacting protein 2 homolog C (Drosophila)	-1.62614
233092_s_at	DKFZP434B061	DKFZP434B061 protein	1.84946
220048_at	EDAR	ectodysplasin A receptor	-1.69385
220645_at	FAM55D	family with sequence similarity 55, member D	1.55166
1557155_a_at	FLJ30375	CDNA clone IMAGE:5301781	1.97451
215333_x_at	GSTM1	glutathione S-transferase mu 1	-2.03103
232207_at	GUSBL2	glucuronidase, beta-like 2	-2.10621
211959_at	IGFBP5	insulin-like growth factor binding protein 5	1.54545
203005_at	LTBR	lymphotoxin beta receptor (TNFR superfamily, member 3)	1.58399
229057_at	SCN2A	sodium channel, voltage-gated, type II, alpha subunit	1.85129
232020_at	SMURF2	SMAD specific E3 ubiquitin protein ligase 2	-1.57992
55872_at	ZNF512B	zinc finger protein 512B	-1.52158

Table 5D. 26 Upregulated Genes that differentiate TIA1 from TIA2

AFFY ID	Gene Symbol	Gene Title	Fold-Change
1557122_s_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	3.49668
1559696_at	---	---	3.23854
227612_at	ELAVL3	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 3 (Hu antigen C)	3.23425
1563032_at	---	---	2.97375
1558496_at	---	---	2.87094
241566_at	---	---	2.82164
213943_at	TWIST1	twist homolog 1 (Drosophila)	2.72279
215448_at	---	---	2.69149
241199_x_at	DPPA4	developmental pluripotency associated 4	2.68174
237479_at	---	---	2.68144
234235_at	---	---	2.64462
1560905_at	---	---	2.63286
222253_s_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	2.61011
237937_x_at	---	---	2.541
207731_at	---	---	2.52426
239309_at	DLX6	distal-less homeobox 6	2.4523
243398_at	---	---	2.43872
241675_s_at	---	---	2.39854
241674_s_at	---	---	2.38362
1555367_at	ZNF479	zinc finger protein 479	2.25193
1554816_at	ASTN2	astrotactin 2	2.22748
241987_x_at	SNX31	sorting nexin 31	2.19167
1557762_at	---	---	2.18276
1563673_a_at	ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	2.15177
214984_at	LOC440345	hypothetical protein LOC440345	1.98536
1556983_a_at	---	---	1.93605

Table 8- Significant genes between TIA1 and TIA2 (FDR $\leq$ 0.05, absolute fold change $\geq$ 1.5, TIA1 vs TIA2)

TABLE 8			
AFY ID	Gene Symbol	Gene Title	Fold Change
1553422_s_at	A2BP1	ataxin 2-binding protein 1	1.72186
223593_at	AADAT	aminoadipate aminotransferase	1.85564
214829_at	AASS	aminoadipate-semialdehyde synthase	1.89032
1552582_at	ABCC13	ATP-binding cassette, sub-family C (CFTR/MRP), member 13	2.62247
1557374_at	ABCC9	ATP-binding cassette, sub-family C (CFTR/MRP), member 9	1.74138
208462_s_at	ABCC9	ATP-binding cassette, sub-family C (CFTR/MRP), member 9	2.03195
220518_at	ABI3BP	ABI family, member 3 (NESH) binding protein	1.81797
220061_at	ACSM5	acyl-CoA synthetase medium-chain family member 5	1.74065
89977_at	ACSM5	acyl-CoA synthetase medium-chain family member 5	2.18846
215613_at	ADAM12	Meltrin-S (ADAM12) mRNA, complete cds, alternatively spliced	1.79057
1568970_at	ADAM18	ADAM metallopeptidase domain 18	2.48574
207664_at	ADAM2	ADAM metallopeptidase domain 2	1.9154
243520_x_at	ADAM30	ADAM metallopeptidase domain 30	2.74216
1552266_at	ADAM32	ADAM metallopeptidase domain 32	1.65164
206134_at	ADAMDEC1	ADAM-like, decysin 1	3.08521
230040_at	ADAMTS18	ADAM metallopeptidase with thrombospondin type 1 motif, 18	1.68813
1553180_at	ADAMTS19	ADAM metallopeptidase with thrombospondin type 1 motif, 19	2.44377
214913_at	ADAMTS3	ADAM metallopeptidase with thrombospondin type 1 motif, 3	1.58473
220287_at	ADAMTS9	ADAM metallopeptidase with thrombospondin type 1 motif, 9	1.97398
209614_at	ADH1B	alcohol dehydrogenase 1B (class I), beta polypeptide	1.60016
231678_s_at	ADH4	alcohol dehydrogenase 4 (class II), pi polypeptide	1.66033
204120_s_at	ADK	adenosine kinase	-1.79666
211491_at	ADRA1A	adrenergic, alpha-1A-, receptor	1.6033
204333_s_at	AGA	aspartylglucosaminidase	-1.54576
1553447_at	AGBL1	ATP/GTP binding protein-like 1	1.51198
1554820_at	AGBL3	ATP/GTP binding protein-like 3	1.79467
232007_at	AGPAT5	1-acylglycerol-3-phosphate O-acyltransferase 5 (lysophosphatidic acid acyltransf	-1.78587
205357_s_at	AGTR1	angiotensin II receptor, type 1	1.51953
206957_at	AGXT	alanine-glyoxylate aminotransferase	1.50599
230630_at	AK3L1 /// AK3L2	adenylate kinase 3-like 1 /// adenylate kinase 3-like 2	1.52481
207870_at	AKAP9	A kinase (PRKA) anchor protein (yotiao) 9	1.76652
244205_at	ALAS2	aminolevulinate, delta-, synthase 2	1.67115
211617_at	ALDOAP2	aldolase A, fructose-bisphosphate pseudogene 2	3.07845
211357_s_at	ALDOB	aldolase B, fructose-bisphosphate	1.74204
1553261_x_at	ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	2.08857
1553260_s_at	ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	2.81678
1563673_a_at	ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 11	3.60798
1553471_at	AMAC1	acyl-malonyl condensing enzyme 1	1.53576
236760_at	AMMECR1	Alport syndrome, mental retardation, midface hypoplasia and elliptocytosis chrom	-1.61791
203002_at	AMOTL2	angiominin like 2	1.52446

TABLE 8

AFY ID	Gene Symbol	Gene Title	Fold Change
243799_x_at	ANGPTL3	Angiopoietin-like 3, mRNA (cDNA clone IMAGE 3934961)	1.63129
232606_at	ANK2	Ankyrin, Brank-1 protein	1.69608
1553211_at	ANKFN1	ankyrin-repeat and fibronectin type III domain containing 1	1.66982
1560370_x_at	ANKH	CDNA FLJ30404 fis, clone BRACE2008481	1.53577
243181_at	ANKIB1	ankyrin repeat and IBR domain containing 1	-1.59952
206029_at	ANKRD1	ankyrin repeat domain 1 (cardiac muscle)	1.58224
1559406_at	ANKRD18A	ankyrin repeat domain 18A	1.76934
1570255_s_at	ANKRD20A1 /// ANKRD20A2 /// ANKRD20A3 /// ANKRD20A4 /// ANKRD20B /// LOC375010 /// LOC647595 /// LOC728371	ankyrin repeat domain 20 family, member A1 /// ankyrin repeat domain 20 family,	2.65731
205706_s_at	ANKRD26	ankyrin repeat domain 26	-1.69786
1561079_at	ANKRD28	ankyrin repeat domain 28	1.96635
1562292_at	ANKRD30B	ankyrin repeat domain 30B	2.5644
1562294_x_at	ANKRD30B	ankyrin repeat domain 30B	3.18306
227034_at	ANKRD57	ankyrin repeat domain 57	-1.62847
213553_x_at	APOC1	apolipoprotein C-I	1.51627
215931_s_at	ARFGEF2	ADP-ribosylation factor guanine nucleotide-exchange factor 2 (brefeldin A-inhibi	-1.50024
228368_at	ARHGAP20	Rho GTPase activating protein 20	1.60285
1560318_at	ARHGAP29	Rho GTPase activating protein 29	4.60468
235412_at	ARHGEF7	Rho guanine nucleotide exchange factor (GEF) 7 (ARHGEF7), transcript variant 2,	1.63916
242727_at	ARL5B	ADP-ribosylation factor-like 5B	-1.54355
219094_at	ARMC8	armadillo repeat containing 8	-1.57518
227444_at	ARMCX4	Armadillo repeat containing, X-linked 4, mRNA (cDNA clone IMAGE 5261888)	-1.81523
239147_at	ARSK	arylsulfatase family, member K	1.97592
239002_at	ASPM	asp (abnormal spindle) homolog, microcephaly associated (Drosophila)	2.35391
1554816_at	ASTN2	astrotactin 2	4.64925
233536_at	ASXL3	additional sex combs like 3 (Drosophila)	2.11586
1569729_a_at	ASZ1	ankyrin repeat, SAM and basic leucine zipper domain containing 1	1.59531
1559485_at	ATG2B	ATG2 autophagy related 2 homolog B (S. cerevisiae)	1.71224
228190_at	ATG4C /// CTR9	ATG4 autophagy related 4 homolog C (S. cerevisiae) /// Ctr9, Paf1/RNA polymerase	-1.50066
220920_at	ATP10B	ATPase, class V, type 10B	1.91809
220556_at	ATP1B4	ATPase, (Na+)/K+ transporting, beta 4 polypeptide	1.63153
211137_s_at	ATP2C1	ATPase, Ca++ transporting, type 2C, member 1	-1.51541
214594_x_at	ATP8B1	ATPase, class I, type 8B, member 1	1.78628
216129_at	ATP9A	ATPase, class II, type 9A	1.98899
1560404_a_at	ATPBD4	ATP binding domain 4	1.5843
1569796_s_at	ATRNL1	attractin-like 1	2.48281

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
222969_at	B3GALT1	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 1	1.97721
239144_at	B3GAT2	beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S)	2.24315
206233_at	B4GALT6	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 6	1.51182
222446_s_at	BACE2	beta-site APP-cleaving enzyme 2	-1.70556
207712_at	BAGE	B melanoma antigen	1.65959
1555605_x_at	BAGE	B melanoma antigen	1.7285
1555369_at	BAGE	B melanoma antigen	1.55591
1555603_at	BAGE	B melanoma antigen	2.17743
211568_at	BAI3	brain-specific angiogenesis inhibitor 3	1.99551
219688_at	BBS7	Bardet-Biedl syndrome 7	-1.8488
1555555_at	BBS9	Bardet-Biedl syndrome 9	1.67715
233464_at	BCL2L14	BCL2-like 14 (apoptosis facilitator)	1.59747
1560683_at	BCL8	B-cell CLL/lymphoma 8	1.76236
1560684_x_at	BCL8	B-cell CLL/lymphoma 8	1.85157
239367_at	BDNF	brain-derived neurotrophic factor	1.96176
232368_at	BET3L	BET3 like (S. cerevisiae)	1.85928
1569674_at	BHLHB9	Clone 23955 mRNA sequence	1.73214
1569289_at	BIYM	Full length insert cDNA clone YB21E09	1.62223
205431_s_at	BMP5	bone morphogenetic protein 5	2.03195
242579_at	BMPR1B	bone morphogenetic protein receptor, type IB	3.69028
235723_at	BNC2	basomuculin 2	1.76632
232103_at	BPNT1	3'(2'), 5'-bisphosphate nucleotidase 1	-1.52974
206044_s_at	BRAF /// KIAA1549	v-raf murine sarcoma viral oncogene homolog B1 /// KIAA1549	1.58869
1569960_at	BRD7P3	bromodomain containing 7 pseudogene 3	3.08416
206787_at	BRDT	bromodomain, testis-specific	1.53605
207369_at	BRS3	bombesin-like receptor 3	2.10739
238966_at	BRUNOL4	bruno-like 4, RNA binding protein (Drosophila)	1.59417
230497_at	BRUNOL5	bruno-like 5, RNA binding protein (Drosophila)	1.81119
232416_at	BRUNOL5	bruno-like 5, RNA binding protein (Drosophila)	2.98452
202946_s_at	BTBD3	BTB (POZ) domain containing 3	-1.51798
207326_at	BTC	betacellulin	1.76063
234243_at	BXDC5	brix domain containing 5	3.97289
224667_x_at	C10orf104	chromosome 10 open reading frame 104	1.56473
1557548_at	C10orf108	chromosome 10 open reading frame 108	4.2936
1560851_at	C10orf136	chromosome 10 open reading frame 136	2.78294
244435_at	C10orf141	chromosome 10 open reading frame 141	1.90679
1556648_a_at	C10orf40	chromosome 10 open reading frame 40	2.61956
1557801_x_at	C11orf31	chromosome 11 open reading frame 31	-1.50635
1561985_at	C14orf39	chromosome 14 open reading frame 39	2.08706
224213_at	C14orf91	chromosome 14 open reading frame 91	1.51441
232507_at	C15orf41	chromosome 15 open reading frame 41	1.77387
208109_s_at	C15orf5	chromosome 15 open reading frame 5	1.62118
1560751_at	C18orf16	chromosome 18 open reading frame 16	3.41883
223977_s_at	C18orf2	chromosome 18 open reading frame 2	2.32467
244495_x_at	C18orf45	chromosome 18 open reading frame 45	1.64232

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
1553652_a_at	C18orf54	chromosome 18 open reading frame 54	1.96326
1556288_at	C18orf62	chromosome 18 open reading frame 62	2.60662
1552908_at	C1orf150	chromosome 1 open reading frame 150	2.85331
1554540_at	C1orf67	chromosome 1 open reading frame 67	1.74707
233598_at	C20orf187	chromosome 20 open reading frame 187	2.12033
1554657_a_at	C20orf26	chromosome 20 open reading frame 26	1.7578
232953_at	C20orf69 /// DKFZP434B20 18 /// LOC643670 /// LOC728105 /// LOC728323 /// PCMTD2	chromosome 20 open reading frame 69 /// similar to hypothetical protein LOC28470	1.62957
234314_at	C20orf74	chromosome 20 open reading frame 74	1.68
240068_at	C21orf130	chromosome 21 open reading frame 130	2.30653
1557481_a_at	C21orf131	chromosome 21 open reading frame 131	2.67119
239999_at	C21orf34	CDNA FLJ38295 fis, clone FCBBF3012332	1.71918
240801_at	C21orf37	chromosome 21 open reading frame 37	2.52149
1552876_at	C21orf89	chromosome 21 open reading frame 89	1.74874
244467_at	C22:CTA- 250D10.9	transmembrane protein 46-like	-1.50447
1552979_at	C2orf52	chromosome 2 open reading frame 52	1.5065
1558519_at	C2orf67 /// RPE	Chromosome 2 open reading frame 67, mRNA (cDNA clone MGC:27010 IMAGE:4829661) //	1.54141
231081_at	C2orf73	chromosome 2 open reading frame 73	1.83581
241998_at	C2orf80	chromosome 2 open reading frame 80	2.15326
1554147_s_at	C3orf15	chromosome 3 open reading frame 15	1.5927
1554528_at	C3orf15	chromosome 3 open reading frame 15	2.15191
1555719_a_at	C3orf15	chromosome 3 open reading frame 15	2.82189
223990_at	C4orf17	chromosome 4 open reading frame 17	1.61603
231565_at	C4orf22	chromosome 4 open reading frame 22	1.55741
231612_at	C4orf35	chromosome 4 open reading frame 35	1.55132
1555096_at	C4orf37	chromosome 4 open reading frame 37	1.87794
1553106_at	C5orf24	chromosome 5 open reading frame 24	-1.84772
234457_at	C6orf12	chromosome 6 open reading frame 12	2.8135
1552575_a_at	C6orf141	chromosome 6 open reading frame 141	1.70056
232152_at	C6orf182 /// C6orf182P	chromosome 6 open reading frame 182 /// chromosomal 6 open reading frame 182 psu	2.19633
244829_at	C6orf218	Chromosome 6 open reading frame 218 (C6orf218), mRNA	2.4961
211351_at	C6orf54	chromosome 6 open reading frame 54	2.04304
1566865_at	C7orf38	chromosome 7 open reading frame 38	1.98885
209446_s_at	C7orf44	chromosome 7 open reading frame 44	-1.51989
1553329_at	C7orf45	chromosome 7 open reading frame 45	2.3417
240626_at	C8orf15	chromosome 8 open reading frame 15	1.70317
231380_at	C8orf34	chromosome 8 open reading frame 34	1.78353
218541_s_at	C8orf4	chromosome 8 open reading frame 4	1.99089
214796_at	C8orf79	chromosome 8 open reading frame 79	1.71345
1560207_at	C8orf81	chromosome 8 open reading frame 81	3.37061
206727_at	C9	complement component 9	1.66942

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
230522_s_at	C9orf100	chromosome 9 open reading frame 100	-1.55527
1557541_at	C9orf122	chromosome 9 open reading frame 122	1.55302
208077_at	C9orf38	chromosome 9 open reading frame 38	2.77328
1558414_at	C9orf4	chromosome 9 open reading frame 4	1.61823
1560558_at	C9orf80	chromosome 9 open reading frame 80	3.13268
1556516_at	C9orf93	CDNA clone IMAGE:5312512	2.11837
1553433_at	C9orf93	chromosome 9 open reading frame 93	2.37646
1557666_s_at	C9orf98	chromosome 9 open reading frame 98	1.57862
230976_at	C9orf98	chromosome 9 open reading frame 98	-1.65509
238636_at	CACNA1C	calcium channel, voltage-dependent, L type, alpha 1C subunit	1.73954
244256_at	CACNA1E	Voltage-operated calcium channel, alpha-1 subunit	2.70134
239884_at	CADPS	Ca ⁺⁺ -dependent secretion activator	2.05688
219572_at	CADPS2	Ca ⁺⁺ -dependent secretion activator 2	1.64739
201617_x_at	CALD1	caldesmon 1	2.15522
235834_at	CALD1	Caldesmon, 3' UTR	1.76734
205525_at	CALD1	caldesmon 1	2.04665
1552421_a_at	CALR3	calreticulin 3	1.59981
212551_at	CAP2	CAP, adenylate cyclase-associated protein, 2 (yeast)	1.94441
1569450_at	CAPZA2	capping protein (actin filament) muscle Z-line, alpha 2	-1.55786
1553323_a_at	CATSPER2	cation channel, sperm associated 2	-1.76772
230981_at	CATSPER3	cation channel, sperm associated 3	-1.5308
1555920_at	CBX3	Heterochromatin protein HP1Hs-gamma	-1.65486
1553886_at	CCDC108	coiled-coil domain containing 108	2.91507
1561477_at	CCDC144A	coiled-coil domain containing 144A	3.37527
1561271_at	CCDC144C	coiled-coil domain containing 144C	3.46131
243565_at	CCDC150	coiled-coil domain containing 150	1.71562
237475_x_at	CCDC152	coiled-coil domain containing 152	1.54515
1553849_at	CCDC26	coiled-coil domain containing 26	1.9386
1553666_at	CCDC34	coiled-coil domain containing 34	1.8159
233259_at	CCDC48	PREDICTED: Homo sapiens similar to hCG20004 (LOC729581), mRNA	2.53391
1558893_a_at	CCDC67	coiled-coil domain containing 67	1.69471
214710_s_at	CCNB1	cyclin B1	-1.54345
220351_at	CCRL1	chemokine (C-C motif) receptor-like 1	3.68023
229900_at	CD109	CD109 molecule	1.62542
215784_at	CD1E	CD1e molecule	2.06446
1552509_a_at	CD300LG	CD300 molecule-like family member g	1.53768
1554519_at	CD80	CD80 molecule	-1.71348
241120_s_at	CDC20B	Cell division cycle 20 homolog B (S. cerevisiae), mRNA (cDNA clone IMAGE:5206729)	1.50701
240161_s_at	CDC20B	Cell division cycle 20 homolog B (S. cerevisiae), mRNA (cDNA clone IMAGE:5206729)	2.04212
1555772_a_at	CDC25A	cell division cycle 25 homolog A (S. pombe)	3.35221
232266_x_at	CDC2L5	CDNA FLI35215 fis, clone PROST2000079, highly similar to Homo sapiens mRNA for C	1.52631
240735_at	CDC42BPA	Ser-thr protein kinase PK428	1.53612
220115_s_at	CDH10	cadherin 10, type 2 (T2-cadherin)	2.15879
236179_at	CDH11	cadherin 11, type 2, OB-cadherin (osteoblast)	1.70475

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
207149_at	CDH12	cadherin 12, type 2 (N-cadherin 2)	1.62637
206898_at	CDH19	cadherin 19, type 2	1.56233
220679_s_at	CDH7	cadherin 7, type 2	1.80801
241911_at	CDKL3	cyclin-dependent kinase-like 3	1.65132
204159_at	CDKN2C	cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)	-1.5149
228744_at	CEP27	centrosomal protein 27kDa	-1.53605
229208_at	CEP27	centrosomal protein 27kDa	-1.51058
241836_x_at	CEP97	centrosomal protein 97kDa	1.50275
207874_s_at	CFHR4	complement factor H-related 4	1.74706
235117_at	CHAC2	ChaC, cation transport regulator homolog 2 (E. coli)	-1.8177
220619_at	CHD7	chromodomain helicase DNA binding protein 7	1.76809
1565951_s_at	CHML	choroideremia-like (Rab escort protein 2)	-1.91904
206079_at	CHML	choroideremia-like (Rab escort protein 2)	-1.64317
214596_at	CHRM3	cholinergic receptor, muscarinic 3	2.54248
211587_x_at	CHRNA3	cholinergic receptor, nicotinic, alpha 3	1.61917
221107_at	CHRNA9	cholinergic receptor, nicotinic, alpha 9	1.56409
220026_at	CLCA4	chloride channel regulator 4	2.16081
214598_at	CLDN8	claudin 8	1.81271
219414_at	CLSTN2	calsynenin 2	1.84839
1552588_a_at	CNBD1	cyclic nucleotide binding domain containing 1	1.55712
1552344_s_at	CNOT7	CCR4-NOT transcription complex, subunit 7	-1.82468
239989_at	CNTLN	centlein, centrosomal protein	2.22761
227209_at	CNTN1	Contactin 2 precursor (CNTN1)	1.77739
229084_at	CNTN4	contactin 4	2.67917
207195_at	CNTN6	contactin 6	1.56557
205229_s_at	COCH	coagulation factor C homolog, cochlin (Limulus polyphemus)	-1.9015
205941_s_at	COL10A1	collagen, type X, alpha 1	1.7013
37892_at	COL11A1	collagen, type XI, alpha 1	2.34283
1556499_s_at	COL1A1	collagen, type I, alpha 1	4.18573
202403_s_at	COL1A2	collagen, type I, alpha 2	1.61064
229218_at	COL1A2	collagen, type I, alpha 2	4.15668
1555253_at	COL25A1	collagen, type XXV, alpha 1	3.31837
225293_at	COL27A1	collagen, type XXVII, alpha 1	1.80939
211161_s_at	COL3A1	collagen, type III, alpha 1	1.88084
215076_s_at	COL3A1	collagen, type III, alpha 1	1.84665
232458_at	COL3A1	MRNA 3' region for pro-alpha1(III) collagen	2.19054
207420_at	COLEC10	collectin sub-family member 10 (C-type lectin)	1.54892
217645_at	COX16	COX16 cytochrome c oxidase assembly homolog (S. cerevisiae)	-1.59605
227253_at	CP	centrioplasm (ferroxidase)	1.66043
1552511_a_at	CPA6	carboxypeptidase A6	2.12705
227721_at	CPAMD8	C3 and PZP-like, alpha-2-macroglobulin domain containing 8	-2.00772
1555250_a_at	CPEB3	cytoplasmic polyadenylation element binding protein 3	1.57893
204920_at	CPS1	carbamoyl-phosphate synthetase 1, mitochondrial	1.95567
1552714_at	CREG2	cellular repressor of E1A-stimulated genes 2	2.09357
237502_at	CRLS1	Cardiolipin synthase 1 (CRLS1), transcript variant 2, mRNA	1.62771
1555958_at	CRTAC1	cartilage acidic protein 1	1.57641
1557143_at	C8MD2	CUB and Sushi multiple domains 2	1.65198

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
1553080_at	CSNIS2A	casein alpha s2-like A	1.73631
207030_s_at	CSRP2	cysteine and glycine-rich protein 2	1.92858
1567912_s_at	CT45-4 /// CT45-6 /// LOC100133581 /// RP13-36C9.1 /// RP13-36C9.3 /// RP13-36C9.6 /// XX- FW88277B6.1	cancer/testis antigen CT45-4 /// cancer/testis antigen CT45-6 /// hypothetical p	5.90054
231568_at	CT47.7 /// CT47.8 /// RP6- 166C19.1 /// RP6-166C19.10 /// RP6- 166C19.11 /// RP6-166C19.2 /// RP6- 166C19.3 /// RP6-166C19.4 /// RP6- 166C19.5 /// RP6-166C19.6 /// RP6- 166C19.9	cancer/testis CT47 family, member 7 /// cancer/testis CT47 family, member 8 ///	1.71304
213597_s_at	CTDSPL	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatas	1.93739
209617_s_at	CTNND2	catenin (cadherin-associated protein), delta 2 (neural plakophilin-related arm-r	1.50335
203917_at	CXADR	coxsackie virus and adenovirus receptor	2.66153
231389_at	CXorf41	chromosome X open reading frame 41	1.97677
1553466_at	CXorf59	chromosome X open reading frame 59	2.19023
235991_at	CYB5RL	cytochrome b5 reductase-like	-1.53055
216809_at	CYLC1	cylicin, basic protein of sperm head cytoskeleton 1	1.90782
207780_at	CYLC2	cylicin, basic protein of sperm head cytoskeleton 2	1.65232
240863_at	CYP19A1	cytochrome P450, family 19, subfamily A, polypeptide 1	2.21129
214235_at	CYP3A5	cytochrome P450, family 3, subfamily A, polypeptide 5	1.80203
205939_at	CYP3A7	cytochrome P450, family 3, subfamily A, polypeptide 7	1.70992
205472_s_at	DACH1	dachshund homolog 1 (Drosophila)	1.65928
239738_at	DACH2	dachshund homolog 2 (Drosophila)	1.51034
1562772_a_at	DAND5	DAN domain family, member 5	1.73689
238757_at	DBF4B	DBF4 homolog B (S. cerevisiae)	-1.67188
238508_at	DBF4B	DBF4 homolog B (S. cerevisiae)	-1.81109
205369_x_at	DBT	dihydrolipoamide branched chain transacylase E2	1.72887
213865_at	DCBLD2	discoidin, CUB and LCCL domain containing 2	1.55339
205399_at	DCLK1	doublecortin-like kinase 1	1.62886
215303_at	DCLK1	doublecortin-like kinase 1	3.56201
201893_x_at	DCN	decorin	1.94418
227561_at	DDR2	discoidin domain receptor tyrosine kinase 2	1.53865
223662_x_at	DDX59	DEAD (Asp-Glu-Ala-Asp) box polypeptide 59	1.55041
1553002_at	DEFB105A /// DEFB105B	defensin, beta 105A /// defensin, beta 105B	1.94929

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
1552411_at	DEFB106A /// DEFB106B	defensin, beta 106A /// defensin, beta 106B	1.9024
1563450_at	DEFB107A /// DEFB107B	defensin, beta 107A /// defensin, beta 107B	3.12379
1562167_a_at	DEFB122	defensin, beta 122 (pseudogene)	1.58206
207356_at	DEFB4	defensin, beta 4	1.95828
238917_s_at	DENND5B	DENN/MADD domain containing 5B	-1.87705
234071_at	DEPDC6	DEP domain containing 6	1.54924
216947_at	DES	desmin	4.20247
1553524_at	DGKB	diacylglycerol kinase, beta 90kDa	2.81068
203699_s_at	DIO2	deiodinase, iodothyronine, type II	1.61583
1557633_at	DKFZp434K19 1	POM121 membrane glycoprotein-like 1 pseudogene	1.87034
1569476_at	DKFZP434L18 7	CDNA clone IMAGE:5022014	3.78072
206819_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	2.57115
222253_s_at	DKFZP434P211	POM121 membrane glycoprotein-like 1 pseudogene	5.5328
216877_at	DKFZp666G13 27	EST clone 251800 mariner transposon Hsmar1 sequence	2.46877
224199_at	DKK2	dickkopf homolog 2 (Xenopus laevis)	1.52116
242631_x_at	DLC1	deleted in liver cancer 1	1.70843
233056_x_at	DLGAP4	discs, large (Drosophila) homolog-associated protein 4	1.52268
207147_at	DLX2	distal-less homeobox 2	2.38281
239309_at	DLX6	distal-less homeobox 6	4.54905
220493_at	DMRT1	doublesex and mab-3 related transcription factor 1	2.29697
237804_at	DNAH11	Axonemal dynein heavy chain (DNAH11), partial	1.71964
1560416_at	DNAH11	dynein, axonemal, heavy chain 11	2.87499
220725_x_at	DNAH3	Dynein, axonemal, heavy chain 3 (DNAH3), mRNA	1.58728
1552675_at	DNAJB7	DnaJ (Hsp40) homolog, subfamily B, member 7	1.69507
1558501_at	DNM3	dynammin 3	1.56409
214844_s_at	DOK5	docking protein 5	2.18827
207789_s_at	DPP6	dipeptidyl-peptidase 6	1.51336
231385_at	DPPA3 /// STELLAR	developmental pluripotency associated 3 /// germ and embryonic stem cell enriche	2.12291
241199_x_at	DPPA4	developmental pluripotency associated 4	4.80564
1557290_at	DPY19L2 /// DPY19L2P1 /// DPY19L2P2 /// DPY19L2P4	dpy-19-like 2 (C. elegans) /// dpy-19-like 2 pseudogene 1 (C. elegans) /// dpy-1	1.62779
240218_at	DSCAM	Down syndrome cell adhesion molecule	1.59287
1552708_a_at	DUSP19	dual specificity phosphatase 19	2.25968
204014_at	DUSP4	dual specificity phosphatase 4	1.67536
1569843_at	DYNC1H1	dynein, cytoplasmic 1, intermediate chain 1	1.78891
1565149_at	DYNC2H1	dynein, cytoplasmic 2, heavy chain 1	2.12554
204271_s_at	EDNRB	endothelin receptor type B	1.68002
1558300_at	EFCAB5	EF-hand calcium binding domain 5	2.24756
233814_at	EFNA5	Receptor tyrosine kinase ligand LERK-7 precursor (EPLG7)	1.57917
219454_at	EGFL6	EGF-like-domain, multiple 6	1.63159
1565483_at	EGFR	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncoge	1.75454

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
219850_s_at	EHF	ets homologous factor	2.15949
232360_at	EHF	ets homologous factor	2.97474
208427_s_at	ELAVL2	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B)	1.52696
228260_at	ELAVL2	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B)	4.26399
227612_at	ELAVL3	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 3 (Hu antigen C)	6.80428
238073_at	ELAVL4	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 4 (Hu antigen D)	1.54026
229581_at	ELFN1	extracellular leucine-rich repeat and fibronectin type III domain containing 1	1.84175
1568254_s_at	ELL	elongation factor RNA polymerase II	2.51255
1557836_at	ELMOD2	ELMO/CED-12 domain containing 2 (ELMOD2), mRNA	1.86018
219134_at	ELTD1	EGF, latrophilin and seven transmembrane domain containing 1	2.15765
219436_s_at	EMCN	endomucin	1.94422
1553672_at	ENAH	enabled homolog (Drosophila)	1.64531
205066_s_at	ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	1.63382
205065_at	ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	1.52899
229292_at	EPB41L5	erythrocyte membrane protein band 4.1 like 5	-1.50762
206070_s_at	EPHA3	EPH receptor A3	2.33775
211164_at	EPHA3	EPH receptor A3	4.39517
216837_at	EPHA5	EPH receptor A5	3.21486
229288_at	EPHA7	EPH receptor A7	1.56981
216999_at	EPOR	erythropoietin receptor	2.17646
202454_s_at	ERBB3	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian)	1.58154
206794_at	ERBB4	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	1.84155
233498_at	ERBB4	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	1.68382
214053_at	ERBB4	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	3.22256
216440_at	ERC1	RAB6 interacting protein 2, mRNA (cDNA clone IMAGE:4343516)	2.35068
1569583_at	EREG	epiregulin	1.55022
213365_at	ERI2	exoribonuclease 2	-1.60968
1564473_at	ESCO2	Clone 305-4G mRNA sequence	1.51202
235588_at	ESCO2	establishment of cohesion 1 homolog 2 (S. cerevisiae)	2.61641
209966_x_at	ESRRG	estrogen-related receptor gamma	1.74023
224454_at	ETNK1	ethanolamine kinase 1	1.50058
206501_x_at	ETV1	ets variant 1	1.64042
230102_at	ETV5	Ets-related protein	1.68286
243277_x_at	EVII	ecotropic viral integration site 1	2.35623
208298_at	EVI5	ecotropic viral integration site 5	2.18273
207327_at	EYA4	eyes absent homolog 4 (Drosophila)	2.48321
1569592_a_at	F11	coagulation factor XI	2.291
220575_at	FAM106A	family with sequence similarity 106, member A	1.54075
209074_s_at	FAM107A	family with sequence similarity 107, member A	1.63185
1557129_a_at	FAM111B	family with sequence similarity 111, member B	2.02161
212979_s_at	FAM115A	family with sequence similarity 115, member A	1.61927
1555944_at	FAM120A	family with sequence similarity 120A	-1.5885

TABLE 8

AFTY ID	Gene Symbol	Gene Title	Fold Change
1552323_s_at	FAM122C	family with sequence similarity 122C	-1.54021
1553720_a_at	FAM123A	family with sequence similarity 123A	1.51994
235465_at	FAM123A	family with sequence similarity 123A	1.86652
230496_at	FAM123A	family with sequence similarity 123A	2.50999
231396_s_at	FAM126A	family with sequence similarity 126, member A	-1.50922
223625_at	FAM126A	family with sequence similarity 126, member A	-1.81004
239481_at	FAM133A	family with sequence similarity 133, member A	4.33493
1569025_s_at	FAM13A1	family with sequence similarity 13, member A1	1.57074
222291_at	FAM149A	family with sequence similarity 149, member A	2.00081
214825_at	FAM155A	family with sequence similarity 155, member A	1.68899
230869_at	FAM155A	family with sequence similarity 155, member A	4.25508
242687_at	FAM160A1	family with sequence similarity 160, member A1	1.63033
213304_at	FAM179B	family with sequence similarity 179, member B	-1.60915
230539_at	FAM182A	family with sequence similarity 182, member A	1.57619
216053_x_at	FAM182A	CDNA FLJ38374 fis, clone FEBRA2002552	1.70561
222205_x_at	FAM182B // RP13-401N8.2	family with sequence similarity 182, member B // hypothetical gene supported by	2.46888
234945_at	FAM54A	family with sequence similarity 54, member A	2.36602
234331_s_at	FAM84A	family with sequence similarity 84, member A	1.85031
1555538_s_at	FAM9B	family with sequence similarity 9, member B	1.61504
1568889_at	FANCD2	Fanconi anemia, complementation group D2	1.62037
1568891_x_at	FANCD2	Fanconi anemia, complementation group D2	2.51522
239246_at	FARF1	CDEP	1.90491
201579_at	FAT1	FAT tumor suppressor homolog 1 (Drosophila)	2.29159
1558964_at	FAT3	FAT tumor suppressor homolog 3 (Drosophila)	1.55077
1560490_at	FAT3	FAT tumor suppressor homolog 3 (Drosophila)	1.79133
236029_at	FAT3	FAT tumor suppressor homolog 3 (Drosophila)	4.17669
233087_at	FBXL17	F-box and leucine-rich repeat protein 17	1.83402
218875_s_at	FBXO5	F-box protein 5	-1.6348
224402_s_at	FCRL4	Fc receptor-like 4	1.66601
224403_at	FCRL4	Fc receptor-like 4	3.64968
1555136_at	FGD6	FYVE, RhoGEF and PH domain containing 6	2.22566
214589_at	FGF12	fibroblast growth factor 12	1.87587
231523_at	FGF14	fibroblast growth factor 14	2.00116
214284_s_at	FGF18	Fibroblast growth factor 18, mRNA (cDNA clone MGC.10529 IMAGE.3948893)	1.54076
220394_at	FGF20	fibroblast growth factor 20	1.85663
210311_at	FGF5	fibroblast growth factor 5	1.59913
205782_at	FGF7	fibroblast growth factor 7 (keratinocyte growth factor)	1.67479
239710_at	FIGN	fidgetin	4.1857
238964_at	FIGN	fidgetin	2.65603
1556325_at	FILIP1	filamin A interacting protein 1	2.16122
1570515_a_at	FILIP1	filamin A interacting protein 1	1.86592
223667_at	FKBP7	FK506 binding protein 7	1.51179
220828_s_at	FLJ11292	hypothetical protein FLJ11292	1.81486
215187_at	FLJ11292	hypothetical protein FLJ11292	2.15766
1564160_at	FLJ16686	FLJ16686 protein	1.79597
234830_at	FLJ20518	similar to FSHD region gene 2 protein	2.17839

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
221172_at	FLJ21075	hypothetical protein FLJ21075	1.7343
233604_at	FLJ22763	hypothetical gene supported by AK026416	2.69416
217016_x_at	FLJ23172 /// TMEM212	hypothetical LOC389177 /// transmembrane protein 212	1.7451
1553614_a_at	FLJ25694	hypothetical protein FLJ25694	1.723
241953_at	FLJ25694 /// KRTAP21-1	hypothetical protein FLJ25694 /// keratin associated protein 21-1	1.67966
1557155_a_at	FLJ30375	CDNA clone IMAGE:5301781	2.6058
241440_at	FLJ30375	hypothetical gene supported by AK054937	2.70383
236739_at	FLJ30594	CDNA FLJ34044 fis, clone FCBBF2007080	3.41974
1553775_at	FLJ31715	hypothetical protein FLJ31715	-1.57858
1553354_a_at	FLJ31958	hypothetical protein FLJ31958	1.71642
230047_at	FLJ32810	hypothetical protein FLJ32810	1.76353
1553472_at	FLJ32955	hypothetical protein FLJ32955	2.65054
1569378_at	FLJ33297	CDNA FLJ33297 fis, clone BNGH42001406	1.76909
1553335_x_at	FLJ34047	hypothetical protein FLJ34047	1.59989
1559277_at	FLJ35700	hypothetical protein FLJ35700	1.66616
1557206_at	FLJ35848	hypothetical protein FLJ35848	2.97097
1566480_x_at	FLJ35848	Hypothetical protein FLJ35848, mRNA (cDNA clone IMAGE:5402642)	2.19166
1557895_at	FLJ35934	FLJ35934 protein	2.05515
1561171_a_at	FLJ36131 /// LOC100131452 /// LOC100132025 /// LOC100132566 /// LOC100132727 /// LOC729272	hypothetical protein FLJ36131 /// hypothetical protein LOC100131452 /// transmem /// LOC100132025 /// LOC100132566 /// LOC100132727 /// LOC729272	1.78937
1560790_at	FLJ36144	hypothetical protein FLJ36144	2.06719
1556558_s_at	FLJ36665	hypothetical protein FLJ36665	-1.73079
231527_at	FLJ36840	CDNA FLJ36840 fis, clone ASTRO2011461	1.66566
1558579_at	FLJ37786	hypothetical LOC642691	2.45337
242683_at	FLJ38028	hypothetical gene supported by AK095347	1.51579
242546_at	FLJ39632	hypothetical LOC642477	2.20629
239010_at	FLJ39632	CDNA clone IMAGE:5270501	2.23008
231882_at	FLJ39632 /// LOC100131139	hypothetical LOC642477 /// similar to double homeobox A	2.09022
1566665_at	FLJ40176	hypothetical LOC121951	1.68357
1568698_at	FLJ43080	hypothetical protein LOC642987	2.07737
1565786_x_at	FLJ45482	hypothetical LOC645566	1.60292
240259_at	FLRT2	CDNA FLJ51243 complete cds, highly similar to Leucine-rich repeat transmembrane	2.20213
219250_s_at	FLRT3	fibronectin leucine rich transmembrane protein 3	1.59215
1559244_at	FMN2	formin 2	2.22149
223618_at	FMN2	formin 2	1.85606
231231_at	FMNL3	KIAA2014 protein	2.66876
226930_at	FNDC1	fibronectin type III domain containing 1	1.78354
217483_at	FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	2.41619

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
217487_x_at	FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	4.54562
40284_at	FOXA2	forkhead box A2	3.21218
1553613_s_at	FOXC1	forkhead box C1	1.8881
206018_at	FOXG1	forkhead box G1	1.85819
235201_at	FOXP2	forkhead box P2	2.75837
1555352_at	FOXP2	forkhead box P2	1.7166
230964_at	FREM2	FRAS1 related extracellular matrix protein 2	4.03728
243689_s_at	FRG1B	Hypothetical protein LOC283788, mRNA (cDNA clone MGC:23868 IMAGE:4297267)	2.17705
234949_at	FRG1B	Hypothetical protein LOC283788, mRNA (cDNA clone MGC:23868 IMAGE:4297267)	2.27959
207178_s_at	FRK	fyn-related kinase	1.87638
1570207_at	FRRS1	ferrie-chelate reductase 1	2.89483
1562625_at	FRYL	FRY-like	1.99342
244419_at	FRZB	Fritz	1.54036
230904_at	FSD1L	fibronectin type III and SPRY domain containing 1-like	-1.99072
223985_at	FSD1L	fibronectin type III and SPRY domain containing 1-like	1.83509
207345_at	FST	follistatin	2.76648
203705_s_at	FZD7	frizzled homolog 7 (Drosophila)	1.55517
1553024_at	G30	protein LG30-like	2.51805
222187_x_at	G3BP1	GTPase activating protein (SH3 domain) binding protein 1	1.62305
206952_at	G6PC	glucose-6-phosphatase, catalytic subunit	2.12833
238569_at	GABBR1	GABA-BR1a (hGB1a) receptor	-1.61754
209990_s_at	GABBR2	gamma-aminobutyric acid (GABA) B receptor, 2	1.59875
233437_at	GABRA4	gamma-aminobutyric acid (GABA) A receptor, alpha 4	3.25934
207010_at	GABRB1	gamma-aminobutyric acid (GABA) A receptor, beta 1	2.42007
242344_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	5.10676
1557122_s_at	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2	8.54122
229724_at	GABRB3	gamma-aminobutyric acid (GABA) A receptor, beta 3	1.55943
1563533_at	GADL1	glutamate decarboxylase-like 1	4.0883
208283_at	GAGE1	G antigen 1	2.39924
207739_s_at	GAGE1 /// GAGE12F /// GAGE12G /// GAGE12I /// GAGE12J /// GAGE2A /// GAGE2B /// GAGE2C /// GAGE2D /// GAGE2E /// GAGE3 /// GAGE4 /// GAGE5 /// GAGE6 /// GAGE7 /// GAGE8	G antigen 1 /// G antigen 12F /// G antigen 12G /// G antigen 12I /// /// G antigen	2.7548
237183_at	GALNT5	CDNA FLJ75131 complete cds, highly similar to Homo sapiens UDP-N-acetyl-alpha-D-	1.57858
240390_at	GALNT5	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	4.19183

TABLE 8

AFFY ID	Gene Symbol	Gene Title	Fold Change
236361_at	GALNTL2	UDP-N-acetyl-alpha-D-galactosamine polypeptide N-acetylgalactosaminyltransferase	1.9112
220124_at	GAN	gigaxonin	1.78227
204471_at	GAP43	growth associated protein 43	1.67109
219954_s_at	GBA3	glucosidase, beta, acid 3 (cytosolic)	1.56599
230788_at	GCNT2	glucosaminyl (N-acetyl) transferase 2, 1-branching enzyme (1 blood group)	-1.71043
236548_at	GIPC2	GIPC PDZ domain containing family, member 2	2.02931
230258_at	GLIS3	GLIS family zinc finger 3	2.8996
244680_at	GLRB	glycine receptor, beta	1.90493
235371_at	GLT8D4	glycosyltransferase 8 domain containing 4	1.5501
1554712_a_at	GLYATL2	glycine-N-acyltransferase-like 2	2.06041
204763_s_at	GNAO1	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide	2.09098
229274_at	GNAS	Adenyl cyclase mRNA	-1.62372
207166_at	GNGT1	guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide	1.92988
204324_s_at	GOLIM4	golgi integral membrane protein 4	1.65786
1555199_at	GOSR1	golgi SNAP receptor complex member 1	3.06916
1553879_a_at	GOT1L1	glutamic-oxaloacetic transaminase 1-like 1	1.59882
1553878_at	GOT1L1	glutamic-oxaloacetic transaminase 1-like 1	1.95653
215554_at	GPLD1	glycosylphosphatidylinositol specific phospholipase D1	1.54336
236024_at	GPM6A	glycoprotein M6A	2.04441
212950_at	GPR116	G protein-coupled receptor 116	1.52524
212951_at	GPR116	G protein-coupled receptor 116	1.57258
1555122_at	GPR125	G protein-coupled receptor 125	2.42496
233887_at	GPR126	G protein-coupled receptor 126	1.58837
1553025_at	GPR126	G protein-coupled receptor 126	1.68374
209631_s_at	GPR37	G protein-coupled receptor 37 (endothelin receptor type B-like)	1.56859
219898_at	GPR85	G protein-coupled receptor 85	2.09828
238049_at	GRAMD3	GRAM domain containing 3	2.61185
206204_at	GRB14	growth factor receptor-bound protein 14	2.23024
235504_at	GREM2	gremlin 2, cysteine knot superfamily, homolog (Xenopus laevis)	1.50319
219388_at	GRHL2	grainyhead-like 2 (Drosophila)	2.33499
205358_at	GRIA2	glutamate receptor, ionotropic, AMPA 2	2.02789
206730_at	GRIA3	glutamate receptor, ionotropic, AMPA 3	2.12652
213845_at	GRIK2	glutamate receptor, ionotropic, kainate 2	1.74884
205814_at	GRM3	glutamate receptor, metabotropic 3	2.30621
207235_s_at	GRM5	glutamate receptor, metabotropic 5	2.95593
207548_at	GRM7	glutamate receptor, metabotropic 7	1.64049
216992_s_at	GRM8	glutamate receptor, metabotropic 8	1.54515
235387_at	GSTCD	glutathione S-transferase, C-terminal domain containing	-1.51561
242656_at	GTF2H1	General transcription factor IIH, polypeptide 1, 62kDa (GTF2H1), transcript variant 1	-1.65352
204237_at	GULP1	GULP, engulfment adaptor PTB domain containing 1	1.726
204235_s_at	GULP1	GULP, engulfment adaptor PTB domain containing 1	1.67838
215695_s_at	GYG2	glycogenin 2	1.67125
1559520_at	GYPA	Glycophorin A	3.86167
205523_at	HAPLN1	hyaluronan and proteoglycan link protein 1	1.50177

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 3
CONTENANT LES PAGES 1 À 108

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JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

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NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

WHAT IS CLAIMED IS:

1. A method for diagnosing a transient ischemic attack (TIA) or a predisposition for experiencing TIA, the method comprising: determining a level of
5 expression of a plurality of TIA-associated biomarkers in a biological sample from a patient, wherein an increase or decrease of the level of expression compared to a control indicates that the patient has suffered or is at risk of experiencing TIA, wherein the plurality of TIA-associated biomarkers is selected from the biomarkers set forth in Tables 1, 2, 5A, 5B, 5C, 5D, 7, 8 and 9.
- 10 2. The method of claim 1, further comprising determining the level of expression of one or biomarkers selected from the group consisting of CNTN4, TLR5, GPR84, BCL6, NELL2, APBA2 and MLL.
3. The method of any one of claims 1 to 2, wherein the determining step is performed at 3 or fewer hours after a suspected ischemic event.
- 15 4. The method of any one of claims 1 to 2, wherein the determining step is performed at 3 or more hours after a suspected ischemic event.
5. The method of any one of claims 1 to 2, wherein the determining step is performed at least 24 hours after a suspected ischemic event.
- 20 6. The method of any one of claims 1 to 5, wherein an increased expression level of one or more TIA-associated biomarkers selected from the group consisting of DKFZP434B061, FAM55D, FLJ30375, IGFBP5, LTBR and SCN2A indicates that the patient has suffered or is at risk of experiencing TIA.
- 25 7. The method of any one of claims 1 to 6, wherein an increased expression level of one or more TIA-associated biomarkers selected from the group consisting of GABRB2, ELAVL3, TWIST1, DPPA4, DKFZP434P211, DLX6, ZNF479, ASTN2, SNX31, ALS2CR11, LOC440345 indicates that the patient has suffered or is at risk of experiencing TIA.
8. The method of any one of claims 1 to 7, wherein an increased expression level of one or more TIA-associated biomarkers selected from the group

consisting of GABRB2, ELAVL3, COL1A1, SHOX2, GABRB2, TWIST1, DPPA4, DKFZP434P211, WIT1, SOX9, DLX6, ANXA3, EPHA3, SOX11, SLC26A8, CCRL1, FREM2, STOX2, ZNF479, LOC338862, ASTN2, FOLH1, SNX31, KREMEN1, ZNF479, ALS2CR11, FIGN, RORB, LOC732096, GYP A, ALPL, LHX2, GALNT5, SRD5A2L2, GALNT14, OVOL2, BMPRI B, UNC5B, ODZ2, ALPL, RASAL2, SHOX, C19orf59, ZNF114, SRGAP1, ELAVL2, NCRNA00032, LOC440345, FLJ30375, TFPI, PTGR1, ROBO1, NR2F2, GRM5, LUM, FLJ39051, COL1A2, CASP5, OPCML, TTC6, TFAP2B, CRISP2, SOX11, ANKRD30B, FLJ39051, SCN2A, MYNN, FOXA2, DKFZP434B061, LOC645323, SNIP, LOC645323, LOC374491, ADAM30, SIX3, FLJ36144, CARD8, KREMEN1, RP1-127L4.6, FAM149A, B3GAT2, SPOCK3, G30, ITGBL1, IQGAP3, C7orf45, ZNF608, LOC375010, LRP2, TGFB2, SHOX2, HOXC4 /// HOXC6, ELTD1, FAM182B /// RP13-401N8.2, PRO0478, LIFR, FOLH1, EHF, NDST3, BRUNOL5, LOC728460, PDE1A, POU2AF1, FAT1, PCDH11X /// PCDH11Y, FLJ37786, SLC22A4, DHRS13, EHF, MEG3, PIWIL1, LOC203274, LOC100133920 /// LOC286297, DMRT1, ADM, VWA3B, GAFA3, HESX1, ADAMDEC1, CAV1, LAMB4, TPTE, PPP1R1C, HPSE, AIM2, RUNDC3B, CARD16, FAM124A, MGC39584, OSM, RFX2, MYBPC1, LTBR, C18orf2, SNRPN, FLJ36031, IL1B, TRPM1, OSTCL, MAPK14, KCNJ15 /// LOC100131955, FIGN, HNT, S100A12, CHIT1, C7orf53, FAM13A1, GNAO1, MAPK14, FAM55D, PRKD2, LIMK2, C18orf54, IGFBP5, EVI1, PLSCR1, FOXC1, LOC646627, ZNF462, CNTLN, ZNF438, DEFB105A /// DEFB105B, LOC340017, C1orf67, ACSL1, ADH1B, SLC2A14 /// SLC2A3, IL1B, ST3GAL4, UBE2J1, PNPLA3 and PAPPA indicates that the patient has suffered or is at risk of experiencing TIA.

9. The method of any one of claims 1 to 8, wherein a decreased expression level of one or more TIA-associated biomarkers selected from the group consisting of ATG9B, DIP2C, EDAR, GSTM1, GUSBL2, SMURF2, ZNF512B indicates that the patient has suffered or is at risk of experiencing TIA.

10. The method of any one of claims 1 to 9, wherein a decreased expression level of one or more TIA-associated biomarkers selected from the group consisting of NBPF10 /// RP11-94I2.2, SFXN1, SPIN3, UNC84A, OLFM2, PPM1K, P2RY10, ZNF512B, MORF4L2, GIGYF2, ERAP2, SLFN13, LOC401431, MED6,

BAIAP2L1 /// LOC100128461, LNPEP, MBNL1, NOS3, MCF2L, KIAA1659,
 SCAMP5, LOC648921, ANAPC5, SPON1, FUS, GPR22, GAL3ST4, METTL3,
 LOC100131096, FAAH2, SMURF2, SNRPN, FBLN7, GLS, G3BP1, RCAN3,
 EPHX2, DIP2C, CCDC141, CLTC, FOSB, CACNA1I, UNQ6228, ATG9B, AK5,
 5 SPIN3, RBM14, SNRPN, MAN1C1, HELLS, EDAR, SLC3A1, ZNF519,
 LOC100130070 /// LOC100130775 /// LOC100131787 /// LOC100131905 ///
 LOC100132291 /// LOC100132488 /// RPS27, ZC3H12B, IQGAP2, SOX8,
 WHDC1L2, TNPO1, TNFRSF21, TSHZ2, DMRTC1 /// DMRTC1B, GSTM1,
 GSTM2, PNMA6A, CAND1, CCND3, GSTM1, GUSBL2 indicates that the patient
 10 has suffered or is at risk of experiencing TIA.

11. The method of any one of claims 1 to 10, further comprising
 the step of determining the cause of stroke.

12. The method of any one of claims 1 to 11, wherein the patient
 has a neurological disorder and has increased or decreased expression relative to a
 15 control level of expression of a plurality of biomarkers selected from the group
 consisting of ACSL1, ADH1B, AK5, ANXA3, APBA2, ASTN2 (includes
 EG:23245), BCL6, BMPR1B, CASP5, CAV1, CNTN4, DIP2C, ELAVL2, EPHX2,
 ERAP2, FAM124A, FAM13A, FAM149A, FAT1, FOLH1, FOXC1, GABRB2,
 GIGYF2, GNAO1, GRM5, GSTM1, HESX1, HOXC6, IGFBP5, IL1B, IQGAP2,
 20 ITGBL1, LAMB4, LIFR, LTBR, MECOM, NBPFI10, NDST3, NELL2, NOS3, NTM,
 ODZ2, OLFM2, OPCML, PDE1A, RFX2, ROBO1, S100A12, SCN2A, SLC22A4
 (includes EG:6583), SLC2A3, SLC3A1, SOX9, SPOCK3, SPON1, TGFB2, TLR5,
 TNFRSF21, TRPM1, TSHZ2, TTC6 (includes EG:115669), UNC5B, UNC84A and
 ZNF608.

25 13. The method of any one of claims 1 to 12, wherein the patient
 has a skeletal or muscular disorder and have increased or decreased expression
 relative to a control level of expression of a plurality of biomarkers selected from the
 group consisting of ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6,
 BMPR1B, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C,
 30 DNAH14, EDAR, ELAVL2, EPHA3, EPHX2, FAM124A, FOSB, GABRB2,
 GIGYF2, GNAO1, HOXC6, IL1B, KCNJ15, LAMB4, LIFR, LTBR, LUM,
 MAPK14, MYBPC1, NOS3, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B,

S100A12, SCN2A, SHOX, SLC22A4 (includes EG:6583), SOX9, SPOCK3, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B and ZNF438.

14. The method of any one of claims 1 to 13, wherein the patient
 5 has an inflammatory disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ANXA3, APBA2, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CAV1, CCND3, CCRL1, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, ERAP2, FAM124A, FBLN7, FOSB, FREM2,
 10 GABRB2, GRM5, IL1B, KCNJ15, LAMB4, LHX2, LNPEP, LRP2, LTBR, LUM, MAPK14, MECOM, MYBPC1, NOS3, ODZ2, OPCML, OSM, PAPP, PDE1A, PPP1R1C, ROBO1, RUNDC3B, S100A12, SCN2A, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SMURF2, SNRPN, SPON1, TGFB2, TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), TWIST1, UNC5B, VWA3B and ZNF438.

15 15. The method of any one of claims 1 to 14, wherein the patient has a cardiovascular disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ALPL, ASTN2 (includes EG:23245), BCL6, BMPR1B, C18ORF54, CACNA1I, CARD16, CAV1, CNTN4, DMRT1, DNAH14,
 20 EDAR, EPHX2, ERAP2, FAM13A, FOLH1, FOSB, FREM2, GABRB2, GRM5, GSTM1, IL1B, IQGAP2, LIFR, LTBR, MAN1C1, MAPK14, MBNL1, MCF2L, MECOM, MYBPC1, NOS3, NTM, ODZ2, OLFM2, OPCML, PAPP, PDE1A, ROBO1, RORB, S100A12, SMURF2, SNRPN, SOX9, SPOCK3, SPON1, TFPI, TRPM1, UNC84A and VWA3B.

25 16. The method of any one of claims 1 to 15, wherein the patient has an immunological disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ANXA3, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CCRL1, CLTC, CNTN4, COL1A2, DIP2C, DNAH14,
 30 EDAR, EPHA3, EPHX2, FAM124A, FAT1, FOSB, GABRB2, GOLGA6L2, GSTM1, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14, MYBPC1, NELL2, NOS3, NTM, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1,

RUNDC3B, S100A12, SLC22A4 (includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B and ZNF438.

17. The method of any one of claims 1 to 16, wherein the patient has a metabolic disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, EPHX2, FAT1, FOXA2, GABRB2, GUSBL2, IGFBP5, IL1B, IQGAP2, ITGBL1, LRP2, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

18. The method of any one of claims 1 to 17, wherein the patient has an endocrine system disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LRP2, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SHOX, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

19. The method of any one of claims 1 to 18, wherein the patient has an autoimmune disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, AK5, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, GUSBL2, IL1B, IQGAP2, KCNJ15, LAMB4, LTBR, MAPK14, MYBPC1, NELL2, ODZ2, OPCML, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), SNRPN, SPON1, TLR5, TNFRSF21, TNPO1, TSHZ2, TTC6 (includes EG:115669), VWA3B and ZNF438.

20. The method of any one of claims 1 to 19, wherein the patient has diabetes and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, DNAH14, EPHA3, FAT1, FOXA2, GABRB2, GUSBL2, IL1B, IQGAP2, ITGBL1, LTBR, MAPK14, MBNL1, NELL2, NOS3, NTM, ODZ2, OPCML, PAPP, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SMURF2, SNRPN, SPON1, SRGAP1, TLR5, TSHZ2, UNC84A and VWA3B.

21. The method of any one of claims 1 to 20, wherein the patient has connective tissue disorder and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, COL1A1, COL1A2, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SHOX, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

22. The method of any one of claims 1 to 21, wherein the patient has rheumatic disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2, IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TLR5, TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

23. The method of any one of claims 1 to 22, wherein the patient has arthritis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CASP5, CCND3, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2,

IL1B, KCNJ15, LAMB4, LTBR, LUM, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B, ZNF438.

24. The method of any one of claims 1 to 23, wherein the patient
5 has atherosclerosis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FOSB, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A, ROBO1,
10 RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A and VWA3B.

25. The method of any one of claims 1 to 24, wherein the patient has inflammatory bowel disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C,
15 DNAH14, ERAP2, FBLN7, FREM2, GRM5, IL1B, LHX2, LNPEP, LTBR, MECOM, NOS3, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B and ZNF438.

26. The method of any one of claims 1 to 25, wherein the patient
20 has non-insulin-dependent diabetes mellitus and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ADAM30, AK5, ALPL, ALS2CR11, ASTN2 (includes EG:23245), CARD8, CCRL1, CNTLN, CNTN4, COL1A2, DIP2C, DMRT1, EPHA3, FAT1, FOXA2, GABRB2, IL1B, IQGAP2, ITGBL1, MBNL1,
25 NOS3, NTM, ODZ2, PLSCR1, ROBO1, SLC22A4 (includes EG:6583), SLC2A3, SPON1, SRGAP1, TLR5, UNC84A and VWA3B.

27. The method of any one of claims 1 to 26, wherein the patient has rheumatoid arthritis and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group
30 consisting of ACSL1, ADM, ASTN2 (includes EG:23245), BCL6, CARD8, CLTC, CNTN4, DIP2C, DNAH14, EDAR, EPHA3, EPHX2, FAM124A, FOSB, GABRB2,

IL1B, KCNJ15, LAMB4, MAPK14, ODZ2, OSM, PAPP, PDE1A, ROBO1, RUNDC3B, S100A12, SLC22A4 (includes EG:6583), TNFRSF21, TNPO1, TTC6 (includes EG:115669), VWA3B and ZNF438.

28. The method of any one of claims 1 to 27, wherein the patient
5 has coronary artery disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, ASTN2 (includes EG:23245), BMPR1B, CARD16, CNTN4, DMRT1, DNAH14, ERAP2, FREM2, GRM5, IL1B, IQGAP2, LIFR, MAN1C1, MBNL1, MCF2L, MECOM, NOS3, NTM, ODZ2, OLFM2, PDE1A,
10 ROBO1, RORB, SNRPN, SPOCK3, SPON1, TRPM1, UNC84A and VWA3B.

29. The method of any one of claims 1 to 28, wherein the patient has Crohn's disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ACSL1, AK5, APBA2, ASTN2 (includes EG:23245), CARD8, DIP2C, DNAH14,
15 ERAP2, FBLN7, FREM2, GRM5, LHX2, LNPEP, MECOM, ODZ2, OPCML, PAPP, PDE1A, PPP1R1C, ROBO1, SFXN1, SLC22A4 (includes EG:6583), SLC26A8, SNRPN, SPON1, TGFB2, TLR5, VWA3B and ZNF438.

30. The method of any one of claims 1 to 29, wherein the patient has a neurodegenerative disorder and have increased or decreased expression relative
20 to a control level of expression of a plurality of biomarkers selected from the group consisting of ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SCN2A, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2 and ZNF608.

31. The method of any one of claims 1 to 30, wherein the patient
25 has Alzheimer's disease and have increased or decreased expression relative to a control level of expression of a plurality of biomarkers selected from the group consisting of ASTN2 (includes EG:23245), CASP5, CNTN4, FAM124A, FOLH1, GABRB2, GRM5, IL1B, MECOM, NDST3, NOS3, OPCML, RFX2, SLC22A4 (includes EG:6583), SLC2A3, SLC3A1, SPON1, TSHZ2 and ZNF608.

32. The method of any one of claims 1 to 31, wherein the level of
30 expression of one or more genes selected from the group consisting of MMP16,

MMP19, MMP26, COL1A1, COL1A2, COL3A1, COL10A1, COL11A1, COL25A1, COL27A1, FGFs and EGFR is increased in comparison to the control, and the patient is determined to have atherosclerosis.

33. The method of any one of claims 1 to 32, wherein the level of
5 expression of the biomarker is determined at the transcriptional level.

34. The method of any one of claims 1 to 33, wherein the level of expression is determined by detecting hybridization of a TIA-associated gene probe to gene transcripts of the biomarkers in the biological sample.

35. The method of claim 34, wherein the hybridization step is
10 performed on a nucleic acid microarray chip.

36. The method of claim 34, wherein the hybridization step is performed in a microfluidics assay plate.

37. The method of any one of claims 1 to 33, wherein the level of expression is determined by amplification of gene transcripts of the biomarkers.

38. The method of claim 37, wherein the amplification reaction is a
15 polymerase chain reaction (PCR).

39. The method of any one of claims 1 to 32, wherein the level of expression of the biomarker is determined at the protein level.

40. The method of any one of claims 1 to 39, wherein the level of
20 expression of at least 15 biomarkers is determined.

41. The method of any one of claims 1 to 40, further comprising the step of obtaining a biological sample.

42. The method of any one of claims 1 to 41, wherein the biological sample is blood, serum or plasma.

43. The method of any one of claims 1 to 42, wherein the control is
25 the expression level of a plurality of stably expressed endogenous reference biomarkers.

44. The method of claim 43, wherein the one or more endogenous reference biomarkers selected from the group consisting of USP7, MAPRE2, CSNK1G2, SAFB2, PRKAR2A, PI4KB, CRTCL1, HADHA, MAP1LC3B, KAT5, CDC2L1 /// CDC2L2, GTSE1, CDC2L1 /// CDC2L2, TCF25, CHP, LRRC40, hCG_2003956 /// LYPLA2 /// LYPLA2P1, DAXX, UBE2NL, EIF1, KCMF1, PRKRIP1, CHMP4A, TMEM184C, TINF2, PODNL1, FBXO42, LOC441258, RRP1, C10orf104, ZDHHC5, C9orf23, LRRC45, NACC1, LOC100133445 /// LOC115110 and PEX16

45. The method of any one of claims 1 to 44, wherein the control is the expression level of the same biomarker in a healthy individual.

46. The method of any one of claims 1 to 45, wherein the control is a threshold level of expression representative of a population of healthy individuals.

47. The method of any one of claims 1 to 46, further comprising the step of providing an appropriate treatment or prevention regime for TIA to the patient.

48. A solid support comprising a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 2, a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 5A, a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 5B, a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 5C, a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 5D, a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 7, a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 8 and a plurality of nucleic acids that hybridize to a plurality of the genes set forth in Table 9.

49. The solid support of claim 48, comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of GUSBL2, GSTM1, FLJ30375, SCN2A, DKFZP434B061, EDAR, ATG9B, DIP2C, LTBR, SMURF2, FAM55D, IGFBP5, and ZNF512B.

50. The solid support of any one of claims 48 to 49, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of SNIP, BXDC5, FAT3, LECT2, THSD4, CCDC144C /// LOC100134159, OVOL2, SPTLC3, CLEC4E, GLYATL1, RBMS3,
5 SPIB, DKFZP434L187, GADL1, SHOX, TBX5, UNC5B, PGM5, TIMP2, ELL2, CXADR, and RNF141.

51. The solid support of any one of claims 48 to 50, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of RPL22, SNIP, SH3GL3, MCTP1, FAT3,
10 SPTLC3, RBMS3, SNRPN, and TIMP2.

52. The solid support of any one of claims 48 to 51, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of FGD4, F5, ABCA1, LOC100290882, LTB4R, UBXN2B, CKLF, CLEC4E, PHTF1, ENTPD1, OSBPL1A, RRAGD, CPEB2, CKLF,
15 BST1, and CKLF.

53. The solid support of any one of claims 48 to 52, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of ZNF608, FCHO2, ST3GAL6, ABCA1, THBD, AMN1, QKI, KIAA0319, MCTP1, VNN3, UBR5, FAR2, RBM25, CHMP1B,
20 LAMP2, VAPA, IFRD1, HNRNPH2, REM2, and GAB1.

54. The solid support of any one of claims 48 to 53, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of THSD4, SNRPN, ASTN2, SNIP, FAT3, TIMM8A, CCDC144C /// LOC100134159, ANKRD28, TBX5, PGM5, SCD5,
25 FCRL4, SHOX, CCRL1, LECT2, PTPRD, CCDC144A, LDB3, LOC729222 /// PPFIBP1, RBMS3, P704P, GYPA, PRTG, GABRB2, HNRNPUL2, ELAVL2, SPTLC3, FOXA2, DLX6, ALDOAP2, and FLJ35934.

55. The solid support of any one of claims 48 to 54, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes

selected from the group consisting of RPL22, LOC100129488, LOC283027, LOC344595, THSD4, FAT3, and P704P.

56. The solid support of any one of claims 48 to 55, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes
 5 selected from the group consisting of SNIP, BXDC5, FAT3, LECT2, THSD4, CCDC144C /// LOC100134159, OVOL2, SPTLC3, CLEC4E, GLYATL1, RBMS3, SPIB, DKFZP434L187, GADL1, SHOX, TBX5, UNC5B, PGM5, TIMP2, ELL2, CXADR, RNF141, RPL22, SH3GL3, MCTP1, SNRPN, FGD4, F5, ABCA1, LOC100290882, LTB4R, UBXN2B, CKLF, PHTF1, ENTPD1, OSBPL1A, RRAGD,
 10 CPEB2, CKLF, BST1, ZNF608, FCHO2, ST3GAL6, THBD, AMN1, QKI, KIAA0319, MCTP1, VNN3, UBR5, FAR2, RBM25, CHMP1B, LAMP2, VAPA, IFRD1, HNRNPH2, REM2, GAB1, ASTN2, TIMM8A, CCDC144C /// LOC100134159, ANKRD28, SCD5, FCRL4, CCRL1, LECT2, PTPRD, CCDC144A, LDB3, LOC729222 /// PPFIBP1, P704P, GYPA, PRTG, GABRB2, HNRNPUL2,
 15 ELAVL2, FOXA2, DLX6, ALDOAP2, FLJ35934, LOC100129488, LOC283027, and LOC344595.

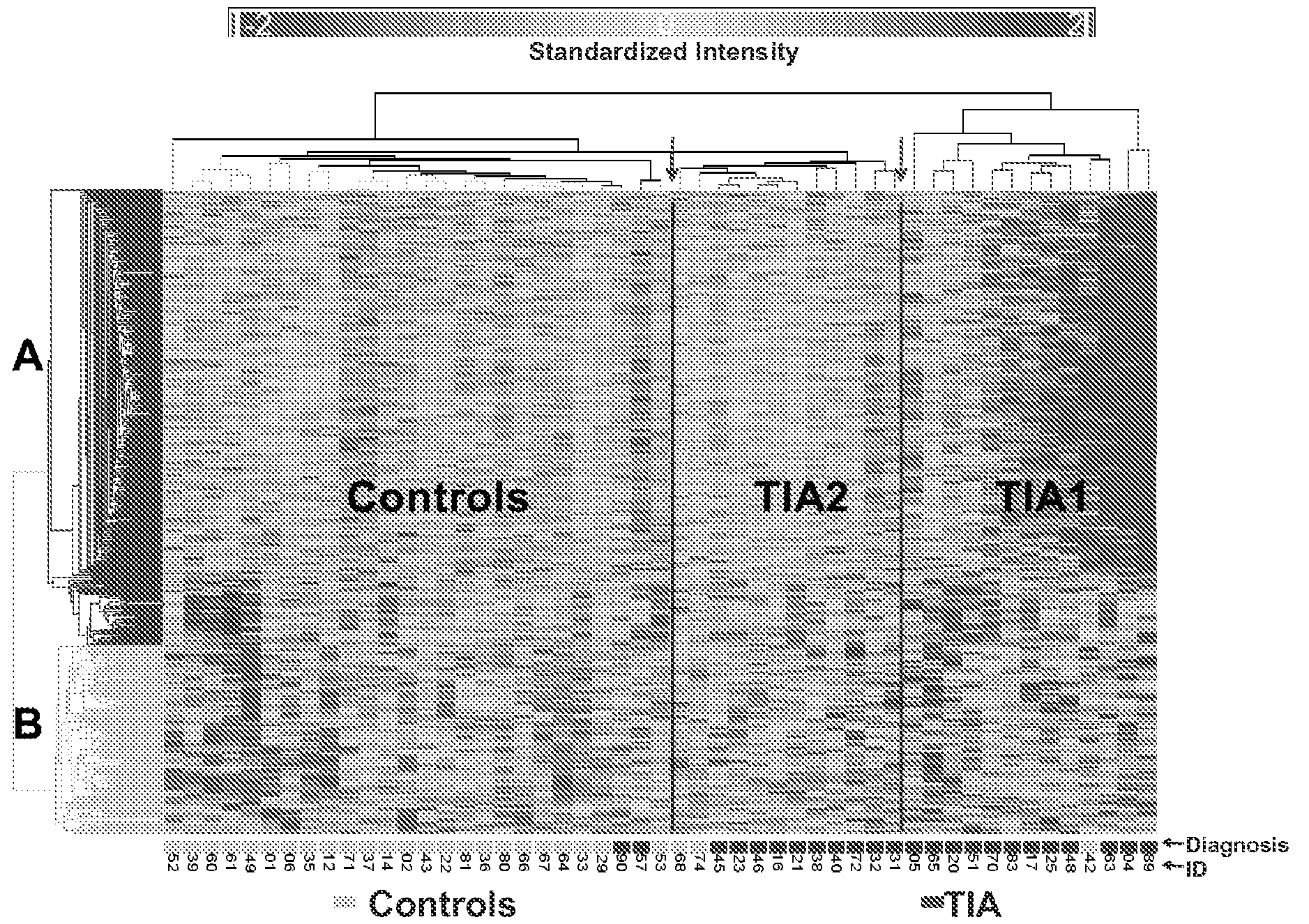
57. The solid support of any one of claims 48 to 56, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of EBF1, GRM5, TSKS, ENPP2, AP3S2,
 20 LRRC37A3, C16orf68, LOC284751, IRF6, LHFP, BANK1, ARHGEF5, ZNF254, TFDP1, COL13A1, GSTK1, ADAMTSL4, P2RX5, LHFP, PIK3C2B, CHURC1, EXT2, HLA-DOA, OOEP, ZNF185, TMEM19, FCRL1, FLJ40125, ARHGEF12, CLEC18A, CD46, PTPN20A /// PTPN20B, and C19orf28.

58. The solid support of any one of claims 48 to 57, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of EBF1, FLJ31945, C16orf68, SLC20A1, DOPEY2, COL13A1, LHFP, LOC284751, GRM5, LOC100144603, MTBP, SHOX2, ARHGEF5, RNF7, CLASP2, GIPC2, RANBP10, CMBL, LOC100127980, CYTH3, PROCR, LOC146880, SLC6A19, ICAM4, C12orf42, ARHGEF12, PRSS35, NT5E,
 30 LOC100271832, LHFP, NT5E and AKR1C3.

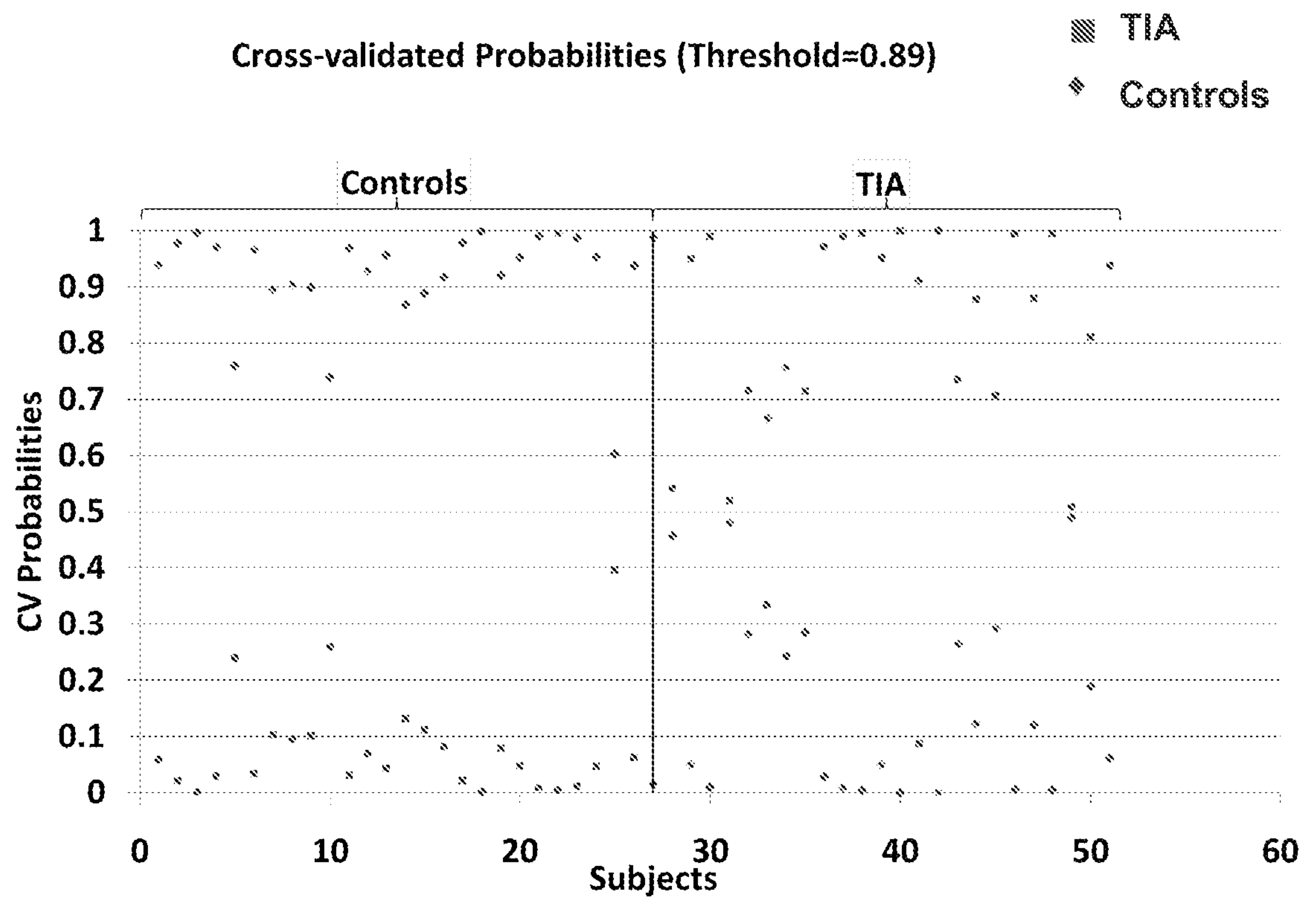
59. The solid support of any one of claims 48 to 58, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of CMTM1, COL13A1, SDC4, C6orf164, GPR176, BRUNOL6, SNORA68, MIF /// SLC2A11, DUSP16, HIPK2, TTC7A,
5 PPIE, GRLF1, MAP3K7IP1, LOC100129034, PER3, SMC1A, and LRRC43.

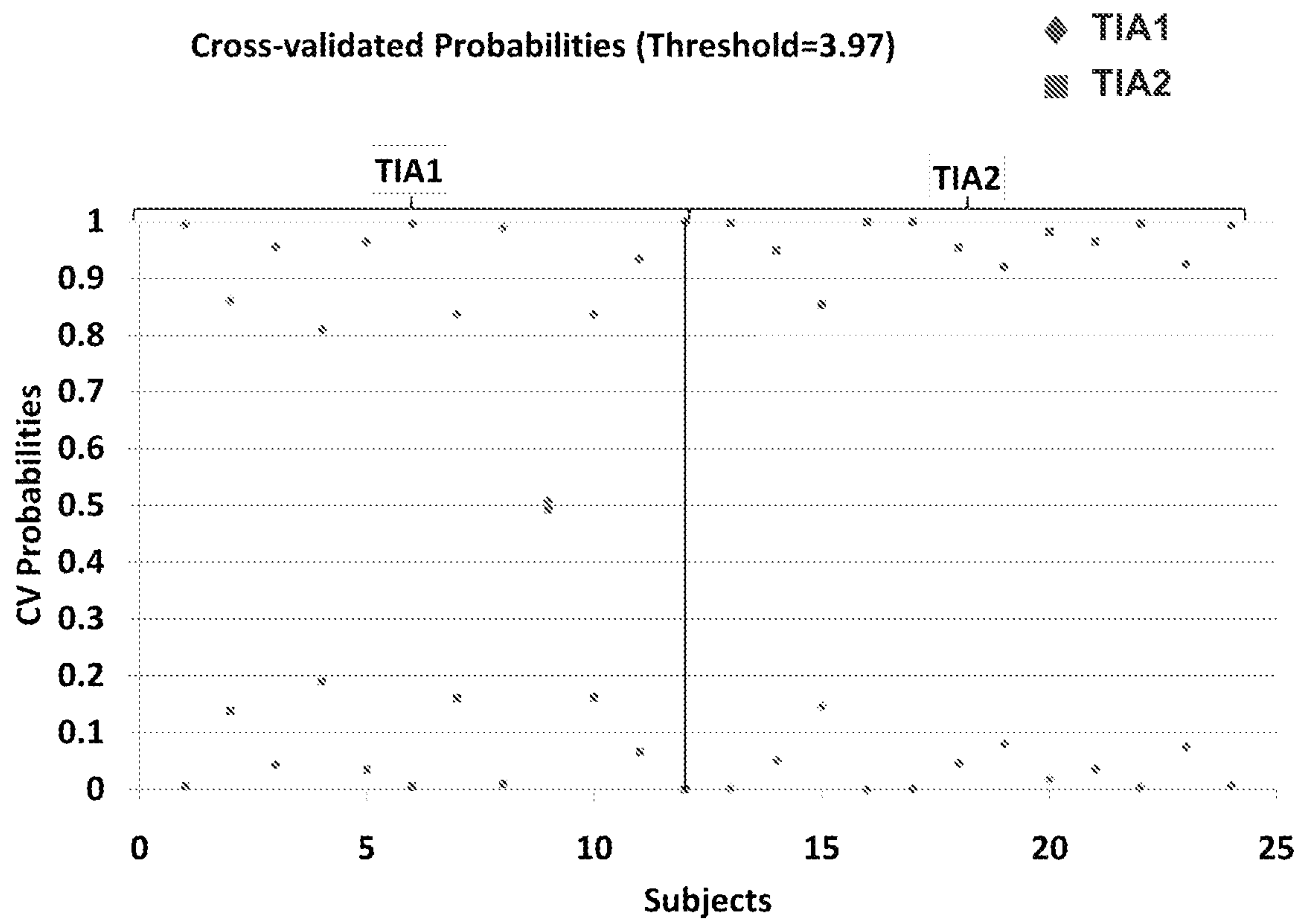
60. The solid support of any one of claims 48 to 59, further comprising a plurality of nucleic acids that hybridize to a plurality of the genes selected from the group consisting of USP7, MAPRE2, CSNK1G2, SAFB2, PRKAR2A, PI4KB, CRTCL1, HADHA, MAP1LC3B, KAT5, CDC2L1 /// CDC2L2,
10 GTSE1, TCF25, CHP, LRRC40, hCG_2003956 /// LYPLA2 /// LYPLA2P1, DAXX, UBE2NL, EIF1, KCMF1, PRKRIP1, CHMP4A, TMEM184C, TINF2, PODNL1, FBXO42, LOC441258, RRP1, C10orf104, ZDHHC5, C9orf23, LRRC45, NACC1, LOC100133445 /// LOC115110, PEX16.

61. The solid support of any one of claims 48 to 60, wherein the
15 solid support is a microarray.

1/4*Figure 1*

2/4

*Figure 2*

3/4*Figure 3*

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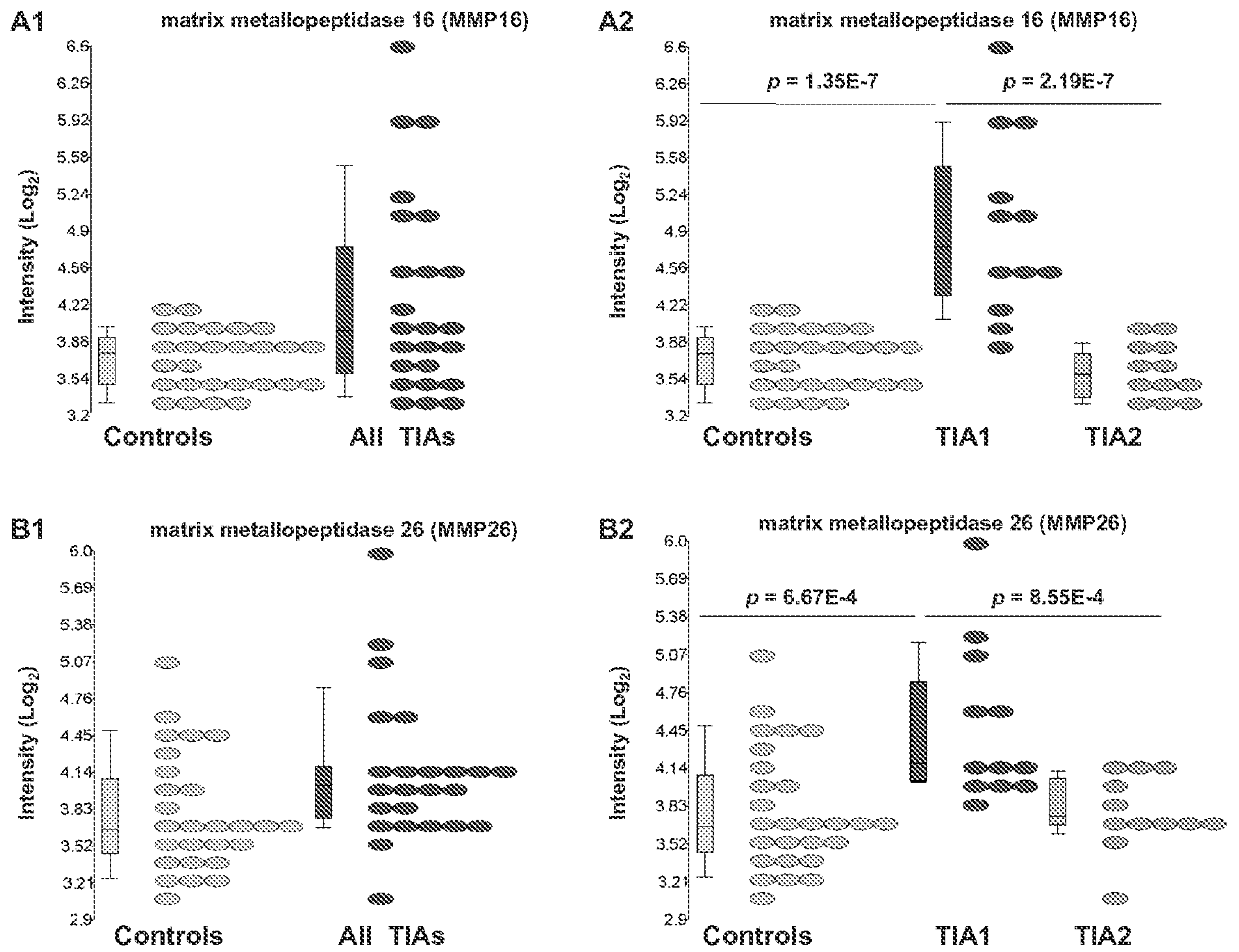


Figure 4

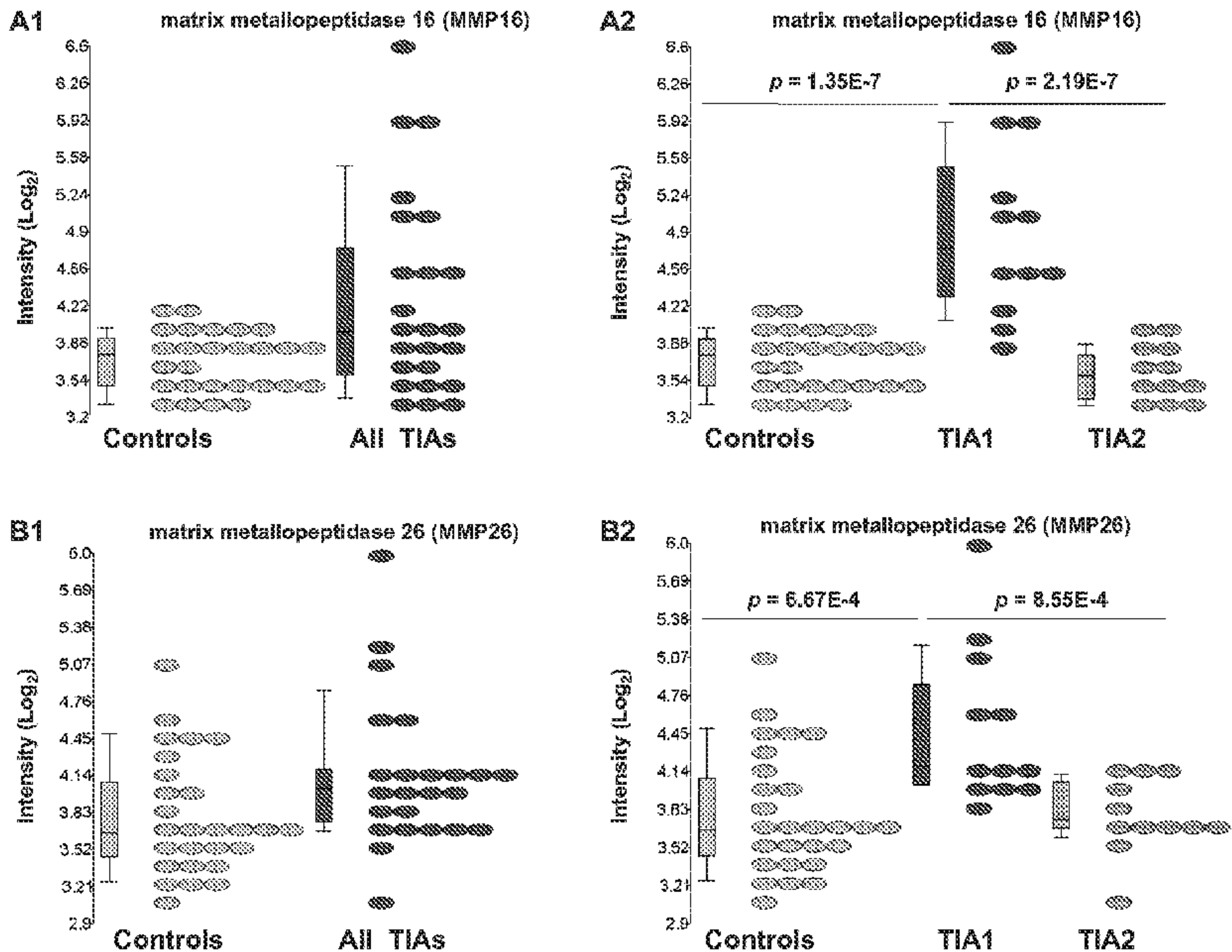


Figure 4