

METHOD AND SYSTEM FOR RNA ISOLATION FROM SELF-COLLECTED AND SMALL VOLUME SAMPLES

FIELD OF THE INVENTION

[0001] The present invention relates generally to the isolation and characterization of nucleic acid, particularly RNA, from small volume and self-collected samples, including fingerstick blood samples, swabs and saliva samples. The RNA derived is intact and of sufficient quality and quantity for RNA analysis, longitudinal RNA sequencing and global transcriptomic profiling.

BACKGROUND OF THE INVENTION

[0002] RNA analysis, longitudinal RNA sequencing and global transcriptomic profiling are useful tools to identify and analyze biomarkers for disease, infection, exposure, susceptibility, drug response and toxicity (Frank MO et al (2019) BMC Medical Genetics 12:56; doi.org/10.1186/s12920-019-0500-0; Casamassimi A et al (2017) Int J Mol Sci 18(8):1652; Sheid AD et al (2018) J Immunol 200:1817-1928). In some disease and cancer studies, solid tissues or tumor samples are utilized, however, this is not practical in clinical studies or for continuous monitoring. Peripheral blood has advantages for biomarker evaluation and discovery due to its non-invasive collection and availability, particularly in comparison to solid tissue samples. A number of studies have demonstrated that transcriptomic changes in peripheral blood can serve as biomarkers of infection, exposure to xenobiotics, response to therapeutics or vaccines, or as indicators for pathological changes occurring in other tissues (Bushel PR et al (2007) Proc Natl Acad Sci 104(46):18211-6; Ramilo O et al (2007) Blood 109:2066-2077; Mejias A et al (2013) PLoSMed 10(11):e1001549; Hecker M et al (2013) Molec Neurobiol 48:737-756; Querec TD et al (2009) Nat Immunol 10:116-125).

[0003] The use of whole blood for transcriptomic profiling and RNA evaluation presents a number of significant technical challenges, including that RNA degradation and transcriptomic changes can occur quickly after the blood is drawn from subjects. Traditional reagents, such as citrate salts, heparin, and EDTA, inhibit blood clotting, but do not stabilize mRNA transcripts and altered gene regulation has been observed in whole blood samples, particularly when RNA is not immediately isolated (Debey S et al (2004) Pharmacogenomics 4:193-207; Rainen L et al (2002) Clin Chem 48:1883-1890). Moreover, the majority of RNA from whole blood encodes the globin protein, and sequencing that does not take this into consideration can yield results of low complexity (ie mostly globin mRNA, and few other unique or rare mRNA species).

[0004] Approaches for blood RNA stabilization have been developed to address the issues for RNA analysis from whole and peripheral blood samples (Asare AL et al (2008) BMC Genomics 9:474; Rainen L (2002) Clin Chem 48:1883-1890; Chai V et al (2005) J Clin Lab Anal 19:182-188). These

include the PAXgene™ Blood RNA system (Qiagen) and the Tempus™ system (Applied Biosystems). In both systems, blood is immediately lysed when collected into the tube and RNA is stabilized using specific reagents. The PAX blood collection tube system and stabilization buffer is described including in US Patents 6,602,718 and 6,617,170. Aspects of the Tempus guanidinium-based stabilization agent are provided in 5,972,613. Both of these systems are designed for and require 2.5 mls or 3 mls of whole blood, which necessitates venipuncture, and are not suitable for small blood samples such as from a laboratory animal, an infant, or for any applicable means of self-collection.

[0005] Fingerstick blood collection is a practical and minimally invasive sample collection method that is used for a wide range of applications in routine clinical practice and can be implemented outside of clinical settings. For example, fingerstick sampling is used by millions of individuals to collect daily small blood volumes to monitor sugar or glucose levels. Finger stick blood collection would also be of value in subjects where it is commonly difficult to collect blood via venipuncture such as in infants and young children, elderly or ill individuals with compromised veins, intravenous drug addicts, and very obese individuals, in field studies in remote and under-developed areas, in military subjects or physically active athletes, or in other situations such as where a rapid sample is necessitated or applicable or in instances where collection of a large number of samples, including from many individuals, need to be obtained in a short amount of time.

[0006] The RNA collection and analysis systems currently in use and available, however, are not designed for small volume samples, such as finger stick blood samples or samples of one or a few droplets of blood. Collection of small volumes of blood via finger sticks is especially indicated for high frequency or repeated sample collection, such as to enable monitoring individuals in health and disease or infection. In addition, these systems are not applicable for alternative types of samples which may be time and sample volume critical such as nasopharyngeal, nasal or throat swabs or aspirates. These are commonly utilized in direct and rapid patient assessment for virus infection, particularly respiratory virus infection, such as for influenza, so that infection can be quickly evaluated and treatment prescribed.

[0007] In order to implement and apply RNA isolation, evaluation and analysis more broadly and across various clinical and nonclinical scenarios and situations, there is a need for methods and a system to reliably and effectively sample and analyze RNA from small volume samples and alternative sample types that can be collected frequently, rapidly, in large number, in the field or at home by a relatively untrained individual or non-health professional or patient. There is a need for straightforward and dependable systems and methods whereby RNA can be isolated from small volume samples, self-collection samples, fingerstick samples and evaluated qualitatively and quantitatively with confidence and dependable results, particularly for whole transcriptome analysis and profiling.

SUMMARY OF THE INVENTION

[0008] The present invention general relates to methods for RNA isolation and RNA profiling and analysis of small volume samples and self-collected samples, wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling. In embodiments of the method, a small volume sample may be from a patient or individual having a disease or infection or at risk for or suspected of disease or infection. In some embodiments, the patient or individual obtains or collects the small volume sample. In some embodiments, the patient or individual is assisted by a non-medical person in collection of the sample. In an embodiment, the sample is collected from a patient or individual by a non-medical person, such as a spouse, parent, friend, guardian, etc that is not medically trained or involved in any medical profession. Critically, the invention describes methods to obtain sufficient quality and quantity of RNA for a variety of analyses, ranging from quantitating individual RNA species to sequencing entire transcriptomes of high complexity.

[0009] In accordance with the method, small volume sample(s) is collected and combined with an RNA stabilization solution. In some embodiments, the RNA stabilization solution is capable of lysing the cells in the sample and of stabilizing RNA contained in the cells or cell lysate of the sample. In some embodiments, the RNA stabilization solution is capable of lysing the cells in the sample and of stabilizing RNA contained in the cells or cell lysate of the sample in a single step. In embodiments, the sample and RNA stabilization solution are mixed, vortexed or shaken when combined. In some embodiments, the sample may be stored or left at room temperature for up to a few or several hours prior to refrigeration. In some embodiments, the sample is then stored in refrigerated conditions, such as at about 40°F or about 4°C for a brief time. In some embodiments, the sample is then stored in refrigerated conditions, such as at about 40°F or about 4°C for a brief time, up to a day or a few or several days. In some embodiments, the sample may be stored or left at room temperature for up to a few or several hours, up to 2 hours, up to 3 hours, up to 3 or 4 hours, prior to refrigeration. In some embodiments, the sample is then stored in refrigerated conditions, such as at about 40°F or about 4°C for a brief time, up to a day or a few or several days. In some embodiments, the sample is stored in a freezer or in frozen temperature conditions, such as at about 30 or 32°F or about 0°C, either after collection, after brief (2-4 hour) storage at room temperature, or after brief (1-2 day) refrigerated storage.

[00010] A small volume sample may be less than 500µl, less than 300µl, less than 250µl, about 200-300µl, less than 200µl, about 100-300µl, about 150-300µl, about 100-250µl, about 50-300µl. In an embodiment, a small volume sample volume is about 100-300µl.

[00011] In some embodiments, the sample may be the sample is a small volume blood sample, a sputum or saliva sample, or a nasal, nasopharyngeal or oropharyngeal swab, wash or aspirate. In embodiments, the small volume sample is a blood sample and is collected via fingerstick or heelprick. In an embodiment, the small volume sample is a blood sample and is collected via fingerstick. In

embodiments, the fingerstick sample or heelprick sample may comprise blood droplets directly from a fingerstick or heelprick or a capillary tube may be utilized.

[00012] In some embodiments, the sample volume is less than 500 μ l, less than 300 μ l, less than 250 μ l, about 200-300 μ l, less than 200 μ l, about 100-300 μ l, about 150-300 μ l, about 100-250 μ l, about 50-300 μ l. In some embodiments, the volume is less than 100 μ l, less than 50 μ l, about 10-50 μ l, about 10-20 μ l, about 10 μ l, as small as 10 μ l or less. In an embodiment, the sample volume is about 100-300 μ l. In an embodiment, the sample volume is about 50-300 μ l. In some embodiments, the sample volume is on the order of a blood droplet volume, or one or a few blood droplet volumes. In some embodiments, the blood or sample volume is that of a capillary tube volume, or less than a blood droplet volume. Capillary tube sample volumes may be on the order of 60-100 μ l, 100-200 μ l, 5-25 μ l, 10-50 μ l, less than 10 μ l, 1-5 μ l.

[00013] In some embodiments, the volume of RNA stabilization solution is less than 1ml, about 500 μ l or less, about 300 μ l or less, about 200-300 μ l, or about 250 μ l, or about 200 μ l. In an embodiment, the volume of RNA stabilization solution is about 300 μ l or less, about 200-300 μ l, or about 250 μ l, or about 200 μ l. In some embodiments, including wherein the sample volume is very low, such as on the order of less than 50 μ l, or 10-50 μ l, or about 10 μ l, or less than 10 μ l, the volume of RNA stabilization solution is appropriately low, such as on the order of less than 100 μ l, less than 50 μ l, less than 25 μ l, as small as 10 μ l or less.

[00014] In some embodiments, the sample is collected into a tube or wherein the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, 1.2 ml or less, or 1ml or less, or less than 1ml, or less than 500 μ l, or less than 300 μ l, or less than 200 μ l. In an embodiment, the sample is collected into a tube or wherein the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, such as a microtainer tube. In an embodiment, the sample is collected in a tube which is suitable for small volumes, including very small volumes, such as a capillary tube. In an embodiment, the sample is collected into a capillary tube, which is suitable for small volumes, such as less than 100 μ l, or even for very small volumes, such as less than 50 μ l, less than 25 μ l.

[00015] The invention provides a method for RNA profiling and analysis of small volume samples from a patient or individual comprising:

- (a) obtaining one or more small volume sample self-collected by the patient or individual or by a non-medical person, wherein the sample is collected in or otherwise combined with an RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized; and
- (b) isolating RNA using a process adapted for small volume samples wherein the amount of any and all solutions or buffers utilized are reduced and adjusted for small volume samples;

wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling through RNA sequencing (RNAseq).

[00016] In embodiments of the method, the RNA is isolated using a process comprising:

- (a) contacting the sample with a protease to form a protease treated small volume sample;
- (b) contacting the protease treated sample with an ethanol or salt solution forming a precipitate containing the RNA, wherein the precipitate containing the RNA is then resuspended in a buffer or solution, or contacting the protease treated sample with an organic extraction solution, forming a solution having an aqueous phase containing the RNA and an organic phase;
- (c) contacting the resuspended precipitate containing the RNA or the aqueous phase containing the RNA with DNase to form a DNase-treated resuspended precipitate or DNase-treated aqueous phase;
- (d) binding the RNA to a silica based solid phase or column by contacting the resuspended precipitate or aqueous phase with said silica based solid phase; and
- (e) eluting the RNA from the silica based solid phase comprising contacting the silica based solid phase with a solution or buffer to provide isolated RNA;

wherein all buffer and solution volumes are reduced and adjusted for small volume samples.

[00017] In some embodiments, between steps (b) and (c), the resuspended precipitate containing the RNA or the aqueous phase containing the RNA is contacted with a solution or column to remove residual sample cell debris and/or to homogenize the sample cell lysate.

[00018] For embodiments using protease, the protease may be proteinase K. For embodiments using proteinase K, lysis buffers may also contain detergents, which both inactivate adventitious agents, lyse cells, and activate the proteinase K. Proteinase K has activity at 25°C, although it can be activated by putting the collected sample in hot tap water (typical tap water is set at a maximum of 120° F, which is about 48° C; Proteinase K is optimally active at ~55° C).

[00019] In embodiments of the method, the RNA is isolated using a process comprising:

- (a) contacting the sample with an RNA stabilization solution, wherein the solution has capability to lyse cells and inactivate adventitious agents;
- (b) contacting the RNA stabilization solution treated sample with an ethanol or salt solution forming a precipitate containing the RNA, wherein the precipitate containing the RNA is then resuspended in a buffer or solution, or contacting the RNA stabilization solution treated sample with an organic extraction solution, forming a solution having an aqueous phase containing the RNA and an organic phase;

- (c) contacting the resuspended precipitate containing the RNA or the aqueous phase containing the RNA with DNase to form a DNase-treated resuspended precipitate or DNase-treated aqueous phase;
 - (d) binding the RNA to a silica based solid phase or column by contacting the resuspended precipitate or aqueous phase with said silica based solid phase; and
 - (e) eluting the RNA from the silica based solid phase comprising contacting the silica based solid phase with a solution or buffer to provide isolated RNA;
- wherein all buffer and solution volumes are reduced and adjusted for small volume samples.

[00020] In embodiments of the method, the RNA is isolated using a process comprising:

- (a) contacting the sample with an RNA stabilization solution, wherein the solution has capability to lyse cells and inactivate adventitious agents;
- (b) optionally further contacting the sample with a salt, a reducing agent, and/or a detergent;
- (c) contacting the solution contacted sample of (a) or (b) with silica, silica based solid phase or carboxylated magnetic beads which bind RNA and serves to purify the RNA from other components in the sample; and
- (d) eluting the RNA from the silica or silica based solid phase or the magnetic beads comprising contacting the silica, silica based solid phase or magnetic beads with a solution or buffer to provide isolated RNA;

wherein all buffer and solution volumes are reduced and adjusted for small volume samples.

[00021] In an embodiment, the RNA stabilization solution may be a mixture of chaotropic salt and phenol. In an embodiment, the chaotropic salt may be a guanidine salt or guanidine based. In an embodiment, the RNA stabilization solution may be the PAXgene RNA stabilization solution. .

[00022] In an embodiment, purification out of chaotropic salts such as guanidine, with detergent, can be used. The downstream purification as in step (c) may be precipitation, contact with a nucleic acid binding solid bead or semi-porous bead, such as a silica or carboxylated magnetic bead. Modification of lysis buffer for contact with silica or magnetic beads may be to include salt (e.g. sodium acetate) detergent (e.g. 0.2% sarkosyl), reducing agent (e.g. dithiothreitol, e.g. 75mM). Purification may be accomplished using magnets to purify nucleic acids, by washing magnetic beads with bound nucleic acid in 75-80% ethanol or isopropanol, twice, and then eluting RNA off the magnetic beads in pure RNase free double distilled water (ddH₂O).

[00023] In some embodiments, the sample is a small volume blood sample, a sputum or saliva sample, or a nasal, nasopharyngeal or oropharyngeal swab, wash or aspirate. In some embodiments, the sample is a small volume blood sample. In an embodiment, the small volume sample is a blood sample

and is collected via fingerstick. In embodiments, the fingerstick sample may comprise blood droplets directly from a fingerstick or a capillary tube may be utilized.

[00024] In some embodiments of the method(s), the sample volume is less than 500 μ l, less than 300 μ l, less than 250 μ l, about 200-300 μ l, less than 200 μ l, about 100-300 μ l, about 150-300 μ l, about 100-250 μ l, about 50-300 μ l. In an embodiment, the sample volume is about 100-300 μ l. In some embodiments, the volume is less than 100 μ l, less than 50 μ l, about 10-50 μ l, about 10-20 μ l, about 10 μ l, as small as 10 μ l or less. In an embodiment, the sample volume is about 50-300 μ l. In an embodiment, the sample volume is about 50-250 μ l or is about 50-200 μ l.

[00025] In some embodiments of the method(s), buffer and solution volumes are reduced to 20-40% or 20-30% of those utilized for isolation of RNA from a standard venipuncture blood sample.

[00026] In some embodiments, the RNA stabilization solution is a chaotropic salt such as guanidinium thiocyanate based or containing solution. In some embodiments chaotropic salts such as guanidinium thiocyanate based lysis buffers may also contain detergents, which synergize to inactivate adventitious agents, lyse cells. Detergents may include sarkosyl, SDS, or other ionic or non-ionic detergents. Kits/lysis solutions containing chaotropic salts such as guanidinium thiocyanate based lysis buffers with or without detergents, are stable, even up to for years. They can be shipped and used at room temperature. They are less toxic than household bleach, and can be mailed with adherence to suitable or such standards

[00027] In some embodiments, any buffers or solutions are made, prepared or generated with RNase free water or buffers.

[00028] In embodiments of the method, any suitable and efficacious protease is utilized. Suitable proteases are known and available in the art. In embodiment, the protease is proteinase K. In some embodiments, the sample is contacted and treated with a protease at a temperature above room temperature. In embodiments, the sample and protease are heated for protease treatment. In an embodiment, the sample and protease are heated to 50-60°C or incubated at a temperature of 50-60°C. In an embodiment, the sample and protease are heated to or incubated at 55°C.

[00029] In accordance with embodiments of the method, the method further comprises sequencing the RNA. RNA may be sequenced using any suitable or recognized method, steps, system(s) or kit(s), including manual, semi-automated or automated method(s), system(s) or kits. In some embodiments, kits such as Illumina TruSeq or Kapa Hyper Prep Kits are utilized.

[00030] In an embodiment, the isolated RNA is converted to cDNA. In some embodiments, the isolated RNA is converted to cDNA and may be cloned or a library prepared therefrom or containing or based on the cDNA(s).

[00031] In some embodiments, abundant RNA species or RNA species not of interest are removed prior to sequencing. In embodiments, globin mRNA, ribosomal RNA(s) or species specific RNAs are removed prior to sequencing. Methods, systems and kits for removal of globin RNA and/or ribosomal

RNA are known and available to one skilled in the art. In some embodiments, systems or kits such as GlobinZero (Illumina), Ribo-Zero Gold, TruSeq Stranded total RNA library prep, Ribo-Zero Globin, GLOBINclear kit (Thermo Fisher Scientific), QIAseqFastSelect RNA removal kit (Qiagen) may be utilized. In some embodiments, species specific probes may be utilized to select out certain RNAs.

[00032] In embodiments of the method, the patient or individual has a disease or infection or is at risk of or suspected of disease or infection.

[00033] In some embodiments, the method is for longitudinal screening by RNA profiling and analysis of small volume samples from one or more patient or individual, wherein the patient or individual has a disease or infection or is at risk of or suspected of disease or infection. In embodiments, small volume samples are collected in series or in regular or designated increments of hours, days, weeks or months. In embodiments, small volume blood samples are collected via fingerstick in series or in regular or designated increments of hours, days, weeks or months.

[00034] In some embodiments, small volume samples may be collected or additionally collected at onset of symptom(s), such as one or more symptom or recognized parameter indicative of or associated with a disease or infection. The disease may be an acute or chronic disease. The disease may be a relapsing and/or remitting disease. The infection may be a bacterial or viral infection. The infection may be with a known or unknown infectious agent. The infection may be with a known or unknown virus or bacteria.

[00035] In embodiments of the invention, systems and kits for use and application of the methods are provided.

[00036] In embodiments, a system or kit is provided for RNA profiling and analysis of small volume samples from a patient or individual comprising:

- (a) a means for self-collection of a small volume sample by the patient or individual or by a non-medical person, comprising a lancet, swab or receptacle for a wash, spit or aspirate;
- (b) a tube or receptacle for receiving the small volume sample on collection and containing a volume of RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized; and
- (c) one or more appropriate label(s) for designating the name or identity of the patient or individual, date of sample collection and time of sample collection.

[00037] In embodiments, the system or kit may further comprise an envelope or mailing container for shipment of the sample to a laboratory or facility for RNA isolation and analysis.

[00038] In some embodiments, the system or kit may be for longitudinal RNA profiling and analysis of multiple small volume samples collected in series from a patient or individual over days, weeks or months comprising:

- (a) a set of numerous means for self-collection of individual small volume samples by the patient or individual or by a non-medical person, each comprising a lancet, swab or receptacle for a wash, spit or aspirate;
- (b) a set of numerous tubes or receptacles each individually for receiving a small volume sample on collection and containing a volume of RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized;
- (c) numerous appropriate label(s) for designating the name or identity of the patient or individual, date of sample collection and time of sample collection; and
- (d) numerous envelopes or mailing containers for shipment of each sample or several samples to a laboratory or facility for RNA isolation and analysis.

[00039] In some embodiments of the system or kit, the volume of RNA stabilization solution is less than 1ml, about 500µl or less, about 300µl or less, about 200-300µl, or about 250µl. In an embodiment, the volume of RNA stabilization solution is about 300µl or less, about 200-300µl, or about 250µl. In some embodiments, including wherein the sample volume is very low, such as on the order of less than 50µl, or 10-50µl, or about 10µl, or less than 10µl, the volume of RNA stabilization solution is appropriately low, such as on the order of less than 100µl, less than 50µl, less than 25µl, as small as 10µl or less

[00040] In some embodiments of the system or kit, the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, 1.2 ml or less, or 1ml or less. In some embodiments, the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution is a tube which is suitable for small volumes, including very small volumes, such as a capillary tube. In an embodiment, the tube or receptacle is a capillary tube, which is suitable for small volumes, such as less than 100µl, or even for very small volumes, such as less than 50µl, less than 25µl.

[00041] Other objects and advantages will become apparent to those skilled in the art from a review of the ensuing detailed description, which proceeds with reference to the following illustrative drawings, and the attendant claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[00042] The patent or patent application contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

[00043] **Figure 1** depicts the study overview and validation of in-home assessments of disease activity and gene expression. **A.** Clinical data collection and RNA analysis over time. Study overview of clinical data and sample collection over time. **B.** Clinical and patient reported assessments of disease activity. Correlation between disease activity scores measured in clinic (DAS28) and at home (RAPID3

questionnaire) from the index patient. **C.** Clinical blood counts and RNASeq-inferred blood counts. Neutrophil, lymphocyte, and monocyte counts measured from paired clinical complete blood counts from venipuncture blood draws and CIBERSORTx inferred blood counts from RNAseq data from finger stick blood draws (N=38 paired samples).

[00044] **Figure 2** depicts RNA quality and quantity by volume of fixative. 3 drops of blood harvested with a 21 gauge lancet were added to a microtainer tube prefilled with either 250µl, 500µl or 750µl of PAX gene fixative. Samples were stored at room temperature for 3 days and then RNA was extracted using the PAX gene RNA kit and RIN scores and quantity of RNA was assessed using the Agilent 2100 Bioanalyzer picochip. Padj= ANOVA, followed by Dunnett's multiple comparisons test, using 250µl as the reference group.

[00045] **Figure 3** depicts RNA quality and quantity by time at room temperature. 100µl of whole blood was added to a microtainer tube prefilled with 250µl PAX gene fixative and frozen after 2 hours, 3 days, or 7 days incubation at room temperature. RNA was extracted using the PAX gene RNA kit with scaled down washes and elutions and RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzer RNA picochip. Padj= ANOVA, followed by Dunnett's multiple comparisons test, using Day 0 as the reference group.

[00046] **Figure 4** depicts RNA quality and quantity of fresh and mailed samples. 100µl of whole blood was added to a microtainer tube prefilled with 250µl PAX gene fixative and frozen after 2-hour incubation at room temperature or mailed. RNA was extracted using the PAX gene RNA kit and RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzer RNA picochip.

[00047] **Figure 5** depicts RNA quality and quantity by volume of extraction and washes. 3 drops of blood harvested with a 21 gauge lancet were added to a microtainer tube prefilled with 250µl of PAX gene fixative. Samples were stored at room temperature for 3 days and then RNA was extracted using the PAXgeneRNA kit according to manufacturer's directions or with a scaled down version of the PAX protocol, using approximately 25% of the recommended volumes for all washes and elutions. RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzerRNA picochip. P= unpaired two-sided t test.

[00048] **Figure 6** depicts RNA quality and quantity with and without TriZol reagent extraction step. Mailed patient finger stick samples were stored in PAXgeneRNA buffer at -80°C. 142 samples had RNA extracted with PAXgeneRNA extraction with low volume washes, 13 samples were thawed and mixed with 700µl Trizol-LS, and 250µl chloroform. After centrifugation, the top layer was precipitated with isopropanol and glycogen and washed with 80% cold ethanol, centrifuged and the pellet was dried, resuspended in PBS and then purified using the Roche High Pure Isolation kit. P values represent significance of unpaired T tests.

[00049] **Figure 7** depicts a comparison of Cycle Times for HbgA2, 18S RNA, and TNF alpha after GlobinZero depletion. Since ribosomal and hemoglobin RNA represent approximately 98% and 70%

of the RNA in whole blood, respectively, we tested standard commercial kits for removing these RNAs prior to RNAseq. 4ml heparinized blood was treated and stimulated with 1 µg/ml LPS or was untreated and incubated for one hour at 37°C. Then, 250 µl of the unstimulated or stimulated blood sample was placed into 250 µl PAXgene fixative into replicate microtainer tubes. After RNA extraction, samples were either undepleted (left side of panel) or depleted (right side of panel) with the globin zero depletion kit and then quantitative PCR was performed to test for hemoglobin A2, 18S RNA, or TNF alpha mRNA expression. GlobinZero kits depleted both hemoglobin A2 and 18S ribosomal RNA (increased mean cycle time from 11 to 28 and 10 to 30, respectively) with relative preservation of TNFalpha mRNA. P values represent results of ordinary one-way ANOVA with Tukey's multiple comparisons test.

[00050] Figure 8 provides RNASeq QC metrics of RNA with various quality scores prepared with Illumina TruSeq or Kapa Hyper Prep Kits. **A.** (Left Panel): Distribution of mapping, uniquely mapping, and duplicate reads. **B.** (Right Panel): Distribution of tags assigned to UTR (untranslated region), intergenic, intronic, and CDS (coding sequence) of whole blood RNA samples prepared with Illumina TruSeq or Kapa Hyper Prep Kits with various input RNA quality and quantity. The Illumina TruSeq library Prep demonstrated increased mapping to coding sequence and fewer intergenic reads and was ultimately used for downstream RNA sequencing experiments.

[00051] Figure 9 provides clinical and transcriptional characteristics of RA flares in index patient. **A.** Index Patient disease activity over time. Disease activity (RAPID3 questionnaire, N=356), over the course of four years in index patient. Time points are colored according to disease activity category. **B.** Differential expression of genes in flare. Volcano plot of differential gene expression of flare (N=46) versus baseline (N=33), plotting statistical significance ($-\log_{10}(\text{FDR})$) against fold change ($\log_2(\text{FC})$) (gray points are non-significant genes, i.e., $\text{FDR} > 0.1$, red indicates $\text{FDR} < 0.1$ and $\log_2$ fold change > 0 , blue indicates $\text{FDR} < 0.1$ and $\log_2$ fold change < 0). Pathways enriched in significantly increased (**C.**) (Pathways increased in flare) or decreased genes (**D.**) (Pathways decreased in flare) in flare relative to baseline.

[00052] Figure 10 provides transcriptional characteristics of immune activation prior to symptom onset in RA flares. **A.** Disease activity scores over time to flare (measured in days). Box represents disease activity from day -56 to +28 over time to flare. Vertical arrows (in A-D) represent start of flare. **B.** Hierarchical clustering of z scores of 2791 significantly differentially expressed genes over time to flare. Statistically significant clusters are labeled by color. AC2 and AC3 refer to clusters that changed antecedent to flare. **C.** Detailed representation of cluster 1, antecedent cluster 2 (AC2), and antecedent cluster 3 (AC3) genes from Figure 3B over time to flare. **D.** Mean standardized cluster gene expression over time to flare. Light grey lines represent expression of individual genes in the cluster. Dashed horizontal line represents mean baseline gene expression (weeks -8 to -4). Dashed vertical line represents start of flare. **E.** Pathways enriched in clusters 1, AC2, and AC3.

[00053] Figure 11. PRIME cells express AC3 genes. **A.** Synovial cell subtype marker genes in clusters identified in blood (Figure 3A). Enrichment scores of 200 single cell RNAseq marker genes from 18 synovial subset cell types. Dashed line represents threshold for significance ($FDR < 0.05$ or $-\log_{10} FDR > 1.3$). **B.** Mean standardized gene expression and 95% confidence intervals of genes common to synovial sublining fibroblasts (CD34+, DKK+ and HLA-DRA+ fibroblasts) and AC3 in blood over time to flare (dashed vertical line represents start of flare). Error bars represent confidence intervals. **C.** Venn diagram of AC3 genes that decrease during flare in 4 patients. **D.** Flow cytometry of blood samples from 19 RA patients and 18 healthy volunteers (HV). Percent PDPN+/CD45- cells of TOPRO-(live)/CD31- cells is presented. P value represents result of two sided t-test. **E.** Log2 fold change of AC3 genes expressed in PRIME cells (flow sorted CD45-/CD31-/PDPN+ cells) versus hematopoietic cells (flow sorted CD45+) and Log2 fold change of input cells (stained PBMC but not flow sorted) versus hematopoietic cells (flow sorted CD45+) as technical control for stress of flow sorting.

[00054] Figure 12 depicts that differentially expressed flare genes are reproducibly altered in repeated flares. **A.** Index patient disease activity (RAPID3) over time. Top panel dots are colored by disease activity assignment. Bottom panel dots are colored according to clinical flare event number. **B.** Unsupervised hierarchical clustering of genes differentially expressed between baseline and flare. Top bar indicates samples colored according to disease activity assignment. Bottom bar indicates samples colored according to clinical flare event number. Data shows differentially expressed flare genes are represented by multiple clinical events.

[00055] Figure 13 depicts that sorted PRIME cells express synovial fibroblast genes. Log2 fold change of various synovial single cell RNAseq marker genes in PRIME cells (flow sorted CD45-/CD31-/PDPN+ cells) versus hematopoietic cells (flow sorted CD45+) and Log2 fold change of Input cells (stained PBMC but not flow sorted) versus hematopoietic cells (flow sorted CD45+) as technical control for stress of flow sorting. These data show that single cell marker genes of fibroblasts (SC-F1, SC-F2, SC-F3, SC-F4) but not B cells (SC-B1-4), macrophages (SC-M1-4), or T cells (SC-T1-6) are enriched in sorted PRIME cells. Fibroblast genes (as marked) were the only set of synovial cell marker genes enriched in PRIME cells.

[00056] Figure 14 depicts that sorted PRIME cells express classic synovial fibroblast genes. Volcano plot of $\log_{10}(-\text{padj})$ vs Log2 fold change of PRIME cells (flow sorted CD45-/CD31-/PDPN+ cells) versus hematopoietic cells (flow sorted CD45+). Classic fibroblast genes are significantly increased in PRIME cells relative to hematopoietic cells.

DETAILED DESCRIPTION

[00057] In accordance with the present invention there may be employed conventional molecular biology, microbiology, and recombinant DNA techniques within the skill of the art. Such techniques

are explained fully in the literature. See, e.g., Sambrook et al, "Molecular Cloning: A Laboratory Manual" (1989); "Current Protocols in Molecular Biology" Volumes I-III [Ausubel, R. M., ed. (1994)]; "Cell Biology: A Laboratory Handbook" Volumes I-III [J. E. Celis, ed. (1994)]; "Current Protocols in Immunology" Volumes I-III [Coligan, J. E., ed. (1994)]; "Oligonucleotide Synthesis" (M.J. Gait ed. 1984); "Nucleic Acid Hybridization" [B.D. Hames & S.J. Higgins eds. (1985)]; "Transcription And Translation" [B.D. Hames & S.J. Higgins, eds. (1984)]; "Animal Cell Culture" [R.I. Freshney, ed. (1986)]; "Immobilized Cells And Enzymes" [IRL Press, (1986)]; B. Perbal, "A Practical Guide To Molecular Cloning" (1984).

[00058] Therefore, if appearing herein, the following terms shall have the definitions set out below.

[00059] The term "rheumatoid arthritis" or "RA" refers to a chronic disease, which is immune-mediated and inflammatory and is an autoimmune disorder, affecting the lining of joints that causes joint pain, stiffness, swelling and decreased movement of the joints and can eventually result in bone erosion and joint deformity. RA is a systemic autoimmune disease characterized by the simultaneous inflammation of the synovium of multiple joints.

[00060] An "RA flare" or "flare" refers to a surge in immune-mediated and/or inflammatory activity that is periodically experienced by a patient(s) with RA. During a flare, the level of fatigue and joint symptoms such as pain, swelling, and stiffness temporarily increase. Flares are periods of increased disease activity during which people's arthritis symptoms, which typically include joint pain, swelling, and stiffness, are more severe. An RA flare can involve an exacerbation of any symptom of the disease, but most commonly includes intense stiffness in the joints. People with RA report these common symptoms of flares: increased stiffness in joints, pain throughout the entire body, increased difficulty doing everyday tasks, swelling, such as causing shoes not to fit, intense fatigue, flu-like symptoms.

[00061] As used herein, "RNA" is defined as at least two ribonucleotides covalently linked together. The RNA may be any type of RNA. Examples include mRNA, tRNA, rRNA, shRNA, circRNA, scaRNA, scRNA, snRNA, siRNA or Piwi-interacting RNA, or a pri-miRNA, pre-miRNA, miRNA, snoRNA, long ncRNAs, anti-miRNA, precursors and any variants thereof. Further examples of RNA include RNA of a virus, or RNA sequences derived from a virus genome. Even further examples include RNA of a bacteria. RNA may be single stranded or double stranded, or may contain portions of both double stranded and single stranded sequence. RNA may be synthesized as a single stranded molecule or expressed in a cell (in vitro or in vivo) using a synthetic gene. RNA may be obtained by chemical synthesis methods or by recombinant methods.

[00062] RNA may also encompass the complementary strand of a depicted single strand. Many variants of RNA may be used for the same purpose as a given RNA. Thus, RNA also encompasses substantially identical RNA and complements thereof. A single strand provides a probe that may hybridize to a target sequence under stringent hybridization conditions. Thus, RNA also encompasses a probe that hybridizes under stringent hybridization conditions.

[00063] As used herein, "pg" means picogram, "ng" means nanogram, "ug" or "µg" mean microgram, "mg" means milligram, "ul" or "µl" mean microliter, "ml" means milliliter, "l" means liter.

[00064] A "replicon" is any genetic element (e.g., plasmid, chromosome, virus) that functions as an autonomous unit of DNA replication *in vivo*; i.e., capable of replication under its own control.

[00065] A "vector" is a replicon, such as plasmid, phage or cosmid, to which another DNA segment may be attached so as to bring about the replication of the attached segment.

[00066] A "DNA molecule" refers to the polymeric form of deoxyribonucleotides (adenine, guanine, thymine, or cytosine) in its either single stranded form, or a double-stranded helix. This term refers only to the primary and secondary structure of the molecule, and does not limit it to any particular tertiary forms. Thus, this term includes double-stranded DNA found, *inter alia*, in linear DNA molecules (e.g., restriction fragments), viruses, plasmids, and chromosomes. In discussing the structure of particular double-stranded DNA molecules, sequences may be described herein according to the normal convention of giving only the sequence in the 5' to 3' direction along the nontranscribed strand of DNA (i.e., the strand having a sequence homologous to the mRNA). An "origin of replication" refers to those DNA sequences that participate in DNA synthesis.

[00067] A DNA "coding sequence" is a double-stranded DNA sequence which is transcribed and translated into a polypeptide *in vivo* when placed under the control of appropriate regulatory sequences. The boundaries of the coding sequence are determined by a start codon at the 5' (amino) terminus and a translation stop codon at the 3' (carboxyl) terminus. A coding sequence can include, but is not limited to, prokaryotic sequences, cDNA from eukaryotic mRNA, genomic DNA sequences from eukaryotic (e.g., mammalian) DNA, and synthetic DNA sequences. A polyadenylation signal and transcription termination sequence will usually be located 3' to the coding sequence.

[00068] Transcriptional and translational control sequences are DNA regulatory sequences, such as promoters, enhancers, polyadenylation signals, terminators, and the like, that provide for the expression of a coding sequence in a host cell.

[00069] The term "oligonucleotide," as used herein in referring to the probe of the present invention, is defined as a molecule comprised of two or more ribonucleotides, preferably more than three. Its exact size will depend upon many factors which, in turn, depend upon the ultimate function and use of the oligonucleotide.

[00070] The term "primer" as used herein refers to an oligonucleotide, produced synthetically, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product, which is complementary to a nucleic acid strand, is induced, i.e., in the presence of nucleotides and an inducing agent such as a DNA polymerase and at a suitable temperature and pH. The primer may be single-stranded and must be sufficiently long to prime the synthesis of the desired extension product in the presence of the inducing agent. The exact length of the primer will depend upon many factors, including temperature, source of primer and use of the method. For

example, for diagnostic applications, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15-25 or more nucleotides, although it may contain fewer nucleotides.

[00071] The primers herein are selected to be "substantially" complementary to different strands of a particular target DNA sequence. This means that the primers must be sufficiently complementary to hybridize with their respective strands. Therefore, the primer sequence need not reflect the exact sequence of the template. For example, a non-complementary nucleotide fragment may be attached to the 5' end of the primer, with the remainder of the primer sequence being complementary to the strand. Alternatively, non-complementary bases or longer sequences can be interspersed into the primer, provided that the primer sequence has sufficient complementarity with the sequence of the strand to hybridize therewith and thereby form the template for the synthesis of the extension product.

[00072] A "protease" as defined herein is an enzyme that hydrolyses peptide bonds. Conventional proteases may be used. Proteinase K is an example. It is preferred that the specific activity of the protease be high to degrade proteins in what can be a protein-rich sample and thereby protect the RNA from ribonucleases. The specific activity as determined by the Chromozym assay of the protease in the mixture of biological sample and denaturing solution is for example at least about 0.1 U/ml, at least about 1U/ml, at least about 2.5U/ml, at least about 5 U/ml, or at least about 10 U/ml. In another embodiment, the specific activity of the protease in the mixture is between 0.1 and 1000 U/ml.

[00073] Reference throughout this specification to "one embodiment," "an embodiment," "one example," or "an example" means that a particular feature, structure or characteristic described in connection with the embodiment or example is included in at least one embodiment of the present embodiments. Thus, appearances of the phrases "in one embodiment," "in an embodiment," "one example," or "an example" in various places throughout this specification are not necessarily all referring to the same embodiment or example. Furthermore, the particular features, structures or characteristics may be combined in any suitable combinations and/or sub-combinations in one or more embodiments or examples. In addition, it is appreciated that the figures provided herewith are for explanation purposes to persons ordinarily skilled in the art and that the drawings are not necessarily drawn to scale.

[00074] As used herein, the terms "comprises," "comprising," "includes," "including," "has," "having," or any other variation thereof, are intended to cover a non-exclusive inclusion. For example, a process, article, or apparatus that comprises a list of elements is not necessarily limited to only those elements but may include other elements not expressly listed or inherent to such process, article, or apparatus.

[00075] Further, unless expressly stated to the contrary, "or" refers to an inclusive "or" and not to an exclusive "or". For example, a condition A or B is satisfied by any one of the following: A is true (or

present) and B is false (or not present), A is false (or not present) and B is true (or present), and both A and B are true (or present).

[00076] In accordance with the invention a method, kit and system have been established along with a clinical and technical protocol for isolation of RNA via repeated home blood collection of small volume blood samples using self-performed finger stick sampling by patients with a disease. The system enabled and allowed for longitudinal RNA sequencing (RNAseq). In an exemplary set of studies, rheumatoid arthritis (RA) patients were assessed and their RNA evaluated over a series of time points and correlated with clinical and physical parameters regarding RA flares. Samples were obtained from numerous (over 300) time points from eight flares over four years in an index patient, and over 200 time points from flares in three additional patients. A sampling method and RNA stabilization and isolation protocol were developed providing high quality intact RNA. Assessments established that the RNAseq data from small volume blood finger stick samples correlated with blood cell counts from venipuncture blood draws. Transcripts were identified that were differentially expressed antecedent to RA flares. Transcriptomics of the patients prior to RA flares revealed a unique cell type, PRIME cells, in RA blood, which are predicted to become activated by B cells in the weeks prior to RA flare, and then migrate out of the blood to the synovium.

[00077] The methods and systems provided and enabled longitudinal genomic analysis via whole transcriptome analysis and total RNA sequencing (RNAseq). The studies provided herein establish that the collection system and RNA stabilization and isolation methods permits RNA sampling with valuable and consistent results. Among various applications for the system and methods, RNA profiling and longitudinal RNAseq analysis using the system and methods can reveal dynamic changes leading to flares of chronic inflammatory disease, provide indicators of clinical parameters and susceptibilities in disease or infection, reveal mechanisms via RNA activation and/or alteration in the progression of disease or infection or the susceptibility thereto, etc.

[00078] The present invention general relates to methods for RNA isolation and RNA profiling and analysis of small volume samples, wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling.

[00079] Transcriptomics is the study of the 'transcriptome,' initially termed to signify an entire set of transcripts, and now widely understood to mean the complete set of all the ribonucleic acid (RNA) molecules expressed in some given entity, such as a cell, tissue, or organism. Transcriptomics can encompass everything relating to RNAs, including their transcription and expression levels, functions, locations, trafficking, and degradation. It can also include the structures of transcripts and their parent genes with regard to start sites, 5' and 3' end sequences, splicing patterns, and posttranscriptional modifications and covers all types of transcripts, including messenger RNAs (mRNAs), microRNAs(miRNAs), and different types of long noncoding RNAs (lncRNAs).

[00080] Modern transcriptomics often uses high-throughput methods to analyze the expression of multiple transcripts in different physiological or pathological conditions and this is rapidly expanding our understanding of the relationships between the transcriptome and the phenotype across a wide range of living entities. Whole-transcriptome analysis with total RNA sequencing (RNA-Seq) detects coding plus multiple forms of noncoding RNA and a goal of total RNA sequencing is to accurately measure gene and transcript abundance, and identify known and novel features of the transcriptome.

[00081] It is important to recognize that different levels of RNA evaluation and analysis require alternative amounts of RNA in terms of yield or quantity and in terms of quality. For instance, gene expression profiling experiments that are looking for a quick snapshot of highly expressed genes may only require a relatively small amount or lower quality RNA, particularly in as much as the amount of RNA from a highly expressed gene is more significant comparatively (as compared to a lower expressed or comparatively rare or small RNA) in a sample. Evaluation of targeted gene expression or assessing for the presence or absence of one or more targeted RNA may only require a relatively small amount or lower quality RNA, particularly in as much as specific RNA probes or primer based isolation procedures may be utilized in the analysis. Experiments looking for a more global view of gene expression, and some information on alternative splicing, typically require a more mid level of quality and quantity of RNA. This encompasses most or many published RNA-Seq experiments for mRNA/whole transcriptome sequencing.

[00082] In important contrast, studies or experiments looking for or requiring an in-depth and full view of the transcriptome, to evaluate, identify or assemble new transcripts, to accurately measure gene and transcript abundance, or to identify known and novel features of the transcriptome require the highest quality and quantity of RNA available from samples. Thus, methods wherein RNA is isolated – even if from small or smaller volume samples – but is not quantitatively and qualitatively of the highest level, while suitable for some RNA analysis and study, will not be suitable for accurate and complete transcriptome profiling or longitudinal RNA profiling. There is an insufficient amount of all RNAs isolated to provide accurate and complete RNA information.

[00083] Total RNA-Seq analyzes both coding and multiple forms of noncoding RNA for a comprehensive view of the transcriptome and accurate and full results necessitate high quality RNA which is sufficient in quantity and yield to provide accurate, full length and comprehensive RNA sequences representing the full transcriptome. This then captures both known and novel features, allows researchers to identify biomarkers across the broadest range of transcripts, enables a more comprehensive understanding of phenotypes of interest and allows profiling of the whole transcriptome across a wide dynamic range.

[00084] The methods provided herein and in accordance with the invention provide RNA which is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling through RNA sequencing. Known and available methods for RNA isolation, if applied in a manner designed

for larger volume samples, such as a standard venipuncture blood sample, or a sample of 2-3 mls of blood for example, do not result in RNA of suitable quality and quantity for whole transcriptome analysis and transcriptomic profiling through RNA sequencing when applied to small volume samples, particularly for example small blood samples from a fingerstick, or samples in the volume range of 100-300µl blood.

[00085] In some embodiments, the sample may be a small volume blood sample, a sputum or saliva sample, or a nasal, nasopharyngeal or oropharyngeal swab, wash or aspirate. In embodiments, the small volume sample is a blood sample and is collected via fingerstick or heelprick. In an embodiment, the small volume sample is a blood sample and is collected via fingerstick. In embodiments, the fingerstick sample or heelprick sample may comprise blood droplets directly from a fingerstick or heelprick or a capillary tube may be utilized.

[00086] In some embodiments, the sample volume is less than 500µl, less than 300µl, less than 250µl, about 200-300µl, less than 200µl, about 100-300µl, about 150-300µl, about 100-250µl, about 50-300µl, about 50-200µl, about 50-150µl. In an embodiment, the sample volume is about 100-300µl. In some embodiments, the volume is less than 100µl, less than 50µl, about 10-50µl, about 10-20µl, about 10µl, as small as 10µl or less. In an embodiment, the sample volume is about 50-300µl. In some embodiments, the sample volume is on the order of a blood droplet volume, or one or a few blood droplet volumes. In some embodiments, the blood or sample volume is that of a capillary tube volume, or less than a blood droplet volume. Capillary tube sample volumes may be on the order of 60-100µl, 100-200µl, 5-25µl, 10-50µl, less than 10µl, 1-5µl. Capillary tubes on the order of these volumes are readily available commercially, such as from Sigma-Aldrich. The volume of choice or preference may be therein selected or as preferred.

[00087] A small volume sample may be from a patient or individual having a disease or infection or at risk for or suspected of disease or infection. In some embodiments, the patient or individual obtains or collects the small volume sample. In some embodiments, the patient or individual is assisted by a non-medical person in collection of the sample. In an embodiment, the sample is collected from a patient or individual by a non-medical person, such as a spouse, parent, friend, guardian, etc that is not medically trained or involved in any medical profession.

[00088] In accordance with the method, small volume sample(s) is collected and combined with an RNA stabilization solution. In some embodiments, the RNA stabilization solution is capable of lysing the cells in the sample and of stabilizing RNA contained in the cells or cell lysate of the sample. In some embodiments, the RNA stabilization solution is capable of lysing the cells in the sample and of stabilizing RNA contained in the cells or cell lysate of the sample in a single step. In embodiments, the sample and RNA stabilization solution are mixed, vortexed or shaken when combined. In some embodiments, the sample may be stored or left at room temperature for up to a few or several hours prior to refrigeration. In some embodiments, the sample is then stored in refrigerated conditions, such

as at about 40°F or about 4°C for a brief time. In some embodiments, the sample is then stored in refrigerated conditions, such as at about 40°F or about 4°C for a brief time, up to a day or a few or several days. In some embodiments, the sample may be stored or left at room temperature for up to a few or several hours, up to 2 hours, up to 3 hours, up to 3 or 4 hours, prior to refrigeration. In some embodiments, the sample is then stored in refrigerated conditions, such as at about 40°F or about 4°C for a brief time, up to a day or a few or several days. In some embodiments, the sample is stored in a freezer or in frozen temperature conditions, such as at about 30 or 32°F or about 0°C, either after collection, after brief (2-4 hour) storage at room temperature, or after brief (1-2 day) refrigerated storage.

[00089] In some embodiments, the volume of RNA stabilization solution is less than 1ml, about 500μl or less, about 300μl or less, about 200-300μl, or about 250μl. In an embodiment, the volume of RNA stabilization solution is about 300μl or less, about 200-300μl, or about 250μl. In some embodiments, including wherein the sample volume is very low, such as on the order of less than 50μl, or 10-50μl, or about 10μl, or less than 10μl, the volume of RNA stabilization solution is appropriately low, such as on the order of less than 100μl, less than 50μl, less than 25μl, as small as 10μl or less

[00090] The RNA stabilization solution may be guanidinium based. The RNA stabilization solution may be a PAXgene based solution, a Tempus RNA based solution, a Trizol solution, a QIAzol-based solution, a Dexterity based solution system. Suitable guanidinium based solutions, such as guanidinium thiocyanate solutions are known. Guanidinium based solutions and methods have been previously described (for example Chomczynski P & Sacchi N. (1987) Anal. Biochem. 162: 156–159). Some solutions are or may be preferred and more advantageous or more suitable in the methods so as to generate RNA of sufficient quality and quantity for RNAseq and transcriptomic analysis or longitudinal analysis as provided herein.

[00091] The sample may collected into a tube or wherein the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, 1.2 ml or less, or 1ml or less, or 500μl or less. In an embodiment, the sample is collected into a tube wherein the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, such as a microtainer tube. In some embodiments, the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution is a tube which is suitable for small volumes, including very small volumes, such as a capillary tube. In an embodiment, the tube or receptacle is a capillary tube, which is suitable for small volumes, such as less than 100μl, or even for very small volumes, such as less than 50μl, less than 25μl. Suitable sized tubes or containers are known and available in the art.

[00092] The invention provides a method for RNA profiling and analysis of small volume samples from a patient or individual comprising:

- (a) obtaining one or more small volume sample self-collected by the patient or individual or by a non-medical person, wherein the sample is collected in or otherwise combined with an RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized; and
- (b) isolating RNA using a process adapted for small volume samples wherein the amount of any and all solutions or buffers utilized are reduced and adjusted for small volume samples;

wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling through RNA sequencing (RNAseq).

[00093] The RNA may be isolated using a process comprising:

- (a) contacting the sample with a protease to form a protease treated small volume sample;
- (b) contacting the protease treated sample with an ethanol or salt solution forming a precipitate containing the RNA, wherein the precipitate containing the RNA is then resuspended in a buffer or solution, or contacting the protease treated sample with an organic extraction solution, forming a solution having an aqueous phase containing the RNA and an organic phase;
- (c) contacting the resuspended precipitate containing the RNA or the aqueous phase containing the RNA with DNase to form a DNase-treated resuspended precipitate or DNase-treated aqueous phase;
- (d) binding the RNA to a silica based solid phase or column by contacting the resuspended precipitate or aqueous phase with said silica based solid phase; and
- (e) eluting the RNA from the silica based solid phase comprising contacting the silica based solid phase with a solution or buffer to provide isolated RNA;

wherein all buffer and solution volumes are reduced and adjusted for small volume samples.

[00094] In embodiments of the method, the RNA is isolated using a process comprising:

- (a) contacting the sample with an RNA stabilization solution, wherein the solution has capability to lyse cells and inactivate adventitious agents;
- (b) contacting the RNA stabilization solution treated sample with an ethanol or salt solution forming a precipitate containing the RNA, wherein the precipitate containing the RNA is then resuspended in a buffer or solution, or contacting the RNA stabilization solution treated sample with an organic extraction solution, forming a solution having an aqueous phase containing the RNA and an organic phase;
- (c) contacting the resuspended precipitate containing the RNA or the aqueous phase containing the RNA with DNase to form a DNase-treated resuspended precipitate or DNase-treated aqueous phase;

- (d) binding the RNA to a silica based solid phase or column by contacting the resuspended precipitate or aqueous phase with said silica based solid phase; and
 - (e) eluting the RNA from the silica based solid phase comprising contacting the silica based solid phase with a solution or buffer to provide isolated RNA;
- wherein all buffer and solution volumes are reduced and adjusted for small volume samples.

[00095] In embodiments of the method, the RNA is isolated using a process comprising:

- (a) contacting the sample with an RNA stabilization solution, wherein the solution has capability to lyse cells and inactivate adventitious agents;
- (b) optionally further contacting the sample with a salt, a reducing agent, and/or a detergent;
- (c) contacting the solution contacted sample of (a) or (b) with silica, silica based solid phase or carboxylated magnetic beads which bind RNA and serves to purify the RNA from other components in the sample; and
- (d) eluting the RNA from the silica or silica based solid phase or the magnetic beads comprising contacting the silica, silica based solid phase or magnetic beads with a solution or buffer to provide isolated RNA;

wherein all buffer and solution volumes are reduced and adjusted for small volume samples.

[00096] In embodiments, all buffer and solution volumes are reduced to about 20-30%, 20-28%, about 25% of the volumes for standard venipuncture blood, which is on the order of a sample volume of 2.5mls. Thus, while the sample volume is about 1/10th or 10% of the standard blood volume for commercial kits and methods, the buffers and solutions are reduced to about 20-30% or about 25%.

[00097] In commercial RNA isolation kits, such as the PAXgene Blood RNA kit the blood collection tube contains RNA stabilization solution appropriate for about 2.5 ml of sample volume. The PAXgene Blood RNA tube contains 6.9 ml of RNA stabilization solution, applicable for about 2.5 mls of blood. For the PAXgene Blood RNA tube, the relative ratio of sample volume to RNA stabilization buffer is about 0.36, or the stabilization solution volume is about 2.5-3 fold or about 2.76 fold the sample volume. In the present method, about 500µl or less, about 300µl or less, about 200-300µl, or about 250µl of RNA stabilization solution is present or provided for collection of the small volume sample. In the present method, about 500µl or less, about 300µl or less, about 200-300µl, or about 250µl of RNA stabilization solution is present or provided for collection of the small volume sample, wherein the sample volume is less than 500µl, less than 300µl, less than 250µl, about 200-300µl, about 250µl, less than 200µl, about 100-300µl, about 150-300µl, about 100-250µl, about 50-300µl, about 50-200µl, about 50-150µl. The range of sample volume to RNA stabilization buffer is on the order of about 5 fold to about 2 fold, about 5 fold to about 1 fold, about 3 fold to about 2 fold the sample volume. While the

PAXgene kit blood collection tube contains 6.9 mls of RNA stabilization solution, in the instant methods the sample is combined with about 250 μ l or 0.25mls which is a relative volume of 3-4%.

[00098] In commercial RNA isolation kits, such as the PAXgene Blood RNA kit, buffer volume for protease treatment is about 340 μ l comprising 300 μ l of buffer and 40 μ l of protease. In the present method, buffer volume for protease treatment is about 74-75 μ l comprising 65 μ l of buffer and about 9 μ l of protease. The relative volume percentage of the protease buffer and protease in the present method is about 20-22% or about 22%.

[00099] In some embodiments, between steps (b) and (c), the resuspended precipitate containing the RNA or the aqueous phase containing the RNA is contacted with a solution or column to remove residual sample cell debris and/or to homogenize the sample cell lysate.

[00100] The sample may be a small volume blood sample, a sputum or saliva sample, or a nasal, nasopharyngeal or oropharyngeal swab, wash or aspirate. In some embodiments, the sample is a small volume blood sample. In an embodiment, the small volume sample is a blood sample and is collected via fingerstick. In embodiments, the fingerstick sample may comprise blood droplets directly from a fingerstick or a capillary tube may be utilized.

[00101] In some embodiments of the method, the sample volume is less than 500 μ l, less than 300 μ l, less than 250 μ l, about 200-300 μ l, less than 200 μ l, about 100-300 μ l, about 150-300 μ l, about 100-250 μ l, about 50-300 μ l. In an embodiment, the sample volume is about 100-300 μ l. In some embodiments, the sample volume is less than 100 μ l, less than 50 μ l, less than 25 μ l, 10 μ l or less.

[00102] In some embodiments of the method, buffer and solution volumes are reduced to 20-40% or 20-30% or about 25% of those utilized for isolation of RNA from a standard venipuncture blood sample, such as a 2.5 ml or about 2.5 ml sample.

[00103] In some embodiments, the RNA stabilization solution is a guanidinium thiocyanate based or containing solution.

[00104] In some embodiments, any buffers or solutions are made or generated with RNase free water or buffers.

[00105] In embodiments of the method, any suitable and efficacious protease is utilized. Suitable proteases are known and available in the art. In embodiment, the protease is proteinase K. In some embodiments, the sample is contacted and treated with a protease at a temperature above room temperature. In embodiments, the sample and protease are heated for protease treatment. In an embodiment, the sample and protease are heated to 50-60°C or incubated at a temperature of 50-60°C. In an embodiment, the sample and protease are heated to or incubated at 55°C.

[00106] The purification/isolation method may be adapted for a may utilize a fully manual purification. In embodiments of manual purification centrifugation or a vacuum manifold, or a combination thereof, may be utilized, for example in order to pass solutions through columns. The

purification/isolation method may be adapted for or may utilize Semi-automated purification. In embodiments of semi-automated purification, the lysis step and the precipitation or organic extraction step are carried out manually, while column purification is performed in an automated fashion, such as using an automated liquid handling system. Application of the isolation methods to fully automated purification is contemplated and an embodiment hereof, where all steps are performed using a fully automated system such as a fully equipped liquid handling system or a fully automated extraction system. Such fully automated systems are known and available in the art. In some embodiments, the fully automated systems are modified to adjust volumes, reagents, materials for small volume sample handling.

[000107] In embodiments of the method, commercial kits or RNA purification systems are modified. In embodiments, the PAXgene Blood RNA kit and process is modified for suitability and capability to provide for RNA isolation and RNA profiling and analysis of small volume samples, wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling. In embodiments, the Tempus Blood RNA system and process is modified for suitability and capability to provide for RNA isolation and RNA profiling and analysis of small volume samples, wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling.

[000108] The PAXgene protocol for Manual Purification of Total RNA from Human Whole Blood Collected into PAXgene Blood RNA Tubes is as follows (2015 Handbook):

[000109] Procedure

1. Centrifuge the PAXgene Blood RNA Tube for 10 minutes at 3000–5000 x g using a swing-out rotor.
2. Remove the supernatant by decanting or pipetting. Add 4 ml RNase-free water to the pellet, and close the tube using a fresh secondary BD Hemogard closure (supplied with the kit).
3. Vortex until the pellet is visibly dissolved, and centrifuge for 10 minutes at 3000–5000 x g using a swing-out rotor. Remove and discard the entire supernatant. Small debris remaining in the supernatant after vortexing but before centrifugation will not affect the procedure.
4. Add 350 µl Buffer BR1, and vortex until the pellet is visibly dissolved.
5. Pipet the sample into a 1.5 ml microcentrifuge tube. Add 300 µl Buffer BR2 and 40 µl proteinase K. Mix by vortexing for 5 seconds, and incubate for 10 minutes at 55°C using a shaker-incubator at 400–1400 rpm. After incubation, set the temperature of the shaker-incubator to 65°C (for step 20).
6. Pipet the lysate directly into a PAXgene Shredder spin column (lilac) placed in a 2 ml processing tube, and centrifuge for 3 minutes at maximum speed (but not to exceed 20,000 x g).
7. Carefully transfer the entire supernatant of the flow-through fraction to a fresh 1.5 ml microcentrifuge tube without disturbing the pellet in the processing tube.
8. Add 350 µl ethanol (96–100%, purity grade p.a.). Mix by vortexing, and centrifuge briefly (1–2 seconds at 500–1000 x g) to remove drops from the inside of the tube lid.
9. Pipet 700 µl sample into the PAXgene RNA spin column (red) placed in a 2 ml processing tube, and centrifuge for 1 minutes at 8000–20,000 x g. Place the spin column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.
10. Pipet the remaining sample into the PAXgene RNA spin column, and centrifuge for 1 minutes at 8000–20,000 x g. Place the spin column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.
11. Pipet 350 µl Buffer BR3 into the PAXgene RNA spin column. Centrifuge for 1 minute at 8000–20,000 x g. Place the spin column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.

12. Add 10 μ l DNase I stock solution to 70 μ l Buffer RDD in a 1.5 ml microcentrifuge tube. Mix by gently flicking the tube, and centrifuge briefly to collect residual liquid from the sides of the tube.
13. Pipet the DNase I incubation mix (80 μ l) directly onto the PAXgene RNA spin column membrane, and place on the benchtop (20–30°C) for 15 minutes.
14. Pipet 350 μ l Buffer BR3 into the PAXgene RNA spin column, and centrifuge for 1 minute at 8000–20,000 $\times g$. Place the spin column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.
15. Pipet 500 μ l Buffer BR4 into the PAXgene RNA spin column, and centrifuge for 1 minute at 8000–20,000 $\times g$. Place the spin column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.
16. Add another 500 μ l Buffer BR4 to the PAXgene RNA spin column. Centrifuge for 3 minutes at 8000–20,000 $\times g$.
17. Discard the processing tube containing the flow-through, and place the PAXgene RNA spin column in a new 2 ml processing tube. Centrifuge for 1 minute at 8000–20,000 $\times g$.
18. Discard the processing tube containing the flow-through. Place the PAXgene RNA spin column in a 1.5 ml microcentrifuge tube, and pipet 40 μ l Buffer BR5 directly onto the PAXgene RNA spin column membrane. Centrifuge for 1 minute at 8000–20,000 $\times g$ to elute the RNA.
19. Repeat the elution step (step 18) as described, using 40 μ l Buffer BR5 and the same microcentrifuge tube.
20. Incubate the eluate for 5 minutes at 65°C in the shaker-incubator (from step 5) without shaking. After incubation, chill immediately on ice.
21. If the RNA samples will not be used immediately, store at –20°C or –70°C.

[000110] The PAXgene Blood RNA system and method is specifically and particularly designed and applicable for blood sample volumes of about 2.5 mls, which is on the order of 10 fold larger volumes than the methods herein are processing. The PAXgene Blood RNA system and handbook provide a Troubleshooting Guide for issues with the system and notes that this troubleshooting guide may be helpful in solving any problems that may arise. With regard to Low RNA yield, the Troubleshooting Guide indicates: “Less than 2.5 ml blood collected in PAXgene Blood RNA Tube. Ensure that 2.5 ml blood is collected in the PAXgene Blood RNA Tube” (see *PAXgene Blood RNA Tube Product Circular*). The PAXgene blood RNA system is admittedly not designed for or successfully applicable to small volume samples.

[000111] A comparison of the PAXgene Blood RNA system procedure and RNA isolation method with the methods provided herein including in Example 1, will demonstrate that the volumes utilized, particularly including in each of steps are significantly reduced and are approximately 20- % of the volume indicated. Sample volumes of approximately 1/10th or 10% volume size of those recommended and best for the Paxgene system can be processed with approximately 25% volume size of the buffers and solutions to successfully provide RNA of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling through RNA sequencing.

[000112] In accordance with an embodiment of the method, in comparison with commercial RNA isolation kit volumes, such as particularly the PAXgene Blood RNA kit method and procedure outlines above, the volume of buffer (water) in step 2. is 1ml, which is 25% of the 4ml in the kit method. In accordance with an embodiment of the method, the volume of buffer in step 4. is 75 μ l, which is 21.4% of the 350 μ l in the kit method. In accordance with an embodiment of the method, the volume of buffer in step 5. is 65 μ l buffer and 9 μ l proteinase K, which is 21.7% of the 300 μ l and 22.5% of the 40 μ l in the

kit method. In accordance with an embodiment of the method, the volume of ethanol solution in step 8. is 75 μ l, which is 21.4% of the 350 μ l in the kit method. In accordance with an embodiment of the method, the volume of buffer in step 11. is 100 μ l, which is 28.5% of the 350 μ l in the kit method. In accordance with an embodiment of the method, the volume of buffer in step 14. is 100 μ l, which is 28.5% of the 350 μ l in the kit method. Volume adjustments of buffers and solutions in the present method range from about 21% to about 29% or overall about 25%.

[000113] Robison and colleagues previously reported a general assessment of transcript profiling from fingerstick blood samples (Robison EH et al (2009) BMC Genomics 10:617, doi:10.1186/1471-2164-10-617). Only RNA quality and broad correlations of gene expression data using genechip analysis comparing fingerstick samples with whole blood samples were reported. Robison followed the PAXgene Blood RNA kit (product# 762164) protocol for RNA isolation and purification, with the exception of one modification, wherein after the first spin, the pellet was washed with 1 mL RNase free water instead of 4 mL due to its small volume. Robison reported that they tested a scaled down version of the PAXgene protocol, but found that using the standard volumes of buffers and washes had no effect on the yields and were preferred as easier to employ. This is in sharp contrast to the studies and results reported and provided herein.

[000114] The methods herein may further comprise sequencing the RNA. RNA may be sequenced using any suitable or recognized method, steps, system(s) or kit(s), including manual, semi-automated or automated method(s), system(s) or kits. In some embodiments, kits such as Illumina TruSeq or Kapa Hyper Prep Kits are utilized.

[000115] As part of or commensurate with the methods herein, the isolated RNA may be converted to cDNA. Methods for generating cDNA from RNA are well known and available to one skilled in the art. Any applicable and effective method should be suitable. The isolated RNA may be converted to cDNA for probing or specific primer applications, such as to assess expression or for sequencing of specific RNAs or gene products. The isolated RNA may be converted to cDNA for cloning purposes, to be inserted or prepared in a vector, for introducing into or preparing a library therefrom.

[000116] As part of or commensurate with the methods herein, the isolated RNA may be amplified. In some embodiments, the RNA may be converted to cDNA and then amplified. Suitable methods and systems for amplification are known and available. For instance, methods, kits and systems for PCR amplification, including RT-PCR, wherein RNA is first reverse transcribed to cDNA and then amplified are well known and available. Amplification methods and approaches may be useful particularly in the instances of small volume samples and/or where small amounts of RNA are being isolated. Another amplification approach, which is also useful for small volume or small quantity RNA samples, is loop-mediated isothermal amplification (LAMP). Combining LAMP with a reverse transcription step allows detection and evaluation of RNA. LAMP is carried out at a constant temperature (60-65°C) and thus

does not require a thermal cycler. LAMP methods may utilize Bst (*Bacillus stearothermophilus*) DNA polymerase.

[000117] Abundant RNA species or RNA species not of interest may be removed prior to RNA sequencing. For example, globin mRNA, ribosomal RNA(s) and/or species specific RNAs may be removed prior to sequencing. In some instances, globin RNA and ribosomal RNAs are both removed. This serves to eliminate highly prevalent RNAs or known RNAs which are not of interest from the isolated RNAs. Eliminating highly prevalent or irrelevant globin RNA or rRNAs may facilitate analysis of RNAs which are of interest or which are less prevalent and present in smaller amounts. Methods, systems and kits for removal of globin RNA and/or ribosomal RNA are known and available to one skilled in the art. In some embodiments, systems or kits such as GlobinZero (Illumina), Ribo-Zero Gold, TruSeq Stranded total RNA library prep, Ribo-Zero Globin, GLOBINclear kit (Thermo Fisher Scientific), QIAseqFastSelect RNA removal kit (Qiagen) may be utilized. In some embodiments, species specific probes may be utilized to select out certain RNAs.

[000118] In embodiments or the method, the patient or individual has a disease or infection or is at risk of or suspected of disease or infection. The disease may be an acute or chronic disease. The disease may be a relapsing and/or remitting disease. The infection may be a bacterial or viral infection. The infection may be with a known or unknown virus or bacteria. A viral infection or virus may be an influenza virus, a coronavirus, an unidentified virus, an RNA virus. A bacteria may be a gram-positive bacteria. A bacteria may be a *Streptococcus* or *Staphylococcus* bacteria. A disease may be an inflammatory disease, an immune disease, an auto-immune disease, cancer.

[000119] In some embodiments, the method is for longitudinal screening by RNA profiling and analysis of small volume samples from one or more patient or individual, wherein the patient or individual has a disease or infection or is at risk of or suspected of disease or infection. In embodiments, small volume samples are collected in series or in regular or designated increments of hours, days, weeks or months. Small volume samples of a small volume blood sample, a sputum or saliva sample, or a nasal, nasopharyngeal or oropharyngeal swab, wash or aspirate may be collected. A combination of sample types or varying sample types may be collected. In embodiments, small volume blood samples are collected via fingerstick in series or in regular or designated increments of hours, days, weeks or months.

[000120] Samples may be collected in several hour increments, twice a day, three or four times a day, every 4-6 hours, daily, every morning, every evening, every morning and evening, once a week, one a month, every two months, every four months, every six months, several times a year. Samples may be collected to evaluate the effects of a drug or agent, for example prior to and/or following administration of a drug or agent. In some embodiments, small volume samples may be collected or additionally collected at onset of symptom(s), such as one or more symptom or recognized parameter indicative of or associated with a disease or infection. Samples may be collected prior to and after or upon the

recognition or development of one or more symptom or disease or infection parameter. Samples may be collected upon the development of a fever, cough, pain or discomfort, rash, etc.

[000121] Systems and kits for use and application of the methods are provided. A system or kit is provided for RNA profiling and analysis of small volume samples from a patient or individual comprising:

- (a) a means for self-collection of a small volume sample by the patient or individual or by a non-medical person, comprising a lancet, swab or receptacle for a wash, spit or aspirate;
- (b) a tube or receptacle for receiving the small volume sample on collection and containing a volume of RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized; and
- (c) one or more appropriate label(s) for designating the name or identity of the patient or individual, date of sample collection and time of sample collection.

[000122] In embodiments, the system or kit may further comprise an envelope or mailing container for shipment of the sample to a laboratory or facility for RNA isolation and analysis.

[000123] In an embodiment, with collection, the first drop of blood is removed, for example with a sterile gauze or cotton ball, so as to avoid tissue fluids that may produce inaccurate or less effective results. In an embodiment, the finger, heel etc, is cleansed with an alcohol or detergent solution, wipe or swab prior to collection, so as to remove any surface debris, loose cells or bacteria or dirt.

[000124] In some embodiments the lancet may be a small manual blade or may be a spring-loaded assembly or a self-contained disposable unit, such as wherein the blade is automatically retracted a holder after use. One such example is the Dynarex SensiLance pressure activated lancet.

[000125] In some embodiments, the system or kit may be for longitudinal RNA profiling and analysis of multiple small volume samples collected in series from a patient or individual over days, weeks or months comprising:

- (a) a set of numerous means for self-collection of individual small volume samples by the patient or individual or by a non-medical person, each comprising a lancet, swab or receptacle for a wash, spit or aspirate;
- (b) a set of numerous tubes or receptacles each individually for receiving a small volume sample on collection and containing a volume of RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized;
- (c) numerous appropriate label(s) for designating the name or identity of the patient or individual, date of sample collection and time of sample collection; and
- (d) numerous envelopes or mailing containers for shipment of each sample or several samples to a laboratory or facility for RNA isolation and analysis.

[000126] In some embodiments of the system or kit, the volume of RNA stabilization solution is less than 1ml, about 500µl or less, about 300µl or less, about 200-300µl, or about 250µl.

[000127] In some embodiments of the system or kit, the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, 1.2 ml or less, or 1ml or less.

[000128] In the specification, numerous specific details are set forth in order to provide a thorough understanding of the present embodiments. It will be apparent, however, to one having ordinary skill in the art that the specific detail need not be employed to practice the present embodiments. In other instances, well-known materials or methods have not been described in detail in order to avoid obscuring the present embodiments.

[000129] Throughout this specification, quantities are defined by ranges, and by lower and upper boundaries of ranges. Each lower boundary can be combined with each upper boundary to define a range. The lower and upper boundaries should each be taken as a separate element.

[000130] Additionally, any examples or illustrations given herein are not to be regarded in any way as restrictions on, limits to, or express definitions of any term or terms with which they are utilized. Instead, these examples or illustrations are to be regarded as being described with respect to one particular embodiment and as being illustrative only. Those of ordinary skill in the art will appreciate that any term or terms with which these examples or illustrations are utilized will encompass other embodiments which may or may not be given therewith or elsewhere in the specification and all such embodiments are intended to be included within the scope of that term or terms. Language designating such non-limiting examples and illustrations includes, but is not limited to: “for example,” “for instance,” “e.g.,” and “in one embodiment.”

[000131] In this specification, groups of various parameters containing multiple members are described. Within a group of parameters, each member may be combined with any one or more of the other members to make additional sub-groups. For example, if the members of a group are a, b, c, d, and e, additional sub-groups specifically contemplated include any one, two, three, or four of the members, e.g., a and c; a, d, and e; b, c, d, and e; etc.

[000132] The invention may be better understood by reference to the following non-limiting Examples, which are provided as exemplary of the invention. The following examples are presented in order to more fully illustrate the preferred embodiments of the invention and should in no way be construed, however, as limiting the broad scope of the invention.

EXAMPLE 1

Isolation and Analysis of RNA From Rheumatoid Arthritis Patient Finger Stick Blood Samples:

RNA-based Longitudinal Genomics Identifies Markers of RA Flares

[000133] Rheumatoid arthritis (RA), like many inflammatory diseases, is characterized by episodes of quiescence and exacerbation (flares). The molecular events leading to flares are unknown. We established a method, kit and system along with a clinical and technical protocol for isolation of RNA

via repeated home blood collection of small volume blood samples using self-performed finger stick sampling by RA patients. The system enabled and allowed for longitudinal RNA sequencing (RNAseq). Samples were obtained from 364 time points from eight flares over four years in our index patient, and 235 time points from flares in three additional patients. We developed a sampling method and RNA stabilization and isolation protocol providing high quality intact RNA. Assessments established that the RNAseq data from small volume blood finger stick samples correlated with blood cell counts from venipuncture blood draws. We identified transcripts that were differentially expressed antecedent to flares and compared these to synovial single cell RNAseq (scRNAseq). Flow cytometry and sorted blood cell RNAseq in additional RA patients were used to validate the findings.

[000134] Consistent changes were observed in blood transcriptional profiles one to two weeks antecedent to RA flare. B cell activation was followed by expansion of a previously unexplored circulating CD45-/CD31-/PDPN+, PRe-Inflammatory MEsenchymal ("PRIME") cell in RA patient blood, which shared features of inflammatory synovial fibroblasts. Circulating PRIME cells decreased during flares from all four patients, and flow cytometry and sorted cell RNAseq confirmed the presence of PRIME cells in 19 additional RA patients.

[000135] Longitudinal genomic analysis of RA flares reveals PRIME cells in RA blood, and suggests a model in which they become activated by B cells in the weeks prior to RA flare, and then migrate out of the blood to the synovium. These studies established that the collection system and RNA stabilization and isolation methods permits RNA sampling with valuable and consistent results. Among various applications for the system and methods, RNA profiling and longitudinal RNAseq analysis using the system and methods can reveal dynamic changes leading to flares of chronic inflammatory disease.

[000136] Introduction

[000137] Rheumatoid arthritis (RA) symptoms are highly dynamic, with stable periods interrupted by unpredictable flares of disease activity. Such waxing/waning clinical courses are characteristic of many autoimmune diseases, including multiple sclerosis (1), systemic lupus erythematosus (2), and inflammatory bowel disease (3,4), underscoring a need to develop approaches to understand what triggers transitions from quiescence to flare in autoimmune disease.

[000138] This study explores disease pathophysiology with a longitudinal, prospective analysis of blood transcriptional profiles in individual RA patients over time utilizing small volume blood sampling via patient at home finger stick collection. Previous microarray studies of RA blood samples from relatively sparse time series data have identified few significant gene changes associated with disease activity (5-8). Here we provide the first RA study to look for molecular changes in blood that anticipate clinical flares. To do so we developed and optimized methods by which RA patients themselves could collect high quality finger stick blood samples for RNA sequencing (RNAseq), facilitating weekly blood sampling for months to years.

[000139] We analyzed patient reports of clinical disease activity and RNAseq data from four patients across multiple clinical flares. In our most deeply studied index case, we assessed 364 time points by RAPID3 from eight flares over four years, and analyzed 84 time points assessed by RNAseq. Collecting samples longitudinally enabled a search for transcriptional signatures that preceded clinical symptoms. Comparing these blood RNA profiles to synovial single cell RNAseq (scRNAseq) data (9) provided evidence that a biologically coherent set of transcripts are significantly increased in the blood prior to symptom onset, and a subset of these decrease as the patients begin to experience symptoms. These latter transcripts overlap with and likely demarcate cellular precursors to a novel subset of synovial sublining fibroblast cell types detected in inflamed RA synovium using scRNAseq. Analysis in 19 additional RA patients corroborated our findings. Our data suggests a model in which a previously unexplored circulating mesenchymal cell type, detectable in the weeks prior to RA flare, becomes activated by B cells and subsequently leaves the blood, traffics to synovium, and contributes to disease activity. These studies were facilitated by the ability to isolate and analyze high quality RNA which validly represented changes *in vivo* from patient self-collected small volume blood samples (finger stick).

[000140] METHODS

[000141] Patient data

[000142] All patients met American College of Rheumatology/European League Against Rheumatism 2010 (10,11) criteria for RA and were seropositive for cyclized citrullinated protein antibody (CCP). Disease activity was assessed from home each week, or up to 4 times daily during escalation of flares, using the routine assessment of patient index data 3 (RAPID3) questionnaire (12). Disease activity was also assessed at clinic visits, each month, and during flares, using both the RAPID3 and the disease activity score 28 (DAS28), which incorporates tenderness and swelling from 28 joints, erythrocyte sedimentation rate (ESR) and patient global assessment of disease activity. Complete blood counts (CBC) including white blood cells (WBC), neutrophils, monocytes, lymphocytes, and platelets were performed by the clinical lab at Memorial Sloan Kettering Cancer Center. We collected 43 clinic visits from the index patient, and 25, 14 and 12 clinic visits for the other three patients studied longitudinally. Nineteen additional seropositive RA patients and 18 age and sex matched non-RA patients, for whom peripheral blood mononuclear cells (PBMC) were available, were also studied for the presence of PRIME cells by FACS and RNAseq analysis.

[000143] RNA preparation from Finger Stick blood

[000144] Patients self-performed finger sticks at home to collect three drops of blood into a microtainer tube prefilled with fixative (RNA stabilization solution), and samples were mailed overnight each week. RNA was extracted using the PAXgene RNA kit and purified per manufacturer's protocols, except the volume of all washes and elutions was decreased to about 25% of the recommended volume by the manufacturer. RNA was assessed using the Agilent BioAnalyzer for

quantity and quality. For library preparation, we used the GlobinZero kit (EpiCentre #GZG1224) and Illumina's Truseq mRNA Stranded Library kit, with 11-12 PCR cycles for 5-8nM input and sequenced on HiSeq2500 with 150 base paired-end reads. Reads were aligned to Gencodev18 using STAR and quantified using featureCounts (v1.5.0-p2). Samples with at least four million paired-end reads were retained for analysis.

[000145] A detailed protocol is provided below:

Procedure (SOP) Finger Stick Sample Processing

Should receive a box with patient questionnaire and finger stick sample

Place ice pack in cardboard box lined with chuck to thaw and dry

Make notes in Sample Log:

- Date of sample acquisition (date of finger stick)- Date on questionnaire
- Today's date
- Study Week # (if it's not clear from previous week, calculate back from Week 0 on top of sample log page)

Finger Stick Sample

- Three drops of blood are received in microtainer tube that was prefilled with 0.250 ml (250µl) PAX-gene blood solution.
- Write the date (of the finger stick) on a finger stick label
- Transfer to -20°C for 24 hours. Store upright in metal rack.
- Transfer to -80°C for long term storage in patient's sample box in -80° C with the week # written on top of the tube.

(adapted from PAXgene RNA handbook version 2, June 2015)

Before starting

Set temperature of shaker incubator to 55°C

Warm Buffer BR2 (Binding Buffer) to 37°C if there are precipitates (Binding Buffer contains a guanidine salt (guanidine thiocyanate) which can form highly reactive compounds when combined with bleach)

Prepare Buffer BR4 (Wash Buffer) by adding 4 volumes of 100% ethanol to obtain working solution

Prepare DNase I stock by dissolving solid DNase I (1500 Kunitz units; Qiagen, cat# 79254) in 550ul of RNase free water and mix by inversion (1500 Kuntz Units/0.55ml). Do not vortex, DNase is sensitive to physical denaturation.

1. Remove PAXgene Blood RNA microtainer tube from freezer and allow to warm to room temperature (+/-1 hr)
2. Place PAX blood in 2ml microfuge tube and centrifuge at 5000 xg at room temperature for 10 minutes
3. Remove and discard supernatant. Add 1ml RNase-free water (from PAXgene kit) to wash the pellet.
4. Vortex to resuspend the pellet, then centrifuge for 10 minutes at 5000 xg in a centrifuge. Remove and discard the supernatant.
5. Thoroughly resuspend the pellet in 75ul of Buffer BR1 (from PAXgene kit) (Resuspension Buffer) by vortexing
6. Add 65ul Buffer BR2 (from PAXgene kit) and 9ul Proteinase K solution (from PAXgene kit).
7. Mix by vortexing and incubate for 10 minutes at 55°C in shaking heat block (800 rpm).
8. Pipet lysate to lavender top PAXgene shredder spin column (which removes clumps) and spin for 3 minutes at 18,000 xg.
9. Transfer supernatant of flow through (about 150ul) ** be careful with this step since pellet is gooey and easily disrupted** to a new 1.5ml microcentrifuge tube.

10. Add 75ul of 100% ethanol. Mix by vortexing and centrifuge at 1000 xg for 2 seconds to remove drops from inside the tube of lid. Do not centrifuge for longer than this or nucleic acids may pellet and reduce the RNA yield.
11. Apply 225ul of sample to red top PAXgene RNA spin column sitting in a 2ml processing tube (from PAXgene kit). Centrifuge at 8000 xg for 1 minute. Place the PAXgene column in a new 2ml processing tube and discard the old processing tube containing the flow through.
12. Pipet 100ul Buffer BR3 (Wash Buffer) to the PAXgene column and centrifuge at 8000 xg for 1 minute. Place the PAXgene column in a new 2ml processing tube and discard the old processing tube containing flow through.
13. Pipet 5ul DNAase I stock solution into 35ul of Buffer RDD. Mix by gently flicking the tube (do not vortex) and centrifuge briefly.
14. Pipet DNAase I incubation mix (40ul) directly onto PAXgene column and place upright at room temperature for 15 minutes.
15. Pipet 100ul Buffer BR3 to the PAXgene column and centrifuge at 8000 xg for 1 minute. Place the PAXgene column in a new 2ml processing tube and discard the old processing tube containing flow through.
16. Apply 200ul Buffer BR4 (Wash Buffer) to the PAXgene column and centrifuge for 1 minute at 8000 xg. Place the PAXgene column in a new 2ml processing tube and discard the old processing tube containing flow through. Note that the Buffer BR4 is supplied as a concentrate. Ensure that the ethanol is added to Buffer BR4 prior to use.
17. Add another 200ul Buffer BR4 to the PAXgene column. Centrifuge for 3 minutes at 18000 xg (max speed) to dry the PAXgene column membrane.
18. To eliminate residual Buffer BR4, discard the tube containing the flow through, place the PAXgene column in a 2ml processing tube and centrifuge for 1 minute at full speed.
19. Discard the tube containing the flow through and transfer the PAXgene column to a 1.5ml elution tube (from PAXgene kit). Pipet 30ul Buffer BR5 directly on to the PAXgene column membrane (without touching the membrane with the pipet tip) and centrifuge for 2 minutes at 13000 xg.
20. Repeat the elution step as described, using the previously eluted 30ul of RNA in Buffer BR5 (Elution Buffer). 2ul for Pico Bioanalyzer and 26ul for GlobinZero
21. Label and store sample at -80°C until RNA analysis.

[000146] Data analysis:

[000147] Differential expression analyses across patients

Samples were labeled "baseline" (stable RAPID3), "flare" (RAPID3 scores rose over two standard deviations above the baseline mean), or "steroid". EdgeR (v3.24.3) (13) was used to analyze flare vs baseline differential gene expression. Permutation test ($n=1 \times 10^6$) was used to test for the significance of overlap between genes decreased in flares in the index patient and patients 2, 3, and 4. GO enrichment (goana, from limma v3.38.3) (14) was used to identify enriched pathways in significantly differentially expressed genes in the index patient ($FDR < 0.1$) and consistent in the direction of expression in both the index and replication patients (i.e., log fold change either both positive or both negative).

[000148] Time series analysis of index patient

[000149] We performed longitudinal data analysis on the index patient using ImpulseDE2 (v1.8.0) (15). Flare onset was defined clinically (as above) and samples from 8 weeks prior to flare up to 4 weeks after flare were analyzed (excluding any samples during which the patient was taking steroids, $n=65$ samples). The date of library preparation was included in the model for batch correction, and the genefilter (v1.64.0) package (16) was used to filter out lowly expressed genes. We hierarchically

clustered mean expression of significantly differentially expressed genes by week to flare initiation (batch corrected logrpkm expression values were calculated using edgeR) and identified five coexpressed gene modules (Clusters 1-5). We analyzed these five modules for GO term enrichment (goana).

[000150] To compare differentially expressed gene modules over time, the mean expression level for each gene was calculated across flares per week, then normalized across weeks. ABIS (17) and CIBERSORTx (18) were used to deconvolute gene expression data. To aggregate a given cluster of genes or cell type with gene markers, the mean of standardized gene expression scores or deconvolved cell type scores, respectively, within each week were plotted. To identify synovial scRNAseq cluster specific marker gene signatures, we used a previously published dataset (18) to compare the cells from one scRNAseq cluster with cells from all the other scRNAseq clusters using the single-cell RNA-seq log2(CPM + 1) matrix. We generated lists of the top 200 marker genes for each cluster using the criteria of 1) log2FC greater than 1, 2) auc greater than 0.6, and 3) percent of expressing cells greater than 0.4. We used Fisher's exact test to evaluate enrichment of synovial cell subtype marker genes in the 5 coexpressed gene modules.

[000151] Flow cytometry and sorting

[000152] Samples from PBMC were stained with antibodies to: CD31-APC, (WM59), Mouse IgG1-APC, (MOPC-21), PDPN-PerCP, (NZ1.3), Rat IgG2a, (eBR2a), CD45-PE, (HI30), Mouse IgG1-PE, (MOPC-21), TO-PRO®-3, and DAPI (4',6-Diamidino-2-Phenylindole, Dihydrochloride). Cells were sorted on a BD FACS Aria II for RNAseq. cDNA libraries were sequenced on MiSeq. DESeq2 (v1.24.0) (19) was used for differential expression analysis.

[000153] Statistics

[000154] R2 and Pearson correlation coefficients were calculated to assess the bivariate linear fit of disease activity measured by RAPID3 and DAS28 as well as CBC counts inferred from CIBERSORT cell counts and counts measured by clinical labs. Inferred CIBERSORTx lymphocyte counts were the sum of B cells naive + B cells memory + T cells CD8 + T cells CD4 naive + T cells CD4 memory resting + T cells CD4 memory activated. One way ANOVA was used to test for significant differences among various clinical features according to disease activity state. Monocytes, Macrophages M0, Macrophages M1, and Macrophages M2 were summed to infer CIBERSORTx monocytes.

[000155] RESULTS

[000156] Clinical Protocol Development

[000157] Four RA patients were followed for one to four years with weekly home collection of finger stick blood samples coupled with completion of RAPID3 and monthly clinic visits, where DAS28 were collected (Figure 1A). Study patients also documented disease activity (RAPID3 questionnaires). We developed strategies for home blood collection that would allow high quality and quantity RNA for

sequencing (Figures 2-8), which provided 15-50 ng RNA from finger stick blood samples and RNA integrity (RIN) scores (mean 6.9 +/- standard deviation 1.7).

RNA was sequenced from a total of 189 finger stick blood samples from 4 patients, of which 162 (87%) passed quality control filtering.

[000158] We first assessed RNA quality and quantity by volume of fixative. 3 drops of blood were harvested with a 21 guage lancet and added to a microtainer tube prefilled with either 250µl, 500µl or 750µl of PAX gene fixative. Samples were stored at room temperature for 3 days and then RNA was extracted using the PAX gene RNA kit and RIN scores and quantity of RNA was assessed using the Agilent 2100 Bioanalyzer picochip. RIN indicates the RNA integrity number which is an algorithm for assessing integrity values to RNA. The integrity of RNA is of significant importance for gene expression studies. RIN can and was traditionally evaluated using the 28S (~5070 nucleotides) to 18S (~1869 nucleotides) RNA ratio, which gives a ratio of about 2.7. A high 28S to 18S ratio is an indication that the purified RNA is intact and hasn't been degraded. RIN can easily be determined using Agilent 2100 Bioanalyzer measurements (Schroeder A et al (2006) BMC Mol Biol 7:3 (doi:10.1186/1471-2199-7-3). RNA samples should score RIN of >7 on a scale of 1 (highly degraded) to 10 (highest integrity). The results are depicted in Figure 2. Acceptable RIN scores are seen with 250µl, 500µl or 750µl of PAX-gene fixative (left panel of Figure 2). Notably, the 250µl fixative results in the highest ng RNA yield per sample. Using higher volumes of fixative, either 500µl or 750µl of fixative, the ng RNA yields were significantly reduced compared with 250µl fixative (right panel of Figure 2).

[000159] RNA integrity/quality and RNA quantity was evaluated from samples of 100µl of blood in 250µl PAX gene fixative with varying times of storage at room temperature (Figure 3). 100ul of whole blood was added to a microtainer tube prefilled with 250ul PAX gene fixative and frozen after 2 hours, 3 days, or 7 days incubation at room temperature. RNA was extracted with scaled down washes and elutions using the protocol described above and RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzer RNA picochip. RNA quality and quantity is reasonably retained with room temperature storage for up to 3 days.

[000160] RNA quality and quantity were evaluated in fresh and mailed samples (Figure 4). 100µl of whole blood was added to a microtainer tube prefilled with 250µl PAX gene fixative and frozen after 2-hour incubation at room temperature or mailed. RNA was extracted as above described and RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzer RNA picochip. RIN and quantity of RNA was well maintained with mailing of samples.

[000161] RNA quality and quantity were evaluated by volume of extraction and washes (Figure 5). 3 drops of blood harvested with a 21 guage lancet were added to a microtainer tube prefilled with 250µl of PAX gene fixative. Samples were stored at room temperature for 3 days and then RNA was extracted using the PAXgeneRNA kit according to manufacturer's directions or with a scaled down version of the PAX protocol, using significantly reduced volumes (about 25% of the recommended volumes) for

all washes and elutions. RIN scores and quantity of RNA was assessed using the Agilent 2100 BioAnalyzerRNA picochip. The RIN score was well maintained in the low volume protocol. Quantity of RNA isolated, however, was significantly improved with the low volume protocol. This demonstrates that a reduced volume protocol was necessary to isolate a reasonable quantity of RNA from small blood volume samples, such as several drops of blood in line with a fingerstick type sample size of blood.

[000162] RNA quality and quantity were evaluated from finger stick blood samples with RNA isolated using the PAXgeneRNA extraction versus a TriZol-based method. Mailed patient finger stick samples were stored in PAXgeneRNA buffer at -80°C. 142 samples had RNA extracted with PAXgeneRNA extraction with low volume washes, while 13 samples were thawed and mixed with 700µl Trizol-LS and 250µl chloroform. After centrifugation, the top layer was precipitated with isopropanol and glycogen and washed with 80% cold ethanol, centrifuged and the pellet was dried, resuspended in PBS and then purified using the Roche High Pure Isolation kit. RNA integrity and quality were both significantly reduced using Trizol and chloroform extraction versus the PAXgene RNA system. The Trizol reagent system utilizes guanidinium thiocyanate and phenol, and an organic extraction via phenol/chloroform.

[000163] Since ribosomal and hemoglobin RNA represent approximately 98% and 70% of the RNA in whole blood, respectively, we tested standard commercial kits for removing these RNAs prior to RNAseq. The PAXgene system does not remove globin mRNA, which can constitute up to 70% of the mRNA mass in whole blood total RNA. GlobinZero (Illumina) method and kit was utilized to remove globin mRNA from the samples. 4ml heparinized blood was treated with 1ug/ml LPS for one hour at 37°C and 250ul blood was placed into 250µl PAXgene fixative in replicate microtainer tubes. After RNA extraction, samples were either treated with the globin zero depletion kit (globin and ribosomal depleted) or undepleted and then quantitative PCR was performed to test for hemoglobin A2, 18S RNA, or TNF alpha mRNA expression. Figure 7 depicts Cycle Times for HbgA2, 18S RNA, and TNF alpha after GlobinZero depletion. GlobinZero kits depleted both hemoglobin A2 and 18S ribosomal RNA (increased mean cycle time from 11 to 28 and 10 to 30, respectively) with relative preservation of TNFalpha mRNA.

RNASeq QC metrics were assessed on RNA prepared with Illumina TruSeq or Kapa Hyper Prep Kits and having various RIN scores ranging from <5.7 to 8.1-10 (Figure 8). Distribution of mapping, uniquely mapping, and duplicate reads was plotted for the TruSeq and Kapa Hyper Prep RNAs with various RIN scores. Distribution of tags assigned to UTR (untranslated region), intergenic, intronic, and CDS (coding sequence) of whole blood RNA samples prepared with Illumina TruSeq or Kapa Hyper Prep Kits with various input RNA quality and quantity was determined. The Illumina TruSeq library Prep demonstrated increased mapping to coding sequence and fewer intergenic reads and was ultimately used for downstream experiments.

[000164] To assess the validity of patient reported disease activity, we compared their RAPID3 scores with clinician collected DAS28. Significant correlations were evident between RAPID3 and DAS28 for each of the four patients (Figure 1B). To assess the validity of fingerstick blood data, we compared RNAseq inferred white blood cell counts with clinical laboratory measurements of complete blood counts and again observed significant correlations (Figure 1C). Taken together, these data indicate that patient reports of disease activity paired with fingerstick blood samples provide a high quality and robust means by which individuals can participate in longitudinal clinical research studies.

[000165] Clinical and Molecular Features of RA Flare Compared to Baseline

[000166] Flares were associated with increases in objective clinical and laboratory measures of RA related disease activity in the index patient (Figure 9A). Fingerstick RNAseq identified 2613 genes differentially expressed at flare versus baseline ($FDR < 0.1$), with 1437 increased during flare ($\log FC > 0$; Figure 9B). Pathway analysis identified enrichment in myeloid, neutrophil, Fc receptor signaling and platelet activation (Figure 9C), consistent with clinical CBC measurements during flares. Interestingly, 1176 genes were significantly decreased during flare, and pathway analysis of these genes were enriched for extracellular matrix, collagen and connective tissue development (Figure 9D).

[000167] Time Series Analysis of Molecular Events Leading to RA Flares

[000168] To analyze the trajectories of gene expression over time and identify potential antecedents to flare, we performed time series analysis of the RNAseq data (Figure 10A). Notably, disease activity scores in the weeks just prior to flare were the same as baseline scores two months prior to flare, underscoring the challenges of identifying both a time frame and gene expression signature that is antecedent to flare. We focused the analysis on 65 samples acquired 8 weeks prior to flare and 4 weeks after flare initiation, binning samples according to the week they were drawn. This identified 2791 genes with significant differential expression over time to flare ($FDR < 0.05$), and hierarchical clustering of gene expression identified five clusters (Figure 10B). Cluster 1 represented a group of genes which increased after symptom onset (Figure 10C and 10D) and was highly overlapping (Figure 10E) with genes increased in the flare versus baseline analysis (Figure 9B). These gene expression clusters were reproducibly altered in 5 separate clinical flare events (Figure 12).

[000169] We further focused on two clusters that were differentially expressed antecedent to flare (Figure 10C-10D). Antecedent cluster 2 (AC2) (Table 2) transcripts increased two weeks prior to flare and were enriched with developmental pathways for naive B cells and leukocytes. Two additional means of deconvoluting the RNAseq data, CIBERSORTx and ABIS, independently confirmed evidence of B cell and T cell populations antecedent to flare, and all analyses showed evidence of innate inflammatory signatures (neutrophils and monocytes) during flare (data not shown).

[000170] Antecedent cluster 3 (AC3) (Table 3) transcripts increased the week prior to flare and then decreased for the duration of flare (Figure 10C and 10D). AC3 was enriched for pathways not typical

of blood samples, including cartilage morphogenesis, endochondral bone growth, and extracellular matrix organization (Figure 10E), suggesting the presence of an uncharacterized cell type.

[000171] Time Series Analysis of Synovial Cell Marker Genes in RA Flares

[000172] To better characterize the relevance of the clusters identified by the time series analysis to synovitis (Figure 10C), we examined them for enrichment in synovial cell subtypes characterized by scRNAseq. This analysis of 5265 single RA and osteoarthritis patient synovial cells identified four fibroblast, four B cell, six T cell, and four monocyte subpopulations (Figure 11A). We identified approximately 200 marker genes that best distinguished each of 18 synovial cell types. AC2 was enriched with naive B cell genes (Figure 11A), and AC3 was enriched with three sublining fibroblast genes (CD34+, HLA-DR+, and DKK3+) (Figure 11A). Two of these fibroblast subsets, CD34+ and HLA-DR+, are more abundant in inflamed synovium (20). We plotted expression of those transcripts that were common to both synovial sublining fibroblasts and AC3 over time and again noted their increased expression in blood one week prior to flare and decreased expression during flare (Figure 11B and Table 1).

[000173] Overall, 622 of 625 AC3 genes decreased during flare in patient 1, and a subset (194 genes) also decreased in flares from at least 3 out of 4 RA patients (and 22 genes in 4 out of 4 patients; Figure 11C), and permutation test indicated this overlap was greater than expected by chance ($p=0.0001$). Pathway analysis of the subset of 194 overlapping genes was again enriched for extracellular matrix and secreted glycoprotein.

[000174] We further tested whether cells that expressed surface markers of synovial fibroblasts were detectable in RA blood by flow cytometry. CD45-/CD31-/PDPN+ cells were increased in 19 additional RA patient blood relative to healthy controls (Figure 11D). RNAseq of these cells confirmed they were enriched with AC3 cluster genes (Figure 11E), synovial fibroblast genes (Figure 13), and expressed classic synovial fibroblast genes such as FAP, DKK3, CDH11, as well as collagens and laminins (Figure 14). Given their expression of classical mesenchymal surface markers and genes, we refer to these as PRe-Inflammatory Mesenchymal Cells (PRIME cells). Taken together, our observations suggest a model in which sequential activation of B cells activate PRIME cells just prior to flares, which are then evident at flare in inflamed synovium as inflammatory sublining fibroblasts.

[000175] The referenced TABLE 1 is provided below:

TABLE 1
GENES COMMON TO SYNOVIAL SUBLINING FIBROBLASTS AND AC3

cluster	geneset	Ensemble	symbol	auc	pct_nonzero	pct_nonzero_other
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000187955	COL14A1	0.88699058	0.98347107	0.30535427
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000164692	COL1A2	0.84468179	1	0.53280998
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000168542	COL3A1	0.82353841	1	0.53301127
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000130635	COL5A1	0.76918996	0.80991736	0.26348631
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000105664	COMP	0.72267741	0.5268595	0.09178744
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000133083	DCLK1	0.78673115	0.70041322	0.16807568
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000146648	EGFR	0.76375622	0.72933884	0.23007246
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000120738	EGR1	0.75381699	0.95041322	0.6507649
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000164694	FNDC1	0.7526103	0.63842975	0.15116747
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000131386	GALNT15	0.7329481	0.59297521	0.14351852
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000168079	SCARA5	0.74916074	0.78512397	0.28965378
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000137573	SULF1	0.73367922	0.67561983	0.23389694
SC-F1	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000091656	ZFHX4	0.77838039	0.71487603	0.2071256
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000187955	COL14A1	0.91760718	0.99165508	0.27044158
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000084636	COL16A1	0.87323477	0.83588317	0.10585252
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000164692	COL1A2	0.92139483	1	0.50961335
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000168542	COL3A1	0.93074592	1	0.50982464
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000134871	COL4A2	0.84125266	0.86648122	0.18761885
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000130635	COL5A1	0.88489277	0.95132128	0.21487429
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000133083	DCLK1	0.83131283	0.79972184	0.12655821
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000146648	EGFR	0.80327353	0.82058414	0.19142193
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000120738	EGR1	0.80507545	0.9930459	0.62941052
SC-F2	Fibroblast-CD34+ sublining (SC-F1)	ENSG00000130508	PXDN	0.84330642	0.83171071	0.16670188
SC-F2	Fibroblast-HLA-DRAhi sublining (SC-F2)	ENSG00000166444	ST5	0.83349089	0.81641168	0.15867315
SC-F3	Fibroblast-CD34+ sublining (SC-F2)	ENSG00000187955	COL14A1	0.85231287	0.96929825	0.33920368
SC-F3	Fibroblast-CD34+ sublining (SC-F2)	ENSG00000164692	COL1A2	0.90670253	1	0.55570444

SC-F3	Fibroblast-HLA-DRAhi	ENSG000000168542	COL3A1	0.90184724	1	0.55589587
SC-F3	sublining (SC-F2)	ENSG000000130635	COL5A1	0.91728082	0.98245614	0.28273354
SC-F3	Fibroblast-HLA-DRAhi	ENSG000000105664	COMP	0.81905082	0.71929825	0.10470904
SC-F3	sublining (SC-F2)	ENSG000000164694	FNDC1	0.8072182	0.76315789	0.16960184
SC-F3	Fibroblast-HLA-DRAhi	ENSG000000131386	GALNT15	0.81963055	0.76754386	0.15792496
SC-F3	sublining (SC-F2)	ENSG000000164294	GPX8	0.80951068	0.8245614	0.22396631
SC-F3	Fibroblast-HLA-DRAhi	ENSG000000167779	IGFBP6	0.83772643	0.78947368	0.16807044
SC-F3	sublining (SC-F2)	ENSG000000130508	PXDN	0.83692715	0.88157895	0.2270291
SC-F3	Fibroblast-HLA-DRAhi	ENSG000000168079	SCARA5	0.81990132	0.89035088	0.3093415
SC-F3	sublining (SC-F2)	ENSG000000137573	SULF1	0.83014503	0.86403509	0.24732006
SC-F3	Fibroblast-HLA-DRAhi	ENSG000000091656	ZFXH4	0.78976712	0.80263158	0.22817764
SC-F3	sublining (SC-F2)					
SC-F3	Fibroblast-HLA-DRAhi					
SC-F3	sublining (SC-F2)					
SC-F3	Fibroblast-HLA-DRAhi					
SC-F3	sublining (SC-F2)					
SC-F3	Fibroblast-HLA-DRAhi					
SC-F3	sublining (SC-F2)					
SC-F3	Fibroblast-DKK3+ sublining					
SC-F3	(SC-F3)					
SC-F3	Fibroblast-DKK3+ sublining					
SC-F3	(SC-F3)					
SC-F3	Fibroblast-DKK3+ sublining					
SC-F3	(SC-F3)					
SC-F3	Fibroblast-DKK3+ sublining					
SC-F3	(SC-F3)					
SC-F3	Fibroblast-DKK3+ sublining					
SC-F3	(SC-F3)					

	Fibroblast-DKK3+ sublining (SC-F3)								
	Fibroblast-DKK3+ sublining (SC-F3)								
	Fibroblast-DKK3+ sublining (SC-F3)								
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	Fibroblast-DKK3+ sublining (SC-F3)								
	Fibroblast-DKK3+ sublining (SC-F3)								
	Fibroblast-DKK3+ sublining (SC-F3)								

[000176] DISCUSSION

[000177] We present longitudinal genomics as a strategy to study the antecedents to RA flare that may be generalizable to autoimmune diseases associated with waxing/waning clinical courses. We developed easy-to-use tools for patients to acquire both quantifiable clinical symptoms and molecular data at home over many years. This allowed us to capture data prior to the onset of clinical flares and retrospectively analyze it, identifying different RNA signatures (AC2 (Table 2) and AC3 (Table 3) evident in peripheral blood 1-2 weeks prior to flare.

[000178] The RNA signature of AC3 and sorted CD45-/CD31-/PDPN+ circulating cells revealed enrichment for pathways including cartilage morphogenesis, endochondral bone growth, and extracellular matrix organization (Figure 10E) and strongly overlapped with synovial sublining fibroblasts. We therefore propose antecedent PRIME cells are the precursors to inflammatory sublining fibroblasts previously found adjacent to blood vessels in inflamed RA synovium (21).

[000179] Significantly, inflamed sublining fibroblasts are pathogenic in an animal model of arthritis (22). Our discovery that human AC3 genes share molecular characteristics of sublining fibroblasts, together with the observation that these cells spike prior to flare but are less detectable in blood during flare (Figure 9 and 10) support a model in which PRIME cells immigrate acutely from blood to the synovium where they contribute to the inflammatory process. This model is consistent with the observation that RA synovial fibroblasts can traffic to cartilage implants and are sufficient to passively transfer synovial inflammation in mice (23). Together our data suggest the mesenchymal signal detected in AC3 prior to flares represent a previously uncharacterized type of trafficking fibroblast that circulates in blood.

[000180] In addition, we observed a second RNA signature, AC2, activated in blood prior to the spike in AC3. AC2 bear RNA hallmarks of naive B cells. This finding is reminiscent of recent studies demonstrating autoreactive naive B cells are specifically activated in RA patients (24). While the triggers of these are unknown, infectious (for example bacterial or viral antigens), environmental or endogenous toxins (25-27) could provide a source of either specific antigens or activate pattern recognition receptors.

[000181] In conclusion, we demonstrate methods for densely collecting longitudinal clinical and gene expression data that can be used to discover changes in transcriptional profiles in the blood weeks prior to symptom onset. The methods include means and procedures for stabilizing, isolating and analyzing RNA from small volume samples which can be collected by a patient or individual themselves such as by finger stick collection, without the need for medical personnel, and which are applicable to home or field collection, to patients which are compromised or otherwise wherein collection of blood by venipuncture is not reasonable or available, and wherein there is a need for rapid sampling or for periodic sampling over time. This approach led to the identification and characterization of RNA markers and indicators of disease or pathological conditions and also the discovery of PRIME cells,

bearing hallmarks of synovial fibroblasts, which are more common in RA patients and increase in blood just prior to flares. In modeling all our data, we suggest that prior to clinical flare, systemic B cell immune activation (detected as AC2) acts on PRIME cells, which traffic to the blood (detected as AC3) and subsequently to the synovial sublining during flares of disease activity.

[000182] More generally, application of an efficient self-collection protocol and approach combined with quantitative and qualitative RNA isolation to work in RA and RA patient sampling demonstrates the effectiveness and usefulness of our system. This initial study provides an exemplar of an approach to isolating, evaluating and assessing markers and RNA or protein expression changes and cellular changes which are applicable to disease assessment and evaluation, including in waxing/waning inflammatory disease, suggesting a general strategy relevant to numerous diseases and conditions, including additional disorders such as lupus, multiple sclerosis, and vasculitis.

TABLE 2
AC2 GENES

<u>Ensembl</u>	<u>Symbol</u>	<u>Description</u>	<u>Score?/AUC?</u>
ENSG00000204632	HLA-G	"major histocompatibility complex, class I, G [Source:HGNC Symbol;Acc:HGNC:4964]"	5.77E-05
ENSG00000184792	OSBP2	oxysterol binding protein 2 [Source:HGNC Symbol;Acc:HGNC:8504]	6.39E-05
ENSG00000198892	SHISA4	shisa family member 4 [Source:HGNC Symbol;Acc:HGNC:27139]	0.00012762
ENSG00000187017	ESPN	espin [Source:HGNC Symbol;Acc:HGNC:13281]	0.000131036
ENSG00000233762	MARCKSL1	MARCKS like 1	0.000323289
ENSG00000175130		[Source:HGNC Symbol;Acc:HGNC:7142]	0.000358619
ENSG00000125534	PPDPF	pancreatic progenitor cell differentiation and proliferation factor [Source:HGNC Symbol;Acc:HGNC:16142]	0.00037025
ENSG00000158856	DMTN	dematin actin binding protein [Source:HGNC Symbol;Acc:HGNC:3382]	0.000376535
ENSG00000121413	ZSCAN18	zinc finger and SCAN domain containing 18 [Source:HGNC Symbol;Acc:HGNC:21037]	0.000443873
ENSG00000230715	RPL13P12	ribosomal protein L13 pseudogene 12	0.000528797
ENSG00000215030		[Source:HGNC Symbol;Acc:HGNC:35701]	0.000588454
ENSG00000146540	C7orf50	chromosome 7 open reading frame 50 [Source:HGNC Symbol;Acc:HGNC:22421]	0.000639272
ENSG00000029534	ANK1	ankyrin 1 [Source:HGNC Symbol;Acc:HGNC:492]	0.000697583
ENSG00000121104	FAM117A	family with sequence similarity 117 member A [Source:HGNC Symbol;Acc:HGNC:24179]	0.000697583
ENSG00000260231	JHDM1D-AS1	JHDM1D antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HGNC:48959]	0.00070319
ENSG00000211895	IGHA1	immunoglobulin heavy constant alpha 1 [Source:HGNC Symbol;Acc:HGNC:5478]	0.000707226
ENSG00000173581	CCDC106	coiled-coil domain containing 106 [Source:HGNC Symbol;Acc:HGNC:30181]	0.000730947
ENSG00000008441	NFIX	nuclear factor I X [Source:HGNC Symbol;Acc:HGNC:7788]	0.000837162
ENSG00000105701	FKBP8	FK506 binding protein 8 [Source:HGNC Symbol;Acc:HGNC:3724]	0.000994972
ENSG00000079308	TNS1	tensin 1 [Source:HGNC Symbol;Acc:HGNC:11973]	0.00113151
ENSG00000264063	MIR3687-2	microRNA 3687-2 [Source:HGNC Symbol;Acc:HGNC:50835]	0.001218296
ENSG00000049089	COL9A2	collagen type IX alpha 2 chain	

ENSG00000126461	SCAF1	[Source:HGNC Symbol;Acc:HGNC:2218] SR-related CTD associated factor 1	0.001236713
ENSG00000243679		[Source:HGNC Symbol;Acc:HGNC:30403]	0.00126185
ENSG00000169136	ATF5	activating transcription factor 5	0.001292673
ENSG00000181588	MEX3D	[Source:HGNC Symbol;Acc:HGNC:790] mex-3 RNA binding family member D	0.001421682
ENSG00000103257	SLC7A5	[Source:HGNC Symbol;Acc:HGNC:16734] solute carrier family 7 member 5	0.001421682
ENSG00000175931	UBE2O	[Source:HGNC Symbol;Acc:HGNC:11063] ubiquitin conjugating enzyme E2 O	0.001574737
ENSG00000065268	WDR18	[Source:HGNC Symbol;Acc:HGNC:29554] WD repeat domain 18	0.001669619
ENSG00000130300	PLVAP	[Source:HGNC Symbol;Acc:HGNC:17956] plasmalemma vesicle associated protein	0.001764407
ENSG00000232434	AJM1	[Source:HGNC Symbol;Acc:HGNC:13635] apical junction component 1 homolog	0.001779673
ENSG00000197256	KANK2	[Source:HGNC Symbol;Acc:HGNC:37284] KN motif and ankyrin repeat domains 2	0.001937905
ENSG00000229809	ZNF688	[Source:HGNC Symbol;Acc:HGNC:29300] zinc finger protein 688	0.001945859
ENSG00000130433	CACNG6	[Source:HGNC Symbol;Acc:HGNC:30489] calcium voltage-gated channel auxiliary subunit gamma 6	0.002041059
ENSG00000126254	RBM42	[Source:HGNC Symbol;Acc:HGNC:13625] RNA binding motif protein 42	0.002327494
ENSG0000013306	SLC25A39	[Source:HGNC Symbol;Acc:HGNC:28117] solute carrier family 25 member 39	0.002342133
ENSG00000179837	NA	[Source:HGNC Symbol;Acc:HGNC:24279] NA	0.002354141
ENSG00000265714	NA	NA	0.002482976
ENSG00000172460	PRSS30P	"serine protease 30, pseudogene [Source:HGNC Symbol;Acc:HGNC:28753]"	0.002482976
ENSG00000104983	CCDC61	coiled-coil domain containing 61	0.002490713
ENSG00000211898	IGHD	[Source:HGNC Symbol;Acc:HGNC:33629] immunoglobulin heavy constant delta	0.002565172
ENSG00000055118	KCNH2	[Source:HGNC Symbol;Acc:HGNC:5480] potassium voltage-gated channel subfamily H member 2	0.002565172
ENSG00000260335		[Source:HGNC Symbol;Acc:HGNC:6251]	0.002637584
ENSG00000104903	LYL1	"LYL1, basic helix-loop-helix family member [Source:HGNC Symbol;Acc:HGNC:6734]"	0.002639596
ENSG00000099958	DERL3	derlin 3	0.002696079
ENSG00000179526	SHARPIN	[Source:HGNC Symbol;Acc:HGNC:14236] SHANK associated RH domain interactor	0.002709927
ENSG00000133069	TMCC2	[Source:HGNC Symbol;Acc:HGNC:25321] transmembrane and coiled-coil domain family 2	0.002709927
ENSG00000240342	RPS2P5	[Source:HGNC Symbol;Acc:HGNC:24239] ribosomal protein S2 pseudogene 5	0.002940811
ENSG00000264462	MIR3648-2	[Source:HGNC Symbol;Acc:HGNC:31386] microRNA 3648-2	0.002940811
ENSG00000256576	LINC02361	[Source:HGNC Symbol;Acc:HGNC:50843] long intergenic non-protein coding RNA 2361	0.003313878
ENSG00000007968	E2F2	[Source:HGNC Symbol;Acc:HGNC:53283] E2F transcription factor 2 [	0.003383286
ENSG00000141858	SAMD1	[Source:HGNC Symbol;Acc:HGNC:3114] sterile alpha motif domain containing 1	0.003400809
ENSG00000126705	AHDC1	[Source:HGNC Symbol;Acc:HGNC:17958] AT-hook DNA binding motif containing 1	0.003623721
ENSG00000141456	PELP1	[Source:HGNC Symbol;Acc:HGNC:25230] "proline, glutamate and leucine rich protein 1	0.004035577
ENSG00000159713	TPPP3	[Source:HGNC Symbol;Acc:HGNC:30134]" tubulin polymerization promoting protein family member 3	0.00422876
ENSG00000104897	SF3A2	[Source:HGNC Symbol;Acc:HGNC:24162] splicing factor 3a subunit 2	0.004525344
ENSG00000063245	EPN1	[Source:HGNC Symbol;Acc:HGNC:10766] epsin 1	0.004539725
ENSG00000162783	IER5	[Source:HGNC Symbol;Acc:HGNC:21604] immediate early response 5	0.004540184

ENSG00000141582	CBX4	[Source:HGNC Symbol;Acc:HGNC:5393] chromobox 4	0.004549021
ENSG00000168159	RNF187	[Source:HGNC Symbol;Acc:HGNC:1554] ring finger protein 187	0.004686524
ENSG00000136826	KLF4	[Source:HGNC Symbol;Acc:HGNC:27146] Kruppel like factor 4	0.004686524
ENSG00000237214		[Source:HGNC Symbol;Acc:HGNC:6348]	0.004891089
ENSG00000066336	SPI1	Spi-1 proto-oncogene	0.004891089
ENSG00000172270	BSG	[Source:HGNC Symbol;Acc:HGNC:11241] basigin (Ok blood group)	0.005082358
ENSG00000173868	PHOSPHO1	[Source:HGNC Symbol;Acc:HGNC:1116] phosphoethanolamine/phosphocholine phosphatase	0.005082358
ENSG00000167182	SP2	[Source:HGNC Symbol;Acc:HGNC:16815] Sp2 transcription factor	0.005082358
ENSG00000104805	NUCB1	Sp2 transcription factor	0.005118791
ENSG00000099381	SETD1A	[Source:HGNC Symbol;Acc:HGNC:11207] nucleobindin 1	0.005118791
ENSG00000185340	GAS2L1	[Source:HGNC Symbol;Acc:HGNC:8043] SET domain containing 1A	0.005119064
ENSG00000007541	PIGQ	[Source:HGNC Symbol;Acc:HGNC:29010] growth arrest specific 2 like 1	0.00514547
ENSG00000105610	KLF1	[Source:HGNC Symbol;Acc:HGNC:16955] phosphatidylinositol glycan anchor biosynthesis class Q	0.00514547
ENSG00000137193	PIM1	[Source:HGNC Symbol;Acc:HGNC:14135] Kruppel like factor 1	0.005166641
ENSG00000171552	BCL2L1	[Source:HGNC Symbol;Acc:HGNC:6345] "Pim-1 proto-oncogene, serine/threonine kinase	0.005217627
ENSG00000172889	EGFL7	[Source:HGNC Symbol;Acc:HGNC:8986]" BCL2 like 1	0.005247531
ENSG00000213402	PTPRCAP	[Source:HGNC Symbol;Acc:HGNC:992] EGF like domain multiple 7	0.005530506
ENSG00000099330	OCEL1	[Source:HGNC Symbol;Acc:HGNC:20594] "protein tyrosine phosphatase, receptor type C associated protein	0.005530506
ENSG00000147443	DOK2	[Source:HGNC Symbol;Acc:HGNC:9667]" occludin/ELL domain containing 1	0.00560032
ENSG00000182240	BACE2	[Source:HGNC Symbol;Acc:HGNC:26221] docking protein 2	0.005671418
ENSG00000170128	GPR25	[Source:HGNC Symbol;Acc:HGNC:2991] beta-site APP-cleaving enzyme 2	0.005857886
ENSG00000140406	TLNRD1	[Source:HGNC Symbol;Acc:HGNC:934] G protein-coupled receptor 25	0.005857886
ENSG00000117394	SLC2A1	[Source:HGNC Symbol;Acc:HGNC:4480] talin rod domain containing 1	0.006101348
ENSG00000141854	MISP3	[Source:HGNC Symbol;Acc:HGNC:13519] solute carrier family 2 member 1	0.0061541
ENSG00000129757	CDKN1C	[Source:HGNC Symbol;Acc:HGNC:11005] MISP family member 3	0.006158727
ENSG00000186891	TNFRSF18	[Source:HGNC Symbol;Acc:HGNC:26963] cyclin dependent kinase inhibitor 1C	0.006204755
ENSG00000184897	H1FX	[Source:HGNC Symbol;Acc:HGNC:1786] TNF receptor superfamily member 18	0.006380434
ENSG00000185236	RAB11B	[Source:HGNC Symbol;Acc:HGNC:11914] H1 histone family member X	0.006421961
ENSG00000030582	GRN	[Source:HGNC Symbol;Acc:HGNC:4722] "RAB11B, member RAS oncogene family	0.006465512
ENSG00000071564	TCF3	[Source:HGNC Symbol;Acc:HGNC:9761]" granulin precursor	0.006602734
ENSG00000267749		[Source:HGNC Symbol;Acc:HGNC:4601] transcription factor 3	0.006751675
ENSG00000105373	NOP53	[Source:HGNC Symbol;Acc:HGNC:11633] NOP53 ribosome biogenesis factor	0.006772165
ENSG00000240445	FOXO3B	[Source:HGNC Symbol;Acc:HGNC:4333] forkhead box O3B pseudogene	0.006848491
ENSG00000127528	KLF2	[Source:HGNC Symbol;Acc:HGNC:3822] Kruppel like factor 2	0.006952696
		[Source:HGNC Symbol;Acc:HGNC:6347]	0.00698206

ENSG00000254858	MPV17L2	MPV17 mitochondrial inner membrane protein like 2 [Source:HGNC Symbol;Acc:HGNC:28177]	0.006997113
ENSG00000130595	TNNT3	"tropoin T3, fast skeletal type [Source:HGNC Symbol;Acc:HGNC:11950]"	0.007133196
ENSG00000130749	ZC3H4	zinc finger CCCH-type containing 4 [Source:HGNC Symbol;Acc:HGNC:17808]	0.007141116
ENSG00000132819	RBM38	RNA binding motif protein 38 [Source:HGNC Symbol;Acc:HGNC:15818]	0.007141116
ENSG00000135925	WNT10A	Wnt family member 10A [Source:HGNC Symbol;Acc:HGNC:13829]	0.007141116
ENSG00000205639	MFSD2B	major facilitator superfamily domain containing 2B [Source:HGNC Symbol;Acc:HGNC:37207]	0.007141116
ENSG00000213763	ACTBP2	"actin, beta pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:135]"	0.007141116
ENSG00000261221	ZNF865	zinc finger protein 865 [Source:HGNC Symbol;Acc:HGNC:38705]	0.007141116
ENSG00000171611	PTCRA	pre T cell antigen receptor alpha [Source:HGNC Symbol;Acc:HGNC:21290]	0.007255358
ENSG00000161642	ZNF385A	zinc finger protein 385A [Source:HGNC Symbol;Acc:HGNC:17521]	0.007304748
ENSG00000226608	FTLP3	ferritin light chain pseudogene 3 [Source:HGNC Symbol;Acc:HGNC:4000]	0.007304748
ENSG00000170684	ZNF296	zinc finger protein 296 [Source:HGNC Symbol;Acc:HGNC:15981]	0.007327997
ENSG00000213638	ADAT3	"adenosine deaminase, tRNA specific 3 [Source:HGNC Symbol;Acc:HGNC:25151]"	0.007343983
ENSG00000179262	RAD23A	"RAD23 homolog A, nucleotide excision repair protein [Source:HGNC Symbol;Acc:HGNC:9812]"	0.0073448
ENSG00000196126	HLA-DRB1	"major histocompatibility complex, class II, DR beta 1 [Source:HGNC Symbol;Acc:HGNC:4948]"	0.00745996
ENSG00000197149			0.007535198
ENSG00000213820	RPL13P2	ribosomal protein L13 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:16342]	0.007619923
ENSG00000225331	LINC01678	long intergenic non-protein coding RNA 1678 [Source:HGNC Symbol;Acc:HGNC:52466]	0.007619923
ENSG00000235605			0.007619923
ENSG00000183092	BEGAIN	brain enriched guanylate kinase associated [Source:HGNC Symbol;Acc:HGNC:24163]	0.007755013
ENSG00000105369	CD79A	CD79a molecule [Source:HGNC Symbol;Acc:HGNC:1698]	0.007835589
ENSG00000160256	FAM207A	family with sequence similarity 207 member A [Source:HGNC Symbol;Acc:HGNC:15811]	0.007901726
ENSG00000105516	DBP	D-box binding PAR bZIP transcription factor [Source:HGNC Symbol;Acc:HGNC:2697]	0.00795596
ENSG00000179094	PER1	period circadian regulator 1 [Source:HGNC Symbol;Acc:HGNC:8845]	0.008010463
ENSG00000154146	NRGN	neurogranin [Source:HGNC Symbol;Acc:HGNC:8000]	0.008019602
ENSG00000160813	PPP1R35	protein phosphatase 1 regulatory subunit 35 [Source:HGNC Symbol;Acc:HGNC:28320]	0.008019602
ENSG00000152082	MZT2B	mitotic spindle organizing protein 2B [Source:HGNC Symbol;Acc:HGNC:25886]	0.008149414
ENSG00000115274	INO80B	INO80 complex subunit B [Source:HGNC Symbol;Acc:HGNC:13324]	0.008388785
ENSG00000185112	FAM43A	family with sequence similarity 43 member A [Source:HGNC Symbol;Acc:HGNC:26888]	0.008409751
ENSG00000130592	LSP1	lymphocyte-specific protein 1 [Source:HGNC Symbol;Acc:HGNC:6707]	0.00866593
ENSG00000077348	EXOSC5	exosome component 5 [Source:HGNC Symbol;Acc:HGNC:24662]	0.008679008
ENSG00000196498	NCOR2	nuclear receptor corepressor 2 [Source:HGNC Symbol;Acc:HGNC:7673]	0.008729326
ENSG00000132382	MYBBP1A	MYB binding protein 1a [Source:HGNC Symbol;Acc:HGNC:7546]	0.008886691
ENSG00000104885	DOT1L	DOT1 like histone lysine methyltransferase [Source:HGNC Symbol;Acc:HGNC:24948]	0.008912378
ENSG00000153443	UBALD1	UBA like domain containing 1 [Source:HGNC Symbol;Acc:HGNC:29576]	0.008912378

ENSG00000070182	SPTB	"spectrin beta, erythrocytic [Source:HGNC Symbol;Acc:HGNC:11274]"	0.008927471
ENSG00000168517	HEXIM2	hexamethylene bisacetamide inducible 2 [Source:HGNC Symbol;Acc:HGNC:28591]	0.008959412
ENSG00000090674	MCOLN1	mucolipin 1 [Source:HGNC Symbol;Acc:HGNC:13356]	0.009327518
ENSG00000198816	ZNF358	zinc finger protein 358 [Source:HGNC Symbol;Acc:HGNC:16838]	0.009506451
ENSG00000175334	BANF1	barrier to autointegration factor 1 [Source:HGNC Symbol;Acc:HGNC:17397]	0.009647997
ENSG00000125520	SLC2A4RG	SLC2A4 regulator [Source:HGNC Symbol;Acc:HGNC:15930]	0.009686596
ENSG00000141084	RANBP10	RAN binding protein 10 [Source:HGNC Symbol;Acc:HGNC:29285]	0.009715508
ENSG00000149016	TUT1	"terminal uridylyl transferase 1, U6 snRNA-specific [Source:HGNC Symbol;Acc:HGNC:26184]"	0.009768686
ENSG00000178951	ZBTB7A	zinc finger and BTB domain containing 7A [Source:HGNC Symbol;Acc:HGNC:18078]	0.009810065
ENSG00000186111	PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase type 1 gamma [Source:HGNC Symbol;Acc:HGNC:8996]	0.009810065
ENSG00000184481	FOXO4	forkhead box O4 [Source:HGNC Symbol;Acc:HGNC:7139]	0.009820284
ENSG00000064961	HMG20B	high mobility group 20B [Source:HGNC Symbol;Acc:HGNC:5002]	0.009858965
ENSG00000108309	RUNDC3A	RUN domain containing 3A [Source:HGNC Symbol;Acc:HGNC:16984]	0.010055443
ENSG00000130165	ELOF1	elongation factor 1 homolog [Source:HGNC Symbol;Acc:HGNC:28691]	0.010212535
ENSG00000130159	ECSIT	ECSIT signalling integrator [Source:HGNC Symbol;Acc:HGNC:29548]	0.010245658 0.010245658
ENSG00000244560	MT2A	metallothionein 2A [Source:HGNC Symbol;Acc:HGNC:7406]	0.01061889
ENSG00000131116	ZNF428	zinc finger protein 428 [Source:HGNC Symbol;Acc:HGNC:20804]	0.010712491
ENSG00000105617	LENG1	leukocyte receptor cluster member 1 [Source:HGNC Symbol;Acc:HGNC:15502]	0.010999325
ENSG00000139718	SETD1B	SET domain containing 1B [Source:HGNC Symbol;Acc:HGNC:29187]	0.011038344
ENSG00000106665	CLIP2	CAP-Gly domain containing linker protein 2 [Source:HGNC Symbol;Acc:HGNC:2586]	0.011064297
ENSG00000130821	SLC6A8	solute carrier family 6 member 8 [Source:HGNC Symbol;Acc:HGNC:11055]	0.011213055
ENSG00000184232	OAF	out at first homolog [Source:HGNC Symbol;Acc:HGNC:28752]	0.011286635
ENSG00000179820	MYADM	myeloid associated differentiation marker [Source:HGNC Symbol;Acc:HGNC:7544]	0.011330192
ENSG00000127580	WDR24	WD repeat domain 24 [Source:HGNC Symbol;Acc:HGNC:20852]	0.011570001
ENSG00000004939	SLC4A1	solute carrier family 4 member 1 (Diego blood group) [Source:HGNC Symbol;Acc:HGNC:11027]	0.011732314
ENSG00000130522	JUND	"JunD proto-oncogene, AP-1 transcription factor subunit [Source:HGNC Symbol;Acc:HGNC:6206]"	0.011813745
ENSG00000148362	PAXX	"PAXX, non-homologous end joining factor [Source:HGNC Symbol;Acc:HGNC:27849]"	0.011821074
ENSG00000262902	MTCO1P40	mitochondrially encoded cytochrome c oxidase I pseudogene 40 [Source:HGNC Symbol;Acc:HGNC:52105]	0.011821074
ENSG00000167671	UBXN6	UBX domain protein 6 [Source:HGNC Symbol;Acc:HGNC:14928]	0.011831088
ENSG00000125457	MIF4GD	MIF4G domain containing [Source:HGNC Symbol;Acc:HGNC:24030]	0.011851589
ENSG00000146066	HIGD2A	HIG1 hypoxia inducible domain family member 2A [Source:HGNC Symbol;Acc:HGNC:28311]	0.011914767
ENSG00000184221	OLIG1	oligodendrocyte transcription factor 1 [Source:HGNC Symbol;Acc:HGNC:16983]	0.011914767 0.0119947
ENSG00000260316	CDKN1A	cyclin dependent kinase inhibitor 1A [Source:HGNC Symbol;Acc:HGNC:1784]	0.012077375
ENSG00000124762			

ENSG00000103148	NPRL3	"NPR3 like, GATOR1 complex subunit [Source:HGNC Symbol;Acc:HGNC:14124]"	0.012137266
ENSG00000179115	FARSA	phenylalanyl-tRNA synthetase alpha subunit [Source:HGNC Symbol;Acc:HGNC:3592]	0.012137266
ENSG00000120896	SORBS3	sorbin and SH3 domain containing 3 [Source:HGNC Symbol;Acc:HGNC:30907]	0.012150664
ENSG00000174886	NDUFA11	NADH:ubiquinone oxidoreductase subunit A11 [Source:HGNC Symbol;Acc:HGNC:20371]	0.012268883
ENSG00000102145	GATA1	GATA binding protein 1 [Source:HGNC Symbol;Acc:HGNC:4170]	0.012285964
ENSG00000166428	PLD4	phospholipase D family member 4 [Source:HGNC Symbol;Acc:HGNC:23792]	0.012401569
ENSG00000213015	ZNF580	zinc finger protein 580 [Source:HGNC Symbol;Acc:HGNC:29473]	0.012630003
ENSG00000142544	CTU1	cytosolic thioridylase subunit 1 [Source:HGNC Symbol;Acc:HGNC:29590]	0.012676606
ENSG00000085644	ZNF213	zinc finger protein 213 [Source:HGNC Symbol;Acc:HGNC:13005]	0.012935817
ENSG00000003249	DBNDD1	dysbindin domain containing 1 [Source:HGNC Symbol;Acc:HGNC:28455]	0.013109402
ENSG00000221288	MIR663B	microRNA 663b [Source:HGNC Symbol;Acc:HGNC:35270]	0.013333238
ENSG00000042062	RIPOR3	RIPOR family member 3 [Source:HGNC Symbol;Acc:HGNC:16168]	0.013356858
ENSG00000105329	TGFB1	transforming growth factor beta 1 [Source:HGNC Symbol;Acc:HGNC:11766]	0.013356858
ENSG00000116871	MAP7D1	MAP7 domain containing 1 [Source:HGNC Symbol;Acc:HGNC:25514]	0.013356858
ENSG00000168298	HIST1H1E	histone cluster 1 H1 family member e [Source:HGNC Symbol;Acc:HGNC:4718]	0.013400191
ENSG00000127666	TICAM1	toll like receptor adaptor molecule 1 [Source:HGNC Symbol;Acc:HGNC:18348]	0.013447765
ENSG00000166886	NAB2	NGFI-A binding protein 2 [Source:HGNC Symbol;Acc:HGNC:7627]	0.013572419
ENSG00000112787	FBRSL1	fibrosin like 1 [Source:HGNC Symbol;Acc:HGNC:29308]	0.013760569
ENSG00000100243	CYB5R3	cytochrome b5 reductase 3 [Source:HGNC Symbol;Acc:HGNC:2873]	0.013883197
ENSG00000197457	STMN3	stathmin 3 [Source:HGNC Symbol;Acc:HGNC:15926]	0.013964273
ENSG00000255441	JUP	0.013965194	0.014437619
ENSG00000173801		junction plakoglobin [Source:HGNC Symbol;Acc:HGNC:6207]	
ENSG00000224614	TNK2-AS1	TNK2 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:49093]	0.014437619
ENSG00000058453	CROCC	"ciliary rootlet coiled-coil, rootletin [Source:HGNC Symbol;Acc:HGNC:21299]"	0.014522615
ENSG00000079313	REXO1	RNA exonuclease 1 homolog [Source:HGNC Symbol;Acc:HGNC:24616]	0.014579462
ENSG00000154102	C16orf74	chromosome 16 open reading frame 74 [Source:HGNC Symbol;Acc:HGNC:23362]	0.014732236
ENSG00000172650	AGAP5	"ArfGAP with GTPase domain, ankyrin repeat and PH domain 5 [Source:HGNC Symbol;Acc:HGNC:23467]"	0.014761715
ENSG00000159733	ZFYVE28	zinc finger FYVE-type containing 28 [Source:HGNC Symbol;Acc:HGNC:29334]	0.014792652
ENSG00000019582	CD74	CD74 molecule [Source:HGNC Symbol;Acc:HGNC:1697]	0.014946895
ENSG00000211771	TRBJ2-7	T cell receptor beta joining 2-7 [Source:HGNC Symbol;Acc:HGNC:12175]	0.014961068
ENSG00000214309	MBLAC1	metallo-beta-lactamase domain containing 1 [Source:HGNC Symbol;Acc:HGNC:22180]	0.014976932
ENSG00000187266	EPOR	erythropoietin receptor [Source:HGNC Symbol;Acc:HGNC:3416]	0.015342955
ENSG00000108106	UBE2S	ubiquitin conjugating enzyme E2 S [Source:HGNC Symbol;Acc:HGNC:17895]	0.015459542
ENSG00000185838	GNB1L	G protein subunit beta 1 like [Source:HGNC Symbol;Acc:HGNC:4397]	0.015552452
ENSG00000228594	FNDC10	fibronectin type III domain containing 10	

ENSG00000126464	PRR12	[Source:HGNC Symbol;Acc:HGNC:42951] proline rich 12 [Source:HGNC Symbol;Acc:HGNC:29217]	0.015552452 0.015622838
ENSG00000084092	NOA1	nitric oxide associated 1 [Source:HGNC Symbol;Acc:HGNC:28473]	0.015753463
ENSG00000105227	PRX	periaxin [Source:HGNC Symbol;Acc:HGNC:13797]	0.015787169 0.015787169
ENSG00000260401			
ENSG00000159840	ZYX	zyxin [Source:HGNC Symbol;Acc:HGNC:13200]	0.015829354
ENSG00000197483	ZNF628	zinc finger protein 628 [Source:HGNC Symbol;Acc:HGNC:28054]	0.015834462 0.015908819
ENSG00000182572	NA	NA	0.015942034
ENSG00000154035	NA	NA	
ENSG00000161618	ALDH16A1	aldehyde dehydrogenase 16 family member A1 [Source:HGNC Symbol;Acc:HGNC:28114]	0.015942034
ENSG00000124575	HIST1H1D	histone cluster 1 H1 family member d [Source:HGNC Symbol;Acc:HGNC:4717]	0.015948868
ENSG00000196092	PAX5	paired box 5 [Source:HGNC Symbol;Acc:HGNC:8619]	0.01597311
ENSG00000105429	MEGF8	multiple EGF like domains 8 [Source:HGNC Symbol;Acc:HGNC:3233]	0.015986308
ENSG00000213753	CENPBD1P1	CENPB DNA-binding domains containing 1 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:28421]	0.016008143
ENSG00000179627	ZBTB42	zinc finger and BTB domain containing 42 [Source:HGNC Symbol;Acc:HGNC:32550]	0.016166469
ENSG00000107816	LZTS2	leucine zipper tumor suppressor 2 [Source:HGNC Symbol;Acc:HGNC:29381]	0.016243979
ENSG00000183779	ZNF703	zinc finger protein 703 [Source:HGNC Symbol;Acc:HGNC:25883]	0.016243979
ENSG00000203950	RTL8A	retrotransposon Gag like 8A [Source:HGNC Symbol;Acc:HGNC:24514]	0.01630694
ENSG00000088826	SMOX	spermine oxidase [Source:HGNC Symbol;Acc:HGNC:15862]	0.016416472
ENSG00000105298	CACTIN	"cactin, spliceosome C complex subunit [Source:HGNC Symbol;Acc:HGNC:29938]"	0.016416472
ENSG00000137218	FRS3	fibroblast growth factor receptor substrate 3 [Source:HGNC Symbol;Acc:HGNC:16970]	0.016416472
ENSG00000175550	DRAP1	DR1 associated protein 1 [Source:HGNC Symbol;Acc:HGNC:3019]	0.016587059
ENSG00000166165	CKB	creatine kinase B [Source:HGNC Symbol;Acc:HGNC:1991]	0.01659925
ENSG00000162366	PDZK1IP1	PDZK1 interacting protein 1 [Source:HGNC Symbol;Acc:HGNC:16887]	0.016705327
ENSG00000184428	TOP1MT DNA topoisomerase I mitochondrial	[Source:HGNC Symbol;Acc:HGNC:29787]	0.016722415
ENSG00000130479	MAP1S	microtubule associated protein 1S [Source:HGNC Symbol;Acc:HGNC:15715]	0.016796937
ENSG00000171222	SCAND1	SCAN domain containing 1 [Source:HGNC Symbol;Acc:HGNC:10566]	0.016821415
ENSG00000171223	JUNB	"JunB proto-oncogene, AP-1 transcription factor subunit [Source:HGNC Symbol;Acc:HGNC:6205]"	0.016966042
ENSG00000107902	LHPP	phospholysine phosphohistidine inorganic pyrophosphate phosphatase [Source:HGNC Symbol;Acc:HGNC:30042]	0.017052413
ENSG00000170271	FAXDC2	fatty acid hydroxylase domain containing 2 [Source:HGNC Symbol;Acc:HGNC:1334]	0.017052413
ENSG00000100325	ASCC2	activating signal cointegrator 1 complex subunit 2 [Source:HGNC Symbol;Acc:HGNC:24103]	0.017132234
ENSG00000142694	EVA1B	eva-1 homolog B [Source:HGNC Symbol;Acc:HGNC:25558]	0.017132234
ENSG00000064201	TSPAN32	tetraspanin 32 [Source:HGNC Symbol;Acc:HGNC:13410]	0.017210927
ENSG00000157911	PEX10	peroxisomal biogenesis factor 10 [Source:HGNC Symbol;Acc:HGNC:8851]	0.017211726
ENSG00000079432	CIC	capicua transcriptional repressor [Source:HGNC Symbol;Acc:HGNC:14214]	0.017339051
ENSG00000188825	LINC00910	long intergenic non-protein coding RNA 910	

ENSG00000196961	AP2A1	[Source:HGNC Symbol;Acc:HGNC:44361]	0.017339051
		adaptor related protein complex 2 alpha 1 subunit	
ENSG00000214279	SCART1	[Source:HGNC Symbol;Acc:HGNC:561]	0.017339051
		scavenger receptor family member expressed on T cells 1	
ENSG00000272449		[Source:HGNC Symbol;Acc:HGNC:32411]	0.017339051
ENSG00000104973	MED25	mediator complex subunit 25	
		[Source:HGNC Symbol;Acc:HGNC:28845]	0.017392388
ENSG00000180767	CHST13	carbohydrate sulfotransferase 13	
		[Source:HGNC Symbol;Acc:HGNC:21755]	0.017392388
ENSG00000227232	WASH7P	WAS protein family homolog 7 pseudogene	
		[Source:HGNC Symbol;Acc:HGNC:38034]	0.017392388
ENSG00000162302	RPS6KA4	ribosomal protein S6 kinase A4	
		[Source:HGNC Symbol;Acc:HGNC:10433]	0.017767827
ENSG00000136840	ST6GALNAC4	"ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 4	
		[Source:HGNC Symbol;Acc:HGNC:17846]"	0.017832974
ENSG00000160404	TOR2A	torsin family 2 member A	
		[Source:HGNC Symbol;Acc:HGNC:11996]	0.018020454
ENSG00000233038			0.018071818
ENSG00000243449	C4orf48	chromosome 4 open reading frame 48	
		[Source:HGNC Symbol;Acc:HGNC:34437]	0.018116836
ENSG00000160050	CCDC28B	coiled-coil domain containing 28B	
		[Source:HGNC Symbol;Acc:HGNC:28163]	0.01812987
ENSG00000138623	SEMA7A	semaphorin 7A (John Milton Hagen blood group)	
		[Source:HGNC Symbol;Acc:HGNC:10741]	0.01834001
ENSG00000101439	CST3	cystatin C	
		[Source:HGNC Symbol;Acc:HGNC:2475]	0.018421259
ENSG00000100368	CSF2RB	colony stimulating factor 2 receptor beta common subunit	
		[Source:HGNC Symbol;Acc:HGNC:2436]	0.01865112
ENSG00000006015	REX1BD	required for excision 1-B domain containing	
		[Source:HGNC Symbol;Acc:HGNC:26098]	0.01871477
ENSG00000011451	WIZ	widely interspaced zinc finger motifs	
		[Source:HGNC Symbol;Acc:HGNC:30917]	0.018812736
ENSG00000160888	IER2	immediate early response 2	
		[Source:HGNC Symbol;Acc:HGNC:28871]	0.018812736
ENSG00000174807	CD248	CD248 molecule	
		[Source:HGNC Symbol;Acc:HGNC:18219]	0.018812736
ENSG00000099821	POLRMT	RNA polymerase mitochondrial	
		[Source:HGNC Symbol;Acc:HGNC:9200]	0.018832922
ENSG00000211899	IGHM	immunoglobulin heavy constant mu	
		[Source:HGNC Symbol;Acc:HGNC:5541]	0.018832922
ENSG00000130313	PGLS	6-phosphogluconolactonase	
		[Source:HGNC Symbol;Acc:HGNC:8903]	0.019015294
ENSG00000165702	GFI1B	growth factor independent 1B transcriptional repressor	
		[Source:HGNC Symbol;Acc:HGNC:4238]	0.019015294
ENSG00000196557	CACNA1H	calcium voltage-gated channel subunit alpha1 H	
		[Source:HGNC Symbol;Acc:HGNC:1395]	0.019108077
ENSG00000188486	H2AFX	H2A histone family member X	
		[Source:HGNC Symbol;Acc:HGNC:4739]	0.019120708
ENSG00000103260	METRN	"meteorin, glial cell differentiation regulator	
		[Source:HGNC Symbol;Acc:HGNC:14151]"	0.01915234
ENSG00000166925	TSC22D4	TSC22 domain family member 4	
		[Source:HGNC Symbol;Acc:HGNC:21696]	0.01920241
ENSG00000106266	SNX8	sorting nexin 8	
		[Source:HGNC Symbol;Acc:HGNC:14972]	0.019236897
ENSG00000110400	NECTIN1	nectin cell adhesion molecule 1	
		[Source:HGNC Symbol;Acc:HGNC:9706]	0.01926502
ENSG00000088992	TESC	tescalcin	
		[Source:HGNC Symbol;Acc:HGNC:26065]	0.019687862
ENSG00000126368	NR1D1	nuclear receptor subfamily 1 group D member 1	
		[Source:HGNC Symbol;Acc:HGNC:7962]	0.019740714
ENSG00000103202	NME4	NME/NM23 nucleoside diphosphate kinase 4	
		[Source:HGNC Symbol;Acc:HGNC:7852]	0.019829586
ENSG00000213626	LBH	limb bud and heart development	
		[Source:HGNC Symbol;Acc:HGNC:29532]	0.019900152
ENSG00000138629	UBL7	ubiquitin like 7	
		[Source:HGNC Symbol;Acc:HGNC:28221]	0.019916102
ENSG00000254614			0.019916102

ENSG00000116521	SCAMP3s	secretory carrier membrane protein 3	
		[Source:HGNC Symbol;Acc:HGNC:10565]	0.019953714
ENSG00000132481	TRIM47	tripartite motif containing 47	
		[Source:HGNC Symbol;Acc:HGNC:19020]	0.019989295
ENSG00000105699	LSR	lipolysis stimulated lipoprotein receptor	
		[Source:HGNC Symbol;Acc:HGNC:29572]	0.019999965
ENSG00000125503	PPP1R12C	protein phosphatase 1 regulatory subunit 12C	
		[Source:HGNC Symbol;Acc:HGNC:14947]	0.020063533
ENSG00000103056	SMPD3	sphingomyelin phosphodiesterase 3	
		[Source:HGNC Symbol;Acc:HGNC:14240]	0.020115844
ENSG00000156381	ANKRD9	ankyrin repeat domain 9	
		[Source:HGNC Symbol;Acc:HGNC:20096]	0.020225168
ENSG00000197471	SPN	sialophorin	
		[Source:HGNC Symbol;Acc:HGNC:11249]	0.020225168
ENSG00000197471	SPN	sialophorin	
		[Source:HGNC Symbol;Acc:HGNC:11249]	0.020225168
ENSG00000063854	HAGH	hydroxyacylglutathione hydrolase	
		[Source:HGNC Symbol;Acc:HGNC:4805]	0.020247513
ENSG00000130590	SAMD10	sterile alpha motif domain containing 10	
		[Source:HGNC Symbol;Acc:HGNC:16129]	0.020258063
ENSG00000167664	TMIGD2	transmembrane and immunoglobulin domain containing 2	
		[Source:HGNC Symbol;Acc:HGNC:28324]	0.020258063
ENSG00000146083	RNF44	ring finger protein 44	
		[Source:HGNC Symbol;Acc:HGNC:19180]	0.020327471
ENSG00000231925	TAPBP	TAP binding protein	
		[Source:HGNC Symbol;Acc:HGNC:11566]	0.020387859
ENSG00000198858	R3HDM4	R3H domain containing 4	
		[Source:HGNC Symbol;Acc:HGNC:28270]	0.020462672
ENSG00000135924	DNAJB2	DnaJ heat shock protein family (Hsp40) member B2	
		[Source:HGNC Symbol;Acc:HGNC:5228]	0.020505106
ENSG00000239732	TLR9	toll like receptor 9	
		[Source:HGNC Symbol;Acc:HGNC:15633]	0.02065324
ENSG00000115268	RPS15	ribosomal protein S15	
		[Source:HGNC Symbol;Acc:HGNC:10388]	0.020839375
ENSG00000108798	ABI3	ABI family member 3	
		[Source:HGNC Symbol;Acc:HGNC:29859]	0.02085252
ENSG00000119669	IRF2BPL	interferon regulatory factor 2 binding protein like	
		[Source:HGNC Symbol;Acc:HGNC:14282]	0.02099734
ENSG00000160446	ZDHHC12	zinc finger DHHC-type containing 12	
		[Source:HGNC Symbol;Acc:HGNC:19159]	0.02150253
ENSG00000063169	BICRA	BRD4 interacting chromatin remodeling complex associated protein	
		[Source:HGNC Symbol;Acc:HGNC:4332]	0.021525887
ENSG00000141933	TPGS1	tubulin polyglutamylase complex subunit 1	
		[Source:HGNC Symbol;Acc:HGNC:25058]	0.021539966
ENSG00000088256	GNA11	G protein subunit alpha 11	
		[Source:HGNC Symbol;Acc:HGNC:4379]	0.021557835
ENSG00000169583	CLIC3	chloride intracellular channel 3	
		[Source:HGNC Symbol;Acc:HGNC:2064]	0.021557835
ENSG00000188511	C22orf34	chromosome 22 open reading frame 34	
		[Source:HGNC Symbol;Acc:HGNC:28010]	0.021557835
ENSG00000165406	8-Mar	membrane associated ring-CH-type finger 8	
		[Source:HGNC Symbol;Acc:HGNC:23356]	0.021577416
ENSG00000173762	CD7	CD7 molecule	
		[Source:HGNC Symbol;Acc:HGNC:1695]	0.021879276
ENSG00000188322	SBK1	SH3 domain binding kinase 1	
		[Source:HGNC Symbol;Acc:HGNC:17699]	0.021879276
ENSG00000204310	AGPAT1	1-acylglycerol-3-phosphate O-acyltransferase 1	
		[Source:HGNC Symbol;Acc:HGNC:324]	0.021879276
ENSG00000167797	CDK2AP2	cyclin dependent kinase 2 associated protein 2	
		[Source:HGNC Symbol;Acc:HGNC:30833]	0.021895705
ENSG00000142669	SH3BGL3	SH3 domain binding glutamate rich protein like 3	
		[Source:HGNC Symbol;Acc:HGNC:15568]	0.022007819
ENSG00000155034	FBXL18	F-box and leucine rich repeat protein 18	
		[Source:HGNC Symbol;Acc:HGNC:21874]	0.022133956
ENSG00000187840	EIF4EBP1	eukaryotic translation initiation factor 4E binding protein 1	
		[Source:HGNC Symbol;Acc:HGNC:3288]	0.02227554
ENSG00000185187	SIGIRR	single Ig and TIR domain containing	
		[Source:HGNC Symbol;Acc:HGNC:30575]	0.022615882

ENSG00000158545	ZC3H18	zinc finger CCCH-type containing 18	
		[Source:HGNC Symbol;Acc:HGNC:25091]	0.022649486
ENSG00000184730	APOBR	polipoprotein B receptor	
		[Source:HGNC Symbol;Acc:HGNC:24087]	0.022689972
ENSG00000204463	BAG6	BCL2 associated athanogene 6	
		[Source:HGNC Symbol;Acc:HGNC:13919]	0.022689972
ENSG00000071242	RPS6KA2	ribosomal protein S6 kinase A2	
		[Source:HGNC Symbol;Acc:HGNC:10431]	0.022776502
ENSG00000146701	MDH2	malate dehydrogenase 2	
		[Source:HGNC Symbol;Acc:HGNC:6971]	0.02289018
ENSG00000180155	LYNX1	Ly6/neurotoxin 1	
		[Source:HGNC Symbol;Acc:HGNC:29604]	0.02289018
ENSG00000213563	C8orf82	chromosome 8 open reading frame 82	
		[Source:HGNC Symbol;Acc:HGNC:33826]	0.023112388
ENSG00000105281	SLC1A5	solute carrier family 1 member 5	
		[Source:HGNC Symbol;Acc:HGNC:10943]	0.023356543
ENSG00000162882	HAAO	"3-hydroxyanthranilate 3,4-dioxygenase	
		[Source:HGNC Symbol;Acc:HGNC:4796]"	0.02337834
ENSG00000181513	ACBD4	acyl-CoA binding domain containing 4	
		[Source:HGNC Symbol;Acc:HGNC:23337]	0.02337834
ENSG00000185730	ZNF696	zinc finger protein 696	
		[Source:HGNC Symbol;Acc:HGNC:25872]	0.02337834
ENSG00000007520	TSR3	"TSR3, acp transferase ribosome maturation factor	
		[Source:HGNC Symbol;Acc:HGNC:14175]"	0.023637109
ENSG00000090006	LTBP4	latent transforming growth factor beta binding protein 4	
		[Source:HGNC Symbol;Acc:HGNC:6717]	0.023637109
ENSG00000146535	GNA12	G protein subunit alpha 12	
		[Source:HGNC Symbol;Acc:HGNC:4380]	0.023652058
ENSG00000141965	FEM1A	fem-1 homolog A	
		[Source:HGNC Symbol;Acc:HGNC:16934]	0.023707215
ENSG00000160957	RECQL4	RecQ like helicase 4	
		[Source:HGNC Symbol;Acc:HGNC:9949]	0.023710452
ENSG00000135916	ITM2C	integral membrane protein 2C	
		[Source:HGNC Symbol;Acc:HGNC:6175]	0.023733416
ENSG00000177732	SOX12	SRY-box 12	
		[Source:HGNC Symbol;Acc:HGNC:11198]	0.023733416
ENSG00000184508	HDDC3	HD domain containing 3	
		[Source:HGNC Symbol;Acc:HGNC:30522]	0.023802652
ENSG00000175591	P2RY2	purinergic receptor P2Y2	
		[Source:HGNC Symbol;Acc:HGNC:8541]	0.023918507
ENSG00000127903	ZNF835	zinc finger protein 835	
		[Source:HGNC Symbol;Acc:HGNC:34332]	0.023926586
ENSG00000176022	B3GALT6	"beta-1,3-galactosyltransferase 6	
		[Source:HGNC Symbol;Acc:HGNC:17978]"	0.023926586
ENSG00000255319	ENPP7P8	ectonucleotide pyrophosphatase/phosphodiesterase	
		7 pseudogene 8	
		[Source:HGNC Symbol;Acc:HGNC:48691]	0.02392953
ENSG00000105479	CCDC114	coiled-coil domain containing 114	
		[Source:HGNC Symbol;Acc:HGNC:26560]	0.02398767
ENSG00000130529	TRPM4	transient receptor potential cation channel subfamily M member 4	
		[Source:HGNC Symbol;Acc:HGNC:17993]	0.024020687
ENSG00000133250	ZNF414	zinc finger protein 414	
		[Source:HGNC Symbol;Acc:HGNC:20630]	0.024020687
ENSG00000215908	CROCCP2	"ciliary rootlet coiled-coil, rootletin pseudogene 2	
		[Source:HGNC Symbol;Acc:HGNC:28170]"	0.024052859
ENSG00000118046	STK11	serine/threonine kinase 11	
		[Source:HGNC Symbol;Acc:HGNC:11389]	0.024056107
ENSG00000034152	MAP2K3	mitogen-activated protein kinase kinase 3	
		[Source:HGNC Symbol;Acc:HGNC:6843]	0.024155164
ENSG00000142453	CARM1	coactivator associated arginine methyltransferase 1	
		[Source:HGNC Symbol;Acc:HGNC:23393]	0.024155164
ENSG00000256323	NA	NA	
ENSG00000160094	ZNF362	zinc finger protein 362	
		[Source:HGNC Symbol;Acc:HGNC:18079]	0.024171066
ENSG00000104884	ERCC2	"ERCC excision repair 2, TFIIH core complex helicase subunit	
		[Source:HGNC Symbol;Acc:HGNC:3434]"	0.024345083
ENSG00000149257	SERPINH1	serpin family H member 1	
		[Source:HGNC Symbol;Acc:HGNC:1546]	0.024345083

ENSG00000169635	HIC2	HIC ZBTB transcriptional repressor 2 [Source:HGNC Symbol;Acc:HGNC:18595]	0.024354637
ENSG00000143416	SELENBP1	selenium binding protein 1 [Source:HGNC Symbol;Acc:HGNC:10719]	0.024421599
ENSG00000148411	NACC2	NACC family member 2 [Source:HGNC Symbol;Acc:HGNC:23846]	0.02443315
ENSG00000085872	CHERP	calcium homeostasis endoplasmic reticulum protein [Source:HGNC Symbol;Acc:HGNC:16930]	0.024463522
ENSG00000176182	MYPOP	"Myb related transcription factor, partner of profiling [Source:HGNC Symbol;Acc:HGNC:20178]"	0.024477311
ENSG00000160113	NR2F6	nuclear receptor subfamily 2 group F member 6 [Source:HGNC Symbol;Acc:HGNC:7977]	0.024505177
ENSG00000108262	GIT1	GIT ArfGAP 1 [Source:HGNC Symbol;Acc:HGNC:4272]	0.024614621
ENSG00000161395	PGAP3	post-GPI attachment to proteins 3 [Source:HGNC Symbol;Acc:HGNC:23719]	0.024705126
ENSG00000142089	IFITM3	interferon induced transmembrane protein 3 [Source:HGNC Symbol;Acc:HGNC:5414]	0.024765171
ENSG00000070444	MNT	MAX network transcriptional repressor [Source:HGNC Symbol;Acc:HGNC:7188]	0.025148395
ENSG00000112514	CUTA	cutA divalent cation tolerance homolog [Source:HGNC Symbol;Acc:HGNC:21101]	0.025148395
ENSG00000167394	ZNF668	zinc finger protein 668 [Source:HGNC Symbol;Acc:HGNC:25821]	0.025148395
ENSG00000167965	MLST8	"MTOR associated protein, LST8 homolog [Source:HGNC Symbol;Acc:HGNC:24825]"	0.025148395
ENSG00000244187	TMEM141	transmembrane protein 141 [Source:HGNC Symbol;Acc:HGNC:28211]	0.025148395
ENSG00000218175			0.02527518
ENSG00000110063	DCPS	"decapping enzyme, scavenger [Source:HGNC Symbol;Acc:HGNC:29812]"	0.025300524
ENSG00000128805	ARHGAP22	Rho GTPase activating protein 22 [Source:HGNC Symbol;Acc:HGNC:30320]	0.025318552
ENSG00000148400	NOTCH1	notch 1 [Source:HGNC Symbol;Acc:HGNC:7881]	0.025506427
ENSG00000186076			0.0257616
ENSG00000167470	MIDN	midnolin [Source:HGNC Symbol;Acc:HGNC:16298]	0.02580767
ENSG00000188305	PEAK3	PEAK family member 3 [Source:HGNC Symbol;Acc:HGNC:24793]	0.02580767
ENSG00000181396	OGFOD3	2-oxoglutarate and iron dependent oxygenase domain containing 3 [Source:HGNC Symbol;Acc:HGNC:26174]	0.026198035
ENSG00000240877	RN7SL521P	"RNA, 7SL, cytoplasmic 521, pseudogene [Source:HGNC Symbol;Acc:HGNC:46537]"	0.026492508
ENSG00000130511	SSBP4	single stranded DNA binding protein 4 [Source:HGNC Symbol;Acc:HGNC:15676]	0.026588317
ENSG00000063177	RPL18	ribosomal protein L18 [Source:HGNC Symbol;Acc:HGNC:10310]	0.026698079
ENSG00000172663	TMEM134	transmembrane protein 134 [Source:HGNC Symbol;Acc:HGNC:26142]	0.026698079
ENSG00000130706	ADRM1	adhesion regulating molecule 1 [Source:HGNC Symbol;Acc:HGNC:15759]	0.026721536
ENSG00000214063	TSPAN4	tetraspanin 4 [Source:HGNC Symbol;Acc:HGNC:11859]	0.026759131
ENSG00000161677	JOSD2	Josephin domain containing 2 [Source:HGNC Symbol;Acc:HGNC:28853]	0.026798474
ENSG00000189060	H1F0	H1 histone family member 0 [Source:HGNC Symbol;Acc:HGNC:4714]	0.027109095
ENSG00000256811			0.027109095
ENSG00000133317	LGALS12	galectin 12 [Source:HGNC Symbol;Acc:HGNC:15788]	0.027164347
ENSG00000012061	ERCC1	"ERCC excision repair 1, endonuclease non-catalytic subunit [Source:HGNC Symbol;Acc:HGNC:3433]"	0.027196959
ENSG00000007376	RPUSD1	RNA pseudouridylyl synthase domain containing 1 [Source:HGNC Symbol;Acc:HGNC:14173]	0.027275974
ENSG00000108175	ZMIZ1	zinc finger MIZ-type containing 1 [Source:HGNC Symbol;Acc:HGNC:16493]	0.027331142

ENSG00000132003	ZSWIM4	zinc finger SWIM-type containing 4	
		[Source:HGNC Symbol;Acc:HGNC:25704]	0.027331142
ENSG00000148296	SURF6	surfeit 6	
		[Source:HGNC Symbol;Acc:HGNC:11478]	0.027362837
ENSG00000186056	MATN1-AS1	MATN1 antisense RNA 1	
		[Source:HGNC Symbol;Acc:HGNC:40364]	0.02742002
ENSG00000115649	CNPPD1	cyclin Pas1/PHO80 domain containing 1	
		[Source:HGNC Symbol;Acc:HGNC:25220]	0.027574972
ENSG00000065057	NTHL1	nth like DNA glycosylase 1	
		[Source:HGNC Symbol;Acc:HGNC:8028]	0.027763734
ENSG00000272098	NA	NA	0.027825114
ENSG00000011009	LYPLA2	lysophospholipase II	
		[Source:HGNC Symbol;Acc:HGNC:6738]	0.028071412
ENSG00000110025	SNX15	sorting nexin 15	
		[Source:HGNC Symbol;Acc:HGNC:14978]	0.028074538
ENSG00000095321	CRAT	carnitine O-acetyltransferase	
		[Source:HGNC Symbol;Acc:HGNC:2342]	0.028133383
ENSG00000108515	ENO3	enolase 3	
		[Source:HGNC Symbol;Acc:HGNC:3354]	0.028133383
ENSG00000123064	DDX54	DEAD-box helicase 54	
		[Source:HGNC Symbol;Acc:HGNC:20084]	0.028358899
ENSG00000169564	PCBP1	poly(rC) binding protein 1	
		[Source:HGNC Symbol;Acc:HGNC:8647]	0.028645846
ENSG00000171045	TSNARE1	t-SNARE domain containing 1	
		[Source:HGNC Symbol;Acc:HGNC:26437]	0.028645846
ENSG00000225978	HAR1A	highly accelerated region 1A (non-protein coding)	
		[Source:HGNC Symbol;Acc:HGNC:33117]	0.028645846
ENSG00000128283	CDC42EP1	CDC42 effector protein 1	
		[Source:HGNC Symbol;Acc:HGNC:17014]	0.028675863
ENSG00000174282	ZBTB4	zinc finger and BTB domain containing 4	
		[Source:HGNC Symbol;Acc:HGNC:23847]	0.028871519
ENSG00000167685	ZNF444	zinc finger protein 444	
		[Source:HGNC Symbol;Acc:HGNC:16052]	0.028919683
ENSG00000110104	CCDC86	coiled-coil domain containing 86	
		[Source:HGNC Symbol;Acc:HGNC:28359]	0.028929404
ENSG00000171703	TCEA2	transcription elongation factor A2	
		[Source:HGNC Symbol;Acc:HGNC:11614]	0.029117009
ENSG00000177600	RPLP2	ribosomal protein lateral stalk subunit P2	
		[Source:HGNC Symbol;Acc:HGNC:10377]	0.029298722
ENSG00000182095	TNRC18	trinucleotide repeat containing 18	
		[Source:HGNC Symbol;Acc:HGNC:11962]	0.029299181
ENSG00000167106	FAM102A	family with sequence similarity 102 member A	
		[Source:HGNC Symbol;Acc:HGNC:31419]	0.029415219
ENSG00000126458	RRAS	RAS related	
		[Source:HGNC Symbol;Acc:HGNC:10447]	0.02952737
ENSG00000105063	PPP6R1	protein phosphatase 6 regulatory subunit 1	
		[Source:HGNC Symbol;Acc:HGNC:29195]	0.02959944
ENSG00000125730	C3	complement C3	
		[Source:HGNC Symbol;Acc:HGNC:1318]	0.029997906
ENSG00000237973	MTCO1P12	mitochondrially encoded cytochrome c oxidase I pseudogene 12	
		[Source:HGNC Symbol;Acc:HGNC:52014]	0.030144659
ENSG00000267412			0.030144659
ENSG00000185813	PCYT2	"phosphate cytidyltransferase 2, ethanolamine	
		[Source:HGNC Symbol;Acc:HGNC:8756]"	0.030317293
ENSG00000163462	TRIM46	tripartite motif containing 46	
		[Source:HGNC Symbol;Acc:HGNC:19019]	0.030614393
ENSG00000157933	SKI	SKI proto-oncogene	
		[Source:HGNC Symbol;Acc:HGNC:10896]	0.030701411
ENSG00000161091	MFS12	major facilitator superfamily domain containing 12	
		[Source:HGNC Symbol;Acc:HGNC:28299]	0.030704292
ENSG00000185163	DDX51	DEAD-box helicase 51	
		[Source:HGNC Symbol;Acc:HGNC:20082]	0.030735268
ENSG00000171813	PWWP2B	PWWP domain containing 2B	
		[Source:HGNC Symbol;Acc:HGNC:25150]	0.030810478
ENSG00000137267	TUBB2A	tubulin beta 2A class IIa	
		[Source:HGNC Symbol;Acc:HGNC:12412]	0.030847037
ENSG00000188747	NOXA1	NADPH oxidase activator 1	
		[Source:HGNC Symbol;Acc:HGNC:10668]	0.030853611

ENSG00000108557	RAI1	retinoic acid induced 1 [Source:HGNC Symbol;Acc:HGNC:9834]	0.030977697
ENSG00000137166	FOXP4	forkhead box P4 [Source:HGNC Symbol;Acc:HGNC:20842]	0.030977697
ENSG00000204420	MPIG6B	megakaryocyte and platelet inhibitory receptor G6b [Source:HGNC Symbol;Acc:HGNC:13937]	0.031369168
ENSG00000133265	HSPBP1	HSPA (Hsp70) binding protein 1 [Source:HGNC Symbol;Acc:HGNC:24989]	0.031442624
ENSG00000008710	PKD1	"polycystin 1, transient receptor potential channel interacting [Source:HGNC Symbol;Acc:HGNC:9008]"	0.031566582
ENSG00000099624	ATP5F1D	ATP synthase F1 subunit delta [Source:HGNC Symbol;Acc:HGNC:837]	0.031657927
ENSG00000108819	PPP1R9B	protein phosphatase 1 regulatory subunit 9B [Source:HGNC Symbol;Acc:HGNC:9298]	0.031695534
ENSG00000158292	GPR153	G protein-coupled receptor 153 [Source:HGNC Symbol;Acc:HGNC:23618]	0.031750316
ENSG00000130382	MLLT1	"MLLT1, super elongation complex subunit [Source:HGNC Symbol;Acc:HGNC:7134]"	0.031828022
ENSG00000269352	PTOV1-AS2	PTOV1 antisense RNA 2 [Source:HGNC Symbol;Acc:HGNC:51284]	0.031850457
ENSG00000162585	FAAP20	Fanconi anemia core complex associated protein 20 [Source:HGNC Symbol;Acc:HGNC:26428]	0.0320507
ENSG00000157240	FZD1	frizzled class receptor 1 [Source:HGNC Symbol;Acc:HGNC:4038]	0.032151732
ENSG00000135736	CCDC102A	coiled-coil domain containing 102A [Source:HGNC Symbol;Acc:HGNC:28097]	0.032302006
ENSG00000020181	ADGRA2	adhesion G protein-coupled receptor A2 [Source:HGNC Symbol;Acc:HGNC:17849]	0.032424937
ENSG00000198546	ZNF511	zinc finger protein 511 [Source:HGNC Symbol;Acc:HGNC:28445]	0.032576231
ENSG00000123144	TRIR	telomerase RNA component interacting RNase [Source:HGNC Symbol;Acc:HGNC:28424]	0.032671184
ENSG00000156860	FBR5	fibrosin [Source:HGNC Symbol;Acc:HGNC:20442]	0.032671184
ENSG00000162910	MRPL55	mitochondrial ribosomal protein L55 [Source:HGNC Symbol;Acc:HGNC:16686]	0.032697662
ENSG00000130731	METTL26	methyltransferase like 26 [Source:HGNC Symbol;Acc:HGNC:14141]	0.032833764
ENSG00000101986	ABCD1	ATP binding cassette subfamily D member 1 [Source:HGNC Symbol;Acc:HGNC:61]	0.032886018
ENSG00000020633	RUNX3	runt related transcription factor 3 [Source:HGNC Symbol;Acc:HGNC:10473]	0.033016587
ENSG00000184640	9-Sep	septin 9 [Source:HGNC Symbol;Acc:HGNC:7323]	0.033101928
ENSG00000260521	NA	NA	0.033101928
ENSG00000125787	GNRH2	gonadotropin releasing hormone 2 [Source:HGNC Symbol;Acc:HGNC:4420]	0.033349502
ENSG00000229391	HLA-DRB6	"major histocompatibility complex, class II, DR beta 6 (pseudogene) [Source:HGNC Symbol;Acc:HGNC:4954]"	0.033349502
ENSG00000160223	ICOSLG	inducible T cell costimulator ligand [Source:HGNC Symbol;Acc:HGNC:17087]	0.033394348
ENSG00000105204	DYRK1B	dual specificity tyrosine phosphorylation regulated kinase 1B [Source:HGNC Symbol;Acc:HGNC:3092]	0.033465567
ENSG00000142173	COL6A2	collagen type VI alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2212]	0.033483825
ENSG00000169710	FASN	fatty acid synthase [Source:HGNC Symbol;Acc:HGNC:3594]	0.033483825
ENSG00000176533	GNG7	G protein subunit gamma 7 [Source:HGNC Symbol;Acc:HGNC:4410]	0.033483825
ENSG00000179253			0.033483825
ENSG00000169972	PUSL1	pseudouridylate synthase-like 1 [Source:HGNC Symbol;Acc:HGNC:26914]	0.033509544
ENSG00000160360	GPSM1	G protein signaling modulator 1 [Source:HGNC Symbol;Acc:HGNC:17858]	0.033771567
ENSG00000171159	C9orf16	chromosome 9 open reading frame 16 [Source:HGNC Symbol;Acc:HGNC:17823]	0.033853634
ENSG00000215375	MYL5	myosin light chain 5 [Source:HGNC Symbol;Acc:HGNC:7586]	0.033853634

ENSG00000105402	NAPA	NSF attachment protein alpha [Source:HGNC Symbol;Acc:HGNC:7641]	0.034044441
ENSG00000038532	CLEC16A	C-type lectin domain containing 16A [Source:HGNC Symbol;Acc:HGNC:29013]	0.034108157
ENSG00000165175	MID1IP1	MID1 interacting protein 1 [Source:HGNC Symbol;Acc:HGNC:20715]	0.03418982
ENSG00000166947	EPB42	erythrocyte membrane protein band 4.2 [Source:HGNC Symbol;Acc:HGNC:3381]	0.03418982
ENSG00000168286	THAP11	THAP domain containing 11 [Source:HGNC Symbol;Acc:HGNC:23194]	0.03418982
ENSG00000168476	REEP4	receptor accessory protein 4 [Source:HGNC Symbol;Acc:HGNC:26176]	0.034591261
ENSG00000107521	HPS1	"HPS1, biogenesis of lysosomal organelles complex 3 subunit 1 [Source:HGNC Symbol;Acc:HGNC:5163]"	0.034688533 0.034821851
ENSG00000267436	CABIN1	calcineurin binding protein 1	0.034858474
ENSG00000099991		[Source:HGNC Symbol;Acc:HGNC:24187]	
ENSG00000169718	DUS1L	dihydrouridine synthase 1 like [Source:HGNC Symbol;Acc:HGNC:30086]	0.034980702
ENSG00000105325	FZR1	fizzy and cell division cycle 20 related 1 [Source:HGNC Symbol;Acc:HGNC:24824]	0.035034499
ENSG00000167291	TBC1D16	TBC1 domain family member 16 [Source:HGNC Symbol;Acc:HGNC:28356]	0.035082388 0.035085538
ENSG00000213399	CHST2	carbohydrate sulfotransferase 2	0.035106231
ENSG00000175040		[Source:HGNC Symbol;Acc:HGNC:1970]	
ENSG00000228544	CCDC183-AS1	CCDC183 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44105]	0.035154264
ENSG00000167658	EEF2	eukaryotic translation elongation factor 2 [Source:HGNC Symbol;Acc:HGNC:3214]	0.03521308
ENSG00000090238	YPEL3	yippee like 3 [Source:HGNC Symbol;Acc:HGNC:18327]	0.035223199
ENSG00000172508	CARNS1	carnosine synthase 1 [Source:HGNC Symbol;Acc:HGNC:29268]	0.03555645
ENSG00000173272	MZT2A	mitotic spindle organizing protein 2A [Source:HGNC Symbol;Acc:HGNC:33187]	0.035664739
ENSG00000141522	ARHGDIA	Rho GDP dissociation inhibitor alpha [Source:HGNC Symbol;Acc:HGNC:678]	0.03575577
ENSG00000149541	B3GAT3	"beta-1,3-glucuronyltransferase 3 [Source:HGNC Symbol;Acc:HGNC:923]"	0.03575577
ENSG00000171206	TRIM8	tripartite motif containing 8 [Source:HGNC Symbol;Acc:HGNC:15579]	0.035790036
ENSG00000027869	SH2D2A	SH2 domain containing 2A [Source:HGNC Symbol;Acc:HGNC:10821]	0.035871776
ENSG00000149823	VPS51	"VPS51, GARP complex subunit [Source:HGNC Symbol;Acc:HGNC:1172]"	0.035906645 0.035938935
ENSG00000196355	NA	NA	0.035996581
ENSG00000165804	ZNF219	zinc finger protein 219 [Source:HGNC Symbol;Acc:HGNC:13011]	
ENSG00000177542	SLC25A22	solute carrier family 25 member 22 [Source:HGNC Symbol;Acc:HGNC:19954]	0.035996581
ENSG00000130202	NECTIN2	nectin cell adhesion molecule 2 [Source:HGNC Symbol;Acc:HGNC:9707]	0.036025366
ENSG00000006638	TBXA2R	thromboxane A2 receptor [Source:HGNC Symbol;Acc:HGNC:11608]	0.036065767
ENSG00000025770	NCAPH2	non-SMC condensin II complex subunit H2 [Source:HGNC Symbol;Acc:HGNC:25071]	0.036065767
ENSG00000100316	RPL3	ribosomal protein L3 [Source:HGNC Symbol;Acc:HGNC:10332]	0.036065767
ENSG00000110665	C11orf21	chromosome 11 open reading frame 21 [Source:HGNC Symbol;Acc:HGNC:13231]	0.036065767
ENSG00000160445	ZER1	zyg-11 related cell cycle regulator [Source:HGNC Symbol;Acc:HGNC:30960]	0.036065767
ENSG00000173786	CNP	"2',3'-cyclic nucleotide 3' phosphodiesterase [Source:HGNC Symbol;Acc:HGNC:2158]"	0.036065767 0.036065767
ENSG00000229368	LMNA	lamin A/C	0.036188381
ENSG00000160789		[Source:HGNC Symbol;Acc:HGNC:6636]	

ENSG00000166189	HPS6	"HPS6, biogenesis of lysosomal organelles complex 2 subunit 3 [Source:HGNC Symbol;Acc:HGNC:18817]"	0.036188381 0.036342968
ENSG00000261226			
ENSG00000185049	NELFA	negative elongation factor complex member A [Source:HGNC Symbol;Acc:HGNC:12768]	0.036383164
ENSG00000005882	PDK2	pyruvate dehydrogenase kinase 2 [Source:HGNC Symbol;Acc:HGNC:8810]	0.036423123
ENSG00000163050	COQ8A	coenzyme Q8A [Source:HGNC Symbol;Acc:HGNC:16812]	0.036459828
ENSG00000060138	YBX3	Y-box binding protein 3 [Source:HGNC Symbol;Acc:HGNC:2428]	0.03651176
ENSG00000122971	ACADS	acyl-CoA dehydrogenase short chain [Source:HGNC Symbol;Acc:HGNC:90]	0.036511776
ENSG00000205927	OLIG2	oligodendrocyte transcription factor 2 [Source:HGNC Symbol;Acc:HGNC:9398]	0.036582868
ENSG00000092096	SLC22A17	solute carrier family 22 member 17 [Source:HGNC Symbol;Acc:HGNC:23095]	0.036619295
ENSG00000090554	FLT3LG	fms related tyrosine kinase 3 ligand [Source:HGNC Symbol;Acc:HGNC:3766]	0.036780281
ENSG00000078902	TOLLIP	toll interacting protein [Source:HGNC Symbol;Acc:HGNC:16476]	0.036796695
ENSG00000136802	LRRC8A	leucine rich repeat containing 8 VRAC subunit A [Source:HGNC Symbol;Acc:HGNC:19027]	0.036860551 0.036972133
ENSG00000236976			
ENSG00000100908	EMC9	ER membrane protein complex subunit 9 [Source:HGNC Symbol;Acc:HGNC:20273]	0.037054085
ENSG00000105364	MRPL4	mitochondrial ribosomal protein L4 [Source:HGNC Symbol;Acc:HGNC:14276]	0.03712252
ENSG00000157184	CPT2	carnitine palmitoyltransferase 2 [Source:HGNC Symbol;Acc:HGNC:2330]	0.03712252
ENSG00000168056	LTBP3	latent transforming growth factor beta binding protein 3 [Source:HGNC Symbol;Acc:HGNC:6716]	0.037135417
ENSG00000196313	POM121	POM121 transmembrane nucleoporin [Source:HGNC Symbol;Acc:HGNC:19702]	0.037140956
ENSG00000170604	IRF2BP1	interferon regulatory factor 2 binding protein 1 [Source:HGNC Symbol;Acc:HGNC:21728]	0.037222007
ENSG00000110697	PITPNM1	phosphatidylinositol transfer protein membrane associated 1 [Source:HGNC Symbol;Acc:HGNC:9003]	0.037374978
ENSG00000100348	TXN2	thioredoxin 2 [Source:HGNC Symbol;Acc:HGNC:17772]	0.037546969
ENSG00000102007	PLP2	proteolipid protein 2 [Source:HGNC Symbol;Acc:HGNC:9087]	0.037630556
ENSG00000132005	RFX1	regulatory factor X1 [Source:HGNC Symbol;Acc:HGNC:9982]	0.037671165
ENSG00000141499	WRAP53	WD repeat containing antisense to TP53 [Source:HGNC Symbol;Acc:HGNC:25522]	0.037678229
ENSG00000189114	BLOC1S3	biogenesis of lysosomal organelles complex 1 subunit 3 [Source:HGNC Symbol;Acc:HGNC:20914]	0.037963219
ENSG00000123154	WDR83	WD repeat domain 83 [Source:HGNC Symbol;Acc:HGNC:32672]	0.038059131
ENSG00000127663	KDM4B	lysine demethylase 4B [Source:HGNC Symbol;Acc:HGNC:29136]	0.038059131
ENSG00000175274	TP53I11	tumor protein p53 inducible protein 11 [Source:HGNC Symbol;Acc:HGNC:16842]	0.038059131
ENSG00000249115	HAUS5	HAUS augmin like complex subunit 5 [Source:HGNC Symbol;Acc:HGNC:29130]	0.038059131
ENSG00000130764	LRRC47	leucine rich repeat containing 47 [Source:HGNC Symbol;Acc:HGNC:29207]	0.038286929
ENSG00000176946	THAP4	THAP domain containing 4 [Source:HGNC Symbol;Acc:HGNC:23187]	0.038286929
ENSG00000137497	NUMA1	nuclear mitotic apparatus protein 1 [Source:HGNC Symbol;Acc:HGNC:8059]	0.038678067
ENSG00000143761	ARF1	ADP ribosylation factor 1 [Source:HGNC Symbol;Acc:HGNC:652]	0.038678067
ENSG00000198931	APRT	adenine phosphoribosyltransferase	

ENSG00000186174	BCL9L	[Source:HGNC Symbol;Acc:HGNC:626] B cell CLL/lymphoma 9 like	0.038678067
ENSG00000104894	CD37	[Source:HGNC Symbol;Acc:HGNC:23688] CD37 molecule	0.039375488
ENSG00000235314	LINC00957	[Source:HGNC Symbol;Acc:HGNC:1666] long intergenic non-protein coding RNA 957	0.039523734
ENSG00000076864	RAP1GAP	[Source:HGNC Symbol;Acc:HGNC:22332] RAP1 GTPase activating protein	0.039534059
ENSG00000179348	GATA2	[Source:HGNC Symbol;Acc:HGNC:9858] GATA binding protein 2	0.039534171
ENSG00000223496	EXOSC6	[Source:HGNC Symbol;Acc:HGNC:4171] exosome component 6	0.039644975
ENSG00000174004	NRROS	[Source:HGNC Symbol;Acc:HGNC:19055] negative regulator of reactive oxygen species	0.039646513
ENSG00000185736	ADARB2	[Source:HGNC Symbol;Acc:HGNC:24613] "adenosine deaminase, RNA specific B2 (inactive)	0.039697731
ENSG00000177595	PIDD1	[Source:HGNC Symbol;Acc:HGNC:227]" p53-induced death domain protein 1	0.039813584
ENSG00000114767	RRP9	[Source:HGNC Symbol;Acc:HGNC:16491] "ribosomal RNA processing 9, U3 small nucleolar RNA binding protein	0.039841437
ENSG00000198336	MYL4	[Source:HGNC Symbol;Acc:HGNC:16829]" myosin light chain 4	0.039852243
ENSG00000267427	NA	[Source:HGNC Symbol;Acc:HGNC:7585] NA	0.040061329
ENSG00000123159	GIPC1	[Source:HGNC Symbol;Acc:HGNC:1226] GIPC PDZ domain containing family member 1	0.040061329
ENSG00000139405	RITA1	[Source:HGNC Symbol;Acc:HGNC:25925] RBPJ interacting and tubulin associated 1	0.040207239
ENSG00000149929	HIRIP3	[Source:HGNC Symbol;Acc:HGNC:4917] HIRA interacting protein 3	0.040571361
ENSG00000198517	MAFK	[Source:HGNC Symbol;Acc:HGNC:6782] MAF bZIP transcription factor K	0.040590193
ENSG00000164897	TMUB1	[Source:HGNC Symbol;Acc:HGNC:21709] transmembrane and ubiquitin like domain containing 1	0.040938395
ENSG00000070047	PHRF1	[Source:HGNC Symbol;Acc:HGNC:24351] PHD and ring finger domains 1	0.041015111
ENSG00000100403	ZC3H7B	[Source:HGNC Symbol;Acc:HGNC:30869] zinc finger CCCH-type containing 7B	0.041151359
ENSG00000205147	NA	[Source:HGNC Symbol;Acc:HGNC:18155] NA	0.041207854
ENSG00000184470	TXNRD2	[Source:HGNC Symbol;Acc:HGNC:21198] thioredoxin reductase 2	0.04134465
ENSG00000103145	HCFC1R1	[Source:HGNC Symbol;Acc:HGNC:21198] host cell factor C1 regulator 1	0.041366672
ENSG00000087086	FTL	[Source:HGNC Symbol;Acc:HGNC:3999] ferritin light chain	0.041631474
ENSG00000102870	ZNF629	[Source:HGNC Symbol;Acc:HGNC:29008] zinc finger protein 629	0.041631474
ENSG00000181444	ZNF467	[Source:HGNC Symbol;Acc:HGNC:23154] zinc finger protein 467	0.041868067
ENSG00000142444	TIMM29	[Source:HGNC Symbol;Acc:HGNC:25152] translocase of inner mitochondrial membrane 29	0.041933219
ENSG00000204252	HLA-DOA	[Source:HGNC Symbol;Acc:HGNC:4936]" "major histocompatibility complex, class II, DO alpha	0.041944166
ENSG00000224051	CPTP	[Source:HGNC Symbol;Acc:HGNC:28116] ceramide-1-phosphate transfer protein	0.041944166
ENSG00000103253	HAGHL	[Source:HGNC Symbol;Acc:HGNC:14177] hydroxyacylglutathione hydrolase like	0.042027801
ENSG00000011590	ZBTB32	[Source:HGNC Symbol;Acc:HGNC:16763] zinc finger and BTB domain containing 32	0.042101327
ENSG00000182566	CLEC4G	[Source:HGNC Symbol;Acc:HGNC:24591] C-type lectin domain family 4 member G	0.042114834
ENSG00000244165	P2RY11	[Source:HGNC Symbol;Acc:HGNC:8540] purinergic receptor P2Y11	0.042114834
ENSG00000267275			0.042114834
ENSG00000173327	MAP3K11	[Source:HGNC Symbol;Acc:HGNC:6850] mitogen-activated protein kinase kinase kinase 11	0.042395519

ENSG00000149418	ST14	suppression of tumorigenicity 14	
		[Source:HGNC Symbol;Acc:HGNC:11344]	0.04243773
ENSG00000112658	SRF	serum response factor	
		[Source:HGNC Symbol;Acc:HGNC:11291]	0.042440717
ENSG00000106003	LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	
		[Source:HGNC Symbol;Acc:HGNC:6560]	0.042450091
ENSG00000164896	FASTK	Fas activated serine/threonine kinase	
		[Source:HGNC Symbol;Acc:HGNC:24676]	0.042450091
ENSG00000196544	BORCS6	BLOC-1 related complex subunit 6	
		[Source:HGNC Symbol;Acc:HGNC:25939]	0.042514351
ENSG00000134107	BHLHE40	basic helix-loop-helix family member e40	
		[Source:HGNC Symbol;Acc:HGNC:1046]	0.042517218
ENSG00000151176	PLBD2	phospholipase B domain containing 2	
		[Source:HGNC Symbol;Acc:HGNC:27283]	0.042582368
ENSG00000183397	C19orf71	chromosome 19 open reading frame 71	
		[Source:HGNC Symbol;Acc:HGNC:34496]	0.042902315
ENSG00000105738	SIPA1L3	signal induced proliferation associated 1 like 3	
		[Source:HGNC Symbol;Acc:HGNC:23801]	0.043052047
ENSG00000157353	FUK	fucokinase	
		[Source:HGNC Symbol;Acc:HGNC:29500]	0.043381308
ENSG00000126062	TMEM115	transmembrane protein 115	
		[Source:HGNC Symbol;Acc:HGNC:30055]	0.043382452
ENSG00000179632	MAF1	"MAF1 homolog, negative regulator of RNA polymerase III	
		[Source:HGNC Symbol;Acc:HGNC:24966]"	0.043386409
ENSG00000254910			0.043544967
ENSG00000073111	MCM2	minichromosome maintenance complex component 2	
		[Source:HGNC Symbol;Acc:HGNC:6944]	0.043556269
ENSG00000105698	USF2	"upstream transcription factor 2, c-fos interacting	
		[Source:HGNC Symbol;Acc:HGNC:12594]"	0.043737282
ENSG00000261043			0.043870446
ENSG00000078808	SDF4	stromal cell derived factor 4	
		[Source:HGNC Symbol;Acc:HGNC:24188]	0.043914575
ENSG00000182154	MRPL41	mitochondrial ribosomal protein L41	
		[Source:HGNC Symbol;Acc:HGNC:14492]	0.044022575
ENSG00000237476	LINC01637	long intergenic non-protein coding RNA 1637	
		[Source:HGNC Symbol;Acc:HGNC:52424]	0.044022575
ENSG00000264577			0.044022575
ENSG00000160877	NACC1	nucleus accumbens associated 1	
		[Source:HGNC Symbol;Acc:HGNC:20967]	0.044046233
ENSG00000162032	SPSB3	sp1A/ryanodine receptor domain and SOCS box containing 3	
		[Source:HGNC Symbol;Acc:HGNC:30629]	0.044046233
ENSG00000123933	MXD4	MAX dimerization protein 4	
		[Source:HGNC Symbol;Acc:HGNC:13906]	0.044146857
ENSG00000149260	CAPN5	calpain 5 [Source:HGNC Symbol;Acc:HGNC:1482]	0.044146857
ENSG00000197324	LRP10	LDL receptor related protein 10	
		[Source:HGNC Symbol;Acc:HGNC:14553]	0.044146857
ENSG00000128011	LRFN1	leucine rich repeat and fibronectin type III domain containing 1	
		[Source:HGNC Symbol;Acc:HGNC:29290]	0.044424476
ENSG00000103126	AXIN1	axin 1 [Source:HGNC Symbol;Acc:HGNC:903]	0.044490553
ENSG00000183134	PTGDR2	prostaglandin D2 receptor 2	
		[Source:HGNC Symbol;Acc:HGNC:4502]	0.044490553
ENSG00000185905	C16orf54	chromosome 16 open reading frame 54	
		[Source:HGNC Symbol;Acc:HGNC:26649]	0.044574634
ENSG00000185905	C16orf54	chromosome 16 open reading frame 54	
		[Source:HGNC Symbol;Acc:HGNC:26649]	0.044574634
ENSG00000176974	SHMT1	serine hydroxymethyltransferase 1	
		[Source:HGNC Symbol;Acc:HGNC:10850]	0.044717969
ENSG00000105327	BBC3	BCL2 binding component 3	
		[Source:HGNC Symbol;Acc:HGNC:17868]	0.044899327
ENSG00000212123	PRR22	proline rich 22	
		[Source:HGNC Symbol;Acc:HGNC:28354]	0.044899327
ENSG00000171798	KNDC1	kinase non-catalytic C-lobe domain containing 1	
		[Source:HGNC Symbol;Acc:HGNC:29374]	0.045139854
ENSG00000073150	PANX2	pannexin 2	
		[Source:HGNC Symbol;Acc:HGNC:8600]	0.045237232
ENSG00000126453	BCL2L12	BCL2 like 12	
		[Source:HGNC Symbol;Acc:HGNC:13787]	0.04527356
ENSG00000159692	CTBP1	C-terminal binding protein 1	

ENSG00000105248	CCDC94	[Source:HGNC Symbol;Acc:HGNC:2494] coiled-coil domain containing 94	0.04527356
ENSG00000101220	C20orf27	[Source:HGNC Symbol;Acc:HGNC:25518] chromosome 20 open reading frame 27	0.045450088
ENSG00000188735	TMEM120B	[Source:HGNC Symbol;Acc:HGNC:15873] transmembrane protein 120B	0.045474144
ENSG00000149476	TKFC	[Source:HGNC Symbol;Acc:HGNC:32008] triokinase and FMN cyclase	0.045474144
ENSG00000100105	PATZ1	[Source:HGNC Symbol;Acc:HGNC:24552] POZ/BTB and AT hook containing zinc finger 1	0.045497488
ENSG00000136295	TTYH3	[Source:HGNC Symbol;Acc:HGNC:13071] tweety family member 3	0.045500961
ENSG00000104823	ECH1	[Source:HGNC Symbol;Acc:HGNC:22222] enoyl-CoA hydratase 1	0.045528908
ENSG00000167930	FAM234A	[Source:HGNC Symbol;Acc:HGNC:3149] family with sequence similarity 234 member A	0.045555559
ENSG00000125505	MBOAT7	[Source:HGNC Symbol;Acc:HGNC:14163] membrane bound O-acyltransferase domain containing 7	0.045584551
ENSG00000136720	HS6ST1	[Source:HGNC Symbol;Acc:HGNC:15505] heparan sulfate 6-O-sulfotransferase 1	0.045601783
ENSG00000156853	ZNF689	[Source:HGNC Symbol;Acc:HGNC:5201] zinc finger protein 689	0.045601783
ENSG00000176108	CHMP6	[Source:HGNC Symbol;Acc:HGNC:25173] charged multivesicular body protein 6	0.045601783
ENSG00000205336	ADGRG1	[Source:HGNC Symbol;Acc:HGNC:25675] adhesion G protein-coupled receptor G1	0.045601783
ENSG00000186350	RXRA	[Source:HGNC Symbol;Acc:HGNC:4512] retinoid X receptor alpha	0.045601783
ENSG00000164849	GPR146	[Source:HGNC Symbol;Acc:HGNC:10477] G protein-coupled receptor 146	0.045691236
ENSG00000124313	IQSEC2	[Source:HGNC Symbol;Acc:HGNC:21718] IQ motif and Sec7 domain 2	0.045781
ENSG00000148341	SH3GLB2	[Source:HGNC Symbol;Acc:HGNC:29059] "SH3 domain containing GRB2 like, endophilin B2	0.045921742
ENSG00000213654	GPSM3	[Source:HGNC Symbol;Acc:HGNC:10834]" G protein signaling modulator 3	0.045931004
ENSG00000171219	CDC42BPG	[Source:HGNC Symbol;Acc:HGNC:13945] CDC42 binding protein kinase gamma	0.045963746
ENSG00000125741	OPA3	[Source:HGNC Symbol;Acc:HGNC:29829] "OPA3, outer mitochondrial membrane lipid metabolism regulator	0.046017697
ENSG00000089693	MLF2	[Source:HGNC Symbol;Acc:HGNC:8142]" myeloid leukemia factor 2	0.046210538
ENSG00000267283		[Source:HGNC Symbol;Acc:HGNC:7126] 0.046269835	
ENSG00000238164	TNFRSF14-AS1	[Source:HGNC Symbol;Acc:HGNC:26966] TNFRSF14 antisense RNA 1	0.046536749
ENSG00000167815	PRDX2	[Source:HGNC Symbol;Acc:HGNC:9353] peroxiredoxin 2	0.046584081
ENSG00000140564	FURIN	[Source:HGNC Symbol;Acc:HGNC:8568]" "furin, paired basic amino acid cleaving enzyme	0.046640005
ENSG00000059122	FLYWCH1	[Source:HGNC Symbol;Acc:HGNC:25404] FLYWCH-type zinc finger 1	0.046653045
ENSG00000070423	RNF126	[Source:HGNC Symbol;Acc:HGNC:21151] ring finger protein 126	0.046934685
ENSG00000027847	B4GALT7	[Source:HGNC Symbol;Acc:HGNC:930]" "beta-1,4-galactosyltransferase 7	0.047070015
ENSG00000108518	PFN1	[Source:HGNC Symbol;Acc:HGNC:8881] profilin 1	0.047130774
ENSG00000110711	AIP	[Source:HGNC Symbol;Acc:HGNC:358] aryl hydrocarbon receptor interacting protein	0.047157356
ENSG00000164068	RNF123	[Source:HGNC Symbol;Acc:HGNC:21148] ring finger protein 123	0.04721490
ENSG00000137216	TMEM63B	[Source:HGNC Symbol;Acc:HGNC:17735] transmembrane protein 63B	0.047214902
ENSG00000179588	ZFPM1	[Source:HGNC Symbol;Acc:HGNC:19762]" "zinc finger protein, FOG family member 1	0.047244731
ENSG00000188070	C11orf95	[Source:HGNC Symbol;Acc:HGNC:28449] chromosome 11 open reading frame 95	0.047461433
			0.047461433

ENSG00000162722	TRIM58	tripartite motif containing 58	
		[Source:HGNC Symbol;Acc:HGNC:24150]	0.047475759
ENSG00000068724	TTC7A	tetratricopeptide repeat domain 7A	
		[Source:HGNC Symbol;Acc:HGNC:19750]	0.0476766
ENSG00000142227	EMP3	epithelial membrane protein 3	
		[Source:HGNC Symbol;Acc:HGNC:3335]	0.0476766
ENSG00000159714	ZDHHC1	zinc finger DHHC-type containing 1	
		[Source:HGNC Symbol;Acc:HGNC:17916]	0.04772167
ENSG00000196182	STK40	serine/threonine kinase 40	
		[Source:HGNC Symbol;Acc:HGNC:21373]	0.047779011
ENSG00000099875	MKNK2	MAP kinase interacting serine/threonine kinase 2	
		[Source:HGNC Symbol;Acc:HGNC:7111]	0.047824795
ENSG00000132514	CLEC10A	C-type lectin domain containing 10A	
		[Source:HGNC Symbol;Acc:HGNC:16916]	0.047824795
ENSG00000197982	C1orf122	chromosome 1 open reading frame 122	
		[Source:HGNC Symbol;Acc:HGNC:24789]	0.047824795
ENSG00000204348	DXO	decapping exoribonuclease	
		[Source:HGNC Symbol;Acc:HGNC:2992]	0.047913021
ENSG00000259856	RAB43P1	RAB43 pseudogene 1	
		[Source:HGNC Symbol;Acc:HGNC:33153]	0.048194625
ENSG00000103254	FAM173A	family with sequence similarity 173 member A	
		[Source:HGNC Symbol;Acc:HGNC:14152]	0.048206847
ENSG00000196453	ZNF777	zinc finger protein 777	
		[Source:HGNC Symbol;Acc:HGNC:22213]	0.048246269
ENSG00000167173	C15orf39	chromosome 15 open reading frame 39	
		[Source:HGNC Symbol;Acc:HGNC:24497]	0.048259142
ENSG00000172534	HCFC1	host cell factor C1	
		[Source:HGNC Symbol;Acc:HGNC:4839]	0.04840783
ENSG00000198804	MT-CO1	mitochondrially encoded cytochrome c oxidase I	
		[Source:HGNC Symbol;Acc:HGNC:7419]	0.048409706
ENSG00000244486	SCARF2	scavenger receptor class F member 2	
		[Source:HGNC Symbol;Acc:HGNC:19869]	0.048617065
ENSG00000125652	ALKBH7	alkB homolog 7	
		[Source:HGNC Symbol;Acc:HGNC:21306]	0.048746819
ENSG00000176101	SSNA1	SS nuclear autoantigen 1	
		[Source:HGNC Symbol;Acc:HGNC:11321]	0.048934402
ENSG00000129103	SUMF2	sulfatase modifying factor 2	
		[Source:HGNC Symbol;Acc:HGNC:20415]	0.048950286
ENSG00000115756	HPCAL1	hippocalcin like 1	
		[Source:HGNC Symbol;Acc:HGNC:5145]	0.049011448
ENSG00000243566	UPK3B	uroplakin 3B	
		[Source:HGNC Symbol;Acc:HGNC:21444]	0.049012128
ENSG00000149150	SLC43A1	solute carrier family 43 member 1	
		[Source:HGNC Symbol;Acc:HGNC:9225]	0.049128197
ENSG00000103227	LMF1	lipase maturation factor 1	
		[Source:HGNC Symbol;Acc:HGNC:14154]	0.049193782
ENSG00000271959			0.049311473
ENSG00000261222			0.049471704
ENSG00000126217	MCF2L	MCF.2 cell line derived transforming sequence like	
		[Source:HGNC Symbol;Acc:HGNC:14576]	0.049648177
ENSG00000104964	AES	amino-terminal enhancer of split	
		[Source:HGNC Symbol;Acc:HGNC:307]	0.049726662
ENSG00000127831	VIL1	villin 1	
		[Source:HGNC Symbol;Acc:HGNC:12690]	0.049726662
ENSG00000169738	DCXR	dicarbonyl and L-xylulose reductase	
		[Source:HGNC Symbol;Acc:HGNC:18985]	0.049760492
ENSG00000086015	MAST2	microtubule associated serine/threonine kinase 2	
		[Source:HGNC Symbol;Acc:HGNC:19035]	0.04998097

TABLE 3
AC3 GENES

<u>Ensembl</u>	<u>Symbol</u>	<u>Description</u>	<u>Score?/AUC?</u>
ENSG00000251705	RNA5-8SP6	"RNA, 5.8S ribosomal pseudogene 6 [Source:HGNC Symbol;Acc:HGNC:41960]"	5.29E-67

ENSG00000133110	POSTN	periostin [Source:HGNC Symbol;Acc:HGNC:16953]	1.78E-06
ENSG00000142449	FBN3	fibrillin 3 [Source:HGNC Symbol;Acc:HGNC:18794]	2.85E-05
ENSG00000183668	PSG9	pregnancy specific beta-1-glycoprotein 9 [Source:HGNC Symbol;Acc:HGNC:9526]	9.26E-05
ENSG00000258628			0.000107247
ENSG00000260290			0.000163871
ENSG00000224367	OACYLP	"O-acyltransferase like, pseudogene [Source:HGNC Symbol;Acc:HGNC:44362]"	0.000275943
ENSG00000108018	SORCS1	sortilin related VPS10 domain containing receptor 1 [Source:HGNC Symbol;Acc:HGNC:16697]	0.000366056
ENSG00000135454	B4GALNT1	"beta-1,4-N-acetyl-galactosaminyltransferase 1 [Source:HGNC Symbol;Acc:HGNC:41117]"	0.000429017
ENSG00000266172	NA	NA	0.000574378
ENSG00000173769	TOPAZ1	testis and ovary specific PAZ domain containing 1 [Source:HGNC Symbol; Acc:HGNC:24746]	0.00059023
ENSG00000181378	CFAP65	cilia and flagella associated protein 65 [Source:HGNC Symbol;Acc:HGNC:25325]	0.000602774
ENSG00000174498	IGDCC3	immunoglobulin superfamily DCC subclass member 3 [Source:HGNC Symbol;Acc:HGNC:9700]	0.00062895
ENSG00000089116	LHX5	LIM homeobox 5 [Source:HGNC Symbol;Acc:HGNC:14216]	0.000639272
ENSG00000161270	NPHS1	"NPHS1, nephrin [Source:HGNC Symbol;Acc:HGNC:7908]"	0.000697583
ENSG00000006210	CX3CL1	C-X3-C motif chemokine ligand 1 [Source:HGNC Symbol;Acc:HGNC:10647]	0.000730947
ENSG00000249618	LINC02465	long intergenic non-protein coding RNA 2465 [Source:HGNC Symbol;Acc:HGNC:53403]	0.000730947
ENSG00000253871			0.000789684
ENSG00000130540	SULT4A1	sulfotransferase family 4A member 1 [Source:HGNC Symbol;Acc:HGNC:14903]	0.000791019
ENSG00000148942	SLC5A12	solute carrier family 5 member 12 [Source:HGNC Symbol;Acc:HGNC:28750]	0.000819378
ENSG00000226790	HNRNPA3P1	heterogeneous nuclear ribonucleoprotein A3 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:13729]	0.000826721
ENSG00000160460	SPTBN4	"spectrin beta, non-erythrocytic 4 [Source:HGNC Symbol;Acc:HGNC:14896]"	0.000837162
ENSG00000243130	PSG11	pregnancy specific beta-1-glycoprotein 11 [Source:HGNC Symbol;Acc:HGNC:9516]	0.000837162
ENSG00000244694	PTCHD4	patched domain containing 4 [Source:HGNC Symbol;Acc:HGNC:21345]	0.000837162
ENSG00000249464	LINC01091	long intergenic non-protein coding RNA 1091 [Source:HGNC Symbol;Acc:HGNC:27721]	0.000837162
ENSG00000011677	GABRA3	gamma-aminobutyric acid type A receptor alpha3 subunit [Source:HGNC Symbol;Acc:HGNC:4077]	0.000896018
ENSG00000256343			0.00097441
ENSG00000039139	DNAH5	dynein axonemal heavy chain 5 [Source:HGNC Symbol;Acc:HGNC:2950]	0.001236713
ENSG00000130635	COL5A1	collagen type V alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2209]	0.001236713
ENSG00000242512	LINC01206	long intergenic non-protein coding RNA 1206 [Source:HGNC Symbol;Acc:HGNC:49637]	0.001253551
ENSG00000164692	COL1A2	collagen type I alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2198]	0.00126185
ENSG00000259841	LINC01566	long intergenic non-protein coding RNA 1566 [Source:HGNC Symbol;Acc:HGNC:27555]	0.001274332
ENSG00000170777	TPD52L3	tumor protein D52 like 3 [Source:HGNC Symbol;Acc:HGNC:23382]	0.001484087
ENSG00000186487	MYT1L	myelin transcription factor 1 like [Source:HGNC Symbol;Acc:HGNC:7623]	0.001774703
ENSG00000082175	PGR	progesterone receptor [Source:HGNC Symbol;Acc:HGNC:8910]	0.001879127
ENSG00000205922	ONECUT3	one cut homeobox 3 [Source:HGNC Symbol;Acc:HGNC:13399]	0.001993667

ENSG00000249341			0.002126073
ENSG00000139865	TTC6	tetratricopeptide repeat domain 6	
		[Source:HGNC Symbol;Acc:HGNC:19739]	0.002268239
ENSG00000154478	GPR26	G protein-coupled receptor 26	
		[Source:HGNC Symbol;Acc:HGNC:4481]	0.002268239
ENSG00000174358	SLC6A19	solute carrier family 6 member 19	
		[Source:HGNC Symbol;Acc:HGNC:27960]	0.002268239
ENSG00000235711	ANKRD34C	ankyrin repeat domain 34C	
		[Source:HGNC Symbol;Acc:HGNC:33888]	0.002268239
ENSG00000170381	SEMA3E	semaphorin 3E	
		[Source:HGNC Symbol;Acc:HGNC:10727]	0.002327494
ENSG00000142611	PRDM16	PR/SET domain 16	
		[Source:HGNC Symbol;Acc:HGNC:14000]	0.002350766
ENSG00000205396	LINC00661	long intergenic non-protein coding RNA 661	
		[Source:HGNC Symbol;Acc:HGNC:27002]	0.002366966
ENSG00000253288			0.00239082
ENSG00000171435	KSR2	kinase suppressor of ras 2	
		[Source:HGNC Symbol;Acc:HGNC:18610]	0.002607962
ENSG00000256616			0.002639596
ENSG00000171804	WDR87	WD repeat domain 87	
		[Source:HGNC Symbol;Acc:HGNC:29934]	0.002806683
ENSG00000237125	HAND2-AS1	HAND2 antisense RNA 1 (head to head)	
		[Source:HGNC Symbol;Acc:HGNC:48872]	0.00289999
ENSG000002406 94	PNMA2	PNMA family member 2	
		[Source:HGNC Symbol;Acc:HGNC:9159]	0.002940811
ENSG00000102452	NALCN	sodium leak channel, non-selective	
		[Source:HGNC Symbol;Acc:HGNC:19082]"	0.003094645
ENSG00000214929	SPATA31D1	SPATA31 subfamily D member 1	
		[Source:HGNC Symbol;Acc:HGNC:37283]	0.003264148
ENSG00000115041	KCNIP3	potassium voltage-gated channel interacting protein 3	
		[Source:HGNC Symbol;Acc:HGNC:15523]	0.00328034
ENSG00000185038	MROH2A	maestro heat like repeat family member 2A	
		[Source:HGNC Symbol;Acc:HGNC:27936]	0.003313878
ENSG00000138892	TTLL8	tubulin tyrosine ligase like 8	
		[Source:HGNC Symbol;Acc:HGNC:34000]	0.003497603
ENSG00000147573	TRIM55	tripartite motif containing 55	
		[Source:HGNC Symbol;Acc:HGNC:14215]	0.003573936
ENSG00000165323	FAT3	FAT atypical cadherin 3	
		[Source:HGNC Symbol;Acc:HGNC:23112]	0.003629544
ENSG00000142623	PADI1	peptidyl arginine deiminase 1	
		[Source:HGNC Symbol;Acc:HGNC:18367]	0.003697796
ENSG00000146521	LINC01558	long intergenic non-protein coding RNA 1558	
		[Source:HGNC Symbol;Acc:HGNC:21235]	0.003779666
ENSG00000125255	SLC10A2	solute carrier family 10 member 2	
		[Source:HGNC Symbol;Acc:HGNC:10906]	0.003857127
ENSG00000103855	CD276	CD276 molecule	
		[Source:HGNC Symbol;Acc:HGNC:19137]	0.004037668
ENSG00000168907	PLA2G4F	phospholipase A2 group IVF	
		[Source:HGNC Symbol;Acc:HGNC:27396]	0.00413675
ENSG00000141668	CBLN2	cerebellin 2 precursor	
		[Source:HGNC Symbol;Acc:HGNC:1544]	0.004198501
ENSG00000197991			0.004252179
ENSG00000149633	KIAA1755	KIAA1755	
		[Source:HGNC Symbol;Acc:HGNC:29372]	0.004331797
ENSG00000157927	RADIL	Rap associating with DIL domain	
		[Source:HGNC Symbol;Acc:HGNC:22226]	0.004332718
ENSG00000138759	FRAS1	Fraser extracellular matrix complex subunit 1	
		[Source:HGNC Symbol;Acc:HGNC:19185]	0.004539725
ENSG00000174963	ZIC4	Zic family member 4	
		[Source:HGNC Symbol;Acc:HGNC:20393]	0.004539725
ENSG00000177551	NHLH2	nescient helix-loop-helix 2	
		[Source:HGNC Symbol;Acc:HGNC:7818]	0.004560802
ENSG00000250230			0.004576049
ENSG00000204929			0.00461274
ENSG00000163975	MELTF	melanotransferrin	
		[Source:HGNC Symbol;Acc:HGNC:7037]	0.004655716
ENSG00000095587	TLL2	tolloid like 2	
		[Source:HGNC Symbol;Acc:HGNC:11844]	0.004686524

ENSG00000221826	PSG3	pregnancy specific beta-1-glycoprotein 3 [Source:HGNC Symbol;Acc:HGNC:9520]	0.004686524
ENSG00000105392	CRX	cone-rod homeobox [Source:HGNC Symbol;Acc:HGNC:2383]	0.004730282
ENSG00000188338	SLC38A3	solute carrier family 38 member 3 [Source:HGNC Symbol;Acc:HGNC:18044]	0.004737254
ENSG00000167654	ATCAY	"ATCAY, caytaxin [Source:HGNC Symbol;Acc:HGNC:779]"	0.004891089
ENSG00000177511	ST8SIA3	"ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 3 [Source:HGNC Symbol;Acc:HGNC:14269]"	0.00498476 0.005091461
ENSG00000215895	LYPD3	LY6/PLAUR domain containing 3 [Source:HGNC Symbol;Acc:HGNC:24880]	0.005118791
ENSG00000084636	COL16A1	collagen type XVI alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2193]	0.00516436
ENSG00000104537	ANXA13	annexin A13 [Source:HGNC Symbol;Acc:HGNC:536]	0.005166641
ENSG00000145526	CDH18	cadherin 18 [Source:HGNC Symbol;Acc:HGNC:1757]	0.005245896 0.005294938
ENSG00000161103	SFTPC	surfactant protein C [Source:HGNC Symbol;Acc:HGNC:10802]	0.005473496
ENSG00000188886	ASTL	astacin like metalloendopeptidase [Source:HGNC Symbol;Acc:HGNC:31704]	0.005530506
ENSG00000198765	SYCP1	synaptonemal complex protein 1 [Source:HGNC Symbol;Acc:HGNC:11487]	0.005554714
ENSG00000234177	LINC01114	long intergenic non-protein coding RNA 1114 [Source:HGNC Symbol;Acc:HGNC:49245]	0.005808942
ENSG00000091656	ZFHX4	zinc finger homeobox 4 [Source:HGNC Symbol;Acc:HGNC:30939]	0.005809417
ENSG00000151572	ANO4	anoctamin 4 [Source:HGNC Symbol;Acc:HGNC:23837]	0.005857886
ENSG00000178965	ERICH3	glutamate rich 3 [Source:HGNC Symbol;Acc:HGNC:25346]	0.005890875
ENSG00000248587	GDNF-AS1	GDNF antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HGNC:43592]	0.005890875
ENSG00000144908	ALDH1L1	aldehyde dehydrogenase 1 family member L1 [Source:HGNC Symbol;Acc:HGNC:3978]	0.006015103
ENSG00000152822	GRM1	glutamate metabotropic receptor 1 [Source:HGNC Symbol;Acc:HGNC:4593]	0.006033529
ENSG00000138675	FGF5	fibroblast growth factor 5 [Source:HGNC Symbol;Acc:HGNC:3683]	0.006101348
ENSG00000187772	LIN28B	lin-28 homolog B [Source:HGNC Symbol;Acc:HGNC:32207]	0.006111478
ENSG00000227471	AKR1B15	aldo-keto reductase family 1 member B15 [Source:HGNC Symbol;Acc:HGNC:37281]	0.006366933
ENSG00000174502	SLC26A9	solute carrier family 26 member 9 [Source:HGNC Symbol;Acc:HGNC:14469]	0.006716425
ENSG00000078549	ADCYAP1R1	ADCYAP receptor type I [Source:HGNC Symbol;Acc:HGNC:242]	0.006848491
ENSG00000159650	UROCI	urocanate hydratase 1 [Source:HGNC Symbol;Acc:HGNC:26444]	0.006848491
ENSG00000217094	PPIAP31	peptidylprolyl isomerase A pseudogene 31 [Source:HGNC Symbol;Acc:HGNC:44962]	0.006866623
ENSG00000006128	TAC1	tachykinin precursor 1 [Source:HGNC Symbol;Acc:HGNC:11517]	0.006929673
ENSG00000158077	NLRP14	NLR family pyrin domain containing 14 [Source:HGNC Symbol;Acc:HGNC:22939]	0.006952696
ENSG00000223414	LINC00473	long intergenic non-protein coding RNA 473 [Source:HGNC Symbol;Acc:HGNC:21160]	0.006952696
ENSG00000144488	ESPNL	espin like [Source:HGNC Symbol;Acc:HGNC:27937]	0.007039881
ENSG00000144730	IL17RD	interleukin 17 receptor D [Source:HGNC Symbol;Acc:HGNC:17616]	0.007141116
ENSG00000137819	PAQR5	progesterone and adipoQ receptor family member 5 [Source:HGNC Symbol;Acc:HGNC:29645]	0.007179081

ENSG00000162631	NTNG1	netrin G1	
		[Source:HGNC Symbol;Acc:HGNC:23319]	0.007255358
ENSG00000185974	GRK1	G protein-coupled receptor kinase 1	
		[Source:HGNC Symbol;Acc:HGNC:10013]	0.007327997
ENSG00000261275			0.007327997
ENSG00000249267	LINC00939	long intergenic non-protein coding RNA 939	
		[Source:HGNC Symbol;Acc:HGNC:48631]	0.007349367
ENSG00000227827			0.007403828
ENSG00000100065	CARD10	caspase recruitment domain family member 10	
		[Source:HGNC Symbol;Acc:HGNC:16422]	0.007527421
ENSG00000119125	GDA	guanine deaminase	
		[Source:HGNC Symbol;Acc:HGNC:4212]	0.007619923
ENSG00000106304	SPAM1	sperm adhesion molecule 1	
		[Source:HGNC Symbol;Acc:HGNC:11217]	0.00781679
ENSG00000250493			0.007835589
ENSG00000158258	CLSTN2	calsyntenin 2	
		[Source:HGNC Symbol;Acc:HGNC:17448]	0.008149414
ENSG00000175329	ISX	intestine specific homeobox	
		[Source:HGNC Symbol;Acc:HGNC:28084]	0.008233566
ENSG00000188488	SERPINA5	serpin family A member 5	
		[Source:HGNC Symbol;Acc:HGNC:8723]	0.008534971
ENSG00000249584	LINC02225	long intergenic non-protein coding RNA 2225	
		[Source:HGNC Symbol;Acc:HGNC:53094]	0.00866593
ENSG00000147655	RSPO2	R-spondin 2	
		[Source:HGNC Symbol;Acc:HGNC:28583]	0.008823914
ENSG00000171587	DSCAM	DS cell adhesion molecule	
		[Source:HGNC Symbol;Acc:HGNC:3039]	0.008841283
ENSG00000120738	EGR1	early growth response 1	
		[Source:HGNC Symbol;Acc:HGNC:3238]	0.008960131
ENSG00000127129	EDN2	endothelin 2	
		[Source:HGNC Symbol;Acc:HGNC:3177]	0.009244272
ENSG00000157423	HYDIN	"HYDIN, axonemal central pair apparatus protein	
		[Source:HGNC Symbol;Acc:HGNC:19368]"	0.009244272
ENSG00000196565	HBG2	hemoglobin subunit gamma 2	
		[Source:HGNC Symbol;Acc:HGNC:4832]	0.009327518
ENSG00000235881			0.009327518
ENSG00000111262	KCNA1	potassium voltage-gated channel subfamily A member 1	
		[Source:HGNC Symbol;Acc:HGNC:6218]	0.009418575
ENSG00000187527	ATP13A5	ATPase 13A5	
		[Source:HGNC Symbol;Acc:HGNC:31789]	0.009514824
ENSG00000188803	SHISA6	shisa family member 6	
		[Source:HGNC Symbol;Acc:HGNC:34491]	0.009514824
ENSG00000175535	PNLIP	pancreatic lipase	
		[Source:HGNC Symbol;Acc:HGNC:9155]	0.009619326
ENSG00000225953	SATB2-AS1	SATB2 antisense RNA 1	
		[Source:HGNC Symbol;Acc:HGNC:26490]	0.009647997
ENSG00000136695	IL36RN	interleukin 36 receptor antagonist	
		[Source:HGNC Symbol;Acc:HGNC:15561]	0.009810065
ENSG00000259790	ANP32BP1	acidic nuclear phosphoprotein 32 family member B pseudogene 1	
		[Source:HGNC Symbol;Acc:HGNC:24267]	0.009820284
ENSG00000225813			0.009894409
ENSG00000179008	C14orf39	chromosome 14 open reading frame 39	
		[Source:HGNC Symbol;Acc:HGNC:19849]	0.009896903
ENSG00000150893	FREM2	FRAS1 related extracellular matrix protein 2	
		[Source:HGNC Symbol;Acc:HGNC:25396]	0.009945757
ENSG00000197079	KRT35	keratin 35	
		[Source:HGNC Symbol;Acc:HGNC:6453]	0.009945757
ENSG00000231131	LINC01468	long intergenic non-protein coding RNA 1468	
		[Source:HGNC Symbol;Acc:HGNC:50913]	0.010123625
ENSG00000268388	FENDRR	FOXF1 adjacent non-coding developmental regulatory RNA	
		[Source:HGNC Symbol;Acc:HGNC:43894]	0.010151023
ENSG00000159251	ACTC1	"actin, alpha, cardiac muscle 1	
		[Source:HGNC Symbol;Acc:HGNC:143]"	0.010212535
ENSG00000158125	XDH	xanthine dehydrogenase	
		[Source:HGNC Symbol;Acc:HGNC:12805]	0.010258334
ENSG00000156222	SLC28A1	solute carrier family 28 member 1	
		[Source:HGNC Symbol;Acc:HGNC:11001]	0.010392835

ENSG00000260759			0.010741484
ENSG00000110975	SYT10	synaptotagmin 10	
		[Source:HGNC Symbol;Acc:HGNC:19266]	0.010787993
ENSG00000186185	KIF18B	kinesin family member 18B	
		[Source:HGNC Symbol;Acc:HGNC:27102]	0.010844893
ENSG00000110887	DAO	D-amino acid oxidase	
		[Source:HGNC Symbol;Acc:HGNC:2671]	0.011064297
ENSG00000132297	HHLA1	HERV-H LTR-associating 1	
		[Source:HGNC Symbol;Acc:HGNC:4904]	0.011064297
ENSG00000146839	ZAN	zonadhesin (gene/pseudogene)	
		[Source:HGNC Symbol;Acc:HGNC:12857]	0.011064297
ENSG00000215864	NBPF7	NBPF member 7	
		[Source:HGNC Symbol;Acc:HGNC:31989]	0.01113278
ENSG00000233395	LINC00841	long intergenic non-protein coding RNA 841	
		[Source:HGNC Symbol;Acc:HGNC:27430]	0.011213055
ENSG00000177354	C10orf71	chromosome 10 open reading frame 71	
		[Source:HGNC Symbol;Acc:HGNC:26973]	0.011268372
ENSG00000148357	HMCN2	hemicentin 2	
		[Source:HGNC Symbol;Acc:HGNC:21293]	0.01150342
ENSG00000215405	NA	NA	0.011599767
ENSG00000203900			0.011732314
ENSG00000218672			0.011732314
ENSG00000261104			0.011732314
ENSG00000123243	ITIH5	inter-alpha-trypsin inhibitor heavy chain family member 5	
		[Source:HGNC Symbol;Acc:HGNC:21449]	0.011851589
ENSG00000213467	HMGB1P37	high mobility group box 1 pseudogene 37	
		[Source:HGNC Symbol;Acc:HGNC:39184]	0.011876979
ENSG00000119283	TRIM67	tripartite motif containing 67	
		[Source:HGNC Symbol;Acc:HGNC:31859]	0.011900585
ENSG00000166984	TCP10L2	t-complex 10 like 2	
		[Source:HGNC Symbol;Acc:HGNC:21254]	0.012009181
ENSG00000204941	PSG5	pregnancy specific beta-1-glycoprotein 5	
		[Source:HGNC Symbol;Acc:HGNC:9522]	0.012022323
ENSG00000230552			0.012137266
ENSG00000115155	OTOF	otoferlin	
		[Source:HGNC Symbol;Acc:HGNC:8515]	0.012228668
ENSG00000163395	IGFN1	immunoglobulin-like and fibronectin type III domain containing 1	
		[Source:HGNC Symbol;Acc:HGNC:24607]	0.012230791
ENSG00000122778	KIAA1549	KIAA1549	
		[Source:HGNC Symbol;Acc:HGNC:22219]	0.012393242
ENSG00000169169	CPT1C	carnitine palmitoyltransferase 1C	
		[Source:HGNC Symbol;Acc:HGNC:18540]	0.012437719
ENSG00000160994	CCDC105	coiled-coil domain containing 105	
		[Source:HGNC Symbol;Acc:HGNC:26866]	0.012486932
ENSG00000237515	SHISA9	shisa family member 9	
		[Source:HGNC Symbol;Acc:HGNC:37231]	0.012486932
ENSG00000105605	CACNG7	calcium voltage-gated channel auxiliary subunit gamma 7	
		[Source:HGNC Symbol;Acc:HGNC:13626]	0.012676606
ENSG00000185739	SRL	sarcalumenin	
		[Source:HGNC Symbol;Acc:HGNC:11295]	0.012676606
ENSG00000101680	LAMA1	laminin subunit alpha 1	
		[Source:HGNC Symbol;Acc:HGNC:6481]	0.012767139
ENSG00000240021	TEX35	testis expressed 35	
		[Source:HGNC Symbol;Acc:HGNC:25366]	0.012795538
ENSG00000250423	KIAA1210	KIAA1210	
		[Source:HGNC Symbol;Acc:HGNC:29218]	0.012935817
ENSG00000198788	MUC2	"mucin 2, oligomeric mucus/gel-forming	
		[Source:HGNC Symbol;Acc:HGNC:7512]"	0.012968601
ENSG00000205312	KRT17P4	keratin 17 pseudogene 4	
		[Source:HGNC Symbol;Acc:HGNC:50722]	0.013016002
ENSG00000214128	TMEM213	transmembrane protein 213	
		[Source:HGNC Symbol;Acc:HGNC:27220]	0.013016002
ENSG00000178568	ERBB4	erb-b2 receptor tyrosine kinase 4	
		[Source:HGNC Symbol;Acc:HGNC:3432]	0.013045986
ENSG00000175084	DES	desmin	
		[Source:HGNC Symbol;Acc:HGNC:2770]	0.013296119
ENSG00000078295	ADCY2	adenylate cyclase 2	

ENSG00000132639	SNAP25	[Source:HGNC Symbol;Acc:HGNC:233] synaptosome associated protein 25	0.013400191
ENSG00000187094	CCK	[Source:HGNC Symbol;Acc:HGNC:11132] cholecystokinin	0.013440348
ENSG0000018625	ATP1A2	[Source:HGNC Symbol;Acc:HGNC:1569] ATPase Na ⁺ /K ⁺ transporting subunit alpha 2	0.013447765
ENSG00000168542	COL3A1	[Source:HGNC Symbol;Acc:HGNC:800] collagen type III alpha 1 chain	0.013509365
ENSG00000239921	LINC01471	[Source:HGNC Symbol;Acc:HGNC:2201] long intergenic non-protein coding RNA 1471	0.013843652
ENSG00000233183		[Source:HGNC Symbol;Acc:HGNC:51106]	0.013848913
ENSG00000167798	C3P1	complement component 3 precursor pseudogene	0.013964273
ENSG00000183778	B3GALT5	[Source:HGNC Symbol;Acc:HGNC:34414] "beta-1,3-galactosyltransferase 5	0.013987555
ENSG00000168481	LGI3	[Source:HGNC Symbol;Acc:HGNC:920]" leucine rich repeat LGI family member 3	0.01405326
ENSG00000227744	LINC01940	[Source:HGNC Symbol;Acc:HGNC:18711] long intergenic non-protein coding RNA 1940	0.014132769
ENSG00000138162	TACC2	[Source:HGNC Symbol;Acc:HGNC:52763] transforming acidic coiled-coil containing protein 2	0.014149077
ENSG00000250049		[Source:HGNC Symbol;Acc:HGNC:11523]	0.014184675
ENSG00000236445	LINC00608	long intergenic non-protein coding RNA 608	0.014522615
ENSG00000165966	PDZRN4	Source:HGNC Symbol;Acc:HGNC:27179] PDZ domain containing ring finger 4	0.014606813
ENSG00000169876	MUC17	[Source:HGNC Symbol;Acc:HGNC:30552] "mucin 17, cell surface associated	0.014718872
ENSG00000078898	BPIFB2	[Source:HGNC Symbol;Acc:HGNC:16800]" BPI fold containing family B member 2	0.014749092
ENSG00000130528	HRC	[Source:HGNC Symbol;Acc:HGNC:16177] histidine rich calcium binding protein	0.014831419
ENSG00000111799	COL12A1	[Source:HGNC Symbol;Acc:HGNC:5178] collagen type XII alpha 1 chain	0.014902982
ENSG00000185303	SFTPA2	[Source:HGNC Symbol;Acc:HGNC:2188] surfactant protein A2	0.015069239
ENSG00000146648	EGFR	[Source:HGNC Symbol;Acc:HGNC:10799] epidermal growth factor receptor	0.015347263
ENSG00000205592	MUC19	[Source:HGNC Symbol;Acc:HGNC:3236] "mucin 19, oligomeric	0.015466899
ENSG00000198597	ZNF536	[Source:HGNC Symbol;Acc:HGNC:14362]" zinc finger protein 536	0.015539471
ENSG00000120332	TNN	[Source:HGNC Symbol;Acc:HGNC:29025] tenascin N	0.015552452
ENSG00000197406	DIO3	[Source:HGNC Symbol;Acc:HGNC:22942] iodothyronine deiodinase 3	0.015559411
ENSG00000204283	LINC01973	[Source:HGNC Symbol;Acc:HGNC:2885] long intergenic non-protein coding RNA 1973	0.015755832
ENSG00000151224	MAT1A	[Source:HGNC Symbol;Acc:HGNC:52800] methionine adenosyltransferase 1A	0.015755832
ENSG00000257008	GPR142	[Source:HGNC Symbol;Acc:HGNC:6903] G protein-coupled receptor 142	0.015829354
ENSG00000139220	PPFIA2	[Source:HGNC Symbol;Acc:HGNC:20088] PTPRF interacting protein alpha 2	0.015942034
ENSG00000141946	ZIM3	[Source:HGNC Symbol;Acc:HGNC:9246] zinc finger imprinted 3	0.015986308
ENSG00000178171	AMER3	[Source:HGNC Symbol;Acc:HGNC:16366] APC membrane recruitment protein 3	0.015986308
ENSG00000232756		[Source:HGNC Symbol;Acc:HGNC:26771]	0.015986308
ENSG00000130477	UNC13A	unc-13 homolog A	0.015986308
ENSG00000070886	EPHA8	[Source:HGNC Symbol;Acc:HGNC:23150] EPH receptor A8	0.016007101
ENSG00000253301	LINC01606	[Source:HGNC Symbol;Acc:HGNC:3391] long intergenic non-protein coding RNA 1606	0.016008143
ENSG00000006788	MYH13	[Source:HGNC Symbol;Acc:HGNC:51656] myosin heavy chain 13	0.016008143
		[Source:HGNC Symbol;Acc:HGNC:7571]	0.01606756

ENSG00000183287	CCBE1	collagen and calcium binding EGF domains 1 [Source:HGNC Symbol;Acc:HGNC:29426]	0.016243979 0.016243979
ENSG00000262691	FOSB	"FosB proto-oncogene, AP-1 transcription factor subunit [Source:HGNC Symbol;Acc:HGNC:3797]"	0.016263717
ENSG00000125740	DCLK1	doublecortin like kinase 1 [Source:HGNC Symbol;Acc:HGNC:2700]	0.01630694
ENSG00000144820	ADGRG7	adhesion G protein-coupled receptor G7 [Source:HGNC Symbol;Acc:HGNC:19241]	0.01630694
ENSG00000178031	ADAMTSL1	ADAMTS like 1 [Source:HGNC Symbol;Acc:HGNC:14632]	0.016324743
ENSG00000187905	LRRC74B	leucine rich repeat containing 74B [Source:HGNC Symbol;Acc:HGNC:34301]	0.016416472
ENSG00000221878	PSG7	pregnancy specific beta-1-glycoprotein 7 (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:9524]	0.016416472
ENSG00000254101	LINC02055	long intergenic non-protein coding RNA 2055 [Source:HGNC Symbol;Acc:HGNC:52895]	0.016416472
ENSG00000120251	GRIA2	glutamate ionotropic receptor AMPA type subunit 2 [Source:HGNC Symbol;Acc:HGNC:4572]	0.016488676
ENSG00000233991	NA	NA	0.016488676
ENSG00000214402	LCNL1	lipocalin like 1 [Source:HGNC Symbol;Acc:HGNC:34436]	0.016554945 0.016611527
ENSG00000224271	HSPD1P4	heat shock protein family D (Hsp60) member 1 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:35146]	0.016611527 0.016653065
ENSG00000228549	C10orf53	chromosome 10 open reading frame 53 [Source:HGNC Symbol;Acc:HGNC:27421]	0.016654478
ENSG00000100078	PLA2G3	phospholipase A2 group III [Source:HGNC Symbol;Acc:HGNC:17934]	0.016825197
ENSG00000154099	DNAAF1	dynein axonemal assembly factor 1 [Source:HGNC Symbol;Acc:HGNC:30539]	0.016918546
ENSG00000183242	WT1-AS	WT1 antisense RNA [Source:HGNC Symbol;Acc:HGNC:18135]	0.016918546
ENSG00000124253	PCK1	phosphoenolpyruvate carboxykinase 1 [Source:HGNC Symbol;Acc:HGNC:8724]	0.016968016
ENSG00000183304	FAM9A	family with sequence similarity 9 member A [Source:HGNC Symbol;Acc:HGNC:18403]	0.016968016
ENSG00000210127	MT-TA	mitochondrially encoded tRNA alanine [Source:HGNC Symbol;Acc:HGNC:7475]	0.016968016 0.016968016
ENSG00000258679	NCAN	neurocan [Source:HGNC Symbol;Acc:HGNC:2465]	0.016985672
ENSG00000088340	FER1L4	"fer-1 like family member 4, pseudogene [Source:HGNC Symbol;Acc:HGNC:15801]"	0.017112355
ENSG00000196415	PRTN3	proteinase 3 [Source:HGNC Symbol;Acc:HGNC:9495]	0.017180036
ENSG00000135917	SLC19A3	solute carrier family 19 member 3 [Source:HGNC Symbol;Acc:HGNC:16266]	0.017339051 0.017342649
ENSG00000233539	DMBT1P1	deleted in malignant brain tumors 1 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:49497]	0.017392388
ENSG00000135097	MSI1	musashi RNA binding protein 1 [Source:HGNC Symbol;Acc:HGNC:7330]	0.017394805
ENSG00000091128	LAMB4	laminin subunit beta 4 [Source:HGNC Symbol;Acc:HGNC:6491]	0.017415673
ENSG00000168367	LINC00917	long intergenic non-protein coding RNA 917 [Source:HGNC Symbol;Acc:HGNC:48607]	0.017415673
ENSG00000224668	IPO8P1	importin 8 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:41955]	0.017704945
ENSG00000165757	JCAD	junctional cadherin 5 associated [Source:HGNC Symbol;Acc:HGNC:29283]	0.017712329
ENSG00000166558	SLC38A8	solute carrier family 38 member 8 [Source:HGNC Symbol;Acc:HGNC:32434]	0.017722732
ENSG00000185467	KPNA7	karyopherin subunit alpha 7 [Source:HGNC Symbol;Acc:HGNC:21839]	0.017767827 0.017813935 0.017824111
ENSG00000247699			
ENSG00000248975			

ENSG00000179813	FAM216B	family with sequence similarity 216 member B [Source:HGNC Symbol;Acc:HGNC:26883]	0.01797203
ENSG00000188706	ZDHHC9	zinc finger DHHC-type containing 9 [Source:HGNC Symbol;Acc:HGNC:18475]	0.018020454
ENSG00000135472	FAIM2	Fas apoptotic inhibitory molecule 2 [Source:HGNC Symbol;Acc:HGNC:17067]	0.018071818
ENSG00000173572	NLRP13	NLR family pyrin domain containing 13 [Source:HGNC Symbol;Acc:HGNC:22937]	0.018071818
ENSG00000089199	CHGB	chromogranin B [Source:HGNC Symbol;Acc:HGNC:1930]	0.018179173
ENSG00000188112	C6orf132	chromosome 6 open reading frame 132 [Source:HGNC Symbol;Acc:HGNC:21288]	0.018577564
ENSG00000187068	C3orf70	chromosome 3 open reading frame 70 [Source:HGNC Symbol;Acc:HGNC:33731]	0.018587013
ENSG00000233973	LINC01360	long intergenic non-protein coding RNA 1360 [Source:HGNC Symbol;Acc:HGNC:50593]	0.018588752
ENSG00000164265	SCGB3A2	secretoglobin family 3A member 2 [Source:HGNC Symbol;Acc:HGNC:18391]	0.018614288
ENSG00000176769	TCERG1L	transcription elongation regulator 1 like [Source:HGNC Symbol;Acc:HGNC:23533]	0.018783363
ENSG00000179709	NLRP8	NLR family pyrin domain containing 8 [Source:HGNC Symbol;Acc:HGNC:22940]	0.018812736
ENSG00000251557	HNRNPKP3	heterogeneous nuclear ribonucleoprotein K pseudogene 3 [Source:HGNC Symbol;Acc:HGNC:42376]	0.018866754
ENSG00000149654	CDH22	cadherin 22 [Source:HGNC Symbol;Acc:HGNC:13251]	0.018978105
ENSG00000170426	SDR9C7	short chain dehydrogenase/reductase family 9C member 7 [Source:HGNC Symbol;Acc:HGNC:29958]	0.018978105
ENSG00000225637			0.019088297
ENSG00000142408	CACNG8	calcium voltage-gated channel auxiliary subunit gamma 8 [Source:HGNC Symbol;Acc:HGNC:13628]	0.019108077
ENSG00000230873	STMND1	stathmin domain containing 1 [Source:HGNC Symbol;Acc:HGNC:44668]	0.01920241
ENSG00000236404	VLDLR-AS1	VLDLR antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:49621]	0.01920241
ENSG00000170927	PKHD1	"PKHD1, fibrocystin/polyductin [Source:HGNC Symbol;Acc:HGNC:9016]"	0.019345013
ENSG00000237289	CKMT1B	"creatine kinase, mitochondrial 1B [Source:HGNC Symbol;Acc:HGNC:1995]"	0.019345013
ENSG00000229817			0.019542531
ENSG00000259176	NA	NA	0.019829586
ENSG00000124092	CTCF	CCCTC-binding factor like [Source:HGNC Symbol;Acc:HGNC:16234]	0.019839425
ENSG00000259156	CHEK2P2	checkpoint kinase 2 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:43578]	0.019859771
ENSG00000203805	PLPP4	phospholipid phosphatase 4 [Source:HGNC Symbol;Acc:HGNC:23531]	0.019917239
ENSG00000163914	RHO	rhodopsin [Source:HGNC Symbol;Acc:HGNC:10012]	0.019927103
ENSG00000224435	NF1P6	neurofibromin 1 pseudogene 6 [Source:HGNC Symbol;Acc:HGNC:7771]	0.019927103
ENSG00000240707	LINC01168	long intergenic non-protein coding RNA 1168 [Source:HGNC Symbol;Acc:HGNC:49537]	0.019935944
ENSG00000130045	NXNL2	nucleoredoxin like 2 [Source:HGNC Symbol;Acc:HGNC:30482]	0.020063533
ENSG00000162062	TEDC2	tubulin epsilon and delta complex 2 [Source:HGNC Symbol;Acc:HGNC:25849]	0.020213465
ENSG00000172752	COL6A5	collagen type VI alpha 5 chain [Source:HGNC Symbol;Acc:HGNC:26674]	0.020225168
ENSG00000101871	MID1	midline 1 [Source:HGNC Symbol;Acc:HGNC:7095]	0.020247513
ENSG00000137648	TMPRSS4	transmembrane serine protease 4 [Source:HGNC Symbol;Acc:HGNC:11878]	0.020387859
ENSG00000166473	PKD1L2	polycystin 1 like 2 (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:21715]	0.020387859
ENSG00000257907	EEF1A1P17	eukaryotic translation elongation factor 1 alpha 1 pseudogene 17 [Source:HGNC Symbol;Acc:HGNC:37890]	0.020486161

ENSG00000128917	DLL4	delta like canonical Notch ligand 4 [Source:HGNC Symbol;Acc:HGNC:2910]	0.020505106 0.020626924
ENSG00000259380	ATP8B5P	"ATPase phospholipid transporting 8B5, pseudogene [Source:HGNC Symbol;Acc:HGNC:27245]"	0.02065324
ENSG00000179766	DISP3	dispatched RND transporter family member 3 [Source:HGNC Symbol;Acc:HGNC:29251]	0.02065324
ENSG00000204624	C3orf67	chromosome 3 open reading frame 67 [Source:HGNC Symbol;Acc:HGNC:24763]	0.020743462
ENSG00000132321	IQCA1	IQ motif containing with AAA domain 1 [Source:HGNC Symbol;Acc:HGNC:26195]	0.020807093
ENSG00000249119	MTND6P4	mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 6 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:39467]	0.020807093
ENSG00000019505	SYT13	synaptotagmin 13 [Source:HGNC Symbol;Acc:HGNC:14962]	0.020829887
ENSG00000143469	SYT14	synaptotagmin 14 [Source:HGNC Symbol;Acc:HGNC:23143]	0.020885035
ENSG00000196136	SERPINA3	serpin family A member 3 [Source:HGNC Symbol;Acc:HGNC:16]	0.02099734
ENSG00000165816	VWA2	von Willebrand factor A domain containing 2 [Source:HGNC Symbol;Acc:HGNC:24709]	0.021329095
ENSG00000183317	EPHA10	EPH receptor A10 [Source:HGNC Symbol;Acc:HGNC:19987]	0.021329095
ENSG00000072041	SLC6A15	solute carrier family 6 member 15 [Source:HGNC Symbol;Acc:HGNC:13621]	0.021369466
ENSG00000009709	PAX7	paired box 7 [Source:HGNC Symbol;Acc:HGNC:8621]	0.021525887
ENSG00000172350	ABCG4	ATP binding cassette subfamily G member 4 [Source:HGNC Symbol;Acc:HGNC:13884]	0.021525887
ENSG00000183876	ARSI	arylsulfatase family member I [Source:HGNC Symbol;Acc:HGNC:32521]	0.021711339
ENSG00000213934	HBG1	hemoglobin subunit gamma 1 [Source:HGNC Symbol;Acc:HGNC:4831]	0.02185053
ENSG00000186526	CYP4F8	cytochrome P450 family 4 subfamily F member 8 [Source:HGNC Symbol;Acc:HGNC:2648]	0.021913633
ENSG00000161940	BCL6B	B cell CLL/lymphoma 6B [Source:HGNC Symbol;Acc:HGNC:1002]	0.021959359
ENSG00000164093	PITX2	paired like homeodomain 2 [Source:HGNC Symbol;Acc:HGNC:9005]	0.02227554
ENSG00000110786	PTPN5	"protein tyrosine phosphatase, non-receptor type 5 [Source:HGNC Symbol;Acc:HGNC:9657]"	0.022304898
ENSG00000145642	SHISAL2B	shisa like 2B [Source:HGNC Symbol;Acc:HGNC:34236]	0.022689972
ENSG00000260411	NA	NA	0.022689972
ENSG00000135409	AMHR2	anti-Mullerian hormone receptor type 2 [Source:HGNC Symbol;Acc:HGNC:465]	0.022721606 0.022776502
ENSG00000259458	FGFR3	fibroblast growth factor receptor 3 [Source:HGNC Symbol;Acc:HGNC:3690]	0.022896021
ENSG00000068078	FBXO27	F-box protein 27 [Source:HGNC Symbol;Acc:HGNC:18753]	0.023440646
ENSG00000101004	NINL	ninein like [Source:HGNC Symbol;Acc:HGNC:29163]	0.023637109
ENSG00000121207	LRAT	lecithin retinol acyltransferase [Source:HGNC Symbol;Acc:HGNC:6685]	0.023637109
ENSG00000140527	WDR93	WD repeat domain 93 [Source:HGNC Symbol;Acc:HGNC:26924]	0.023652058
ENSG00000236824	BCYRN1	brain cytoplasmic RNA 1 [Source:HGNC Symbol;Acc:HGNC:1022]	0.023652058
ENSG00000101203	COL20A1	collagen type XX alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:14670]	0.023671204 0.023671204
ENSG00000233977	CACNA1B	calcium voltage-gated channel subunit alpha1 B [Source:HGNC Symbol;Acc:HGNC:1389]	0.02389629
ENSG00000148408	HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2 [Source:HGNC Symbol;Acc:HGNC:5008]	0.023926586
ENSG00000134240	HMGS2	3-hydroxy-3-methylglutaryl-CoA synthase 2 [Source:HGNC Symbol;Acc:HGNC:5008]	0.023926586
ENSG00000112186	CAP2	cyclase associated actin cytoskeleton regulatory protein 2 [Source:HGNC Symbol;Acc:HGNC:20039]	0.024121501

ENSG00000182256	GABRG3	gamma-aminobutyric acid type A receptor gamma3 subunit [Source:HGNC Symbol;Acc:HGNC:4088]	0.024155164
ENSG00000166159	LRTM2	leucine rich repeats and transmembrane domains 2 [Source:HGNC Symbol;Acc:HGNC:32443]	0.024214399
ENSG00000132972	RNF17	ring finger protein 17 [Source:HGNC Symbol;Acc:HGNC:10060]	0.024283188
ENSG00000156076	WIF1	WNT inhibitory factor 1 [Source:HGNC Symbol;Acc:HGNC:18081]	0.024283188
ENSG00000261649	GOLGA6L7	golgin A6 family like 7 [Source:HGNC Symbol;Acc:HGNC:37442]	0.024421599
ENSG00000112238	PRDM13	PR/SET domain 13 [Source:HGNC Symbol;Acc:HGNC:13998]	0.02443315
ENSG00000166391	MOGAT2	monoacylglycerol O-acyltransferase 2 [Source:HGNC Symbol;Acc:HGNC:23248]	0.024463522
ENSG00000166869	CHP2	calcineurin like EF-hand protein 2 [Source:HGNC Symbol;Acc:HGNC:24927]	0.024463522
ENSG00000218823	PAPOLB	poly(A) polymerase beta [Source:HGNC Symbol;Acc:HGNC:15970]	0.024463522
ENSG00000265041			
ENSG00000133124	IRS4	insulin receptor substrate 4 [Source:HGNC Symbol;Acc:HGNC:6128]	0.024526611
ENSG00000118733	OLFM3	olfactomedin 3 [Source:HGNC Symbol;Acc:HGNC:17990]	0.024577949
ENSG00000196091	MYBPC1	"myosin binding protein C, slow type [Source:HGNC Symbol;Acc:HGNC:7549]"	0.024577949
ENSG00000105357	MYH14	myosin heavy chain 14 [Source:HGNC Symbol;Acc:HGNC:23212]	0.025148395
ENSG00000167757	KLK11	kallikrein related peptidase 11 [Source:HGNC Symbol;Acc:HGNC:6359]	0.025148395
ENSG00000226068	HNRNPA3P4	heterogeneous nuclear ribonucleoprotein A3 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:39773]	0.025148395
ENSG00000260072			
ENSG00000130226	DPP6	dipeptidyl peptidase like 6 [Source:HGNC Symbol;Acc:HGNC:3010]	0.02515224
ENSG00000144648	ACKR2	atypical chemokine receptor 2 [Source:HGNC Symbol;Acc:HGNC:1565]	0.02527518
ENSG00000169862	CTNND2	catenin delta 2 [Source:HGNC Symbol;Acc:HGNC:2516]	0.025318552
ENSG00000137766	UNC13C	unc-13 homolog C [Source:HGNC Symbol;Acc:HGNC:23149]	0.025345898
ENSG00000261177			
ENSG00000060656	PTPRU	"protein tyrosine phosphatase, receptor type U [Source:HGNC Symbol;Acc:HGNC:9683]"	0.025565995
ENSG00000260305	NTRK3-AS1	NTRK3 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:27532]	0.02580767
ENSG00000187955	COL14A1	collagen type XIV alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2191]	0.025820696
ENSG00000089225	TBX5	T-box 5 [Source:HGNC Symbol;Acc:HGNC:11604]	0.025834296
ENSG00000224209	LINC00466	long intergenic non-protein coding RNA 466 [Source:HGNC Symbol;Acc:HGNC:27294]	0.025987072
ENSG00000151474	FRMD4A	FERM domain containing 4A [Source:HGNC Symbol;Acc:HGNC:25491]	0.026041989
ENSG00000039987	BEST2	bestrophin 2 [Source:HGNC Symbol;Acc:HGNC:17107]	0.026152714
ENSG00000266795	NA	NA	0.026198035
ENSG00000181143	MUC16	"mucin 16, cell surface associated [Source:HGNC Symbol;Acc:HGNC:15582]"	0.026247081
ENSG00000069431	ABCC9	ATP binding cassette subfamily C member 9 [Source:HGNC Symbol;Acc:HGNC:60]	0.026486685
ENSG00000100312	ACR	acrosin [Source:HGNC Symbol;Acc:HGNC:126]	0.02666392
ENSG00000254042			
ENSG00000180251	SLC9A4	solute carrier family 9 member A4 [Source:HGNC Symbol;Acc:HGNC:11077]	0.026721536
ENSG00000237390			
ENSG00000246695	RASSF8-AS1	RASSF8 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:48637]	0.026759131

ENSG00000256612	CYP2B7P	"cytochrome P450 family 2 subfamily B member 7, pseudogene [Source:HGNC Symbol;Acc:HGNC:2616]"	0.026759131
ENSG00000165973	NELL1	neural EGFL like 1 [Source:HGNC Symbol;Acc:HGNC:7750]	0.026774963 0.02698221
ENSG00000172900			
ENSG00000149926	FAM57B	family with sequence similarity 57 member B [Source:HGNC Symbol;Acc:HGNC:25295]	0.02707614
ENSG00000107295	SH3GL2	"SH3 domain containing GRB2 like 2, endophilin A1 [Source:HGNC Symbol;Acc:HGNC:10831]"	0.027164347
ENSG00000173227	SYT12	synaptotagmin 12 [Source:HGNC Symbol;Acc:HGNC:18381]	0.027164347
ENSG00000173013	CCDC96	coiled-coil domain containing 96 [Source:HGNC Symbol;Acc:HGNC:26900]	0.027208218 0.02723306
ENSG00000268460			
ENSG00000234512	TLR12P	"toll like receptor 12, pseudogene [Source:HGNC Symbol;Acc:HGNC:31754]"	0.027406947
ENSG00000135931	ARMC9	armadillo repeat containing 9 [Source:HGNC Symbol;Acc:HGNC:20730]	0.02759323
ENSG00000148702	HABP2	hyaluronan binding protein 2 [Source:HGNC Symbol;Acc:HGNC:4798]	0.027601758
ENSG00000136535	TBR1	"T-box, brain 1 [Source:HGNC Symbol;Acc:HGNC:11590]"	0.028071412
ENSG00000122121	XPNPEP2	X-prolyl aminopeptidase 2 [Source:HGNC Symbol;Acc:HGNC:12823]	0.028133383
ENSG00000170442	KRT86	keratin 86 [Source:HGNC Symbol;Acc:HGNC:6463]	0.028133383
ENSG00000197408	CYP2B6	cytochrome P450 family 2 subfamily B member 6 [Source:HGNC Symbol;Acc:HGNC:2615]	0.028133383
ENSG00000107807	TLX1	T cell leukemia homeobox 1 [Source:HGNC Symbol;Acc:HGNC:5056]	0.028207054
ENSG00000164694	FNDC1	fibronectin type III domain containing 1 [Source:HGNC Symbol;Acc:HGNC:21184]	0.028207054
ENSG00000185313	SCN10A	sodium voltage-gated channel alpha subunit 10 [Source:HGNC Symbol;Acc:HGNC:10582]	0.028207054
ENSG00000164107	HAND2	heart and neural crest derivatives expressed 2 [Source:HGNC Symbol;Acc:HGNC:4808]	0.028335907
ENSG00000133454	MYO18B	myosin XVIIIIB [Source:HGNC Symbol;Acc:HGNC:18150]	0.028417113
ENSG00000167723	TRPV3	transient receptor potential cation channel subfamily V member 3 [Source:HGNC Symbol;Acc:HGNC:18084]	0.028422765
ENSG00000184012	TMPRSS2	transmembrane serine protease 2 [Source:HGNC Symbol;Acc:HGNC:11876]	0.028422765 0.028645846 0.028645846
ENSG00000233485			
ENSG00000261466			
ENSG00000119547	ONECUT2	one cut homeobox 2 [Source:HGNC Symbol;Acc:HGNC:8139]	0.028669408
ENSG00000237222	LINC01968	long intergenic non-protein coding RNA 1968 [Source:HGNC Symbol;Acc:HGNC:52794]	0.028800664
ENSG00000137573	SULF1	sulfatase 1 [Source:HGNC Symbol;Acc:HGNC:20391]	0.028919683
ENSG00000161609	CCDC155	coiled-coil domain containing 155 [Source:HGNC Symbol;Acc:HGNC:26520]	0.028967146 0.028987628
ENSG00000250546			
ENSG00000226057	PHF2P2	PHD finger protein 2 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:38808]	0.029139308
ENSG00000177045	SIX5	SIX homeobox 5 [Source:HGNC Symbol;Acc:HGNC:10891]	0.029298722
ENSG00000124440	HIF3A	hypoxia inducible factor 3 alpha subunit [Source:HGNC Symbol;Acc:HGNC:15825]	0.029322985
ENSG00000234828	IQCM	IQ motif containing M [Source:HGNC Symbol;Acc:HGNC:53443]	0.029461236
ENSG00000116721	PRAMEF1	PRAME family member 1 [Source:HGNC Symbol;Acc:HGNC:28840]	0.029473652 0.029473652
ENSG00000238116			
ENSG00000106689	LHX2	LIM homeobox 2 [Source:HGNC Symbol;Acc:HGNC:6594]	0.029512187
ENSG00000169344	UMOD	uromodulin [Source:HGNC Symbol;Acc:HGNC:12559]	0.02959944

ENSG00000174279	EVX2	even-skipped homeobox 2 [Source:HGNC Symbol;Acc:HGNC:3507]	0.029661965
ENSG00000128573	FOXP2	forkhead box P2 [Source:HGNC Symbol;Acc:HGNC:13875]	0.029779428
ENSG00000251596	HADHAP1	"hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (trifunctional protein), alpha subunit pseudogene 1[Source:HGNC Symbol;Acc:HGNC:4802]" 0.029954508	
ENSG00000002746	HECW1	"HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1 [Source:HGNC Symbol;Acc:HGNC:22195]"	0.029980732
ENSG00000081248	CACNA1S	calcium voltage-gated channel subunit alpha1 S [Source:HGNC Symbol;Acc:HGNC:1397]	0.029997906
ENSG00000166596	CFAP52	cilia and flagella associated protein 52 [Source:HGNC Symbol;Acc:HGNC:16053]	0.030027148
ENSG00000205176	REXO1L1P	"REXO1 like 1, pseudogene [Source:HGNC Symbol;Acc:HGNC:24660]"	0.030066221
ENSG00000152910	CNTNAP4	contactin associated protein like 4 [Source:HGNC Symbol;Acc:HGNC:18747]	0.030144659
ENSG00000106078	COBL	cordon-bleu WH2 repeat protein [Source:HGNC Symbol;Acc:HGNC:22199]	0.030263618
ENSG00000177103	DSCAML1	DS cell adhesion molecule like 1 [Source:HGNC Symbol;Acc:HGNC:14656]	0.030299369
ENSG00000131044	TTLL9	tubulin tyrosine ligase like 9 [Source:HGNC Symbol;Acc:HGNC:16118]	0.030317293
ENSG00000170703	TTLL6	tubulin tyrosine ligase like 6 [Source:HGNC Symbol;Acc:HGNC:26664]	0.030472844
ENSG00000165379	LRFN5	leucine rich repeat and fibronectin type III domain containing 5 [Source:HGNC Symbol;Acc:HGNC:20360]	0.030532839
ENSG00000198929	NOS1AP	nitric oxide synthase 1 adaptor protein [Source:HGNC Symbol;Acc:HGNC:16859]	0.030532839
ENSG00000236253	SLC25A3P1	solute carrier family 25 member 3 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:26869]	0.030574302
ENSG00000205667	ARSH	arylsulfatase family member H [Source:HGNC Symbol;Acc:HGNC:32488]	0.030639161
ENSG00000226440			0.030639161
ENSG00000131183	SLC34A1	solute carrier family 34 member 1 [Source:HGNC Symbol;Acc:HGNC:11019]	0.030803937
ENSG00000225649			0.030847037
ENSG00000006283	CACNA1G	calcium voltage-gated channel subunit alpha1 G [Source:HGNC Symbol;Acc:HGNC:1394]	0.030936635
ENSG00000230392			0.030977697
ENSG00000234130			0.031067495
ENSG00000095637	SORBS1	sorbin and SH3 domain containing 1 [Source:HGNC Symbol;Acc:HGNC:14565]	0.031086939
ENSG00000198010	DLGAP2	DLG associated protein 2 [Source:HGNC Symbol;Acc:HGNC:2906]	0.031235492
ENSG00000102290	PCDH11X	protocadherin 11 X-linked [Source:HGNC Symbol;Acc:HGNC:8656]	0.031415941
ENSG00000260027	HOXB7	homeobox B7 [Source:HGNC Symbol;Acc:HGNC:5118]	0.031452441
ENSG00000105664	COMP	cartilage oligomeric matrix protein [Source:HGNC Symbol;Acc:HGNC:2227]	0.031516506
ENSG00000006071	ABCC8	ATP binding cassette subfamily C member 8 [Source:HGNC Symbol;Acc:HGNC:59]	0.031578145
ENSG00000077522	ACTN2	actinin alpha 2 [Source:HGNC Symbol;Acc:HGNC:164]	0.031657927
ENSG00000248966	BCLAF1P1	BCL2 associated transcription factor 1 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:51329]	0.031733491
ENSG00000124749	COL21A1	collagen type XXI alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:17025]	0.031814031
ENSG00000142675	CNKSR1	connector enhancer of kinase suppressor of Ras 1 [Source:HGNC Symbol;Acc:HGNC:19700]	0.031815396
ENSG00000116748	AMPD1	adenosine monophosphate deaminase 1 [Source:HGNC Symbol;Acc:HGNC:468]	0.031850457
ENSG00000181355	OFCC1	orofacial cleft 1 candidate 1 [Source:HGNC Symbol;Acc:HGNC:21017]	0.03221007
ENSG00000162510	MATN1	"matrilin 1, cartilage matrix protein [Source:HGNC Symbol;Acc:HGNC:6907]"	0.032424937

ENSG00000232392			0.032424937
ENSG00000123572	NRK	Nik related kinase [Source:HGNC Symbol;Acc:HGNC:25391]	0.032537919
ENSG00000267324			0.032537919
ENSG00000196361	ELAVL3	ELAV like RNA binding protein 3 [Source:HGNC Symbol;Acc:HGNC:3314]	0.032579843
ENSG00000204661	C5orf60	chromosome 5 open reading frame 60 [Source:HGNC Symbol;Acc:HGNC:27753]	0.032697662
ENSG00000224059	HSPA8P16	heat shock protein family A (Hsp70) member 8 pseudogene 16 [Source:HGNC Symbol;Acc:HGNC:44931]	0.03275969
ENSG00000114019	AMOTL2	angiomotin like 2 [Source:HGNC Symbol;Acc:HGNC:17812]	0.033101928
ENSG00000134871	COL4A2	collagen type IV alpha 2 chain [Source:HGNC Symbol;Acc:HGNC:2203]	0.033101928
ENSG00000162706	CADM3	cell adhesion molecule 3 [Source:HGNC Symbol;Acc:HGNC:17601]	0.033101928
ENSG00000188782	CATSPER4	cation channel sperm associated 4 [Source:HGNC Symbol;Acc:HGNC:23220]	0.033196706
ENSG00000147689	FAM83A	family with sequence similarity 83 member A [Source:HGNC Symbol;Acc:HGNC:28210]	0.033349502
ENSG00000079841	RIMS1	regulating synaptic membrane exocytosis 1 [Source:HGNC Symbol;Acc:HGNC:17282]	0.033394348
ENSG00000103647	CORO2B	coronin 2B [Source:HGNC Symbol;Acc:HGNC:2256]	0.033419797
ENSG00000112499	SLC22A2	solute carrier family 22 member 2 [Source:HGNC Symbol;Acc:HGNC:10966]	0.033434322
ENSG00000183856	IQGAP3	IQ motif containing GTPase activating protein 3 [Source:HGNC Symbol;Acc:HGNC:20669]	0.033434322
ENSG00000165300	SLITRK5	SLIT and NTRK like family member 5 [Source:HGNC Symbol;Acc:HGNC:20295]	0.033483825
ENSG00000229972	IQCF3	IQ motif containing F3 [Source:HGNC Symbol;Acc:HGNC:31816]	0.033483825
ENSG00000261949	GFY	golgi associated olfactory signaling regulator [Source:HGNC Symbol;Acc:HGNC:44663]	0.033483825
ENSG00000171487	NLRP5	NLR family pyrin domain containing 5 [Source:HGNC Symbol;Acc:HGNC:21269]	0.033631095
ENSG00000129946	SHC2	SHC adaptor protein 2 [Source:HGNC Symbol;Acc:HGNC:29869]	0.033699292
ENSG00000117501	MROH9	maestro heat like repeat family member 9 [Source:HGNC Symbol;Acc:HGNC:26287]	0.03391477
ENSG00000136574	GATA4	GATA binding protein 4 [Source:HGNC Symbol;Acc:HGNC:4173]	0.034539616
ENSG00000106648	GALNTL5	polypeptide N-acetylgalactosaminyltransferase like 5 [Source:HGNC Symbol;Acc:HGNC:21725]	0.034620414
ENSG00000188086	PRSS45	serine protease 45 [Source:HGNC Symbol;Acc:HGNC:30717]	0.034840251
ENSG00000234537			0.034858474
ENSG00000226741	LINC02554	long intergenic non-protein coding RNA 2554 [Source:HGNC Symbol;Acc:HGNC:53594]	0.034969314
ENSG00000004948	CALCR	calcitonin receptor [Source:HGNC Symbol;Acc:HGNC:1440]	0.034980702
ENSG00000142549	IGLON5	IgLON family member 5 [Source:HGNC Symbol;Acc:HGNC:34550]	0.034980702
ENSG00000250519			0.034980702
ENSG00000183908	LRRC55	leucine rich repeat containing 55 [Source:HGNC Symbol;Acc:HGNC:32324]	0.035005257
ENSG00000253974	NRG1-IT1	NRG1 intronic transcript 1 [Source:HGNC Symbol;Acc:HGNC:43633]	0.035154264
ENSG00000162738	VANGL2	VANGL planar cell polarity protein 2 [Source:HGNC Symbol;Acc:HGNC:15511]	0.035338561
ENSG00000115648	MLPH	melanophilin [Source:HGNC Symbol;Acc:HGNC:29643]	0.03575577
ENSG00000187997	C17orf99	chromosome 17 open reading frame 99 [Source:HGNC Symbol;Acc:HGNC:34490]	0.03575577
ENSG00000140279	DUOX2	dual oxidase 2 [Source:HGNC Symbol;Acc:HGNC:13273]	0.035790036
ENSG00000168077	SCARA3	scavenger receptor class A member 3 [Source:HGNC Symbol;Acc:HGNC:19000]	0.035804565

ENSG00000159337	PLA2G4D	phospholipase A2 group IVD [Source:HGNC Symbol;Acc:HGNC:30038]	0.035823277
ENSG00000183580	FBXL7	F-box and leucine rich repeat protein 7 [Source:HGNC Symbol;Acc:HGNC:13604]	0.035823277
ENSG00000218586			0.035823277
ENSG00000184809	B3GALT5-AS1	B3GALT5 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:16424]	0.035845893
ENSG00000132975	GPR12	G protein-coupled receptor 12 [Source:HGNC Symbol;Acc:HGNC:4466]	0.035938935
ENSG00000142910	TINAGL1	tubulointerstitial nephritis antigen like 1 [Source:HGNC Symbol;Acc:HGNC:19168]	0.035938935
ENSG00000075891	PAX2	paired box 2 [Source:HGNC Symbol;Acc:HGNC:8616]	0.035996581
ENSG00000186393	KRT26	keratin 26 [Source:HGNC Symbol;Acc:HGNC:30840]	0.036025366
ENSG00000167779	IGFBP6	insulin like growth factor binding protein 6 [Source:HGNC Symbol;Acc:HGNC:5475]	0.036065767
ENSG00000232667			0.036065767
ENSG00000263711			0.036105875
ENSG00000205054	LINC01121	long intergenic non-protein coding RNA 1121 [Source:HGNC Symbol;Acc:HGNC:49266]	0.036340531
ENSG00000146950	SHROOM2	shroom family member 2 [Source:HGNC Symbol;Acc:HGNC:630]	0.036393162
ENSG00000143867	OSR1	odd-skipped related transcription factor 1 [Source:HGNC Symbol;Acc:HGNC:8111]	0.036631586
ENSG00000205976			0.037140956
ENSG00000196862	RGPD4	RANBP2-like and GRIP domain containing 4 [Source:HGNC Symbol;Acc:HGNC:32417]	0.037154755
ENSG00000148513	ANKRD30A	ankyrin repeat domain 30A [Source:HGNC Symbol;Acc:HGNC:17234]	0.037278195
ENSG00000101057	MYBL2	MYB proto-oncogene like 2 [Source:HGNC Symbol;Acc:HGNC:7548]	0.037361359
ENSG00000139144	PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 Gamma[Source:HGNC Symbol;Acc:HGNC:8973]	0.037546969
ENSG00000247213	LINC01498	long intergenic non-protein coding RNA 1498 [Source:HGNC Symbol;Acc:HGNC:51164]	0.037546969
ENSG00000145242	EPHA5	EPH receptor A5 [Source:HGNC Symbol;Acc:HGNC:3389]	0.037630556
ENSG00000249215	NCOA4P4	nuclear receptor coactivator 4 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:52405]	0.037740576
ENSG00000079112	CDH17	cadherin 17 [Source:HGNC Symbol;Acc:HGNC:1756]	0.037745905
ENSG00000166118	SPATA19	spermatogenesis associated 19 [Source:HGNC Symbol;Acc:HGNC:30614]	0.037802718
ENSG00000162006	MSLN	mesothelin-like [Source:HGNC Symbol;Acc:HGNC:14170]	0.037970738
ENSG00000187123	LYPD6	LY6/PLAUR domain containing 6 [Source:HGNC Symbol;Acc:HGNC:28751]	0.037980544
ENSG00000104313	EYA1	EYA transcriptional coactivator and phosphatase 1 [Source:HGNC Symbol;Acc:HGNC:3519]	0.038059131
ENSG00000237250			0.038171217
ENSG00000105290	APLP1	amyloid beta precursor like protein 1 [Source:HGNC Symbol;Acc:HGNC:597]	0.038576481
ENSG00000138650	PCDH10	protocadherin 10 [Source:HGNC Symbol;Acc:HGNC:13404]	0.038631087
ENSG00000198914	POU3F3	POU class 3 homeobox 3 [Source:HGNC Symbol;Acc:HGNC:9216]	0.03865691
ENSG00000117114	ADGRL2	adhesion G protein-coupled receptor L2 [Source:HGNC Symbol;Acc:HGNC:18582]	0.039101789
ENSG00000185737	NRG3	neuregulin 3 [Source:HGNC Symbol;Acc:HGNC:7999]	0.039101789
ENSG00000197085	NPSR1-AS1	NPSR1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:22128]	0.039361047
ENSG00000230102	LINC02028	long intergenic non-protein coding RNA 2028 [Source:HGNC Symbol;Acc:HGNC:27718]	0.039602594
ENSG00000241158	ADAMTS9-AS1	ADAMTS9 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:40625]	0.039646513
ENSG00000146005	PSD2	pleckstrin and Sec7 domain containing 2	

ENSG00000171533	MAP6	[Source:HGNC Symbol;Acc:HGNC:19092] microtubule associated protein 6	0.039852243
ENSG00000164294	GPX8	[Source:HGNC Symbol;Acc:HGNC:6868] glutathione peroxidase 8 (putative)	0.040171006
ENSG00000054356	PTPRN	[Source:HGNC Symbol;Acc:HGNC:33100] "protein tyrosine phosphatase, receptor type N	0.040207131
ENSG00000077080	ACTL6B	[Source:HGNC Symbol;Acc:HGNC:9676]" actin like 6B	0.040248543
ENSG00000141434	MEP1B	[Source:HGNC Symbol;Acc:HGNC:160] meprin A subunit beta	0.040248543
ENSG00000183067	IGSF5	[Source:HGNC Symbol;Acc:HGNC:7020] immunoglobulin superfamily member 5	0.040590193
ENSG00000112337	SLC17A2	[Source:HGNC Symbol;Acc:HGNC:5952] solute carrier family 17 member 2	0.040590193
ENSG00000161682	FAM171A2	[Source:HGNC Symbol;Acc:HGNC:10930] family with sequence similarity 171 member A2	0.040803316
ENSG00000116833	NR5A2	[Source:HGNC Symbol;Acc:HGNC:30480] nuclear receptor subfamily 5 group A member 2	0.040923418
ENSG00000143355	LHX9	[Source:HGNC Symbol;Acc:HGNC:7984] LIM homeobox 9	0.040938395
ENSG00000139767	SRRM4	[Source:HGNC Symbol;Acc:HGNC:14222] serine/arginine repetitive matrix 4	0.041155655
ENSG00000227036	LINC00511	[Source:HGNC Symbol;Acc:HGNC:29389] long intergenic non-protein coding RNA 511	0.041207854
ENSG00000105549	THEG	[Source:HGNC Symbol;Acc:HGNC:43564] theg spermatid protein	0.041207854
ENSG00000104967	NOVA2	[Source:HGNC Symbol;Acc:HGNC:13706] NOVA alternative splicing regulator 2	0.041581527
ENSG00000183206	POTEC	[Source:HGNC Symbol;Acc:HGNC:7887] POTE ankyrin domain family member C	0.041600384
ENSG00000184302	SIX6	[Source:HGNC Symbol;Acc:HGNC:33894] SIX homeobox 6	0.041620804
ENSG00000245651		[Source:HGNC Symbol;Acc:HGNC:10892] transmembrane protein 125	0.041631474
ENSG00000179178	TMEM125	[Source:HGNC Symbol;Acc:HGNC:28275] long intergenic non-protein coding RNA 1516	0.041791867
ENSG00000231422	LINC01516	[Source:HGNC Symbol;Acc:HGNC:51211] stathmin 2	0.041868067
ENSG00000104435	STMN2	[Source:HGNC Symbol;Acc:HGNC:10577] keratin 76	0.041944166
ENSG00000185069	KRT76	[Source:HGNC Symbol;Acc:HGNC:24430] RIMS binding protein 2	0.042071807
ENSG00000060709	RIMBP2	[Source:HGNC Symbol;Acc:HGNC:30339] transmembrane protein 178B	0.042101327
ENSG00000261115	TMEM178B	[Source:HGNC Symbol;Acc:HGNC:44112] long intergenic non-protein coding RNA 2179	0.042193233
ENSG00000261623	LINC02179	[Source:HGNC Symbol;Acc:HGNC:53041] RANBP2-like and GRIP domain containing 3	0.042224694
ENSG00000153165	RGPD3	[Source:HGNC Symbol;Acc:HGNC:32416] long intergenic non-protein coding RNA 599	0.042347063
ENSG00000253230	LINC00599	[Source:HGNC Symbol;Acc:HGNC:27231] long intergenic non-protein coding RNA 1447	0.042450091
ENSG00000236078	LINC01447	[Source:HGNC Symbol;Acc:HGNC:50783] long intergenic non-protein coding RNA 1721	0.042463159
ENSG00000230133	LINC01721	[Source:HGNC Symbol;Acc:HGNC:52508] ankyrin repeat domain 26 pseudogene 3	0.042512831
ENSG00000237636	ANKRD26P3	[Source:HGNC Symbol;Acc:HGNC:39689] PRR29 antisense RNA 1	0.042582368
ENSG00000264954	PRR29-AS1	[Source:HGNC Symbol;Acc:HGNC:51822] pleckstrin homology domain containing A7	0.042699245
ENSG00000166689	PLEKHA7	[Source:HGNC Symbol;Acc:HGNC:27049] potassium voltage-gated channel subfamily H member 6	0.04272194
ENSG00000173826	KCNH6	[Source:HGNC Symbol;Acc:HGNC:18862] NA	0.042801591
ENSG00000253864	NA	transmembrane protein 100	0.042900836
ENSG00000166292	TMEM100	[Source:HGNC Symbol;Acc:HGNC:25607] transcription factor AP-2 alpha	0.043052047
ENSG00000137203	TFAP2A		

ENSG00000165970	SLC6A5	[Source:HGNC Symbol;Acc:HGNC:11742] solute carrier family 6 member 5	0.043105155
ENSG00000184908	CLCNKB	[Source:HGNC Symbol;Acc:HGNC:11051] chloride voltage-gated channel Kb	0.043105155
ENSG00000197893	NRAP	[Source:HGNC Symbol;Acc:HGNC:2027] nebulin related anchoring protein	0.043516345
ENSG00000169126	ARMC4	[Source:HGNC Symbol;Acc:HGNC:7988] armadillo repeat containing 4	0.043567821
ENSG00000245248	USP2-AS1	[Source:HGNC Symbol;Acc:HGNC:25583] USP2 antisense RNA 1 (head to head)	0.043632647
ENSG00000242866	STRC	[Source:HGNC Symbol;Acc:HGNC:48673] stereocilin	0.043635087
ENSG00000164393	ADGRF2	[Source:HGNC Symbol;Acc:HGNC:16035] adhesion G protein-coupled receptor F2	0.043658722
ENSG00000100033	PRODH	[Source:HGNC Symbol;Acc:HGNC:18991] proline dehydrogenase 1	0.044026611
ENSG00000136352	NKX2-1	[Source:HGNC Symbol;Acc:HGNC:9453] NK2 homeobox 1	0.044045719
ENSG00000165566	AMER2	[Source:HGNC Symbol;Acc:HGNC:11825] APC membrane recruitment protein 2	0.044046233
ENSG00000163995	ABLIM2	[Source:HGNC Symbol;Acc:HGNC:26360] actin binding LIM protein family member 2	0.044155809
ENSG00000165495	PKNOX2	[Source:HGNC Symbol;Acc:HGNC:19195] PBX/knotted 1 homeobox 2	0.044231879
ENSG00000144115	THNSL2	[Source:HGNC Symbol;Acc:HGNC:16714] threonine synthase like 2	0.044261202
ENSG00000157214	STEAP2	[Source:HGNC Symbol;Acc:HGNC:25602] STEAP2 metalloredutase	0.044590058
ENSG00000229240	LINC00710	[Source:HGNC Symbol;Acc:HGNC:17885] long intergenic non-protein coding RNA 710	0.044717969
ENSG00000168356	SCN11A	[Source:HGNC Symbol;Acc:HGNC:27386] sodium voltage-gated channel alpha subunit 11	0.044849493
ENSG00000130508	PXDN	[Source:HGNC Symbol;Acc:HGNC:10583] peroxidase	0.044881812
ENSG00000166444	ST5	[Source:HGNC Symbol;Acc:HGNC:14966] suppression of tumorigenicity 5	0.044899327
ENSG00000140600	SH3GL3	[Source:HGNC Symbol;Acc:HGNC:11350] "SH3 domain containing GRB2 like 3, endophilin A3	0.044899327
ENSG00000214181	NA	[Source:HGNC Symbol;Acc:HGNC:10832]" NA	0.045237232
ENSG00000144681	STAC	[Source:HGNC Symbol;Acc:HGNC:11353] SH3 and cysteine rich domain	0.045237232
ENSG00000166863	TAC3	[Source:HGNC Symbol;Acc:HGNC:11521] tachykinin 3	0.045389235
ENSG00000169436	COL22A1	[Source:HGNC Symbol;Acc:HGNC:22989] collagen type XXII alpha 1 chain	0.045474144
ENSG00000172137	CALB2	[Source:HGNC Symbol;Acc:HGNC:1435] calbindin 2	0.045474144
ENSG00000223566	TNRC18P2	[Source:HGNC Symbol;Acc:HGNC:34014] trinucleotide repeat containing 18 pseudogene 2	0.045474144
ENSG00000175267	VWA3A	[Source:HGNC Symbol;Acc:HGNC:27088] von Willebrand factor A domain containing 3A	0.045495146
ENSG00000175267	VWA3A	[Source:HGNC Symbol;Acc:HGNC:27088] von Willebrand factor A domain containing 3A	0.045495146
ENSG00000183780	SLC35F3	[Source:HGNC Symbol;Acc:HGNC:23616] solute carrier family 35 member F3	0.045495146
ENSG00000228983	SLC47A1P1	[Source:HGNC Symbol;Acc:HGNC:51849] solute carrier family 47 member 1 pseudogene 1	0.045495146
ENSG00000269332	GOLGA2P9	[Source:HGNC Symbol;Acc:HGNC:49921] golgin A2 pseudogene 9	0.045495146
ENSG00000081800	SLC13A1	[Source:HGNC Symbol;Acc:HGNC:10916] solute carrier family 13 member 1	0.045528908
ENSG00000155816	FMN2	[Source:HGNC Symbol;Acc:HGNC:14074] formin 2	0.045528908
ENSG00000091137	SLC26A4	[Source:HGNC Symbol;Acc:HGNC:8818] solute carrier family 26 member 4	0.045601783
ENSG00000129990	SYT5	[Source:HGNC Symbol;Acc:HGNC:11513] synaptotagmin 5	0.045601783

ENSG00000173702	MUC13	"mucin 13, cell surface associated [Source:HGNC Symbol;Acc:HGNC:7511]"	0.045601783
ENSG00000116176	TPSG1	tryptase gamma 1 [Source:HGNC Symbol;Acc:HGNC:14134]	0.045645845
ENSG00000250420	AACSP1	acetoacetyl-CoA synthetase pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:18226]	0.045645845
ENSG00000104055	TGM5	transglutaminase 5 [Source:HGNC Symbol;Acc:HGNC:11781]	0.045691236
ENSG00000109101	FOXN1	forkhead box N1 [Source:HGNC Symbol;Acc:HGNC:12765]	0.045781
ENSG00000131386	GALNT15	polypeptide N-acetylgalactosaminyltransferase 15 [Source:HGNC Symbol;Acc:HGNC:21531]	0.045798489
ENSG00000183016	NA	NA	0.045937358
ENSG00000248746	ACTN3	actinin alpha 3 (gene/pseudogene) [Source:HGNC Symbol;Acc:HGNC:165]	0.045937358
ENSG00000259010			0.04595318
ENSG00000156687	UNC5D	unc-5 netrin receptor D [Source:HGNC Symbol;Acc:HGNC:18634]	0.046099925
ENSG00000213864	EEF1B2P2	eukaryotic translation elongation factor 1 beta 2 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:3209]	0.046129239
ENSG00000143107	FNDC7	fibronectin type III domain containing 7 [Source:HGNC Symbol;Acc:HGNC:26668]	0.046229298
ENSG00000230615			0.046269835
ENSG00000184227	ACOT1	acyl-CoA thioesterase 1 [Source:HGNC Symbol;Acc:HGNC:33128]	0.046363122
ENSG00000118194	TNNT2	"troponin T2, cardiac type [Source:HGNC Symbol;Acc:HGNC:11949]"	0.046453265
ENSG00000172995	ARPP21	cAMP regulated phosphoprotein 21 [Source:HGNC Symbol;Acc:HGNC:16968]	0.046453265
ENSG00000156103	MMP16	matrix metalloproteinase 16 [Source:HGNC Symbol;Acc:HGNC:7162]	0.04649564
ENSG00000164904	ALDH7A1	aldehyde dehydrogenase 7 family member A1 [Source:HGNC Symbol;Acc:HGNC:877]	0.04649564
ENSG00000224743	TEX26-AS1	TEX26 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:42784]	0.04649564
ENSG00000185823	NPAP1	nuclear pore associated protein 1 [Source:HGNC Symbol;Acc:HGNC:1190]	0.04652545
ENSG0000018607	ZNF806	zinc finger protein 806 [Source:HGNC Symbol;Acc:HGNC:33228]	0.046600673
ENSG00000179270	C2orf71	chromosome 2 open reading frame 71 [Source:HGNC Symbol;Acc:HGNC:34383]	0.046600673
ENSG00000186862	PDZD7	PDZ domain containing 7 [Source:HGNC Symbol;Acc:HGNC:26257]	0.046710668
ENSG00000227525	RPL7P6	ribosomal protein L7 pseudogene 6 [Source:HGNC Symbol;Acc:HGNC:32430]	0.046989116
ENSG00000236229	VEZF1P1	vascular endothelial zinc finger 1 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:32320]	0.047105132
ENSG00000171564	FGB	fibrinogen beta chain [Source:HGNC Symbol;Acc:HGNC:3662]	0.047251427
ENSG00000257175			0.047316621
ENSG00000248713	LOC285556	"Homo sapiens uncharacterized mRNA. [Source:RefSeq mRNA;Acc:NM_001354435]"	0.047420932
ENSG00000102287	GABRE	gamma-aminobutyric acid type A receptor epsilon subunit [Source:HGNC Symbol;Acc:HGNC:4085]	0.047603565
ENSG00000150086	NA	NA	0.0476766
ENSG00000168959	GRM5	glutamate metabotropic receptor 5 [Source:HGNC Symbol;Acc:HGNC:4597]	0.0476766
ENSG00000184304	PRKD1	protein kinase D1 [Source:HGNC Symbol;Acc:HGNC:9407]	0.0476766
ENSG00000204055			0.047795615
ENSG00000164122	ASB5	ankyrin repeat and SOCS box containing 5 [Source:HGNC Symbol;Acc:HGNC:17180]	0.047913021
ENSG00000123977	DAW1	dynein assembly factor with WD repeats 1 [Source:HGNC Symbol;Acc:HGNC:26383]	0.047973
ENSG00000156413	FUT6	fucosyltransferase 6 [Source:HGNC Symbol;Acc:HGNC:4017]	0.047988989
ENSG00000101276	SLC52A3	solute carrier family 52 member 3 [Source:HGNC Symbol;Acc:HGNC:16187]	0.048129781

ENSG00000168079	SCARA5	scavenger receptor class A member 5 [Source:HGNC Symbol;Acc:HGNC:28701]	0.048129781 0.048129781
ENSG00000254561			
ENSG00000223949	ROR1-AS1	ROR1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:40508]	0.048194625
ENSG00000204335	SP5	Sp5 transcription factor [Source:HGNC Symbol;Acc:HGNC:14529]	0.048312303 0.04840783
ENSG00000204241			
ENSG00000099625	CBARP	CACN beta subunit associated regulatory protein [Source:HGNC Symbol;Acc:HGNC:28617]	0.048411296
ENSG00000143450	OAZ3	ornithine decarboxylase antizyme 3 [Source:HGNC Symbol;Acc:HGNC:8097]	0.048617065
ENSG00000015520	NPC1L1	NPC1 like intracellular cholesterol transporter 1 [Source:HGNC Symbol;Acc:HGNC:7898]	0.048746819
ENSG00000188162	OTOG	otogelin [Source:HGNC Symbol;Acc:HGNC:8516]	0.048746819
ENSG00000125492	BARHL1	BarH like homeobox 1 [Source:HGNC Symbol;Acc:HGNC:953]	0.048820483
ENSG00000145832	SLC25A48	solute carrier family 25 member 48 [Source:HGNC Symbol;Acc:HGNC:30451]	0.048934402
ENSG00000185686	PRAME	preferentially expressed antigen in melanoma [Source:HGNC Symbol;Acc:HGNC:9336]	0.048934402
ENSG00000229147	SMPD4P2	sphingomyelin phosphodiesterase 4 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:39674]	0.049012128

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EXAMPLE 2

[000184] The system and methods detailed herein and in Example 1 provide a framework and approach to evaluating individuals at risk of disease, for assessing disease progression, or for identifying markers of more severe disease or metastasis. The availability of a system and method to isolate and analyze high quality RNA which validly identifies RNA, including RNA changes *in vivo* and new or altered RNAs such as those of different cellular components or of infectious agents, from patient self-collected samples, including small volume blood samples (finger stick), provides a means to monitor and assess various disease or infectious conditions or scenarios particularly where traditional blood sampling is not warranted, feasible or practical. Applications for evaluation and monitoring of cancer patients, including prior to and following treatment or remission, as well as patients with relapsing or remitting diseases such as multiple sclerosis, Crohn's disease, etc are contemplated. Further, the system and methods can be applied and implemented in infectious disease, including in viral diseases that affect

large populations, either seasonally or in unanticipated circumstances. Those at risk of infection or who are presumed or determined to be infected can be evaluated to assess the RNA response and RNA indicators of disease, characterize predictors or markers of susceptibility or disease severity, and identify targets for treatment or modulation. For example, more precise and marker-based knowledge and understanding of influenza virus infection and susceptibility could reduce the effects of seasonal influenza on individuals and the health care system. Further, the recent outbreak of new coronavirus SARS-CoV-2 and the COVID-19 pandemic underscores an imminent need for a system, method and approach as provided herein.

[000185] Coronaviruses are a family of viruses that can cause illnesses such as the common cold, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). In late 2019, a new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified as the cause of a COVID-19 disease outbreak that originated in China. In March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic. By early April, the worldwide number of confirmed COVID-19 cases were nearly 1.5 million, with over 400,000 in the U.S., over 135,000 cases in each of Italy and Spain, over 100,000 cases in Germany and over 80,000 reported in China. Deaths worldwide were over 80,000. No accepted or approved treatments or vaccines are available.

[000186] Signs and symptoms of COVID-19 appear 2 to 14 days after exposure and can include fever, cough, shortness of breath or difficulty breathing, as well as tiredness, aches, runny nose and sore throat. Some people experience the loss of smell or taste. People who are older or who have existing chronic medical conditions, such as heart disease, lung disease or diabetes, or who have compromised immune systems may be at higher risk of serious illness, similar to what is seen with other respiratory illnesses, such as influenza.

[000187] The severity of COVID-19 symptoms can range from very mild to severe and some people may have no symptoms at all. In fact, studies have shown that a significant portion of individuals with coronavirus lack symptoms (“asymptomatic”) and that even those who eventually develop symptoms (“pre-symptomatic”) can transmit the virus to others before showing symptoms (Li R et al Science 10.1126/science.abb3221(2020); Rothe C et al (2020) New Engl J Med 382(10):970-971; Zou L et al (2010) New Engl J Med 382(12):1177-1179). Therefore, the virus can spread between people interacting in close proximity—for example, speaking, coughing, or sneezing—even if those people are not exhibiting symptoms.

[000188] In the United States, nearly one-third of COVID-19 disease cases are 65 or older and patients over 65 account for nearly half of hospitalizations and a significant majority of deaths, according to CDC reports. Nonetheless, about 20% of infected people ages 20-44 are hospitalized, demonstrating that this is not just a disease of older adults. Important outstanding questions exist as to the underlying biological vulnerability of older individuals and how do preexisting conditions or illnesses exacerbate

COVID-19. Also, it would be helpful to have indicators for those patients who will develop more significant or severe disease, so they can be managed or triaged differently or more aggressively.

[000189] RNA monitoring and longitudinal genomics in accordance with the system and methods provided herein, including as set out in Example 1, provides an approach to isolate, identify and evaluate RNAs in individuals exposed to or at risk of virus infection, such as coronavirus infection, such as with SARS-COV2, or patients infected with the virus and diagnosed for COVID-19. The systems and methods could be implemented in individuals post-vaccine also to evaluate RNA, protein and cellular response(s). Finger stick collection of small blood samples as described herein may be implemented by regular collection at home, at or in hospital, by medical care workers or personnel, or in isolation or quarantine. This permits monitoring of the infection, including viral RNA, disease, RNA response, RNA alterations, including as an indicator of cellular response as described above and in Example 1. The availability of high quality RNA from prospective and retrospective sampling will facilitate an understanding of infection and disease, including in influenza, coronavirus, or instances of other known or unknown infectious agents, including new variants, as well as the body's response to disease and susceptibility to disease aspects. Collection of standard venipuncture samples puts health care workers at risk and is unduly invasive and difficult for patients and individuals already suffering or in stressful and demanding situations and conditions.

[000190] This invention may be embodied in other forms or carried out in other ways without departing from the spirit or essential characteristics thereof. The present disclosure is therefore to be considered as in all aspects illustrated and not restrictive, the scope of the invention being indicated by the appended Claims, and all changes which come within the meaning and range of equivalency are intended to be embraced therein.

[000191] Various references are cited throughout this Specification, each of which is incorporated herein by reference in its entirety.

CLAIMS

1. A method for RNA profiling and analysis of small volume samples from a patient or individual comprising:
 - (a) obtaining one or more small volume sample self-collected by the patient or individual or by a non-medical person, wherein the sample is collected in or otherwise combined with an RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized; and
 - (b) isolating RNA using a process adapted for small volume samples wherein the amount of any and all solutions or buffers utilized are reduced and adjusted for small volume samples;wherein the RNA is of sufficient quality and quantity for whole transcriptome analysis and transcriptomic profiling through RNA sequencing (RNAseq).
2. The method of claim 1 wherein the RNA is isolated using a process comprising:
 - (a) contacting the sample with a protease to form a protease treated small volume sample;
 - (b) contacting the protease treated sample with an ethanol or salt solution forming a precipitate containing the RNA, wherein the precipitate containing the RNA is then resuspended in a buffer or solution, or contacting the protease treated sample with an organic extraction solution, forming a solution having an aqueous phase containing the RNA and an organic phase;
 - (c) contacting the resuspended precipitate containing the RNA or the aqueous phase containing the RNA with DNase to form a DNase-treated resuspended precipitate or DNase-treated aqueous phase;
 - (d) binding the RNA to a silica based solid phase or column by contacting the resuspended precipitate or aqueous phase with said silica based solid phase; and
 - (e) eluting the RNA from the silica based solid phase comprising contacting the silica based solid phase with a solution or buffer to provide isolated RNA;wherein all buffer and solution volumes are reduced and adjusted for small volume samples.
3. The method of claim 2 wherein between steps (b) and (c), the resuspended precipitate containing the RNA or the aqueous phase containing the RNA is contacted with a solution or column to remove residual sample cell debris and/or to homogenize the sample cell lysate.
4. The method of claim 1, wherein the RNA is isolated using a process comprising:

- (e) contacting the sample with an RNA stabilization solution, wherein the solution has capability to lyse cells and inactivate adventitious agents;
 - (f) optionally further contacting the sample with a salt, a reducing agent, and/or a detergent;
 - (g) contacting the solution contacted sample of (a) or (b) with silica, silica based solid phase or carboxylated magnetic beads which bind RNA and seves to purify the RNA from other components in the sample; and
 - (h) eluting the RNA from the silica or silica based solid phase or the magnetic beads comprising contacting the silica, silica based solid phase or magnetic beads with a solution or buffer to provide isolated RNA;
- wherein all buffer and solution volumes are reduced and adjusted for small volume samples.
5. The method of any of claims 1-4, wherein the sample is a small volume blood sample.
 6. The method of any of claims 1-5, wherein the small volume blood sample is collected via fingerstick.
 7. The method of any of claims 1-6, wherein the sample volume is less than 500µl, less than 300µl, less than 250µl, about 200-300µl, less than 200µl, about 100-300µl, about 150-300µl, about 100-250µl, about 50-300µl, less than 100µl, less than 50µl, less than 25µl, 10µl or less.
 8. The method of any of claims 1-7, wherein buffer and solution volumes are reduced to 20-40% or 20-30% or about 25% of those utilized for isolation of RNA from a standard venipuncture blood sample.
 9. The method of any of claims 1-8, wherein said protease is proteinase K.
 10. The method of any of claims 1-9, further comprising sequencing the RNA.
 11. The method of claim 10, wherein abundant RNA species or RNA species not of interest are removed prior to sequencing.
 12. The method of claim 11, wherein globin mRNA, ribosomal RNA(s) or species specific RNAs are removed prior to sequencing.
 13. The method of any of claims 1-12, wherein the patient or individual has a disease or infection or is at risk of or suspected of disease or infection.

14. The method of any of claims 1-13 for longitudinal screening by RNA profiling and analysis of small volume samples from one or more patient or individual, wherein the patient or individual has a disease or infection or is at risk of or suspected of disease or infection.
15. The method of claim 14, wherein small volume samples are collected via fingerstick in series or in regular or designated increments of hours, days, weeks or months.
16. The method of claim 15, wherein small volume blood samples are collected via fingerstick in series or in regular or designated increments of hours, days, weeks or months.
17. A system or kit for RNA profiling and analysis of small volume samples from a patient or individual comprising:
 - (a) a means for self-collection of a small volume sample by the patient or individual or by a non-medical person, comprising a lancet, swab or receptacle for a wash, spit or aspirate;
 - (b) a tube or receptacle for receiving the small volume sample on collection and containing a volume of RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized; and
 - (c) one or more appropriate label(s) for designating the name or identity of the patient or individual, date of sample collection and time of sample collection.
18. The system or kit of claim 17, further comprising an envelope or mailing container for shipment of the sample to a laboratory or facility for RNA isolation and analysis.
19. The system or kit of claim 17, for longitudinal RNA profiling and analysis of multiple small volume samples collected in series from a patient or individual over days, weeks or months comprising:
 - (a) a set of numerous means for self-collection of individual small volume samples by the patient or individual or by a non-medical person, each comprising a lancet, swab or receptacle for a wash, spit or aspirate;
 - (b) a set of numerous tubes or receptacles each individually for receiving a small volume sample on collection and containing a volume of RNA stabilization solution whereby cells in the sample are lysed and RNA is stabilized;
 - (c) numerous appropriate label(s) for designating the name or identity of the patient or individual, date of sample collection and time of sample collection; and
 - (d) numerous envelopes or mailing containers for shipment of each sample or several samples to a laboratory or facility for RNA isolation and analysis.

20. The system or kit of any of claims 17-19, wherein the volume of RNA stabilization solution is less than 1ml, about 500µl or less, about 300µl or less, about 200-300µl, about 250µl, less than 200µl, less than 100µl, less than 50µl, less than 25µl, or 10µl or less.
21. The system or kit of any of claims 17-20, wherein the tube or receptacle for receiving the small volume sample and containing RNA stabilization solution has a total volume capacity of 1.5 ml or less, 1.2 ml or less, or 1ml or less.