



(51) International Patent Classification:
C12Q 1/68 (2006.01)

(21) International Application Number:
PCT/US2013/051099

(22) International Filing Date:
18 July 2013 (18.07.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/673,024 18 July 2012 (18.07.2012) US

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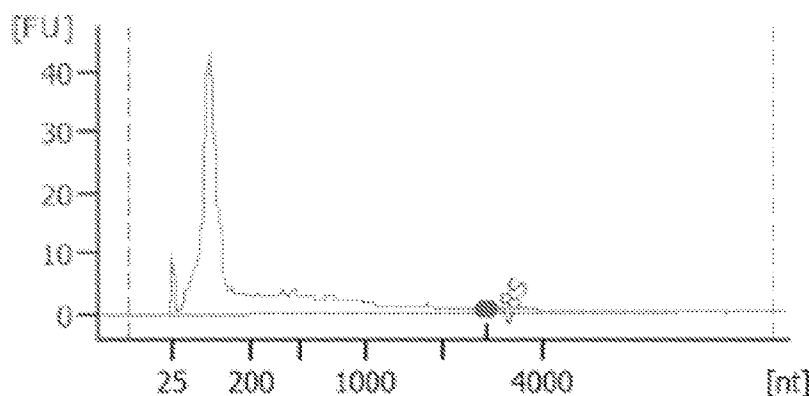
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))

(54) Title: USE OF MICROVESICLES IN DIAGNOSIS, PROGNOSIS, AND TREATMENT OF MEDICAL DISEASES AND CONDITIONS



(57) Abstract: The invention provides a novel method for detecting the presence or absence of one or more transfer RNAs (tRNAs) contained in microvesicles from a subject. The invention also provides a novel method for detecting the presence or absence of one or more human endogenous retrovirus elements (HERV) in microvesicles from a subject. The methods disclosed is directed to aiding diagnosis, prognosis, monitoring and evaluation of a disease or other medical condition in a subject.

USE OF MICROVESICLES IN DIAGNOSIS, PROGNOSIS, AND TREATMENT OF MEDICAL DISEASES AND CONDITIONS

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/673,024, filed July 18, 2013. The contents of this application are hereby incorporated by reference in their entirety.

BACKGROUND

[0002] All membrane vesicles shed by cells < 0.8µm in diameter are referred to herein collectively as microvesicles. This may include exosomes, exosome-like particles, prostasomes, dexosomes, texosomes, ectosomes, oncosomes, apoptotic bodies, retrovirus-like particles, and human endogenous retrovirus (HERV) particles. Microvesicles from various cell sources have been extensively studied with respect to protein and lipid content. Recently, microvesicles have been found to also contain both DNA and RNA, including genomic DNA, cDNA, mitochondrial DNA, microRNA (miRNA), and messenger RNA (mRNA). They may facilitate the transfer of genetic information between cells and/or act as a 'release hatch' for DNA/RNA/proteins that the cell is trying to eliminate (Mack et al., 2000; Baj-Krzyworzeka et al., 2006; Valadi et al. 2007).

[0003] Due to the genetic and proteomic information contained in microvesicles shed by cells, current research is directed at utilizing microvesicles to gain further insight into the status of these cells, for example, disease state or predisposition for a disease.

SUMMARY OF THE INVENTION

[0004] In general, the invention is a novel method for detecting in a subject the presence or absence of a variety of transfer RNAs (tRNAs) contained in microvesicles, thereby aiding the diagnosis, monitoring and evaluation of diseases, other medical conditions, and treatment efficacy.

[0005] One aspect of the invention are methods for aiding in the diagnosis, prognosis, or monitoring of a disease or other medical condition in a subject, comprising the steps of: a) isolating a microvesicle fraction from a biological sample from the subject; and b) detecting the presence or absence of one or more tRNAs within the microvesicle fraction, wherein the tRNA is associated with the disease or other medical condition. The methods

may further comprise the step or steps of correlating the presence or absence of one or more tRNAs to the presence, absence, or increased or decreased levels of one or more HERV sequences. The methods may also further comprise the step or steps of comparing the result of the detection step to a control (e.g., comparing the levels of one or more tRNAs, HERV sequences, or combinations thereof detected in the sample to the levels of one or more tRNAs, HERV sequences, or combinations thereof in a control sample), wherein the subject is diagnosed as having the disease or other medical condition (e.g., cancer) if there is a measurable difference in the result of the detection step as compared to a control.

[0006] In all aspects of the present invention, the tRNAs are RNA and can be identical to, similar to, or fragments of tRNAs. The tRNAs include chromosomal and mitochondrial tRNAs. The tRNAs can be modified post-translationally, for example, aminoacylated.

[0007] In all aspects of the present invention, the HERV sequences are RNA and can be identical to, similar to, or fragments of HERV sequences.

[0008] In certain preferred embodiments of the foregoing aspects of the invention, the biological sample is a tissue sample or a bodily fluid sample. The biological sample can be cells obtained from a tissue sample or bodily fluid sample. Particularly preferred bodily fluid samples are plasma and serum.

[0009] In certain preferred embodiments, the disease or medical condition is associated with the absence or presence one or more tRNAs, HERV sequences, or combinations thereof. In other embodiments, the disease or medical condition is associated with the increased or decreased levels of one or more tRNAs, HERV sequences, or combinations thereof. The absence or presence of one or more tRNAs, HERV sequences, or combinations thereof can be used to diagnose, prognose, or monitor the disease or medical condition. In other embodiments, the increased or decreased levels of one or more tRNAs, HERV sequences, or combinations thereof can be used to diagnose, prognose, or monitor the disease or medical condition.

[00010] In certain embodiments of the foregoing aspects of the invention, the disease or other medical condition is a neoplastic disease or condition (e.g., cancer or cell proliferative disorder), a metabolic disease or condition (e.g., diabetes, inflammation, perinatal conditions or a disease or condition associated with iron metabolism), a neurological disease or condition, an immune disorder or condition, a post transplantation condition, a fetal condition, or a pathogenic infection or disease or condition associated with an infection.

[00011] Various aspects and embodiments of the invention will now be described in detail. It will be appreciated that modification of the details may be made without departing from the scope of the invention. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular.

[00012] All patents, patent applications, and publications identified are expressly incorporated herein by reference for the purpose of describing and disclosing, for example, the methodologies described in such publications that might be used in connection with the present invention. These publications are provided solely for their disclosure prior to the filing date of the present application. Nothing in this regard should be construed as an admission that the inventors are not entitled to antedate such disclosure by virtue of prior invention or for any other reason. All statements as to the date or representations as to the contents of these documents are based on the information available to the applicants and do not constitute any admission as to the correctness of the dates or contents of these documents.

BRIEF DESCRIPTION OF THE FIGURES

[00013] **Figure 1A** is a plot showing the size distribution of microvesicle total RNA extracted from 24 mL normal control (subject 1) plasma. Relative fluorescence units (FU) are plotted against the size of RNA (nucleotides, nt). The 25 nt peak represents an internal standard. The most prominent peak represents small RNA.

[00014] **Figure 1B** is plot showing the size distribution of DNA amplified with prepared cDNA template from microvesicle total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is not detected.

[00015] **Figure 1C** is plot showing the size distribution of DNA amplified with PCR product (FIG. 1B) from microvesicle total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is not detected.

[00016] **Figure 1D** is a plot showing the size distribution of DNA amplified with PCR product (FIG. 1C) from microvesicle total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is detected.

[00017] **Figure 2A** is a plot showing the size distribution of microvesicle total RNA extracted from 2 mL normal control (subject 2) plasma. Relative fluorescence units (FU) are plotted against the size of RNA (nucleotides, nt). The 25 nt peak represents an internal

standard. The most prominent peak represents small RNA. The peaks at ~1900 nt and ~4700 nt represent 18S and 28S, respectively.

[00018] **Figure 2B** is plots showing the size distribution of DNA amplified with prepared cDNA from microvesicle total RNA using four different annealing temperatures. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). Each panel shows a PCR product amplified with different annealing temperature. Top right: 48°C; Top left: 50°C; Bottom left: 52°C; Bottom right: 54°C. The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is not detected.

[00019] **Figure 2C** is plots showing the size distribution of DNA amplified with respective PCR product template (FIG. 2B) from microvesicle total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). Each panel represents a different PCR product template. Top: 48°C template; Middle right: 50°C template; Middle left: 52°C template; Bottom: 54°C template. The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is detected.

[00020] **Figure 3A** is a plot showing the size distribution of total RNA extracted from 1 mL normal control (subject 1) leukocytes. Relative fluorescence units (FU) are plotted against the size of RNA (nucleotides, nt). The 25 nt peak represents an internal standard. The two most prominent peaks represent 18S (~1900 nt) and 28S (~4700 nt). The ~150bp peak represents small RNA.

[00021] **Figure 3B** is a plot showing the size distribution of DNA amplified with prepared cDNA template from leukocyte total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is detected.

[00022] **Figure 3C** is plots showing the size distribution of DNA amplified with PCR product template (FIG. 3B) from leukocyte total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). Each panel represents a different amount of PCR product template. Top left: No dilution; Top right: 1:1 dilution; Bottom: 1:4 dilution. The 15 bp and 1500 bp peaks represent internal standards. Amplified DNA is detected.

[00023] **Figure 4A** is plots showing the size distribution of microvesicle total RNA extracted from 2 mL serum. Relative fluorescence units (FU) are plotted against the size of RNA (nucleotides, nt). Each panel shows a different subject. Top left: subject 1; Top right: subject 2; Middle left: subject 7; Middle right: subject 5; Bottom left: subject 6; Bottom right: subject 4. The 25 nt peak represents an internal standard. The most prominent peak

represents small RNA. The peaks at ~1900 nt and ~4700 nt represent 18S and 28S, respectively.

[00024] **Figure 4B** is plots showing the size distribution of DNA amplified with prepared cDNA template from microvesicle total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). Each panel represents a different subject. Top left: subject 1; Top right: subject 2; Middle left: subject 7; Middle right: subject 5; Bottom left: subject 6; Bottom right: subject 4. The 15 bp and 1500 bp peaks represent internal standards. Amplified cDNA is detected in subject 1, 2, 4, and 5. It is thought that amplified genomic DNA is detected in subject 6 and 7.

[00025] **Figure 5A** is plots showing the size distribution of microvesicle total RNA extracted from 7-8 mL serum. Relative fluorescence units (FU) are plotted against the size of RNA (nucleotides, nt). Each panel represents a different subject. Top right: subject 3; Top left: subject 1; Middle right: subject 2; Middle left: subject 4; Bottom right: subject 5; Bottom left: subject 6. The 25 nt peak represents an internal standard. The most prominent peak represents small RNA. For subjects 4-6, the peaks at ~1900 nt and ~4700 nt represent 18S and 28S, respectively. For subjects 1-3, 18S and 28S are incorrectly shown at ~4,000 nt and ~7,000 nt, respectively, due to technical difficulties. Instead, the 18S and 28S peaks should be shown at ~1900 nt and at ~4700 nt, respectively.

[00026] **Figure 5B** is plots showing the size distribution of DNA amplified with prepared cDNA template from microvesicle total RNA. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). Each panel represents a different subject. Top left: subject 3; Top right: subject 1; Middle left: subject 2; Middle right: subject 4; Bottom right: subject 5; Bottom left: subject 6. Amplified DNA is detected in all subjects.

[00027] **Figure 5C** is plots showing the size distribution of DNA amplified with PCR products (FIG5B) and Illumina adaptors and indexes. Relative fluorescence units (FU) are plotted against the size of DNA (base pairs, bp). Each panel represents a different subject. Top left: subject 3; Top right: subject 1; Middle left: subject 2; Middle right: subject 4; Bottom right: subject 5; Bottom left: subject 6. Amplified DNA is detected in all subjects.

DETAILED DESCRIPTION OF THE INVENTION

[00028] Microvesicles are shed by eukaryotic cells, or budded off of the plasma membrane, to the exterior of the cell. These membrane vesicles are heterogeneous in size with diameters ranging from about 10nm to about 5000 nm. All membrane vesicles shed by cells < 0.8µm in diameter are referred to herein collectively as “microvesicles”. This may

include exosomes, exosome-like particles, prostasomes, dexosomes, texosomes, ectosomes, oncosomes, apoptotic bodies, retrovirus-like particles, and human endogenous retrovirus (HERV) particles. Small microvesicles (approximately 10 to 1000nm, and more often 30 to 200 nm in diameter) that are released by exocytosis of intracellular multivesicular bodies are referred to in the art as "exosomes". The methods and compositions described herein are equally applicable to microvesicles of all sizes; preferably 30 to 800 nm.

[00029] In some of the literature, the term "exosome" also refers to protein complexes containing exoribonucleases which are involved in mRNA degradation and the processing of small nucleolar RNAs (snoRNAs), small nuclear RNAs (snRNAs) and ribosomal RNAs (rRNA) (Liu et al., 2006b; van Dijk et al., 2007). Such protein complexes do not have membranes and are not "microvesicles" or "exosomes" as those terms are used herein.

Microvesicles Contain HERV Elements and Transfer RNAs

[00030] The present invention is related to the discovery that nucleic acids can be isolated from microvesicles obtained from biological samples of subjects, and analysis of these nucleic acids can be useful for diagnosis, prognosis, and monitoring of diseases. The RNA content of microvesicles includes RNAs from the nucleus, cytoplasm, or mitochondria of cells from which the microvesicles originated. Such RNAs can include, but are not limited to, messenger RNAs (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), retrotransposon elements, HERV elements, microRNA (miRNA), and other noncoding RNAs. The present invention is primarily concerned with chromosomal tRNAs, mitochondrial tRNAs, and HERV elements.

[00031] Approximately 8% (or 98,000 elements and fragments) of the human genome is made up of human endogenous retrovirus (HERV) elements or sequences. These sequences are derived from ancient viral infections from retroviruses that are inherited by successive generations and now are permanently integrated into the genome. Retroviruses are single-stranded RNA viruses that reverse-transcribe their RNA into DNA for integration into the host's genome. Most retroviruses (such as HIV-1) infect somatic cells, but in very rare cases, it is thought that exogenous retroviruses have infected germline cells allowing integrated retroviral genetic sequences to be passed on to subsequent progeny, thereby becoming 'endogenous'. Endogenous retroviruses have persisted in the genome of their hosts for thousands of years. Once integrated into the host genome, the retroviral genome acquires inactivating mutations during host DNA replication, and therefore becomes

defective for replication and infection. Most HERVs are merely traces of original viruses, having first integrated millions of years ago.

[00032] HERV elements possess the characteristic provirus structure, including long terminal repeats (LTR), structural proteins (e.g., *gag*, *pol*, and *env*), and a putative primer binding site (PBS) which can be complementary to a distinct transfer RNA (tRNA).

Families of HERV elements are designated according to which tRNA they bind. For example, HERV-E family binds tRNA-Glutamic acid (Repaske et al. 1985), while the HERV-H, -I, and -P, respectively bind tRNAs for His, Ile, and Pro (Maeda et al., 1985; Harada et al., 1987).

[00033] HERV elements or sequences have been linked to disease and medical conditions. For example, increased transcription of HERV elements has been noted in a number of cancer cell types. Increased expression of these elements in cancer seems to result in part from overall hypomethylation of the genome, which is also associated with genomic instability and tumor progression. Increased expression of HERV RNA and proteins, as well as formation of retrovirus-like particles, has been reported in tumor tissue from breast cancer, melanoma, and germ cell carcinoma. Antibodies against HERV proteins and virus-like particles, are also found in blood of some cancer patients. Recent studies have found that HERV elements are highly enriched in microvesicles released from tumor cells (Balaj et al., 2011).

[00034] “HERV elements”, as used herein, refer to RNA sequences that are identical, similar to, or fragments of HERV elements.

[00035] tRNAs are generally 73-93 nucleotides in length, and primarily facilitate the translation of messenger RNA (mRNA) into proteins by recognizing the three letter genetic codon and physically transferring the appropriate amino acid for elongation of the protein at the ribosome. Within the human genome, there are 22 mitochondrial tRNA genes, 497 chromosomal tRNA genes, and there are 324 tRNA-derived putative pseudogenes (Lander et al., 2001). In addition to its primary role in protein synthesis, tRNAs are involved in diverse cellular functions including gene expression and cell death regulation (Mei 2010, Wek 1989, Yamasaki 2009), amino acid (Wilcox 1968), lipid (Lennarz 1966), and porphyrin synthesis (Jahn D 1992), protein degradation (Gonda 1989), and retroviral and retrotransposon replication initiation (Dahlberg 1974 (retroviral), Dewannieux 2006 (HERVs)). It is important to take note of tRNAs’ unique role in reverse transcription

initiation because both retrotransposon and HERV RNAs have been found to be upregulated in cancer microvesicles (Balaj 2010).

[00036] tRNAs have also been linked to disease and medical conditions. For example, previous studies have shown that tRNA expression is enhanced in tumor cells (Reviews: White 2004, Marshall 2008) (Kuchino 1978, Winter 2000, Daly 2005, Pavon-Eternod 2009, Zhou 2009). Further, elevated levels of a specific tRNA has been shown to lead to cellular transformation, suggesting a causal role of tRNA in tumorigenesis (Marshall 2008).

[00037] Herein we show that microvesicles are enriched in mitochondrial 16S rRNA and mitochondrial tRNA. Some tRNAs present in microvesicles are post-transcriptionally modified, such as aminoacylated. Distribution patterns, or abundance of specific tRNAs may be different in microvesicles from a diseased state compared to normal state. Thus, the present invention relates to detection, measuring, analysis, and correlation of tRNA presence, absence, or levels to the diagnosis, prognosis, and monitoring of a disease or other medical condition.

[00038] The term “tRNAs”, as used herein, refers to RNA molecules identical to, similar to, or fragments of tRNAs. The tRNA of the present invention can be transcribed from chromosomal DNA, herein referred to as “chromosomal tRNA”, or from mitochondrial DNA, herein referred to as “mitochondrial tRNA”. tRNAs may be found, for example, in the cytoplasm, nucleus, mitochondria, or other organelles and vesicles within a cell. The tRNA of the present invention may also comprise sequences that are complementary to HERV elements or fragments thereof.

[00039] As discussed above, HERV elements and tRNAs are differentially expressed in different disease states. Therefore, the presence, absence, or relative levels of tRNAs and/or HERV elements can be used for effective detection, diagnosis, monitoring, and evaluation of a disease or medical condition. For example, elevated levels of a specific species of tRNA associated with elevated expression of a specific HERV element detected in microvesicles isolated from a subject may indicate presence of a disease, such as cancer. Specifically, elevated expression of HERV-H accompanied by higher prevalence of Histidine tRNA may indicate presence of glioma.

Microvesicles As Diagnostic And/Or Prognostic Tools

[00040] Certain aspects of the present invention are based on the finding that glioblastoma derived microvesicles can be isolated from the serum of glioblastoma patients. These microvesicles contain mRNA associated with tumor cells. The nucleic acids found

within these microvesicles, as well as other contents of the microvesicles such as angiogenic proteins, can be used as valuable biomarkers for tumor diagnosis, characterization and prognosis by providing a genetic profile. Contents within these microvesicles can also be used to monitor tumor progression over time by analyzing if other mutations are acquired during tumor progression as well as if the levels of certain mutations are becoming increased or decreased over time or over a course of treatment.

[00041] Recently, it has been discovered that tRNAs and HERV elements can be isolated from microvesicles obtained from biological samples. The tRNAs include, but are not limited to, RNA sequences that are identical to, similar to, or fragments of chromosomal and mitochondrial tRNAs. The HERV elements include, but are not limited to, RNA sequences that are identical to, similar to, or fragments of HERV elements.

[00042] Certain aspects of the present invention are based on the finding that microvesicles are secreted by tumor cells and circulating in bodily fluids. The number of microvesicles increases as the tumor activity increases. The higher the tumor activity, the higher the concentration of microvesicles in bodily fluids. In addition, the concentration of nucleic acid, in particular small nucleic acid (75-750 nucleotides), increases as the tumor activity increases. Tumor activity may refer to the malignancy, metastatic potential, or proliferation rate of the tumor.

[00043] Certain aspects of the present invention are based on another surprising finding that most of the extracellular RNAs in bodily fluid of a subject are contained within microvesicles and thus protected from degradation by ribonucleases.

[00044] One aspect of the present invention relates to methods for detecting, diagnosing, monitoring, treating or evaluating a disease or other medical condition in a subject comprising the steps of, isolating microvesicles from a tissue sample or bodily fluid of a subject, and analyzing one or more tRNAs, HERV elements, or combinations thereof contained within the microvesicles. HERV elements and tRNAs are differentially expressed in different disease states. Therefore, the presence, absence, or relative levels of tRNAs and/or HERV elements can be used for effective detection, diagnosis, monitoring, and evaluation of a disease or medical condition. The one or more tRNAs, HERV elements, or combinations thereof are analyzed qualitatively and/or quantitatively, and the results are compared to results expected or obtained for one or more other subjects who have or do not have the disease or other medical condition. The presence of a difference in microvesicular tRNA or HERV element content of the subject, as compared to that of one or more other

individuals, can indicate the presence or absence of, the progression of (e.g., changes of tumor size and tumor malignancy), the susceptibility to, or predisposition for a disease or other medical condition in the subject.

[00045] Indeed, the isolation methods and techniques described herein provide the following heretofore unrealized advantages: 1) the opportunity to selectively analyze disease or other medical condition-specific tRNAs and/or HERV elements, which may be realized by isolating disease- or medical condition-specific microvesicles apart from other microvesicles within the tissue or fluid sample; and 2) scalability, e.g., to detect tRNAs and/or HERV elements expressed at low levels, the sensitivity can be increased by pelleting more microvesicles from a larger volume of tissue or fluid;

[00046] The microvesicles can be isolated from a sample taken from a tissue from a subject. As used herein, a "tissue sample" refers to a sample of tissue isolated from anywhere in the body of the subject, including but not limited to, for example, lung, pancreas, stomach, intestine, bladder, kidney, ovary, testis, skin, colorectal, breast, prostate, brain, esophagus, liver, placenta, spleen, bone marrow, heart, pancreas, lymph node, and combinations thereof. The tissue sample may be isolated from a biopsy tissue or tissue affected by disease or other medical condition, e.g., tumor or cyst.

[00047] The microvesicles are preferably isolated from a sample taken of a bodily fluid from a subject. As used herein, a "bodily fluid" refers to a sample of fluid isolated from anywhere in the body of the subject, preferably a peripheral location, including but not limited to, for example, blood, plasma, serum, urine, sputum, spinal fluid, pleural fluid, nipple aspirates, lymph fluid, fluid of the respiratory, intestinal, and genitourinary tracts, tear fluid, saliva, breast milk, fluid from the lymphatic system, semen, cerebrospinal fluid, intraorgan system fluid, ascitic fluid, tumor cyst fluid, amniotic fluid and combinations thereof. The microvesicles of the present invention are preferably isolated from plasma or serum from a subject.

[00048] The term "subject" is intended to include all animals shown to or expected to have microvesicles. In particular embodiments, the subject is a mammal, a human or nonhuman primate, a dog, a cat, a horse, a cow, other farm animals, or a rodent (e.g., mice, rats, guinea pig. etc.). The term "subject" and "individual" are used interchangeably herein.

[00049] Methods of isolating microvesicles from a biological sample are known in the art. For example, a method of differential centrifugation is described in a paper by Raposo et al. (Raposo et al., 1996), and similar methods are detailed in the Examples section herein.

Methods of anion exchange and/or gel permeation chromatography are described in US Patent Nos. 6,899,863 and 6,812,023. Methods of sucrose density gradients or organelle electrophoresis are described in U.S. Patent No. 7,198,923. A method of magnetic activated cell sorting (MACS, Miltenyi) is described in (Taylor and Gercel-Taylor, 2008). A method of nanomembrane ultrafiltration concentrator is described in (Cheruvanky et al., 2007). Preferably, microvesicles can be identified and isolated from bodily fluid of a subject by a newly developed microchip technology that uses a unique microfluidic platform to efficiently and selectively separate tumor derived microvesicles. This technology, as described in a paper by Negrath et al. (Negrath et al., 2007), can be adapted to identify and separate microvesicles using similar principles of capture and separation as taught in the paper. Each of the foregoing references is incorporated by reference herein for its teaching of these methods.

[00050] In one embodiment, the microvesicles isolated from a bodily fluid are enriched for those originating from a specific cell type, for example, lung, pancreas, stomach, intestine, bladder, kidney, ovary, testis, skin, colorectal, breast, prostate, brain, esophagus, liver, placenta, fetus cells. Because the microvesicles often carry surface molecules such as antigens from their donor cells, surface molecules may be used to identify, isolate and/or enrich for microvesicles from a specific donor cell type (Al-Nedawi et al., 2008; Taylor and Gercel-Taylor, 2008). In this way, microvesicles originating from distinct cell populations can be analyzed for their RNA content. For example, tumor (malignant and nonmalignant) microvesicles carry tumor-associated surface antigens and may be detected, isolated and/or enriched via these specific tumor-associated surface antigens. In one example, the surface antigen is epithelial-cell-adhesion-molecule (EpCAM), which is specific to microvesicles from carcinomas of lung, colorectal, breast, prostate, head and neck, and hepatic origin, but not of hematological cell origin (Balzar et al., 1999; Went et al., 2004). In another example, the surface antigen is CD24, which is a glycoprotein specific to urine microvesicles (Keller et al., 2007). In yet another example, the surface antigen is selected from a group of molecules CD70, carcinoembryonic antigen (CEA), EGFR, EGFRvIII and other variants, Fas ligand, TRAIL, transferrin receptor, p38.5, p97 and HSP72. Additionally, tumor specific microvesicles may be characterized by the lack of surface markers, such as CD80 and CD86.

[00051] The isolation of microvesicles from specific cell types can be accomplished, for example, by using antibodies, aptamers, aptamer analogs or molecularly imprinted polymers

specific for a desired surface antigen. In one embodiment, the surface antigen is specific for a cancer type. In another embodiment, the surface antigen is specific for a cell type which is not necessarily cancerous. One example of a method of microvesicle separation based on cell surface antigen is provided in U.S. Patent No. 7,198,923. As described in, e.g., U.S. Patent Nos. 5,840,867 and 5,582,981, WO/2003/050290 and a publication by Johnson et al. (Johnson et al., 2008), aptamers and their analogs specifically bind surface molecules and can be used as a separation tool for retrieving cell type-specific microvesicles. Molecularly imprinted polymers also specifically recognize surface molecules as described in, e.g., US Patent Nos. 6,525,154, 7,332,553 and 7,384,589 and a publication by Bossi et al. (Bossi et al., 2007) and are a tool for retrieving and isolating cell type-specific microvesicles. Each of the foregoing reference is incorporated herein for its teaching of these methods.

[00052] It may be beneficial or otherwise desirable to extract tRNAs and/or HERV elements from the microvesicles prior to the analysis. RNA molecules can be isolated from a microvesicle using any number of procedures, which are well-known in the art, the particular isolation procedure chosen being appropriate for the particular biological sample. Examples of methods for extraction are provided in the Examples section herein. In some instances, with some techniques, it may also be possible to analyze the RNA without extraction from the microvesicle.

[00053] In one embodiment, the tRNAs and/or HERV elements are analyzed directly without an amplification step. Direct analysis may be performed with different methods including, but not limited to, the nanostring technology. NanoString technology enables identification and quantification of individual target molecules in a biological sample by attaching a color coded fluorescent reporter to each target molecule. This approach is similar to the concept of measuring inventory by scanning barcodes. Reporters can be made with hundreds or even thousands of different codes allowing for highly multiplexed analysis. The technology is described in a publication by Geiss et al. (Geiss et al., 2008) and is incorporated herein by reference for this teaching.

[00054] In another embodiment, it may be beneficial or otherwise desirable to amplify the nucleic acid of the microvesicle prior to analyzing it. Methods of nucleic acid amplification are commonly used and generally known in the art, many examples of which are described herein. If desired, the amplification can be performed such that it is quantitative. Quantitative amplification will allow quantitative determination of relative amounts of the various nucleic acids, to generate a profile as described below.

[00055] In one embodiment, the extracted RNA is similar to, identical to, or a fragment of a tRNA. In another embodiment, the extracted RNA is similar to, identical to, or a fragment of a HERV element. RNAs are then preferably reverse-transcribed into complementary DNAs before further amplification. Such reverse transcription may be performed alone or in combination with an amplification step. One example of a method combining reverse transcription and amplification steps is reverse transcription polymerase chain reaction (RT-PCR), which may be further modified to be quantitative, e.g., quantitative RT-PCR as described in US Patent No. 5,639,606, which is incorporated herein by reference for this teaching.

[00056] Nucleic acid amplification methods include, without limitation, polymerase chain reaction (PCR) (US Patent No. 5,219,727) and its variants such as in situ polymerase chain reaction (US Patent No. 5,538,871), quantitative polymerase chain reaction (US Patent No. 5,219,727), nested polymerase chain reaction (US Patent No. 5,556,773), self sustained sequence replication and its variants (Guatelli et al., 1990), transcriptional amplification system and its variants (Kwoh et al., 1989), Qb Replicase and its variants (Miele et al., 1983), cold-PCR (Li et al., 2008) or any other nucleic acid amplification methods, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. Especially useful are those detection schemes designed for the detection of nucleic acid molecules if such molecules are present in very low numbers. The foregoing references are incorporated herein for their teachings of these methods.

[00057] The analysis of nucleic acids present in the microvesicles is quantitative and/or qualitative. For quantitative analysis, the amounts (expression levels), either relative or absolute, of specific nucleic acids of interest within the microvesicles are measured with methods known in the art (described below). For qualitative analysis, the species of specific nucleic acids of interest within the microvesicles, whether wild type or variants, are identified with methods known in the art (described below).

[00058] In one embodiment, the tRNA and/or HERV elements are identified and measured from a biological sample in a method comprising: isolating the microvesicle fraction from the biological sample (e.g., by ultracentrifugation), lysing the microvesicles and extracting the RNA (with the optional step of RNA extraction enhancement, e.g., addition of an RNase inhibitor, for example RNasin), optionally DNase treating the extracted RNA, optionally purifying the extracted RNA (e.g., phenol-chloroform extraction and ethanol precipitation), analyzing RNA quality and concentration, preparing a small

RNA cDNA library, amplifying the small RNA cDNA library (e.g., using primers complementary to the 3' adaptor oligonucleotides), and sequencing the PCR products from the amplification step (e.g., Sanger or Illumina sequencing). Preparing a small RNA cDNA library can include: ligating adaptor oligonucleotides, purifying and concentrating the ligation products, reverse-transcription the ligation product, and purifying and concentrating the cDNA products.

[00059] Detection of one or more tRNAs and/or HERV elements can be accomplished by performing a nucleotide variant screen on the nucleic acids within the microvesicles. Such a screen can be as wide or narrow as determined necessary or desirable by the skilled practitioner. It can be a wide screen (set up to detect all tRNAs and/or HERV elements known to be associated with one or more disease states or other medical conditions, e.g., cancer). Where one specific disease or other medical condition is suspected or known to exist, the screen can be specific to that cancer or disease. One example is a brain tumor/brain cancer screen (e.g., set up to detect all tRNAs and/or HERV elements associated with various clinically distinct subtypes of brain cancer or known drug-resistant or drug-sensitive mutations of that cancer).

[00060] In one embodiment, the analysis is of a profile of the amounts (levels) of specific nucleic acids present in the microvesicle, herein referred to as a "quantitative nucleic acid profile" of the microvesicles. In another embodiment, the analysis is of a profile of the species of specific nucleic acids present in the microvesicles, herein referred to as a "nucleic acid species profile." A term used herein to refer to a combination of these types of profiles is "genetic profile" which refers to the determination of the presence or absence of nucleotide species, variants and also increases or decreases in nucleic acid levels.

[00061] Once generated, these genetic profiles of the microvesicles are compared to those expected in, or otherwise derived from a healthy normal individual. A profile can be a genome wide profile (set up to detect all possible expressed genes or DNA sequences). It can be narrower as well, such as a cancer wide profile (set up to detect all possible genes or nucleic acids derived therefrom, or known to be associated with one or more cancers).

[00062] Where one specific disease or other medical condition is suspected or known to exist, the profile can be specific to that disease or other medical condition (e.g., set up to detect all possible tRNAs or HERV elements derived therefrom, associated with various clinically distinct subtypes of that cancer or known drug-resistant or sensitive mutations of that disease or other medical condition).

[00063] Which nucleic acids are to be amplified and/or analyzed can be selected by the skilled practitioner. The entire nucleic acid content of the microvesicles or only a subset of specific nucleic acids which are likely or suspected of being influenced by the presence of a disease or other medical condition such as cancer, can be amplified and/or analyzed. The identification of a nucleic acid aberration(s) in the analyzed microvesicle nucleic acid can be used to diagnose the subject for the presence of a disease such as cancer, hereditary diseases or viral infection with which that aberration(s) is associated. For instance, analysis for the presence or absence of one or more tRNAs or HERV elements specific to a particular disease or other medical condition (e.g., cancer) can indicate the presence of the disease or medical condition in the individual. Alternatively, or in addition, analysis of one or more tRNAs or HERV elements for an increase or decrease in nucleic acid levels specific to a cancer can indicate the presence of the disease or other medical condition in the individual.

[00064] The nucleic acid sequences may be complete or partial, as both are expected to yield useful information in diagnosis and prognosis of a disease. The sequences may be sense or anti-sense to the actual gene or transcribed sequences. The skilled practitioner will be able to devise detection methods for a nucleotide variance from either the sense or anti-sense nucleic acids which may be present in a microvesicle. Many such methods involve the use of probes which are specific for the nucleotide sequences which directly flank, or contain the nucleotide variances. Such probes can be designed by the skilled practitioner given the knowledge of the gene sequences and the location of the nucleic acid variants within the gene. Such probes can be used to isolate, amplify, and/or actually hybridize to detect the nucleic acid variants, as described in the art and herein.

[00065] Determining the presence or absence of a particular nucleotide variant or plurality of variants in the nucleic acid within microvesicles from a subject can be performed in a variety of ways. A variety of methods are available for such analysis, including, but not limited to, PCR, hybridization with allele-specific probes, enzymatic mutation detection, chemical cleavage of mismatches, mass spectrometry or DNA sequencing, including minisequencing. In particular embodiments, hybridization with allele specific probes can be conducted in two formats: 1) allele specific oligonucleotides bound to a solid phase (glass, silicon, nylon membranes) and the labeled sample in solution, as in many DNA chip applications, or 2) bound sample (often cloned DNA or PCR amplified DNA) and labeled oligonucleotides in solution (either allele specific or short so as to allow sequencing by hybridization). Diagnostic tests may involve a panel of variances, often on a solid support,

which enables the simultaneous determination of more than one variance. In another embodiment, determining the presence of at least one nucleic acid variance in the microvesicle nucleic acid entails a haplotyping test. Methods of determining haplotypes are known to those of skill in the art, as for example, in WO 00/04194.

[00066] In one embodiment, the determination of the presence or absence of a nucleic acid variant(s) involves determining the sequence of the variant site or sites (the exact location within the sequence where the nucleic acid variation from the norm occurs) by methods such as polymerase chain reaction (PCR), chain terminating DNA sequencing (US Patent No. 5547859), minisequencing (Fiorentino et al., 2003), oligonucleotide hybridization, high-throughput sequencing, , , mass spectrometry or other nucleic acid sequence detection methods. Methods for detecting nucleic acid variants are well known in the art and disclosed in WO 00/04194, incorporated herein by reference. In an exemplary method, the diagnostic test comprises amplifying a segment of DNA or RNA (generally after converting the RNA to complementary DNA) spanning one or more known variants in the desired gene sequence. This amplified segment is then sequenced and/or subjected to electrophoresis in order to identify transfer RNAs in the amplified segment.

[00067] In one embodiment, the invention provides a method of screening for tRNAs and/or HERV elements in the nucleic acids of microvesicles isolated as described herein. This can be achieved, for example, by PCR or, alternatively, in a ligation chain reaction (LCR) (Abravaya et al., 1995; Landegren et al., 1988; Nakazawa et al., 1994). LCR can be particularly useful for detecting point mutations in a gene of interest (Abravaya et al., 1995). The LCR method comprises the steps of designing degenerate primers for amplifying the target sequence, the primers corresponding to one or more conserved regions of the nucleic acid corresponding to the gene of interest, amplifying PCR products with the primers using, as a template, a nucleic acid obtained from a microvesicle, and analyzing the PCR products. Comparison of the PCR products of the microvesicle nucleic acid to a control sample (either having the nucleotide variant or not) indicates variants in the microvesicle nucleic acid. The change can be either an absence or presence of a nucleotide variant in the microvesicle nucleic acid, depending upon the control.

[00068] Analysis of amplification products can be performed using any method capable of separating the amplification products according to their size, including automated and manual gel electrophoresis, mass spectrometry, and the like.

[00069] Alternatively, the amplification products can be analyzed based on sequence differences, using SSCP, DGGE, TGGE, chemical cleavage, OLA, restriction fragment length polymorphisms as well as hybridization, for example, nucleic acid microarrays.

[00070] The methods of nucleic acid isolation, amplification and analysis are routine for one skilled in the art and examples of protocols can be found, for example, in *Molecular Cloning: A Laboratory Manual* (3-Volume Set) Ed. Joseph Sambrook, David W. Russel, and Joe Sambrook, Cold Spring Harbor Laboratory, 3rd edition (January 15, 2001), ISBN: 0879695773. A particular useful protocol source for methods used in PCR amplification is *PCR Basics: From Background to Bench* by Springer Verlag; 1st edition (October 15, 2000), ISBN: 0387916008.

[00071] Identification of tRNA and/or HERV elements associated with specific diseases and/or medical conditions by the methods described herein can also be used for prognosis and treatment decisions of an individual diagnosed with a disease or other medical condition such as cancer. Presence, absence, or relative levels of tRNAs and/or HERV elements may also provide useful information guiding the treatment of the disease and/or medical condition.

[00072] As such, aspects of the present invention relate to a method for monitoring disease (e.g., cancer) progression in a subject, and also to a method for monitoring disease recurrence in an individual. These methods comprise the steps of isolating microvesicles from a tissue or bodily fluid of an individual, as discussed herein, and analyzing nucleic acid within the microvesicles as discussed herein (e.g., to create a genetic profile of the microvesicles). The presence/absence of a certain genetic aberration/profile is used to indicate the presence/absence of the disease or other medical condition (e.g., cancer) in the subject as discussed herein. The process is performed periodically over time, and the results reviewed, to monitor the progression or regression of the disease, or to determine recurrence of the disease. Put another way, a change in the genetic profile indicates a change in the disease state in the subject. The period of time to elapse between sampling of microvesicles from the subject, for performance of the isolation and analysis of the microvesicle, will depend upon the circumstances of the subject, and is to be determined by the skilled practitioner. Such a method would prove extremely beneficial when analyzing a nucleic acid from a gene that is associated with the therapy undergone by the subject. For example, a gene which is targeted by the therapy can be monitored for the development of mutations which make it resistant to the therapy, upon which time the therapy can be

modified accordingly. The monitored gene may also be one which indicates specific responsiveness to a specific therapy.

[00073] Aspects of the present invention also relate to the fact that a variety of non-cancer diseases and/or medical conditions also are associated with HERV sequences and different levels of tRNAs, and such diseases and/or medical conditions can likewise be diagnosed and/or monitored by the methods described herein. Many such diseases are metabolic, infectious or degenerative in nature. One such disease is diabetes (e.g., diabetes insipidus) in which the vasopressin type 2 receptor (V2R) is modified. Another such disease is kidney fibrosis in which the genetic profiles for the genes of collagens, fibronectin and TGF- β 3 are changed. Changes in the genetic profile due to substance abuse (e.g., a steroid or drug use), viral and/or bacterial infection, and hereditary disease states can likewise be detected by the methods described herein.

[00074] Diseases or other medical conditions for which the inventions described herein are applicable include, but are not limited to, nephropathy, diabetes insipidus, diabetes type I, diabetes II, renal disease glomerulonephritis, bacterial or viral glomerulonephritides, IgA nephropathy, Henoch-Schonlein Purpura, membranoproliferative glomerulonephritis, membranous nephropathy, Sjogren's syndrome, nephrotic syndrome minimal change disease, focal glomerulosclerosis and related disorders, acute renal failure, acute tubulointerstitial nephritis, pyelonephritis, GU tract inflammatory disease, Pre-clampsia, renal graft rejection, leprosy, reflux nephropathy, nephrolithiasis, genetic renal disease, medullary cystic, medullar sponge, polycystic kidney disease, autosomal dominant polycystic kidney disease, autosomal recessive polycystic kidney disease, tuberous sclerosis, von Hippel-Lindau disease, familial thin-glomerular basement membrane disease, collagen III glomerulopathy, fibronectin glomerulopathy, Alport's syndrome, Fabry's disease, Nail-Patella Syndrome, congenital urologic anomalies, monoclonal gammopathies, multiple myeloma, amyloidosis and related disorders, febrile illness, familial Mediterranean fever, HIV infection-AIDS, inflammatory disease, systemic vasculitides, polyarteritis nodosa, Wegener's granulomatosis, polyarteritis, necrotizing and crescentic glomerulonephritis, polymyositis-dermatomyositis, pancreatitis, rheumatoid arthritis, systemic lupus erythematosus, gout, blood disorders, sickle cell disease, thrombotic thrombocytopenia purpura, Fanconi's syndrome, transplantation, acute kidney injury, irritable bowel syndrome, hemolytic-uremic syndrome, acute cortical necrosis, renal thromboembolism, trauma and surgery, extensive injury, burns, abdominal and vascular surgery, induction of anesthesia, side effect of use of drugs or

drug abuse, circulatory disease myocardial infarction, cardiac failure, peripheral vascular disease, hypertension, coronary heart disease, non-atherosclerotic cardiovascular disease, atherosclerotic cardiovascular disease, skin disease, psoriasis, systemic sclerosis, respiratory disease, COPD, obstructive sleep apnoea, hypoxia at high altitude or endocrine disease, acromegaly, diabetes mellitus, or diabetes insipidus.

[00075] Selection of an individual from whom the microvesicles are isolated is performed by the skilled practitioner based upon analysis of one or more of a variety of factors. Such factors for consideration are whether the subject has a family history of a specific disease (e.g., a cancer), has a genetic predisposition for such a disease, has an increased risk for such a disease due to family history, genetic predisposition, other disease or physical symptoms which indicate a predisposition, or environmental reasons. Environmental reasons include lifestyle, exposure to agents which cause or contribute to the disease such as in the air, land, water or diet. In addition, having previously had the disease, being currently diagnosed with the disease prior to therapy or after therapy, being currently treated for the disease (undergoing therapy), being in remission or recovery from the disease, are other reasons to select an individual for performing the methods.

[00076] The methods described herein are optionally performed with the additional step of selecting a gene or nucleic acid for analysis, prior to the analysis step. This selection can be based on any predispositions of the subject, or any previous exposures or diagnosis, or therapeutic treatments experienced or concurrently undergone by the subject.

[00077] The cancer diagnosed, monitored or otherwise profiled, can be any kind of cancer. This includes, without limitation, epithelial cell cancers such as lung, ovarian, cervical, endometrial, breast, brain, colon and prostate cancers. Also included are gastrointestinal cancer, head and neck cancer, non-small cell lung cancer, cancer of the nervous system, kidney cancer, retina cancer, skin cancer, liver cancer, pancreatic cancer, genital-urinary cancer and bladder cancer, melanoma, and leukemia. In addition, the methods and compositions of the present invention are equally applicable to detection, diagnosis and prognosis of non-malignant tumors in an individual (e.g., neurofibromas, meningiomas and schwannomas).

[00078] In one embodiment, the cancer is brain cancer. Types of brain tumors and cancer are well known in the art. Glioma is a general name for tumors that arise from the glial (supportive) tissue of the brain. Gliomas are the most common primary brain tumors. Astrocytomas, ependymomas, oligodendrogliomas, and tumors with mixtures of two or more

cell types, called mixed gliomas, are the most common gliomas. The following are other common types of brain tumors: Acoustic Neuroma (Neurilemmoma, Schwannoma, Neurinoma), Adenoma, Astracytoma, Low-Grade Astrocytoma, giant cell astrocytomas, Mid-and High-Grade Astrocytoma, Recurrent tumors, Brain Stem Glioma, Chordoma, Choroid Plexus Papilloma, CNS Lymphoma (Primary Malignant Lymphoma), Cysts, Dermoid cysts, Epidermoid cysts, Craniopharyngioma, Ependymoma Anaplastic ependymoma, Gangliocytoma (Ganglioneuroma), Ganglioglioma, Glioblastoma Multiforme (GBM), Malignant Astracytoma, Glioma, Hemangioblastoma, Inoperable Brain Tumors, Lymphoma, Medulloblastoma (MDL), Meningioma, Metastatic Brain Tumors, Mixed Glioma, Neurofibromatosis, Oligodendroglioma. Optic Nerve Glioma, Pineal Region Tumors, Pituitary Adenoma, PNET (Primitive Neuroectodermal Tumor), Spinal Tumors, Subependymoma, and Tuberous Sclerosis (Bourneville's Disease).

[00079] In addition to identifying previously known HERV sequences and tRNAs (as associated with diseases), the methods of the present invention can be used to identify previously unidentified HERV sequences and tRNAs or modifications thereof (e.g., post transcriptional modifications) that are associated with a certain disease and/or medical condition. This is accomplished, for example, by analysis of the nucleic acid within microvesicles from a bodily fluid of one or more subjects with a given disease/medical condition (e.g., a clinical type or subtype of cancer) and comparison to the nucleic acid within microvesicles of one or more subjects without the given disease/medical condition, to identify differences in their nucleic acid content. The differences may include, without limitation, expression level of the nucleic acid, alternative splice variants, gene copy number variants (CNV), modifications of the nucleic acid, single nucleotide polymorphisms (SNPs), and mutations (insertions, deletions or single nucleotide changes) of the nucleic acid. Once a difference in a genetic parameter of a particular nucleic acid is identified for a certain disease, further studies involving a clinically and statistically significant number of subjects may be carried out to establish the correlation between the genetic aberration of the particular nucleic acid and the disease. The analysis of genetic aberrations can be done by one or more methods described herein, as determined appropriate by the skilled practitioner.

EXAMPLES

Example 1

[00080] In one embodiment, plasma was isolated from a normal control (subject 1). Plasma was filtered through a 0.8 μm filter and divided into 1 mL aliquots. Aliquots were frozen at -80°C until needed.

[00081] Isolation of microvesicle RNA was conducted using twenty-four 1 mL aliquots of subject 1 plasma. The plasma was evenly split into eight 3mL aliquots, transferred to 5mL polyallomer tubes (Beckman-Coulter, Miami, FL, USA) containing 8 μL RNasin Plus (40 u/ μL , Promega, Madison, Wi., USA) RNase inhibitor, and incubated for 5min at room temp. Following incubation, the plasma aliquots were diluted in 2 mL PBS. Microvesicles were pelleted by ultracentrifugation at 120,000g for 80 minutes. The microvesicle pellets were each washed in 42 μL PBS and 8 μL RNasin Plus, and incubated for 20 minutes at room temp. Microvesicle pellets were lysed in 700ul Qiazol Reagent (Qiagen, Valencia, Ca., USA) and isolated using the miRNeasy kit (Qiagen). All eight aliquots of total RNA were combined, and concentrated and purified using a 30 kDa centrifugal filter unit (Millipore, Bedford, Ma., USA). The total RNA was further concentrated to 10 μL in a Speed Vac concentrator (Savant, Farmingdale, Ny., USA). Following concentration, the total RNA was quantified using a nanodrop ND-2000 instrument (Thermo Fischer Scientific, Wilmington, De., USA). Subject 1 plasma microvesicles were found to contain 1.6 ng RNA/mL plasma. The total RNA was further purified by phenol-chloroform extraction and ethanol precipitation. RNA quality and concentration was assessed with the 2100 Bioanalyzer (Agilent, Palo Alto, Ca., USA) using a RNA 6000 Pico Chip (FIG. 1A).

[00082] Small RNA cDNA library preparation was performed as previously described (Pak) with modifications. Total microvesicle RNA was ligated at 37°C for 1 hour and 16°C for 16 hours to a 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCTGTAGGCACCATCAAT/ddC/-3' (SEQ ID NO: 1) (IDT DNA, Coralvill, Ia., USA) at a 1:60 molar ratio in a reaction volume of 20 μL containing 10 U T4 RNA Ligase I (10 U/ μL ; New England BioLabs, Beverly, Ma., USA), 20 U RNasin Plus (Promega), and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the product was purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the 3'-adaptor oligonucleotide, and concentrated to 11 μL in a Speed Vac concentrator (Savant). The ligation product was reverse transcribed using Sensiscript (Qiagen) and a primer with sequence complementarity to the 3'-adaptor oligonucleotide (5'-

GATTGATGGTGCCTACAG-3' (SEQ ID NO: 2) (IDT DNA)). Following reverse transcription, the cDNA was purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the primer, and concentrated to 13 μ L in a Speed Vac concentrator (Savant). The cDNA was ligated at 37°C for 1 hour and 16°C for 2 hours to a second 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCACTCGGGCACCAAGGA/ddC/-3' (SEQ ID NO: 3) (IDT DNA)) at a 1:60 molar ratio in a reaction volume of 20 μ L containing 10 U T4 RNA Ligase I (New England BioLabs), 5% DMSO, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the cDNA was purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the second 5'-adenylated 3'-adaptor oligonucleotide, and concentrated to 9 μ L in a Speed Vac concentrator (Savant).

[00083] The final ligation product was PCR amplified using the reverse transcription primer and a primer with sequence complementarity to the second 3'-adaptor (5'-GTCCTTGGTGCCCGAGTG-3' (SEQ ID NO: 4) (IDT DNA)) in a reaction volume of 20 μ L containing 1 U Platinum Taq DNA Polymerase (Invitrogen, Carlsbad, Ca., USA), 1X Platinum Taq DNA Polymerase Buffer, 3 mM MgCl₂, 0.5 mM dNTPs, and 0.5 μ M of each primer. Amplification conditions consisted of: 1 cycle of 95°C, 10 min; 40 cycles of 95°C 30 sec; 50°C 30 sec; 68°C 30 sec; and 1 cycle of 68°C 10 min. The PCR product was assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 1B). The PCR product was submitted to a second round of amplification in the same reaction solution as above. Amplification conditions consisted of: 1 cycle of 95°C, 10 min; 20 cycles of 95°C 30 sec; -0.5°C/cycle 60°C 30 sec; 68°C 30 sec; 30 cycles of 95°C 30 sec; 50°C 30 sec; 68°C 30 sec; and 1 cycle of 68°C 10 min. The second PCR product was assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 1C). The second PCR product was submitted to a third round of amplification in the same reaction solution as above. Amplification conditions consisted of: 1 cycle of 95°C, 10 min; 20 cycles of 95°C 30 sec; -0.5°C/cycle 60°C 30 sec; 68°C 30 sec; 30 cycles of 95°C 30 sec; 50°C 30 sec; 68°C 30 sec; and 1 cycle of 68°C 10 min. The third PCR product was assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 1D).

[00084] The small RNA cDNA library third PCR product was subcloned using the TOPO TA Cloning Kit (Invitrogen), and analyzed by Sanger sequencing. The sequences are

shown in SEQ ID NOS. 7-14. The distribution of sequences, organized by origin, is shown in TABLE 1.

Example 2

[00085] In one embodiment, plasma was isolated from a normal control (subject 2). Plasma was filtered through a 0.8 μ m filter and divided into 1 mL aliquots. Aliquots were frozen at -80°C until needed.

[00086] Isolation of microvesicle RNA was conducted using eight 1 mL aliquots of subject 1 plasma. The plasma was evenly split into four 2 mL aliquots, transferred to 5 mL polyallomer tubes (Beckman-Coulter) containing 8 μ L RNasin Plus (40u/ μ L, Promega) RNase inhibitor, and incubated for 5 min at room temp. Following incubation, the plasma aliquots were diluted in 3 mL PBS. Microvesicles were pelleted by ultracentrifugation at 120,000g for 80 min. The microvesicle pellets were each washed in 42 μ L PBS and 8 μ L RNasin Plus, and incubated for 20 min at room temp. Microvesicle pellets were lysed in 700 μ L Qiazol Reagent (Qiagen, Valencia, Ca., USA) and isolated using the miRNeasy kit (Qiagen). Each RNA aliquot was assessed for quality and concentration with the 2100 Bioanalyzer (Agilent) using a RNA 6000 Pico Chip (FIG. 2A)

[00087] Small RNA cDNA library preparation was performed as previously described (Pak) with modifications. Total microvesicle RNA was ligated at 37°C for 1 hr and 16°C for 16 hrs to a 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCTGTAGGCACCATCAAT/ddC/-3' (SEQ ID NO: 1) (IDT DNA)) at a 1:100 molar ratio in a reaction volume of 80 μ L containing 40 U T4 RNA Ligase I (New England BioLabs, Beverly, Ma., USA), 80 U RNasin Plus (Promega), 1.3% DMSO, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the product was purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the 3'-adaptor oligonucleotide, and concentrated to 6 μ L in a Speed Vac concentrator (Savant). The ligation product was reverse transcribed using Sensiscript (Qiagen) and a primer with sequence complementarity to the 3'-adaptor oligonucleotide (5'-GATTGATGGTGCCTACAG-3' (SEQ ID NO: 2) (IDT DNA)). Following reverse transcription, the cDNA was purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the primer, and concentrated to 11 μ L in a Speed Vac concentrator (Savant). The cDNA was ligated at 22°C for 16 hrs to a second 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCACTCGGGCACCAAGGA/ddC/-3' (SEQ ID NO: 3) (IDT DNA)) at a 1:30 molar ratio in a reaction volume of 20 μ L containing 10 U

T4 RNA Ligase I (New England BioLabs), 5% DMSO, 25% PEG8000, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the cDNA was purified by phenol-chloroform extraction and filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the second 5'-adenylated 3'-adaptor oligonucleotide.

[00088] The final ligation product was PCR amplified using the reverse transcription primer and a primer with sequence complementarity to the second 3'-adaptor (5'-GTCCTTGTTGCCCGAGTG-3' (SEQ ID NO: 4) (IDT DNA)) in a reaction volume of 20 μ L containing 1 U Platinum Taq DNA Polymerase (Invitrogen, Carlsbad, Ca., USA), 1X Platinum Taq DNA Polymerase Buffer, 3 mM $MgCl_2$, 0.5 mM dNTPs, and 0.5 μ M of each primer. Amplification conditions consisted of: 1 cycle of 95°C, 10 min; 40 cycles of 95°C 30 sec; 48°C or 50°C or 52°C or 54°C 30 sec; 68°C 30 sec; and 1 cycle of 68°C 10 min. The PCR products were assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 2B). The PCR products were submitted to a second round of amplification in the same reaction solution as above. Amplification conditions consisted of: 1 cycle of 95°C, 10 min; 20 cycles of 95°C 30 sec; -0.5°C/cycle 60°C 30 sec; 68°C 30 sec; 30 cycles of 95°C 30 sec; 50°C 30 sec; 68°C 30 sec; and 1 cycle of 68°C 10 min. The second PCR products were assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 2C).

[00089] The small RNA cDNA library second PCR products were subcloned using the TOPO TA Cloning Kit (Invitrogen), according to the manufacturer's recommendations, and analyzed by Sanger sequencing. The sequences are shown in SEQ ID NOS. 15-130. The distribution of sequences, organized by origin, is shown in TABLE 2.

Example 3

[00090] In one embodiment, leukocytes were isolated from a normal control (subject 2) and divided into two 1 mL aliquots. Leukocyte cells were lysed in 700ul Qiazol Reagent (Qiagen, Valencia, Ca., USA) and isolated using the miRNeasy kit (Qiagen). The total RNA was quantified using a nanodrop ND-2000 instrument (Thermo Fischer Scientific, Wilmington, De., USA). Subject 1 leukocytes were found to contain ~4 μ g RNA/mL plasma (FIG. 1A). Each RNA aliquot was diluted to 5 ng/ μ L and assessed for quality with the 2100 Bioanalyzer (Agilent) using a RNA 6000 Pico Chip (FIG. 3A).

[00091] Small RNA cDNA library preparation was performed as previously described (Pak) with modifications. Total microvesicle RNA was ligated at 37°C for 1 hr and 16°C for

2 hrs to a 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCTGTAGGCACCATCAAT/ddC/-3' (SEQ ID NO: 1) (IDT DNA)) at a 1:0.5 molar ratio in a reaction volume of 100 µl containing 50 U T4 RNA Ligase I (New England BioLabs, Beverly, Ma., USA), 100 U RNasin Plus (Promega), 5% DMSO, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the product was purified by phenol-chloroform extraction and filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the 3'-adaptor oligonucleotide. The ligation product was reverse transcribed using Omniscript (Qiagen) and a primer with sequence complementarity to the 3'-adaptor oligonucleotide (5'-GATTGATGGTGCCTACAG-3' (SEQ ID NO: 2) (IDT DNA)), according to the manufacturer's recommendation. Following reverse transcription, the cDNA was purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the primer, and concentrated to 7 µL in a Speed Vac concentrator (Savant). The cDNA was ligated at 22°C for 2 hrs to a second 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCACTCGGGCACCAAGGA/ddC/-3' (SEQ ID NO: 3) (IDT DNA)) at a 1:3 molar ratio in a reaction volume of 20 µl containing 10 U T4 RNA Ligase I (New England BioLabs), 5% DMSO, 25% PEG8000, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the cDNA was purified by phenol-chloroform extraction and filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the second 5'-adenylated 3'-adaptor oligonucleotide.

[00092] The final ligation product was PCR amplified using the reverse transcription primer and a primer with sequence complementarity to the second 3'-adaptor (5'-GTCCTTGGTGCCCGAGTG-3' (SEQ ID NO: 4) (IDT DNA)) in a reaction volume of 20 µL containing 1 U Platinum Taq DNA Polymerase (Invitrogen, Carlsbad, Ca., USA), 1X Platinum Taq DNA Polymerase Buffer, 3 mM MgCl₂, 0.5 mM dNTPs, and 0.5 µM of each primer. Amplification conditions consisted of: 1 cycle of 95°C, 10 min; 20 cycles of 95°C 30 sec; -0.5°C/cycle 60°C 30 sec; 68°C 30 sec; 30 cycles of 95°C 30s; 50°C 30 sec; 68°C 30 sec; and 1 cycle of 68°C 10 min. The PCR product was assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 3B). The PCR product was submitted to a second round of amplification using PCR product template dilutions (no dilution; 1:1; and 1:4) in the same reaction solution and amplification conditions as above. The second PCR products were assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 3C).

[00093] The small RNA cDNA library second PCR products were subcloned using the TOPO TA Cloning Kit (Invitrogen), and analyzed by Sanger sequencing. The sequences are shown in SEQ ID NOS. 131-221. The distribution of sequences, organized by origin, is shown in TABLE 3.

Example 4

[00094] In one embodiment, normal control serum was isolated (subject 1 and 2). In another embodiment, we obtained normal control serum from a bioreclamation bank (subject 7). In another embodiment, we obtained serum from glioblastoma multiforme patients (subject 4-6). Serum was filtered through a 0.8 μ m filter and divided into 1 mL aliquots. Aliquots were frozen at -80°C until needed.

[00095] Isolation of microvesicle RNA was conducted using eight 1 mL aliquots of serum from each subject. For each subject, the serum was split into four 2 mL aliquots, transferred to 5 mL polyallomer tubes (Beckman-Coulter, Miami, FL, USA) containing 8 μ L RNasin Plus (40 U/ μ L, Promega, Madison, WI, USA) RNase inhibitor, and incubated for 5 minutes at room temp. Following incubation, the plasma aliquots were diluted in 3 mL PBS. Microvesicles were pelleted by ultracentrifugation at 120,000g for 80 minutes. The microvesicle pellets were each washed in 42 μ L PBS and 8 μ L RNasin Plus, and incubated for 20 minutes at room temp. Microvesicle pellets were lysed in 700ul Qiazol Reagent (Qiagen, Valencia, Ca., USA) and isolated using the miRNeasy kit (Qiagen) according to the manufacturer's recommendation. For each subject aliquot, the RNA quality and concentration was assessed with the 2100 Bioanalyzer (Agilent, Palo Alto, Ca., USA) using a RNA 6000 Pico Chip. A representative subject profile is shown (FIG. 4A).

[00096] All four aliquots of total RNA from each subject were combined, purified by phenol-chloroform extraction, and concentrated using a 30 kDa centrifugal filter unit (Millipore, Bedford, Ma., USA). The total RNAs were further concentrated to ~7 μ L in a Speed Vac concentrator (Savant).

[00097] Small RNA cDNA library preparation was performed as previously described (Pak) with modifications. Total microvesicle RNAs were ligated at 16°C for 16 hours to a 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppTGGAATTCTCGGGCACCAAG/ddC/-3' (SEQ ID NO: 5) (IDT DNA)) at a 1:100 molar ratio in a reaction volume of 20 μ l containing 10 U T4 RNA Ligase I (10 U/ μ L; New England BioLabs, Beverly, Ma., USA), 20 U RNasin Plus (Promega), 10% DMSO, 12% PEG8000, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the products were purified by phenol-chloroform

extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the 3'-adaptor oligonucleotide, and concentrated to 13 μ L in a Speed Vac concentrator (Savant). The ligation products were reverse transcribed using Sensiscript (Qiagen) and a primer with sequence complementarity to the 3'-adaptor oligonucleotide (5'-GCTTGGTGCCCGAGAATTCCA-3' (SEQ ID NO: 6) (IDT DNA)). Following reverse transcription, the cDNAs were purified by phenol-chloroform extraction, filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the primer, and concentrated to $\sim$ 7 μ L in a Speed Vac concentrator (Savant). The cDNAs were ligated at 16°C for 16 hours to a second 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCACTCGGGCACCAAGGA/ddC/-3' (SEQ ID NO: 3) (IDT DNA)) at a 1:100 molar ratio in a reaction volume of 20 μ l containing 10 U T4 RNA Ligase I (New England BioLabs), 10% DMSO, 12% PEG8000, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the cDNAs were purified by phenol-chloroform extraction and filtered using a 30 kDa centrifugal filter unit (Millipore) to remove the second 5'-adenylated 3'-adaptor oligonucleotide.

[00098] The final ligation products were PCR amplified using Phusion II (Thermo Fischer), and the reverse transcription primer and a primer with sequence complementarity to the second 3'-adaptor (5'-GTCCTTGGTGCCCGAGTG-3' (SEQ ID NO: 4) (IDT DNA)). Amplification conditions consisted of: 1 cycle of 98°C, 30 sec; 35 cycles of 98°C 10 sec; 67.4°C 10 sec; 72°C 30 sec; and 1 cycle of 72°C 10 min. The PCR products were assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 4B).

[00099] The small RNA cDNA library PCR products were subcloned using Zero Blunt Cloning Kit (Invitrogen), according to the manufacturer's recommendations, and analyzed by Sanger sequencing. The sequences are shown as follows: subject 7 in SEQ ID NOS. 222-236, subject 1 in SEQ ID NOS. 237-252, subject 2 in SEQ ID NOS. 253-268, subject 4 in SEQ ID NOS. 269-284, subject 5 in SEQ ID NOS. 285-300, and subject 6 in SEQ ID NOS. 301-313. The distribution of sequences, organized by origin, is shown in TABLE 4.

Example 5

[000100] In one embodiment, normal control serum was isolated (subject 1,2). In another embodiment, normal control serum was obtained from a bioreclamation bank (subject 7). In another embodiment, serum was obtained from glioblastoma multiforme patients (subject 4-6). Serum was filtered through a 0.8 μ m filter and divided into 1 mL aliquots. Aliquots were frozen at -80°C until needed.

[000101] Isolation of microvesicle RNA was conducted using eight 1 mL aliquots of serum from each subject. For each subject, the serum was split into four 2 mL aliquots, transferred to 5 mL polyallomer tubes (Beckman-Coulter, Miami, FL, USA) containing 8 μ L RNasin Plus (40 U/ μ L, Promega, Madison, WI., USA) RNase inhibitor, and incubated for 5 min at room temp. Following incubation, the plasma aliquots were diluted in 3 mL PBS. Microvesicles were pelleted by ultracentrifugation at 120,000g for 80 minutes. The microvesicle pellets were each washed in 42 μ L PBS and 8 μ L RNasin Plus, and incubated for 20 minutes at room temp. For each subject, the four microvesicle pellets were lysed in 1.4mL Qiazol Reagent (Qiagen, Valencia, Ca., USA) and isolated using the miRNeasy kit (Qiagen). Total RNAs were then treated for 20 minutes at room temp with 2 U of DNase I (DNA free kit, Ambion). After treatment, the DNase I was inactivated using the kit's inactivation reagent. The RNA qualities and concentrations were assessed with the 2100 Bioanalyzer (Agilent) using a RNA 6000 Pico Chip (FIG. 5A).

[000102] Small RNA cDNA library preparation was performed as previously described (Pak) with a few modifications. Total microvesicle RNAs were ligated at 16°C for 16 hours to a 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppTGGAATTCTCGGGCACCAAG/3ddC/-3' (SEQ ID NO: 5) (IDT DNA)) at a 1:100 molar ratio in a reaction volume of 30 μ L containing 15 U T4 RNA Ligase I (New England BioLabs), 30 U RNasin Plus (Promega), 10% DMSO, 12% PEG 8000, and 1X T4 RNA Ligase Buffer (New England BioLabs). After ligation, the products were purified and concentrated with a 30 kDa centrifugal filter unit (Millipore). The ligated products were then reverse transcribed using Sensiscript (Qiagen) and a primer with sequence complementarity to the 3'-adaptor (5'-GCTTGGTGCCCGAGAATTCCA-3' (SEQ ID NO: 6) (IDT DNA)), according to the manufacturer's recommendation. The cDNAs were purified and concentrated with a 30 kDa centrifugal filter unit (Millipore). The cDNAs were ligated at 16°C for 16 hours to a second 5'-adenylated 3'-adaptor oligonucleotide (5'-rAppCACTCGGGCACCAAGGA/3ddC/-3' (SEQ ID NO: 3) (IDT DNA)) at a 1:100 molar ratio in a reaction volume of 60 μ L containing 15 U T4 RNA Ligase I (New England BioLabs), 10% DMSO, 12% PEG 8000, and 1X T4 RNA Ligase Buffer (New England BioLabs). The ligation products were purified and concentrated with a 30 kDa centrifugal filter unit (Millipore).

[000103] The final ligation products were PCR amplified using Phusion II (Thermo Fischer) and the reverse transcription primer and a primer with sequence complementarity

to the second 3'-adaptor (5'- GTCCTTGGTGCCCGAGTG -3' (SEQ ID NO: 4) (IDT DNA)). Amplification conditions consisted of: 1 cycle of 98°C, 30 sec; 35 cycles of 98°C 10 sec; 67.4°C 10 sec; 72°C 30 sec; and 1 cycle of 72°C 10 min. The PCR products were assessed for quantity and size ranges with the 2100 Bioanalyzer (Agilent) using a DNA 7500 Chip (FIG. 5B).

[000104] In one embodiment, the small RNA cDNA library PCR products were subcloned using Zero Blunt Cloning Kit (Invitrogen), and analyzed by Sanger sequencing. The sequences are shown as follows: subject 3 in SEQ ID NOS. 314-327, subject 1 in SEQ ID NOS. 328-353, subject 2 in SEQ ID NOS. 354-379, subject 4 in SEQ ID NOS. 380-402, subject 5 in SEQ ID NOS. 403-430, and subject 6 in SEQ ID NOS. 431-460. The distribution of sequences, organized by origin, is shown in TABLE 5.

[000105] In another embodiment, the small RNA cDNA library PCR products were prepared for Illumina sequencing. Library preparation was based on the manufacturer's recommendations (Illumina). Briefly, the small RNA cDNA library PCR products were purified using the QIAquick PCR Purification kit (Qiagen). The products were phosphorylated with 50 U T4 Polynucleotide Kinase (New England BioLabs) in 1X T4 DNA Ligase Buffer (New England BioLabs) and purified using the MinElute Reaction Cleanup Kit (Qiagen). The products were A-tailed using NEBNext dA-Tailing Module and purified using the MinElute Reaction Cleanup Kit (Qiagen). The products were ligated to Illumina paired-end adaptor oligonucleotides and purified using the MinElute Reaction Cleanup Kit (Qiagen). The products were enriched by PCR using Phusion II (Thermo Fischer) for 25 cycles with Illumina PCR primer PE 1.0 and 2.0 and a PCR index primer (Subject 3: Index 7; Subject 1: Index 8; Subject 2: Index 9; Subject 4: Index 10; Subject 5: Index 11; Subject 6: Index 12). The PCR products were purified with the QIAquick PCR Purification kit (Qiagen). The PCR products were assessed for quantity and size range with the 2100 Bioanalyzer using a DNA 7500 Chip (Agilent) (FIG. 5C). The amplicons were sequenced with 150-bp paired-end reads on an Illumina MiSeq instrument. A summary of relevant HERV and tRNA sequences is shown TABLE 6.

TABLE 1. Classification of microvesicle RNA sequencing reads for normal control (subject 1) plasma. Values are as a percentage of total sequencing reads.

Category	Percentage
Chromosomal tRNA	50
-Alanine	25
-Glycine	25
Unknown Origin	37.5
Mitochondrial tRNA	12.5
-Leucine	12.5

TABLE 2. Classification of microvesicle RNA sequencing reads for normal control (subject 2) plasma. Values are as a percentage of total sequencing reads.

Category	Percentage
Mitochondrial tRNA	52.6
-Threonine	14.7
-Valine	11.2
-Glycine	6.0
-Tryptophan	4.3
-Isoleucine	3.4
-Leucine	3.4
-Serine	3.4
-Histidine	2.6
-Lysine	1.7
-Arginine	0.9
-Glutamate	0.9
-Methionine	0.9
Chromosomal tRNA	28.4
-Glycine	8.6
-Alanine	5.2
-Arginine	4.3
-Proline	3.4
-Valine	3.4
-Cysteine	1.7
-Serine	0.9
-Threonine	0.9
Unknown Origin	12.1
RNY RNA	4.3
Mitochondrial rRNA	0.9
-16S	0.9
microRNA	0.9

TABLE 3. Classification of cellular RNA sequencing reads for normal control (subject 1) leukocytes. Values are as a percentage of total sequencing reads.

Category	Percentage
Chromosomal tRNA	53.8
-Proline	14.3
-Glycine	9.9
-Alanine	5.5
-Aspartate	5.5
-Arginine	4.4
-Leucine	3.3
-Valine	3.3
-Glutamate	2.2
-Cysteine	1.1
-Methionine	1.1
Chromosomal rRNA	20.9
-28S	17.6
-5S	2.2
-18S	1.1
Mitochondrial tRNA	9.9
-Serine	4.4
-Valine	4.4
-Lysine	1.1
7SL RNA	4.4
Mitochondrial rRNA	4.4
-16S	4.4
RNY RNA	3.3
Chromosomal mRNA	1.1
snoRNA	1.1
Unknown Origin	1.1

TABLE 5. Classification of RNA sequencing reads for normal control (subjects 1-3) and glioblastoma multiforme (subjects 4-6) serum. Values are as a percentage of total sequencing reads. Chr, chromosomal; Mt, mitochondrial; Val, valine; Asp, aspartate;

		Percentage											
		Chr rRNA			Mt rRNA		Mt tRNA			Chr mRNA	Rep Element	7SL RNA	Ukn Function
		28S	18S	5S	16S	Asn	Trp	Val					
Normal Controls	Subject 7	0	0	0	6.7	0	0	0	0	0	86.7	0.0	6.7
	Subject 1	50.0	6.3	0	18.8	0	0	0	0	6.3	0	0	12.5
	Subject 2	56.3	0	0	25.0	6.3	0	0	0	0	0	6.3	0
Glioblastoma Multiformes	Subject 4	68.8	0	0	18.8	0	0	0	6.3	0	0	6.3	0
	Subject 5	68.8	0	0	12.5	0	0	0	6.3	0	0	6.3	6.3
	Subject 6	15.4	0	0	0	0	0	0	0	0	46.2	0.0	38.5

TABLE 4. Classification of microvesicle RNA sequencing reads for normal control (subject 1,2,7) and glioblastoma multiforme (subjects 4-6) serum. Values are as a percentage of total sequencing reads. It is thought that the sequencing reads from subjects 6 and 7 represent genomic DNA. Chr, chromosomal; Mt, mitochondrial; Asn, asparagine; Trp, tryptophan; Val, valine; Rep, repetitive; Ukn, Unknown.

		Percentage												
		Chr rRNA			Mt rRNA				Mt rRNA		Chr mRNA	Ukn Origin	Ukn Function	Bac Origin
		28S	18S	5S	Val	Ile	Asp	Ser	16S					
Normal Controls	Subject 1	46.2	34.6	0	15.4	0	0	0	0	0	3.8	0	0	
	Subject 2	50.0	7.7	0	7.7	3.8	0	0	23.1	7.7	0	0	0	
	Subject 3	42.9	0	0	4.3	0	4.3	0	4.3	21.4	14.3	14.3	7.1	
Glioblastoma Multiformes	Subject 4	34.8	4.3	0	0	0	0	0	30.4	13.0	0	0	4.3	
	Subject 5	53.6	25.0	3.6	0	0	0	0	7.1	0	0	3.6	7.1	
	Subject 6	16.7	20.0	0	3.3	3.3	0	0	0	10.0	33.3	10.0	3.3	

TABLE 6. Classification of HERVH and tRNA-His sequencing reads for normal control (subjects 1-3) and glioblastoma multiforme (subjects 4-6) serum. Values are as a normalization of total sequencing reads.

	HERVH	tRNA-His
Subject 1	6	0
Subject 2	0	0
Subject 3	4	0
Subject 4	110	3
Subject 5	2	0
Subject 6	0	0

SEQUENCES

EXAMPLE 1

Subject 1

SEQ ID NO: 7 CCCCAAAAATTTTGGTGCAACTCCAAATAAAAGTACCA mitochondrial tRNA
Leucine

SEQ ID NO: 8 TCCCCGGCCTNTNNNCCA chromosomal tRNA Glycine

SEQ ID NO: 9 TTCCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 10 TCCCCGGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 11 GCTAAAGGGGGCAGA Unknown Origin

SEQ ID NO: 12 NANAGCGAGNCNNNNNNNNNNANNAACTGNNANAACACTTCCCCGGCCANCAANNNT
TNNCTGGTGTGATC Unknown Origin

SEQ ID NO: 13 TCCCCAGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 14 GCTAAAGGGGGCAGA Unknown Origin

EXAMPLE 2

Subject 2

SEQ ID NO: 15 CGCA Unknown Origin

SEQ ID NO: 16 ATCCGGGTGCCCCCTCCA chromosomal tRNA Cysteine

SEQ ID NO: 17 TATAAATAGTACCGTTAACTTCCAATTAAGTAGTTTGTGACAACATTCAAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 18 TTCCCCGGCCAATGCACCA chromosomal tRNA Glycine (SEQ ID NO:
11)

SEQ ID NO: 19 TTCCCCGGCCAATGCACCA chromosomal tRNA Glycine (SEQ ID NO:
11)

SEQ ID NO: 20 CACCTCTTTACAGTGACCA mitochondrial tRNA Lysine

SEQ ID NO: 21 AACCGGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 22 TTGTAAACCGGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 23 TTGTAAACCGGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 24 GNGTAAATAATAGGAGNTTAAACNNNNNNNTTNTNCCA mitochondrial tRNA
Isoleucine

SEQ ID NO: 25 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 26 TATAAATAGTACCGTTAACTTCCAATTAAGTTTGTGACAACATTCAAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 27 TATAAATAGTACCGTTAACTTCCAATTAAGTTTGTGACAACATTCAAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 28 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 29 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 30 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine (SEQ ID NO:
11)

SEQ ID NO: 31 TTCCCGGCCCATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 32 TATAAATAGTACCGTTAACTTCCAATTAAGTTTGTGACAACATTCAAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 33 ATCCCACCAGAGTCCCCA chromosomal tRNA Arginine

SEQ ID NO: 34 TTCCCGNCCAANNCNCCA chromosomal tRNA Glycine

SEQ ID NO: 35 AACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGACC
A mitochondrial tRNA Valine

SEQ ID NO: 36 CCCCCCTTATTTCTACCA mitochondrial tRNA Isoleucine

SEQ ID NO: 37 TTGTAAACCGGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 38 GACAACAGAGGCTTACGACCCCTTATTTACCCCA mitochondrial tRNA
Histidine

SEQ ID NO: 39 GAGAAAGCTCACAAGAACTGCTAACTCATGCCCCCATGTCTAACAACATGGCTTTCTC
ACCA mitochondrial tRNA Serine

SEQ ID NO: 40 GAGTAAATAATAGGAGCTTAAACCCCTTATTTCTACC mitochondrial tRNA
Isoleucine

SEQ ID NO: 41 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 42 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 43 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 44 AGCCCTCAGTAAGTTGCAATACTTAATTT mitochondrial tRNA
Tryptophan

SEQ ID NO: 45 GAGCAGAACCCAACCTCCGAGCAGTACA mitochondrial rRNA 16S

SEQ ID NO: 46 AACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGACC
A mitochondrial tRNA Valine

SEQ ID NO: 47 GGCTGGTCCGATGGTAGTGGGTTATCAGAACA RNY4 RNA

SEQ ID NO: 48 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 49 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 50 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 51 GACAACAGAGGCTTACGACCCCTTATTTACCGCCA mitochondrial tRNA
Histidine

SEQ ID NO: 52 ATCCCAGTCT Unknown Origin

SEQ ID NO: 53 AGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 54 CCGAAAGGCATGCCTGTTTGAGTGTC Unknown Origin

SEQ ID NO: 55 AGTAAGGTCAGCTAAATAAGCTATCGGGCCCATACCCGAAAATGTTGGTTATACCCCT
TCCCGTACTACCA mitochondrial tRNA Methionine

SEQ ID NO: 56 AACCGGAGATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 57 GNNGNTNNGANNNTNGTGGGTTATCNA RNY4 RNA

SEQ ID NO: 58 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 59 AGCATNTCCNCCA chromosomal tRNA Alanine

SEQ ID NO: 60 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 61 AGTAAACCGGAGATGAAAACCTTTNTNCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 62 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 63 G Unknown Origin

SEQ ID NO: 64 ATCCCATCCTNGTCGCCA chromosomal tRNA Serine

SEQ ID NO: 65 GATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA Threonine

SEQ ID NO: 66 AGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 67 GGCTGGTCCGATGGTAGTGGGTTATCAGAACT RNY4 RNA

SEQ ID NO: 68 TTGTAAACCGGAGATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 69 AGCCCTCAGTAAGTTGCAATACTTAATTTCTGCCA mitochondrial tRNA
Tryptophan

SEQ ID NO: 70 GACTCGGCGGAAACACCA Unknown Origin

SEQ ID NO: 71 GTCGTGGTTGTAGTCCGTGCGAGAATACCN mitochondrial tRNA
Glutamate

SEQ ID NO: 72 GACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 73 ACCCAAGAACAGGNNNNANAN Unknown Origin

SEQ ID NO: 74 TATAAACTAATACACCAG mitochondrial tRNA Threonine

SEQ ID NO: 75 ANCCGGGCGGAAACACCA chromosomal tRNA Valine

SEQ ID NO: 76 GGCNGAAACACCN chromosomal tRNA Valine

SEQ ID NO: 77 GGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 78 G Unknown Origin

SEQ ID NO: 79 GGNGGNNNNNNNNN Unknown Origin

SEQ ID NO: 80 CTCCAAATAAAAGTACCA mitochondrial tRNA Leucine

SEQ ID NO: 81 CCA Unknown Origin

SEQ ID NO: 82 TTGTAAACCGGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 83 TATAAATAGTACCGTTAACTTCCAATTAAGTATTTGACAACATTCAAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 84 GGTNNNATTCCTTCCTTTTTTGCCN mitochondrial tRNA Serine

SEQ ID NO: 85 GGCTGGTCCGATGGTAGTGGGTATCAGAACT RNY4 RNA

SEQ ID NO: 86 TTCCTCTNTTAACA mitochondrial tRNA Leucine

SEQ ID NO: 87 AATGATTTGACTCATTAATATGATAATCATATTTACCAACCA
mitochondrial tRNA Arginine

SEQ ID NO: 88 TTCCTCTTCTTAACACCA mitochondrial tRNA Leucine

SEQ ID NO: 89 TATAAATAGTACCGTTAACTTCCAATTAAGTATTTGACAACATTCAAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 90 GNNNNCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 91 TATAAACTAATACACCAGTACCCA mitochondrial tRNA Threonine

SEQ ID NO: 92 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine (SEQ ID NO:
11)

SEQ ID NO: 93 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine (SEQ ID NO:
11)

SEQ ID NO: 94 TTGTAAACCGGAGATGAAAACCTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 95 CCAC Unknown Origin

SEQ ID NO: 96 CTCCTGGCTGGCTCGCCA chromosomal tRNA Arginine

SEQ ID NO: 97 AACCGGGCGGAAACACCA chromosomal tRNA Valine

SEQ ID NO: 98 NNNNTNNNNNNNNTCNCCA chromosomal tRNA Arginine

SEQ ID NO: 99 TCGTACCGTGAGTAATAATGCG microRNA 126

SEQ ID NO: 100 GAGTAAATAATAGGAGCTTAAACCCCTTATTTCTACCN mitochondrial tRNA
Isoleucine

SEQ ID NO: 101 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 102 TAATTTCTGCCA mitochondrial tRNA Tryptophan

SEQ ID NO: 103 ATCNCGGTGNNNCCTCCA chromosomal tRNA Cysteine

SEQ ID NO: 104 TGGCAGAAATTAAGTATTGCAACTTACTGAGGG mitochondrial tRNA
Tryptophan

SEQ ID NO: 105 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTG
ACCA mitochondrial tRNA Valine

SEQ ID NO: 106 AACCGGAGATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 107 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 108 TTGTAAACCGGAGATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 109 GTTTAACCAAAACATCAGATTGTGAATCTGACAACAGAGGCTTACGACCCCTTATTTA
CCCCA mitochondrial tRNA Histidine

SEQ ID NO: 110 TAAGTTGCAATACTTAATTTCTGCCA mitochondrial tRNA Tryptophan

SEQ ID NO: 111 GAGAAAGCTCACAAGAACTGCTAACTCATGCCCCCATGTCTAACAACATG
mitochondrial tRNA Serine

SEQ ID NO: 112 GCATNTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 113 TTGTAAACCGGAGATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 114 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 115 GACCTGCCGC Unknown Origin

SEQ ID NO: 116 AGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 117 CTCCTGGCTGGCTCGCCA chromosomal tRNA Arginine

SEQ ID NO: 118 AACCGGGCGGAAACACCA chromosomal tRNA Valine

SEQ ID NO: 119 CTTCTNNCCCN mitochondrial tRNA Leucine

SEQ ID NO: 120 TTGTAAACCGGAGATGAAAACCTTTTTTCCAAGGACACCA mitochondrial tRNA
Threonine

SEQ ID NO: 121 GCG Unknown Origin

SEQ ID NO: 122 ATCTCGCTGGGGCCTCCA chromosomal tRNA Threonine

SEQ ID NO: 123 CACTTCTGACNCC Unknown Origin

SEQ ID NO: 124 CTCCTGGCTGGCTCGCCA chromosomal tRNA Arginine

SEQ ID NO: 125 AAGTTAAAGATTAAGAGAACCAACACCTCTTTACAGTGACCA mitochondrial
tRNA Lysine

SEQ ID NO: 126 GAAAGCTCNNNNNNNNNGNNNNCTCANGCCNNNNNGTNNNNCAACATGNCTTTCNNNN
CA mitochondrial tRNA Serine

SEQ ID NO: 127 GACT Unknown Origin

SEQ ID NO: 128 NTCCNGGCCNNNNCNCCA chromosomal tRNA Glycine

SEQ ID NO: 129 TATAAATAGTACCGTTAACTTCCAATTAAGTAGTTTTGACAACATTCAAAAAGAGTA
CCA mitochondrial tRNA Glycine

SEQ ID NO: 130 CTGGTCCGATGGTAGTGGGTTATCAGAACA RNY4 RNA

EXAMPLE 3**Subject 1**

SEQ ID NO: 131 AACCGGGCGGAAACNNCN chromosomal tRNA Valine

SEQ ID NO: 132 GGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCG
ACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 133 GTATAGTGGTGAGTATCCCCGCTGTCACGCGGGAGACCGGGGTTTCGATTCCCCGACG
GGGAGCCA chromosomal tRNA Aspartate

SEQ ID NO: 134 GCCGGTCCCCCA Unknown Origin

SEQ ID NO: 135 GCGATTTGTCTGGTTAATTCGATAACGAACGAGACTCTGGCATGCTAACTAGTTACG
CGACCCC chromosomal 18S rRNA

SEQ ID NO: 136 TGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCA
GCCCTCGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 137 GTCCCATCTGGGGTG(GCCTGTGACTTTT) similar to chromosomal tRNA
Arginine

SEQ ID NO: 138 CTCCTGGCTGGCTCGCCA chromosomal tRNA Arginine

SEQ ID NO: 139 GCAATAGATATAGTACCGCAAGGGAAAGATGAAAAATTATAACCAAGCATAATATAGC
AGGGACTAACCCCTATACCTTCTGCATAATGAATTAAGTAACTTTGCAAGGAGAGCCAAAGCTAA
GACCCCCGAAACCAGACGAGCTACCTAAGAACAGCTAA mitochondrial 16S rRNA

SEQ ID NO: 140 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 141 ATCCGGGTGCCCCCTCCA chromosomal tRNA Cysteine

SEQ ID NO: 142 GGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAG
CCCTCGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 143 GCAATAGATATAGTACCGCAAGGGAAAGATGAAAAATTATAACCAAGCATAATATAGC
AGGGACTAACCCCTATACCTTCTGCATAATGAATTAAGTAACTTTGCAAGGAGAGCCAAAGCTAA
GACCCCCGAAACCAGACGAGCTACCTAAGAACAGCTAA mitochondrial 16S rRNA

SEQ ID NO: 144 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 145 TTCCCGGNCNNTGCACCA chromosomal tRNA Glycine

SEQ ID NO: 146 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 147 GTCTAGCGGTTAGGATTCCTGGTTTTTACCCAGGCGGCCGGGTTCTGACTCCCGGTGT
GGGAACCA chromosomal tRNA Glutamate

SEQ ID NO: 148 ATCCCGGCCGANCCCCCA chromosomal tRNA Proline

SEQ ID NO: 149 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 150 CTCCTGGCTGGCTCGCCA chromosomal tRNA Arginine

SEQ ID NO: 151 ACCTCAGAGGGGGCA(GCTGCCATTT) similar to chromosomal tRNA
Methionine

SEQ ID NO: 152 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 153 AACCGGGCGGAAACACCA chromosomal tRNA Valine

SEQ ID NO: 154 AACCGGGCGGAAACACCA chromosomal tRNA Valine

SEQ ID NO: 155 GGCTGGTCCGATGGTAGTGGGTTATCAGAACTTATTAACATTAGTGTCATAAAGTTG
GTATACAACCCCCCACTGCTAAATTTGACTGGCTT RNY4 RNA

SEQ ID NO: 156 NTCCCGGNCNNNNNNCCA chromosomal tRNA Proline

SEQ ID NO: 157 ATCCCGGACGANCCCCCA chromosomal tRNA Proline

SEQ ID NO: 158 TAGGCTTT chromosomal 5S rRNA

SEQ ID NO: 159 GGCTGGTCCGAGTGCAGTGGTGTGTTTACAATAATTGATCACAACCAGTTACAGATTTC
TTTGTTCCTTCTCCACTCCCCTGCTTCACTTGACTAGT RNY3 RNA

SEQ ID NO: 160 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 161 GTCACGCACCGCACGTTCTGTTGGGAACCTGGCGNNAANNCATTCGTAGACGACCTGCT
TCTGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACAC
AAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 162 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 163 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 164 GTCCCATCTGGGGTG(GCCTGTGACTTTT) similar to chromosomal tRNA
Arginine

SEQ ID NO: 165 ATCCCACCGNNNCCACCA chromosomal tRNA Leucine

SEQ ID NO: 166 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACC mitochondrial 16S rRNA

SEQ ID NO: 167 GCTAAACCTAGCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCGAACCAT
TTACCCAAATAAAGTATAGGCGATAGAAATTGAAACCT mitochondrial 16S rRNA

SEQ ID NO: 168 NTCCCGGNCNANNCNCCA chromosomal tRNA proline/glycine

SEQ ID NO: 169 NTCCCGGNCNANNCNCCA chromosomal tRNA proline/glycine

SEQ ID NO: 170 TTCCCGGCCAACGCACCA chromosomal tRNA Glycine

SEQ ID NO: 171 GACTCTTAGCGGTGGATCACTCGGCTCGTGCGTCGATGAAGAACGCAGCTAGCTGCGA
GAATTAATGTGAATTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCCTCCC
GGGGCTACGCCTGTCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 172 TGCCCGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 173 GGGAATACCGGGTGTGTAGGCTT chromosomal 5S rRNA

SEQ ID NO: 174 GTATAGTGGTGAGTATCCCCGCTGTCNCGCGGAGACCGGGGTTCGATTCCCCGACG
GGGAGCCA chromosomal tRNA Aspartate

SEQ ID NO: 175 GAGAAAGCTCNCAAGAANTNNTAACNTCNNGNCNNNNNNNNNNNNNNN
mitochondrial tRNA Serine

SEQ ID NO: 176 CACCTCTTTACAGTGACCA mitochondrial tRNA Lysine

SEQ ID NO: 177 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 178 TTCCCGGTCAGGGAA(TGAGGTTTT) similar to chromosomal tRNA
Glutamate

SEQ ID NO: 179 GGACCACCAGGTTGCCTAAGGAGGGGTGAACCGGCCAGGTTCGAAACGGAGCAGGTC
AAAACCTCCCGTGCTGATCAGTAGTGGGATCGCGCTGTGAATAGCCACTGCACTCCAGCCTGGGCAACATA
GCGAGACCCCGTCTCTA 7SL RNA

SEQ ID NO: 180 GTTCGGCATCAATATGGTGACCTCCCGGGAGCGGGGACCACCAGGTTGCCTAAGGAG
GGGTGAACCGGCCAGGTTCGAAACGGAGCAGGTCAAACTCCCGTGCTGATCAGTAGTGGGATCGCGCCT
GTGAATAGCCACTGCACTCCAGCCTGGGCAACATAGCGAGACCCCGTCTCTT 7SL RNA

SEQ ID NO: 181 GGC GCGTGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGTGGGAGGATCGCTTGAGCC
CAGGAGTTCTGGGCTGTAGTGCCTATGCCGATCGGGTGTCCGCACTAAGTTCCGCATCAATATGGTGACC
TCCCGGGAGCGGGGACCACCAGGTTGCCTAAGGAGGGGTGAACCGGCCAGGTTCGAAACGGAGCAGGTC

AAAAC TCCCGTGCTGATCAGTAGTGGGATCGCGCCTGTGAATAGCCACTGCACTCCAGCCTGAGCAACATA
GCGAGACCCCGTCTCTTA 7SL RNA

SEQ ID NO: 182 GCTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCT
GACCA mitochondrial tRNA Valine

SEQ ID NO: 183 GACTCTTAGCGGTGGATCACTCGGCTCGTGCCTCGATGAAGAACGCAGCTAGCTGCGA
GAATTAATGTGAATTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCTCCC
GGGCTACGCCTGTCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 184 GCTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCT
GACCA mitochondrial tRNA Valine

SEQ ID NO: 185 TCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCTCCCGG
GGCTACGCCTGTCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 186 ATCCCACCGCTGCCACCA chromosomal tRNA Leucine

SEQ ID NO: 187 GGGATCACTCGGCTCGTGCCTCNATGAANAACGCAGCTAGCTGCGAGAATTANTGTGA
ATTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCTCCCGGGGCTACGCCT
GTCTGANCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 188 GGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCG
ACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 189 TCCCCGGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 190 GGCTGGTCCGAAGGTAGTGAGTTATCTCAATTGATTGTTACAGTCAGTTACAGATCG
AACTCCTTGTTCTACTCTCTCCCCCTTCTCACTACTGCACTTGACTAGTCTTA RNY1 RNA

SEQ ID NO: 191 GGCCGCCGTAGGCGAAGGTGAAGATGGCTGCCTCTGCCTTT chromosomal mRNA
MRPL35

SEQ ID NO: 192 TCCCCGGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 193 ATCCCACCGNNNCCACCA chromosomal tRNA Leucine

SEQ ID NO: 194 NTCCCNNGNNNNNGNNNCN chromosomal tRNA

SEQ ID NO: 195 GGATCACTCGGCTCGTGCCTCGATGAAGAACGCAGCTAGCTGCGAGAATTAATGTGAA
TTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCTCCCGGGGCTACGCCTG
TCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 196 GGACCACCAGGTTGCCTAAGGAGGGGTGAACCGGCCAGGTCGGAAACGGAGCAGGTC
AAAAC TCCCGTGCTGATCAGTAGTGGGATCGCGCCTGTGAATAGCCACCGCACTCCAGCCTGAGCAACATA
GCGAGACCCCGTCTCTTA 7SL RNA

SEQ ID NO: 197 GTATAGTGGTTAGTATCCCCGCCTGTCACGCGGGAGACCGGGGTTCAATTCCCCGACG
GGGAGCCA chromosomal tRNA Aspartate

SEQ ID NO: 198 GGATCACTCGGCTCGTGCCTCGATGAAGAACGCAGCTAGCTGCGAGAATTAATGTGAA
TTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCTCCCGGGGCTACGCCTG
TCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 199 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 200 GGGCGGTGATGACCCCAACATGCCATCTGAGTGTGCGGTGCTGAAATCCAGAGGCTGTT
TCTGAGCT snoRNA C/D box 95

SEQ ID NO: 201 ATCCCGGACNANCCCCCA chromosomal tRNA Proline

SEQ ID NO: 202 GAGAAAGCTCACAAGAACTGCTAACTCATGCCCCCATGTCTAACAACATGGCTTTCTC
ACCA mitochondrial tRNA Serine

SEQ ID NO: 203 GAGAAAGCTCACAAGAACTGCTAACTCATGCCCCCATGTCTAACAACATGGCTTTCTC
ACCA mitochondrial tRNA Serine

SEQ ID NO: 204 GACTCTTAGCGGTGGATCACTCGGCTCGTGCGTCGATGAAGAACGCAGCTAGCTGCGA
GAATTAATGTGAATTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCCTCCC
GGGCTACGCCTGTCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 205 GTCACGCACCGCACGTTCTGTGGGGAACCTGGCGCTAAACCATTCTGTAGACGACCTGCT
TCTGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACAC
AAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 206 GGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCG
ACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 207 GTATAGTGGTGAGTATCCCCGCTGTACGCGGGAGACCGGGGTTTCGATTCCCCGACG
GGGAGCCA chromosomal tRNA Aspartate

SEQ ID NO: 208 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCT
GACCA mitochondrial tRNA Valine

SEQ ID NO: 209 GAGAAAGCTCACAAGAACTGCTAACTCATGCCCCCATGTCTAACAACATGGCTTTCTC
ACC mitochondrial tRNA Serine

SEQ ID NO: 210 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 211 TCCCGGCATCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 212 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 213 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 214 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 215 TTCCCGGCCAATGCACCA chromosomal tRNA Glycine

SEQ ID NO: 216 GGATCACTCGGCTCGTGCGTCGATGAAGAACGCAGCTAGCTGCGAGAATTAATGTGAA
TTGCAGGACACATTGATCATCGACACTTCGAACGCACCTGCGGCCCCGGGTTCCTCCCGGGCTACGCCTG
TCTGAGCGTCGCT chromosomal 28S rRNA

SEQ ID NO: 217 GGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCG
ACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 218 GTATAGTGGTGAGTATCCCCGCTGTACGCGGGAGACCGGGGTTTCGATTCCCCGACG
GGGAGCCA chromosomal tRNA Aspartate

SEQ ID NO: 219 ATCCCGGACGAGCCCCCA chromosomal tRNA Proline

SEQ ID NO: 220 TGCCCGCATCCTCCACCA chromosomal tRNA Alanine

SEQ ID NO: 221 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCT
GACCA mitochondrial tRNA Valine

EXAMPLE 4**Subject 7**

SEQ ID NO: 222 ATCGAATGGACTCGAATGGGATCATCGAATGGAATGCAATGGATTAGTCCATGGACTC
GAATTCAATCACCATCGAATACAATCGAATGGAGTCATCGAATCGACTCAAATGGAATAATCATTGAATGG

AATCGAATGGAATCATCGAGTGGAATCGAATGGAATCATGATCAAATGGAATCGAATGTAATCATCATCAA
ATGGAATCAAAAAATAACCATCATCAATTGGTATTGAATGGAATTGTCATCAAATGGAATTCAAAGGAATCA
TCATCAAATGGAACCGAATGGAATCCTCATTGAATGGAATGAAAGGAGTCATCATCTAATGGAATCGCAT
GGAA HSATII

SEQ ID NO: 223 GGAGCACCCAGATTCATAAAGCAAGTCCTTAGAGATCTACAAAGAGATTGAGACTCCC
ACAAAAATAATAATGGGAGACTTTAACACCCCACTGTCAACATTGAACAGATCAATGAGACAGAAAGTTAAC
AAGGATATCCAGGAATTGAAGTCAGCTCTGCACCAAG L1

SEQ ID NO: 224 GCTGGGACTACAGGTGTGAGCCACCATGCCTGGCTAATTTTTGTATTTTTAGTAGAGA
C(A)GGGTTTCACCATGTTGGACAGGCTGTTCTTGAACCTCTGAAATCAGGTGATCCGCCCTCCTCAGCAT
C AluSx

SEQ ID NO: 225 AAACGCCTTCACAGCAACATTTAGACTACTGTTTCAGCCAAGTATCTGGGCACCATAGC
TCAGATAAGTTGACGTATAAAATTCACCATCACAAGGGAGGAATTTATATATACACTTTATTGCAGCAAAA
TCTTTACAGTTTAACGTTTTGTACTTTTCCCAGAAGGAAACGTTTCAGTGCAGAGTTGAATA MLT2C2

SEQ ID NO: 226 TCTACGGCCATACCACCCTGAACGCGCCCGATCTCGTCTGATCTCGGAAGCTAAGCAG
GGTCGGGCCTGGTTAGTACTTGGATGGGAGACCGCCTGGGAATACCGGGTGCTGTAGGCTT
chromosomal 5S rRNA

SEQ ID NO: 227 TACCCACAGAACCCATAGACACATGCACAGACATGGATACCCGGGAACACACAGTTAC
ACACATTACACACAAACACTCATGCATAAACATTACAGGCTCTCACAGCCTGAAAGACACACAGGACCA
CCCCCAGAAACACACACAGACATACACAGCCACAGCCACCTG ERV1-N3-I_DR

SEQ ID NO: 228 CCACCCACTCCCTTCTCTCCACATCCCCTATGACCACCCACTGGCACCTGCTCTTTAT
TATGGATTCTGTAACTTCTTTAATTACATCACCGTCTACCTAGTTGCTCACTTAGAAACCTCATTCATCAG
TGATTCTTCCATTACCCTCACCTAATCCCATCAAGGCCATCTCCTTCTTCAATGACCAGGTGTCCCATGTT
CCCCCTGGTCTTAATCCTGTATACAGCTTATGCTAGTCCCTTAGCCTATATCATGGTTTTCATTTGAAAAAG
GGCCATAACATCTCCTGATTTACTTGTACTTTTCTATGATTACCACTGATGTTGAACATTTTTTATATATC
AGCTATTTTACAATGATA L1ME4A

SEQ ID NO: 229 GCAGGTCCACTAGGTCTAAGGCCAAAGAGGTGAGGAAAGCTGTTCACAGGGAAAAACAT
GGAATGAACAGGAGTAAGTTGTTCCCATAAATCTTCTGTCTTGAATTAATTTTATTCCTATCCTATCCC
ATGCCATTCTCTAATGCCAACTGAGTCCGGGTG MamRep1527

SEQ ID NO: 230 AAATCATCATTCTCAACAACTAACACAAGAACAGAAAACCAAATACCACATGTTCTC
ACTCATAAATGGGAGTTGAACAATGAGAACAATGGACACAGGGAGGGGAACATCACACACCAGGGCCTGTC
AGAGGGTGAGGGACTAGGGGAGGGATAGCATT L1PA7

SEQ ID NO: 231 GGTTCCCCCTCCTCTCCTCTCCCTGGCCTTGTCCCCAGGATGCGGATCAGCACTTCC
CTCTCCATCACCCTTCACACCCCTGTCTCCAGCCGGCCCCATGTGTCTCCACCCCATCTCTCCATGTCC
CTCAACAGTGTCTCTGCATCGCTGTCTGCCCTAG Gypsy-25_LBS-I

SEQ ID NO: 232 AGATAATAACACTTAGTGGGTAAGAGGAGTTATTTATAAAAAATAATAATAATAAAGG
AAGCAACAAAGCCTAGTGCCCATTAGTTATTTTTCTGCTCTTCTCCCTCCTGCCACCCTCCACCCTTTG
L1PA13

SEQ ID NO: 233 ACACACATGCACGGCCTCCCCATTATCAACACCCTGCACCCTGAATAGTGCAATTTAC
AACAGTGATGACCCTACACGGCCACACCACGAGCACCCGAACCCACACGGCCACACCACGAGCACCCGAA
CCCTACACGGCCACACCACGAGCACCCGAACCCTACACGGCCACACCACGAG L1MC1_EC

SEQ ID NO: 234 TGCTCTTCCTTCCAGACCTAACTCCAGGAAGTGTCCTCTCCAGGAAGCTCCTCTGAT
CCCCACTGGAAAGGTGTGCCTCCCCTTTGTGCCCTTTGA Unknown Function Chr1

SEQ ID NO: 235 GCTGGGANTACAGGTGTGAGCCACCATGCCTGGCTAATTTTTGTATTTTTAGTANAGA
CGGGGTTTCACCATGTTGGACAGGCTGTTCTTGAACCTCCTGAAATCAGGTGATCCGCCCTCCTCAGCATC
AluSx

SEQ ID NO: 236 GGNTGTGTGGCATGCTAACAAACATGGGTGAGATAACGAGGGTTCAGGAAATCTTACT
TTCCATTTCTGTCAATTGTTGTTGCCTATGGTCTGATTCCTTTCTCTTAATGATGCAGTAAAGAGGTAGCAA
ATACAGCAAAGTGCTTCATAAGTCAGGCTCAG Rover_DM

Subject 1

SEQ ID NO: 237 TTTCTATCTACTTCAAATTCCTCCCTGTACGAAAGGACAAGAGAAATAAGGCCTACTT
CACAAAGCGCCTTCCCCGTAAATGATATCATCTCAACTTAGTA mitochondrial 16S rRNA

SEQ ID NO: 238 GATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACA
ACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGGCCATACCCGGCCGTCGC
CGGCAGTCGAGAG chromosomal 28S rRNA

SEQ ID NO: 239 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTAC mitochondrial 16S rRNA

SEQ ID NO: 240 CTGCTTTGGAGTTCTGTTCCAGTTCCTTAG (C) CCCAGAACACTTTTAGGTTCTCCAT
CTCCTA Unknown Function Chr13

SEQ ID NO: 241 GCTGTAGTGGCTTCGTCTTCGGTTTTTCTCTTCCTTCGCTAACGCCTCCCGGCTCTCG
TCAGCCTCCCGCCGGCCGTCTCCTTAACACCG(TA) chromosomal mRNA SKP1

SEQ ID NO: 242 GAGCCGCCTGGATACCGCAGCTAGGAATAATGGAATAGGACCGCGGTTCTATTTTGT
GGTTTTCGGAACTGAGGCCATGATTAAGAGGGACGGCCGGGGGCATTCTGATTGCGCCGCTAGAGGTGAAA
TTCTTGGAACCGCGCAAGACGGACCAGAGCGAAAGCATTTGCCAAGAATGTTTTTATTAATCAAGAACGAA
AGTCGGAGGTTTGAAGACGATCAGATACCGTCGTAGTTCCGACCATAAACGATGCCGACCGGCATGCGGC
GGCGTTA chromosomal 18S rRNA

SEQ ID NO: 243 GGCGAAAGACTAATCGAACCATCTAGTAGCTGGTTCCTCCGAAGTTTCCCTCAGGAT
AGCTGGCGCTCTCGCAGACC chromosomal 28S rRNA

SEQ ID NO: 244 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 245 AACCTGGCGCTAAACCATTCTGTAGACGACCTGCTTCTGGGTCGGGGTTTTCGTACGTAG
CAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGA chromosomal 28S rRNA

SEQ ID NO: 246 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 247 GCGCTAAACCATTCTGTAGACGACCTGCTTCTGGGTCGGGGTTTTCGTACGTAGCAGAGC
AGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACACAAGGGTTTGT chromosomal 28S
rRNA

SEQ ID NO: 248 AGGAGGAGGCGCAGCTTACAGAGACGGTGCCCTTGCAGGCACAACCACTAGCAAGTC
CCGGGGGCACCGTTCTTGAATAGGAAGACCCGCTCGCTCCAGGCAGAGCTGCCTGAAGGGCAAGCACCC

AGAGTGGGGAAGGAAAGAAGAGCCCCGAAGAGGCAGGAGAAAGGCCACTTTGAGAGCTCACA (GCAGTTG AACATGGGTCAGTCGGTCCCTGAGAGATGG) Unknown Function Chr10

SEQ ID NO: 249 TCGCCCGTCACGCACCGCACGTTTCGTGGGGAACCTGGCGCTAAACCATTCGTAGACGA CCTGCTTCTGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCT CGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 250 GAACTGGCGCTGCGGGATGAACCGAACGCCGGGTAAAGGCGCCCGATGCCGACGCTCA TCAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAG GAGTGTGTAACAACCTACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGCCCATA CCCGGCCGTCGCCGGCAGTCGAGA chromosomal 28S rRNA

SEQ ID NO: 251 GACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTACCTGCCGAA TCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGCCCATACCCGGCCGTCGCCGGCAGTCGAG chromosomal 28S rRNA

SEQ ID NO: 252 TCAGACCGGAGTAATCCAGGTCGGTTTCTATCTACTTCAAATTCCTCCCTGTACGAAA GGACAAGAGAAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCGTAAATGATATCATCTCAACTTAGTATTA TACCCACACCCACCCAAGAACAGGGTTTGAAAA mitochondrial 16S rRNA

Subject 2

SEQ ID NO: 253 GACGCTCATCAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCA TGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTACCTGCCGAATCAACTAGCCCTGAAAATGGATGG CGCTGGAGCGTCGGGCCCATACCCGGCCGTCGCCGGCAGTCGA chromosomal 28S rRNA

SEQ ID NO: 254 GACCACCAGGTTGCCTAAGGAGGGGTGAACCGGCCAGGTTCGGAACGGAGCAGGTCA AAACCTCCCGTGCTGATCAGTAGTGGGATCGCGCCTGTGAATAGCCACTGCACTCCAGCCTGAGCAACATAG CGAGACCCGTCTCT (TA) 7SL RNA

SEQ ID NO: 255 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAAGTG AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCATGAGGCTTTAATTTAT TAATGCAAACAGTACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG CGACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCACTCAAAGCGAACTACTATA CTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAACAGCGCAATCCTATTCTAGAG TCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCAATGGTGCAGCCGCTATTAAA GGTTCTGTTTGTCAACGATTAAAGTCCTACGTGATCTGAGTTCAGACCGGAGTAATCCAGGTTCGGTTTCTA TCTACTTCAAATTCCTCCCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCG TAAATGATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTTT (AAAA) mitochondrial 16S rRNA

SEQ ID NO: 256 ACGCACCACGCTTCGTGGGGAACCTGGCGCTAAACCATTCGTAGACGACCTGCTTCT GGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACACAAG GGT chromosomal 28S rRNA

SEQ ID NO: 257 GAACTGGCGCTGCGGGATGAACCGAACGCCGGGTAAAGGCGCCCGATGCCGACGCTCA TCAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAG GAGTGTGTAACAACCTACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGCCCATA CCCGGCCGTCGCCGGCAGTCGAGA chromosomal 28S rRNA

SEQ ID NO: 258 GTGCGGAGTGCCCTTCGTCCTGGGAAACGGGGCGCGGCTGGAAAGGCGGCCGCCCCCT
CGCCCGTCACGCACCGCACGTTTCGTGGGGAACCTGGCGCTAAACCATTCTGTAGACGACCTGCTTCTGGGTG
GGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACACAAGGGTTT
GT chromosomal 28S rRNA

SEQ ID NO: 259 GAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTG
AAAAATGGATGGCGCTGGAGCGTCGGGCCCATACCCGGCCGTCGCCGGCAGTCGAG chromosomal 28S
rRNA

SEQ ID NO: 260 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACGGCAGCGCCGCGGAGCCTCGGTTGGCCTCGGATAGC
CGGTCCCCCGCCTGTCCCCGCGGGCGGGCCGCC (A) chromosomal 28S rRNA

SEQ ID NO: 261 GTTAAATACAGACCAAGAGCCTTCAAAGCCCTCAGTAAGTTGCAATACTTAATTTCTG
CCA mitochondrial tRNA Tryptophan

SEQ ID NO: 262 GACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCA
TGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGG
CGCTGGAGCGTCGGGCCCATACCCGGCCGTCGCCGGCAGTCGAGA chromosomal 28S rRNA

SEQ ID NO: 263 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAAGT
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTACTATA
CTCAATTGATCCAATA mitochondrial 16S rRNA

SEQ ID NO: 264 TTCAACGATTAAAGTCTACGTGATCTGAGTTCAGACCGGAGTAATCCAGGTGGGTTT
CTATCTACTTCAAATTCCTCCCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCC
CCGTAAATGATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTT (ACCA)
mitochondrial 16S rRNA

SEQ ID NO: 265 CTTAGCTGTTAACTAAGTGTGTTGTGGGTTTAAGTCCCATTGGTCTAGCCA
mitochondrial tRNA Asparagine

SEQ ID NO: 266 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 267 ACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCAT
GGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGC
GCTGGAGCGTCGGGCCCATACCCGGCCGTCGCCGGCAGTCGAG chromosomal 28S rRNA

SEQ ID NO: 268 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAAGT
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTA
mitochondrial 16S rRNA

Subject 4

SEQ ID NO: 269 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 270 TAGGGACCTGTATGAATGGCTTCACGAGGGTTCANCTGTCTCTTACTTTTAACCAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATGACACAGCAAGACGAGAAGACCCATGGAGCTTTAATTTAT
TAATGCAAAACAGTACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCAGAAACCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTACT
mitochondrial 16S rRNA

SEQ ID NO: 271 TCGCCCGTCACGCACCGCACGTTCTGTGGGGAACCTGGCGCTAAACCATTCTGTAGACGA
CCTGCTTCTGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCT
CGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 272 GGTCGGGGTTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGC
CCTCGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 273 GAACTGGCGCTGCGGGATGAACCGAACGCCGGGTAAAGGCGCCCGATGCCGACGCTCA
TCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAG
GAGTGTGTAACAACCTACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGGCCATA
CCCGGCCGTCGCCGGCAGTCGAGAG chromosomal 28S rRNA

SEQ ID NO: 274 GCTTAACACAAAGCACCCAACCTTACACTTANGAGATTTCAACTTAACTTGACCGCTCT
GACCA mitochondrial tRNA Valine

SEQ ID NO: 275 AGACCGGAGTAATCCAGGTCGTTTCTATCTACTTCAAATTCCTCCCTGTACGAAAGG
ACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCGTAAATGATATCATCTCAACTTAG (A)
mitochondrial 16S rRNA

SEQ ID NO: 276 GAACTGGCGCTGCGGGATGAACCGAACGCCGGGTAAAGGCGCCCGATGCCGACGCTCA
TCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAG
GAGTGTGTAACAACCTACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGGCCATA
CCCGGCCGTCGCCGGCAGTCGAGAGTG(TT) chromosomal 28S rRNA

SEQ ID NO: 277 TAACTTGACCAACGGAACAAGTTACCCTAGGGATAACAGCGCAATCCTATTCTAGAGT
CCATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCGATGGTGCAGCCGCTATTAAAG
GTTTCGTTTGTTCACGATTAAAGTCCTACGTGATCTGAGTTCAGACCGGAGTAATCCAGGTCGTTTCTAT
CTACTTCAAATTCCTCCCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCGT
AAATGATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTTTCAA
mitochondrial 16S rRNA

SEQ ID NO: 278 GAACTGGCGCTGCGGGATGAACCGAACGCCGGGTAAAGGCGCCCGATGCCGACGCTCA
TCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAG
GAGTGTGTAACAACCTACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGGCCATA
CCCGGCCGTCGCCGGCAGTCGAGA chromosomal 28S rRNA

SEQ ID NO: 279 GGTCAAACTCCCGTGCTGATCAGTAGTGGGATCGCGCCTGTGAATAGCCACTGCACT
CCAGCCTGAGCAACATAGCGAGACCCCGTCTCTGA 7SL RNA

SEQ ID NO: 280 GGACCGGGGTCCGGTGCGGAGTGCCCTTCGTCTTGGGAAACGGGGCGCGCTGGAAAG
GCGGCCGCCCCCTCGCCCGTCACGCACCGCACGTTCTGTGGGGAACCTGGCGCTAAACCATTCTGTAGACGAC
CTGCTTCTGGGTCGGGGTTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTC
GACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 281 TTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGT
GTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGCCCATAACCGGC
CGTCGCCGGCAGTCGAGAGT chromosomal 28S rRNA

SEQ ID NO: 282 TCGCCCGTCACGCACCGCACGTTCTGGGGAACCTGGCGCTAAACCATTCTGTAGACGA
CCTGCTTCTGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCT
CGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 283 ATGCCGACGCTCATCAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGT
GGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATG
GATGGCGCTGGAGCGTCGGGCCCATAACCGGCCGTCGCCGGCAGTCGAG chromosomal 28S rRNA

SEQ ID NO: 284 GGGAACCTGGCGCTAAACCATTCTGTAGACGACCTGCTTCTGGGTCGGGGTTTCGTACG
TAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACACAAGGGTTTGT
chromosomal 28S rRNA

Subject 5

SEQ ID NO: 285 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTACTATA
CTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCTAGGGATAACAGCGCAATCCTATTCTAGAG
TCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCAATGGTGCAGCCGCTATTAAA
GGTTCGTTTGTTC AACGATTAAAGTCCTACGTGATCTGAGTTCAGACCGGAGTAATCCAGGTCGGTTTCTA
TCTACTTCAAATTCCTCCCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCG
TAAATGATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTTTAAAA
mitochondrial 16S rRNA

SEQ ID NO: 286 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACGGCAGCGCCG chromosomal 28S rRNA

SEQ ID NO: 287 ACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACC
TGCCGAATCAACTAGCCCTGAAAATGGATGGCGCTGGAGCGTCGGGCCCATAACCGGCCGTCGCCGGCAGT
CGAG chromosomal 28S rRNA

SEQ ID NO: 288 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACGGCAGCGCCGCGAGCCTCGGTTGGCCTCGGATAGC
CGGTCCCCCG chromosomal 28S rRNA

SEQ ID NO: 289 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACA mitochondrial 16S rRNA

SEQ ID NO: 290 GACGCTCATCAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCA
TGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGG
CGCTGGAGCGTCGGGCCCATAACCGGCCGTCGCCGGCAGTCGAGAG chromosomal 28S rRNA

SEQ ID NO: 291 GACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCA
TGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGG
CGCTGGAGCGTCGGGGCCCATACCCGGCCGTCGCCGGCAGTCGAGA chromosomal 28S rRNA

SEQ ID NO: 292 AACCTGGCGCTAAACCATTCTGTAGACGACCTGCTTCTGGGTGCGGGTTTTCTACGTAG
CAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCGACACAAGGGTTTTGT chromosomal
28S rRNA

SEQ ID NO: 293 GACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCA
TGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGG
CGCTGGAGCGTCGGGGCCCATACCCGGCCGTCGCCGGCAGTCGAG chromosomal 28S rRNA

SEQ ID NO: 294 ACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCAT
GGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGC
GCTGGAGCGTCGGGGCCCATACCCGGCCGTCGCCGGCAGTCGAGA chromosomal 28S rRNA

SEQ ID NO: 295 TGTCTGTAGAAAAAGATTGGGATGATTTGTGGTTAGGAGTGA Unknown
Function Chr21

SEQ ID NO: 296 GACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCA
TGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGG
CGCTGGAGCGTCGGGGCCCATACCCGGCCGTCGCCGGCAGTCGAG chromosomal 28S rRNA

SEQ ID NO: 297 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 298 ACGCTCATCAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCAT
GGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGC
GCTGGAGCGTCGGGGCCCATACCCGGCCGTCGCCGGCAGTCGAG chromosomal 28S rRNA

SEQ ID NO: 299 TAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAC
CA mitochondrial tRNA Valine

SEQ ID NO: 300 GAGCAGGTCAAAACTCCCGTGCTGATCAGTAGTGGGATCGCGCCTGTGAATAGCCACT
GCACTCCAGCCTGGGCAACATAGCGAGACCCCGTCTCTT 7SL RNA

Subject 6

SEQ ID NO: 301 NNACCCACCATCTCATCCTTCTCTGCCC GGCGTTTGCCCATCTTCCACTGCTTGTTCAT
CCAGGCAGCTGAGGAAATGCTGGAAGCCTTCGTACTGGGAGAGCACAGGGTGGCTGGTCATGTGGTCCATC
CAGAGGATGAGTCTCCGCTTCCGCTTTTCGATGAAGTCCTAAATTTGGGTAACAATAGCTTCAGTGAAAGT
TAGGAGAATTGTATTTTAGTGG Gypsy-614_AA-I

SEQ ID NO: 302 NANTCATGCAGGTGTTATTAACCTTTANNNNNNTCNATCTCAACTAGATCACTGTCAGG
GACGATGTGGTAACAATTGATTTTTCCAGGTCTGAGAGAATTCTCAGTTTACTTATTTTCATTTCTCCATA
GACTAATTTTTTTCCTTTGCTTGGAGATTTATGGCAGCATTTCTTTCTTCTGCTCTCTCATTTCAATTTG
AAAATAGCATGCTTTTAAGCACAAATTTGGGGAGGAAAAGCAAAGTGACTTANAGGCTTCAAAAACAACCT
CATCCAAGCCCATAAATTTGGCAGCCTAAACAGGCATTGACAAAGAAGGATGTACTCTTTCTGAACCTTAT
GCATTTCAACCATGTG Unknown Function Chr11

SEQ ID NO: 303 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 304 NCAGAGAATCAACATTTTGCCAGAGNNNNNNNNNNANNGAAGTAGGGGGTGGGGGGT
TCTCCAAAGTCNNNNNNNNNTTCCACGAGAGCATGCTGCCCAAACAGGTTTCTGTAGATACAGAAT
AGGAAGAAAGGATGTCAGAGGAAGGAACAACATAGGCATGAAGGTGCATTGCATTAGGGAAACATGGCGTG
TCA Unknown Function Chr8

SEQ ID NO: 305 TAATGGCCAAAGTCAGTTTCTGCCTGTGGCTATGGTGTAGCGTTTTCTTTTAGTCCT
TGGTGAGTACTGGACATTTGTAATATGTAAGCATGGTACTTCACAGAAGACTTAGCAGTTTACATGCATCT
GGTAGTTTATTTAGCATTTGTGAAAAATAAGAATTTTGTATTTTCTAGAGTTTTTAAAAAGTTACTCAGCGA
ATTTTTGTTTGTTTTGTAGGGAACAGCAGAACTCATGAGCTGGCAGAAGGCAGTACTGCTGATGTTCTGCA
TTCGAGAATCAGTGGTGAAATAATGGAATTAGTCCTGGTGAAATACCAGGGCAAAAAGTTGGAATGGACATT
TCCGCATACGTGATACACTACCAGAAATCTTTTCTGTGTGTTTTTCTTCTGACTCCACAGAAGTGACGACA
GTCGACCTGTCAGTCCACGTGAGGAGAAATGGCAGCCGGATGGTGTCTGTCTTTAGTCCCTATTGGTT
AATCAACAAGACTACCCGGGTCTCCAGTATCGTTCAGAAGATATTCATGTGAAACATCCAGCTGATTTC
Unknown Function Chr15

SEQ ID NO: 306 TGCTGGGTTCCCTTACCCCAAGACATGGATTCTTAATGACCCTGGAGCCCTGTGATTT
AGGATGCACTCAAGAAATGCAGGCTGAACATGATTGGTTTGTACCCATCTGGAAAGAGGGGATAAAGGCA
TCTCTTTATTCATCTCTCTTTCCAGTGAATACCTGGCGTATGTGACAGAGAGAATAAAAAATGTCCTTTCT
TCTTCCAACTTATATCCCTGAGTCCCTGGCAACCTGTGCAGGTGTTAACTGTGGGTGCAAGTGTAACATTC
AGCCATGAAGCAGGAGGCATAGCTGACAGGAATATTTGCACTCATCTGAGCGGAGCCTAAGCCACCTGCT
GTCAGTAACCATTGAATTCTCTAGACC MER52A1

SEQ ID NO: 307 CTGGGCACACAGCAAGTGTCTGACATGCAGCTCGGGTCTGCAGATAGAGCGGCAGC
ATGGGATTGTGGGAGGAGCTTGGGTGTGAGGGCCGTGTAGACAGCTTAGTTTTGTGACCTTGCGCAGGTAA
TTTCTGTTCTCTGAGCCTCAATTCCATTGCCTTTAAAATGAGA MIRc

SEQ ID NO: 308 GCCCTAGTAACCTCTAATTCTCTGTCTCTAGGACTCTGCTTATTCTAGATCTTTTCT
GTAAGTGGGATCATAACAATACGTGTCTTTCTGTGTTTAACTTATTTCACTTAGACGAATGTTTGCAAGGTT
TGCTGTGCTATAGCATGTGTCAATACTTCATTCCCTTTTATGGATGAATAATATCCTATTGTATGCATAT
ACTGTACCATATTTTGTATTATCCATTTCATCGGTTGATGAACATATTGGTTATTTCCACCGCCTTTTAATTA
TTGTGAATAATGTTGTAATGAATAAGGCTGTACAAATATCTGTTTCATTGCTGTTGTTTTCAATTCTTTAG
GGGTACCTACCAATGAAATTGCTG LIMB4

SEQ ID NO: 309 TACTAGAGTTTATGCTAATAAGGTGACTCTTGGAAGATGGGGGCTGGCTGCTAGAGGA
ACCATGATCCAAATTTTCACTGCCCCCACCACCATCTCCGGGAAAAGGAAAGGGACTGGAGACGGGAGAGG
AGCTAGGAATTGAGTTAATCACCAATGCCAATGATTAATCATTAATTAATCATTAATCATTCCCTAGGTAA
TGTGACCTCCATTAAAAAAAATCTTAAAGGGCAGGGTTCAGAGAACTTCTGGGATGGCAAACATATGCC
TCTACCAGGAGGATGGTATACCCCAACTTCACAGAGACAGAAGCTCCTGCACCCAGGACCCTTCTAGACCT
TGCCCTACATACCTCTTAGTCTGACTATTTCAGTTGTATCCCTTATAATGTTCTTTTTAAAAACCAATAAAT
GTAAGTAAAGTATTTCCCTGAGTTCTGTGAGCCTTTACAGCAAATTACTGAACATGAGCAGGTGATCATGA
GACCCCTCAAGTTATAACCAAAAAGTACCCTGGCAACTTAGGACT MER21C

SEQ ID NO: 310 (GCCCCGANAAATTCCA) CAGCGATATGGGGGCCTGGACCTTGCCCTCCCATCCTCCT
GGTGTGTGGCTTTCCCTAAGGGGCAACCTGTGGTTTCTGGTGGGTGGTGGGTGAAATAAAGAGCCTGCAG
GGAGTANCTGGGGGATGGGAAGTGTGAGAAGACTGATGATTTTCNNAGAGA Unknown Function
Chr1

SEQ ID NO: 311 CAAGAGGGTCGTTTGACCCTGGTGGGTCCCTTCCCTACCCGGTGCCTTTCTCGCCCGT
 AGAAGGAGACCAGGTTTCGGTTAAGCAGAGCAGAACTATTCACTGATCAAGGAATGGAGTAGGAGAGTTCC
 TGCTCAAAGTGCCTGGGGTGTAGTGTGGGGGTGCTCCTTAAGGTCT LTR75B_EC

SEQ ID NO: 312 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
 CTCTAAGTCAGAATCCCGCCAGGCGGAACGATACG chromosomal 28S rRNA

SEQ ID NO: 313 CCACATAAGGGAGAGAGCACAGAAGAGGCNGGNNTTTTCCCTAAGAAGGGATCACCCCA
 CCTTGTAACCACATCTAGAACCCAGAAGCCCAAATGTCAAGATAACATTCCCTCGGTCAGGAGTACACGAA
 GGACAAACCTCCAAAGACAGACGCAGCTGTCTAAAACCAAAGACGCTTGATGAATGCCGGCCACTGCGCGC
 TTGGTAGCTAACACAGACAGTGGTGCGGCAGGTGGCATGGTGCCCCACAACATCCTAACCCCTCAAACCTG
 TGAATGTCA Unknown Function Chr21

Example 5

Subject 3

SEQ ID NO: 314 TTCCCCCTTCTCACTACTGCACTTGACTATA Unknown Function Chr5

SEQ ID NO: 315 AACACGGACCAAGGAGTCTAACACGTGCGCGAGTCGGGGGCTCGCACGAAAGCCGCCG
 TGGCGCAATGAAGGTGAAGGCCGGCGCGCTCGCCGGCCGAGGG chromosomal 28S rRNA

SEQ ID NO: 316 CAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCG
 GAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
 chromosomal 28S rRNA

SEQ ID NO: 317 AATTCNNNTNNNNACNCCAGTGTTTAACTTTTANTNNNNACCATGNNNGGTCAATTA
 TAACACATTAAAAAGTGACAACAGCTATAAGCTGCANTTTTACATTTGTAAANNNNAAACGTCCATTTTCA
 AAAGCTGAACATAACTATCAAATTGTAATANCTAAGCTNNNNNNNNACTGCTTATACAGATGAAATTTTCT
 ATGANNNANNATGATTTTATATCTGNCCACATTCTGNGATAGTTATTCTTCGACNAACANACCCTTTGGGA
 GAACCAAATGATTCANNCNTTTTCACAGTATCCATACCATCCTTAANNNACCCAAATACTANNTGNTTAAA
 GTCCANATGTTCTGCTTTCTTCANTGTTATAACAAATTGANAATTATTGNNNNNNNTGGCNCNTGNTTGGCCA
 TGGATANNANANCANNACCAGTATGTTTCACATNANAATTTTNATCTTCNAATTTGNNNNNNATNANNGGAC
 TGTCNNNCTGTTCCATCATGTNTGGTGATATCTCCTCCTTGGNAAACAAAATCTGNAATTACTCTGNANA
 AA chromosomal mRNA RANBP2

SEQ ID NO: 318 AATTCCAAAANTGGAAGTGCACCTGAAATTCGAATAGAANGAACTGTGTACTGTGATG
 AAAGTCTGACGAATCCTCANGAATTAATGTGCATCAACCCACTGCTTTTGCTCACAAGTTACTTCAGCTC
 TCTGGAGTGTCTCTCTTCTGGGATGAGTTTTCTGCATCANCCAAATCTTCCCAGTGTTCAACTGCACC
 AGTGGAAGTCTGAGCCAAAGCTCTCACCTANCTGGAACCCCAAATTTATTTATGAGCCACACCCACAGCTAA
 CTAGAAATTTACCANAGATAGCACCTTCTGACCCAGTGCAGATTGGACGGTTAATTGGTAGGTTGGAGTTG
 AGTCTCACGTTGAAACAGAAATGAAGTGCTTCCTGGAGCTAAGTTGGATGTTGATGGACAGATAGACTCTAT
 TCATCTACTCCTGTCACCAAGACAGGTGCACTTGCTTTTGGATATGTTGGCAGCTATTGCTGGACCANAAA
 ATTCANNNNAATAGGGTTAGCTAATAAAGATAGGAAAAATCNACCCATGCAGCAGGAAGACNAGTATCGA
 ATTCAGA chromosomal mRNA ATG2B

SEQ ID NO: 319 TGTTCTTTGATATTAAGTGGATTGAGTGCAGTGCCTTAATATTTTGTATTAAACC
 AAGTAAGTTCAAATACAAGAAAATATT Unknown Function Chr7

SEQ ID NO: 320 TGGGTCGGGGTTTCGTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCA
GCCCTCGACACAAGGGTTTGT chromosomal 28S rRNA

SEQ ID NO: 321 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 322 CAGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCG
GAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 323 TCACCACCACCACCATCATCACCACCACCACCNNTA Unknown Origin

SEQ ID NO: 324 TCGGAAAAGTCATTTGATACTGTAACTAGAGTGTGGAAGAGGCTAT Unknown
Origin

SEQ ID NO: 325 GTTGAACAATGTAGGTAAGGGAAGTCGGCAAGCCGGATCCGTAACCTTCGGGATAAGG
ATTGGCTCTAAGGGC chromosomal 28S rRNA

SEQ ID NO: 326 GAAACAGATGATGAGAAGGACTCACTTAAGAAGCAGCTGAGAGAGA chromosomal
mRNA LOC100652789

SEQ ID NO: 327 TGTCCGTACAGAGCCGACGNCCC GGCTTGATACTCCGACAGTGAGCCGTATCCAAGG
A bacterial origin

Subject 1

SEQ ID NO: 328 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCCGACCCGGGGAGGTAGTGACGAAAAA chromosomal 18S rRNA

SEQ ID NO: 329 AGGGACGGCCGGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCTTGGACCGGCGC
AAGACGGACCAGAGCGAAAGCATTTGCCAAGAATGTTTTTATTAATCAAGAACGAAAGTCGGAGGTTCGAA
GACGATCAGATACCGTCGTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATG
ACCCGCCGGGCAGCTTCCGGGAAACCAAAGTCTTTGGGTTCCGGGGGAGTATGGTTGCAAAGCTGAAACT
TAA chromosomal 18S rRNA

SEQ ID NO: 330 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTC
mitochondrial tRNA Valine

SEQ ID NO: 331 GCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTA
GCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 332 GCTTAACACANNGCACCCAACCTTACNCTTAGGAGATTTCANCTTANCTTGACCGCTC
mitochondrial tRNA Valine

SEQ ID NO: 333 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGG chromosomal 28S rRNA

SEQ ID NO: 334 AGGTCTCCAAGGTGAACAGCCTCTGGCATGTTGGAACAATGTAGGTAAGGGAAGTCGG
CAAGCCGATCCGTAACCTTCGGGATAAGGATTGGCTCTAAGGGC chromosomal 28S rRNA

SEQ ID NO: 335 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTC
mitochondrial tRNA Valine

SEQ ID NO: 336 GCCCTATCAACTTTTCGATGGTAGTCGCCGTGCCTACCATGGTGACCACGGGTGACGGG
GAATCAGGGTTTCGATTCCGGAGAGGGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGC
AAATTACCCACTCCCGACCCGGGGAGGTAGTGACGAAAAATAAC chromosomal 18S rRNA

SEQ ID NO: 337 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCCGACCCGGGGAGGTAGTGACGAAAAATAAC chromosomal 18S rRNA

SEQ ID NO: 338 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGGCGGAACGATACGG chromosomal 28S rRNA

SEQ ID NO: 339 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCCGACCCGGGGAGGTAGTGACGAAAAATAACAATACAGGAC chromosomal 18S rRNA

SEQ ID NO: 340 ACCGCGGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGGACGGCCG
GGGGCATTCGTATTGCGCCGCTAGAGGTGGAATTCTTGGACCGGCGCAAGACGGACCAGAGCGAAAGCATT
TGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTCAAGACGATCAGATACCGTCGTAGTTC
CGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTTCCCATGACCCGCCGGGCAGCTTCCGGGAAA
CCAAAGTCTTTGGGTTCCGGGGGGAGTATGGTTGCAAAGCTGAAACTTAAA chromosomal 18S
rRNA

SEQ ID NO: 341 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 342 AACACGGACCAAGGAGTCTAACACGTGCGCGAGTCGGGGGCTCGCACGAAAGCCGCCG
TGGCGCAATGAAGGTGAAGGCCGCGCGCTCGCCGGCCGAGG chromosomal 28S rRNA

SEQ ID NO: 343 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTC
mitochondrial tRNA Valine

SEQ ID NO: 344 TTGCACGGCGGAAAGCAATGCGACATTCTCACTTTGCGCTAATGCGCGTAGATCAACT
AATACCTGCTTACTTCTATCGATACTCTCTTTAGCATTAGTCTCGGGCAGCATAATATCAACATAGTCGAT
AACAACAAAGTCGAAGGTTATGCCAACAGCTTGGTACTTCTTTATAA Unknown Origin

SEQ ID NO: 345 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCCGACCCGGGGAGGTAGTGACGAAAAATAACAATACAGGAC chromosomal 18S rRNA

SEQ ID NO: 346 ATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAA
CTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 347 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 348 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCTTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTCAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGGGTTCCGGGGGGAGTATGGTTGCAAAGCTGAAACTTA chromosomal
18S rRNA

SEQ ID NO: 349 AGGACCGCGGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGGACGG
CCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCTTGGACCGGCGCAAGACGGACCAGAGCGAAAGC
ATTTGCCAAGAAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTCAAGACGATCAGATACCGTCGTAG

TTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTGGAAAAAAGGAGAAGA chromosomal
18S rRNA

SEQ ID NO: 350 CAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCC
GAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 351 AACACGGACCAAGGAGTCTAACACGTGCGCGAGTCGGGGGCTCGCACGAAAGCCGCCG
TGGCGCAATGAAGGTGAAGGCCGGCGC chromosomal 28S rRNA

SEQ ID NO: 352 AAAGATGGTGAACCTATGCCTGGGCAGGGCGAAGCCAGAGGAACTCTGGTGGAGGTCC
GTAGCGGTCTTGACGTGCAAATCGGTCTCCGACCTGGGTATAG chromosomal 28S rRNA

SEQ ID NO: 353 TAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTC
ACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

Subject 2

SEQ ID NO: 354 GGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATG
GATGGCGC chromosomal 28S rRNA

SEQ ID NO: 355 NNTCCAGTTTNNNTNNCAACCANNNGNGANGNNGNNGNNTNNNNNAAANNNNTNCGA
GAGTATNNNNNTNNTNANCANNATGAAGANNNNCCGNNTGNNNCANCCNAACAANCCANCAATCACTNNGA
GAAACAAAAGNTTNGNAACCCNGNCNTNNNNGAGAACNTNNTCAGTGGGATATNGGCATNGNCCANGCNG
TGAAAGCANNGAAAANGACTGGNGANGAAAGAATNGANCAGTATACNTTTATNNNCNNNATAAACANCNNG
AAGAGGNTTNNNNNCAAGCAAAAAAGANNNNNNCCTCCAAAACNNAANNTAAAAAACNGACGACCAAGA
TNTNTGCTGAATANTCAGCCAGANCAGACCANNNCNNGGAGGTGGCNCCTCCTACTNTCAAGTNNNGAAAT
TCGGAGACATANCCAGAGGCGGCACACAAGTNNGGANGAGGAAGAGCCNCCGCCTGTTAAAATANNCN
chromosomal mRNA WHSC1L1

SEQ ID NO: 356 TTACTTTGATAGAGTAAATAATAGGAGCTTAAACCCCCTTATTTCTA
mitochondrial tRNA Isoleucine

SEQ ID NO: 357 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 358 AATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGA
TGGCGC chromosomal 28S rRNA

SEQ ID NO: 359 ACTTGACCAACGGAACAAGTTACCCTAGGGATAACAGCGCAATCCTATTCTAGAGTCC
ATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCAATGGTGCAGC
mitochondrial 16S rRNA

SEQ ID NO: 360 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCCGACCCGGGGAGGTAGTGACGAAAAATAACAATAC chromosomal 18S rRNA

SEQ ID NO: 361 NGNNNNTAACAAACCCACAGGTCCTAGNNNNNNNAACCTGNNTTAAAAATTTTCGGTTG
GGGCGACCTCGGANCAANAACCCANCTCCNAGCANTACATGCTANNACTTCACCAGTCAAAGCGAACTACT
ATACTCAATTGATCCAATAACTTGACCAACGGANCNNGTTACCCTAGGGATAACAGCGCANTCCTATTCCN
NAGNCNNTATCAACAATAGGGTTTACNACCTCNATGTTGGATCAGGACNTCCCANTGGTGCANCCGCTATT
AAAGGTTTCNNNGNTCAACGATTAANGTCCACGTGATCTGAGTTCANACCGGANTAATCCAGGTCGGTTT
CTATCTACTTCAAATTCCTCCCTGTACNAAAGGACAAGAGAAATAANGNCTACNTNNNNAAGCGCCTTCCC

CCNNANATGATATCATCTCNACTTANNATTATACCCNCACCCACCCNNNAACAGGGTTTGTTA
mitochondrial 16S rRNA

SEQ ID NO: 362 AAAAAATCCCAAACATATAACTGAACTCCTCACACCCAATTGGACCAATCTATCACCC
TATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAGCCTGCGTCAGATTAAA
AC mitochondrial 16S rRNA

SEQ ID NO: 363 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 364 ATTACCACCATGCTCAGTAAGTCCATTTTTGCATGGAATATGGAGCCTTAAACATGT
CATGAATTTGGAGTCCCTGGCACATAAATCTACCTTCAAATCAGAGGTCCTTAATGATGCCTAAACATACA
GTAAATTAGAATCAGAAATACTTCTTTAAAAAATATTCAAATGTGTTTGTTCCTATGGGATTATTCTC
TATCCACACGAATGTAAAAAATCCACATTAATGATCCATTTAAGTATAGTTTTATTGGGTCCTTTTCTA
ATGATTAAAGGTTCTTTCTCAATTCATTCCTCAGTCCTGCAAGTAAGGACTCATACTGAAGAGTACTGAA
ACAAGGACTTCTTGTGAGAAACAGCTTC chromosomal mRNA **PIK3AP1**

SEQ ID NO: 365 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 366 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 367 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCT
GAC mitochondrial tRNA Valine

SEQ ID NO: 368 GGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATG
GATGGCGC chromosomal 28S rRNA

SEQ ID NO: 369 TAGGGACCTGTATGAATGGCTCCACGAGGGTTTCAGCTGTCTCTTACTTTTAACAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCCTATGGAGCTTTAATTTAT
TAATGCAAAACAGTACCTAACAAACCCACAGGTCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTACTATA
CTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAACAGCGCAATCCTATTCTAGAG
TCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCAA mitochondrial 16S
rRNA

SEQ ID NO: 370 TTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAA
CAACTCACCTGCCGAATCAACTAGCCCTGAAAA chromosomal 28S rRNA

SEQ ID NO: 371 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTC
mitochondrial tRNA Valine

SEQ ID NO: 372 GGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCTTGGACCGGCGCAAGACGGACC
AGAGCGAAAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTNGAAGACGATCAGA
TACCGTCGTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGG
CAGCTTCCGGGAAACCAAAGTCTTTGGGTTCCGGGGGGAGTATGGTTGCAAAGCTGAAACTTAA
chromosomal 28S rRNA

SEQ ID NO: 373 GGAATCCGCTAAGGAGTGTGTAACTCACCTGCCGAATCAACTAGCCCTGAAAATG
GATGGCGC chromosomal 28S rRNA

SEQ ID NO: 374 CCCAAACATATAACTGAACTCCTCACACCCAATTGGACCAATCTATCACCCCTATAGAA
GAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAGCCTGCGTCAGATTAAAA
mitochondrial 16S rRNA

SEQ ID NO: 375 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 376 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTG
AAATTGACCTGCCCCGTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACCTAACAAACCCACAGGTCCTAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCA mitochondrial 16S rRNA

SEQ ID NO: 377 GTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTA
ACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 378 TGTGACGAAAAATAACAATACAGGACTCTTTCGAGGCCCTGTAATNGGAATGAGTCCA
CTTTAAATCCTTTAACGAGGATCCAT chromosomal 18S rRNA

SEQ ID NO: 379 GGATCCGTAACCTTCGGGATAAGGATTGGCTCTAAGGGC chromosomal 28S
rRNA

Subject 4

SEQ ID NO: 380 AATTCCAAAAGAATNCATCACACGNNTNGTNTNNNACCNGAAACACAAAACCCCTTGCT
TTAATTAAAGATGGCCGTGTTATNGGTGGTATCTGTTTCNNNNNTTCCCATNTCANGGATTCACAGAGAT
TGTCTTNTGTGCTGTAACCTCAAATGAGCAAGTCAAGGGTTANGGANACACNTGANGAATCATTTGAAAG
AATATCACATAANNCNNGACATCNTGAACTTCCTCNCATATGCAGANGAATANGCAATTGGATACTTTAAG
AAACAGGGTTTCTCCAAAGAAATTAATACTAAAACCAAATATGTTGGNTATATCAAGGATTATGAAGG
AGCCACTTTAATGGGATGTGAGCTAAATCCACGGATCCCGTACACNNAATTTTCTGTCATCATTAATAAGC
AGAAGGAGATAATTAAAAAACTGATTGAAAGAAAACAGGCACAAATTCGAAAAGTTTACCCTGGACTNTCA
TGTTTNAAGAN chromosomal mRNA KAT2B

SEQ ID NO: 381 TAACTGAACTCCTCACACCCAATTGGACCAATCTATCACCCCTATAGAAGAACTAATGT
TAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAGCCTGCGTCAGATTA mitochondrial 16S
rRNA

SEQ ID NO: 382 ACTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAACAGCGCA
ATCCTATTCTAGAGTCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCGA
mitochondrial 16S rRNA

SEQ ID NO: 383 CAGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCG
GAATCCGCTAAGGAGTGTGTAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 384 GGANCAATCTATCACCCCTATAGAAGAACTAATGTTAGTATAAGTAACATGAAAA
mitochondrial 16S rRNA

SEQ ID NO: 385 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 386 GCTTAACACAAAGCACCCAACCTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCT
GA mitochondrial tRNA Valine

SEQ ID NO: 387 CCCATAGTAGGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACCCAC
TACCTAAAAAATCCCATCA mitochondrial 16S rRNA

SEQ ID NO: 388 GCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTA
GCCC chromosomal 28S rRNA

SEQ ID NO: 389 AAAGAATACATCACACGNTNGTNTNTGACCCGAAACACAAAACCCCTTGCTTTAATTA
AAGATGGCCGTGTTATTGGTGGTATCTGTTTCCGTATGTTCCCATNTCAAGGATTCACAGAGATTGTNTTN
TGTGCTGTAACCTCAAATGAGCAAGTCAAGGNTATGGAACACACNTGATGAATCATTGAAAGAATATCA
CATAAGCATGACATCCTGAACTTCCTCACATATGCAGATGAATATGCAATTGGATACTTTAAGAAACAGG
GTTTCTCCAAAGAAATTTAAATACCTAAAACCAAATATGTTGGCTATATCAAGGATTATGAAGGAGCCACT
TTAATGGGATGTGAGCTAAATCCACGGATCCCGTACACAGAATTTTCTGTCATCTAAAAAGCAGAAGGA
GATAATTAAAAAACTGATTGAAAGAAAACAGGCACAAATTCGAAAAGTTTACCCTGGACTTTCATGTTTTA
AAGA chromosomal mRNA KAT2B

SEQ ID NO: 390 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACAACTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 391 GGGCGTAAAGGATGCGTAGGCTGGAATCAAGTCGAAAGTGAAATCCAACGGCTCAAC
CGTTGAACTGCTTTCGAAACTGGTTACCTAGAATATGGGAGAGGTAGA bacterial origin

SEQ ID NO: 392 GAGAAAGCTCACAAGAACTGCTAACTCATGCCCCCATGTCTAACAACATGGCTTTCTC
A mitochondrial tRNA Serine 2

SEQ ID NO: 393 ATCCCAAACATATAACTGAACTCCTCACACCCAATTGGACCAATCTATCACCCCTATAG
AAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAGCCTGCGTCAGATTAAACACT
GAACTGACAAATTAACAGCCCCAATATCTACAATC mitochondrial 16S rRNA

SEQ ID NO: 394 TGAAAAACCATTTCATAACTTTGTCAAAGTTAAATTATAGGCTAAATCCTATATA
mitochondrial tRNA Aspartate

SEQ ID NO: 395 TATNCTTGCTGTTGAGTCTCCNNACCCTGANGCTANGANATNACTANCANGGNTCENN
GNACANATAAAAACTTCNNATTCATGGNCCCGCAACACAACAGCNTNNNNANGAGGGATTCNACATCCCC
ATCCACTTCCNCTNTATCNGTATGATTATTTGCTATANNATGTGCTCCATTNCCTCCCCNTTTGCTGTGT
TTTCNCCNTTTTTTGCAGATNCTTGTGGNTGGCTGCANCTGCGGNNNGNTGCANCANCTGCTGCCTGTTGC
TGNGCAANNNNANCTCTATANNNTGTTGNCTTGNNNGNACTACTTCNNGNNNNNCNNNNTCNATCNNGNA
CNNANACTCTATTGNTCNACCNNCANNNNNNGNACCATNNNNNNNANTACTANACTTCTGCTTCNACNNNC
TGNANACCTTTCTGGATGATANAAANCAATGCTGCGGA chromosomal mRNA TBL1XR1

SEQ ID NO: 396 TAACTGAACTCCTCACACCCAATTGGACCAATCTATCACCCCTATAGAAGAACTAATGT
TAGTATAAGTAACA mitochondrial 16S rRNA

SEQ ID NO: 397 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCCGACCCGGGGAGGTAGTGACGAAAAATAACAATACAGGA chromosomal 18S rRNA

SEQ ID NO: 398 AATCCGCTAAGGAGTGTGTAACTCACCTGCCGAATCACTAGCCCTGAAAATGGA
TGGCGC chromosomal 28S rRNA

SEQ ID NO: 399 GCTGCGGGATGAACCGAACGCCGGGTAAAGCGCCCGATGCCGACGCTCATCAGACCC
chromosomal 28S rRNA

SEQ ID NO: 400 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACTCACCTGCCGAATCACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 401 CCTTGGTGCCCGAGTGCCTTGGTGCCCGAGTGTAGAATCTTAGTTCACTTTAAATTT
GCCCACAGAACCCCTCTAAATCCCCTTGTAATTTAACTGTTAGTCCAAAGAGGAACAGCTCTTTGGACACT
AGGAAAAAACCTTGTAGAGAGAGTAAAAATTTAACACCCATAGTAGGCCTAAAAGCAGCCACCAATTAAG
AAAGCGTTCAAGCTCAACACCCACTACCAAAAAACAAAAA mitochondrial 16S rRNA

SEQ ID NO: 402 ANCACGGNCCAAGNGTCTAACACGTGCGCGAGTCGGGGGCTCGCACGAAAGCCGCCG
TGGCGCAATGAAGGTGAAGGCCGCGCTCGCCGGCCGAGG chromosomal 28S rRNA

Subject 5

SEQ ID NO: 403 AGACCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACTCACCTGCCGAATCACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 404 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACTCACCTGCCGAATCACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 405 GGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGCAAATTACCCAC
TCCGACCCGGGGAGGTAGTGACGAAAAATAACAATAC chromosomal 18S rRNA

SEQ ID NO: 406 GTCTACGGCCATACCACCCTGAACGCGCCGATCTCGTCTGATCTCGGAAGCTAAGCA
GGGTCGGGCTTGGTACTTGGATGGGAGACCGCTGGGAATACCGGGTGCTGTAGGCTA
chromosomal 5S rRNA

SEQ ID NO: 407 TGCTGGTTGGTCTGGTGATGAATGTTACGGTGCAGGGGGCAGCCTTGAGCAGGTCGG
TAAATTTATGCTGC bacterial origin

SEQ ID NO: 408 ATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACT
CTCACCTGCCGAATCACTAGCCCTGAAAA chromosomal 28S rRNA

SEQ ID NO: 409 TGCTTGGCTGAGGAGCCAATGGGGCGAAGCTACCATCTGTGGGATTATGACTGAACGC
CTCTAAGTCAGAATCCCGCCCAGG chromosomal 28S rRNA

SEQ ID NO: 410 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACTCACCTGCCGAATCACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 411 AATCCGCTAAGGAGTGTGTAACTCACCTGCCGAATCACTAGCCCTGAAAATGGA
TGGCGC chromosomal 28S rRNA

SEQ ID NO: 412 TGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACT
CACTCACCTGCCGAATCACTAGCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 413 GCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCNCNNNNNGAATCAACTA
GCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 414 GCCCTATCAACTTTTCGATGGTAGTCGCCGTGCCTACCATGGTGACCACGGGTGACGGG
GAATCAGGGTTTCGATTCCGGAGAGGGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCGCGC
AAATTACCCACTCCCGACCCGGGGAGGTAGTGACGAAAAATAAC chromosomal 18S rRNA

SEQ ID NO: 415 GAAAAATAACAATNCAGGACTNNTTNGAGNCCCTGTAANNNGAATGAGTNCACCTTTAA
NTCNNTTAACGAGGATNCATTGGAGGGCAANTCTGGTNCCAGCAGCCGCGGTAATTCCAGCTCCAATAGCG
TATATTAAAGNNGNNNCAGTTAAAAAGCTNGTAGTTGGATCTTGGGNNNTGGCGGGCGGTCCGCCGCGAGG
CGAGCCACCGCCCGTCCCNCGCCCTTGCCCTCTCGGCGCCCCCTCGATGCTCTTAGCTGAGTGTCCGCGG
GGCCCGAAGCGTTTACTTTGAAAAAATTAGAGTGTTCAAAGCAGGCCCAGCCGCCTGGATACCGCAGCTA
GGAATAATGGAATAGGACCGCGGTTCTATTTTGTGGTTTTTCGGAAGTGAAGCCATGATTAAGAGGGACGG
CCGGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGAAAGC
ATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTCAAGACGATCAGATACCGTCGTAG
TTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTCCGGG
AAACCAAAGTCTTTGGGTTCGGGGGGGAGTATGGTTGCAAAGCTGAACTTAA chromosomal 18S
rRNA

SEQ ID NO: 416 AGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGC
TAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC chromosomal
28S rRNA

SEQ ID NO: 417 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 418 GAATAGGACCGCGGTTCTATTTTGTGGTTTTTCGGAAGTGAAGCCATGATTAAGAGGG
ACGGCCGGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTCAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGGGTTCGGGGGGGAGTATGGTTGCAAAGCTGAACTTAA chromosomal
18S rRNA

SEQ ID NO: 419 TTAGTGACGCGCATGAATGGATTAACGAGATTCCCACTGTCCCTATCTACTATCTAGC
GAAACCACAGCGAAGGGAACGGGCTTCGCAAAATCAGCGGGGAAAGAAGACCCTGTTGAGCTTGACTCTAG
TTTGACATTGTGAAAAGACATAGGGGTGTAGAATAGG chromosomal 28S rRNA

SEQ ID NO: 420 TTAGACCGTCGTGAGACAGGTTAGTTTTACCCTACTGATGATGTGTTGTTGCCATGGT
AATCCTGCTCAGTACGAGAGGAACCGCAGGTTTCAGACATT chromosomal 28S rRNA

SEQ ID NO: 421 TAGGGACCTGTATGAATGGCTCCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAAGTG
AAATTGACCTGCCCCTGAAGAGGCGGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTAT
TAATGCAAACAGTACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTTCGGTTGGGG
CGACCTCGGAGCAGAAACCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGAACTACTATA
CTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAACAGCGCAATCCTATTCTAGAG
TCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATCAGGACATCCCAATGGTGCAGCCGCTATTA
mitochondrial 16S rRNA

SEQ ID NO: 422 GTACGTAGCAGAGCAGCTCCCTCGCTGCGATCTATTGAAAGTCAGCCCTCNNNNNAAG
GNNNNGAATTNTCGGNCACCAANC chromosomal 28S rRNA

SEQ ID NO: 423 AGACCCCAGAAAAGGTGTTGGTTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGG
AATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAATGGATGGCGC
chromosomal 28S rRNA

SEQ ID NO: 424 GGTGCATGGCCGTTCTTAGTTGGTGGAGCGATTTGTCTGGTTAATTCCGATAACGAAC
GAGACTCTGGCATGCTAACTAGTTACGCGAC chromosomal 18S rRNA

SEQ ID NO: 425 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTCTGAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGGGTTCCGGGGGGAGTATGGTTGCAAAGCTGAACTTAAA chromosomal
18S rRNA

SEQ ID NO: 426 TAGTCCGGATTGGAGTCTGCAACTCGACTCCATGAAGTCGGAATCGCTAGTAATCG
bacterial origin

SEQ ID NO: 427 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTCTGAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGG chromosomal 18S rRNA

SEQ ID NO: 428 GCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTA
GCCCTGAAAATGGATGGCGC chromosomal 28S rRNA

SEQ ID NO: 429 TCGTTGGCGGGTTATAAATGTCTCCTTCTCCCTGTGATTTGTTTAATCCGTGGAAATG
GTGCTGGTCTTATGTAAACAAGCCAAGTGCAGGAATGAAGGCAGTCACCCATGCGTGGCCAGCCTGCCTATT
TGTCAGAAAACCTTCATAAATACTGAGCTGGGGCTGGGCAAGG Unknown Function Chr5

SEQ ID NO: 430 GCTAAACCTAGCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCAAACCAT
TTACCCAAATAAAGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGA
mitochondrial 16S rRNA

Subject 6

SEQ ID NO: 431 GTTGAATGAAAATCGCAGTCAGTGTGGCTTTGGTAGTCTAACAGTCAATCAGAATCTT
AACCTTACAGCAATGAATCATGCCAACTATATGGCATCGGTAAGTAAACAAATAAACAGCCATTTGCAAG
TCACGAAGAGCAAGCTGAAACGGGTTTGTAGATACAGGAATTACCAACCCCTATTATTTCAGGTATTGATT
TAACCACTAGACTAAACCCCTTTA Unknown Origin

SEQ ID NO: 432 TTGATATAGACAGCAGGACGGTGGCCATGGAAGTCGGAATCCGCTAAGGAGTGTGTAA
CAACTCACCTGCCGAATCAACTAGCCCTGAAAA chromosomal 28S rRNA

SEQ ID NO: 433 TCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAA
chromosomal 28S rRNA

SEQ ID NO: 434 TCGGAATCCGCTAAGGAGTGTGTAACAACCTCACCTGCCGAATCAACTAGCCCTGAAAA
chromosomal 28S rRNA

SEQ ID NO: 435 GGACCCCCCCCCAACACAAAGCCCCTGTCCCGACCCCCAACTCTGAN chromosomal mRNA NPR1

SEQ ID NO: 436 TTCCGCGGTGCCGTGGCGCAGCGCGCAGGTTGCGGCCGATGGTCGCCTCCTCGTCG TGCGCCGGGATCACCACGCTCGCTACGGAC Unknown Origin

SEQ ID NO: 437 CTTAACACAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTC mitochondrial tRNA Valine

SEQ ID NO: 438 TTACTTTGATAGAGTAAATAATAGGAGCTTAAACCCCCTTATTTCTA mitochondrial tRNA Isoleucine

SEQ ID NO: 439 CCACTACCACCACCACCACCACCCTACTACCACCACCACCACCACCCTACCACCAC CACCACCCTACCACCACCACCCTAC Unknown Origin

SEQ ID NO: 440 ATCTGTACCATTCCACTCCATTCCATTTTCATTCCATTCCACTCCACTCCACTCCATTC CATTGCGTTCCATTCCACTCCACTTACACTCCATTCTTTCTTTCTTTCCATTCCACTCCATTCCATTCC ATTA Unknown Origin

SEQ ID NO: 441 TGTTCCATTCCATTCCATTCCATTCCATTCCATTNNNTNNCATTCCACTCCATTCCAC TCCATTCCATTCCACTCCATTACATTCCATTCCATTCCACTCCATTCCATTCCACTCCATTCCATTCCATT CCATTCCACTCCATTCCACTCCACTCCA Unknown Origin

SEQ ID NO: 442 TTGGTGGTAGTAGCAAATATTCAAACGAGAACTTTGAAGGCCGAAG chromosomal 28S rRNA

SEQ ID NO: 443 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG ACGGCCGGGGCATTTCGTATTGCGCCGCTAGAGGTGAAATTCCTTGGACCGGCGCAAGACGGACCAGAGCGA AAGCATTTGCCAAGAATGTTTTTCATTAATCAAGAACGAAAGTCGGAGGTTGCAAGACGATCAGATACCGTC GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC CGGGAACCAAGTCTTTGGGTTCGGGGGGAGTATGGTTGCAAAGCTGAACTTAAA chromosomal 18S rRNA

SEQ ID NO: 444 GCCCAGAGACCAGACCCCCCAAAGGACCAGACCCCCCACAGGGACCCAGAGACCAG CCACCCCCACACAGGG Unknown Function Chr10 (spliced)

SEQ ID NO: 445 CCACCACCACCATCACCATCACCACCACCACCACCNCNNCATCACCACCACCACCAT CACCACC Unknown Origin

SEQ ID NO: 446 GGTTTGAGCCTCAGATTCGTAGAATAGTCGAACAAGATACTATGCCTCCAAAGGGTGT CCGCCACACTATGATGTTTAGTGCTACTTTTCCTAAGGAAATACAGATGCTGGCTCGTGATTTCTTAGATG AATATATCTTCTTGGCTGTAGGAAGAGTTGGCTCTACCTCTGAAAACATCACACAGAAAGTAGTTTGGGTG GAAGAATCAGACAAACGGTCATTTCTGCTTGACCTCCTAAATGCAACAGGCAAGGATTCACTGACCTTAGT GTTTGTGGAGACCAAAAAGGGTGCAGATTCTCTGGAGGATTTCTTATACCATGAAGGATACGCATGTACCA GCATCCATGGAGACCGTTCTCAGAGGGATAGAGAAGAGGCCCTTCACCAGTTCCGCTCAGGAAAAAGCCCA ATTTTAGTGGCTACAGCAGTAGCAGCAAGAGGACTGGACATTTCAAATGTGAAACATGTTATCAATTTTGA CTTGCCAAGTGATATTGAAGAAT chromosomal mRNA DDX3X

SEQ ID NO: 447 TTTCCGCCAGACGTGGGCCAAAATCCGGGAAGTGTGTTAGGATTAGCTTCCAGGCT bacterial origin

SEQ ID NO: 448 TCACCATCACCACCACCACCACCATCACCACCACCATCACTACCACCACCACCACCAT CA Unknown Function Chr1

SEQ ID NO: 449 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTGAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGGGTTCGGGGGGAGTATGGTTGCAAAGCTGAAACTTAAA chromosomal
18S rRNA

SEQ ID NO: 450 ATCTGTACCATTCCACTCCATTCCATTTTATTCCATTCCACTCCACTCCACTCCATTC
CATTGCGTTCCATTCCACTCCACTTACACTCCATTCTTTCTTTCTTTCCATTCCACTCCATTCCATTCC
ATTA Unknown Origin

SEQ ID NO: 451 GNATAAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGG
GACGGCCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCG
AAAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTGAAGACGATCAGATACCGT
CGTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTT
CCGGAAACCAAAGTCTTTGGGTTCGGGGGGAGTATGGTTGCAAAGCTGAAACTTAAA chromosomal
18S rRNA

SEQ ID NO: 452 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTGAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGGGTTCGGGGGGAGTATGGTTGCAAAGCTGAAACTTAAA chromosomal
18S rRNA

SEQ ID NO: 453 ACTACCACCACCACCACCACCACCACCAACCATCACCATC Unknown Function
Chr7

SEQ ID NO: 454 TTCCATTCCATTCCNTTCCATTCCATTCCATTCCATTCCATTCCACTCCATTCCACTC
CATTCCATTCCACTCCATTACATTCCATTCCATTCCACTCCATTCCATTCCACTCCATTCCATTCCATTCC
ATTCCACTCCATTCCACTCCACTCCA Unknown Origin

SEQ ID NO: 455 CTACCACCACCACCACCACCATCACTACCACCACCACCACCACCATCACTACCACCAC
CACCACCACCACCACCATCACTACCACCACCACCACCACCATCACTACCACC Unknown Function
Chr22

SEQ ID NO: 456 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTGAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC
CGGGAAACCAAAGTCTTTGGGTTCGGGGGGAGTATGGTTGCAAAGCTGAAACTTAAA chromosomal
18S rRNA

SEQ ID NO: 457 AATTCCNTGNGTTGGGGGCCTGGGCTCANGACNGANGGGGCN Unknown Origin

SEQ ID NO: 458 GAATAGGACCGCGTTCTATTTTGTGGTTTTTCGGAAGTGAAGGCCATGATTAAGAGGG
ACGGCCGGGGGCATTCGTATTGCGCCGCTAGAGGTGAAATTCCTGGACCGGCGCAAGACGGACCAGAGCGA
AAGCATTTGCCAAGAATGTTTTCATTAATCAAGAACGAAAGTCGGAGGTTTGAAGACGATCAGATACCGTC
GTAGTTCCGACCATAAACGATGCCGACCGGCGATGCGGCGGCGTTATTCCCATGACCCGCCGGGCAGCTTC

CGGGAAACCAAAGTCTTTGGGTTCCGGGGGGGAGTATGGTTGCAAAGCTGAAACTTAAA chromosomal
18S rRNA

SEQ ID NO: 459 ATCTGTACCATTCCACTCCATTCCATTTTCATTCCATTCCACTCCACTCCACTCCATTC
CATTGCGTTCCATTCCACTCCACTTACACTCCATTCCTTTTCCTTTCCATTCCACTCCATTCCATTCC
ATTA Unknown Origin

SEQ ID NO: 460 TCGGAATCCGCTAAGGAGTGTGTAAACAACTCNNCNGNNNNNTCAACTAGCCCTGAAAA
chromosomal 28S rRNA

What is claimed is:

1. A method for diagnosing a disease or other medical condition in a subject comprising:
 - a. isolating a microvesicle fraction from a biological sample from a subject;
 - b. measuring the levels of one or more tRNAs; and
 - c. correlating the levels of said tRNAs to the presence or absence of the disease or other medical condition.
2. A method for prognosing a disease or other medical condition in a subject comprising:
 - a. isolating a microvesicle fraction from a biological sample from a subject;
 - b. measuring the levels of one or more tRNAs; and
 - c. correlating the levels of said tRNAs to a higher susceptibility to or predisposition to develop the disease or other medical condition.
3. A method for monitoring a disease or other medical condition in a subject comprising:
 - a. isolating a microvesicle fraction from a biological sample from a subject;
 - b. measuring the levels of one or more tRNAs; and
 - c. correlating the levels of said tRNAs to a higher susceptibility or predisposition to develop the disease or other medical condition.
4. The method of any of claims 1-3, wherein said tRNA is a chromosomal tRNA, a mitochondrial tRNA, or fragments or combinations thereof.
5. The method of any of claims 1-3, further comprising measuring the levels of one or more HERV elements.
6. The method any of claims 1-3, wherein the disease or medical condition is associated with increased or decreased levels of one or more tRNAs, HERV sequences, or fragments or combinations thereof, when compared to a control sample.
7. The method of claim 6, wherein the control sample is a biological sample from a subject without the disease or medical condition.

8. The method of any of claims 1-3 or 7, wherein the biological sample is chosen from a tissue sample or a bodily fluid sample.
9. The method of claim 8, wherein the bodily fluid sample is plasma or serum.

FIG. 1A

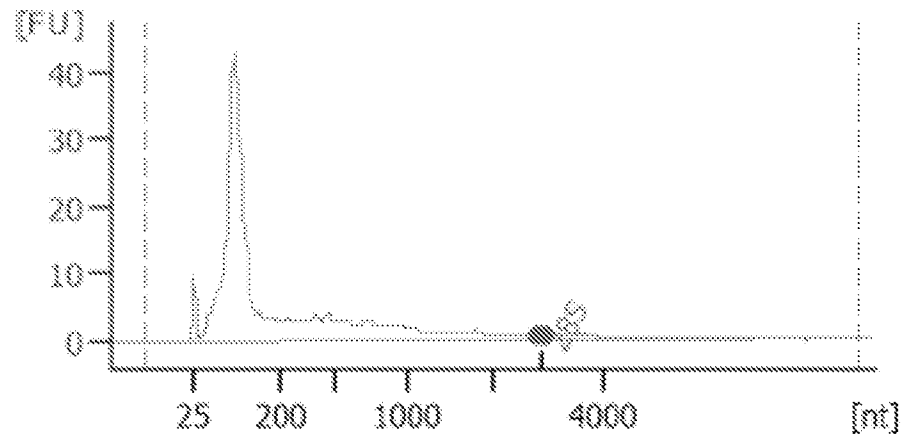


FIG. 1B

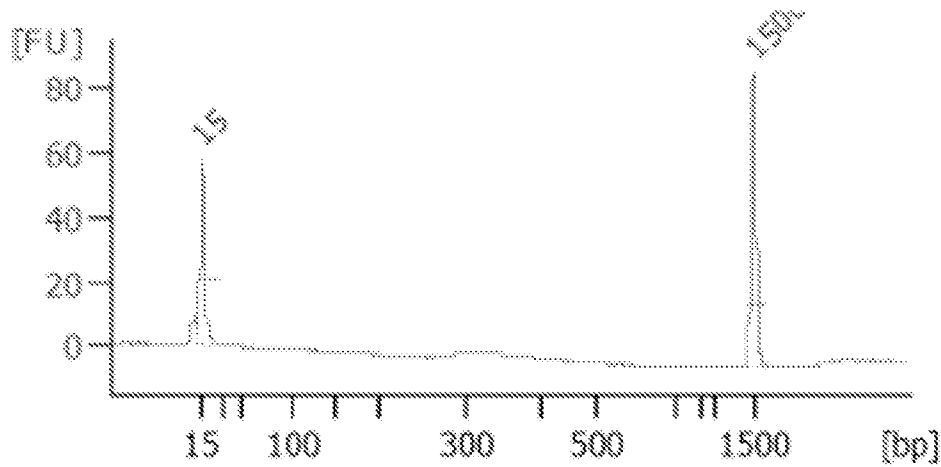


FIG. 1C

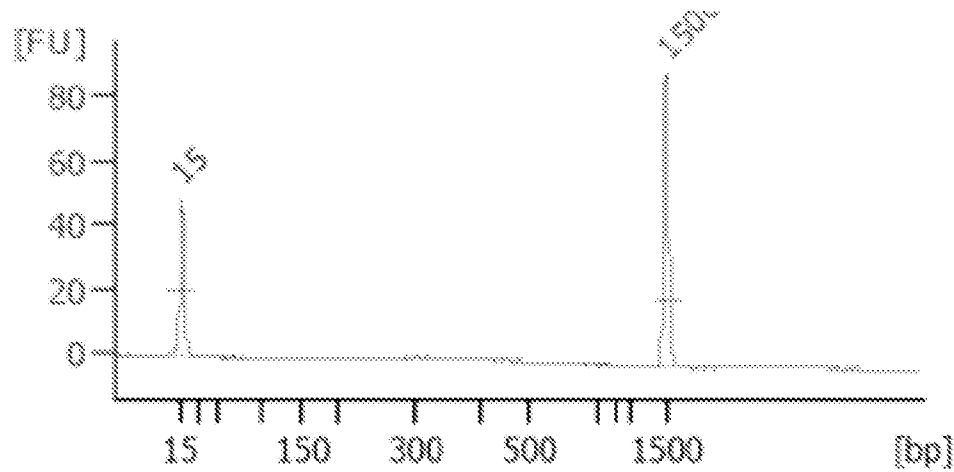


FIG. 1D

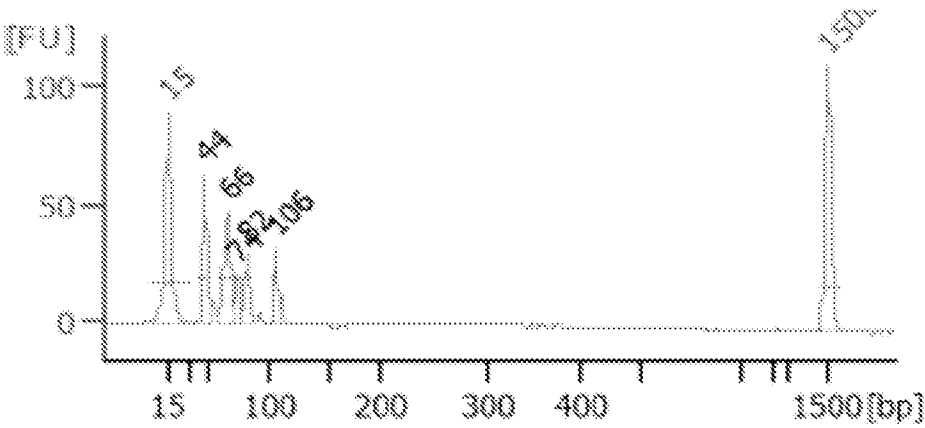


FIG. 2A

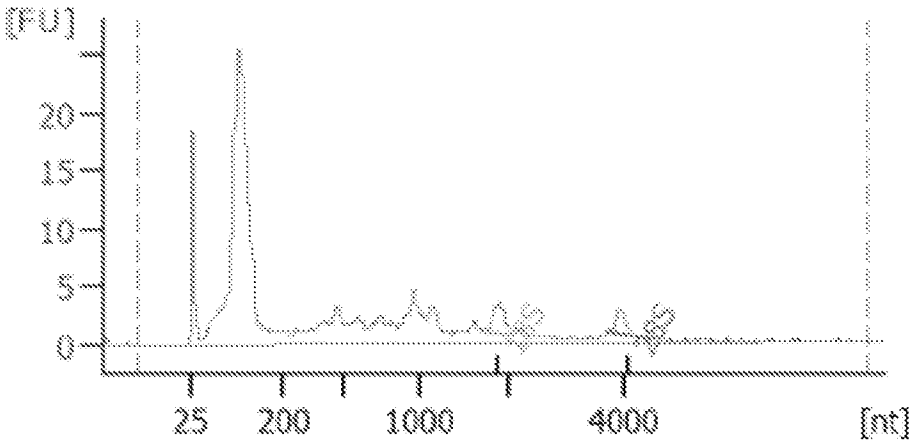
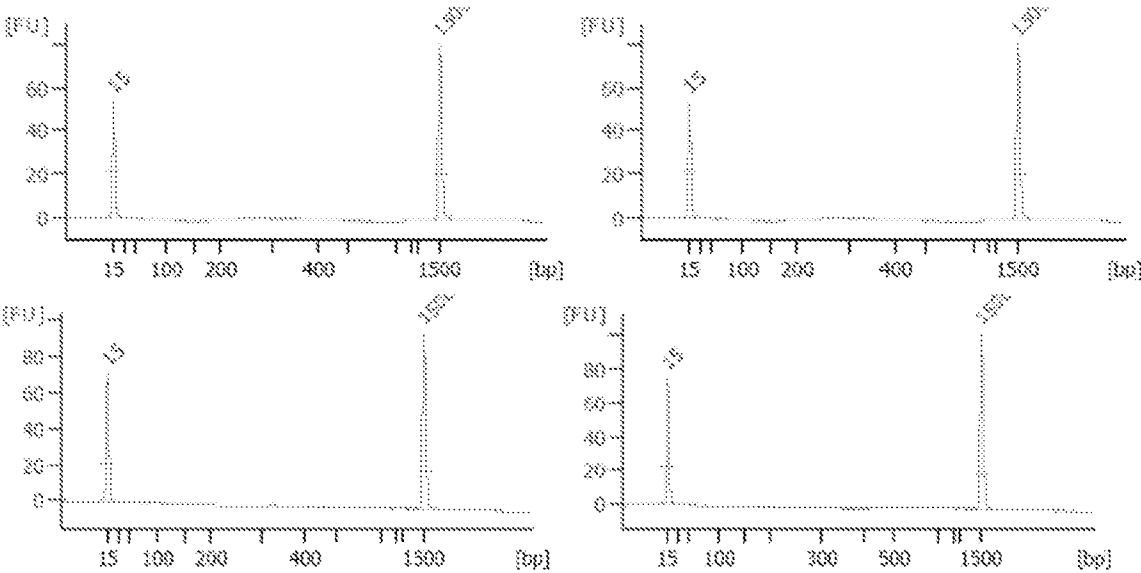


FIG. 2B



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FIG. 2C

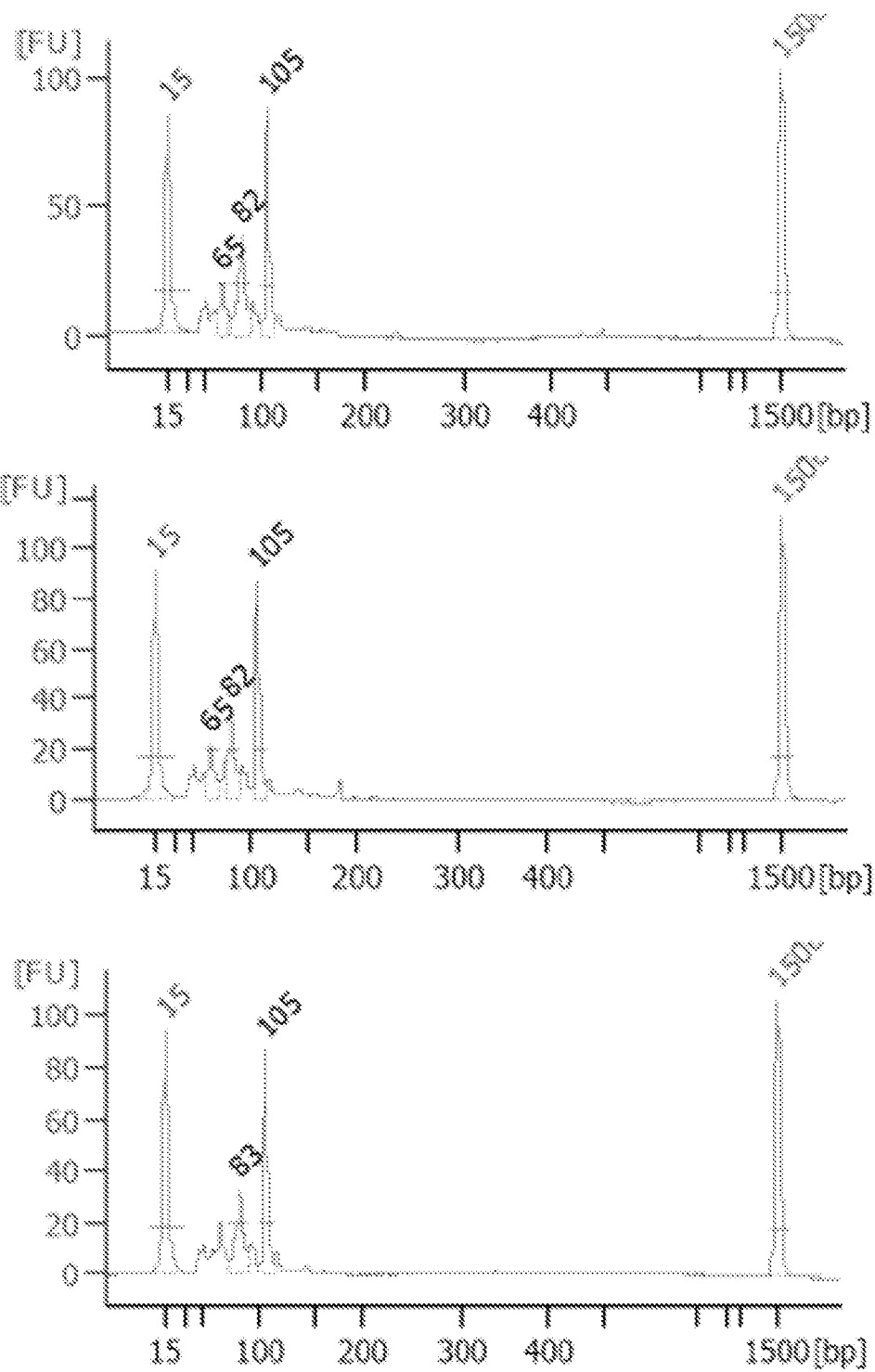


FIG. 3A

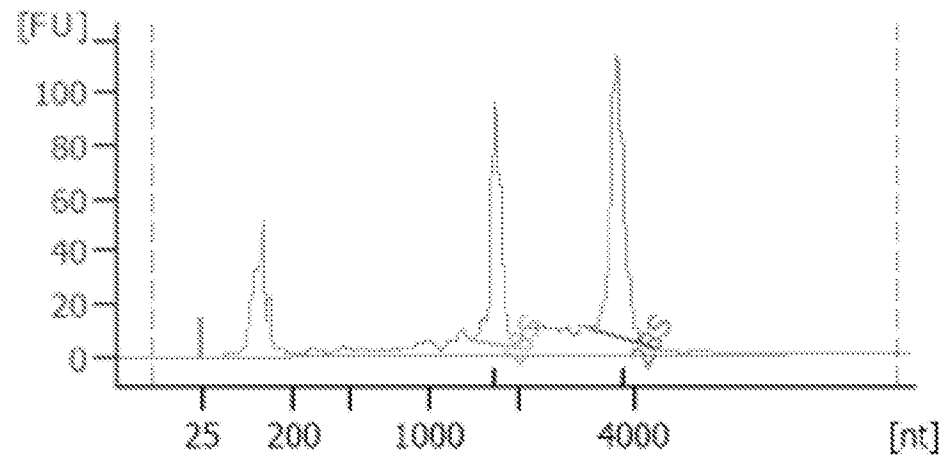


FIG. 3B

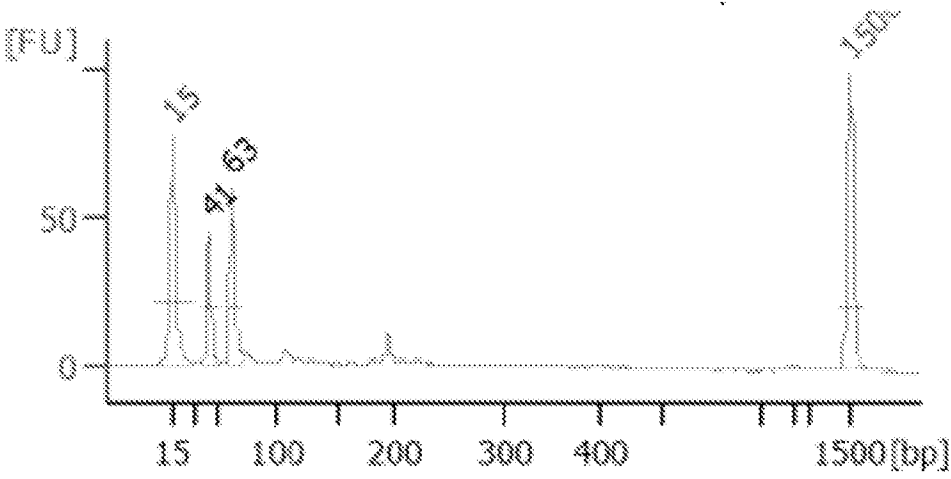


FIG. 3C

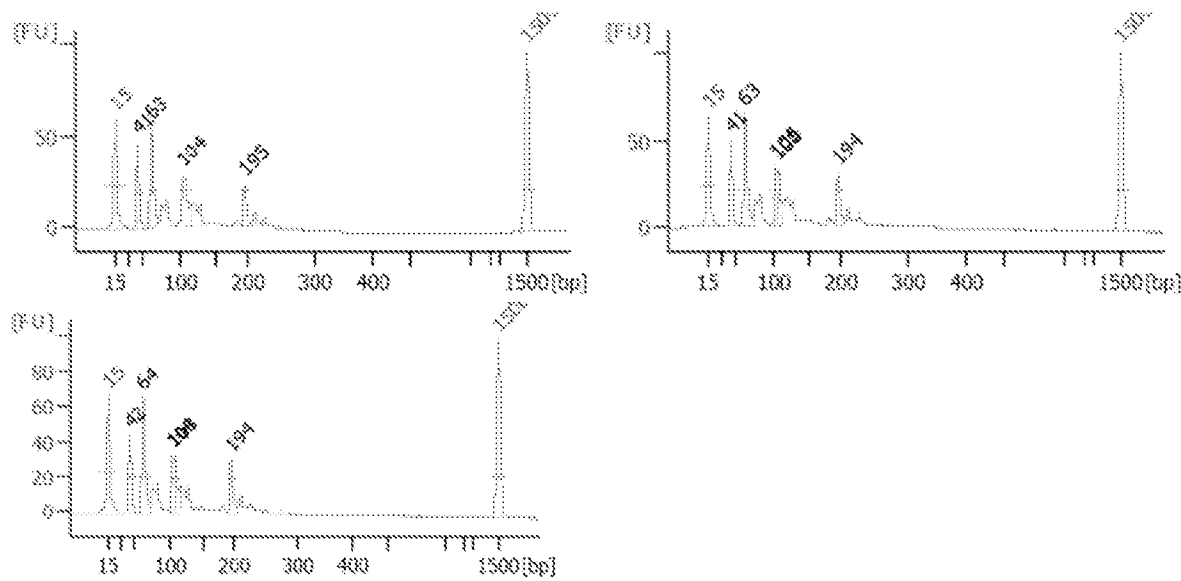


FIG. 4A

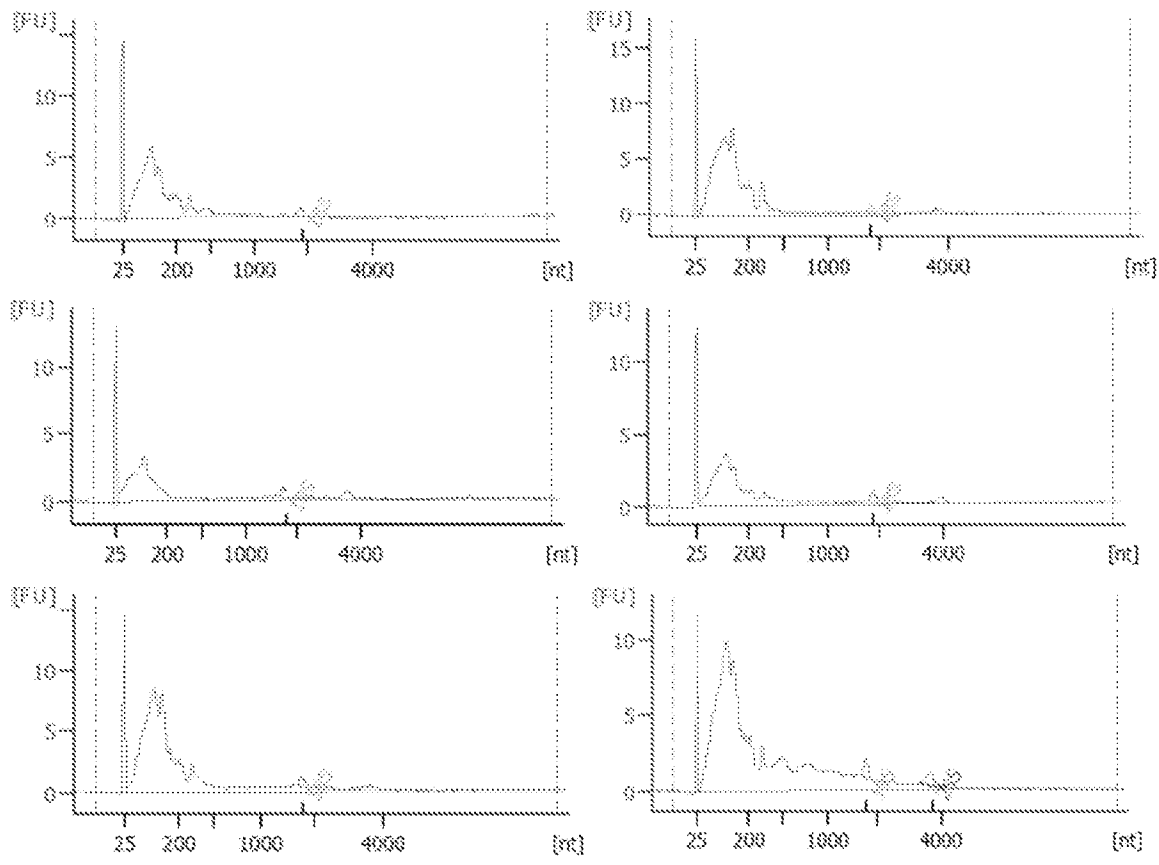
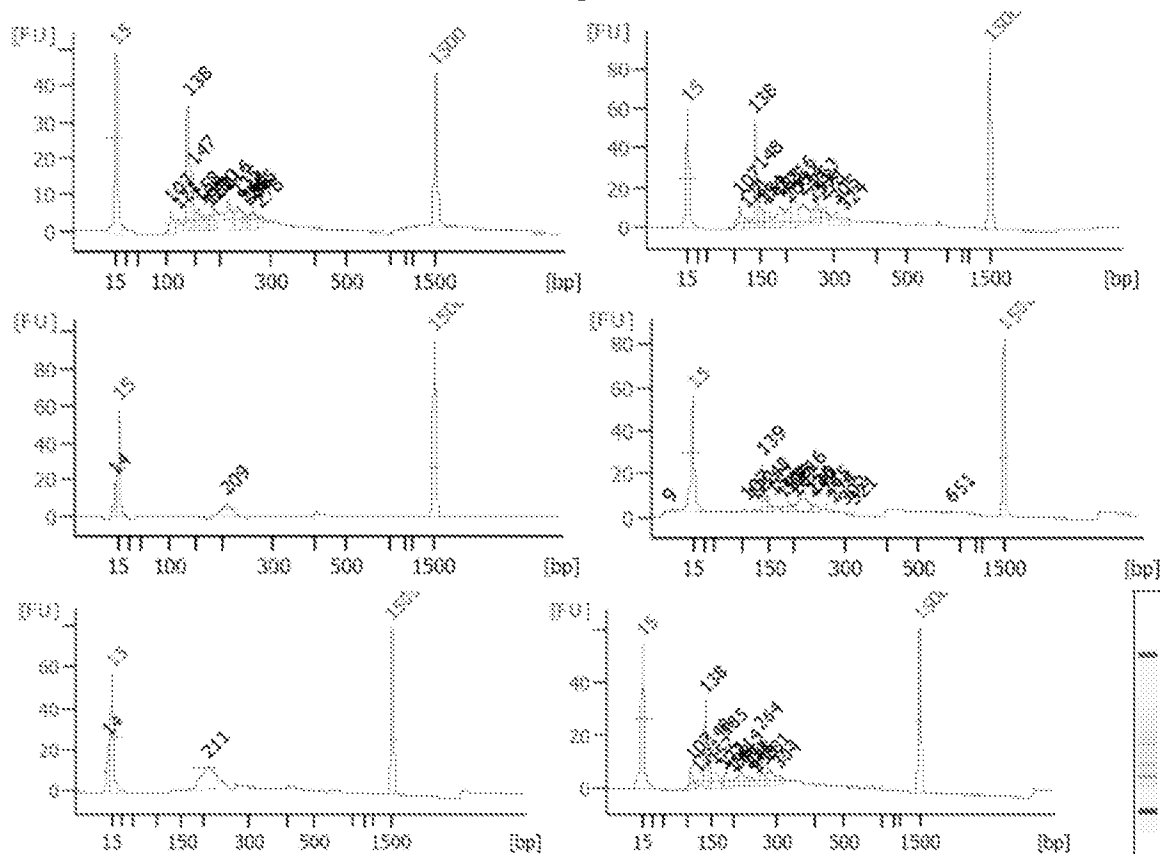


FIG. 4B



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FIG. 5A

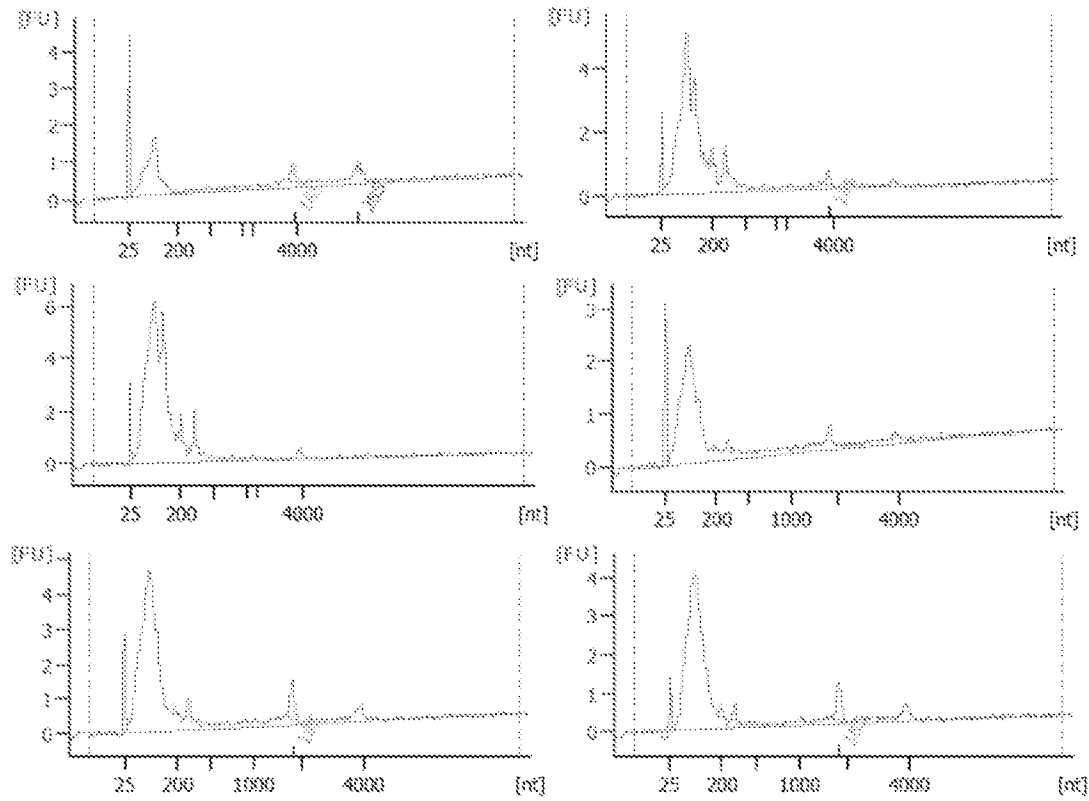


FIG. 5B

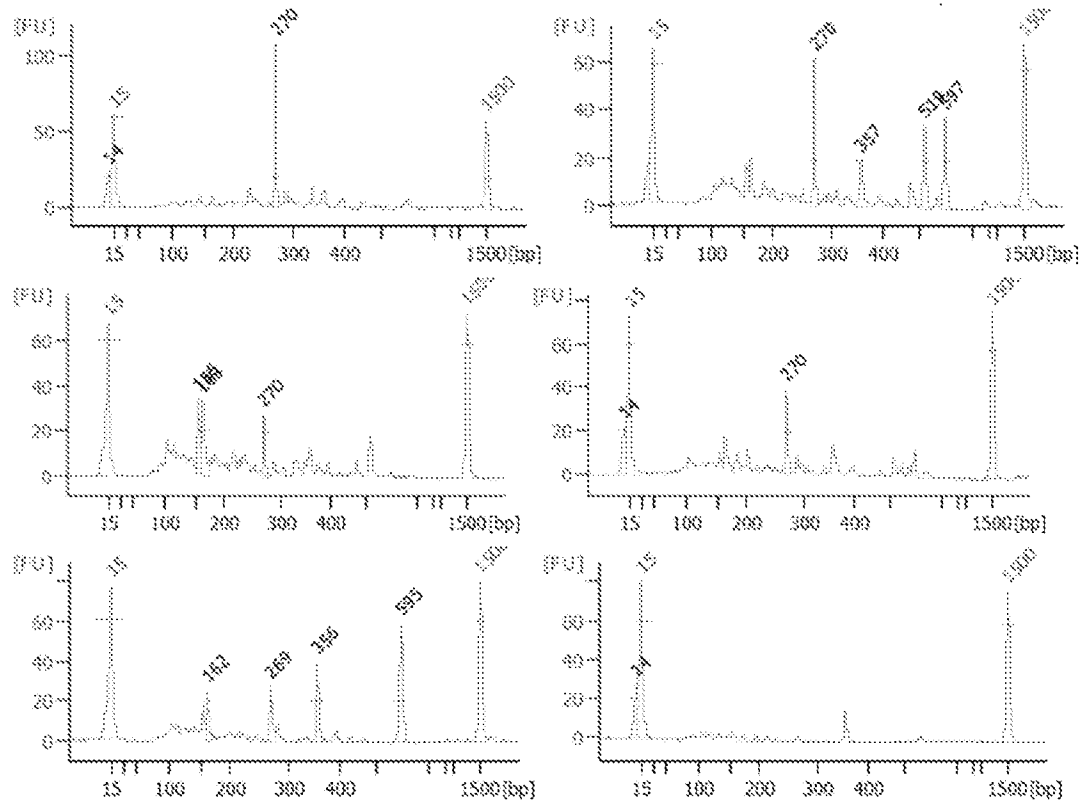


FIG. 5C

