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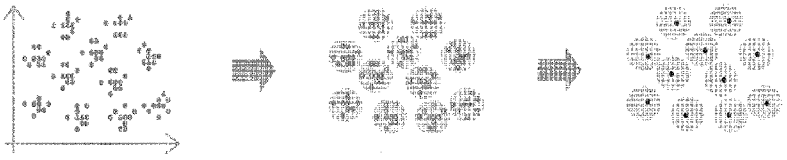

Figure 1

(57) Abstract: The present invention provides compositions and methods for making and using a transcriptome-wide gene-expression profiling platform that measures the expression levels of only a select subset of the total number of transcripts. Because gene expression is believed to be highly correlated, direct measurement of a small number (for example, 1,000) of appropriately-selected transcripts allows the expression levels of the remainder to be inferred. The present invention, therefore, has the potential to reduce the cost and increase the throughput of full- transcriptome gene-expression profiling relative to the well-known conventional approaches that require all transcripts to be measured.

WO 2011/127150 A2

Gene-Expression Profiling with Reduced Numbers of Transcript Measurements

Statement of Government Support

This invention was made with government support under Grant No. CA133834 awarded by the National Institutes of Health. The government has certain rights in the invention.

Field of the Invention

The present invention is related to the field of genomic informatics and gene-expression profiling. Gene-expression profiles provide complex molecular fingerprints regarding the relative state of a cell or tissue. Similarities in gene-expression profiles between organic states (ie, for example, normal and diseased cells and/or tissues) provide molecular taxonomies, classification, and diagnostics. Similarities in gene-expression profiles resulting from various external perturbations (ie, for example, ablation or enforced expression of specific genes, and/or small molecules, and/or environmental changes) reveal functional similarities between these perturbagens, of value in pathway and mechanism-of-action elucidation. Similarities in gene-expression profiles between organic (eg disease) and induced (eg by small molecule) states can identify clinically-effective therapies. Improvements described herein allow for the efficient and economical generation of full-transcriptome gene-expression profiles by identifying cluster centroid landmark transcripts that predict the expression levels of other transcripts within the same cluster.

Background

High-density, whole-transcriptome DNA microarrays are the method of the choice for unbiased gene-expression profiling. These profiles have been found useful for the classification and diagnosis of disease, predicting patient response to therapy, exploring biological mechanisms, in classifying and elucidating the mechanisms-of-action of small molecules, and in identifying new therapeutics. van de Vijver et al., "A gene expression signature as a predictor of survival in breast cancer" *N Engl J Med* 347:1999-2009 (2002); Lamb et al., "A mechanism of cyclin D1 action encoded in the patterns of gene expression in human cancer" *Cell* 114:323-334 (2003); Glas et al., "Gene expression profiling in follicular lymphoma to assess clinical aggressiveness and to guide the choice of treatment" *Blood* 105:301-307 (2005); Burczynski et

al., "Molecular classification of Crohn's disease and ulcerative colitis patients using transcriptional profiles in peripheral blood mononuclear cells" *J Mol Diagn* 8:51-61 (2006); Golub et al., "Molecular classification of cancer: class discovery and class prediction by gene expression monitoring" *Science* 286:531 (1999); Ramaswamy et al., "Multiclass cancer diagnosis using tumor gene expression signatures" *Proc Natl Acad Sci* 98: 15149 (2001); Lamb et al., "The Connectivity Map: using gene-expression signatures to connect small molecules, genes and disease" *Science* 313:1929 (2006). However, the overall success and wide-spread use of these methods is severely limited by the high cost and low throughput of existing transcriptome-analysis technologies. For example, using gene-expression profiling to screen for small molecules with desirable biological effects is practical only if one could analyze thousands of compounds per day at a cost dramatically below that of conventional microarrays.

What is needed in the art is a simple, flexible, cost-effective, and high-throughput transcriptome-wide gene-expression profiling solution that would allow for the analysis of many thousands of tissue specimens and cellular states induced by external perturbations. This would greatly accelerate the rate of discovery of medically-relevant connections encoded therein. Methods have been developed to rapidly assay the expression of small numbers of transcripts in large number of samples; for example, Peck et al., "A method for high-throughput gene expression signature analysis" *Genome Biol* 7:R61 (2006). If transcripts that faithfully predict the expression levels of other transcripts could be identified, it is conceivable that the measurement of a set of such 'landmark' transcripts using such moderate-muliplex assay methods could, in concert with an algorithm that calculates the levels of the non-landmark transcripts from those measurements, provide the full-transcriptome gene-expression analysis solution sought.

Summary of the Invention

The present invention is related to the field of genomic informatics and gene-expression profiling. Gene-expression profiles provide complex molecular fingerprints regarding the relative state of a cell or tissue. Similarities in gene-expression profiles between organic states (ie, for example, normal and diseased cells and/or tissues) provide molecular taxonomies, classification, and diagnostics. Similarities in gene-expression profiles resulting from various external perturbations (ie, for example, ablation or enforced expression of specific genes, and/or small

molecules, and/or environmental changes) reveal functional similarities between these perturbagens, of value in pathway and mechanism-of-action elucidation. Similarities in gene-expression profiles between organic (eg disease) and induced (eg by small molecule) states can identify clinically-effective therapies. Improvements described herein allow for the efficient and economical generation of full-transcriptome gene-expression profiles by identifying cluster centroid landmark transcripts that predict the expression levels of other transcripts within the same cluster.

In one embodiment, the present invention contemplates a method for making a transcriptome-wide mRNA-expression profiling platform using sub-transcriptome numbers of transcript measurements comprising: a) providing: i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples; ii) a second collection of biological samples; iii) a second library of transcriptome-wide mRNA-expression data from said second collection of biological samples; iv) a device capable of measuring transcript expression levels; b) performing computational analysis on said first library such that a plurality of transcript clusters are created, wherein the number of said clusters is substantially less than the total number of all transcripts; c) identifying a centroid transcript within each of said plurality of transcript clusters, thereby creating a plurality of centroid transcripts, said remaining transcripts being non-centroid transcripts; d) measuring the expression levels of at least a portion of transcripts from said second collection of biological samples with said device, wherein said portion of transcripts comprise transcripts identified as said centroid transcripts from said first library; e) determining the ability of said measurements of the expression levels of said centroid transcripts to infer the levels of at least a portion of transcripts from said second library, wherein said portion is comprised of non-centroid transcripts; f) selecting said centroid transcripts whose said expression levels have said ability to infer the levels of said portion of non-centroid transcripts. In one embodiment, the plurality of centroid transcripts is approximately 1000 centroid transcripts. In one embodiment, the device is selected from the group comprising a microarray, a bead array, a liquid array, or a nucleic-acid sequencer. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the method further comprises repeating steps c) to f) until validated centroid transcripts for each of said plurality of transcript clusters are identified. In one embodiment, the plurality of clusters of transcripts are orthogonal. In one embodiment, the plurality of clusters of transcripts are non-overlapping. In

one embodiment, the determining involves a correlation between said expression levels of said centroid transcripts and said expression levels of said non-centroid transcripts. In one embodiment, the expression levels of a set of substantially invariant transcripts are additionally measured with said device in said second collection of biological samples. In one embodiment, the measurements of said centroid transcripts made with said device, and said mRNA-expression data from said first and second libraries, are normalized with respect to the expression levels of a set of substantially invariant transcripts.

In one embodiment, the present invention contemplates a method for identifying a subpopulation of predictive transcripts within a transcriptome, comprising: a) providing; i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples;ii) a second collection of biological samples; ii) a second library of transcriptome-wide mRNA-expression data from said second collection of biological samples; iii) a device capable of measuring transcript expression levels; b) performing computational analysis on said first library such that a plurality of transcript clusters are created, wherein the number of said clusters is less than the total number of all transcripts in said first library; c) identifying a centroid transcript within each of said transcript clusters thereby creating a plurality of centroid transcripts, said remaining transcripts being non-centroid transcripts; d) processing transcripts from said second collection of biological samples on said device so as to measure expression levels of said centroid transcripts, and e) determining which of said plurality of centroid transcripts measured on said device predict the levels of said non-centroid transcripts in said second library of transcriptome-wide data. In one embodiment, the plurality of centroid transcripts is approximately 1000 centroid transcripts. In one embodiment, the device is selected from the group comprising a microarray, a bead array, a liquid array, or a nucleic-acid sequencer. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the determining involves a correlation between said centroid transcript and said non-centroid transcript. In one embodiment, the method further comprises repeating steps c) to e).

In one embodiment, the present invention contemplates a method for identifying a subpopulation of approximately 1000 predictive transcripts within a transcriptome, comprising: a) providing: i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples representing greater than 1000 different transcripts, and ii) transcripts from a second collection of biological samples; b) performing computational analysis

on said first library such that a plurality of clusters of transcripts are created, wherein the number of said clusters is approximately 1000 and less than the total number of all transcripts in said first library; c) identifying a centroid transcript within each of said transcript clusters, said remaining transcripts being non-centroid transcripts; d) processing the transcripts from said second collection of biological samples so as to measure the expression levels of non-centroid transcripts, so as to create first measurements, and expression levels of centroid transcripts, so as to create second measurements; and e) determining which centroid transcripts based on said second measurements predict the levels of said non-centroid transcripts, based on said first measurements, thereby identifying a subpopulation of predictive transcripts within a transcriptome. In one embodiment, the method further comprises a device capable of measuring the expression levels of said centroid transcripts. In one embodiment, the device is capable of measuring the expression levels of approximately 1000 of said centroid transcripts. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the determining involves a correlation between said centroid transcript and said non-centroid transcript. In one embodiment, the method further comprises repeating steps c) to e).

In one embodiment, the present invention contemplates a method for predicting the expression level of a first population of transcripts by measuring the expression level of a second population of transcripts, comprising: a) providing: i) a first heterogeneous population of transcripts comprising a second heterogeneous population of transcripts, said second population comprising a subset of said first population, ii) an algorithm capable of predicting the level of expression of transcripts within said first population which are not within said second population, said predicting based on the measured level of expression of transcripts within said second population; b) processing said first heterogeneous population of transcripts under conditions such that a plurality of different templates representing only said second population of transcripts is created; c) measuring the amount of each of said different templates to create a plurality of measurements; and d) applying said algorithm to said plurality of measurements, thereby predicting the level of expression of transcripts within said first population which are not within said second population. In one embodiment, the first heterogenous population of transcripts comprise a plurality of non-centroid transcripts. In one embodiment, the second heterogenous population of transcripts comprises a plurality of centroid transcripts. In one embodiment, the method further comprises a device capable of measuring the amount of approximately 1000 of

said different templates. In one embodiment, the device is selected from the group comprising a microarray, a bead array, a liquid array, or a nucleic-acid sequencer. In one embodiment, the algorithm involves a dependency matrix.

In one embodiment, the present invention contemplates a method of assaying gene expression, comprising: a) providing: i) approximately 1000 different barcode sequences; ii) approximately 1000 beads, each bead comprising a homogeneous set of nucleic-acid probes, each set complementary to a different barcode sequence of said approximately 1000 barcode sequences; iii) a population of more than 1000 different transcripts, each transcript comprising a gene-specific sequence; iv) an algorithm capable of predicting the level of expression of unmeasured transcripts; b) processing said population of transcripts to create approximately 1000 different templates, each template comprising one of said approximately 1000 barcode sequences operably associated with a different gene-specific sequence, wherein said approximately 1000 different templates represents less than the total number of transcripts within said population; c) measuring the amount of each of said approximately 1000 different templates to create a plurality of measurements; and d) applying said algorithm to said plurality of measurements, thereby predicting the level of expression of unmeasured transcripts within said population. In one embodiment, the method further comprises a device capable of measuring the amount of each of said approximately 1000 different templates. In one embodiment, the beads are optically addressed. In one embodiment, the processing comprises ligation-mediated amplification. In one embodiment, the measuring comprises detecting said optically addressed beads. In one embodiment, the measuring comprises hybridizing said approximately 1000 different templates to said approximately 1000 beads through said nucleic-acid probes complementary to said approximately 1000 barcode sequences. In one embodiment, the measuring comprises a flow cytometer. In one embodiment, the algorithm involves a dependency matrix.

In one embodiment, the present invention contemplates a composition comprising an amplified nucleic acid sequence, wherein said sequence comprises at least a portion of a cluster centroid transcript sequence and a barcode sequence, wherein said composition further comprises an optically addressed bead, and wherein said bead comprises a capture probe nucleic-acid sequence hybridized to said barcode. In one embodiment, the barcode sequence is at least partially complementary to said capture probe nucleic acid. In one embodiment, the amplified

nucleic-acid sequence is biotinylated. In one embodiment, the optically addressed bead is detectable with a flow cytometric system. In one embodiment, the flow cytometric system discriminates between approximately 500 - 1000 optically addressed beads.

In one embodiment, the present invention contemplates a method for creating a genome-wide expression profile, comprising: a) providing; i) a plurality of genomic transcripts derived from a biological sample; ii) a plurality of centroid transcripts comprising at least a portion of said genomic transcripts, said remaining genomic transcripts being non-centroid transcripts; b) measuring the expression level of said plurality of centroid transcripts; c) inferring the expression levels of said non-centroid transcripts from said centroid transcript expression levels, thereby creating a genome-wide expression profile. In one embodiment, the plurality of centroid transcripts comprise approximately 1,000 transcripts. In one embodiment, the measuring comprises a device selected from the group comprising a microarray, a bead array, a liquid array, or a nucleic-acid sequencer. In one embodiment, the inferring involves a dependency matrix. the genome-wide expression profile identifies said biological sample as diseased. In one embodiment, the genome-wide expression profile identifies said biological sample as healthy. In one embodiment, the genome-wide expression profile provides a functional readout of the action of a perturbagen. In one embodiment, the genome-wide expression profile comprises an expression profile suitable for use in a connectivity map. In one embodiment, the expression profile is compared with query signatures for similarities. In one embodiment, the genome-wide expression profile comprises a query signature compatible with a connectivity map. In one embodiment, the query signature is compared with known genome-wide expression profiles for similarities.

In one embodiment, the present invention contemplates a kit, comprising: a) a first container comprising a plurality of centroid transcripts derived from a transcriptome;b) a second container comprising buffers and reagents compatible with measuring the expression level of said plurality of centroid transcripts within a biological sample; c) a set of instructions for inferring the expression level of non-centroid transcripts within said biological sample, based upon the expression level of said plurality of centroid transcripts. In one embodiment, the plurality of centroid transcripts is approximately 1,000 transcripts.

In one embodiment, the present invention contemplates a method for making a transcriptome-wide mRNA-expression profile, comprising: a) providing: i) a composition of validated centroid transcripts numbering substantially less than the total number of all transcripts; ii) a device capable of measuring the expression levels of said validated centroid transcripts; iii) an algorithm capable of substantially calculating the expression levels of transcripts not amongst the set of said validated centroid transcripts from expression levels of said validated centroid transcripts measured by said device and transcript cluster information created from a library of transcriptome-wide mRNA-expression data from a collection of biological samples; and iv) a biological sample; b) applying said biological sample to said device whereby expression levels of said validated centroid transcripts in said biological sample are measured; and c) applying said algorithm to said measurements thereby creating a transcriptome-wide mRNA expression profile. In one embodiment, the validated centroid transcripts comprise approximately 1,000 transcripts. In one embodiment, the device is selected from the group comprising a microarray, a bead array, a liquid array, or a nucleic-acid sequencer. In one embodiment, the expression levels of a set of substantially invariant transcripts are additionally measured in said biological sample. In one embodiment, the expression levels of said validated centroid transcripts are normalized with respect to said expression levels of said invariant transcripts.

In one embodiment, the present invention contemplates a method for making a transcriptome-wide mRNA-expression profiling platform comprising: a) providing: i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples; ii) a second library of transcriptome-wide mRNA-expression data from a second collection of biological samples; iii) a device capable of measuring transcript expression levels; b) performing computational analysis on said first library such that a plurality of transcript clusters are created, wherein the number of said clusters is substantially less than the total number of all transcripts; c) identifying a centroid transcript within each of said plurality of transcript clusters, thereby creating a plurality of centroid transcripts; d) identifying a set of substantially invariant transcripts from said first library; e) measuring the expression levels of at least a portion of transcripts from said second collection of biological samples with said device, wherein said portion of transcripts comprise transcripts identified as said centroid transcripts and said invariant transcripts from said first library; f) determining the ability of said measurements

of expression levels of said plurality of centroid transcripts to infer the levels of at least a portion of non-centroid transcripts from said second library. In one embodiment, the plurality of centroid transcripts is approximately 1000 centroid transcripts. In one embodiment, the device comprises a genome-wide microarray. In one embodiment, the method further comprises repeating steps c to f until validated centroid transcripts for each of said plurality of transcript clusters are identified. In one embodiment, the plurality of clusters of transcripts are orthogonal. In one embodiment,the plurality of clusters of transcripts are non-overlapping.

In one embodiment, the present invention contemplates a method for predicting transcript levels within a transcriptome, comprising: a) providing; i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples; ii) a second library of transcriptome-wide mRNA-expression data from a second collection of biological samples; iii) a device capable of measuring transcript expression levels; b) performing computational analysis on said first library such that a plurality of transcript clusters are created, wherein the number of said clusters is less than the total number of all transcripts in said first library; c) identifying a centroid transcript within each of said transcript clusters thereby creating a plurality of centroid transcripts, said remaining transcripts being non-centroid transcripts; d) processing said second library transcripts on said device so as to measure expresssion levels of said centroid transcripts and e) determining which of said plurality of centroid transcripts measured on said device predict the levels of said non-centroid transcripts in said second library of transcriptome-wide data. In one embodiment, the plurality of centroid transcripts is approximately 1000 centroid transcripts. In one embodiment, the device is selected from the group comprising a microarray, a bead array, or a liquid array. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the identifying comprises repeating steps c) to e). In one embodiment, the processing utilizes a flow cytometer. In one embodiment, the determining identifies a correlation between said centroid transcript and said non-centroid transcript.

In one embodiment, the present invention contemplates a method for making a transcriptome-wide mRNA-expression profiling platform comprising: a) providing: i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples; ii) a second collection of biological samples; iii) a second library of transcriptome-wide mRNA-expression data from said second collection of biological samples; iv) a device capable of measuring transcript expression levels; b) performing computational analysis on said first

library such that a plurality of transcript clusters are created, wherein the number of said clusters is substantially less than the total number of all transcripts; c) identifying a centroid transcript within each of said plurality of transcript clusters, thereby creating a plurality of centroid transcripts; d) measuring the expression levels of at least a portion of transcripts from said second collection of biological samples with said device, wherein said portion of transcripts comprise transcripts identified as said centroid transcripts from said first library; e) determining the ability of said measurements of the expression levels of said centroid transcripts to infer the levels of at least a portion of transcripts from said second library, wherein said portion is comprised of non-centroid transcripts. In one embodiment, the plurality of centroid transcripts is approximately 1000 centroid transcripts. In one embodiment, the device comprises a microarray. In one embodiment, the device comprises a bead array. In one embodiment, the device comprises a liquid array. In o the method further comprises repeating steps c to e until validated centroid transcripts for each of said plurality of transcript clusters are identified. In one embodiment, the plurality of clusters of transcripts are orthogonal. In one embodiment, the plurality of clusters of transcripts are non-overlapping. In one embodiment, the determining involves a correlation between said centroid transcripts and said non-centroid transcripts. In one embodiment, the expression levels of a set of substantially invariant transcripts are additionally measured with said device in said second collection of biological samples. In one embodiment, the measurements of said centroid transcripts made with said device, and said mRNA-expression data from said first and second libraries, are normalized with respect to the expression levels of a set of substantially invariant transcripts.

In one embodiment, the present invention contemplates a method for identifying a subpopulation of approximately 1000 predictive transcripts within a transcriptome, comprising: a) providing i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples representing greater than 1000 different transcripts, and ii) transcripts from a second collection of biological samples; b) performing computational analysis on said first library such that a plurality of clusters of transcripts are created, wherein the number of said clusters is approximately 1000 and less than the total number of all transcripts in said first library; c) identifying a centroid transcript within each of said transcript clusters, said remaining transcripts being non-centroid transcripts; d) processing the transcripts from said second collection of biological samples so as to measure the expression levels of non-centroid

transcripts, so as to create first measurements, and expression levels of centroid transcripts, so as to create second measurements; and e) determining which centroid transcripts based on said second measurements predict the levels of said non-centroid transcripts, based on said first measurements, thereby identifying a subpopulation of predictive transcripts within a transcriptome. In one embodiment, the method further comprises a device capable of attaching said centroid transcripts. In one embodiment, the device attaches approximately 1000 of said centroid transcripts. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the identifying comprises repeating steps c) to e). In one embodiment, the processing utilizes a flow cytometer. In one embodiment, the determining identifies a correlation between said centroid transcript and said non-centroid transcript..

In one embodiment, the present invention contemplates a method for predicting the expression level of a first population of transcripts by measuring the expression level of a second population of transcripts, comprising: a) providing; i) a first heterogeneous population of transcripts comprising a second heterogeneous population of transcripts, said second population comprising a subset of said first population, ii) an algorithm capable of predicting the level of expression of transcripts within said first population which are not within said second population, said predicting based on the measured level of expression of transcripts within said second population; b) processing said first heterogeneous population of transcripts under conditions such that a plurality of different templates representing only said second population of transcripts is created; c) measuring the amount of each of said different templates to create a plurality of measurements; and d) applying said algorithm to said plurality of measurements, thereby predicting the level of expression of transcripts within said first population which are not within said second population. In one embodiment, the first heterogenous population of transcripts comprise a plurality of non-centroid transcripts. In one embodiment, the second heterogenous population of transcripts comprises a plurality of centroid transcripts. In one embodiment, the method further comprises a device capable of attaching approximately 1000 of said centroid transcripts. In one embodiment, the measuring comprises a flow cytometer. In one embodiment, the applying said algorithm identifies a correlation between said centroid transcript and said non-centroid transcript.

In one embodiment, the present invention contemplates a method of assaying gene expression, comprising: a) providing i) approximately 1000 different barcode sequences; ii)

approximately 1000 beads, each bead comprising a homogeneous set of nucleic acid probes, each set complementary to a different barcode sequence of said approximately 1000 barcode sequences; iii) a population of more than 1000 different transcripts, each transcript comprising a gene specific sequence; iv) an algorithm capable of predicting the level of expression of unmeasured transcripts; b) processing said population of transcripts to create approximately 1000 different templates, each template comprising one of said approximately 1000 barcode sequences operably associated with a different gene specific sequence, wherein said approximately 1000 different templates represents less than the total number of transcripts within said population; c) measuring the amount of each of said approximately 1000 different templates to create a plurality of measurements; and d) applying said algorithm to said plurality measurements, thereby predicting the level of expression of unmeasured transcripts within said population. In one embodiment, the method further comprises a device capable of attaching approximately 1000 of said centroid transcripts. In one embodiment, the processing comprises ligation mediated amplification. In one embodiment, the beads are optically addressable. In one embodiment, the measuring comprises detecting said optically addressable beads. In one embodiment,.the applying said algorithm comprises identifying a correlation between said measured transcripts and said unmeasured trancripts.

In one embodiment, the present invention contemplates a composition comprising an amplified nucleic acid sequence, wherein said sequence comprises at least a portion of a cluster centroid landmark transcript sequence and a barcode sequence, wherein said composition further comprises an optically addressable bead, and wherein said bead comprises a capture probe nucleic acid sequence hybridized to said barcode. In one embodiment, the barcode sequence is at least partially complementary to said capture probe nucleic acid. In one embodiment, the optically addressable bead is color coded. In one embodiment, the amplifiied nucleic acid sequence is biotinylated. In one embodiment, the optically addressable bead is detectable with a flow cytometric system. In one embodiment, the flow cytometric system simultaneously differentiates between approximately 500 - 1000 optically addressable beads.

In one embodiment, the present invention contemplates a method for creating a genome-wide expression profile, comprising: a) providing; i) a plurality of genomic transcripts derived from a biological sample; and ii) a plurality of centroid transcripts comprising at least a portion of said genomic transcripts, said remaining genomic transcripts being non-centroid transcripts; b)

measuring the expression of said plurality of centroid transcripts; c) inferring the expression levels of said non-centroid transcripts from said centroid transcript expression, thereby creating a genome wide expression profile. In one embodiment, the plurality of centroid transcripts comprise approximately 1,000 transcripts. In one embodiment, the genome-wide expression profile identifies said biological sample as diseased. In one embodiment, the genome-wide expression profile identifies said biological sample as healthy. In one embodiment, the genome-wide expression profile comprises a query signature compatible with a connectivity map. In one embodiment, the query signature is compared with known genome-wide expression profiles for similarities.

In one embodiment, the present invention contemplates a method for identifying a subpopulation of predictive transcripts within a transcriptome, comprising: a) providing i) a device to measure the expression level of transcripts, ii) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples, and iii) transcripts from a second collection of biological samples; b) performing computational analysis on said first library such that a plurality of clusters of transcripts are created, wherein the number of said clusters is less than the total number of all transcripts in said first library; c) identifying a centroid transcript within each of said transcript clusters, said remaining transcripts being non-centroid transcripts; d) processing the transcripts from said second collection of biological samples so as to measure, with said device, the expression levels of non-centroid transcripts, so as to create first measurements, and expression levels of centroid transcripts, so as to create second measurements; and e) determining which centroid transcripts based on said second measurements predict the levels of said non-centroid transcripts, based on said first measurements, thereby identifying a subpopulation of predictive transcripts within a transcriptome. In one embodiment, the device comprises a microarray. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the identifying comprises an iterative validation algorithm. In one embodiment, the processing utilizes a cluster dependency matrix. In one embodiment, the determining identifies a dependency matrix between said centroid transcript and said non-centroid transcript..

In one embodiment, the present invention contemplates a method for identifying a subpopulation of approximately 1000 predictive transcripts within a transcriptome, comprising: a) providing i) a device to measure the expression level of transcripts, ii) a first library of

transcriptome-wide mRNA-expression data from a first collection of biological samples representing greater than 1000 different transcripts, and iii) transcripts from a second collection of biological samples; b) performing computational analysis on said first library such that a plurality of clusters of transcripts are created, wherein the number of said clusters is approximately 1000 and less than the total number of all transcripts in said first library; c) identifying a centroid transcript within each of said transcript clusters, said remaining transcripts being non-centroid transcripts; d) processing the transcripts from said second collection of biological samples so as to measure, with said device, the expression levels of non-centroid transcripts, so as to create first measurements, and expression levels of centroid transcripts, so as to create second measurements; and e) determining which centroid transcripts based on said second measurements predict the levels of said non-centroid transcripts, based on said first measurements, thereby identifying a subpopulation of predictive transcripts within a transcriptome. In one embodiment, the device comprises a microarray. In one embodiment, the computational analysis comprises cluster analysis. In one embodiment, the identifying comprises an iterative validation algorithm. In one embodiment, the processing utilizes a cluster dependency matrix. In one embodiment, the determining identifies a dependency matrix between said centroid transcript and said non-centroid transcript.

In one embodiment, the present invention contemplates a method for predicting the expression level of a first population of transcripts by measuring the expression level of a second population of transcripts, comprising: a) providing i) a first heterogeneous population of transcripts comprising a second heterogeneous population of transcripts, said second population comprising a subset of said first population, ii) a device, iii) an algorithm capable of predicting the level of expression of transcripts within said first population which are not within said second population, said predicting based on the measured level of expression of transcripts within said second population; b) processing said first heterogeneous population of transcripts under conditions such that a plurality of different templates representing only said second population of transcripts is created; c) measuring the amount of each of said different templates with said device to create a plurality of measurements; and d) applying said algorithm to said plurality of measurements, thereby predicting the level of expression of transcripts within said first population which are not within said second population. In one embodiment, the first heterogenous population of transcripts comprise a plurality of non-centroid transcripts. In one

embodiment, the second heterogenous population of transcripts comprises a plurality of centroid transcripts. In one embodiment, the device comprises a microarray. In one embodiment, the processing comprises computations selected from the group consisting of dimensionality reduction and cluster analysis. In one embodiment, the applying said algorithm identifies a dependency matrix between said centroid transcript and said non-centroid transcript.

In one embodiment, the present invention contemplates a method of assaying gene expression, comprising:a) providing i) approximately 1000 different barcode sequences; ii) approximately 1000 beads, each bead comprising a homogeneous set of nucleic acid probes, each set complementary to a different barcode sequence of said approximately 1000 barcode sequences; iii) a population of more than 1000 different transcripts, each transcript comprising a gene specific sequence; iv) a device; and v) an algorithm capable of predicting the level of expression of unmeasured transcripts; b) processing said population of transcripts to create approximately 1000 different templates, each template comprising one of said approximately 1000 barcode sequences operably associated with a different gene specific sequence, wherein said approximately 1000 different templates represents less than the total number of transcripts within said population; c) measuring the amount of each of said approximately 1000 different templates with said device to create a plurality of measurements; and d) applying said algorithm to said plurality measurements, thereby predicting the level of expression of unmeasured transcripts within said population. In one embodiment, the device comprises a microarray. In one embodiment, the processing comprises ligation mediated amplification. In one embodiment, the beads are optically addressable. In one embodiment, the measuring comprises detecting said optically addressable beads. In one embodiment, the applying said algorithm identifies a dependency matrix between said measured transcripts and said unmeasured trancripts.

In one embodiment, the present invention contemplates a method for making a transcriptome-wide mRNA-expression profiling platform comprising a) providing a library of transcriptome-wide mRNA-expression data from a first collection of biological samples; b) performing computational analysis on said library such that a plurality of (orthogonal/non-overlapping) clusters of transcripts are created, wherein the number of said clusters is substantially less than the total number of all transcripts; c) identifying a centroid transcript within each of said transcript clusters; d) identifying a set of transcripts from said transcriptome-wide mRNA-expression-data library whose levels are substantially invariant across said first

collection of biological samples; e) providing a device to measure (simultaneously) the levels of at least a portion of said centroid transcripts and said invariant transcripts; f) determining the ability of said measurements of centroid-transcript levels made using said devise to represent the levels of other transcripts within its cluster from a second collection of biological samples; and g) repeating steps c to f until validated centroid transcripts for each of said plurality of transcript clusters are identified.

In one embodiment, the present invention contemplates a method for using a transcriptome-wide mRNA-expression profiling platform: a) providing: i) a composition of validated centroid transcripts numbering substantially less than the total number of all transcripts; ii) a device capable of measuring the levels of said validated centroid transcripts; iii) an algorithm capable of substantially calculating the levels of transcripts not amongst the set of said validated centroid transcripts from levels of said validated centroid transcripts measured by said device and transcript cluster information created from a library of transcriptome-wide mRNA-expression data from a collection of biological samples; and iv) a biological sample; b) applying said biological sample to said devise whereby levels of said validated centroid transcripts in said biological sample are measured; and c) applying said algorithm to said measurements thereby creating a transcriptome-wide mRNA expression profile.

Definitions

The term "device" as used herein, refers to any composition capable of measuring expression levels of transcripts. For example, a device may comprise a solid planar substrate capable of attaching nucleic acids (ie, an oligonucleotide microarray). Alternatively, a device may comprise a solution-based bead array, wherein nucleic acids are attached to beads and detected using a flow cytometer. Alternatively, a device may comprise a nucleic-acid sequencer. In other examples, a device may comprise a plurality of cluster centroid landmark transcripts as contemplated by the present invention.

The term "capture probe" as used herein, refers to any molecule capable of attaching and/or binding to a nucleic acid (ie, for example, a barcode nucleic acid). For example, a capture probe may be an oligonucleotide attached to a bead, wherein the oligonucleotide is at least partially complementary to another oligonucleotide. Alternatively, a capture probe may comprise a polyethylene glycol linker, an antibody, a polyclonal antibody, a monoclonal antibody, an Fab

fragment, a biological receptor complex, an enzyme, a hormone, an antigen, and/or a fragment or portion thereof.

The term "LMF" as used herein, refers to an acronym for any method that combines *ligation*-mediated amplication, optically-addressed and barcoded *microspheres*, and *flow* cytometric detection. See Peck et al., "A method for high-throughput gene expression signature analysis" *Genome Biol* 7:R61 (2006).

The term "transcript" as used herein, refers to any product of DNA transcription, generally characterized as mRNA. Expressed transcripts are recognized as a reliable indicator of gene expression.

The term "gene-expression profile" as used herein, refers to any dataset representing the expression levels of a significant portion of genes within the genome (ie, for example, a transcriptome).

The term "centroid transcript" as used herein, refers to any transcript that is within the center portion, or is representative of, a transcript cluster. Further, the expression level of a centroid transcript may predict the expression levels of the non-centroid transcripts within the same cluster.

The term "non-centroid transcript" as used herein, refers to any transcript in a transcript cluster that is not a centroid transcript. The expression level of a non-centroid transcript may be predicted (eg, inferred) by the expression levels of centroid transcripts.

The term "cluster centroid landmark transcript" as used herein, refers to any transcript identified as a centroid transcript, the expression level of which predicts (eg, infers) the expression levels of non-centroid transcripts within the same cluster, and optionally may contribute to prediction of the expression levels of non-centroid transcripts in other clusters.

The term "computational analysis" as used herein, refers to any mathematical process that results in the identification of transcript clusters, wherein the transcripts are derived from a transcriptome. For example, specific steps in a computational analysis may include, but are not limited to, dimensionality reduction and/or cluster analysis.

The term "dependency matrix" as used herein, refers to a table of weights (ie, factors) relating the expression levels of a plurality of cluster centroid landmark transcripts to the

expression levels of non-centroid transcripts generated by a mathematical analysis (ie, for example, regression) of a library of transcriptome-wide gene-expression profiles. Cluster dependency matrices may be produced from a heterogeneous library of gene-expression profiles or from libraries of gene-expression profiles from specific tissues, organs, or disease classes.

The term "algorithm capable of predicting the level of expression of transcripts" as used herein, refers to any mathematical process that calculates the expression levels of non-centroid transcripts given the expression levels of cluster centroid landmark transcripts and a dependency matrix.

The term "invariant transcript" as used herein, refers to any transcript that remains at approximately the sample level regardless of cell or tissue type, or the presence of a perturbating agent (ie, for example, a perturbagen). Invariant transcripts, or sets thereof, may be useful as an internal control for normalizing gene-expression data.

The term "moderate-multiplex assay platform" as used herein, refers to any technology capable of producing simultaneous measurements of the expression levels of a fraction of the transcripts in a transcriptome (ie, for example, more than approximately 10 and less than approximately 2,000).

The term "Connectivity Map" as used herein, refers to a public database of transcriptome-wide gene-expression profiles derived from cultured human cells treated with a plurality of perturbagens, and pattern-matching algorithms for the scoring and identification of significant similarities between those profiles and external gene-expression data, as described by Lamb et al., "The Connectivity Map: using gene-expression signatures to connect small molecules, genes and disease", *Science* 313:1929 (2006). Build02 of the Connectivity Map contains 7,056 full-transcriptome gene-expression profiles generated with Affymetrix high-density oligonucleotide microarrays representing the biological effects of 1,309 small-molecule perturbagens, and is available at broadinstitute.org/cmap.

The term "query signature" as used herein, refers to any set of up- and down- regulated genes between two cellular states (eg, cells treated with a small molecule versus cells treated with the vehicle in which the small molecule is dissolved) derived from a gene-expression profile that is suitable to query Connectivity Map. For example, a 'query signature' may comprise a list of genes differentially expressed in a distinction of interest; (eg, disease versus normal), as

opposed to an 'expression profile' that illustrates all genes with their respective expression levels.

The term "connectivity score" as used herein, refers to a relative measure of the similarity of the biological effects of a perturbagen used to generate a query signature with those of a perturbagen represented in the Connectivity Map based upon the gene-expression profile of a single treatment with that perturbagen. For example, one would expect every treatment instances with vorinostat, a known histone deacetylase (HDAC) inhibitor, to have a high connectivity score with a query signature generated from the effects of treatments with a panel of HDAC inhibitors.

The term "enrichment score" as used herein, refers to a measure of the similarity of the biological effects of a perturbagen used to generate a query signature with those of a perturbagen represented in the Connectivity Map based upon the gene-expression profiles of multiple independent treatments with that perturbagen.

The term "template" as used herein, refers to any stable nucleic acid structure that represents at least a portion of a cluster centroid landmark gene transcript nucleic acid sequence. The template may serve to allow the generation of a complementary nucleic acid sequence.

The term "derived from" as used herein, refers to the source of a biological sample, whrein the sample may comprise a nucleic acid sequence. In one respect, a sample or sequence may be derived from an organism or particular species. In another respect, a sample or sequence may be derived from (i.e., for example, a smaller portion and/or fragment) a larger composition or sequence.

The term, "purified" or "isolated", as used herein, may refer to a component of a composition that has been subjected to treatment (i.e., for example, fractionation) to remove various other components. Where the term "substantially purified" is used, this designation will refer to a composition in which a nucleic acid sequence forms the major component of the composition, such as constituting about 50%, about 60%, about 70%, about 80%, about 90%, about 95% or more of the composition (i.e., for example, weight/weight and/or weight/volume). The term "purified to homogeneity" is used to include compositions that have been purified to 'apparent homogeneity" such that there is single nucleic acid species (i.e., for example, based

upon SDS-PAGE or HPLC analysis). A purified composition is not intended to mean that some trace impurities may remain.

As used herein, the term "substantially purified" refers to molecules, such as nucleic acid sequences, that are removed from their natural environment, isolated or separated, and are at least 60% free, preferably 75% free, and more preferably 90% free from other components with which they are naturally associated. An "isolated polynucleotide" is therefore a substantially purified polynucleotide.

"Nucleic acid sequence" and "nucleotide sequence" as used herein refer to an oligonucleotide or polynucleotide, and fragments or portions thereof, and to DNA or RNA of genomic or synthetic origin which may be single- or double-stranded, and represent the sense or antisense strand.

The term "an isolated nucleic acid", as used herein, refers to any nucleic acid molecule that has been removed from its natural state (e.g., removed from a cell and is, in a preferred embodiment, free of other genomic nucleic acid).

The term "portion or fragment" when used in reference to a nucleotide sequence refers to smaller subsets of that nucleotide sequence. For example, such portions or fragments may range in size from 5 nucleotide residues to the entire nucleotide sequence minus one nucleic acid residue.

The term "small organic molecule" as used herein, refers to any molecule of a size comparable to those organic molecules generally used in pharmaceuticals. The term excludes biological macromolecules (e.g., proteins, nucleic acids, etc.). Preferred small organic molecules range in size from approximately 10 Da up to about 5000 Da, more preferably up to 2000 Da, and most preferably up to about 1000 Da.

The term "sample" as used herein is used in its broadest sense and includes environmental and biological samples. Environmental samples include material from the environment such as soil and water. Biological samples may be animal, including, human, fluid (e.g., blood, plasma and serum), solid (e.g., stool), tissue, liquid foods (e.g., milk), and solid foods (e.g., vegetables). For example, a pulmonary sample may be collected by bronchoalveolar lavage (BAL) which comprises fluid and cells derived from lung tissues. A biological sample

may comprise a cell, tissue extract, body fluid, chromosomes or extrachromosomal elements isolated from a cell, genomic DNA (in solution or bound to a solid support such as for Southern blot analysis), RNA (in solution or bound to a solid support such as for Northern blot analysis), cDNA (in solution or bound to a solid support) and the like.

The term "functionally equivalent codon", as used herein, refers to different codons that encode the same amino acid. This phenomenon is often referred to as "degeneracy" of the genetic code. For example, six different codons encode the amino acid arginine.

A "variant" of a nucleotide is defined as a novel nucleotide sequence which differs from a reference oligonucleotide by having deletions, insertions and substitutions. These may be detected using a variety of methods (e.g., sequencing, hybridization assays etc.).

A "deletion" is defined as a change in a nucleotide sequence in which one or more nucleotides are absent relative to the native sequence.

An "insertion" or "addition" is that change in a nucleotide sequence which has resulted in the addition of one or more nucleotides relative to the native sequence. A "substitution" results from the replacement of one or more nucleotides by different nucleotides or amino acids, respectively, and may be the same length of the native sequence but having a different sequence.

The term "derivative" as used herein, refers to any chemical modification of a nucleic acid. Illustrative of such modifications would be replacement of hydrogen by an alkyl, acyl, or amino group. For example, a nucleic acid derivative would encode a polypeptide which retains essential biological characteristics.

As used herein, the terms "complementary" or "complementarity" are used in reference to "polynucleotides" and "oligonucleotides" (which are interchangeable terms that refer to a sequence of nucleotides) related by the base-pairing rules. For example, the sequence "C-A-G-T," is complementary to the sequence "G-T-C-A." Complementarity can be "partial" or "total." "Partial" complementarity is where one or more nucleic acid bases is not matched according to the base pairing rules. "Total" or "complete" complementarity between nucleic acids is where each and every nucleic acid base is matched with another base under the base pairing rules. The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands. This is of particular importance in

amplification reactions, as well as detection methods which depend upon binding between nucleic acids.

The terms "homology" and "homologous" as used herein in reference to nucleotide sequences refer to a degree of complementarity with other nucleotide sequences. There may be partial homology or complete homology (i.e., identity). A nucleotide sequence which is partially complementary, i.e., "substantially homologous," to a nucleic acid sequence is one that at least partially inhibits a completely complementary sequence from hybridizing to a target nucleic acid sequence. The inhibition of hybridization of the completely complementary sequence to the target sequence may be examined using a hybridization assay (Southern or Northern blot, solution hybridization and the like) under conditions of low stringency. A substantially homologous sequence or probe will compete for and inhibit the binding (i.e., the hybridization) of a completely homologous sequence to a target sequence under conditions of low stringency. This is not to say that conditions of low stringency are such that non-specific binding is permitted; low stringency conditions require that the binding of two sequences to one another be a specific (i.e., selective) interaction. The absence of non-specific binding may be tested by the use of a second target sequence which lacks even a partial degree of complementarity (e.g., less than about 30% identity); in the absence of non-specific binding the probe will not hybridize to the second non-complementary target.

The terms “homology” and “homologous” as used herein in reference to amino acid sequences refer to the degree of identity of the primary structure between two amino acid sequences. Such a degree of identity may be directed a portion of each amino acid sequence, or to the entire length of the amino acid sequence. Two or more amino acid sequences that are “substantially homologous” may have at least 50% identity, preferably at least 75% identity, more preferably at least 85% identity, most preferably at least 95%, or 100% identity.

An oligonucleotide sequence which is a "homolog" is defined herein as an oligonucleotide sequence which exhibits greater than or equal to 50% identity to a sequence, when sequences having a length of 100 bp or larger are compared.

Low stringency conditions comprise conditions equivalent to binding or hybridization at 42°C in a solution consisting of 5 x SSPE (43.8 g/l NaCl, 6.9 g/l NaH2PO4·H2O and 1.85 g/l EDTA, pH adjusted to 7.4 with NaOH), 0.1% SDS, 5x Denhardt's reagent {50x Denhardt's

contains per 500 ml: 5 g Ficoll (Type 400, Pharmacia), 5 g BSA (Fraction V; Sigma)} and 100 μg/ml denatured salmon sperm DNA followed by washing in a solution comprising 5x SSPE, 0.1% SDS at 42°C when a probe of about 500 nucleotides in length. is employed. Numerous equivalent conditions may also be employed to comprise low stringency conditions; factors such as the length and nature (DNA, RNA, base composition) of the probe and nature of the target (DNA, RNA, base composition, present in solution or immobilized, etc.) and the concentration of the salts and other components (e.g., the presence or absence of formamide, dextran sulfate, polyethylene glycol), as well as components of the hybridization solution may be varied to generate conditions of low stringency hybridization different from, but equivalent to, the above listed conditions. In addition, conditions which promote hybridization under conditions of high stringency (e.g., increasing the temperature of the hybridization and/or wash steps, the use of formamide in the hybridization solution, etc.) may also be used.

As used herein, the term "hybridization" is used in reference to the pairing of complementary nucleic acids using any process by which a strand of nucleic acid joins with a complementary strand through base pairing to form a hybridization complex. Hybridization and the strength of hybridization (i.e., the strength of the association between the nucleic acids) is impacted by such factors as the degree of complementarity between the nucleic acids, stringency of the conditions involved, the Tm of the formed hybrid, and the G:C ratio within the nucleic acids.

As used herein the term "hybridization complex" refers to a complex formed between two nucleic acid sequences by virtue of the formation of hydrogen bounds between complementary G and C bases and between complementary A and T bases; these hydrogen bonds may be further stabilized by base stacking interactions. The two complementary nucleic acid sequences hydrogen bond in an antiparallel configuration. A hybridization complex may be formed in solution (e.g., C0 t or R0 t analysis) or between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized to a solid support (e.g., a nylon membrane or a nitrocellulose filter as employed in Southern and Northern blotting, dot blotting or a glass slide as employed in in situ hybridization, including FISH (fluorescent in situ hybridization)).

As used herein, the term "Tm " is used in reference to the "melting temperature." The melting temperature is the temperature at which a population of double-stranded nucleic acid

molecules becomes half dissociated into single strands. As indicated by standard references, a simple estimate of the Tm value may be calculated by the equation: Tm = 81.5 + 0.41 (% G+C), when a nucleic acid is in aqueous solution at 1M NaCl. Anderson et al., "Quantitative Filter Hybridization" In: Nucleic Acid Hybridization (1985). More sophisticated computations take structural, as well as sequence characteristics, into account for the calculation of Tm.

As used herein the term "stringency" is used in reference to the conditions of temperature, ionic strength, and the presence of other compounds such as organic solvents, under which nucleic acid hybridizations are conducted. "Stringency" typically occurs in a range from about Tm to about 20°C to 25°C below Tm. A "stringent hybridization" can be used to identify or detect identical polynucleotide sequences or to identify or detect similar or related polynucleotide sequences. For example, when fragments of SEQ ID NO:2 are employed in hybridization reactions under stringent conditions the hybridization of fragments of SEQ ID NO:2 which contain unique sequences (i.e., regions which are either non-homologous to or which contain less than about 50% homology or complementarity with SEQ ID NOs:2) are favored. Alternatively, when conditions of "weak" or "low" stringency are used hybridization may occur with nucleic acids that are derived from organisms that are genetically diverse (i.e., for example, the frequency of complementary sequences is usually low between such organisms).

As used herein, the term "amplifiable nucleic acid" is used in reference to nucleic acids which may be amplified by any amplification method. It is contemplated that "amplifiable nucleic acid" will usually comprise "sample template."

As used herein, the term "sample template" refers to nucleic acid originating from a sample which is analyzed for the presence of a target sequence of interest. In contrast, "background template" is used in reference to nucleic acid other than sample template which may or may not be present in a sample. Background template is most often inadvertent. It may be the result of carryover, or it may be due to the presence of nucleic acid contaminants sought to be purified away from the sample. For example, nucleic acids from organisms other than those to be detected may be present as background in a test sample.

"Amplification" is defined as the production of additional copies of a nucleic acid sequence and is generally carried out using polymerase chain reaction. Dieffenbach C. W. and

G. S. Dveksler (1995) In: PCR Primer, a Laboratory Manual, Cold Spring Harbor Press, Plainview, N.Y.

As used herein, the term "polymerase chain reaction" ("PCR") refers to the method of K. B. Mullis U.S. Pat. Nos. 4,683,195 and 4,683,202, herein incorporated by reference, which describe a method for increasing the concentration of a segment of a target sequence in a mixture of genomic DNA without cloning or purification. The length of the amplified segment of the desired target sequence is determined by the relative positions of two oligonucleotide primers with respect to each other, and therefore, this length is a controllable parameter. By virtue of the repeating aspect of the process, the method is referred to as the "polymerase chain reaction" (hereinafter "PCR"). Because the desired amplified segments of the target sequence become the predominant sequences (in terms of concentration) in the mixture, they are said to be "PCR amplified". With PCR, it is possible to amplify a single copy of a specific target sequence in genomic DNA to a level detectable by several different methodologies (e.g., hybridization with a labeled probe; incorporation of biotinylated primers followed by avidin-enzyme conjugate detection; incorporation of 32P-labeled deoxynucleotide triphosphates, such as dCTP or dATP, into the amplified segment). In addition to genomic DNA, any oligonucleotide sequence can be amplified with the appropriate set of primer molecules. In particular, the amplified segments created by the PCR process itself are, themselves, efficient templates for subsequent PCR amplifications.

As used herein, the term "primer" refers to an oligonucleotide, whether occurring naturally as in a purified restriction digest or produced synthetically, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product which is complementary to a nucleic acid strand is induced, (i.e., in the presence of nucleotides and an inducing agent such as DNA polymerase and at a suitable temperature and pH). The primer is preferably single stranded for maximum efficiency in amplification, but may alternatively be double stranded. If double stranded, the primer is first treated to separate its strands before being used to prepare extension products. Preferably, the primer is an oligodeoxy-ribonucleotide. The primer must be sufficiently long to prime the synthesis of extension products in the presence of the inducing agent. The exact lengths of the primers will depend on many factors, including temperature, source of primer and the use of the method.

As used herein, the term "probe" refers; to an oligonucleotide (i.e., a sequence of nucleotides), whether occurring naturally as in a purified restriction digest or produced synthetically, recombinantly or by PCR amplification, which is capable of hybridizing to another oligonucleotide of interest. A probe may be single-stranded or double-stranded. Probes are useful in the detection, identification and isolation of particular gene sequences. It is contemplated that any probe used in the present invention will be labeled with any "reporter molecule," so that is detectable in any detection system, including, but not limited to enzyme (e.g., ELISA, as well as enzyme-based histochemical assays), fluorescent, radioactive, and luminescent systems. It is not intended that the present invention be limited to any particular detection system or label.

As used herein, the terms "restriction endonucleases" and "restriction enzymes" refer to bacterial enzymes, each of which cut double-stranded DNA at or near a specific nucleotide sequence.

DNA molecules are said to have "5' ends" and "3' ends" because mononucleotides are reacted to make oligonucleotides in a manner such that the 5' phosphate of one mononucleotide pentose ring is attached to the 3' oxygen of its neighbor in one direction via a phosphodiester linkage. Therefore, an end of an oligonucleotide is referred to as the "5' end" if its 5' phosphate is not linked to the 3' oxygen of a mononucleotide pentose ring. An end of an oligonucleotide is referred to as the "3' end" if its 3' oxygen is not linked to a 5' phosphate of another mononucleotide pentose ring. As used herein, a nucleic acid sequence, even if internal to a larger oligonucleotide, also may be said to have 5' and 3' ends. In either a linear or circular DNA molecule, discrete elements are referred to as being "upstream" or 5' of the "downstream" or 3' elements. This terminology reflects the fact that transcription proceeds in a 5' to 3' fashion along the DNA strand. The promoter and enhancer elements which direct transcription of a linked gene are generally located 5' or upstream of the coding region. However, enhancer elements can exert their effect even when located 3' of the promoter element and the coding region. Transcription termination and polyadenylation signals are located 3' or downstream of the coding region.

As used herein, the term "an oligonucleotide having a nucleotide sequence encoding a gene" means a nucleic acid sequence comprising the coding region of a gene, i.e. the nucleic acid sequence which encodes a gene product. The coding region may be present in a cDNA, genomic

DNA or RNA form. When present in a DNA form, the oligonucleotide may be single-stranded (i.e., the sense strand) or double-stranded. Suitable control elements such as enhancers/promoters, splice junctions, polyadenylation signals, etc. may be placed in close proximity to the coding region of the gene if needed to permit proper initiation of transcription and/or correct processing of the primary RNA transcript. Alternatively, the coding region utilized in the expression vectors of the present invention may contain endogenous enhancers/promoters, splice junctions, intervening sequences, polyadenylation signals, etc. or a combination of both endogenous and exogenous control elements.

The term "poly A site" or "poly A sequence" as used herein denotes a DNA sequence which directs both the termination and polyadenylation of the nascent RNA transcript. Efficient polyadenylation of the recombinant transcript is desirable as transcripts lacking a poly A tail are unstable and are rapidly degraded. The poly A signal utilized in an expression vector may be "heterologous" or "endogenous." An endogenous poly A signal is one that is found naturally at the 3' end of the coding region of a given gene in the genome. A heterologous poly A signal is one which is isolated from one gene and placed 3' of another gene. Efficient expression of recombinant DNA sequences in eukaryotic cells involves expression of signals directing the efficient termination and polyadenylation of the resulting transcript. Transcription termination signals are generally found downstream of the polyadenylation signal and are a few hundred nucleotides in length.

As used herein, the terms "nucleic acid molecule encoding", "DNA sequence encoding," and "DNA encoding" refer to the order or sequence of deoxyribonucleotides along a strand of deoxyribonucleic acid. The order of these deoxyribonucleotides determines the order of amino acids along the polypeptide (protein) chain. The DNA sequence thus codes for the amino acid sequence.

The term "Southern blot" refers to the analysis of DNA on agarose or acrylamide gels to fractionate the DNA according to size, followed by transfer and immobilization of the DNA from the gel to a solid support, such as nitrocellulose or a nylon membrane. The immobilized DNA is then probed with a labeled oligodeoxyribonucleotide probe or DNA probe to detect DNA species complementary to the probe used. The DNA may be cleaved with restriction enzymes prior to electrophoresis. Following electrophoresis, the DNA may be partially

depurinated and denatured prior to or during transfer to the solid support. Southern blots are a standard tool of molecular biologists. J. Sambrook et al. (1989) In: Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, NY, pp 9.31-9.58.

The term "Northern blot" as used herein refers to the analysis of RNA by electrophoresis of RNA on agarose gels to fractionate the RNA according to size followed by transfer of the RNA from the gel to a solid support, such as nitrocellulose or a nylon membrane. The immobilized RNA is then probed with a labeled oligodeoxyribonucleotide probe or DNA probe to detect RNA species complementary to the probe used. Northern blots are a standard tool of molecular biologists. J. Sambrook, J. et al. (1989) supra, pp 7.39-7.52.

The term "reverse Northern blot" as used herein refers to the analysis of DNA by electrophoresis of DNA on agarose gels to fractionate the DNA on the basis of size followed by transfer of the fractionated DNA from the gel to a solid support, such as nitrocellulose or a nylon membrane. The immobilized DNA is then probed with a labeled oligoribonuclotide probe or RNA probe to detect DNA species complementary to the ribo probe used.

As used herein the term "coding region" when used in reference to a structural gene refers to the nucleotide sequences which encode the amino acids found in the nascent polypeptide as a result of translation of a mRNA molecule. The coding region is bounded, in eukaryotes, on the 5' side by the nucleotide triplet "ATG" which encodes the initiator methionine and on the 3' side by one of the three triplets which specify stop codons (i.e., TAA, TAG, TGA).

As used herein, the term "structural gene" refers to a DNA sequence coding for RNA or a protein. In contrast, "regulatory genes" are structural genes which encode products which control the expression of other genes (e.g., transcription factors).

As used herein, the term "gene" means the deoxyribonucleotide sequences comprising the coding region of a structural gene and including sequences located adjacent to the coding region on both the 5' and 3' ends for a distance of about 1 kb on either end such that the gene corresponds to the length of the full-length mRNA. The sequences which are located 5' of the coding region and which are present on the mRNA are referred to as 5' non-translated sequences. The sequences which are located 3' or downstream of the coding region and which are present on the mRNA are referred to as 3' non-translated sequences. The term "gene" encompasses both cDNA and genomic forms of a gene. A genomic form or clone of a gene contains the coding

region interrupted with non-coding sequences termed "introns" or "intervening regions" or "intervening sequences." Introns are segments of a gene which are transcribed into heterogeneous nuclear RNA (hnRNA); introns may contain regulatory elements such as enhancers. Introns are removed or "spliced out" from the nuclear or primary transcript; introns therefore are absent in the messenger RNA (mRNA) transcript. The mRNA functions during translation to specify the sequence or order of amino acids in a nascent polypeptide.

In addition to containing introns, genomic forms of a gene may also include sequences located on both the 5' and 3' end of the sequences which are present on the RNA transcript. These sequences are referred to as "flanking" sequences or regions (these flanking sequences are located 5' or 3' to the non-translated sequences present on the mRNA transcript). The 5' flanking region may contain regulatory sequences such as promoters and enhancers which control or influence the transcription of the gene. The 3' flanking region may contain sequences which direct the termination of transcription, posttranscriptional cleavage and polyadenylation.

The term "label" or "detectable label" are used herein, to refer to any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical or chemical means. Such labels include biotin for staining with labeled streptavidin conjugate, magnetic beads (e.g., Dynabeads®), fluorescent dyes (e.g., fluorescein, texas red, rhodamine, green fluorescent protein, and the like), radiolabels (e.g., 3H, 125I, 35S, 14C, or 32P), enzymes (e.g., horse radish peroxidase, alkaline phosphatase and others commonly used in an ELISA), and calorimetric labels such as colloidal gold or colored glass or plastic (e.g., polystyrene, polypropylene, latex, etc.) beads. Patents teaching the use of such labels include, but are not limited to, U.S. Pat. Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241 (all herein incorporated by reference). The labels contemplated in the present invention may be detected by many methods. For example, radiolabels may be detected using photographic film or scintillation counters, fluorescent markers may be detected using a photodetector to detect emitted light. Enzymatic labels are typically detected by providing the enzyme with a substrate and detecting, the reaction product produced by the action of the enzyme on the substrate, and calorimetric labels are detected by simply visualizing the colored label.

Brief Description of the Figures

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawings will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Figure 1 presents exemplary simulated data depicting the clustering of PCA loadings of transcripts (purple dots) in the eigenspace by k-means to identify k distinct clusters (gray circles). The transcript closest to the mean of the cluster was selected as the 'cluster centroid landmark transcript' (single red dots).

Figure 2 presents exemplary results using Connectivity Map data demonstrating that approximately 80% of the connections observed between 184 query signatures and gene-expression profiles produced by measuring approximately 22,000 transcripts are recovered using gene-expression profiles created by measuring only approximately 1,000 transcripts and predicted the expression levels of the remainder.

Figure 3 presents one embodiment of a method for measuring the expression levels of multiple transcripts simultaneously using ligation-mediated amplification and optically-addressed microspheres.

Figure 4 presents exemplary data for normalized expression levels of a representative cluster centroid landmark transcript (217995_at:SQRDL) in 384 biological samples measured by LMF and Affymetrix microarray.

Figure 5 presents exemplary data showing a simple (type 1) cluster centroid landmark transcript validation failure; circle. Axes are normalized expression levels.

Figure 6 presents exemplary data showing a complex (type 2) cluster centroid landmark transcript validation failure.

Figure 6A: Plots of normalized expression levels for a representative validated transcript / probe pair (blue, 218039_at:NUSAP1) and a representative failed transcript / probe pair (orange, 217762_s_at:RAB31).

Figure 6B: Histogram showing normalized expression levels for the validated transcript / probe pair from Figure 6A (blue arrow) and its associated non-centroid transcripts (blue bars); and the failed transcript / probe pair from Figure 6A (orange arrow) and its

associated non-centroid transcripts (orange bars). Red crosses mark non-correlation of gene-expression levels.

Figure 7 presents exemplary data comparing the performance of Connectivity Map datasets populated with gene-expression profiles generated with Affymetrix microarrays reporting on approximately 22,000 transcripts (left), and a ligation-mediated amplification and Luminex optically-addressed microsphere assay of 1,000 landmark transcripts with inference of the expression levels of the remaining transcripts (right). Both datasets were queried with an independent HDAC-inhibitor query signature. The 'bar views' shown are constructed from 6,100 and 782 horizontal lines, respectively, each representing individual treatment instances and ordered by connectivity score. All instances of the HDAC-inhibitor, vorinostat, are colored in black. Colors applied to the remaining instances reflect their connectivity scores (green, positive; gray, null; red, negative).

Figure 8 presents exemplary data comparing consensus clustering dendrograms of gene-expression profiles for human cell lines generated with Affymetrix microarrays (A), and one embodiment of a landmark transcript measurement and inference method as contemplated herein (B). Tissue types are: CO = colon; LE = blood (leukemia); ME = skin (melanoma); CNS = brain (central nervous system); OV = ovary; and RE = kidney (renal).

Detailed Description of the Invention

The present invention is related to the field of genomic informatics and gene-expression profiling. Gene-expression profiles provide complex molecular fingerprints regarding the relative state of a cell or tissue. Similarities in gene-expression profiles between organic states (ie, for example, normal and diseased cells and/or tissues) provide molecular taxonomies, classification, and diagnostics. Similarities in gene-expression profiles resulting from various external perturbations (ie, for example, ablation or enforced expression of specific genes, and/or small molecules, and/or environmental changes) reveal functional similarities between these perturbagens, of value in pathway and mechanism-of-action elucidation. Similarities in gene-expression profiles between organic (eg disease) and induced (eg by small molecule) states can identify clinically-effective therapies. Improvements described herein allow for the efficient and economical generation of full-transcriptome gene-expression profiles by identifying cluster

centroid landmark transcripts that predict the expression levels of other transcripts within the same cluster.

Some embodiments of the present invention contemplate performing genome-wide transcriptional profiling for applications including, but not limited to, disease classification and diagnosis without resort to expensive and laborious microarray technology (ie, for example, Affymetrix GeneChip microarrays). Other uses include, but are not limited to, generating gene-expression data for use in and with information databases (i.e., for example, connectivity maps). A connectivity map typically comprises a collection of a large number of gene-expression profiles together with allied pattern-matching software. The collection of profiles is searched with the pattern-matching algorithm for profiles that are similar to gene-expression data derived from a biological state of interest. The utility of this searching and pattern-matching exercise resides in the belief that similar biological states can be identified through the transitory feature of common gene-expression changes. The gene-expression profiles in a connectivity map may be derived from known cellular states, or cells or tissues treated with known chemical or genetic perturbagens. In this mode, the connectivity map is a tool for the functional annotation of the biological state of interest. Alternatively, the connectivity map is populated with gene-expression profiles from cells or tissues treated with previously uncharacterized or novel perturbagens. In this mode, the connectivity map functions as a screening tool. Most often, a connectivity map is populated with profiles of both types. Connectivity maps, in general, establish biologically-relevant connections between disease states, gene-product function, and small-molecule action. In particular, connectivity maps have wide-ranging applications including, but not limited to, functional annotation of unknown genes and biological states, identification of the mode of action or functional class of a small molecule, and the identification of perturbagens that modulate or reverse a disease state towards therapeutic advantage as potential drugs. See Lamb *et al*, "The Connectivity Map: using gene-expression signatures to connect small molecules, genes and disease" *Science* 313: 1929-1935 (2006), and Lamb, "The Connectivity Map: a new tool for biomedical research" *Nature Reviews Cancer* 7: 54-60 (2007). However, the high cost of generating gene-expression profiles severely limits the size and scope of connectivity maps. A connectivity map populated with gene-expression profiles derived from every member of an industrial small-molecule drug-screening library, a saturated combinatorial or diversity-orientated chemical library, a comprehensive collection of crude or purified plant or animal

extracts, or from the genetic ablation or forced expression of every gene in a mammalian genome, for example, would be expected to facilitate more, and more profound, biological discoveries than those of existing connectivity maps. Although it is not necessary to understand the mechanism of an invention, it is believed that the presently disclosed method for gene-expression profiling reduces the cost of generating these profiles by more than 30-fold. The present invention contemplates the creation of connectivity maps with at least 100,000 gene-expression profiles, and ultimately, many millions of gene-expression profiles.

I. Cluster Centroid Landmark Transcript Identification

The present invention contemplates compositions and methods for making and using a transcriptome-wide gene-expression profiling platform that measures the expression levels of only a select subset of the total number of transcripts. Because gene expression is believed to be highly correlated, direct measurement of a small number (for example, 1,000) of appropriately-selected "landmark" transcripts allows the expression levels of the remainder to be inferred. The present invention, therefore, has the potential to reduce the cost and increase the throughput of full-transcriptome gene-expression profiling relative to the well-known conventional approaches that require all transcripts to be measured.

In one embodiment, the present invention contemplates identifying landmark transcripts from a computational analysis of a large collection of transcriptome-wide gene-expression profiles. In one embodiment, the profiles contain identities and expression levels of a large proportion (preferably more than 70%) of the known transcripts in the genome. In one preferred embodiment, the profiles are generated by the use of high-density DNA microarrays commercially-available from, but not limited to, Affymetrix, Agilent, and Illumina. Suitable profiles may also be generated by other transcriptome-analysis methods including, but not limited to, Serial Analysis of Gene Expression (SAGE) and deep cDNA sequencing. In one preferred embodiment, all profiles are generated with the same analysis method. In one especially preferred embodiment, all profiles are generated using Affymetrix oligonucleotide microarrays. In one embodiment, the number of profiles in the collection exceeds 1,000, and preferably is more than 10,000. In one preferred embodiment, the profiles derive from a broad diversity of normal and diseased tissue and/or cell types. As know to those skilled in the art, collections of suitable gene-expression profiles are available from public and private,

commercial sources. In one preferred embodiment, gene-expression profiles are obtained from NCBI's Gene Expression Omnibus (GEO). In one embodiment, expression levels in the profiles in the collection are scaled relative to each other. Those skilled in the art will be aware of a variety of methods to achieve such normalization, including, but not limited to, quantile normalization (preferably RMA). In one preferred embodiment, expression levels in the profiles in the collection are scaled relative to each other using a set of transcripts (numbering approximately 100, and preferable approximately 350) having the lowest coefficients-of-variation (CV) of all transcripts at each of a number (preferably approximately 14) of expression levels chosen to span the range of expression levels observed, from an independent collection of transcriptome-wide gene-expression profiles (numbering at least 1,000 and preferably approximately 7,000).

In one preferred embodiment, profiles used to identify landmark transcripts are required to exceed a minimum standard for data quality (ie, for example, quality control (QC) analysis). The samples passing the QC analysis are identified as a core dataset. Suitable data-quality measures are known to those skilled in the art and include, but are not limited to, percentage-of-P-calls and 3'-to-5' ratios. In one embodiment, an empirical distribution of data-quality measures is built and outlier profiles eliminated from the collection. In one preferred embodiment, profiles with data-quality measures beyond the 95^{th} percentile of the distribution are eliminated from the collection. In one preferred embodiment, the set of transcripts represented in all profiles in the collection is identified, and the remainder eliminated from all of the profiles. In one embodiment, the set of transcripts below the limit of detection in a large proportion of the profiles (preferably 99%) are eliminated from the profiles.

In one embodiment, the present invention contemplates using dimensionality reduction in combination with cluster analysis to select transcripts to be measured (ie, for example, landmark transcripts). While dimensionality reduction may be performed by a number of known methods, the embodiments described herein utilize principal component analysis. In one embodiment, the method further comprises using a linear dimension reduction method (ie, for example, using eigenvectors). In one embodiment, the cluster analysis creates a plurality of clusters wherein each cluster comprises a single cluster centroid landmark transcript and a plurality of cluster non-centroid transcripts. See Figure 1. In one preferred embodiment, clusters are achieved by using

k-means clustering, wherein the k-means clustering is repeated a number of times allowing a consensus matrix to be constructed (ie, for example, a gene-by-gene pairwise consensus matrix).

In one preferred embodiment, pockets of high local correlation are identified by hierarchically clustering the gene-by-gene pairwise consensus matrix. As is known to those skilled in the art, the tree from the hierarchical clustering can then be cut at multiple levels. At each level, there are numerous nodes, wherein the leaves (ie, for example, illustrated herein as transcripts) in each node represent a tight cluster. For each tight cluster, a representative centroid 'landmark' transcript can be chosen by picking the transcript whose individual profile most closely correlates with the tight-cluster's mean profile. In one preferred embodiment, the cluster analysis identifies multiple (preferably more than 3 and less than 10) centroid landmark transcripts. Although it is not necessary to understand the mechanism of an invention, it is believed that the expression level of cluster centroid landmark transcripts can be used to infer the expression level of the associated cluster non-centroid transcripts.

In one embodiment, the present invention contemplates a method comprising creating gene-expression profiles from data consisting only of cluster centroid landmark transcript expression-level measurements. In one embodiment, medically-relevant similarities between biological samples are identified by similarities in their corresponding gene-expression profiles produced in the space of cluster centroid landmark transcripts.

In one preferred embodiment, the levels of non-measured transcripts in a new biological sample are inferred (ie, for example, predicted) from the measurements of the landmark transcripts with reference to a dependency matrix, thereby creating a full-transcriptome gene-expression profile. In one embodiment, a dependency matrix is constructed by performing linear regression between the expression levels of each of the cluster centroid landmark genes (g) and the expression levels of all of the non-landmark transcripts (G) in a collection of transcriptome-wide expression profiles. In one preferred embodiment, a pseudo-inverse is used to build the dependency matrix (G non-landmark transcripts x g landmark transcripts). In one preferred embodiment, the collection of transcriptome-wide expression profiles used to build the dependency matrix is the same collection used to identify the cluster centroid landmark transcripts. In another embodiment, the collection of transcriptome-wide expression profiles used to build the dependency matrix is different from that used to identify the cluster centroid

landmark transcripts. In one preferred embodiment, multiple dependency matrices are constructed from collections of transcriptome-wide expression profiles, each collection populated with profiles derived from the same type of normal or diseased tissues or cells. In one embodiment, the choice of dependency matrix to use for the inference is made based upon knowledge of the tissue, cell and/or pathological state of the sample. In one preferred embodiment, the expression level of each non-landmark transcript in a new biological sample is inferred by multiplying the expression levels of each of the landmark transcripts by the corresponding weights looked up from the dependency matrix, and summing those products.

In one preferred embodiment, the present invention contemplates a method comprising the creation of full-transcriptome gene-expression profiles using measurements of a plurality of landmark transcripts and inference of non-landmark transcript levels, wherein those profiles have at least 80% of the performance of gene-expression profiles produced by direct measurement of all transcripts, in a useful application of gene-expression profiling.

II. Determining Suitable Numbers of Cluster Centroid Landmark Transcripts

In one embodiment, the present invention contemplates determining the number of cluster centroid landmark transcripts suitable for the creation of transcriptome-wide gene-expression profiles by experimentation. In one embodiment, the number of cluster centroid landmark transcripts suitable for the creation of transcriptome-wide gene-expression profiles is determined by simulation.

A computational simulation presented herein (Example I and II) demonstrates that dimensionality reduction can be applied to the identification of a plurality of cluster centroid landmark transcripts, and that surprisingly few landmark-transcript measurements are sufficient to faithfully recreate full-transcriptome profiles. It is shown that the expression levels of only 1,000 cluster centroid landmark transcripts (ie, for example, <5% of transcripts in the transcriptome) can be used to recreate full-transcriptome expression profiles that perform as well as profiles in which all transcripts were measured directly in 80% of tests for profile similarity examined. Further, these data demonstrate that 500 centroid landmark transcripts (ie, for example, <2.5% of transcripts in the transcriptome) recovers approximately 50% of such similarities (Figure 2).

In one preferred embodiment, the present invention contemplates a method comprising approximately 1,000 cluster centroid landmark transcripts from which the expression levels of the remainder of the transcriptome may be inferred.

III. Measurement of Cluster Centroid Landmark Transcripts

In one embodiment, the present invention contemplates measuring the expression levels of a set of cluster centroid landmark transcripts in a biological sample comprising a plurality of transcripts, and using a corresponding dependency matrix to predict the expression levels of the transcripts not measured, thereby creating a full-transcriptome expression profile. In one preferred embodiment, the expression levels of the set of cluster centroid landmark transcripts are measured simultaneously. In another preferred embodiment, the number of cluster centroid landmark transcripts measured is approximately 1,000. In another preferred embodiment, the expression levels of the set of cluster centroid landmark transcripts are measured using a moderate-multiplex assay platform. As is well known to those skilled in the art, there are many methods potentially capable of determining the expression level of a moderate number (ie approximately 10 to approximately 1,000) of transcripts simultaneously. These include, but are not limited to, multiplexed nuclease-protection assay, multiplexed RT-PCR, DNA microarrays, nucleic-acid sequencing, and various commercial solutions offered by companies including, but not limited to, Panomics, High Throughput Genomics, NanoString, Fluidigm, Nimblegen, Affymetrix, Agilent, and Illumina.

In one preferred embodiment, the present invention contemplates a method for generating a full-transcriptome gene-expression profile by simultaneously measuring the expression levels of a set of cluster centroid landmark transcripts in a biological sample comprising a plurality of transcripts, and using a corresponding dependency matrix to predict the expression levels of the transcripts not measured, where the said simultaneous measurements are made using nucleic-acid sequencing.

In one preferred embodiment, the present invention contemplates a method for generating a full-transcriptome gene-expression profile by simultaneously measuring the expression levels of a set of cluster centroid landmark transcripts in a biological sample comprising a plurality of transcripts, and using a corresponding dependency matrix to predict the expression levels of the transcripts not measured, where the said simultaneous measurements are made using multiplex

ligation-mediated amplification with Luminex FlexMAP optically-addressed and barcoded microspheres and flow-cytometric detection (LMF); Peck et al., "A method for high-throughput gene expression signature analysis" *Genome Biology* 7:R61 (2006). See Figure 3. In this technique, transcripts are captured on immobilized poly-dT and reverse transcribed. Two oligonucleotide probes are designed for each transcript of interest. Upstream probes contain 20 nt complementary to a universal primer (T7) site, one of a set of unique 24 nt barcode sequences, and a 20 nt sequence complementary to the corresponding first-strand cDNA. Downstream probes are 5'-phosphorylated and contain 20 nt contiguous with the gene-specific fragment of the corresponding upstream probe and a 20 nt universal-primer (T3) site. Probes are annealed to target cDNAs, free probes removed, and juxtaposed probes joined by the action of ligase enzyme to yield 104 nt amplification templates. PCR is performed with T3 and 5'-biotinylated T7 primers. Biotinylated barcoded amplicons are hybridized against a pool of optically-addressed microspheres each expressing capture probes complementary to a barcode, and incubated with streptavidin-phycoerythrin to label biotin moieties fluorescently. Captured labeled amplicons are quantified and beads decoded by flow cytometry in Luminex detectors. The above reported LMF method was limited to measuring 100 transcripts simultaneously due to the availability of only 100 optical addresses. In one embodiment, the present invention contemplates a method for generating gene-expression profiles using simultaneous measurement of the levels of cluster centroid landmark transcripts that is compatible with an expanded number (approximately 500, and preferably 1,000) of barcode sequences, and optically-addressed microspheres and a corresponding flow-cytometric detection device. In one embodiment, the present invention contemplates a method comprising two assays per biological sample, each capable of measuring the expression levels of approximately 500 cluster centroid transcripts. In one embodiment, the present invention contemplates a method were the expression levels of approximately 1,000 cluster centroid landmark transcripts are measured in one assay per biological sample using less than 1,000 populations of optically-addressed microspheres by arranging for microspheres to express more than one type of capture probe complimentary to a barcode. In one embodiment, the present invention contemplates a method comprising one assay per sample, each capable of measuring the expression levels of 1,000 cluster centroid landmark transcripts.

A. Platform-Specific Selection of Landmark Transcripts to be Measured

As is well known to those skilled in the art, an estimate of the expression level of a transcript made with one method (eg RT-PCR) does not always agree with the estimate of the expression level of that same transcript in the same biological sample made with another method (eg DNA microarray). In one embodiment, the present invention contemplates a method for selecting the set of cluster centroid landmark transcripts to be measured by a given moderate-multiplex assay platform for the purposes of predicting the expression levels of transcripts not measured, and thereby to create a full-transcriptome gene-expression profile, from the set of all possible cluster centroid landmark transcripts by experimentation. In one preferred embodiment, the set of cluster centroid landmark transcripts to be measured by a given moderate-multiple assay platform is selected by empirically confirming concordance between measurements of expression levels of cluster centroid landmark transcripts made by that platform and those made using the transcriptome-wide gene-expression profiling technology used to generate the collection of gene-expression profiles from which the universe of cluster centroid landmark transcripts was originally selected. In one especially preferred embodiment, the expression levels of all possible cluster centroid landmark transcripts (preferably numbering approximately 1,300) in a collection of biological samples (preferably numbering approximately 384) are estimated by both LMF and Affymetrix oligonucleotide microarrays, where Affymetrix oligonucleotide microarrays were used to produce the transcriptome-wide gene-expression profiles from which the universe of possible cluster centroid landmark transcripts was selected, resulting in the identification of a set of cluster centroid landmark transcripts (preferably numbering approximately 1,100) whose expression level estimated by LMF is consistently concordant with the expression levels estimated by Affymetrix oligonucleotide microarrays. Data presented herein (Example III) show unanticipated discordances between expression-level measurements made using LMF and Affymetrix oligonucleotide microarrays.

B. Elimination of Cluster Centroid Landmark Transcripts that do not Faithfully Report on Non-Centroid Transcripts in their Clusters

In one embodiment, the present invention contemplates a method for selecting the final set of cluster centroid landmark transcripts to be measured by a given moderate-multiplex assay platform for the purposes of predicting the expression levels of transcripts not measured, and

thereby to create a full-transcriptome gene-expression profile, from the set of all possible cluster centroid landmark transcripts by experimentation. In one preferred embodiment, the set of cluster centroid landmark transcripts to be measured by a given moderate-multiple assay platform is selected by empirically confirming that measurements of their expression levels made by that platform can be used to predict the expression level of non-landmark transcripts in their cluster measured using the transcriptome-wide gene-expression profiling technology used to generate the collection of gene-expression profiles from which the universe of cluster centroid landmark transcripts was selected.

In one especially preferred embodiment, the expression levels of all possible cluster centroid landmark transcripts (preferably numbering approximately 1,300) in a collection of biological samples (preferably numbering approximately 384) are measured by LMF, and the expression levels of all non-landmark transcripts are measured in that same collection of biological samples by Affymetrix oligonucleotide microarrays, where Affymetrix oligonucleotide microarrays were used to produce the transcriptome-wide gene-expression profiles from which the universe of possible cluster centroid landmark transcripts was selected, resulting in the identification of a final set of cluster centroid landmark transcripts (preferably numbering approximately 1,000) whose expression levels estimated by LMF can consistently be used to predict the expression level of transcripts in their clusters as measured by Affymetrix oligonucleotide microarrays. Data presented herein (Example III) show unanticipated failures of measurements of the expression levels of certain cluster centroid landmark made using LMF to be useful for predicting the expression levels of transcripts in their cluster measured using Affymetrix oligonucleotide microarrays.

In one embodiment, the present invention contemplates creating a dependency matrix specific to the final set of cluster centroid landmark transcripts selected for a given moderate-multiplex assay platform.

Data presented herein (Examples IV, V, VI, VII) demonstrate the generation of useful transcriptome-wide gene-expression profiles from the measurement of the expression levels of a set of cluster centroid landmark transcripts selected for use with a specific moderate-multiplex assay platform.

C. Data Normalization Using Invariant Transcripts

In one embodiment, the present invention contemplates a method comprising normalization (ie, for example, scaling) of gene-expression data to correct for day-to-day or detector-to-detector variability in signal intensities. Although it is not necessary to understand the mechanism of an invention, it is believed that in transcriptome-wide gene-expression profiles (ie, for example, high-density microarray data with approximately 20,000 dimensions) convention assumes that the vast majority of the transcripts do not change in a given state. Such an assumption allows a summation of the expression levels for all transcripts to be taken as a measure of overall signal intensity. Those using conventional systems then normalize the expression level of each transcript against that overall signal-intensity value.

However, when using gene-expression profiles of lower dimensionality (i.e., for example, 1,000 transcripts) it is not reasonable to suppose that only a small fraction of those transcripts change, especially in the special case of cluster centroid landmark transcripts where the transcripts were selected, in part, because each exhibited different levels across a diversity of samples. Consequently, normalization relative to a sum of the levels of all transcripts is not suitable.

In one embodiment, the present invention contemplates normalizing gene-expression profiles relative to a set of transcripts whose levels do not change across a large collection of diverse sample (i.e., for example, invariant transcripts). Such a process is loosely analogous to the use of a so-called housekeeping gene (ie, for example, GAPDH) as a reference in a qRT-PCR. Although it is not necessary to understand the mechanism of an invention, it is believed that the normalization described herein is superior to other known normalization techniques because the invariant transcripts are empirically determined to have invariant expression across a broad diversity of samples.

In one embodiment, the set of transcripts (numbering between 10 and 50, preferably 25) having the lowest coefficients-of-variation (CV) of all transcripts at each of a number (preferably approximately 14) of expression levels chosen to span the range of expression levels observed from a collection of transcriptome-wide gene-expression profiles (numbering at least 1,000 and preferably approximately 7,000), are identified as invariant transcripts. In one preferred

embodiment, the collection of transcriptome-wide gene-expression profiles used to selected invariant transcripts is build02 of the Connectivity Map dataset (broadinstitute.org/cmap). In one preferred embodiment, a final set of invariant transcripts (numbering between 14 and 98, preferably 80) to be used to normalize measurements of expression levels of cluster centroid landmark transcripts made using a given moderate-multiplex assay platform is selected from the set of all invariant transcripts by empirically confirming concordance between measurements of their expression levels made by that platform and those made using the transcriptome-wide gene-expression profiling technology used to generate the collection of gene-expression profiles from which the invariant transcripts were originally identified, and that their expression levels are indeed substantially invariant, in a collection of biological samples (numbering preferably approximately 384).

Data presented herein (Examples IV, V, VI, VII) demonstrate the generation of useful transcriptome-wide gene-expression profiles from the measurement of the expression levels of a set of cluster centroid landmark transcripts measured on a selected moderate-multiple assay platform scaled relative to the expression levels of a set of invariant transcripts measured together on the same platform.

IV. Dimensionality Reduction In Gene Expression Profiling

It has been reported that gene regulation may be studied on a genomic level using dimensionality reduction in combination with clustering techniques. For example, gene co-regulation may be inferred from gene co-expression dynamics (i.e., for example, gene-gene interactions) using a dimensionally reduced biological dataset. Capobianco E., "Model Validation For Gene Selection And Regulation Maps" *Funct Integr Genomics* 8(2):87-99 (2008). This approach suggests three feature extraction methods that may detect genes with the greatest differential expression by clustering analysis (i.e., for example, k-means) in combination with principal and/or independent component analysis. In transcriptomics, for instance, clusters may be formed by genes having similar expression patterns. Dimensionality reduction, however, is used primarily to eliminate "noise" from useful biological information. A correlation matrix may be computed whose decomposition applies according to an eigensystem including eigenvalues (i.e., for example, the energies of the modes) and eigenvectors (i.e., for example, γ, determined by maximizing the energy in each mode). Selecting representative differentially

expressed genes may be performed by 'regularization via shrinkage' that isolates cluster outliers to pick the genes having the greatest differential levels of expression.

Other dimensionality reduction methods have been used in proteomic biomarker studies. For example, mass-spectra based proteomic profiles have been used as disease biomarkers that generate datasets having extremely high dimensionality (i.e. number of features or variables) of proteomic data with a small sample size. Among these methods, one report suggests using a feature selection method described as centroid shrinkage, wherein data sets may be evaluated using causal inference techniques. Training samples are used to identify class centroids, wherein a test sample is assigned to a class belonging to the closest centroid. Hilario et al., "Approaches To Dimensionality Reduction In Proteomic Biomarker Studies" *Brief Bioinform* 9(2):102-118 (2008). Centroid shrinkage analysis has been previously used in gene expression analysis to diagnose cancers.

One dimensionality reduction report identifies a subset of features from within a large set of features. Such a selection process is performed by training a support vector machine to rank the features according to classifier weights. For example, a selection may be made for the smallest number of genes that are capable of accurately distinguishing between medical conditions (i.e., for example, cancer versus non-cancer). Principal component analysis is capable of clustering gene expression data, wherein specific genes are selected within each cluster as highly correlated with the expression of cancer. Golub's eigenspace vector method to predict gene function with cancer is directly compared and contrasted as an inferior method. Barnhill et al., "Feature Selection Method Using Support Vector Machine Classifier" *United States Patent 7,542,959 (*col 35 – 49). .

Linear transformations (i.e., for example, principal component analysis) may also be capable of identifying low-dimensional embeddings of multivariate data, in a way that optimally preserves the structure of the data. In particular, the performance of dimensionality reduction may be enhanced. Furthermore, the resulting dimensionality reduction can maintain data coordinates and pairwise relationships between the data elements. Subsequent clustering of decomposition information can be integrated in the linear transformation that clearly show separation between the clusters, as well as their internal structure. Koren et al., "Robust Linear Dimensionality Reduction" *IEEE Trans Vis Comput Graph.* 10(4):459-470 (2004)

Further, methods and systems for organizing complex and disparate data. Principal component analysis may be used to evaluate phenotypic, gene expression, and metabolite data collected from Arabidopsis plants treated with eighteen different herbicides. Gene expression and transcription analysis was limited to evaluating gene expression in the context of cell function. Winfield et al., "Methods And Systems For Analyzing Complex Biological Systems" *United States Patent 6,873,914.*

Functional genomics and proteomics may be studied involving the simultaneous analysis of hundreds or thousands of expressed genes or proteins. From these large datasets, dimensionality reduction strategies have been used to identify clinically exploitable biomarkers from enormous experimental datasets. The field of transcriptomics could benefit from using dimensionality reduction methods in high-throughput methods using microarrays. Finn WG., "Diagnostic Pathology And Laboratory Medicine In The Age Of "omics" *J Mol Diagn.* 9(4):431-436 (2007).

Multifactor dimensionality reduction (MDR) may also be useful for detecting and modeling epistasis, including the identification of single nucleotide polymorphisms (SNPs).. MDR pools genotypes into 'high-risk' and 'low-risk' or 'response' and 'non-response' groups in order to reduce multidimensional data into only one dimension. MDR has detected gene-gene interactions in diseases such as sporadic breast cancer, multiple sclerosis and essential hypertension. MDR may be useful in evaluating most common diseases that are caused by the non-linear interaction of numerous genetic and environmental variables. Motsinger et al., "Multifactor Dimensionality Reduction: An Analysis Strategy For Modeling And Detecting Gene-Gene Interactions In Human Genetics And Pharmacogenomics Studies" *Hum Genomics* 2(5):318-328 (2006).

Another report attempted to use 6,100 transcripts to represent the entire transcriptome in an effort to avoid measuring for genes that were not expected to be expressed. Hoshida et al, "Gene Expression in Fixed Tissues and Outcome in Hepatocellular Carcinoma" *New Engl J Med* 259:19 (2008)).

V Detection Methodologies

A. Detection of Nucleic Acids

mRNA expression may be measured by any suitable method, including but not limited to, those disclosed below.

In some embodiments, RNA is detection by Northern blot analysis. Northern blot analysis involves the separation of RNA and hybridization of a complementary labeled probe.

In other embodiments, RNA expression is detected by enzymatic cleavage of specific structures (INVADER assay, Third Wave Technologies; See e.g., U.S. Pat. Nos. 5,846,717, 6,090,543; 6,001,567; 5,985,557; and 5,994,069; each of which is herein incorporated by reference). The INVADER assay detects specific nucleic acid (e.g., RNA) sequences by using structure-specific enzymes to cleave a complex formed by the hybridization of overlapping oligonucleotide probes.

In still further embodiments, RNA (or corresponding cDNA) is detected by hybridization to a oligonucleotide probe. A variety of hybridization assays using a variety of technologies for hybridization and detection are available. For example, in some embodiments, TaqMan assay (PE Biosystems, Foster City, Calif.; See e.g., U.S. Pat. Nos. 5,962,233 and 5,538,848, each of which is herein incorporated by reference) is utilized. The assay is performed during a PCR reaction. The TaqMan assay exploits the 5'-3' exonuclease activity of the AMPLITAQ GOLD DNA polymerase. A probe consisting of an oligonucleotide with a 5'-reporter dye (e.g., a fluorescent dye) and a 3'-quencher dye is included in the PCR reaction. During PCR, if the probe is bound to its target, the 5'-3' nucleolytic activity of the AMPLITAQ GOLD polymerase cleaves the probe between the reporter and the quencher dye. The separation of the reporter dye from the quencher dye results in an increase of fluorescence. The signal accumulates with each cycle of PCR and can be monitored with a fluorimeter.

In yet other embodiments, reverse-transcriptase PCR (RT-PCR) is used to detect the expression of RNA. In RT-PCR, RNA is enzymatically converted to complementary DNA or "cDNA" using a reverse transcriptase enzyme. The cDNA is then used as a template for a PCR reaction. PCR products can be detected by any suitable method, including but not limited to, gel electrophoresis and staining with a DNA specific stain or hybridization to a labeled probe. In some embodiments, the quantitative reverse transcriptase PCR with standardized mixtures of

competitive templates method described in U.S. Pat. Nos. 5,639,606, 5,643,765, and 5,876,978 (each of which is herein incorporated by reference) is utilized.

The method most commonly used as the basis for nucleic acid sequencing, or for identifying a target base, is the enzymatic chain-termination method of Sanger. Traditionally, such methods relied on gel electrophoresis to resolve, according to their size, wherein nucleic acid fragments are produced from a larger nucleic acid segment. However, in recent years various sequencing technologies have evolved which rely on a range of different detection strategies, such as mass spectrometry and array technologies.

One class of sequencing methods assuming importance in the art are those which rely upon the detection of PPi release as the detection strategy. It has been found that such methods lend themselves admirably to large scale genomic projects or clinical sequencing or screening, where relatively cost-effective units with high throughput are needed.

Methods of sequencing based on the concept of detecting inorganic pyrophosphate (PPi) which is released during a polymerase reaction have been described in the literature for example (WO 93/23564, WO 89/09283, WO98/13523 and WO 98/28440). As each nucleotide is added to a growing nucleic acid strand during a polymerase reaction, a pyrophosphate molecule is released. It has been found that pyrophosphate released under these conditions can readily be detected, for example enzymically e.g. by the generation of light in the luciferase-luciferin reaction. Such methods enable a base to be identified in a target position and DNA to be sequenced simply and rapidly whilst avoiding the need for electrophoresis and the use of labels.

At its most basic, a PPi-based sequencing reaction involves simply carrying out a primer-directed polymerase extension reaction, and detecting whether or not that nucleotide has been incorporated by detecting whether or not PPi has been released. Conveniently, this detection of PPi-release may be achieved enzymatically, and most conveniently by means of a luciferase-based light detection reaction termed ELIDA (see further below).

It has been found that dATP added as a nucleotide for incorporation, interferes with the luciferase reaction used for PPi detection. Accordingly, a major improvement to the basic PPi-based sequencing method has been to use, in place of dATP, a dATP analogue (specifically dATP.alpha.s) which is incapable of acting as a substrate for luciferase, but which is nonetheless capable of being incorporated into a nucleotide chain by a polymerase enzyme (WO98/13523).

Further improvements to the basic PPi-based sequencing technique include the use of a nucleotide degrading enzyme such as apyrase during the polymerase step, so that unincorporated nucleotides are degraded, as described in WO 98/28440, and the use of a single-stranded nucleic acid binding protein in the reaction mixture after annealing of the primers to the template, which has been found to have a beneficial effect in reducing the number of false signals, as described in WO00/43540.

B. Detection of Protein

In other embodiments, gene expression may be detected by measuring the expression of a protein or polypeptide. Protein expression may be detected by any suitable method. In some embodiments, proteins are detected by immunohistochemistry. In other embodiments, proteins are detected by their binding to an antibody raised against the protein. The generation of antibodies is described below.

Antibody binding may be detected by many different techniques including, but not limited to, (e.g., radioimmunoassay, ELISA (enzyme-linked immunosorbant assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (e.g., using colloidal gold, enzyme or radioisotope labels, for example), Western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays, etc.), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc.

In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled.

In some embodiments, an automated detection assay is utilized. Methods for the automation of immunoassays include those described in U.S. Pat. Nos. 5,885,530, 4,981,785, 6,159,750, and 5,358,691, each of which is herein incorporated by reference. In some embodiments, the analysis and presentation of results is also automated. For example, in some embodiments, software that generates a prognosis based on the presence or absence of a series of proteins corresponding to cancer markers is utilized.

In other embodiments, the immunoassay described in U.S. Pat. Nos. 5,599,677 and 5,672,480; each of which is herein incorporated by reference.

C. Remote Detection Systems

In some embodiments, a computer-based analysis program is used to translate the raw data generated by the detection assay (eg, the presence, absence, or amount of a given transcript or transcripts) into data of predictive value for a clinician or researcher. The clinician or researcher can access the predictive data using any suitable means. Thus, in some preferred embodiments, the present invention provides the further benefit that the clinician or researcher, who is not likely to be trained in genetics or genomics, need not understand the raw data. The data is presented directly to the clinician or researcher in its most useful form. The clinician or researcher is then able to immediately utilize the information in order to optimize the care of the subject or advance the discovery objectives.

The present invention contemplates any method capable of receiving, processing, and transmitting the information to and from laboratories conducting the assays, wherein the information is provided to medical personal and/or subjects and/or researchers. For example, in some embodiments of the present invention, a sample (eg, a biopsy or a serum or urine sample or perturbed cells or tissue) is obtained from a subject or experimental procedure and submitted to a profiling service (eg, clinical laboratory at a medical facility, genomic profiling business, etc.), located in any part of the world (eg, in a country different than the country where the subject resides, the experiment performed, or where the information is ultimately used) to generate raw data. Where the sample comprises a tissue or other biological sample, the subject may visit a medical center to have the sample obtained and sent to the profiling center, or subjects may collect the sample themselves (eg, a urine sample) and directly send it to a profiling center. Where the sample comprises previously determined biological information, the information may be directly sent to the profiling service by the subject (eg, an information card containing the information may be scanned by a computer and the data transmitted to a computer of the profiling center using an electronic communication systems). Once received by the profiling service, the sample is processed and a profile is produced (ie, expression data) specific for the diagnostic or prognostic information desired for the subject, or the discovery objective of the researcher.

The profile data is then prepared in a format suitable for interpretation by a treating clinician or researcher. For example, rather than providing raw expression data, the prepared

format may represent a diagnosis or risk assessment for the subject, along with recommendations for particular treatment options, or mechanism-of-action, protein-target prediction, or potential therapeutic use for an experimental perturbagen. The data may be displayed to the clinician or researcher by any suitable method. For example, in some embodiments, the profiling service generates a report that can be printed for the clinician or researcher (eg, at the point of care or laboratory) or displayed to the clinician or researcher on a computer monitor.

In some embodiments, the information is first analyzed at the point of care or laboratory or at a regional facility. The raw data is then sent to a central processing facility for further analysis and/or to convert the raw data to information useful for a clinician, patient or researcher. The central processing facility provides the advantage of privacy (all data is stored in a central facility with uniform security protocols), speed, and uniformity of data analysis. The central processing facility can then control the fate of the data following treatment of the subject or completion of the experiment. For example, using an electronic communication system, the central facility can provide data to the clinician, the subject, or researchers.

In some embodiments, the subject is able to directly access the data using the electronic communication system. The subject may chose further intervention or counseling based on the results. In some embodiments, the data is used for research use. For example, the data may be used to further optimize the inclusion or elimination of markers as useful indicators of a particular condition or stage of disease.

VI. Kits

In one embodiment, the present invention contemplates kits for the practice of the methods of this invention. The kits preferably include one or more containers containing various compositions and/or reagents to perform methods of this invention. The kit can optionally include a plurality of cluster centroid landmark transcripts. The kit can optionally include a plurality of nucleic-acid sequences wherein the sequence is complementary to at least a portion of a cluster centroid landmark transcript sequence, and wherein the sequences may optionally comprise a primer sequence and/or a barcode nucleic-acid sequence. The kit can optionally include a plurality of optically addressed beads, wherein each bead comprises a different a nucleic-acid sequence that is complementary to a barcode nucleic-acid sequence.

The kit can optionally include enzymes capable of performing PCR (ie, for example, DNA polymerase, thermostable polymerase). The kit can optionally include enzymes capable of performing nucleic-acid ligation (for example, a ligase). The kit can optionally include buffers, excipients, diluents, biochemicals and/or other enzymes or proteins. The kits may also optionally include appropriate systems (eg opaque containers) or stabilizers (eg antioxidants) to prevent degradation of the reagents by light or other adverse conditions.

The kits may optionally include instructional materials containing directions (ie, protocols) providing for the use of the reagents in the performance of any method described herein. While the instructional materials typically comprise written or printed materials they are not limited to such. Any medium capable of storing such instructions and communicating them to an end user is contemplated by this invention. Such media include, but are not limited to electronic storage media (eg, magnetic discs, tapes, cartridges, chips), optical media (eg, CD ROM), and the like. Such media may include addresses to internet sites that provide such instructional materials.

The kits may optionally include computer software (ie, algorithms, formulae, instrument settings, instructions for robots, etc) providing for the performance of any method described herein, simplification or automation of any method described herein, or manipulation, analysis, display or visualization of data generated thereby. Any medium capable of storing such software and conveying it to an end user is contemplated by this invention. Such media include, but are not limited to, electronic storage media (eg, magnetic discs), optical media (eg, CD ROM), and the like. Such media may include addresses to internet sites that provide such software.

Experimental

Example I: Identification of Cluster Centroid Landmark Transcripts and Creation of a Dependency Matrix

The present example describes one method for the identification of cluster centroid landmark transcripts having inferential relationships.

Thirty-five thousand eight-hundred and sixty-seven transcriptome-wide gene-expression profiles generated with the Affymetrix U133 family of oligonucleotide microarrays were downloaded from NCBI's Gene Expression Omnibus (GEO) repository in the form of .cel files.

The .cel files were preprocessed to produce average-difference values (ie expression levels) for each probe set using MAS5 (Affymetrix). Expression levels in each profile were then scaled with respect to the expression levels of 350 previously-determined invariant probe sets whose expression levels together spanned the range of expression levels observed. The minimal common feature space in the dataset was determined to be 22,268 probe sets.

The quality of each profile was assessed by reference to two data-quality metrics: percentage of P-calls and 3':5' ratios. Empirical distributions of both metrics were built and the 10% of profiles at both extremes of each distribution were eliminated from further consideration. A total of 16,428 profiles remained after this quality filtering. A further 1,941 profiles were found to be from a single source, and were also eliminated.

Probe sets below a predetermined arbitrary detection threshold of 20 average-difference units in over 99% of the profiles were eliminated, bringing the total number of probe sets under consideration to 14,812.

Principal component analysis (PCA) dimensionality reduction was then applied to the dataset (ie 14,487 samples x 14,812 features). Two-hundred eight-seven components were identified that explained 90% of the variation in the dataset. The matrix of the PCA loadings of the features in the eigenspace (ie 287 x 14,812) was then clustered using k-means. The k-means clustering was repeated a number of times because the high-dimensionality matrix obtained partitions non-deterministically based on the starting seeds, and the results were used to build a gene-by-gene pairwise consensus matrix.

Pockets of high local correlation were identified by hierarchically clustering the gene-by-gene pairwise consensus matrix. The leaves on each node of the dendrogram 'tree' together constitute a cluster. The tree was then cut a multiple levels to identify 100, 300, 500, 700, 1,000, 1,500, 2,000, 5,000, and 10,000 clusters.

The probe sets whose individual expression-level vector across all 14,487 profiles most closely correlated with that of the mean of all probe sets in each cluster was selected as the centroid of that cluster. This produced sets of 100, 300, 500, 700, 1,000, 1,500, 2,000, 5,000, and 10,000 centroid probe sets. Multiple individual probe sets had attributes that approximate the definition of a centroid probe set of any given cluster.

A dependency matrix was created for each set of centroid probe sets by linear regression between the expression levels of the g centroid probe sets and the remaining 14,812 – g probe sets in the space of the 14,487 profiles. A pseudo-inverse was used because the number of profiles did not necessarily match the number of features being modeled. Dependency matrices were thereby populated with weights (ie factors) relating the expression level of each non-centroid probe set to the expression level of each centroid probe set.

The identity and gene symbol of the transcript represented by each centroid probe set was determined using a mapping provided by Affymetrix (affymetrix.com) and taken as a 'cluster centroid landmark transcript.' Non-centroid probe sets were mapped to gene symbols in the same manner.

Example II: Determining a Suitable Number of Cluster Centroid Landmark Transcripts

The present example describes one method for selected the number of cluster centroid landmark transcripts required to create useful transcriptome-wide gene-expression profiles. This method makes use of a large collection of transcriptome-wide gene-expression profiles produced from cultured human cells treated with small-molecule perturbagens made with Affymetrix oligonuceotide microarrays provided in build02 of the public Connectivity Map resource (broadinstitute.org/cmap). One use of Connectivity Map is the identification of similarities between the biological effects of small-molecule perturbagens. This is achieved by detecting similarities in the gene-expression profiles produced by treating cells with those perturbagens (Lamb et al., "The Connectivity Map: using gene-expression signatures to connect small molecules, genes and disease" *Science* 313:1929 2006), and represents one valuable application of transcriptome-wide gene-expression profiling. In summary of the present method, expression values for the sets of cluster centroid landmark transcripts (specifically their corresponding probe sets) identified according to Example I (above) are extracted from the Connectivity Map data and used to create transcriptome-wide gene-expression profiles using the dependency matrices generated also according to Example I (above). Note that the collection of expression profiles used in Example I did not include any Connectivity Map data. The proportion of similarities identified using the actual transcriptome-wide gene-expression profiles also identified by the inferred transcriptome-wide gene-expression profiles created from different numbers of cluster centroid landmark transcript measurements are then compared.

First, a matrix of enrichment scores was constructed by executing 184 independent query signatures obtained from Lamb et al. and the Molecular Signatures Database (MSigDB; release 1.5; broadinstitute.org/gsea/msigdb) against the full Connectivity Map dataset, as described (Lamb et al.) producing a 'reference connectivity matrix' (ie 184 queries x 1,309 treatments).

The 7,056 transcriptome-wide gene-expression profiles were downloaded from the Connectivity Map website in the form of .cel files. The .cel files were then preprocessed to produce average-difference values (ie expression levels) for each probe set using MAS5 (Affymetrix). Expression levels for each set of centroid probe sets were extracted, and 9 x 7,056 sets of transcriptome-wide gene-expression profiles created using the corresponding dependency matrices; expression levels of non-centroid probe sets were computed by multiplying the expression levels for each centroid probe set by their dependency-matrix factors and summed. Rank-ordered lists of probe sets were computed for each treatment-and-vehicle pair using these (inferred) transcriptome-wide gene-expression profiles as described (Lamb et al.). Matrices of enrichment scores were created for each of the 9 datasets with the set of 184 query signatures exactly as was done to create the reference connectivity matrix.

The number of query signatures for which the treatment with the highest enrichment score in the reference connectivity matrix was also the top scoring treatment in the connectivity matrix produced from each of the 9 inferred datasets was plotted (Figure 2). The dataset generated using expression values for only 1,000 centroid probe sets identified the same treatment as the dataset generated using expression values for all 22,283 probe sets in 147 of 184 (80%) of cases. These findings indicate that 1,000 cluster centroid landmark transcripts can be used to create useful transcriptome-wide gene-expression profiles.

Example III: Platform-Specific Selection of Cluster Centroid LandmarkTranscripts

This example describes one method for validating the performance of cluster centroid landmark transcripts on a selected moderate-multiplex assay platform. This example relates specifically to the measurement of expression levels of cluster centroid landmark transcripts derived from gene-expression profiles generated using Affymetrix microarrays using the LMF method of Peck et al., "A method for high-throughput gene expression signature analysis" *Genome Biology* 7:R61 (2006). See Figure 3.

Probe pairs were designed for 1,000 cluster centroid landmark transcripts selected according to Example I (above) as described by Peck et al. The expression levels of these transcripts were measured by LMF in a collection of 384 biological samples comprising unperturbed cell lines, cell lines treated with bioactive small molecules, and tissue specimens for which transcriptome-wide gene-expression profiles generated using Affymetrix microarrays was available. A plot of normalized expression level measured by LMF against normalized expression level measured by Affymetrix microarray for a representative cluster centroid landmark transcript (217995_at:SQRDL) across all 384 biological samples is shown as Figure 4. Vectors of expression levels across all 384 samples were constructed for every feature from both measurement platforms.

For each cluster centroid landmark transcript, the corresponding LMF vector was used as the index in a nearest-neighbors analysis to rank the Affymetrix probe sets. Cluster centroid landmark transcripts were considered to be 'validated' for measurement by LMF when the Affymetrix probe set mapping to that cluster centroid landmark transcript had a rank of 5 or greater, and the Affymetrix probe sets mapping to 80% or more of the non-centroid transcripts in the corresponding cluster had a rank of 100 or greater.

Not all attempts to create validated cluster centroid landmark transcripts were successful. Transcripts failing to meet the validation criteria were found to be of two types: (1) simple, where the measurements of the centroid transcript itself were poorly correlated across the 384 samples; and (2) complex, where the measurements of the centroid transcripts were well correlated but those levels were not well correlated with those of the non-centroid transcripts from its cluster. Neither type of failure could be anticipated. A plot of normalized expression levels determined by LMF and Affymetrix microarray for three validated transcripts (218039_at:NUSAP1, 201145_at:HAX1, 217874_at:SUCLG1), one representative type-1 failure (202209_at:LSM3), and one representative type-2 failure (217762_at:RAB31) in one of the 384 biological samples is presented as Figure 5. A plot of normalized expression levels determined by LMF and Affymetrix microarray for one of these validated transcripts and the same representative type-2 failure in a different one of the 384 biological samples is presented as Figure 6A. Figure 6B shows the expression levels of the same transcripts in the same biological sample together with those of three transcripts from their clusters (measured using Affymetrix microarray only). Only the expression level of the validated transcript (218039_at:NUSAP1) is

correlated with the levels of the transcripts in its cluster (35685_at:RING1, 36004_at:IKBKG, 41160_at:MBD3). The expression level of the type-2 failed transcript (217762_at:RAB31) is not correlated with the levels of all of the transcripts in its cluster (48612_at:N4BP1, 57516_at:ZNF764, 57539_at:ZGPAT). A representative list of transcripts exhibiting simple (type 1) failures, together with the gene-specific portions of their LMF probe pairs, is provided as Table 1. A representative list of transcripts exhibiting complex (type 2) failures, together with the gene-specific portions of their LMF probe pairs is provided as Table 2.

The use of alternative probe pairs allowed a proportion of failed cluster centroid landmark transcripts to be validated. When this was not successful, failed cluster centroid landmark transcripts were substituted with other transcripts from the same cluster. This process was continued until validated cluster centroid landmark transcripts for all 1,000 clusters were obtained. The list of these landmark transcripts, together with the gene-specific portions of their corresponding LMF probe pairs, is provided in Table 3. A dependency matrix specific for this set of validated landmark transcripts was created according to Example I (above).

Example IV: Generation and Use of Transcriptome-Wide Gene-Expression Profiles Made by Measurement of 1,000 Transcripts

This example described one method for the generation of transcriptome-wide gene-expression profiles using measurement of the expression levels of a sub-transcriptome number of cluster centroid landmark transcripts. The present method uses the LMF moderate multiplex gene-expression analysis platform described by Peck et al. ("A method for high-throughput gene expression signature analysis" *Genome Biology* 7:R61 2006), the Luminex FlexMAP 3D optically-addressed microspheres and flow-cytometric detection system, 1,000 cluster centroid landmark transcripts (and corresponding gene-specific sequences) validated for LMF from Example III (above), a corresponding dependency matrix from Example III (above), 50 empirically-determined invariant transcripts with expression levels spanning the range of those observed, and 1,050 barcode sequences developed. The FlexMAP 3D system allows simultaneous quantification of 500 distinct analytes in samples arrayed in the wells of a 384-well plate. Measurement of the expression levels of 1,000 landmark transcripts plus 50 invariant transcripts was therefore divided over 3 wells. Four hundred landmark transcripts were assayed in one well, and three hundred landmark transcripts were assayed in each of 2 additional wells.

The 50 invariant genes were assayed in all 3 wells. This overall method, referred to herein as L1000, was then used to generate a total of 1,152 transcriptome-wide gene-expression profiles from cultured human cells treated with each of 137 distinct bioactive small molecules. These data were used to create an analog of a small portion of Connectivity Map de novo, and the relative performance of the L1000 version compared to that of the original.

LMF probe pairs were constructed for each of the 1,000 landmark and 50 invariant transcripts such that each pair incorporated one of the 1,050 barcode sequences. Probes were mixed in equimolar amounts to form a probe-pair pool. Capture probes complementary to each of the barcode sequences were obtained and coupled to one of 500 homogenous populations of optically-distinguishable microspheres using standard procedures. Three pools of capture-probe expressing microspheres were created; one pool contained beads coupled to capture probes complementary to the barcodes in 400 of the landmark probe pairs, a second pool contained beads matching a different 300 landmark probes, and a third pool contained beads matching the remaining 300 landmark probes. Each pool contained beads expressing barcodes matching the probe pairs corresponding to the 50 invariant transcripts.

MCF7 cells were treated with small molecules and corresponding vehicles in 384-well plates. Cells were lysed, mRNA captured, first-strand cDNA synthesized, and ligation-mediated amplification performed using the 1,000 landmark plus 50 invariant transcript probe-pair pool in accordance with the published LMF method (Peck et al.). The amplicon pools obtained after the PCR step were divided between 3 wells of fresh 384-well plates, and each hybridized to one of the three bead pools at a bead density of approximately 500 beads of each address per well, also in accordance with the published LMF method. The captured amplicons were labeled with phycoerythrin and the resulting microsphere populations were analyzed using a FlexMAP 3D instrument in accordance with the manufacturer's instructions.

Median fluorescence intensity (MFI) values from each microsphere population from each detection well were associated with their corresponding transcript and sample. MFI values for each landmark transcript were scaled relative to those for the set of invariant transcripts obtained from the same detection well, and all scaled MFI values derived from the same samples were concatenated to produce a list of normalized expression levels for each of the 1,000 landmark transcripts in each treatment sample.

Predicted expression levels for transcripts that were not measured were calculated by multiplying the expression levels of each of the landmark transcripts by the weights contained in the dependency matrix, and summed. Computed and measured expression levels were combined to create full-transcriptome gene-expression profiles for each sample. Rank-ordered lists of transcripts were computed for each pair of treatment and corresponding vehicle-control profiles as described by Lamb et al. ("The Connectivity Map: using gene-expression signatures to connect small molecules, genes and disease" *Science* 313: 1929-1935 2006), resulting in an analog of the Connectivity Map dataset containing a total of 782 small-molecule treatment instances.

Enrichment scores for each of the perturbagens in the original Connectivity Map (created with Affymetrix microarrays) and the L1000 analogwere computed according to the method of Lamb et al. for a published query signature derived from an independent transcriptome-wide gene-expression analysis of the effects of three biochemically-verified histone-deacetylase (HDAC) inhibitor compounds. Glaser et al., "Gene expression profiling of multiple histone deacetylase (HDAC) inhibitors: defining a common gene set produced by HDAC inhibition in T24 and MDA carcinoma cell lines." *Mol Cancer Ther* 2:151-163 (2003). As anticipated, the small molecule with the highest score in the original Affymetrix Connectivity Map was vorinostat, an established HDAC inhibitor (enrichment score=0.973, n=12, p-value < 0.001). However, vorinostat was also the highest scoring perturbagen in the L1000 dataset (score=0.921, n=8, p-value < 0.001). See Figure 7. An additional 95 query signatures were executed against both datasets. The perturbagen with the highest score in the original Connectivity Map also had the highest score of those in the L1000 dataset in 79 (83%) of those cases.

These data show that L1000 can substitute for a technology that directly measures the expression levels of all transcripts in the transcriptome—specifically, Affymetrix high-density oligonucleotide microarrays—in one useful application of transcriptome-wide gene-expression profiling.

Example V: Use of Transcriptome-Wide Gene-Expression Profiles Made by Measurement of 1,000 Transcripts for Clustering of Cell Lines

Transcriptome-wide gene-expression profiles were generated from total RNA isolated from 44 cultured human cancer cells lines derived from six tissue types using measurement of

the expression levels of a sub-transcriptome number of cluster centroid transcripts and inference of the remaining transcripts according to the L1000 methods described in Example IV. Full-transcriptome gene-expression data were produced from these same total RNA samples using Affymetrix U133 Plus 2.0 high-density oligonucleotide microarrays for comparison.

Cell lines were grouped together according to consensus hierarchical clustering of their corresponding gene-expression profiles (Monti et al "Consensus Clustering: A resampling-based method for class discovery and visualization of gene expression microarray data. *Machine Learning Journal* 52: 91-118 2003). The similarity metric used was Pearson correlation. One hundred twenty-five clustering iterations were made. In each iteration, 38 (85%) of the samples were used and 6 excluded.

As anticipated, the results of the consensus clustering made with the Affymetrix data placed cell lines from the same tissue in the same branch of the dendrogram, with only few exceptions (Figure 8A). Many similar such findings have been reported. Ross et al., "Systematic variation in gene expression patterns in human cancer cell lines" *Nature Genetics* 24: 227-235 2000). Remarkably, clustering of the L1000 data also placed cell lines with the same tissues of origin in the same branch of the dendrogram (Figure 8B).

This example shows that L1000 can substitute for a technology that directly measures the expression levels of all transcripts in the transcriptome—specifically, Affymetrix high-density oligonucleotide microarrays—in a second useful application of transcriptome-wide gene-expression profiling; that is, grouping of samples on the basis of biological similarity.

Example VI: Use of Transcriptome-Wide Gene-Expression Profiles Made by Measurement of 1,000 Transcripts for Gene-Set Enrichment Analysis

The expression levels of 1,000 cluster centroid transcripts were measured in primary human macrophages following treatment with lipopolysaccharide (LPS) or vehicle control, and used to create gene-expression profiles composed of expression levels for 22,268 transcripts, according to the L1000 methods described in Example IV. These data were used as input for a Gene-Set Enrichment Analysis (GSEA) with a library of 512 gene sets from version 3 of the Molecular Signatures Database (Subramanian et al., "Gene set enrichment analysis: A

knowledge-based approach for interpreting genome-wide expression profiles" *Proc Natl Acad Sci* 102: 15545-15550 2005).

LPS is known to be a potent activator of the NF-κB transcription-factor complex (Qin et al., "LPS induces CD40 gene expression through the activation of NF-κB and STAT-1α in macrophages and microglia" *Blood* 106: 3114-3122 2005). It was therefore not unexpected that a gene set composed of 23 members of the canonical NF-κB signaling pathway (BIOCARTA_NFKB_PATHWAY) received the highest score of all gene sets tested ($p<0.001$).

This example shows that L1000 can generate data compatible with a third useful application of full-transcriptome gene-expression profiling; that is, gene-set enrichment analysis. However, closer examination of the analysis revealed that none of the 23 transcripts in the BIOCARTA_NFKB_PATHWAY gene set had been explicitly measured. This example then also demonstrates the utility of the method even in the extreme case when the expression levels of all of the transcripts of interest were inferred.

Example VII: Creation of a Full-Transcriptome Gene-Expression Dataset of Unprecedented Size

The L1000 methods described in Example IV were used to create a connectivity map with in excess of 100,000 full-transcriptome gene-expression profiles from a panel of cultured human cells treated with a diversity of chemical and genetic perturbations at a range of doses and treatment durations.

Creation of a dataset of this size is impractical with existing transcriptome-wide gene-expression profiling technologies (eg Affymetrix GeneChip) due to high cost and low throughput. This example therefore demonstrates the transformative effect of the present invention on the field of gene-expression profiling in general, and its potential to impact medically-relevant problems in particular.

Table 1. Representative Type I (simple) Landmark Transcript / Probe-Pair Failures

##	name	alternate name	left probe sequence	right probe sequence
1	FFA6B6	200058_s_at:SNRNP200	CCATCAAGAGGCTGACCTTG	CAGCAGAAGGCCAAGGTGAA
2	RE1F1	200064_at:HSP90AB1	GGCGATGAGGATGCGTCTCG	CATGGAAGAAGTCGATTAGG
3	YC7D7	200729_s_at:ACTR2	GAAAATCCTATTTATGAATC	CTGTCGGTATTCCTTGGTAT
4	GGG6H6	200792_at:XRCC6	TGCTGGAAGCCCTCACCAAG	CACTTCCAGGACTGACCAGA
5	CC1D1	200870_at:STRAP	GTGTCAGATGAAGGGAGGTG	GAGTTATCCTCTTATAGTAC
6	AG12H12	200991_s_at:SNX17	TTCTCTTGGCCAGGGGCCTC	GTATCCTACCTTTCCTTGTC
7	DDC7D7	201488_x_at:KHDRBS1	TCTTGTATCTCCCAGGATTC	CTGTTGCTTTACCCACAACA
8	BBA1B1	201511_at:AAMP	CACGTCAGGAGACCACAAAG	CGAAAGTATTTTGTGTCCAA
9	LG12H12	201620_at:MBTPS1	CAGGGGAAGGATGTACTTTC	CAAACAAATGATACAACCCT
10	YC12D12	201652_at:COPS5	AAAGTTAGAGCAGTCAGAAG	CCCAGCTGGGACGAGGGAGT
11	FFE11F11	201683_x_at:TOX4	AATGACAGACATGACATCTG	GCTTGATGGGGCATAGCCAG
12	FFG11H11	201684_s_at:TOX4	TTATCTGCTGGGAAAGTGTC	CAAGAGCCTGTTTTTGAAAC
13	OG3H3	201696_at:SFRS4	TAACCTGGACGGCTCTAAGG	CTGGAATGACCACATAGGTA
14	YA1B1	201710_at:MYBL2	ATGTTTACAGGGGTTGTGGG	GGCAGAGGGGGTCTGTGAAT
15	VC3D3	201729_s_at:KIAA0100	GGCAGGCGCAAATGATTTGG	CGATTCGAGTGGCTGCAGTA
16	AAC9D9	201773_at:ADNP	ACTTAGTTTTTGCACATAAC	CTTGTACAATCTTGCAACAG
17	BBA7B7	201949_x_at:CAPZB	AGCTCTGGGAGCAGAGGTGG	CCCTCGGTGCCGTCCTGCGC
18	CCE4F4	202116_at:DPF2	TTGTTCTTCCTGGACCTGGG	CATTCAGCCTCCTGCTCTTA
19	ME8F8	202123_s_at:ABL1	CGACTGCCTGTCTCCATGAG	GTACTGGTCCCTTCCTTTTG
20	UUA11B11	202178_at:PRKCZ	CACGGAAACAGAACTCGATG	CACTGACCTGCTCCGCCAGG
21	MA1B1	202261_at:VPS72	TGTTCCGTTTCTTCTCCCTG	CTTCTCCCCTTTGTCATCTC
22	RG1H1	202298_at:NDUFA1	GCTCATTTTGGGTATCACTG	GAGTCTGATGGAAAGAGATA
23	OE2F2	202408_s_at:PRPF31	CCGCCCAGTATGGGCTAGAG	CAGGTCTTCATCATGCCTTG
24	LC9D9	202452_at:ZER1	CCTGGGGAGCAGCGCTAACC	CTGGAGGCAGCCTTTGGGTG
25	ZC12D12	202477_s_at:TUBGCP2	ACACGGAGCGCCTGGAGCGC	CTGTCTGCAGAGAGGAGCCA
26	UUE8F8	202717_s_at:CDC16	ACTCTGCTATTGGATATATC	CACAGTCTGATGGGCAACTT

27	VA5B5	202757_at:COBRA1	ACGGGGCCAGCTGGACACAC	GGTGAGATTTTCTCGTATGT
28	EEE4F4	203118_at:PCSK7	CCTGTCTTCCTCTGCAAGTG	CTCAGGGAAATGGCCTTCCC
29	AAA12B12	203154_s_at:PAK4	TCATTTTATAACACTCTAGC	CCCTGCCCTTATTGGGGGAC
30	LE8F8	203190_at:NDUFS8	CCACGGAGACCCATGAGGAG	CTGCTGTACAACAAGGAGAA
31	ZC9D9	203201_at:PMM2	GGAAGGATCCCGGGTCTCAG	CTAGAACACGGTGGAAGAGA
32	BE3F3	203517_at:MTX2	TCTGTAGGAGAATTGAACAG	CACTATTTTGAAGATCGTGG
33	TE8F8	203530_s_at:STX4	CATCACCGTCGTCCTCCTAG	CAGTCATCATTGGCGTCACA
34	FFC9D9	203572_s_at:TAF6	CCTCTGGTCCTGGGAGTGTC	CAGAAGTACATCGTGGTCTC
35	MC4D4	204549_at:IKBKE	AGGGCAGTAGGTCAAACGAC	CTCATCACAGTCTTCCTTCC
36	UC11D11	204757_s_at:C2CD2L	GCCTCTGAGAATGTTGGCAG	CTCACAGAGAGCAGGGCCGG
37	FFE1F1	206050_s_at:RNH1	GTCCTGTACGACATTTACTG	GTCTGAGGAGATGGAGGACC
38	AAA1B1	206075_s_at:CSNK2A1	CTCCCAGGCTCCTTACCTTG	GTCTTTTCCCTGTTCATCTC
39	SG10H10	207988_s_at:ARPC2	TAAGAGGAGGAAGCGGCTGG	CAACTGAAGGCTGGAACACT
40	AE8F8	208093_s_at:NDEL1	GCATGTTAATGACTCTGATG	GTGTCCTCCTCTGGGCAGCT
41	CG1H1	208152_s_at:DDX21	GGAAGTTAAGGTTTCCTCAG	CCACCTGCCGAACAGTTTCT
42	GGG9H9	208174_x_at:ZRSR2	TCGGGAGAGGCACAATTCAC	GAAGCAGAGGAAGAAATAGG
43	EEA12B12	208720_s_at:RBM39	GATGGGATACCGAGATTAAG	GATGATGTGATTGAAGAATG
44	BA10B10	208887_at:EIF3G	GCTAAGGACAAGACCACTGG	CCAATCCAAGGGCTTCGCCT
45	EEA6B6	208996_s_at:POLR2C	CCAGTGCACCTGTAGGGAAC	CAACTAGACTTCTCTCCTGG
46	JE11F11	209044_x_at:SF3B4	TCCCCCTCACTACCTTCCTC	CTGTACAACTTTGCTGACCT
47	SE12F12	209659_s_at:CDC16	AAACGGGGCTTACGCCATTG	GAAACCTCAAGGAAAACTCC
48	IIA3B3	210947_s_at:MSH3	TGGAATTGCCATTGCCTATG	CTACACTTGAGTATTTCATC
49	YYA10B10	211233_x_at:ESR1	CTGCTGGCTACATCATCTCG	GTTCCGCATGATGAATCTGC
50	FFC1D1	212047_s_at:RNF167	GTGACCTATTTGCACAGACC	GTCGTCTTCCCTCCAGTCTT
51	TTC2D2	212087_s_at:ERAL1	CACAGGAGGCAGGCCATGAC	CTCATGGACATCTTCCTCTG
52	UUA10B10	212216_at:PREPL	CCTGAAATTCTGAAACACTG	CATTCAACTGGGAATTGGAA
53	OA4B4	212544_at:ZNHIT3	AGGTCATGCAGGCCTTTACC	GGCATTGATGTGGCTCATGT
54	DDG6H6	212564_at:KCTD2	ACGCAGGTGATGCCAGCCAG	GCCCAGGAGTGCCCAGCATC
55	IIE7F7	212822_at:HEG1	GCGGATGAACTGACATGCTC	CTACCATGACCAGGCTCTGG

56	ZG12H12	212872_s_at:MED20	AAGCCTCTGCAACAAGTCAG	GTGGTGGTCATGTTTCCCTT
57	NC5D5	212968_at:RFNG	ACCACAGAGATGTTTTCTCC	GCTCTGACTTGTGGCTCAGG
58	GGA5B5	214004_s_at:VGLL4	GCCAAAGCTCTGGGTGACAC	GTGGCTCCAGATCAAAGCGG
59	AAC1D1	216525_x_at:PMS2L3	TTTCTACCTGCCACGCGTCG	GTGAAGGTTGGGACTCGACT
60	FFA9B9	217832_at:SYNCRIP	TATATCACATACCCAATAGG	CACCACGATGAAGATCAGAG
61	BG1H1	217987_at:ASNSD1	TTTTACGCCTTGCAGCTGTG	GAACTTGGTCTTACAGCCTC
62	UUC9D9	218114_at:GGA1	TGGGGCACCTAGAGTTCTCG	GTGTGTCTCCTTCATTCATT
63	LE4F4	218386_x_at:USP16	CAGCGACACACATGTGCAAG	CTGTGCCTACAACTAAAGTA
64	FFE3F3	218649_x_at:SDCCAG1	GAAACTGAACAGTGAAGTGG	CTTGATTGCTTAAACTATTG
65	NG4H4	218725_at:SLC25A22	CTGGCCATGTGATCGTGTTG	GTGACAGACCCTGATGTGCT
66	BBE10F10	218760_at:COQ6	GGCTTTGGGGATATCTCCAG	CTTGGCCCATCACCTCAGTA
67	BE11F11	202209_at:LSM3	GCCCCTCCACTGAGAGTTGG	CTGAAACAAAGAATTTGTCC

Table 2. Representative Type II (complex) Landmark Transcript / Probe-Pair Failures

##	name	alternate name	left probe sequence	right probe sequence
1	AA3B3	221049_s_at:POLL	ATTTTAAGCAGGAGCAGGTG	GCTGGTTTGAAGCCCCAGGT
2	AAG3H3	41160_at:MBD3	GCTCCCTGTCAGAGTCAAAG	CACAAATCCTCAGGACGGGC
3	AC6D6	218912_at:GCC1	TTTCTGCCCAGTGGGTCTTG	GCATAAGTAGATTAATCCTG
4	AE7F7	221560_at:MARK4	GAGTTAAAGAAGAGGCGTGG	GAATCCAGGCAGTGGTTTTT
5	AG4H4	219445_at:GLTSCR1	AACAAGAAACTGGGGTCTTC	CTCTCCCCCGAACCTCTCCC
6	CA6B6	218936_s_at:CCDC59	GCCTCTGAAGGAAGGTTGGC	CTGAAGAACTGAAAGAACCT
7	FFA4B4	221471_at:SERINC3	CTTCCCTAGAAGAATGGTTG	CTGATATGGCTACTGCTTCT
8	GGA1B1	221490_at:UBAP1	GGTTCTGCAATATCTCTGAG	GTGCAAAGAATGCACTTTTC
9	HHG1H1	222039_at:KIF18B	TGAAGATGTGGATGATAATG	GTGCCTTGATTTCCAAATGA
10	VG10H10	217762_s_at:RAB31	GAACAATCAAAGTTGAGAAG	CCAACCATGCAAGCCAGCCG
11	NA5B5	221196_x_at:BRCC3	GTTGCCAGGGATAGGGACTG	GAGGGGGTGTGGGGTATGTA
12	RRE10F10	222351_at:PPP2R1B	AGAGGACATGGGGAAGGGAC	CAGTGTATCAGTTGCGTGGA

13	SSE6F6	220079_s_at:USP48	AGATGCGTTGGTCCATAAAG	GATTGTATCAAGTAGATGGG
14	TA5B5	221567_at:NOL3	GTGAGACTAGAAGAGGGGAG	CAGAAAGGGACCTTGAGTAG
15	UUG11H11	221858_at:TBC1D12	ATGGGTCATTCTAGTCTAAG	GACTACTAGTAGAACCCTCA
16	WC8D8	90610_at:LRCH4	AAGACGCGCCTGGGCTCCGC	GCTCTCAGAGAAGCACGTGG
17	XE6F6	222199_s_at:BIN3	ACGACTGAGCCCTGCTTCTG	CTGGGGCTGTGTACAGAGTG
18	YG1H1	221856_s_at:FAM63A	CTAGGATTGGTGGGTTTCTG	GTTCTCAACTCCCGGTCCCT

Table 3. Representative Cluster Centroid Landmark Transcripts / Probe Pairs Validated for LMF

5

##	name	Affymetrix	gene symbol	left probe sequence	right probe sequence
1	QC7D7	209083_at	CORO1A	CCCTCCTCATCTCCCTCAAG	GATGGCTACGTACCCCCAAA
2	AAAG5H5	221223_x_at	CISH	TGTGTCTCACCCCCTCACAG	GACAGAGCTGTATCTGCATA
3	TE6F6	203458_at	SPR	GGAAAGAGTGATCTGGTGTC	GAATAGGAGGACCCATGTAG
4	MME12F12	203217_s_at	ST3GAL5	AACTGTGAAGCCACCCTGGG	CTACAGAAACCACAGTCTTC
5	LLLC12D12	202862_at	FAH	TCCATGTTGGAACTGTCGTG	GAAGGGAACGAAGCCCATAG
6	IIC3D3	201393_s_at	IGF2R	AGAAGCAAACCGCCCTGCAG	CATCCCTCAGCCTGTACCGG
7	PPE8F8	203233_at	IL4R	CGGGCAATCCAGACAGCAGG	CATAAGGCACCAGTTACCCT
8	MMMA8B8	209531_at	GSTZ1	TAGGGAGATGCGGGGAGCAG	GGTGGGCAGGAATACTGTTA
9	BBE6F6	218462_at	BXDC5	ATCCTCAATTTATCGGAAGG	CAGGTTGCCACATTCCACAA
10	IIG7H7	213417_at	TBX2	TAGACCGCGTGATAAAACTG	GGTTGAGGGATGCTGGAACC
11	NNA11B11	201795_at	LBR	TGGTGGCGTTTTCTGTACTG	GATTGCACCAAGGAAGCTTT

12	XG1H1	204752_x_at	PARP2	TGGGAGTACAGTGCCATTAG	GACCAGCAAGTGACACAGGA
13	YA8B8	200713_s_at	MAPRE1	CTTTGTTTGGCAGGATTCTG	CAAAATGTGTCTCACCCACT
14	MMME2F2	203138_at	HAT1	AGCTGGAAGAGAGTTTTCAG	GAACTAGTGGAAGATTACCG
15	NG5H5	209515_s_at	RAB27A	ACTGTACTTGCTGGGTCTTG	CCAAGATCATTTATTCCGCT
16	SSG2H2	211605_s_at	RARA	CTCTCATCCAGGAAATGTTG	GAGAACTCAGAGGGCCTGGA
17	PG4H4	201078_at	TM9SF2	TTACCAAAATATACAGTGTG	GTGAAGGTTGACTGAAGAAG
18	TE2F2	202401_s_at	SRF	GGTGATATTTTTATGTGCAG	CGACCCTTGGTGTTTCCCTT
19	ZZE5F5	203787_at	SSBP2	GCTCCTGCCCCCTCCCTGAA	CTATTTTGTGCTGTGTATAT
20	MMG1H1	200972_at	TSPAN3	GACTGATGCCGAAATGTCAC	CAGGTCCTTTCAGTCTTCAC
21	XXG10H10	217766_s_at	TMEM50A	AAAAGCATGATTCCCACAAG	GACTAAGTATCAGTGATTTG
22	MC1D1	212166_at	XPO7	GTGGATATTTATATATGTAC	CCTGCACTCATGAATGTATG
23	JJG3H3	204812_at	ZW10	GGCCCTAGCTTTGGAACGAG	GAATTGGGAGATTCCAGGAG
24	ZZE7F7	218489_s_at	ALAD	CTGATGGCACATGGACTTGG	CAACAGGGTATCGGTGATGA
25	NA4B4	201739_at	SGK1	TAGTATATTTAAACTTACAG	GCTTATTTGTAATGTAAACC
26	IIIA7B7	206770_s_at	SLC35A3	CAAGACTGCTGAAAGCAATC	CAGTTGCTCCTGTGCTAGAT
27	QQC6D6	205774_at	F12	GATTCCGCAGTGAGAGAGTG	GCTGGGGCATGGAAGGCAAG
28	NNE10F10	201611_s_at	ICMT	GCCTTAGGTAGTTGGGCTTG	CCCACCCTAGTTTGCTTTTG
29	VA3B3	209092_s_at	GLOD4	ATGAGTGTGTGACGTTGCTG	CACGCCTGACTCTGTGCGAG
30	LLA1B1	219382_at	SERTAD3	GAAAGCTGGGCCTGTCGAAG	GATGACAGGGATGTGCTGCC
31	NNE9F9	217872_at	PIH1D1	AAGCCTCACCTGAACCTGTG	GCTGGAAGCCCCCGACCTCC
32	KKE12F12	207196	TNIP1	CACAGTAGCCTTGCTGAAGC	CATCACAGATGGGAGAAGGC

		_s_at			
33	NG12H12	202417 _at	KEAP1	TACATAGAAGCCACCGGATG	GCACTTCCCCACCGGATGGA
34	XG8H8	203630 _s_at	COG5	TTCACTAAATAAGCATGTAG	CTCAGTGGTTTCCAAATTTG
35	OOA7B7	219952 _s_at	MCOLN1	ATTCGACCTGACTGCCGTTG	GACCGTAGGCCCTGGACTGC
36	PPA9B9	203291 _at	CNOT4	ACGAGGGCACTCTGAGATAG	CACTGCTCTGGGGCCATCTG
37	HHHA5B5	217789 _at	SNX6	GCAGGTTTGCTTGACCTCTG	CCTCAGTTCTCGACTCTAAA
38	LLA7B7	203117 _s_at	PAN2	AGCAAGTAGAGTGTTGGTGG	CCCAAGCAAACCAGTGTTGC
39	QG3H3	202673 _at	DPM1	GATGGAGATGATTGTTCGGG	CAAGACAGTTGAATTATACT
40	MC11D11	203373 _at	SOCS2	AAAAACCAATGTAGGTATAG	GCATTCTACCCTTTGAAATA
41	VVA2B2	217719 _at	EIF3L	TTATGGGGATTTCTTCATCC	GTCAGATCCACAAATTTGAG
42	FFFC6D6	210695 _s_at	WWOX	CTGCTTGGTGTGTAGGTTCC	GTATCTCCCTGGAGAAGCAC
43	MMG8H8	201829 _at	NET1	GTGTAGTAAGTTGTAGAAGG	CTCGAGGGGACGTGGACTTA
44	JJJE10F10	203379 _at	RPS6KA1	CACACACCTCCGAGACAGTC	CAGTGTCACCTCTCTCAGAG
45	TTC4D4	204757 _s_at	C2CD2L	AGACCAGCACCAGTGTCTGC	CTCTGAGAATGTTGGCAGCT
46	HHC11D11	203725 _at	GADD45A	TCAACTACATGTTCTGGGGG	CCCGGAGATAGATGACTTTG
47	LLE12F12	202466 _at	POLS	GGGTGTGCATTTTAAAACTC	GATTCATAGACACAGGTACC
48	IIE1F1	212124 _at	ZMIZ1	CATAAACACACCCACCAGTG	CAGCCTGAAGTAACTCCCAC
49	HHG8H8	200816 _s_at	PAFAH1B1	AAGCTGGATTTACAGGTCAC	GGCTGGACTGAATGGGCCTT
50	JJJA2B2	202635 _s_at	POLR2K	AATCAGATGCAGAGAATGTG	GATACAGAATAATGTACAAG
51	JJJA10B10	203186 _s_at	S100A4	TGGACAGCAACAGGGACAAC	GAGGTGGACTTCCAAGAGTA
52	IIA5B5	207163 _s_at	AKT1	TAGCACTTGACCTTTTCGAC	GCTTAACCTTTCCGCTGTCG

53	RA9B9	218346_s_at	SESN1	CAGCACCAAAGTTGTGGGAC	ATGTTGCTGTAGACTGCTGC
54	NA8B8	201896_s_at	PSRC1	GAATTTTATCTTCTTCCTTG	GCATTGGTTCACTGGACATT
55	MME3F3	203013_at	ECD	GACCAGGAACTAGCACACAC	CTGCATCAGCAAAAGTTTCA
56	IIIE12F12	207620_s_at	CASK	AAAAGCCTCTTTGTTATCGG	CCTTGTGTCAGCAGGTCATG
57	ZE4F4	201980_s_at	RSU1	CAACACTTCATTCTCTCTTG	CCCTGTCTCTCAAATAAACC
58	OE6F6	204825_at	MELK	GCTGCAAGGTATAATTGATG	GATTCTTCCATCCTGCCGGA
59	ZZA12B12	201170_s_at	BHLHE40	ACTTGTTTTCCCGATGTGTC	CAGCCAGCTCCGCAGCAGCT
60	ZZE11F11	211715_s_at	BDH1	CTGCGAATGCAGATCATGAC	CCACTTGCCTGGAGCCATCT
61	NNG3H3	208078_s_at	SIK1	TTGGGGCAGCCAGGCCCTTG	CCTTCATTTTTACAGAGGTA
62	QC3D3	203338_at	PPP2R5E	CGTTCTATATCTCATCACAG	CGCCAGCCCTGTTTTTAGCC
63	MMMG11H11	217956_s_at	ENOPH1	ACAGCAAGCAGTTGCCTTAC	CAGTGAAAAAGGTGCACTGA
64	JJJA9B9	202095_s_at	BIRC5	CCAACCTTCACATCTGTCAC	GTTCTCCACACGGGGGAGAG
65	MMME3F3	216836_s_at	ERBB2	TCCCTGAAACCTAGTACTGC	CCCCCATGAGGAAGGAACAG
66	LLLE10F10	212694_s_at	PCCB	TCCACACGTGCCCGAATCTG	CTGTGACCTGGATGTCTTGG
67	ZZC6D6	204497_at	ADCY9	TGAGAGCCCCACAGGCTCTG	CCACACCCGTGACTTCATCC
68	UUC1D1	221142_s_at	PECR	GTGTCCTCCATCCCCCAGTG	CCTTCACATCTTGAGGATAT
69	RE10F10	203246_s_at	TUSC4	ATCTGCTGGAAGTGAGGCTG	GTAGTGACTGGATGGACACA
70	XE5F5	203071_at	SEMA3B	CAGGCCCTGGCTGAGGGCAG	CTGCGCGGGCTTATTTATTA
71	LLLC6D6	217784_at	YKT6	AGGACCCTGGGGAGAGATGG	GGGCGGGGAAAATGGAGGTA
72	LE10F10	202784_s_at	NNT	CTATGCTGCAGTGGACAATC	CAATCTTCTACAAACCTAAC
73	NNNE6F6	200887	STAT1	TGTAACTGCATTGAGAACTG	CATATGTTTCGCTGATATAT

		_s_at			
74	WWC5D5	202540 _s_at	HMGCR	GACTCTGAAAAACATTCCAG	GAAACCATGGCAGCATGGAG
75	MMG6H6	220643 _s_at	FAIM	TGGTAAAAAATTGGAGACAG	CGGGTGAGTTTGTAGATGAT
76	ZG7H7	202446 _s_at	PLSCR1	AAATCAGGAGTGTGGTAGTG	GATTAGTGAAAGTCTCCTCA
77	HHHG9H9	219888 _at	SPAG4	GCTGGGCTTTTGAAGGCGAC	CAAGGCCAGGTGGTGATCCA
78	EEEE11F11	204653 _at	TFAP2A	GTATTCTGTATTTTCACTGG	CCATATTGGAAGCAGTTCTA
79	MME5F5	217080 _s_at	HOMER2	AAACAAGCTTCTGGTGGGTG	CATTTTCTGGCCCGGAGTTG
80	NE9F9	212846 _at	RRP1B	CTAAGTAAAATTGCCAAGTG	GACTTGGAAGTCCAGAAAGG
81	YYA9B9	203442 _x_at	EML3	GCCTTGACTCCCGCTGCCTG	CTGAGGGGCAATAAACCAGA
82	HHE2F2	202324 _s_at	ACBD3	AGCTCATAGGTGTTCATACT	GTTACATCCAGAACATTTGT
83	NNNA5B5	214473 _x_at	PMS2L3	CATCAGAATTACTTTGAAGG	CTACTATTAATATGCAGACT
84	PA1B1	203008 _x_at	TXNDC9	TGATGTTGAATCAACTGATG	CCAGCAGAAAGCTATTTTGA
85	KKKC9D9	209526 _s_at	HDGFRP3	TTTCCTCTCTGTGACAGAAC	CCAGGAATTAATTCCTAAAT
86	PPG5H5	202794 _at	INPP1	GCAGAGACGCATACCTAGAG	GAACTCTAACCCCGGTGTAC
87	OA6B6	202990 _at	PYGL	CAAAGGCCTGGAACACAATG	GTACTCAAAAACATAGCTGC
88	QQC5D5	205452 _at	PIGB	CACTTCCCATGAGATTTCTC	CAGTGCCCGCCAGACCTGAC
89	UG11H11	204458 _at	PLA2G15	TTTTCTCTGTTGCATACATG	CCTGGCATCTGTCTCCCCTT
90	QE4F4	207842 _s_at	CASC3	GGTGGTTGTGCCTTTTGTAG	GCTGTTCCCTTTGCCTTAAA
91	QQA9B9	211071 _s_at	MLLT11	CTTCACACCTACTCACTTTA	CAACTTTGCTCCTAACTGTG
92	PC12D12	206846 _s_at	HDAC6	CCCATCCTGAATATCCTTTG	CAACTCCCCAAGAGTGCTTA
93	SSC3D3	201498 _at	USP7	TGCTGCCTTGGCAGACTTAC	GATCTCAACAGTTCATACGA

94	IIIG4H4	213851_at	TMEM110	GACCACCGAGTGGCAAGGTG	GAAGGAAGCACAGGCACACA
95	RRG5H5	219492_at	CHIC2	AGTATGTTGTCTTTCCAATG	GTGCCTTGCTTGGTGCTCTC
96	PPG4H4	202703_at	DUSP11	ATTCTACCTGGAGACCAGAG	CTGGCCTGAAAATTACTGGT
97	ZA4B4	218145_at	TRIB3	TCTAACTCAAGACTGTTCTG	GAATGAGGGTCCAGGCCTGT
98	MC7D7	212255_s_at	ATP2C1	CCAGGAGTGCCATATTTCAG	CTACTGTATTTCCTTTTTCT
99	VE9F9	200083_at	USP22	CACCACTGCAACATATAGAC	CTGAGTGCTATTGTATTTTG
100	SG7H7	202630_at	APPBP2	CTTCATTGTGTCAGGATGAC	CTTTCATATCATTCTCACCA
101	RC2D2	201774_s_at	NCAPD2	CTGTGCAGGGTATCCTGTAG	GGTGACCTGGAATTCGAATT
102	AAA7B7	203279_at	EDEM1	TCACAGGGCTCAGGGTTATG	CTCCCGCTTGAATCTGGACG
103	RRA12B12	204225_at	HDAC4	GGCTAAGATTTCACTTTAAG	CAGTCGTGAACTGTGCGAGC
104	UE5F5	201671_x_at	USP14	TCAGTCAGATTCTTTCCTTG	GCTCAGTTGTGTTTGTATTT
105	NNNA8B8	218046_s_at	MRPS16	CACCAATCGGCCGTTCTACC	GCATTGTGGCTGCTCACAAC
106	HHC8D8	209263_x_at	TSPAN4	CACCTACATTCCATAGTGGG	CCCGTGGGGCTCCTGGTGCA
107	QE3F3	200621_at	CSRP1	AGGCATGGGCTGTACCCAAG	CTGATTTCTCATCTGGTCAA
108	KKA2B2	200766_at	CTSD	GGGGTAGAGCTGATCCAGAG	CACAGATCTGTTTCGTGCAT
109	YA5B5	201985_at	KIAA0196	GTGCCCTTCTGTTCCTGGAG	GATTATGTTCGGTACACAAA
110	HHG5H5	203154_s_at	PAK4	CCTGCAGCAAATGACTACTG	CACCTGGACAGCCTCCTCTT
111	PPG1H1	202284_s_at	CDKN1A	CAGACATTTTAAGATGGTGG	CAGTAGAGGCTATGGACAGG
112	EEEA11B11	218584_at	TCTN1	TGCAGAGGCAGGCTTCAGAG	CTCCACCAGCCATCAATGCC
113	VE10F10	212943_at	KIAA0528	CCCCCAGGACAACAAACTGC	CCTTAAGAGTCATTTCCTTG
114	ZZA5B5	204656	SHB	TCCAAAGAGATGCCTTCCAG	GATGAACAAAGGCAGACCAG

		_at			
115	EEEG6H6	205573 _s_at	SNX7	TGCTAATAATGCCCTGAAAG	CAGATTGGGAGAGATGGAAA
116	OOE7F7	200670 _at	XBP1	AGTTTGCTTCTGTAAGCAAC	GGGAACACCTGCTGAGGGGG
117	YYC10D10	201328 _at	ETS2	TCTGTTTACTAGCTGCGTGG	CCTTGGACGGGTGGCTGACA
118	QQE9F9	212765 _at	CAMSAP1L 1	GTTTCATGGACACTGTTGAG	CAATGTACAGTGTATGGTGT
119	IIE12F12	202986 _at	ARNT2	GTGCAGGCACATTTCCAAGC	GTAGGTGTCCCTGGCTTTTG
120	XA8B8	201997 _s_at	SPEN	AGACTGGCTAACCCCTCTTC	CTATTACCTTGATCTCTTCC
121	VA8B8	203218 _at	MAPK9	CATGTGACCACAAATGCTTG	CTTGGACTTGCCCATCTAGC
122	UUA3B3	219281 _at	MSRA	TTATCTGTGCTCTCTGCCCG	CCAGTGCCTTACAATTTGCA
123	MME8F8	201649 _at	UBE2L6	CTTGCCATCCTGTTAGATTG	CCAGTTCCTGGGACCAGGCC
124	MA4B4	202282 _at	HSD17B10	TCAATGGAGAGGTCATCCGG	CTGGATGGGGCCATTCGTAT
125	UUG6H6	218794 _s_at	TXNL4B	CTTGCTTTTGGCTCATACAG	GAGAGAGGGAAGGCTGCCAG
126	AAAE9F9	202866 _at	DNAJB12	AGATTATAAGAACTGATGTG	GCCAGAGTGCCTACCCACTG
127	LC7D7	203050 _at	TP53BP1	TGTCACAAGAGTGGGTGATC	CAGTGCCTCATTGTTGGGGA
128	IIC12D12	200045 _at	ABCF1	GGTGGTGCTGTTCTTTTCTG	GTGGATTTAATGCTGACTCA
129	HHC10D10	218523 _at	LHPP	GGCACACAGGGTACTTTCTG	GACCCACTGCTGGACAGACT
130	AC11D11	202535 _at	FADD	GAGTCTCCTCTCTGAGACTG	CTAAGTAGGGGCAGTGATGG
131	PE9F9	202331 _at	BCKDHA	TCAGGGGACAGCATCTGCAG	CAGTTGCTGAGGCTCCGTCA
132	IIC4D4	204087 _s_at	SLC5A6	AGAGCAAGCACGTTTTCCAC	CTCACTGTCTCCATCCTCCA
133	HHE7F7	201555 _at	MCM3	TTGCATCTTCATTGCAAAAG	CACTGGCTCATCCGCCCTAC
134	OOG4H4	212557 _at	ZNF451	AGGAGGTAGTCACTGAGCTG	GACCTTAAACACATCTGCAG

135	QQC2D2	204809_at	CLPX	GCCCCGCCAAGCAGATGCTG	CAAACAGCTAAACTGTCATA
136	PPC9D9	203301_s_at	DMTF1	CGAGAGAATAGTTTGTCATC	CACTTAGTGTGTTAGCTGGT
137	PPE2F2	202361_at	SEC24C	CCTGCTGGGACACCGCTTGG	GCTTTGGTATTGACTGAGTG
138	XG12H12	202716_at	PTPN1	CGAGGTGTCACCCTGCAGAG	CTATGGTGAGGTGTGGATAA
139	PPE12F12	204042_at	WASF3	GCACAAGGCAAGTGAGTTTG	CACTGTCAGCCCCAGACCGT
140	HHE11F11	201675_at	AKAP1	AGACATGAACTGACTAATTG	GTATCCACTACTTGTACAGC
141	BBBE11F11	217989_at	HSD17B11	TCCAATGCCAAACATTTCTG	CACAGGGAAGCTAGAGGTGG
142	SSA8B8	202260_s_at	STXBP1	GTCTCCCTCCCAACTTATAC	GACCTGATTTCCTTAGGACG
143	AAE5F5	201225_s_at	SRRM1	GAAATGAATCAGGATTCGAG	CTCTAGGATGAGACAGAAAA
144	IIE11F11	202624_s_at	CABIN1	GTAAATCTGCCCACACCCAG	CTGGCCATATCCACCCCTCG
145	UC2D2	202705_at	CCNB2	TTGTGCCCTTTTTCTTATTG	GTTTAGAACTCTTGATTTTG
146	MMA11B11	202798_at	SEC24B	TTGAACTCTGGCAAGAGATG	CCAAAAGGCATTGGTACCGT
147	IIG5H5	200053_at	SPAG7	TGCTATTAGAGCCCATCCTG	GAGCCCCACCTCTGAACCAC
148	HHG2H2	202945_at	FPGS	CACACCTGCCTGCGTTCTCC	CCATGAACTTACATACTAGG
149	OOE9F9	201292_at	TOP2A	AATCTCCCAAAGAGAGAAAC	CAATTTCTAAGAGGACTGGA
150	NC9D9	209760_at	KIAA0922	GCCCCATCAACCCCACCACG	GAACATTCGACCCACATGGA
151	XA4B4	204755_x_at	HLF	TCGTCAATCCATCAGCAATG	CTTCTCTCATAGTGTCATAG
152	AAG6H6	209147_s_at	PPAP2A	ACGCCCCACACTGCAATTTG	GTCTTGTTGCCGTATCCATT
153	QQE4F4	205190_at	PLS1	TCCATCTTCCACTGTTAGTG	CCAGTGAGCAATACTGTTGT
154	XC4D4	201391_at	TRAP1	CGAGAACGCCATGATTGCTG	CTGGACTTGTTGACGACCCT
155	UUG2H2	218807	VAV3	TGGGCCTGGGGGTTTCCTAG	CAGAGGATATTGGAGCCCCT

		_at			
156	TTG9H9	209806_at	HIST1H2BK	GGGGTTGGGGTAATATTCTG	TGGTCCTCAGCCCTGTACCT
157	PPG10H10	203755_at	BUB1B	GCTTGCAGCAGAAATGAATG	GGGTTTTTGACACTACATTC
158	MA9B9	203465_at	MRPL19	CCAGAATGGTCTTTAATGAG	CATGGAACCTGAGCAAAGGG
159	VA9B9	202679_at	NPC1	CCTTTTAGGAGTAAGCCATC	CCACAAGTTCTATACCATAT
160	RRE8F8	218051_s_at	NT5DC2	CTTCTCTGACCTCTACATGG	CCTCCCTCAGCTGCCTGCTC
161	JJA4B4	204828_at	RAD9A	GCCTTGGACCCGAGTGTGTG	GCTAGGGTTGCCCTGGCTGG
162	PPA12B12	203965_at	USP20	ATCAGGATCAAAGCAGACGG	GGCGTGGGTGGGGAAGGGGC
163	JJA9B9	209507_at	RPA3	TGGAATTGTGGAAGTGGTTG	GAAGAGTAACCGCCAAGGCC
164	XE1F1	203068_at	KLHL21	CAGTTCACCCCAGAGGGTCG	GGCAGGTTGACATATTTATT
165	NNNG3H3	201339_s_at	SCP2	TCAGCTTCAGCCAGGCAACG	CTAAGCTCTGAAGAACTCCC
166	PPG2H2	202369_s_at	TRAM2	TGAAGGATGAACTAAGGCTG	CTGGTGCCCTGAGCAACTGA
167	UUC11D11	208716_s_at	TMCO1	AAGGCACTGTGTATGCCCTG	CAAGTTGGCTGTCTATGAGC
168	CG4H4	218271_s_at	PARL	GGGATTGGACAGTAGTGGTG	CATCTGGTCCTTGCCGCCTG
169	KKC6D6	202188_at	NUP93	AGGTCCTCATGAATTAAGTG	CCATGCTTTGTGGGAGTCTG
170	BBBA5B5	221245_s_at	FZD5	GAGCCAAATGAGGCACATAC	CGAGTCAGTAGTTGAAGTCC
171	RRE5F5	219485_s_at	PSMD10	TGTGAGTCTTCAGCACCCTC	CCATGTACCTTATATCCCTC
172	LA6B6	201263_at	TARS	CAGTGGCACTGTTAATATCC	GCACAAGAGACAATAAGGTC
173	NNC5D5	213196_at	ZNF629	AAACTGCTATGGACATGGAG	GTCAGATGGGAACTTGGAAC
174	TC8D8	201932_at	LRRC41	GCAAACAGGCATTCTCACAG	CTGGGTTTATAGTCTTTGGG
175	SG8H8	204758_s_at	TRIM44	GTCCTGACTCACTAAAGATG	CCAGGATATTGGGGCTGAGG

176	IIIG8H8	213669_at	FCHO1	CGCATGTCGCTGGTGAAGAG	GAGGTTTGCCACAGGGATGT
177	NNA7B7	219581_at	TSEN2	CACTTTCATACGCAGGCATC	TCTTGTTACCTACATCTAAG
178	LE7F7	201704_at	ENTPD6	TTCTGGACACCAACTGTGTC	CTGTGAATGTATCGCTACTG
179	ZA7B7	205225_at	ESR1	CCCTTTGCATTCACAGAGAG	GTCATTGGTTATAGAGACTT
180	CCCG4H4	210582_s_at	LIMK2	AAGCTCGATGGGTTCTGGAG	GACAGTGTGGCTTGTCACAG
181	NNE11F11	202382_s_at	GNPDA1	GTGCCTGTTTGAAGCTACTG	CTGCCTCCATTTCTGGGAAA
182	PPE6F6	202809_s_at	INTS3	TATGACGTGGTCAGGGTGTC	CATTCCTAATCATGGGGCAG
183	SSG9H9	201833_at	HDAC2	ACCAAATCAGAACAGCTCAG	CAACCCCTGAATTTGACAGT
184	BBBE9F9	200697_at	HK1	TCCGTGGAACCAGTCCTAGC	CGCGTGTGACAGTCTTGCAT
185	NA7B7	208741_at	SAP18	GGAATTGGTGTCCCTGTTAG	CAATGGCAGAGACCAGCCTG
186	UC6D6	202117_at	ARHGAP1	CTGGTCTGTACCCCAGGGAG	CGGGTGCTTGTACTGTGTGA
187	TE9F9	202651_at	LPGAT1	GCTGGTCACACGTGGATCTG	GTTTATGAATGCATTTGGGA
188	LE3F3	203073_at	COG2	TGGGCTTTCTAAAGAGGCTG	CGGGAAGCCATCCTCCACTC
189	IIIC2D2	218108_at	UBR7	GCAGCACAATAGTACCGATC	AGTTAACTCAGCGCTGAAGG
190	HHHC9D9	201855_s_at	ATMIN	GCATGTAATAATACAAGAAC	TGTTTCCCCCTCAAAACCTG
191	PPE5F5	202763_at	CASP3	ACTGCACCAAGTCTCACTGG	CTGTCAGTATGACATTTCAC
192	OOA3B3	206109_at	FUT1	TGAGATAAAACGATCTAAAG	GTAGGCAGACCCTGGACCCA
193	VE3F3	202891_at	NIT1	GAACCTTGACTCTCTTGATG	GAACACAGATGGGCTGCTTG
194	RRC12D12	204313_s_at	CREB1	TGTCCTTGGTTCTTAAAAGC	ATTCTGTACTAATACAGCTC
195	QA9B9	209029_at	COPS7A	TTTCCTCTCTCTGGCCCTTG	GGTCCTGGGAATGCTGCTGC
196	PG7H7	209304	GADD45B	GGGAGCTGGGGCTGAAGTTG	CTCTGTACCCATGAACTCCC

		_x_at			
197	PPC4D4	202691 _at	SNRPD1	CTAGAATTGATTCTCCTTTC	CTGAGTTTTACTCCACGGAG
198	RRA2B2	218375 _at	NUDT9	GCCATGCGTTGTAGCTGATG	GTCTCCGTGTAAGCCAAAGG
199	PPC8D8	203080 _s_at	BAZ2B	AACCACTGTGTTTTATCTAC	TGTGTGTTGTGGTGGCCTGT
200	BBBC10D10	221750 _at	HMGCS1	GGGCAGGCCTGCAAATACTG	GCACAGAGCATTAATCATAC
201	QQA11B11	213119 _at	SLC36A1	GACATAAATGGTGCTGGTAG	GAGGTTATCAGAGTAAGGAA
202	EEEC12D12	202011 _at	TJP1	GGGGCAGTGGTGGTTTTCTG	TTCTTTCTGGCTATGCATTT
203	QQC7D7	208190 _s_at	LSR	TGGGCGGCTACTGGAGGAGG	CTGTGAGGAAGAAGGGGTCG
204	UC10D10	202468 _s_at	CTNNAL1	ATGACAAGCTTATGCTTCTC	CTGGAAATAAACAAGCTAAT
205	QA7B7	218206 _x_at	SCAND1	TCGGGCCCGGGGGCCTGAGC	CTGGGACCCCACCCCGTGTT
206	EEEG10H10	204158 _s_at	TCIRG1	TGCTGGTCCCCATCTTTGCC	GCCTTTGCCGTGATGACCGT
207	XG2H2	202128 _at	KIAA0317	TTAGCGTCTTTGAAGGAGAC	CAGACATGAGTGAATACCTA
208	RG3H3	203105 _s_at	DNM1L	TTATGAACTCCTGTGTATTG	CAATGGTATGAATCTGCTCA
209	QQE5F5	205633 _s_at	ALAS1	TCCTATTTCTCAGGCTTGAG	CAAGTTGGTATCTGCTCAGG
210	NG7H7	203228 _at	PAFAH1B3	TGGCTTTGTGCACTCAGATG	GCACCATCAGCCATCATGAC
211	RC1D1	208820 _at	PTK2	ACCAGAGCACCTCCAAACTG	CATTGAGGAGAAGTTCCAGA
212	ZZG8H8	204765 _at	ARHGEF5	GCTTAAACATTCTCCGCCTC	CAGGGTGCAGATTCAGAGCT
213	IIE9F9	201719 _s_at	EPB41L2	TGGTTACAAGAAAGTTATAC	CATTTAAAGCTGGCACCAGA
214	JJG10H10	212591 _at	RBM34	AGGATTGTGAGAGACAAAAT	GACAGGCATCGGCAAAGGGT
215	OE11F11	202633 _at	TOPBP1	TCTTTTAACAGGAGCCTGAG	CACAAGGTTTAATGAGGAAG
216	AAAG1H1	209213 _at	CBR1	TGACATGGCGGGACCCAAGG	CCACCAAGAGCCCAGAAGAA

217	EEEE6F6	208879_x_at	PRPF6	GCCTGCAACATTCGGCCGTG	GTTACGATGAGTTTACCCCT
218	NE3F3	206398_s_at	CD19	TGACTCTGAAATCTGAAGAC	CTCGAGCAGATGATGCCAAC
219	TTA1B1	209095_at	DLD	CTTTTGTAGAAGTCACATTC	CTGAACAGGATATTCTCACA
220	HHA9B9	201207_at	TNFAIP1	AGTCTTTTTTGCCGAGAAAG	CACAGTAGTCTGGGACTGGG
221	IIC9D9	201462_at	SCRN1	CAGTCCCAGGTCCCAGCTCC	CCTCTTATGGTTTCTGTCAT
222	FFFA3B3	218245_at	TSKU	GCAGTGAGCTCTGTCTTCCC	CCACCTGCCTAGCCCATCAT
223	PC4D4	212910_at	THAP11	TTTTCCTTCCCAGGTGCAGC	CTGTGATTCTGATGGGGACT
224	IIG2H2	219968_at	ZNF589	AGGAATGGCTGGTCCAGAGG	CTTTTGTCCACTCCCTCTCA
225	MMMC11D11	221531_at	WDR61	ATGCCTCCTGGGTGCTGAAC	GTTGCATTCTGTCCTGATGA
226	NNNG7H7	205172_x_at	CLTB	GTCGGGGTGGAGACTCGCAG	CAGCTGCTACCCACAGCCTA
227	WE7F7	202788_at	MAPKAPK3	GGTATACTTGTGTGAAAGTG	GCTGGTTGGGAGCAGAGCTA
228	ZG4H4	212054_x_at	TBC1D9B	GTGTTAGCCCCCACATGGGG	CTGCTCTTGCTTCTACTAAA
229	SSG4H4	208510_s_at	PPARG	TGCTCCAGAAAATGACAGAC	CTCAGACAGATTGTCACGGA
230	QG10H10	203574_at	NFIL3	GAGACTTATAGCCACACAAC	CAATCTCTGCTTCAGACTCT
231	YE1F1	201032_at	BLCAP	CGCTTCAGTAACAAGTGTTG	GCAAACGAGACTTTCTCCTG
232	TE12F12	201889_at	FAM3C	ATATGCTAAATCACATTCAG	CATGTGTATTTTGACATTTA
233	MMG11H11	202946_s_at	BTBD3	GGCAGTCTTTGTCGTTGTTC	ATTCTGGGGATAAAGGGGAA
234	UUG10H10	201380_at	CRTAP	TGCATCTCCAAAATTACAAC	GGTTGGCCGATCCCATTTGA
235	FFFA8B8	219711_at	ZNF586	CCTGCCAGTCATGAATCTCA	GACAGCCTGCCACCTATTGC
236	QC8D8	203646_at	FDX1	GAAGGCAGAGATCTAACCTG	GCTTGTTTAGGGCCATACCA
237	HHHA6B6	204985	TRAPPC6A	AGGTGGGGGTGTCAGAGGAG	GCAAAGGGGTCCCAGCTGCG

		_s_at			
238	SA3B3	202680 _at	GTF2E2	TTTTTCTCCACTTCTAAATG	GTTCCTGGTTCCTTTCTTCC
239	EEEA12B12	213135 _at	TIAM1	TATCATCTCCGGTTCGATCG	CGTCCAGATGGAAAACGGAA
240	VG7H7	201761 _at	MTHFD2	AAGTACGCAACTTACTTTTC	CACCAAAGAACTGTCAGCAG
241	TTG3H3	217825 _s_at	UBE2J1	CCTTGATTCAGTGCTCAGTG	GTCTCCTAGTAAGAAGTCAC
242	OOC8D8	201158 _at	NMT1	GGTGCCATGTCTGGGAACAG	GGACGGGGGAGCTTCACCTT
243	PPA7B7	202813 _at	TARBP1	TTCCTCAACAGGGCATTATC	CGCTCCCTGAATGTCCATGT
244	JJJG4H4	206066 _s_at	RAD51C	CACTGGAACTTCTTGAGCAG	GAGCATACCCAGGGCTTCAT
245	PA5B5	217934 _x_at	STUB1	TGTTTCCCCTCTCAGCATCG	CTTTTGCTGGGCCGTGATCG
246	MMA3B3	202394 _s_at	ABCF3	TATTCCCAAATGTCTCTATC	CTTTTGACTGGAGCATCTTC
247	TA6B6	208647 _at	FDFT1	CATTCAGTGCCACGGTTTAG	GTGAAGTCGCTGCATATGTG
248	LE1F1	202733 _at	P4HA2	TGTCTGGAGCAGAGGGAGAC	CATACTAGGGCGACTCCTGT
249	JJJG6H6	201589 _at	SMC1A	CAATCCATCTTCTGTAATTG	CTGTATAGATTGTCATCATA
250	IIIC4D4	215000 _s_at	FEZ2	GGTGGTGATGGATTTTGTAG	CTTGCTGCTTGTTTCACCAC
251	LC11D11	203963 _at	CA12	CACAGACAGTTTCTGACAGG	CGCAACTCCTCCATTTTCCT
252	YC3D3	206662 _at	GLRX	ATGGATCAGAGGCACAAGTG	CAGAGGCTGTGGTCATGCGG
253	BBBG2H2	202942 _at	ETFB	TGCTGGGCAAACAGGCCATC	GATGATGACTGTAACCAGAC
254	XC6D6	201234 _at	ILK	AGAAGATGCAGGACAAGTAG	GACTGGAAGGTCCTTGCCTG
255	UUG9H9	212206 _s_at	H2AFV	CCCTGTTTCCTGTTGATATG	GTGATAGTTGGAGAGTCAAA
256	RRA1B1	217906 _at	KLHDC2	TGATCACCTTGCATGGACAG	CAATCCTGTAAACATCACAG
257	OE12F12	201494 _at	PRCP	ATCAGTGGCCCTCATAACTG	GAGTAGAGTTCCTGGTTGCT

258	RA1B1	204054_at	PTEN	CTACCCCTTTGCACTTGTGG	CAACAGATAAGTTTGCAGTT
259	RRC9D9	218856_at	TNFRSF21	GGTCCAATCTGCTCTCAAGG	CCTTGGTCCTGGTGGGATTC
260	LLLE7F7	211747_s_at	LSM5	AGCTAAGTTTCCCGTTAAAG	GGAAGTGCTTTGAAGATGTG
261	RRE12F12	206364_at	KIF14	TTGCTGGCACAGTAGTTTAC	CCTGTTATCTGTGTTTCATA
262	JJC4D4	204849_at	TCFL5	TTGTCATGACTCTGAGTCAC	GTGCTGCTGTATTGCAACGT
263	PPA1B1	202153_s_at	NUP62	ACAATGAAGCCCAGTGTAAC	GTCAGTCCACAGAAATAGCC
264	HHE5F5	218014_at	NUP85	ACGTCTCGGATTGCCCCTCG	GTCTTTCTGGATGACTCTGC
265	KKG10H10	205088_at	MAMLD1	GCACCCTCGTGGGGTTAAGG	CGAGCTGTTCCTGGTTTAAA
266	JJC6D6	205340_at	ZBTB24	TGAAACACCTCGTTTTGAAG	GTGAATCTTTGGTTTTCTCC
267	KKE3F3	203130_s_at	KIF5C	TCCATGTAACAAAAGATCTG	GAAGTCACCCTCCTCTGGCC
268	YC5D5	208309_s_at	MALT1	CTGTCATTGCAGCCGGACTC	CAGATGCATTTATTTCAAGT
269	TTE4F4	221567_at	NOL3	ACCCCACGCAAGTTCCTGAG	CTGAACATGGAGCAAGGGGA
270	NE1F1	219650_at	ERCC6L	ATCTCAAAAAGCAACTTCTG	CCCTGCAACGCCCCCCACTC
271	KKC10D10	201121_s_at	PGRMC1	CTCTCCTAAGAGCCTTCATG	CACACCCCTGAACCACGAGG
272	SSA1B1	203201_at	PMM2	GTTCCCTCCAAACCTCCCAG	CCACTCGGGCTTGTAACTGT
273	LLE4F4	218170_at	ISOC1	GGATAGAAGGGTTTGCAATG	CCATATTATTGGTGGAGGGC
274	IIIC5D5	203288_at	KIAA0355	TGTGTGAAGCCGTTTGTGTG	GTCTCCATGTAGGTGCTGTG
275	BBBA3B3	217838_s_at	EVL	TAAGGGGCCGGCCTCGCTGC	GCTGATTCGTCGAGCCCATC
276	HHG4H4	213292_s_at	SNX13	CTCAAATACTGTTGTGTCTG	CACCAGTCTTTTAGTGTCTC
277	UC1D1	202602_s_at	HTATSF1	GGGCCCCTATCCACTGGCAG	CAGCTTTATTCTCAGTAGCG
278	ZC4D4	202349	TOR1A	CACCTTAGCAACAATGGGAG	CTGTGGGAGTGATTTTGGCC

		_at			
279	MMME10F10	201560_at	CLIC4	CCAGAGTTGCATGTAGATAG	CATTTATTTCTGTGCCCTTA
280	ZZA4B4	207749_s_at	PPP2R3A	TTTGCCTCAAACCTCTTACG	GAGCTTCTCCTCAGAAGTGG
281	MMC12D12	203188_at	B3GNT1	TGTGGCCTTGAGTAAATCCC	GTTACCTCTCTGAGCCTCGG
282	LLC12D12	202187_s_at	PPP2R5A	CCTCACAACCTGTCCTTCAC	CTAGTCCCTCCTGACCCAGG
283	IIG4H4	205607_s_at	SCYL3	TAGGCAGTTCCTGACTGTTC	CACATGTAGTACATTGTACC
284	LLE9F9	205130_at	RAGE	CATTTCTGTGATGTGTTGGG	CGTGGTTGGAAGGTGGGTTC
285	IIIE11F11	218854_at	DSE	CTGGTCTCTGCACACATATG	CTTGGTTACTTGCATGCATT
286	OOA2B2	203857_s_at	PDIA5	TGTTCTACGCCCCTTGGTGC	CCACACTGTAAGAAGGTCAT
287	QQE7F7	208445_s_at	BAZ1B	ACTGCGGAATGTGGCCTCTG	CTTCCTCCGTCCTCCTGCCC
288	NNNE4F4	203360_s_at	MYCBP	AAAATCCAGAAATAGAGCTG	CTTCGCCTAGAACTGGCCGA
289	JJC7D7	205909_at	POLE2	AGGACATCTGACTCCCCTAC	CTCTTTATGTCTGCCCAGTG
290	YYG6H6	210563_x_at	CFLAR	CTTGAAGATGGACAGAAAAG	CTGTGGAGACCCACCTGCTC
291	UC4D4	200071_at	SMNDC1	GGATGTGTGATGTTTATATG	GGAGAACAAAAAGCTGATGT
292	PA9B9	209259_s_at	SMC3	TTGGAAAATACTACCTACTG	GTTTGGGAGATGTATATAGT
293	OOC2D2	203931_s_at	MRPL12	TCCAAGGCATCAACCTCGTC	CAGGCAAAGAAGCTGGTGGA
294	KKE1F1	200678_x_at	GRN	CCTGTCAGAAGGGGGTTGTG	GCAAAAGCCACATTACAAGC
295	JJJE9F9	202735_at	EBP	CCTGCCAGAAGAGTCTAGTC	CTGCTCCCACAGTTTGGAGG
296	BC8D8	201804_x_at	TBCB	TTGGTGTCCGCTATGATGAG	CCACTGGGGAAAAATGATGG
297	LLE2F2	219573_at	LRRC16A	CGGAGTACTGCTAAGTGTAC	CTGTGTCAAATCCGCACAGG
298	XC8D8	201614_s_at	RUVBL1	GCTGCCGTCCCCACTCAGGC	GTGGTCTGCAGCGCTGTCAG

299	EEEE10F10	336_at	TBXA2R	CCCTGAATTTGACCTACTTG	CTGGGGTACAGTTGCTTCCT
300	AAG2H2	202052_s_at	RAI14	TTCAGAAAATACACAACAGC	CCCTTCTGCCCCCGCACAGA
301	RC12D12	212899_at	CDC2L6	TTTCCTGCTTTTGAGTTGAC	CTGACTTCCTTCTTGAAATG
302	TE3F3	202433_at	SLC35B1	TGGCCTCTGTGATCCTCTTC	GCCAATCCCATCAGCCCCAT
303	AAG10H10	201591_s_at	NISCH	TCTGACTTTCTCTTCTACAC	GTCCTTTCCTGAAGTGTCGA
304	OG4H4	202518_at	BCL7B	TGAGGTTCTGACAACAGTAC	CCATCCCCCACAGTACCCCT
305	RRG4H4	219184_x_at	TIMM22	GCTGAGGGGCTGTTCACCAC	CATCCTCGTTCTCCAGGGTC
306	WE1F1	203334_at	DHX8	GAAAGGGACAATTTGTGCAG	CTCCAGGATGGGAAGGTGGA
307	LLLC9D9	204517_at	PPIC	GTCACCCTTTAGTTTGCTTG	AACTTTAGTAAACCACCTGC
308	WA2B2	202396_at	TCERG1	GCATTTGTGGCTTGAACTTG	CCAGATGCAAATACCACAGA
309	NE2F2	218034_at	FIS1	TTTCTGCTCCCCTGAGATTC	GTCCTTCAGCCCCATCATGT
310	VC7D7	209189_at	FOS	CCCAGTGACACTTCAGAGAG	CTGGTAGTTAGTAGCATGTT
311	HHG3H3	212462_at	MYST4	TGTACAGGGTGACAGTAAGG	GCCAAGCAGGAGAGGCGTAA
312	AAG12H12	202329_at	CSK	GGGCATTTTACAAGAAGTAC	GAATCTTATTTTTCCTGTCC
313	JJJG12H12	206571_s_at	MAP4K4	GGAGCTGCACCGAGGGCAAC	CAGGACAGCTGTGTGTGCAG
314	VG6H6	202778_s_at	ZMYM2	ACTGGGTTCTTAACCAGATG	GTTGTGTATGGGTAGCACTA
315	OC9D9	205376_at	INPP4B	TCAACATGCTACAGCTGATG	GCTTTCCCCAAGTACTACAG
316	FFFG8H8	218916_at	ZNF768	GAAGTGACATGCCCTGGAGA	CTTGTGGGAAGTGGGTTGGA
317	IIA8B8	219499_at	SEC61A2	CACCGAGCTAAGTCTGTGTG	CAGCATTAGTACCCGCTGCC
318	JJA12B12	218898_at	FAM57A	CCCATTCCTGTGTGTCCGTC	CTGCCATTTAGCCACAGAAG
319	BBBG1H1	220161_s_at	EPB41L4B	CCCTAGTCTGTTGGTAGAAC	CAGAAATCAATATGTTGTCT

320	RRA6B6	200981_x_at	GNAS	GCATGCACCTTCGTCAGTAC	GAGCTGCTCTAAGAAGGGAA
321	QQC8D8	209191_at	TUBB6	TCGGCCCCTCACAAATGCAG	CCAAGTCATGTAATTAGTCA
322	RC7D7	202776_at	DNTTIP2	GGAAGTACTCAGAGATCATG	GCTGAAAAAGCAGCAAATGC
323	NNNA6B6	203582_s_at	RAB4A	ACAGATGCCCGAATGCTAGC	GAGCCAGAACATTGTGATCA
324	QQC3D3	204977_at	DDX10	AGATCGAGGGTGGATGATAC	CATTTCCTGACCCCGTTTTC
325	OOA10B10	201412_at	LRP10	GCACCGGAATGCCAATTAAC	TAGAGACCCTCCAGCCCCCA
326	RC3D3	203367_at	DUSP14	CACTTTGGGGCCTCATTAAC	CCTTTAGAGACAAGCTTTGC
327	MMMG8H8	201379_s_at	TPD52L2	GGGTTAAAATCGGCCTGTGG	GGTGTGGTGAGAAGGCAGGT
328	AAAG3H3	203973_s_at	CEBPD	TGCCCGCTGCAGTTTCTTGG	GACATAGGAGCGCAAAGAAG
329	EEEE12F12	212770_at	TLE3	GTCTCTTGTGGCCCAAACAG	GTTAGGTAGACTATCGCCTC
330	AAE9F9	203192_at	ABCB6	AACCTCTGAAGACACTAAGC	CTCAGACCATGGAACGGTGA
331	SSE10F10	202180_s_at	MVP	CTGAAATCAACCCTCATCAC	CGATGGCTCCACTCCCATCA
332	PPC6D6	202801_at	PRKACA	TTCAAGGCTAGAGCTGCTGG	GGAGGGGCTGCCTGTTTTAC
333	JJE9F9	209691_s_at	DOK4	GTGGCAGGAGGATGATAAAG	CACGCGGCCCCTCCCAAAGG
334	LLLA2B2	201185_at	HTRA1	ATGCGTAGATAGAAGAAGCC	CCACGGGAGCCAGGATGGGA
335	OA9B9	207700_s_at	NCOA3	ATAGTATACTCTCCTGTTTG	GAGACAGAGGAAGAACCAGG
336	UUG1H1	219460_s_at	TMEM127	TACACCCAGCCCCGAGTGTG	CATCACGGTAAAAGAGCTGA
337	YG10H10	205548_s_at	BTG3	CATTGTGACCGGAATCACTG	GATTAATCCTCACATGTTAG
338	RG10H10	218039_at	NUSAP1	AGCTGGGATAGAAAGGCCAC	CTCTTCACTCTCTATAGAAT
339	LLG4H4	218290_at	PLEKHJ1	CATCCAAAGCCTGAAGCCAG	GTGGGTGTGGGCAGGGGCTG
340	PPA2B2	202328	PKD1	GGGCAAGTAGCAGGACTAGG	CATGTCAGAGGACCCCAGGG

		_s_at			
341	XG5H5	201976 _s_at	MYO10	GGGGGAGAGACGCTGCATTC	CAGAAACGTCTTAACACTTG
342	LLG7H7	212726 _at	PHF2	CTGGATGTTTTTGTCCACTG	GGAGAGGCAGCTTGGTGGAG
343	YC4D4	201000 _at	AARS	GAACACACTTGGGAGCAGTC	CTATGTCTCAGTGCCCCTTA
344	PA8B8	210640 _s_at	GPER	CCCTCTGTGGAGCGCCCGCC	GTCTGCTCCGGGGTGGTTCA
345	SSC9D9	201727 _s_at	ELAVL1	CACTCCTCTCGCAGCTGTAC	CACTCGCCAGCGCGACGGTT
346	MMA7B7	207290 _at	PLXNA2	GCCTGGCCACCCACACTCTG	CATGCCCTCACCCCACTTCT
347	HHA12B12	210074 _at	CTSL2	GATGGATGGTGAGGAGGAAG	GACTTAAGGACAGCATGTCT
348	LLLG4H4	202087 _s_at	CTSL1	TTCATCTTCAGTCTACCAGC	CCCCGCTGTGTCGGATACAC
349	OOG3H3	209435 _s_at	ARHGEF2	GGGGATTTTTCAGTGGAACC	CTTGCCCCCAAATGTCGACC
350	JJJC5D5	203126 _at	IMPA2	ACCCCAGAGGGAGTTGTCAC	GCTACAGTGAGTGGCTGGCC
351	YE10F10	217722 _s_at	NGRN	AATAGGAAGAGGTGTTGAGC	CTGGACTGTGGGAGGAAAGA
352	ZZC9D9	202207 _at	ARL4C	GTGGTCACCAGGGGGACAGG	GAGCCCCCCACCAATGTATC
353	QG7H7	206688 _s_at	CPSF4	ATTTTCTCTTGGGGTACGTG	CCTGACAGTGTTTAAGGTGT
354	NNNC6D6	218193 _s_at	GOLT1B	TGAAATCCATGTTAATGATG	CTTAAGAAACTCTTGAAGGC
355	SSC11D11	202675 _at	SDHB	AAGGCAAGCAGCAGTATCTG	CAGTCCATAGAAGAGCGTGA
356	XE2F2	203266 _s_at	MAP2K4	TGCTGTCAACTTCCCATCTG	GCTCAGCATAGGGTCACTTT
357	PA7B7	201967 _at	RBM6	GTTGGAGCCTCAGGAAGAAC	CAGCAAAAGACAGTCCAACG
358	IIIG5H5	212851 _at	DCUN1D4	AGTGGACAAGAAACCACCAG	CATTGAGCTAACCCAGTACA
359	UA12B12	203640 _at	MBNL2	GGAACTACATTTCACTCTTG	GTTTTCAGGATATAACAGCA
360	UA6B6	201960 _s_at	MYCBP2	TCAAACTTGTGAGGTGTTTG	CATGTGGCCATTACCGTCAT

361	UUC4D4	200636_s_at	PTPRF	GTCCTTATTATCCCAGCTTG	CTGAGGGGCAGGGAGAGCGC
362	NNG11H11	202427_s_at	BRP44	CTTTGTGGGGGCAGCAGGAG	CCTCTCAGCTTTTTCGTATT
363	AAAA12B12	200789_at	ECH1	TGGCCGAGAGCCTCAACTAC	GTGGCGTCCTGGAACATGAG
364	AAAE5F5	218597_s_at	CISD1	ACCACCTCTGTCTGATTCAC	CTTCGCTGGATTCTAAATGT
365	RRA11B11	202550_s_at	VAPB	AACTCTGTTGGGTGAACTGG	TATTGCTGCTGGAGGGCTGT
366	MMMA11B11	209337_at	PSIP1	GGTCATTTGGCACTTCTCAG	CAAGTAGGATACTTCTCATG
367	OOE3F3	208626_s_at	VAT1	AGGACCTGGGCCATTGCAAC	CAAAATGGGGACTTCCTGGG
368	NNNE1F1	222125_s_at	P4HTM	CCCCGCCAGCCGCGATACGG	CGCAGTTCCTATATTCATGT
369	KKG9H9	200078_s_at	ATP6V0B	TCCAGAGTGAAGATGGGTGA	CTAGATGATATGTGTGGGTG
370	YA2B2	200752_s_at	CAPN1	CTTCAGGGACTTGTGTACTG	GTTATGGGGGTGCCAGAGGC
371	WE9F9	217874_at	SUCLG1	TCAGTATGTCTCCTGCACAG	CTGGGAACCACGATCTACAA
372	HHC4D4	212723_at	JMJD6	ACCCATTCACTTAGCGTTTG	CTCCAGTAGCTTTCCCTCTG
373	ZZC5D5	212811_x_at	SLC1A4	GAAGGGGAAGATCTGAGAGC	GTGCTGTTTGTGGCTGTTGA
374	MME4F4	212140_at	PDS5A	GGCCCACCCCAATTTTGTAA	CATGATGCAAGTGTCTGGCA
375	AAE11F11	219222_at	RBKS	GCTTACTATCCAAATCTGTC	CTTGGAAGACATGCTCAACA
376	TTE12F12	217950_at	NOSIP	CTGGGGCTGTGGTCACCCTC	GAATGCGTGGAGAAGCTGAT
377	OOC10D10	201432_at	CAT	TTAATACAGCAGTGTCATCA	GAAGATAACTTGAGCACCGT
378	NNNC1D1	218845_at	DUSP22	TTATCCCCACTGCTGTGGAG	GTTTCTGTACCTCGCTTGGA
379	YG2H2	201314_at	STK25	GCCTTGTGGTGTTGGATCAG	GTACTGTGTCTGCTCATAAG
380	MMG9H9	202414_at	ERCC5	AAACCAGTGCTTCAGATTCG	CAGAACTCAGTGAAGGAAGC
381	PE5F5	203659	TRIM13	TTCTTTGCCTCAAGACACTG	GCACATTCATTAGCAAGATT

		_s_at			
382	FFFA2B2	210241 _s_at	TP53TG1	CATGATGCTGGGGAGCTTGG	CGCCTGACCCAGGATCTAGA
383	RRE7F7	204761 _at	USP6NL	TAGTAGAAAACCCGACATTG	ATGTTTCTTCCTGTTGCAAG
384	XA9B9	208946 _s_at	BECN1	ATCTATAGTTGCCAGCCCTG	GTCAGTTTTGATTCTTAACC
385	CCCE2F2	204017 _at	KDELR3	CCTTCAGGCCAGAAGCAAAC	CAAATTTACCAGGTTTGGCT
386	BBBA1B1	204256 _at	ELOVL6	GATGGCAAGGGCTTTTTCAG	CATCTCGTTTATGTGTGGAA
387	RRC11D11	221848 _at	ZGPAT	ACTGCTGAGTGGAGACAGAG	CTGCGGGGTCCCATCTGGAC
388	JJG5H5	205161 _s_at	PEX11A	TGATGTGGGCAGAGATGAGG	CCAAGAACGGAGAAGGGAGG
389	VC2D2	202894 _at	EPHB4	GGTGGAACCCAGAAACGGAC	GCCGGTGCTTGGAGGGGTTC
390	YG9H9	209710 _at	GATA2	CGCTGCAGGGAGCACCACGG	CCAGAAGTAACTTATTTTGT
391	TTC9D9	215980 _s_at	IGHMBP2	AGAGCCTCCCGGCCTTCTCC	GGTGTCCTGTACCAACTCTT
392	RE9F9	203221 _at	TLE1	TTGCCCAAGTGTGAGATTAC	CTTTCTGTTCCTTGCAGTTC
393	IIC6D6	202950 _at	CRYZ	AGTTTCCAAGGGTTTTCAAG	CCTACTTACCTTTATAAAGG
394	OG10H10	40562_ at	GNA11	CTCTCCCTCCGTACACTTCG	CGCACCTTCTCACCTTTTGT
395	RE11F11	203302 _at	DCK	TCAAAGATGATAATTTAGTG	GATTAACCAGTCCAGACGCA
396	NNG12H12	202545 _at	PRKCD	TTCTTCAAGACCATAAACTG	GACTCTGCTGGAAAAGCGGA
397	PPE11F11	203884 _s_at	RAB11FIP2	GGGCCTGTTAGTCTTCGAAG	CTTCCAGATGGTTTGTGTTT
398	QQE10F10	212973 _at	RPIA	GGGGTTTCTTCATATTCCTG	CTGTTGGAAGCAGTTGACCA
399	HHE6F6	202452 _at	ZER1	GGCAGGACGGCAGGGGTGAG	CAGCTTTGGGAGAGACACCT
400	LG6H6	221046 _s_at	GTPBP8	TGACCTTTTCTGGAATCCAC	CTGTTGAGATGCTTTATAGC
401	OA8B8	201366 _at	ANXA7	AGCTCTGCCTTCCGGAATCC	CTCTAAGTCTGCTTGATAGA

402	WG12H12	202954_at	UBE2C	CCCAGGCTGCCCAGCCTGTC	CTTGTGTCGTCTTTTTAATT
403	SSA10B10	201984_s_at	EGFR	ATCTGTGTGTGCCCTGTAAC	CTGACTGGTTAACAGCAGTC
404	XA2B2	201161_s_at	CSDA	GGGACAGACCTTTGACCGTC	GCTCACGGGTCTTACCCCAT
405	LLA9B9	206173_x_at	GABPB1	CTGTGGATGGTGCCATTCAG	CAAGTAGTTAGTTCAGGGGG
406	LA2B2	207038_at	SLC16A6	GACACAAGGAGGCAGAGGAG	CTAACCCCTCTACTCCACTT
407	AAE10F10	202179_at	BLMH	AGACCTAATGCTCCTTGTTC	CTAGAGTAGAGTGGAGGGAG
408	IIIA1B1	209567_at	RRS1	TGCCTTCATTGAGTTTAAAG	GGACAGGATTGCCCTTCCGT
409	NNNE10F10	209109_s_at	TSPAN6	CGCCTACTGCCTCTCTCGTG	CCATAACAAATAACCAGTAT
410	TTA12B12	209260_at	SFN	GCATGTCTGCTGGGTGTGAC	CATGTTTCCTCTCAATAAAG
411	SSG3H3	201729_s_at	KIAA0100	ATGATTTGGCGATTCGAGTG	GCTGCAGTACAGGATCTGAC
412	HHE10F10	209166_s_at	MAN2B1	GCGCCCCCGTTACCTTGAAC	TTGAGGGACCTGTTCTCCAC
413	LC6D6	201794_s_at	SMG7	GACAAGCTAACCAGGTTTAC	CATCTCACTCCCAGTAATAC
414	LLA4B4	208936_x_at	LGALS8	AATCACCAATCAAGGCCTCC	GTTCTTCTAAAGATTAGTCC
415	QQA2B2	204788_s_at	PPOX	CAATTCCTGACTGCTCACAG	GTTGCCCCTGACTCTGGCTG
416	OOE2F2	204106_at	TESK1	GTCTCAGGCCTCCAACTTTG	GCCTTCAGGACACCCTGTAA
417	MG11H11	201849_at	BNIP3	CAGTTTTCTGCTGAAGGCAC	CTACTCAGTATCTTTTCCTC
418	TE7F7	203685_at	BCL2	TTTCATTAAGTTTTTCCCTC	CAAGGTAGAATTTGCAAGAG
419	HHHE11F11	205205_at	RELB	GATGTCTAGCACCCCCATCC	CCTTGGCCCTTCCTCATGCT
420	XA10B10	203575_at	CSNK2A2	GGGTATGCAGAATGTTGTTG	GTTACTGTTGCTCCCCGAGC
421	MMG2H2	202022_at	ALDOC	GCCAGGGCCAAATAGCTATG	CAGAGCAGAGATGCCTTCAC
422	OOC12D12	201817	UBE3C	GGGGGGAGGGGATCTAAATC	CTCATTTATCTCTTCTATGT

		_at			
423	NNC9D9	201236_s_at	BTG2	GTGTTCTTGCATCTTGTCTG	CAAACAGGTCCCTGCCTTTT
424	RG7H7	210022_at	PCGF1	CTGATCACATGACAATGAAG	CAGATATGGCTCTCCCGCTG
425	YYC12D12	201565_s_at	ID2	CTGTGGACGACCCGATGAGC	CTGCTATACAACATGAACGA
426	NE12F12	201186_at	LRPAP1	AGGACCTCGATGTCCAGCTG	CTGTCAGGTCTGATAGTCCT
427	SC7D7	204324_s_at	GOLIM4	AAGGCCGAGAGGAACACTAC	GAGGAGGAAGAAGAGGAGGA
428	KKA3B3	213370_s_at	SFMBT1	GTATCAGCTTGCTCTCTTTG	CACTTTCGGGGAAGGAGGAC
429	VG1H1	201270_x_at	NUDCD3	AGAGTGAGGTGTCCAGCCTG	CAAAGCTATTCCAGCTCCTT
430	NC10D10	204217_s_at	RTN2	CTAATTACCTGAGCGACCAG	GACTACATTTCCCAAGAGGC
431	RRC8D8	201707_at	PEX19	AGATCATCTTTGAGTAGCAC	TGTTTTGGGGCCCTCGGTCT
432	OOE12F12	201963_at	ACSL1	GAGAGTACATGTATTATATA	CAAGCACAACAGGGCTTGCA
433	UA8B8	203038_at	PTPRK	TTTTTCAGCCTGTGGCCCAG	CACTGGTCAAGAAAACAAGA
434	RA5B5	205202_at	PCMT1	GATGTCCTGTAAACACTCAG	CTGTTCAGATTGGACATAAC
435	MME2F2	201924_at	AFF1	GCTCTCAATGGGAAGATGTG	CAACACAAATTAAGGGGAAC
436	HHA5B5	213772_s_at	GGA2	CTTGTTGCACTGTTCCCAGG	CGAGTGGCTGCCATGAGACC
437	YYC6D6	203773_x_at	BLVRA	ACTGGCTGCTGAAAAGAAAC	GCATCCTGCACTGCCTGGGG
438	PPA6B6	202797_at	SACM1L	CAAAGACCAAATCTGAACTG	CTAATGTGGCTGCTTTGTAG
439	PPE3F3	202431_s_at	MYC	CCACAGCATACATCCTGTCC	GTCCAAGCAGAGGAGCAAAA
440	MMMG6H6	209367_at	STXBP2	GCTCATCGTGTATGTCATGG	GCGGTGTGGCCATGTCAGAG
441	RRE11F11	201361_at	TMEM109	GAGGTGGATGTCCTTCTCTG	CCAGGCTTGGCACATGATGT
442	MMME12F12	210788_s_at	DHRS7	TACATGCCAACCTGGGCCTG	GTGGATAACCAACAAGATGG

443	AAG8H8	203119_at	CCDC86	CTTTCCCAAACCAGTCTCTG	CAGAAGCCCCAGAGAATCTA
444	SSC8D8	1007_s_at	DDR1	GCTTCTTCCTCCTCCATCAC	CTGAAACACTGGACCTGGGG
445	OG7H7	203304_at	BAMBI	GGCACGGGAAGCTGGAATTC	GTATGACGGAGTCTTATCTG
446	DDC2D2	201007_at	HADHB	TTTCAATAATCAGTTTACTG	CTCTTTCAGGGATTTCTAAG
447	RRC7D7	201710_at	MYBL2	CCCATTCTCATGTTTACAGG	GGTTGTGGGGGCAGAGGGGG
448	NNE2F2	204729_s_at	STX1A	CATGTTTGGGATGGTGGCTC	CTGTTGTCTTGCGCTCTGGG
449	IIE8F8	217398_x_at	GAPDH	CTGCCACCCAGAAGACTGTG	GATGGCCCCTCCGGGAAACT
450	LA1B1	209899_s_at	PUF60	TAGCCTCTGAGACTCATAAG	GCCATCCAGGCCCTCAATGG
451	HHHC7D7	212660_at	PHF15	GCAATAGAATGTATGGTCAC	CTGGGTGTGGCCAGTGCCCG
452	CCCC5D5	206723_s_at	LPAR2	GCAGCAGAGACTGAGGGGTG	CAGAGTGTGAGCTGGGAAAG
453	TG2H2	202423_at	MYST3	ATCCCCTGTGAATCAGAGTG	CACAAGCACCTCTCCTGTGA
454	RE6F6	203570_at	LOXL1	ACCAACAACGTGGTGAGATG	CAACATTCACTACACAGGTC
455	UUE4F4	202738_s_at	PHKB	ACATCCTTGGCGGGGTTATG	GACCTCTTGCATGTCATAGC
456	UUA4B4	221610_s_at	STAP2	TTGGCCAGTCATCCTGAAGC	CAAAGAAGTTGCCAAAGCCT
457	SSC4D4	204549_at	IKBKE	TCACCACTGCCAGCCTCAGG	CAACATAGAGAGCCTCCTGT
458	VE7F7	203596_s_at	IFIT5	GACTTAATTGGCATGGGGTG	CAGTCCAGGCATCATGATTT
459	UUE11F11	218255_s_at	FBRS	ACCTCTTAATGGCTCAGTCC	CCTTCACCCCATTTCCAAGT
460	PC2D2	201528_at	RPA1	TCCCCTAAGGAAATCCGAGC	GGCTACAAAGCGTTTCTTTA
461	IIG9H9	201738_at	EIF1B	CTGCCTTGTGAAATGATTCC	CTGCAGTAAACGGACTTTTC
462	TG3H3	201146_at	NFE2L2	CCTGCAGCAAACAAGAGATG	GCAATGTTTTCCTTGTTCCC
463	RRG6H6	221081	DENND2D	ATTGATTTCTCAGGACTTTG	GAGGGCTCTGACACCATGCT

		_s_at			
464	TTC7D7	218529 _at	CD320	GCCCTGTGCTTAAGACACTC	CTGCTGCCCCGTCTGAGGGT
465	KKKC10D10	218086 _at	NPDC1	CCTCGGATGAGGAGAATGAG	GACGGAGACTTCACGGTGTA
466	HHHG8H8	219051 _x_at	METRN	GACGCTGAGCTGCTCCTGGC	CGCATGCACCAGCGACTTCG
467	JJJA7B7	201014 _s_at	PAICS	AACATCTGCGCATAAAGGAC	CAGATGAAACTCTGAGGATT
468	MMC7D7	200757 _s_at	CALU	AGAGCCTCACACCTCACTAG	GTGCAGAGAGCCCAGGCCTT
469	CCCE4F4	201212 _at	LGMN	TCCAGGACCTTCTTCACAAG	ATGACTTGCTCGCTGTTACC
470	XC3D3	212850 _s_at	LRP4	CTGGCGAGCCCTTAGCCTTG	CTGTAGAGACTTCCGTCACC
471	WE12F12	201243 _s_at	ATP1B1	AAAGCTGTGTCTGAGATCTG	GATCTGCCCATCACTTTGGC
472	PPE4F4	202696 _at	OXSR1	CCCCTTGTCCCTGGAGTAGG	GACTAACTATAGCACAAAGT
473	IIA12B12	222217 _s_at	SLC27A3	GGCCGTTGCAGGTGTACTGG	GCTGTCAGGGATCTTTTCTA
474	NNA5B5	212795 _at	KIAA1033	CTGGAAACGAATTTAAATGG	TGTCAAACTGCAGAGCAACA
475	MMMA1B1	212815 _at	ASCC3	CTGCCGCATAAACTATAAAT	CTGTAAGGTGGTACACAGCG
476	JJC1D1	203512 _at	TRAPPC3	AAGCCACCCAGGTCTCATTC	CTCCCTGCTGTTGGAGGCAA
477	TTC10D10	218948 _at	QRSL1	ATGCGCATGGCAAGAACTTG	CCTTACCCCAGATTCTCTAT
478	XE10F10	209224 _s_at	NDUFA2	CCCTTTGAACAACTTCAGTG	CTGATCAGGTAACCAGAGCC
479	JJA7B7	205811 _at	POLG2	TAGGAAGAGGCCCCACATTG	GAACTAAGACAGGTTTGTCA
480	JJJE11F11	204608 _at	ASL	CTCAAGGGACTTCCCAGCAC	CTACAACAAAGACTTACAGG
481	LE6F6	209161 _at	PRPF4	TACAGTGAAGAAGACTTCAC	CTCTTCCTATTGAGTTTGCT
482	JJJC12D12	205120 _s_at	SGCB	CTCTTCAAGGTGCAAGTAAC	CAGCCAGAACATGGGCTGCC
483	ZZC2D2	208634 _s_at	MACF1	ACCAGTAACTCTTGTGTTCA	CCAGGACCCAGACCCTTGGC

484	YG4H4	202160_at	CREBBP	TTCTTGAATTCATGTACATG	GTATTAACACTTAGTGTTCG
485	AAE7F7	201807_at	VPS26A	CAAAAGGGTCCATGTACCAC	CATGTGCTGGAGCATCTGTT
486	ME4F4	205406_s_at	SPA17	GCCTTCCGGGGACACATAGC	CAGAGAGGAGGCAAAGAAAA
487	AAC2D2	214404_x_at	SPDEF	CCCCTGAGTTGGGCAGCCAG	GAGTGCCCCCGGGAATGGAT
488	HHA6B6	57703_at	SENP5	ATGCCCCGAGTGCGGAAGAG	GATTTACAAGGAGCTATGTG
489	YA3B3	213720_s_at	SMARCA4	GATGCATGTGCGTCACCGTC	CACTCCTCCTACTGTATTTT
490	QQA4B4	212047_s_at	RNF167	AGCTTCTCCCTTACCCACAC	CTATCCTTTTGAGGGGCTTT
491	LLLG11H11	202083_s_at	SEC14L1	CACCCAGCGGCGACATTGTA	CAGACTCCTCTCACCTCTAG
492	PPG11H11	203919_at	TCEA2	CCGTTGACACAGCTTCTCTG	GAGACCCTAGAAGGCGGCAT
493	QC6D6	200666_s_at	DNAJB1	CTCTGTATAGGGCCATAATG	GAATTCTGAAGAAATCTTGG
494	AAG5H5	203409_at	DDB2	GTTAAAGGGCCAAAAGTATC	CAAGGTTAGGGTTGGAGCAG
495	PPA4B4	202623_at	EAPP	GGAAGATGCTGCCGAGAAGG	CAGAGACAGATGTGGAAGAA
496	LLE10F10	212955_s_at	POLR2I	CACGAAGTGGACGAACTGAC	CCAGATTATCGCCGACGTGT
497	PPE1F1	202241_at	TRIB1	CTAGAAACACTAGGTTCTTC	CTGTACATACGTGTATATAT
498	QG6H6	203054_s_at	TCTA	CCCACCCACTAATACTACTG	CACAGAGTCAGGATCTCACA
499	HHHA10B10	204514_at	DPH2	GTTCAGACAGCCACATGAGG	GGACAGTGCAGCTACAGGAT
500	KKKC3D3	208872_s_at	REEP5	AATTAAAGCTATAGAGAGTC	CCAACAAAGAAGATGATACC
501	NNG8H8	201125_s_at	ITGB5	TGAGTCCTGAGACTTTTCCG	CGTGATGGCTATGCCTTGCA
502	JJJE7F7	201127_s_at	ACLY	GGGGTACAGGCACCGAAGAC	CAACATCCACAGGCTAACAC
503	OG9H9	201558_at	RAE1	GGGTTGAGGTTATTGTAGAC	GTTAGATTGCGGGCACCGCC
504	KKE8F8	201664	SMC4	GGTTTACCAGGATGTAGTCC	CACTGTTGAGGAGCATCTAT

		_at			
505	SA1B1	203026_at	ZBTB5	TGCCTCTCCACTGCTAGATG	GAACCTGGAATCTCTCATCT
506	KKA6B6	202025_x_at	ACAA1	AATGAGCTGAAGCGCCGTGG	GAAGAGGGCATACGGAGTGG
507	MMG3H3	204978_at	SFRS16	CAAGATCCGCATGAAGGAGC	GGGAACGCCGAGAGAAGGAG
508	AAG1H1	202732_at	PKIG	ACCTCTGCCCTGTCCACCAG	GATAAGTGACACCTAGGACC
509	LLA12B12	205667_at	WRN	AAATCAGCCTTCCGCAATTC	ATGTAGTTTCTGGGTCTTCT
510	NG1H1	202038_at	UBE4A	CATGCCAGAGGCTGATGCTG	CACTGTTGATGTCATGTGAG
511	HHA4B4	89476_r_at	NPEPL1	AGGACCCTCTGCTGAACCTG	GTGTCCCCACTGGGCTGTGA
512	KKKG3H3	208950_s_at	ALDH7A1	CCTAAAGGATCAGACTGTGG	CATTGTAAATGTCAACATTC
513	RRG3H3	218788_s_at	SMYD3	ATGCGACGCCAACATCAGAG	CATCCTAAGGGAACGCAGTC
514	JJE8F8	209045_at	XPNPEP1	AGATGCCCCGACTTCTTTGG	CCAGTGATGGGGAATCAGTG
515	LLG2H2	219459_at	POLR3B	CCTGGCTTTTGTCGTGGTGG	CTGGCTCGGATAAATTTTCC
516	QQG9H9	206050_s_at	RNH1	CTGGCTCTGTGCTGCGGGTG	CTCTGGTTGGCCGACTGCGA
517	LLG10H10	218064_s_at	AKAP8L	GCAAGAAGCTGGAGCGCTAC	CTGAAGGGCGAGAACCCTTT
518	HHHE7F7	202185_at	PLOD3	TGAATATGTCACCTTGCTCC	CAAGACACGGCCCTCTCAGG
519	WWE4F4	201145_at	HAX1	CTCAGGGGCTTGGATATGTG	GAATAGTGAACTGGGGCCAT
520	PPG6H6	202812_at	GAA	AATAAGATTGTAAGGTTTGC	CCTCCTCACCTGTTGCCGGC
521	VC9D9	202125_s_at	TRAK2	ATGCATGCAGACCTGTACTC	CACATGCAACCCAACAGCAG
522	WA3B3	202927_at	PIN1	CCGAATTGTTTCTAGTTAGG	CCACGCTCCTCTGTTCAGTC
523	MMG12H12	203306_s_at	SLC35A1	ACTCGGACAATTTCTGGGTG	GTGACTGAGTACCCCTTTAG
524	PG11H11	203727_at	SKIV2L	ACATCGTATTTGCGGCCAGC	CTCTACACCCAGTGAATGCC

525	KKC11D11	202829_s_at	VAMP7	ATGGTACCTGTTCTTCTATC	CAAACCTTTCAATTCATGCT
526	KKC8D8	201513_at	TSN	ACTTAAGTGGCTAAAGAGAT	GAGACAAACATGCAGGTCGC
527	EEA10B10	220964_s_at	RAB1B	CCCCTCTGGTGTCATGTCAG	GCATTTTGCAAGGAAAAGCC
528	LLE5F5	203897_at	LYRM1	GGTAGAGTCAGGTGAGAGTC	CCTTGGTGAGTCATTTGTAC
529	AAA9B9	203573_s_at	RABGGTA	GCCCTGCCCCCTACCCTTGC	CCTTTAACTTATTGGGACTG
530	TTE1F1	204089_x_at	MAP3K4	CATTACTACTGTACACGGAC	CATCGCCTCTGTCTCCTCCG
531	MMMG2H2	219076_s_at	PXMP2	TCCGGGTGCTCTTCGCCAAC	CTGGCAGCTCTGTTCTGGTA
532	MMC5D5	212648_at	DHX29	ACGTCTTCTTTCTATTGATG	GCTGGATCTATTTTCAGGCC
533	ZZA9B9	212614_at	ARID5B	GTTGGCTGTTAGTGTATTTG	ATATTCTGCCTGTCTCCTCA
534	FFFC2D2	210986_s_at	TPM1	CAGCTCATGACAATCTGTAG	GATAACAATCAGTGTGGATT
535	OOG1H1	203616_at	POLB	GGAAATACCGGGAACCCAAG	GACCGGAGCGAATGAGGCCT
536	AAA11B11	202491_s_at	IKBKAP	TTCCACTCATTCCTGTTGTC	CTACCACCCCTTGCTCTTTG
537	QQC9D9	212500_at	ADO	GTGTGCATAAACTGTTAGTC	GTGACTGACTTGGTGTGTTG
538	EEEC11D11	202720_at	TES	TACTTCCAAGCCTGTCCATG	GATATATCAAATGTCTTCAC
539	HHG10H10	214259_s_at	AKR7A2	TGAAAGGTGGGGGGTGAGTC	CCACTTGAGCGCTTCCTGTT
540	TG11H11	201594_s_at	PPP4R1	TCTTCACATACTGTACATAC	CTGTGACCACTCTTGGGAGT
541	PA6B6	217933_s_at	LAP3	ACCAACAAAGATGAAGTTCC	CTATCTACGGAAAGGCATGA
542	UG3H3	202868_s_at	POP4	AGCCAATTCCATTTATAGAC	CACCTCCAGCCAGTGACGCT
543	IIA4B4	202949_s_at	FHL2	CCAGGCAATCTTGCCTTCTG	GTTTCTTCCAGCCACATTGA
544	UC9D9	209341_s_at	IKBKB	TTTGTTGGAGAAGAAAGTTG	GAGTAGGAGACTTTCACAAG
545	ZZG4H4	201811	SH3BP5	GATTTATTCTAAGAGAAGTG	CATGTGAAGAATGGTTGCCA

		_x_at			
546	YYC9D9	204143 _s_at	ENOSF1	ACCGATCAAGATGAGTTCAG	CTAGAAGTCATACCACCCTC
547	UUE7F7	217931 _at	CNPY3	AAACTCACCATCCCTCAGTC	CTCCCCAACAGGGTACTAGG
548	MG10H10	209100 _at	IFRD2	GGAGACTTTCTATGCCCTTG	GTCCGTATTTTTAACAGAAG
549	ZA3B3	201466 _s_at	JUN	TGCGATGTTTCAGGAGGCTG	GAGGAAGGGGGGTTGCAGTG
550	VE5F5	202830 _s_at	SLC37A4	GGCCATCATTCTCACTGTAC	CACTAGGCGCAGTTGGATAT
551	ZZC8D8	218910 _at	ANO10	TGAGTGAGCCACCAGCTCTC	CACGTTCCCCTCATAGCAGT
552	SSA12B12	203530 _s_at	STX4	GACAGTTCTTCTGGGGTTGG	CAGCTGCTCATTCATGATGG
553	LLE7F7	203562 _at	FEZ1	GCGGGGTCCTTTGCCGTTGG	CTTCTAGTGCTAGTAATCAT
554	NE11F11	209364 _at	BAD	GGCGGAAGTACTTCCCTCAG	GCCTATGCAAAAAGAGGATC
555	PPG9H9	203405 _at	PSMG1	TTGTCCATTGCTAGAACAAC	CGAATATAGTACACGACCTT
556	JJE2F2	203885 _at	RAB21	GTTCAGTGGTATGAGCAGAG	GAAGAGATCCCAGATAGTAG
557	NNE6F6	219170 _at	FSD1	AAGCGAGGCAGTGCTACCAG	CAGCTCCAACACCAGCCTCA
558	UE8F8	207939 _x_at	RNPS1	CGTTCATGGTGGTCTTTCAG	GTTATCTTGGCAACATGTAC
559	MMMG5H5	221492 _s_at	ATG3	GTGATGAAGAAAATCATTGA	GACTGTTGCAGAAGGAGGGG
560	HHC3D3	210719 _s_at	HMG20B	GACCCTGGTGGGGGTGGCTC	CTTCTCACTGCTGGATCCGG
561	HHE8F8	204605 _at	CGRRF1	AGAATGGGACTGTGAACTGG	GTACTCTTACCATGCAGACA
562	PPC2D2	218450 _at	HEBP1	ATAGACCAGAAAAATCCTGG	CAGCTTTTCTCCAGGCATCT
563	ZG2H2	212049 _at	WIPF2	TCTCAGTCCCTGGCCATGTG	GTCAAGGTGGCTTTCTGTTA
564	PPC11D11	203848 _at	AKAP8	GCCCTGCTGTGTCAGTTTCC	CTGTGGCCTTTTGAACTGTA
565	NNA2B2	204587 _at	SLC25A14	ACTTGGGCTAGAGCAGAAGG	CATAGGCCAGGGTGGTTATT

566	BBBE8F8	204418_x_at	GSTM2	TCTCCCGATTTGAGGGCTTG	GAGAAGATCTCTGCCTACAT
567	YC1D1	203047_at	STK10	TTCTCTTCAGGAAGAAAAAG	CATCAGGGGGAAATGGAATG
568	IIC2D2	205451_at	FOXO4	GTGTCAGCGCCTGGCCTACC	CAGATTGTATCATGTGCTAG
569	PE11F11	203346_s_at	MTF2	ACGTCGGGTGACACTTGATG	GAAAGGTGCAGTATCTTGTG
570	OOE6F6	218571_s_at	CHMP4A	GGCTCCCTTCTCTTTGATAG	CAGTTATAATGCCCTTGTTC
571	RG9H9	203241_at	UVRAG	GGTGTCTGGTAGGCAAACTG	CAAGGCAGTTGAGATAGTTG
572	OOG11H11	201695_s_at	NP	GATGCCCAGGATTTGACTCG	GGCCTTAGAACTTTGCATAG
573	RE8F8	203764_at	DLGAP5	TTTCCTTCATATTATCAATG	CTTATATATTCCTTAGACTA
574	NNG10H10	201631_s_at	IER3	CTTTGTGGGACTGGTGGAAG	CAGGACACCTGGAACTGCGG
575	SSG5H5	214221_at	ALMS1	GGTGATTAAAATTCCTAATG	GTTTGGGAGCAATACTTTCT
576	JJG12H12	219742_at	PRR7	GCTTGGCGTCTGCCGGTCTC	CATCCCCTTGTTCGGGAGGA
577	LE12F12	202016_at	MEST	TGATTCCTTTATGATGACTG	CTTAACTCCCCACTGCCTGT
578	WA11B11	202108_at	PEPD	GCTTCGGCATTTGATCAGAC	CAAACAGTGCTGTTTCCCGG
579	MMA8B8	201074_at	SMARCC1	GGAGTCCGAGAAGGAAAATG	GAATTCTGGTTCATACTGTG
580	PE6F6	202780_at	OXCT1	CCACATGGTTAAATGCATAC	CTTCCCAGTACTGGGGGGAA
581	HHHG11H11	209253_at	SORBS3	CTAGCCTGGCTCAAATATTC	CCCAGGGAGACTGCTGTGTG
582	NE6F6	203256_at	CDH3	TACAGTGGACTTTCTCTCTG	GAATGGAACCTTCTTAGGCC
583	PC8D8	208398_s_at	TBPL1	AGCAGAGCTGTCACAGTGTG	CACTACCTTAGATTGTTTTA
584	OOE10F10	201519_at	TOMM70A	TCTCCCTTCTTTCATCTTGG	GGTTGGGTAGAGAAACACAA
585	LA10B10	217745_s_at	NAT13	ACTATGTTAGTTGCATTTAG	GTTTTAAAGCAAAGAATCTG
586	ZA11B11	210811	DDX49	AGGAGATCAACAAACGGAAG	CAGCTGATCCTGGAGGGGAA

		_s_at			
587	NNC11D11	201887 _at	IL13RA1	GGTCTTGGGAGCTCTTGGAG	GTGTCTGTATCAGTGGATTT
588	PPG3H3	202447 _at	DECR1	ACCAAGGAGCAGTGGGACAC	CATAGAAGAACTCATCAGGA
589	SC12D12	202749 _at	WRB	GAAATGTTTAGGGACATCTC	CATGCTGTCACTTGTGATTT
590	IIE6F6	204285 _s_at	PMAIP1	CCGCTGGCCTACTGTGAAGG	GAGATGACCTGTGATTAGAC
591	KKA10B10	201036 _s_at	HADH	GAATGGGTCAGCATATCTCT	GTTTGCATGGTTTGCAGGAG
592	NNE3F3	207877 _s_at	NVL	CGGCAGAGAATCCCCCACAC	GCTCTGAAGGACCCACTTTC
593	RRG7H7	203806 _s_at	FANCA	GGAACCCACAGACCTCACAC	CTGGGGGACAGAGGCAGATA
594	RRG12H12	201819 _at	SCARB1	CACTGCATCGGGTTGTCTGG	CGCCCTTTTCCTCCAGCCTA
595	OG12H12	201709 _s_at	NIPSNAP1	CTGTTCCCTCACCCTGTATC	CTGTCTCCCCTAATTGACAT
596	OOC7D7	221741 _s_at	YTHDF1	TGAGTTGAAGCATGAAAATG	GTGCCCATGCCTGACGCTCC
597	KKE10F10	202916 _s_at	FAM20B	CAATTCCTCAAGTCTGGGTG	GTGACAAGGTAGGGGCTAGG
598	SG4H4	202148 _s_at	PYCR1	GGTTTCCAGCCCCCAGTGTC	CTGACTTCTGTCTGCCACAT
599	LC1D1	218316 _at	TIMM9	CAGTAGCCACCATGTTCAAC	CATCTGTCATGACTGTTTGG
600	QQC10D10	212894 _at	SUPV3L1	CCAGCCCCGATGCAGGAGAG	CTGTCCCTTGCTTCCAGATT
601	QQA12B12	215903 _s_at	MAST2	GCCAAGAACCAGGGGGCCAT	CAAAAGCATCGGGATTTGGC
602	PPG8H8	203285 _s_at	HS2ST1	TGCAGTGGCTGAACAAAGAG	CATGGCTTGAGAATCAAAGG
603	SE4F4	203594 _at	RTCD1	AAACAGGACCAGTTACACTC	CATACGCAAACCGCGATACA
604	UUA2B2	219384 _s_at	ADAT1	TACTACCTAGAGAAAGCCAG	CAAAGAATGAAGGCAACAAA
605	SSE9F9	201825 _s_at	SCCPDH	ATTGATGCTGCCTCATTCAC	GCTGACATTCTTTGGTCAAG
606	RC5D5	204168 _at	MGST2	CCTAGGTGCCCTGGGAATTG	CAAACAGCTTTCTGGATGAA

607	AAAA6B6	221227_x_at	COQ3	AGAAACAGAAGAGCTCCAAG	CTAATGCCTGCACCAATCCA
608	UUC2D2	219390_at	FKBP14	TAGGACTTAAGCTGATGAAG	CTTGGCTCCTAGTGATTGGT
609	YG8H8	202184_s_at	NUP133	AGTTCTTGTCCTGGTTCTAG	CTGCTCACATGTACAAATCA
610	VE2F2	202521_at	CTCF	ATATGTAATGGGGTTGAAAG	CTGGGGAGGAGGATCTACTG
611	MMMC2D2	209215_at	MFSD10	TCAGTGACTCCGAGCTGCAG	CACTCCAAGGCTGTCAGGGC
612	OOE8F8	201174_s_at	TERF2IP	CCTTCTCAGTCAAGTCTGCC	GGATGTCTTTCTTTACCTAC
613	PG1H1	217758_s_at	TM9SF3	ATCTGTTCAGGTTGGTGTAC	CGTGTAAAGTGGGGATGGGG
614	LLC7D7	212453_at	KIAA1279	CCTTGTAAGAAAAAATGCTG	GGTAATGTACCTGGTAACAA
615	NNNE9F9	218435_at	DNAJC15	CAAGGCTAAGATTAGAACAG	CTCATAGGAGAGTCATGATT
616	TTC11D11	209911_x_at	HIST1H2BD	CCACCCAAATCCAACTCATC	CTGGTTTGCTGCACACTGGT
617	BBBE10F10	212115_at	HN1L	GGGAGAAGAAGAGTTCCTGC	GCATGCAAGCCCTGCTGTGT
618	KKA7B7	217995_at	SQRDL	GCTAAGGGGTTACTGGGGAG	GACCAGCGTTTCTGCGCAAG
619	LLLC5D5	210058_at	MAPK13	CCTTCCTTGGCTCTTTTTAG	CTTGTGGCGGCAGTGGGCAG
620	IIC5D5	218642_s_at	CHCHD7	TTGCAGGATGAGTTGGGCAG	GGAAAAGGGTCAGGGTTCAT
621	ZC5D5	204000_at	GNB5	GCCCAGCCCTTCTTCTAGTG	GTAGCTCTGGCTTTGCAGGC
622	MMA4B4	208249_s_at	TGDS	TGATTCGGACAACCATGAGG	GGTAGTGGTGCTAGGGAGAA
623	FFFC8D8	218068_s_at	ZNF672	AGGCCAAAACCATGTGGGTG	CACAAAGCCAGGCACTGCCA
624	AAAC10D10	217901_at	DSG2	CAAAGGATTTATATAGTGTG	CTCCCACTAACTGTACAGAT
625	YYA6B6	213419_at	APBB2	GAACTAACGCTGCGTCCTTG	GAATGAATGATGCGTGAGTT
626	MC2D2	202683_s_at	RNMT	ATTCCCTTCCAGTTAACTAC	CTCTCCAAGGGAAACCACTA
627	PPA10B10	203456	PRAF2	TGCCCCTCACCCCAATGTTC	CACACCATCGACAACCAAGG

		_at			
628	PG5H5	201266 _at	TXNRD1	TCACGTCCTCATCTCATTTG	GCTGTGTAAAGAAATGGGAA
629	SSG1H1	202261 _at	VPS72	GAAGTACATTACTGCCCATG	GACTGCCGCCCACTGCCTCA
630	QQE8F8	209460 _at	ABAT	CAGCAGAAGCTGGTAAAAAC	ATGGGGAGCCCGGAGGACAG
631	RC9D9	213390 _at	ZC3H4	TGTGGATGAAATAGAAGCTG	GAGCCCTCCTCTTGGAATAT
632	HHHG4H4	205036 _at	LSM6	ATCAGTACACAGAAGAGACG	GATGTGAAGACACCAAGAGA
633	JJE4F4	204937 _s_at	ZNF274	GCCTTTTCAGCTTGACCCTG	CAATATAACATGCACAGGCC
634	MMMA4B4	212624 _s_at	CHN1	TGCGTCCTGGGTAGTCTGTG	CTTGTAATCCAGCATGTTTC
635	SE9F9	218350 _s_at	GMNN	CCTCCACTAGTTCTTTGTAG	CAGAGTACATAACTACATAA
636	JJA3B3	204484 _at	PIK3C2B	ATAACTGGAGAAAGAAGCTC	CATTGACCGAAGCCACAGGG
637	PPC1D1	202230 _s_at	CHERP	AATCGGCCACACCTGGTGTC	CATGGGCAGCCTGGTGCAAT
638	QQE1F1	204617 _s_at	ACD	CCTTCCAGTATGAGTATGAG	CCACCCTGCACGTCCCTCTG
639	KKE6F6	202761 _s_at	SYNE2	TTGAGCTGCCGGTTATACAC	CAAAATGTTCTGTTCAGTAC
640	MMC10D10	202756 _s_at	GPC1	TCAGGAGCCCCCAACACAGG	CAAGTCCACCCCATAATAAC
641	RRA10B10	204808 _s_at	TMEM5	TTGCTCCTATGGCTCCATTC	CTGTGGTGGAAGACGTGATG
642	JJE6F6	205450 _at	PHKA1	CCTAATCACTCCAACCCTGC	CCCTTTCTGTCCCATCCTTC
643	XG10H10	201875 _s_at	MPZL1	CTTTCCTGGTTGCAGATAAC	GAACTAAGGTTGCCTAAAGG
644	KKKA12B12	221482 _s_at	ARPP19	GAAAGATTTGTATCTCTGTG	CTTGAACTTGAATGGCCTTA
645	KKA11B11	202598 _at	S100A13	AAATCAGGAAGAAGAAAGAC	CTGAAGATCAGGAAGAAGTA
646	JJG11H11	218215 _s_at	NR1H2	CTTGCCTGACCACCCTCCAG	CAGATAGACGCCGGCACCCC
647	XG6H6	202689 _at	RBM15B	CACTAAGGACATTGGGCAAG	CTAGAAGAAGAACACATGGT

648	OOC3D3	218050_at	UFM1	CCCCGTTTCTTACAATAAAT	GTTGAGTCTTAGTTAAGCAG
649	IIIC6D6	205963_s_at	DNAJA3	TGGTAGCATGTCGCAGTTTC	CATGTGTTTCAGGATCTTCG
650	IIIA5B5	201561_s_at	CLSTN1	CCCTGACTGCTAGTTCTGAG	GACACTGGTGGCTGTGCTAT
651	RC8D8	201899_s_at	UBE2A	GCTGACTGGGCACACTCATG	CCAAGTTTCAGAATTATTGG
652	UUA7B7	219127_at	ATAD4	CAAGTCACACACCCTCAAAG	GGAAGCTACACGGGCCAAAT
653	MMC11D11	202811_at	STAMBP	GGGTGAGGGACAGCTTACTC	CATTTGACCAGATTGTTTGG
654	ZZG6H6	208847_s_at	ADH5	ATCCTGTCGTGATGTGATAG	GAGCAGCTTAACAGGCAGGG
655	NNG4H4	212485_at	GPATCH8	CAAACACAACTCTTGACTGC	CCTCCCACCCTCCTACCTGT
656	RRA4B4	218852_at	PPP2R3C	GCTTCTGGACTTACGAGAAC	AGAGAGGCTCTTGTTGCAAA
657	MA12B12	221732_at	CANT1	GTGGCTGAATTGAGACCTTG	CTGATGTATTCATGTCAGCA
658	UUE6F6	218780_at	HOOK2	CCTGGCATCTCTGAACCTTC	GCCCCACTGACAAGCACTGA
659	HHG12H12	217870_s_at	CMPK1	TCATCAGGTATCTTTCTGTG	GCATTTGAGAACAGAAACCA
660	HHA8B8	203709_at	PHKG2	TGAAGAGGAGGGAGACTCTG	CTGCTATAACTGAGGATGAG
661	JJG9H9	209724_s_at	ZFP161	GGGGCAGTACCAGTCCATAC	CAGCTGCGATTTGTGAGTGG
662	ZZA3B3	202889_x_at	MAP7	ACTTCCATGTACAACAAACG	CTCCGGGAAATGGAAAGCCA
663	TTA11B11	218809_at	PANK2	CAGTTGACTGGTTTTGTGTC	CTGTTTGAACTTGCTGAATG
664	LG11H11	201489_at	PPIF	CAATGTGAATTCCTGTGTTG	CTAACAGAAGTGGCCTGTAA
665	IIC10D10	201767_s_at	ELAC2	CCCTGCACACCAGAGACAAG	CAGAGTAACAGGATCAGTGG
666	LLC10D10	212070_at	GPR56	TTGCTGGCCTGTTGTAGGTG	GTAGGGACACAGATGACCGA
667	NNNA9B9	200929_at	TMED10	CTAAGGCATCCTACCAACAG	CACCATCAAGGCACGTTGGA
668	AAAC2D2	220094	CCDC90A	GAAATAGTGGCATTGCATGC	CCAGCAAGATCGGGCCCTTA

		_s_at			
669	OOA5B5	212833 _at	SLC25A46	TCAGAGACAACATCCTTGTC	CATATCCAAACCCAGTGTTT
670	YE2F2	202371 _at	TCEAL4	CTTTTGACCTATCTGCAATG	CAGTGTTCTCAGTAGGAAAT
671	RRG1H1	218249 _at	ZDHHC6	CTGGTTAAGATGTTCTTTTC	CTCAAAGGTGCCCTAGTGCC
672	PPE9F9	203395 _s_at	HES1	TCCCTCCGGACTCTAAACAG	GAACTTGAATACTGGGAGAG
673	IIE4F4	205562 _at	RPP38	GGCTCAGTGAGAGAATCGCC	CCCGTCATTGGCTTAAAATG
674	QQG5H5	205750 _at	BPHL	GGTGGTTCCTTCGTGTGGGG	CTTGATCGTGTTGCTGCCTG
675	JJC11D11	212871 _at	MAPKAPK5	GTGATAGAAGAGCAAACCAC	GTCCCACGAATCCCAATAAT
676	HHC6D6	201620 _at	MBTPS1	TCTTCTGACTGCAGGGGAAG	GATGTACTTTCCAAACAAAT
677	UC7D7	202996 _at	POLD4	GAGGCACCACGTAAGACCTC	CTGCCCTTAGCTCTCTTGCT
678	IIIG12H12	218826 _at	SLC35F2	CAAAGAGTATGCCTGGGAGC	CTCCAGCTGTTAAAAGACAA
679	RC10D10	202626 _s_at	LYN	GGGATCATCTGCCGTGCCTG	GATCCTGAAATAGAGGCTAA
680	GGE5F5	218397 _at	FANCL	TCTTGGTATAAATACACTTC	CACAGTCAGCACGGGGATCA
681	HHC2D2	201548 _s_at	KDM5B	TCAGCAAAGCTACAGGACTG	GTACTCAAGCCAGCCTGTAA
682	YE5F5	213689 _x_at	FAM69A	CACACGTATACTCAGATTTG	GCATGTACCTTTCAACATCT
683	VG8H8	201223 _s_at	RAD23B	CCCCTTCCCTCAGCAGAAAC	GTGTTTATCAGCAAGTCGTG
684	BBBC12D12	203627 _at	IGF1R	AAGCAGTCAATGGATTCAAG	CATTCTAAGCTTTGTTGACA
685	MMMG1H1	217867 _x_at	BACE2	TATTAAGAAAATCACATTTC	CAGGGCAGCAGCCGGGATCG
686	UG2H2	204952 _at	LYPD3	CTTCTCATCCTTGTCTCTCC	GCTTGTCCTCTTGTGATGTT
687	KKG7H7	221449 _s_at	ITFG1	GGAAAAGAAAGCAGATGATA	GAGAAAAACGACAAGAAGCC
688	MMA12B12	203124 _s_at	SLC11A2	TTGGCTCCCTTGAGGTTCTG	CTAGTGGTGTTAGGAGTGGT

689	EEE10F10	202362_at	RAP1A	AATATGATTATACAAAAGAG	CATGGATGCATTTCAAATGT
690	MMME7F7	212449_s_at	LYPLA1	TAATAAAGGCTAGTCAGAAC	CCTATACCATAAAGTGTAGT
691	VVC12D12	209015_s_at	DNAJB6	GCCGTTCATGTTGCTTTCTC	CTTTGTCCTCTTGGACTTGA
692	MMC4D4	209662_at	CETN3	ATGGAGAAATAAACCAAGAG	GAGTTCATTGCTATTATGAC
693	CC5D5	200618_at	LASP1	GGGGTTGTTGTCTCATTTTG	GTCTGTTTTGGTCCCCTCCC
694	DDA9B9	217971_at	MAPKSP1	TACATTGATCCACTTGAGCC	GTTAAGTGCTGCCAATTGTA
695	LE9F9	218595_s_at	HEATR1	AGTGCCAAAAGACTATTCAG	CAACTGGAAACTGTCCTGGG
696	KKA9B9	201735_s_at	CLCN3	GTCTCGAAGGAAGCGAGAAC	GAAATCTCTCATTGTGTGCC
697	QQC11D11	213531_s_at	RAB3GAP1	GGAGCTCAAGATGTCTTGTG	TCTGTGTGGCTAGATGGCCT
698	SSG11H11	203447_at	PSMD5	AAATTATTTTAAAGTGACTG	GAATTATCTAGTCCCCAGAT
699	HHHC6D6	212345_s_at	CREB3L2	GGTTTTAGCTCTGTTCTCTG	CTCCCATCCTTCGCTCACCA
700	JJG8H8	209179_s_at	MBOAT7	CCCTGGGCAGTGGGTTTTGG	GCAAATTCCCTTTCTTTGCA
701	JJE3F3	202093_s_at	PAF1	GTGATGCTGATTCTGAGGAC	GATGCCGACTCTGATGATGA
702	UUG3H3	219363_s_at	MTERFD1	TTTGTGCACAATGTGATGAG	CATTCCCCACCACATCATTG
703	WWA8B8	203094_at	MAD2L1BP	GATTTCCTGATAGGCTGATG	GCATGTGGCTGTGACTGTGA
704	MC3D3	202458_at	PRSS23	TGACACAGTGTTCCCTCCTG	GCAGCAATTAAGGGTCTTCA
705	HHA10B10	202708_s_at	HIST2H2BE	AGTGATTCAGCTGTTTTTGG	CTAAGGGCTTTTGGAGCTGA
706	OE5F5	202847_at	PCK2	AGTCTAGCAAGAGGACATAG	CACCCTCATCTGGGAATAGG
707	IIIG3H3	201331_s_at	STAT6	GCTGCATCTTTTCTGTTGCC	CCATCCACCGCCAGCTTCCC
708	MMA6B6	218961_s_at	PNKP	AAGGCTTCTCTGCCATCCTG	GAGATCCCGTTCCGGCTATG
709	TTA2B2	211015	HSPA4	GGCAGATAGACAGAGAGATG	CTCAACTTGTACATTGAAAA

		_s_at			
710	QE1F1	212231 _at	FBXO21	CTCCAGGAAGCCTGTATCAC	CTGTGTAAGTTGGTATTTGG
711	TTE11F11	215497 _s_at	WDTC1	CCGAGCCTTTTTGTTGCTCC	GCTCCCAGGAGAGTGAGGGT
712	RRC4D4	219016 _at	FASTKD5	CTCGGCTTGGCTACCGTGTG	GTAGAGTTATCCTACTGGGA
713	LLA2B2	218542 _at	CEP55	TGTTCCCCAACTCTGTTCTG	CGCACGAAACAGTATCTGTT
714	OOG5H5	218358 _at	CRELD2	GATGTCCCGTGGAAAATGTG	GCCCTGAGGATGCCGTCTCC
715	SC11D11	209586 _s_at	PRUNE	CCTACCCCACAGCTCTGTTC	CATGTAAGTTGCCAACAGTT
716	FFFC1D1	218113 _at	TMEM2	ATGGCCTCTACCTTTGTATC	CAGGAGAAACTGCAGAGCAG
717	TTA8B8	220661 _s_at	ZNF692	ACTGGGCTGTAGGGGAGCTG	GACTACTTTAGTCTTCCTAA
718	VE6F6	209394 _at	ASMTL	CATGCTGGTGCAGACTGAAG	GCAAGGAGCGGAGCCTGGGC
719	PE7F7	202109 _at	ARFIP2	TTGCTGCCCTGTCTATCTTC	CTGGCCACAGGGCTTCATTC
720	MG5H5	202528 _at	GALE	AGGCTCTGGCACAAAACCTC	CTCCTCCCAGGCACTCATTT
721	LLG11H11	201870 _at	TOMM34	GTTTTTTGTTCCAACAGTGG	CCTTCTCCGGGCTTCATAGT
722	BBBC7D7	210473 _s_at	GPR125	GGACCAATTAAAAGCAATGG	GCAGGAGGGACCCTTGCTCG
723	IIIC9D9	218744 _s_at	PACSIN3	GGCTGAGGGCAAGATGGGAG	GTCAGAGGTGACAGAAGCGT
724	WC1D1	1053_at	RFC2	TACAGGTGCCCTATTCTGAG	GTACAGGAGCCGCGGCTTTC
725	JJE11F11	217809 _at	BZW2	ATGGAGCCCTGAGGCATCAG	CTATTATACTTGGGACTCTA
726	TTE8F8	219270 _at	CHAC1	ACAGGCCCTGGCAACCTTCC	CAGTCTGTCCCATACTGTTA
727	KKE7F7	219082 _at	AMDHD2	TCGACGACTCCCTTCACGTC	CAGGCCACCTACATCTCGGG
728	YG7H7	201968 _s_at	PGM1	CATGCCCTCCTGCATTGCTG	CTGCGTGGGTATTTGTCTCC
729	SE3F3	202722 _s_at	GFPT1	GCAGTGTATGCTCATACTTG	GACAGTTAGGGAAGGGTTTG
730	QQG4H4	205251	PER2	CTCTCAGAGTTTCTGTGATG	ATTTGTTGAGCCTTGCTGGA

		_at			
731	UUG7H7	201416 _at	SOX4	GCACGCTCTTTAAGAGTCTG	CACTGGAGGAACTCCTGCCA
732	OOG10H10	201531 _at	ZFP36	CTCAAATTACCCTCCAAAAG	CAAGTAGCCAAAGCCGTTGC
733	JJJE5F5	203336 _s_at	ITGB1BP1	CTGAAGACCACAGATGCAAG	CAATGAGGAATACAGCCTGT
734	FFFE1F1	212282 _at	TMEM97	CCATATTGGCCCGATTAGTG	GTACTGTCTGACTCACGTGT
735	KKA5B5	213995 _at	ATP5S	TGTGCAAGTGTCATTATATC	GAGGATGACTGTTTGCTGAG
736	AAA4B4	213918 _s_at	NIPBL	GGAGTCAACGTATTTCGCAG	CGTATTACGTAAAATGATTT
737	PPC7D7	202854 _at	HPRT1	ACTATGAGCCTATAGACTAT	CAGTTCCCTTTGGGCGGATT
738	KKA1B1	221549 _at	GRWD1	GAGGTGTGGGTTCCTCCAAC	ACAATTTGCTTCTGCCCGTT
739	LLLA3B3	202900 _s_at	NUP88	CCATTATTCTCAGTGCCTAC	CAGCGAAAGTGCATTCAGTC
740	NA2B2	201673 _s_at	GYS1	GCCCACTGTGAAACCACTAG	GTTCTAGGTCCTGGCTTCTA
741	RE5F5	217777 _s_at	PTPLAD1	AGGCTCAGCCCACCCCAACC	CTATCTCATGTTCAGTCTGT
742	MME1F1	200843 _s_at	EPRS	TCAAACCACTCTGTGAACTG	CAGCCTGGAGCCAAATGTGT
743	RRE1F1	218175 _at	CCDC92	GGCACCGATCACCGAGCAGC	CGTGCGTGTATCTCAAGGAA
744	HHG11H11	204711 _at	KIAA0753	GGCTCAGTGAAGGAAACATG	CAGAAAGAATGCCTGAGACG
745	NA11B11	218001 _at	MRPS2	TCAATCTAAATGCCTTTCAG	GTGGGCCGCTTCCTTGGCTA
746	PPA11B11	203775 _at	SLC25A13	CAGACAGAAAAAACTGAGAT	GTAGCCCCTCTCCTGGAAGT
747	QQE6F6	205895 _s_at	NOLC1	GGGAACCCTCAGGTCTCTAG	GTGAGGGTCTTGATGAGGAC
748	HHHG12H12	209262 _s_at	NR2F6	TAGCATGAACTTGTGGGATG	GTGGGGTTGGCTTCCCTGGC
749	IIIE8F8	218828 _at	PLSCR3	CTGCCTTCAGCTGGTGCTTG	CTGCGATTCCTGTGCCTTAT
750	AAAC11D11	203303 _at	DYNLT3	GAGCGGAACCATAACTCATT	GAATTTTGGAGAGGAATAAG

751	TTE3F3	216913_s_at	RRP12	CCTGGACTCAGGATGACTTG	GAACTAGGGCTTGGCTCTCA
752	OOA11B11	201572_x_at	DCTD	AGCTTACTGCAGCACTGTTG	GTGTTCGGAGCTCTTCTGTG
753	MMA10B10	202734_at	TRIP10	GGACCTATGCACTTTATTTC	TGACCCCGTGGCTTCGGCTG
754	OE1F1	203258_at	DRAP1	GAAGATTACGACTCCTAGCG	CCTTCTGCCCCCCAGACCAT
755	GGA6B6	217734_s_at	WDR6	TTGTAGTAGGAGCTGAAATC	CATGCTGAGCTGTACCAGGA
756	XC10D10	203905_at	PARN	TTGAAACAGATCACAGCAAC	GACAAACGCTCATGGCGCTG
757	ME7F7	218577_at	LRRC40	ATTGACTTGAATATGACTAG	CCAGTTTCTATGTTTTTGTT
758	BBBG7H7	209409_at	GRB10	ACAGTATGACCGATCTCTGC	GCCTTTCTGGGGGCGGGCAA
759	NG11H11	201098_at	COPB2	TCCTACTCCGGTTATTGTGG	CCTCCCACACAGCCAACAAA
760	TTC3D3	216321_s_at	NR3C1	GTCCACCCAGGATTAGTGAC	CAGGTTTTCAGGAAAGGATT
761	VA10B10	201995_at	EXT1	AGAAATACCGAGACATTGAG	CGACTTTGAGGAATCCGGCT
762	JJC3D3	204742_s_at	PDS5B	TGCTGCAGTGCAACAGGAGG	CTTTTTCAGTGATCTTCACT
763	SSE2F2	212180_at	CRKL	CAGGAGGAACAGTGGCCTTG	CTTCTTAGACGGTCTTCACT
764	HHA3B3	203171_s_at	RRP8	ACAAGCGCAGGTGACCTCTG	GATCTTCCTTGAAAGGGGAG
765	MMMC5D5	209608_s_at	ACAT2	CTTTGCAGCTGTCTCTGCTG	CAATAGTTAAAGAACTTGGA
766	PPA8B8	203046_s_at	TIMELESS	CCTTTGGCTTTCTCTTGGAG	GTGGGTCGCAGCACCAGATG
767	QG9H9	203341_at	CEBPZ	CAAACAGCTTAGATGGGAGG	CTGAACGTGATGACTGGCTA
768	OOA8B8	201153_s_at	MBNL1	TCCAGCCTTCACTCCAGCTG	GTTAAAAATGTTGCACTTAT
769	NC6D6	207831_x_at	DHPS	AAACCTTTGCCCAGAAGATG	GATGCCTTCATGCATGAGAA
770	IIE10F10	201778_s_at	KIAA0494	GTCACAGTTGAGGATTTTGG	CTGTGATGGGCTCATACTCA
771	JJA10B10	210151	DYRK3	GTATTGCCAAAACTGATTAG	CTAGTGGACAGAGATATGCC

		_s_at			
772	OOG6H6	218743 _at	CHMP6	GTTATGAGACGATCTCGCTG	GGACCGCCCCTGCCCGTGGA
773	IIC8D8	200791 _s_at	IQGAP1	AAGGCCACATCCAAGACAGG	CAATAATGAGCAGAGTTTAC
774	IIG1H1	205055 _at	ITGAE	CTTGGAGAGCATCAGGAAGG	CCCAGCTGAAATCAGAGAAT
775	MMMG4H4	201503 _at	G3BP1	AAGAAGGAATGTTACTTTAA	TATTGGACTTTGCTCATGTG
776	HHC5D5	217900 _at	IARS2	GTCTTCAGATACACTGTGTC	CTCGATGTGCAGAAGTTGTC
777	JJE7F7	206015 _s_at	FOXJ3	TTTTGTGCAGATACAACCTG	CTCTCTGTACTGCTGTTGGA
778	KKKA5B5	210153 _s_at	ME2	CCAGTGAAACTTACAGATGG	GCGAGTCTTTACACCAGGTC
779	NNNA7B7	203328 _x_at	IDE	GGAAATGTTGGCAGTAGATG	CTCCAAGGAGACATAAGGTA
780	RRC2D2	218474 _s_at	KCTD5	GCATCCTCTCTGGGGAGCTG	CTGGCCGCTTAGCGTTGTTT
781	ZZC4D4	202429 _s_at	PPP3CA	ACCCAAACAAAGATGTTCTC	GATACAGTCTGGCAAAGACT
782	RRA9B9	203911 _at	RAP1GAP	TGGCCCCAATACCCATTTTG	GAAGCCCCTGTGGCCGTGTG
783	LLLG7H7	215116 _s_at	DNM1	ACTACCAGAGAACGCTGTCC	CCCGACATCCCACTCCAAAG
784	IIIG2H2	213844 _at	HOXA5	AACTCCCTTGTGTTCCTTCT	GTGAAGAAGCCCTGTTCTCG
785	TTG11H11	218547 _at	DHDDS	GCATCTCTCTTTGGCCTGAG	GTTCTGTATTCTGGGAAAGG
786	TG5H5	203521 _s_at	ZNF318	ATTGAACTCATTCCCTGTTC	CACAAACCCATATGTATCCT
787	TG7H7	213150 _at	HOXA10	CTAGGAGGACTGGGGTAAGC	GGAATAAACTAGAGAAGGGA
788	TG9H9	203720 _s_at	ERCC1	GTACCTGGAGACCTACAAGG	CCTATGAGCAGAAACCAGCG
789	NNA1B1	203546 _at	IPO13	AGAGGCGGGTGAAGGAGATG	GTGAAGGAGTTCACACTGCT
790	IIG10H10	202388 _at	RGS2	TGCAGTGTCCGTTATGAGTG	CCAAAAATCTGTCTTGAAGG
791	XC12D12	200617 _at	MLEC	TTTCCCATCCTCTCTCTGTG	GAGGCCAAACCAACTCTTTG

792	OC7D7	213233_s_at	KLHL9	ACCAAGGCAAAATGAATTGG	CTTCTAGGGGTCTGAACCTT
793	SG12H12	212997_s_at	TLK2	TCCGTCTGGTCTCCTGTTTG	CAATTGCTTCCCTCATCTCA
794	JJA11B11	212689_s_at	KDM3A	GGCTGTAAAAGCAAAACCTC	GTATCAGCTCTGGAACAATA
795	HHC9D9	212189_s_at	COG4	CAGCAGAGAAACAAAGTCTG	GACCCACTCCATGCTCTGCC
796	OOC1D1	202911_at	MSH6	TAGGACATATGGCATGCATG	GTAGAAAATGAATGTGAAGA
797	NNNE3F3	200698_at	KDELR2	ACAAAAGCTCTGTAGGGCTG	CAGACATTTAAAGTTCACAT
798	VVG7H7	201913_s_at	COASY	GTCCAAGCTATACTGTGCAG	GACATGGCCAGGCCTGGTGG
799	SE10F10	202604_x_at	ADAM10	GCTCGACCACCTCAACATTG	GAGACATCACTTGCCAATGT
800	MMA1B1	202910_s_at	CD97	TGTCCCATCCTGGACTTTTC	CTCTCATGTCTTTGCTGCAG
801	VG9H9	205051_s_at	KIT	TCTATGCTCTCGCACCTTTC	CAAAGTTAACAGATTTTGGG
802	LLLA6B6	202772_at	HMGCL	GCTGGCAGAGGCCATTTGTG	GAAAGTGGAGAGCTACGTGG
803	KKC3D3	218667_at	PJA1	GTTCCCTCCCCCACTCTAAA	GACCAAGGCCGTTTACTCCT
804	CCCG3H3	203726_s_at	LAMA3	GGTGGCAGTCACCATAAAAC	AACACATCCTGCACCTGGAA
805	KKKA10B10	217960_s_at	TOMM22	CGGAGAAGTTGCAAATGGAG	CAACAGCAGCAACTGCAGCA
806	RRE3F3	218755_at	KIF20A	TCCTACGCTCACGGCGTTCC	CCTTTACTCAAATCTGGGCC
807	RRE4F4	219069_at	ANKRD49	GATAGTCCTACCTCACCCTG	GTCAACCTACATGATCCTTA
808	OOA1B1	202880_s_at	CYTH1	TTTCCTAGACAGAGAGGCAC	CTGGGTCAGTATTAGTCTAT
809	RE4F4	200825_s_at	HYOU1	AGCTAGGGCTGCTGCCTCAG	CTCCAAGACAAGAATGAACC
810	LA4B4	214061_at	WDR67	TCTTTTGGCTGCATAGAATG	CATGTCACCTTGAGACGGTC
811	SE7F7	204772_s_at	TTF1	CACTAAAATCCAGACTCCTG	CAGCACCCAAGCAAGTTTTC
812	NNA9B9	201178	FBXO7	GTGGTATGACCCAAAGGTTC	CTCTGTGACAAGGTTGGCCT

		_at			
813	LLC6D6	204611 _s_at	PPP2R5B	GTCTATTTATTCTCGCCCAG	CTCACCCTCTACACAGACAC
814	ZG3H3	202500 _at	DNAJB2	ACCCTGCTGCCCATTCTTTC	CAACATCACAGATGAACTGC
815	YYC11D11	201347 _x_at	GRHPR	GTAGCCAAACAGTAGAGATG	GAGGGCCGGGAAGCAAACCG
816	RA7B7	214106 _s_at	GMDS	TGGGTCGCTTTGCGTTTGTC	GAAGCCTCCTCTGAATGGCT
817	ZZG7H7	205640 _at	ALDH3B1	AAACCTACATTTGGACAATG	AGAGGCTGCTCCTGCGGCCT
818	HHHA9B9	205379 _at	CBR3	GACAGGATTCTGGTGAATGC	GTGCTGCCCAGGACCAGTGA
819	OA12B12	204662 _at	CP110	AGCTTATTCATAGCATTGTG	GGTCTCTCCAGTAAGAAAGA
820	YA4B4	202174 _s_at	PCM1	AAGCTCTCTGGCTGGAAGTC	CTGATACTGAATCTCCAGTG
821	JJJG7H7	201351 _s_at	YME1L1	CAGAAACCCAATCTGCCATC	GAACAAGAAATAAGAATCCT
822	ZE7F7	202032 _s_at	MAN2A2	AGAAACTAGCCAAGGGCAAG	CTATTATTCAGCAGTGTCCC
823	AAAE10F10	205741 _s_at	DTNA	CTGTCACCACAGAGATTGGC	CTACGGTTTCTGTTTTGAGG
824	GGGA6B6	220091 _at	SLC2A6	GCCCAACCTCTGGGAACAGG	CAGCTCCTATCTGCAAACTG
825	AAAE3F3	203213 _at	CDC2	AAGTCTTACAAAGATCAAGG	GCTGTCCGCAACAGGGAAGA
826	BBBE12F12	205227 _at	IL1RAP	CGTTCCATGCCCAGGTTAAC	AAAGAACTGTGATATATAGA
827	LA3B3	203566 _s_at	AGL	TGCTTCATACTTGAGTGATG	CTGGATAAGGTATTGTATTT
828	LC5D5	214741 _at	ZNF131	CGTTGAAACACATTGATTCC	CCTCCCCCTACTTATTGCCA
829	YYA11B11	213343 _s_at	GDPD5	AGCAGACCTCAAGGCAGAAG	GGTCACCTAACCCAGGAGTC
830	LLLG6H6	210115 _at	RPL39L	ACTTGAAAAAGTGGTGTGTG	GTTGACTCTGTTTCTCGCCA
831	LLC4D4	218104 _at	TEX10	GAGGAGCTGCCTGTTGTGGG	CCAGCTGCTTCGACTGCTGC
832	EEEE7F7	203127 _s_at	SPTLC2	AAAATTGGCGCCTTTGGACG	GGAGATGCTGAAGCGGAACA

833	RRG9H9	203209_at	RFC5	ACGCACTTGTTTTCATGCAG	GAGCGGGGCAAGTAAGGTTG
834	IIA11B11	202441_at	ERLIN1	CCCTCTCAGCTCTGAGGCTG	GCCGTCTTTCGGGGTGTTCC
835	KKA8B8	201011_at	RPN1	AAACCAGGCCCTGCGTCAGG	CAGTGTGAGTTTGCCGTTTG
836	BBBE7F7	219327_s_at	GPRC5C	ATGGGTGTCCCCACCCACTC	CTCAGTGTTTGTGGAGTCGA
837	IIA7B7	205085_at	ORC1L	GCCGTGTGTTCTCACCTGGG	CTCCTGTCGCCTCCTGCTTG
838	VVC7D7	210416_s_at	CHEK2	CTGTCTGAGGAAAATGAATC	CACAGCTCTACCCCAGGTTC
839	LLG6H6	212830_at	MEGF9	CCCTAGAAAGTAAGCCCAGG	GCTTCAGATCTAAGTTAGTC
840	AAAA7B7	214074_s_at	CTTN	TGTGTTTTAAACAGAATTTC	GTGAACAGCCTTTTATCTCC
841	KKC7D7	202908_at	WFS1	CCTGCCAGTGTTTAGAAGAG	CCTGACTGTGTTCAGTGCCT
842	HHE4F4	212968_at	RFNG	CGCTCTGACTTGTGGCTCAG	GACTACTTTCTGGGTCGTGC
843	IIIE1F1	212665_at	TIPARP	CTGTTGTTTGCTGCCATTGG	CATGAAATGGCCAACTGTGG
844	WWG11H11	208717_at	OXA1L	TTTTCCCTGGTCCAAGTATC	CTGTCTCCGGATTCCAGCAG
845	LC4D4	203557_s_at	PCBD1	TTTAGACCTTTTCCCTGCAC	CACTCTCTTCATCCTGGGGG
846	AAE2F2	201579_at	FAT1	AGTGTAACGGGGACCTTCTG	CATACCTGTTTAGAACCAAA
847	SSA5B5	202006_at	PTPN12	GTTTCTGAATTTTAAACTTG	CTGGATTCATGCAGCCAGCT
848	OOE4F4	211783_s_at	MTA1	GTTTACTTTTTGGCTGGAGC	GGAGATGAGGGGCCACCCCG
849	YA7B7	201260_s_at	SYPL1	TTGTTTCCTGTCCTTTGTTG	CTCATGCTGTTTAAGTGCAG
850	QQC1D1	215884_s_at	UBQLN2	GAAGGATCAGTGTAGTAATG	CCAGGAAAGTGCTTTTTACC
851	IIIA2B2	203418_at	CCNA2	CTCATGGACCTTCACCAGAC	CTACCTCAAAGCACCACAGC
852	TTG12H12	221779_at	MICALL1	GGAAGAGGCTCGCTCCCGCC	CATGGTCATCACTGGTCTGT
853	JJJG3H3	203167	TIMP2	AAGAAGAGCCTGAACCACAG	GTACCAGATGGGCTGCGAGT

		_at			
854	KKA12B12	204998 _s_at	ATF5	AGTGTTTCGTGAAGGTGTTG	GAGAGGGGCTGTGTCTGGGT
855	MA11B11	217830 _s_at	NSFL1C	CCCTGCAATGAGCCAAGAAC	CAACACTACATCCACCTAGA
856	ZZA7B7	217761 _at	ADI1	AATTCCGAGATAGGATTATG	CCTAGTTTGTCATATCACAG
857	ZZE12F12	218168 _s_at	CABC1	GAGCTGGGAGAGGTGCTGAG	CTAACAGTGCCAACAAGTGC
858	MMC6D6	219821 _s_at	GFOD1	AAAGTGAGCCTAGCCAGGAG	GTGTTTGGGGCTCTATCGCG
859	IIIE3F3	203648 _at	TATDN2	TGCAGGTGAAACCAACCAGC	CCTGTGTTAGAGGAGGAAAA
860	MA3B3	203250 _at	RBM16	GTCAAGGAAATGAATAACAG	CTTGTCAGAGACTTCCTATG
861	RA2B2	202040 _s_at	KDM5A	AGCCCTGACCCCAATGTCTG	CTGTTTCCAACACTGGTGAT
862	ZZC12D12	211725 _s_at	BID	CCTGGAGCAGCTGCTGCAGG	CCTACCCTAGAGACATGGAG
863	SG6H6	203208 _s_at	MTFR1	TTCCTGGCTGGGAGTATTAG	GAGATGGGAGTAGAGATTCA
864	TTG8H8	220140 _s_at	SNX11	AGACAATGAGGCATTCTGTC	CTCCTGCTGCCATTCTTCAT
865	UUA12B12	201080 _at	PIP4K2B	ACAACTGTTCCCCAATCTAC	CAGCCATCTGCAGGGGTCAG
866	NNG9H9	201250 _s_at	SLC2A1	GATTGAGGGTAGGAGGTTTG	GATGGGAGTGAGACAGAAGT
867	PPG12H12	204126 _s_at	CDC45L	CTGAAAGCTGAGGATCGGAG	CAAGTTTCTGGACGCACTTA
868	MMA9B9	202220 _at	KIAA0907	TCTCCCAGAACTGGTTGCAG	CTAAAACAGAGAGATCTGAC
869	SSE3F3	218742 _at	NARFL	GAGCAAGACGGGTTCTCACC	CCTGACTTCTGGAGGCTTCC
870	QA2B2	208424 _s_at	CIAPIN1	CCCACTTTAGAAGAGTCCAG	GTTGGTGAGCATTTAGAGGG
871	SSC5D5	212644 _s_at	MAPK1IP1L	TTAGGGAACCTTAAGTCATG	CAGACATGACTGTTCTCTTT
872	YYA1B1	205480 _s_at	UGP2	AGCGGGAATTTCCTACAGTG	CCCTTGGTTAAATTAGGCAG
873	ZG1H1	203499 _at	EPHA2	AGTCGGCCCCATCTCTCATC	CTTTTGGATAAGTTTCTATT

874	GGGE7F7	204949_at	ICAM3	CATAATGGTACTTATCAGTG	CCAAGCGTCCAGCTCACGAG
875	LLLG3H3	219654_at	PTPLA	GTGTGGTGCTTTTTCTGGTC	GCGTGGACTGTGACAGAGAT
876	ZE6F6	215093_at	NSDHL	CACCCTACTCTTTCCGTGAC	GATGAGGGCGGCAAAAACAG
877	QQE2F2	204826_at	CCNF	GGGTGAGAACCCAAGCGTTG	GAACTGTAGACCCGTCCTGT
878	ZE12F12	201756_at	RPA2	GAGAAACCTGCTGGCCTCTG	CCTGTTTTCATTTCCCACTT
879	OA2B2	202678_at	GTF2A2	AGGCTATAAATGCAGCACTG	GCTCAGAGGGTCAGGAACAG
880	NC1D1	221230_s_at	ARID4B	TCTTTGTTTCCTGGCAATAC	GACGTGGGAATTTCAATGCG
881	JJA1B1	203155_at	SETDB1	TGATCCCTTCCAATGTGGTG	CTAGCAGGCAGGATCCCTTC
882	JJC10D10	212458_at	SPRED2	CCGACCCCCCAAGCTATTTG	CTCACATTAACAAATTAAAG
883	OG8H8	213153_at	SETD1B	GAGTTTTAGGGATGTTTGTG	CGGGTAGACTCCATCATCCA
884	LLLG2H2	208690_s_at	PDLIM1	TGAGTCCCCTCCCTGCCTTG	GTTAATTGACTCACACCAGC
885	SA8B8	218102_at	DERA	TGCCCTAGCAGAGGAAAATG	CAACATCTCGCAAGCGCTGC
886	AAAC7D7	211919_s_at	CXCR4	CCGACTTCATCTTTGCCAAC	GTCAGTGAGGCAGATGACAG
887	TG4H4	203343_at	UGDH	TGCTGAGAATGTACAGTTTG	CATTAAACATCCCAGGTCTC
888	QG5H5	203464_s_at	EPN2	GCTGTTTCTCAGTCCCAGAG	GCCGGTGGCTGGTTTTGAAC
889	QQG3H3	205173_x_at	CD58	CCAAGCAGCGGTCATTCAAG	ACACAGATATGCACTTATAC
890	YYE2F2	212399_s_at	VGLL4	TGCCTGCAGTGCGCTCTGAC	CTTCTCTTCATGTGTGTAAA
891	RRA7B7	221552_at	ABHD6	TGTTCTGAGTGAACCCACAG	CAGTCGCAGAATGAGCACCT
892	NNE7F7	220127_s_at	FBXL12	GGGCACCTGAGGGTCTGAGC	CCCCTTATGAGTACCCAAGA
893	MMG5H5	217873_at	CAB39	AGGTCGTAGCCTTTTAGGTG	GAAGAAGTGAGGGTGCAGCG
894	QE2F2	203342	TIMM17B	CGAAGTTCTCACCCCAGCTC	CTTTGTGTGGCACCCTGATG

		_at			
895	PA12B12	201697 _s_at	DNMT1	ACATGGTGTTTGTGGCCTTG	GCTGACATGAAGCTGTTGTG
896	RRC5D5	221887 _s_at	DFNB31	CCTCCAGCTAGGACCCAGCC	CATCCCCAGATGCCTGAGCC
897	OOC11D11	201608 _s_at	PWP1	AGTGGCCCTTTTGGCAGCAG	GAGCTCAGATACACCCATGG
898	QQG12H12	217168 _s_at	HERPUD1	GCTGTTGGAGGCTTTGACAG	GAATGGACTGGATCACCTGA
899	MG2H2	201847 _at	LIPA	GGTTGCCCATGAGAAGTGTC	CTTGTTCATTTTCACCCAAA
900	KKKC12D12	221641 _s_at	ACOT9	ACTCTACCCACAGTGACGTG	GTATCTGATGAAGACCTGAT
901	LLC9D9	207871 _s_at	ST7	CTGTGGCACCAGCTAACACG	GATCTGAGAGAAGCCCTGTC
902	YC6D6	208407 _s_at	CTNND1	ACCACTGGGCCATAATGTTG	CTTCTCAGGCTATATGCAGT
903	LLC2D2	218581 _at	ABHD4	GGTGGTTCCCACTGCATGAC	CCTCTATCCCTGCCATCTGT
904	AAE4F4	201626 _at	INSIG1	ATTTCCAATGAAGATGTCAG	CATTTTATGAAAAACCAGAA
905	QE10F10	203989 _x_at	ZNF160	GAAGAGAGAGGCCAGGCGCG	GTGGCTCACACCTGTAATCC
906	NG6H6	202494 _at	PPIE	TGGGCCTCTCCTGGGACTAC	CAGTGTGGCTCTTACGTGTT
907	ZA1B1	201628 _s_at	RRAGA	AGTGGGCTTTGAAGTGTGTG	CTGCTTACTCCTTTCATCTT
908	ME5F5	207467 _x_at	CAST	CTCCAAAGCACCTAAGAATG	GAGGTAAAGCGAAGGATTCA
909	IIA1B1	217911 _s_at	BAG3	TGCAGCCCTGTCTACTTGGG	CACCCCCACCACCTGTTAGC
910	NNC8D8	201040 _at	GNAI2	TGTCTTGTTCTGTGATGAGG	GGAGGGGGGCACATGCTGAG
911	MC5D5	203120 _at	TP53BP2	CCTGCCAGAAAGGACCAGTG	CCGTCACATCGCTGTCTCTG
912	SC5D5	202825 _at	SLC25A4	AACCAGACTGAAAGGAATAC	CTCAGAAGAGATGCTTCATT
913	YG11H11	201644 _at	TSTA3	GGGCAGTTTAAGAAGACAGC	CAGTAACAGCAAGCTGAGGA
914	VC8D8	202599 _s_at	NRIP1	TCCCATTGCAAACATTATTC	CAAGAGTATCCCAGTATTAG

915	IIIE4F4	215945_s_at	TRIM2	CGCTGTGCATCAAAGTGTTT	GTATGTTCGTAGCTACATAC
916	NNC10D10	201397_at	PHGDH	GAGAAAATCCACATTCTTGG	GCTGAACGCGGGCCTCTGAC
917	MMMC7D7	209163_at	CYB561	CCAGTCTCCTCTAATGCTCA	GATTTCCCATAGTTGGCTTT
918	RRG10H10	200895_s_at	FKBP4	GGACATGGGAAAAACCACTG	CTATGCCATTTCTTCTCTCT
919	KKC2D2	200811_at	CIRBP	TGTGGCTTTTTTCCAACTCC	GTGTGACGTTTCTGAGTGTA
920	QQG10H10	213110_s_at	COL4A5	GAATCCTCCTGTGGCCTCTG	CTTGTACAGAACTGGGAAAC
921	SSE1F1	202009_at	TWF2	CGGGCTGGCATTTTGTGACC	CTTCCCTGTTGCTGTCCCTG
922	HHG7H7	202123_s_at	ABL1	CTGTGGTGGCTCCCCCTCTG	CTTCTCGGGGTCCAGTGCAT
923	IIA10B10	201743_at	CD14	CTGACGAGCTGCCCGAGGTG	GATAACCTGACACTGGACGG
924	AAA8B8	203494_s_at	CEP57	AAGTGAGAAACAGTGCTCTG	GTGACATGATAAATATATGT
925	SSC6D6	221856_s_at	FAM63A	GTTTCTGGTTCTCAACTCCC	GGTCCCTGAATAGTCACACG
926	UUA1B1	218695_at	EXOSC4	GGCAGATGGTGGGACCTATG	CAGCTTGTGTGAATGCAGCC
927	NNA10B10	201323_at	EBNA1BP2	GAAAGGGTCAAATAAGAGAC	CTGGAAAACGAACAAGAGAG
928	GGGE2F2	203358_s_at	EZH2	TCGAAAGAGAAATGGAAATC	CCTTGACATCTGCTACCTCC
929	KKG12H12	207515_s_at	POLR1C	AAGCTAAAGAAGGTTGTGAG	GCTTGCCCGGGTTCGAGATC
930	PPC5D5	202726_at	LIG1	CCCTCGGTTTATTCGAGTCC	GTGAAGACAAGCAGCCGGAG
931	LG1H1	212875_s_at	C2CD2	CGGAAAGGTTTGGCCTGACG	CTGGAGTGCGGTGATGAACT
932	XG3H3	218093_s_at	ANKRD10	TGGATTTATTGTTTTTATTC	CACACTTCCTACTTGGTCTC
933	QC10D10	207059_at	DDX41	CTGGCTGCCTGTTCCCTGTG	CTCTTCAGAATTACTGTTTT
934	KKG4H4	218421_at	CERK	AAGTCTGAGTGAAAGGATGG	CCTCATTCTCTTTCTAATCT
935	QC4D4	209380	ABCC5	AGACCTACCTCAGGTTGCTG	GTTGCTGTGTGGTTTGGTGT

		_s_at			
936	LLG9H9	202963 _at	RFX5	GTTCTGTGGTCAGGCGGCAC	CAATGAGAAAGGAATGCAGA
937	QE12F12	201944 _at	HEXB	AGCTGCACAACCTCTTTATG	CTGGATATTGTAACCATGAG
938	ZA2B2	200915 _x_at	KTN1	TAAACCAACAGCTCACAAAG	GAGAAAGAGCACTACCAGGT
939	KKE5F5	212403 _at	UBE3B	CCCATCCTAATTTTTATCAC	CTGAAGGTTGGAACCAGTGA
940	EEEG5H5	205398 _s_at	SMAD3	TCAAAGAGATTCGAATGACG	GTAAGTGTTCTCATGAAGCA
941	HHA2B2	121_at	PAX8	TGTGCTTCCTGCAGCTCACG	CCCACCAGCTACTGAAGGGA
942	HHE3F3	212300 _at	TXLNA	CAGCTTTTTTGTCTCCTTTG	GGTATTCACAACAGCCAGGG
943	NNE8F8	201087 _at	PXN	TCTCCACTTTCACCCGCAGG	CCTTACCGCTCTGTTTATAG
944	LLLE8F8	201136 _at	PLP2	CAACAACATTCCCAGCAGAC	CAACTCCCACCCCCTCTTTG
945	HHHE5F5	212038 _s_at	VDAC1	TTCCCTAACCCTAATTGATG	AGAGGCTCGCTGCTTGATGG
946	XA11B11	209408 _at	KIF2C	TTTAGTACAGCTATCTGCTG	GCTCTAAACCTTCTACGCCT
947	JJG2H2	204252 _at	CDK2	TGATCCCATTTTCCTCTGAC	GTCCACCTCCTACCCCATAG
948	RA12B12	204542 _at	ST6GALNAC2	TCCCATTAGAGATGTATCAC	CACCTTGTCACCAACAGGAT
949	KKE2F2	202114 _at	SNX2	GACCCTCTTTGAATTAAGTG	GACTGTGGCATGACATTCTG
950	FFG4H4	213152 _s_at	SFRS2B	CATGCAGTGAGCACATCTAG	CTGACGATAATCACACCTTT
951	LLE3F3	212651 _at	RHOBTB1	GGCAGTGGAAACACCAGATA	GAAGATCTTAGGAGAGGCCC
952	YC8D8	202925 _s_at	PLAGL2	TAGCTGATTGTTCCCACTTG	CACCTCTCCACCTTTGGCAC
953	TC10D10	205324 _s_at	FTSJ1	ACAACCCTGAAGACAACAAG	GAAAGAAACCATGAAAGTCT
954	QQG7H7	208898 _at	ATP6V1D	TCAGGCCAATTACTGTGGAG	CAGCTTTCATTCCTACCCAC
955	LLE1F1	218399 _s_at	CDCA4	TAGATCACAGGCACCAGTTG	GTCTTCAGGGACCTCATAGC
956	QQE3F3	205031	EFNB3	TGGCCACCTCAATCACCAGC	CAAGATGGTTGCTTTGTCCA

		_at			
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958	TTE10F10	221514 _at	UTP14A	ATGCTCTGTAGATTGAGTTG	CTGGAGGAGTGACAGCCAGG
959	MC12D12	203675 _at	NUCB2	AACGTCAGCATGATCAACTG	GAGGCTCAGAAGCTGGAATA
960	TC7D7	202119 _s_at	CPNE3	GTAAATTCAGGGCCCCATTG	CTACTTATGCCATATTTGGA
961	OOG7H7	200783 _s_at	STMN1	TTCTCTGCCCCGTTTCTTGC	CCCAGTGTGGTTTGCATTGT
962	PPA3B3	202413 _s_at	USP1	CTTGATTCACTTAGAAGTGT	CTCAGAAAACCTGGACAGTT
963	FFA8B8	218140 _x_at	SRPRB	GGTCTAGTGTGTTCTTAGTG	GTTATACTGGGAAGTGTGTG
964	MA7B7	219352 _at	HERC6	GGAATGTACTTTCACTTTTG	CTGCTTCACTGCCTTGTGCT
965	QQA10B10	212880 _at	WDR7	CAACCAAGGCCAGTAGAAAG	CTATGGCTGCAAAACCCTGG
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967	UUA6B6	212536 _at	ATP11B	ACCTGAGACACTGTGGCTGT	CTAATGTAATCCTTTAAAAA
968	TG10H10	204489 _s_at	CD44	GCCAACCTTTCCCCCACCAG	CTAAGGACATTTCCCAGGGT
969	MMC1D1	204781 _s_at	FAS	AGAAAGTAGCTTTGTGACAT	GTCATGAACCCATGTTTGCA
970	JJE5F5	205079 _s_at	MPDZ	ACCCCTAGCTCACCTCCTAC	TGTAAAGAGAATGCACTGGT
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976	HHHA11B11	218407 _x_at	NENF	TTCTTGGGAGCGTGAGGCAG	GAAGACACTAGGTGCTGAAT

977	OOC5D5	213190_at	COG7	TTACTGACCCCACCACACAC	CGGACCACCAAGAGAGCCAG
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979	OE3F3	201827_at	SMARCD2	GTTTTCAGGGAGCCTGTTAG	GTGCCTCCTTCTTTTCTTTC
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989	XC11D11	201931_at	ETFA	GCTTTGTTCCCAATGACATG	CAAGTTGGACAGACGGGAAA
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995	OOA12B12	201788_at	DDX42	GCTCTGAAGATTCCCAGAAG	CCACAAGGATTGAAGGGAAA
996	ZC3D3	218149_s_at	ZNF395	GACGTCTGTGGCCAAGCGAG	GTCTCAGGTGCAAAGCAAAA
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		_s_at			
998	FFFG2H2	208763 _s_at	TSC22D3	AACCAGCCTTGGGAGTATTG	ACTGGTCCCTTACCTCTTAT
999	TA3B3	203232 _s_at	ATXN1	GCACTACCAGACTGACATGG	CCAGTACAGAGGAGAACTAG
1000	TA9B9	202655 _at	ARMET	CTGGAGCTTTCCTGATGATG	CTGGCCCTACAGTACCCCCA

Claims

We claim:

1. A method for making a transcriptome-wide mRNA-expression profiling platform using sub-transcriptome numbers of transcript measurements comprising:

a) providing:

i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples;

ii) a second collection of biological samples;

iii) a second library of transcriptome-wide mRNA-expression data from said second collection of biological samples;

iv) a device capable of measuring transcript expression levels;

b) performing computational analysis on said first library such that a plurality of transcript clusters are created, wherein the number of said clusters is substantially less than the total number of all transcripts;

c) identifying a centroid transcript within each of said plurality of transcript clusters, thereby creating a plurality of centroid transcripts, said remaining transcripts being non-centroid transcripts;

d) measuring the expression levels of at least a portion of transcripts from said second collection of biological samples with said device, wherein said portion of transcripts comprise transcripts identified as said centroid transcripts from said first library;

e) determining the ability of said measurements of the expression levels of said centroid transcripts to infer the levels of at least a portion of transcripts from said second library, wherein said portion is comprised of non-centroid transcripts;

f) selecting said centroid transcripts whose said expression levels have said ability to infer the levels of said portion of non-centroid transcripts.

2. The method of Claim 1, wherein said plurality of centroid transcripts is approximately 1000 centroid transcripts.

3. The method of Claim 1, wherein said device is selected from the group consisting of a microarray, a bead array, a liquid array, and a nucleic-acid sequencer.

4. The method of Claim 1, wherein said computational analysis comprises cluster analysis.

5. The method of Claim 1, wherein said method further comprises repeating steps c) to f) until validated centroid transcripts for each of said plurality of transcript clusters are identified.

6. The method of Claim 1, wherein said plurality of clusters of transcripts are orthogonal.

7. The method of Claim 1, wherein said plurality of clusters of transcripts are non-overlapping.

8. The method of Claim 1, wherein said determining involves a correlation between said expression levels of said centroid transcripts and said expression levels of said non-centroid transcripts.

9. The method of Claim 1, wherein expression levels of a set of substantially invariant transcripts are additionally measured with said device in said second collection of biological samples.

10. The method of Claim 9, wherein said measurements of said centroid transcripts made with said device, and said mRNA-expression data from said first and second libraries, are normalized with respect to the expression levels of a set of substantially invariant transcripts.

11. A method for identifying a subpopulation of predictive transcripts within a transcriptome, comprising:

a) providing;

i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples;

ii) a second collection of biological samples;

ii) a second library of transcriptome-wide mRNA-expression data from said second collection of biological samples;

iii) a device capable of measuring transcript expression levels;

b) performing computational analysis on said first library such that a plurality of transcript clusters are created, wherein the number of said clusters is less than the total number of all transcripts in said first library;

c) identifying a centroid transcript within each of said transcript clusters thereby creating a plurality of centroid transcripts, said remaining transcripts being non-centroid transcripts;

d) processing transcripts from said second collection of biological samples on said device so as to measure expression levels of said centroid transcripts, and

e) determining which of said plurality of centroid transcripts measured on said device predict the levels of said non-centroid transcripts in said second library of transcriptome-wide data.

12. The method of Claim 11, wherein said plurality of centroid transcripts is approximately 1000 centroid transcripts.

13. The method of Claim 11, wherein said device is selected from the group consisting of a microarray, a bead array, a liquid array, and a nucleic-acid sequencer.

14. The method of Claim 11, wherein said computational analysis comprises cluster analysis.

15. The method of Claim 11, wherein said determining involves a correlation between said centroid transcript and said non-centroid transcript.

16. The method of Claim 11, wherein said method further comprises repeating steps c) to e).

17. A method for identifying a subpopulation of approximately 1000 predictive transcripts within a transcriptome, comprising:

a) providing:

i) a first library of transcriptome-wide mRNA-expression data from a first collection of biological samples representing greater than 1000 different transcripts, and

ii) transcripts from a second collection of biological samples;

b) performing computational analysis on said first library such that a plurality of clusters of transcripts are created, wherein the number of said clusters is approximately 1000 and less than the total number of all transcripts in said first library;

c) identifying a centroid transcript within each of said transcript clusters, said remaining transcripts being non-centroid transcripts;

d) processing the transcripts from said second collection of biological samples so as to measure the expression levels of non-centroid transcripts, so as to create first measurements, and expression levels of centroid transcripts, so as to create second measurements; and

e) determining which centroid transcripts based on said second measurements predict the levels of said non-centroid transcripts, based on said first measurements, thereby identifying a subpopulation of predictive transcripts within a transcriptome.

18. The method of Claim 17, wherein said method further comprises a device capable of measuring the expression levels of said centroid transcripts.

19. The method of Claim 18, wherein said device is capable of measuring the expression levels of approximately 1000 of said centroid transcripts.

20. The method of Claim 17, wherein said computational analysis comprises cluster analysis.

21. The method of Claim 17, wherein said determining involves a correlation between said centroid transcript and said non-centroid transcript.

22. The method of Claim 17, wherein said method further comprises repeating steps c) to e).

23. A method for predicting the expression level of a first population of transcripts by measuring the expression level of a second population of transcripts, comprising:

a) providing:

i) a first heterogeneous population of transcripts comprising a second heterogeneous population of transcripts, said second population comprising a subset of said first population,

ii) an algorithm capable of predicting the level of expression of transcripts within said first population which are not within said second population, said predicting based on the measured level of expression of transcripts within said second population;

b) processing said first heterogeneous population of transcripts under conditions such that a plurality of different templates representing only said second population of transcripts is created;

c) measuring the amount of each of said different templates to create a plurality of measurements; and

d) applying said algorithm to said plurality of measurements, thereby predicting the level of expression of transcripts within said first population which are not within said second population.

24. The method of Claim 23, wherein said first heterogenous population of transcripts comprise a plurality of non-centroid transcripts.

25. The method of Claim 23, wherein said second heterogenous population of transcripts comprises a plurality of centroid transcripts.

26. The method of Claim 23, wherein said method further comprises a device capable of measuring the amount of approximately 1000 of said different templates.

27. The method of Claim 26, wherein said device is selected from the group consisting of a microarray, a bead array, a liquid array, and a nucleic-acid sequencer.

28. The method of Claim 23, wherein said algorithm involves a dependency matrix.

29. A method of assaying gene expression, comprising:

a) providing:

i) approximately 1000 different barcode sequences;

ii) approximately 1000 beads, each bead comprising a homogeneous set of nucleic-acid probes, each set complementary to a different barcode sequence of said approximately 1000 barcode sequences;

iii) a population of more than 1000 different transcripts, each transcript comprising a gene-specific sequence;

iv) an algorithm capable of predicting the level of expression of unmeasured transcripts;

b) processing said population of transcripts to create approximately 1000 different templates, each template comprising one of said approximately 1000 barcode sequences operably associated with a different gene-specific sequence, wherein said approximately 1000 different templates represents less than the total number of transcripts within said population;

c) measuring the amount of each of said approximately 1000 different templates to create a plurality of measurements; and

d) applying said algorithm to said plurality of measurements, thereby predicting the level of expression of unmeasured transcripts within said population.

30. The method of Claim 29, wherein said method further comprises a device capable of measuring the amount of each of said approximately 1000 different templates.

31. The method of Claim 29, wherein said beads are optically addressed.

32. The method of Claim 29, wherein said processing comprises ligation-mediated amplification.

33. The method of Claim 31, wherein said measuring comprises detecting said optically addressed beads.

34. The method of Claim 31, wherein said measuring comprises hybridizing said approximately 1000 different templates to said approximately 1000 beads through said nucleic-acid probes complementary to said approximately 1000 barcode sequences.

35. The method of Claim 31, wherein said measuring comprises a flow cytometer.

36. The method of Claim 29, wherein said algorithm involves a dependency matrix.

37. A composition comprising an amplified nucleic acid sequence, wherein said sequence comprises at least a portion of a cluster centroid transcript sequence and a barcode sequence, wherein said composition further comprises an optically addressed bead, and wherein said bead comprises a capture probe nucleic-acid sequence hybridized to said barcode.

38. The composition of Claim 37, wherein said barcode sequence is at least partially complementary to said capture probe nucleic acid.

39. The composition of Claim 37, wherein said amplified nucleic-acid sequence is biotinylated.

40. The composition of Claim 37, wherein said optically addressed~~able~~ bead is detectable with a flow cytometric system.

41. The composition of Claim 40, wherein said flow cytometric system discriminates between approximately 500 - 1000 optically addressed beads.

42. A method for creating a genome-wide expression profile, comprising:

a) providing;

i) a plurality of genomic transcripts derived from a biological sample;

ii) a plurality of centroid transcripts comprising at least a portion of said genomic transcripts, said remaining genomic transcripts being non-centroid transcripts;

b) measuring the expression level of said plurality of centroid transcripts;

c) inferring the expression levels of said non-centroid transcripts from said centroid transcript expression levels, thereby creating a genome-wide expression profile.

43. The method of Claim 42, wherein said plurality of centroid transcripts comprise approximately 1,000 transcripts.

44. The method of Claim 42, wherein said measuring comprises a device selected from the group consisting of a microarray, a bead array, a liquid array, and a nucleic-acid sequencer.

45. The method of Claim 42, wherein said inferring involves a dependency matrix.

46. The method of Claim 42, wherein said genome-wide expression profile identifies said biological sample as diseased.

47. The method of Claim 42, wherein said genome-wide expression profile identifies said biological sample as healthy.

48. The method of Claim 42, wherein said genome-wide expression profile provides a functional readout of the action of a perturbagen.

49. The method of Claim 42, wherein said genome-wide expression profile comprises an expression profile suitable for use in a connectivity map.

50. The method of Claim 49, wherein said expression profile is compared with query signatures for similarities.

51. The method of Claim 42, wherein said genome-wide expression profile comprises a query signature compatible with a connectivity map.

52. The method of Claim 51, wherein said query signature is compared with known genome-wide expression profiles for similarities.

53. A kit, comprising:

a) a first container comprising a plurality of centroid transcripts derived from a transcriptome;

b) a second container comprising buffers and reagents compatible with measuring the expression level of said plurality of centroid transcripts within a biological sample;

c) a set of instructions for inferring the expression level of non-centroid transcripts within said biological sample, based upon the expression level of said plurality of centroid transcripts.

54. The kit of Claim 53, wherein said plurality of centroid transcripts is approximately 1,000 transcripts.

55. A method for making a transcriptome-wide mRNA-expression profile, comprising:

a) providing:

i) a composition of validated centroid transcripts numbering substantially less than the total number of all transcripts;

ii) a device capable of measuring the expression levels of said validated centroid transcripts;

iii) an algorithm capable of substantially calculating the expression levels of transcripts not amongst the set of said validated centroid transcripts from expression levels of said validated centroid transcripts measured by said device and transcript cluster information created from a library of transcriptome-wide mRNA-expression data from a collection of biological samples; and

iv) a biological sample

b) applying said biological sample to said device whereby expression levels of said validated centroid transcripts in said biological sample are measured;

c) applying said algorithm to said measurements thereby creating a transcriptome-wide mRNA expression profile.

56. The method of Claim 55, wherein said validated centroid transcripts comprise approximately 1,000 transcripts.

57. The method of Claim 55, wherein said device is selected from the group consisting of a microarray, a bead array, a liquid array, and a nucleic-acid sequencer.

58. The method of Claim 55, wherein expression levels of a set of substantially invariant transcripts are additionally measured in said biological sample.

59. The method of Claim 55, wherein said expression levels of said validated centroid transcripts are normalized with respect to said expression levels of said invariant transcripts.

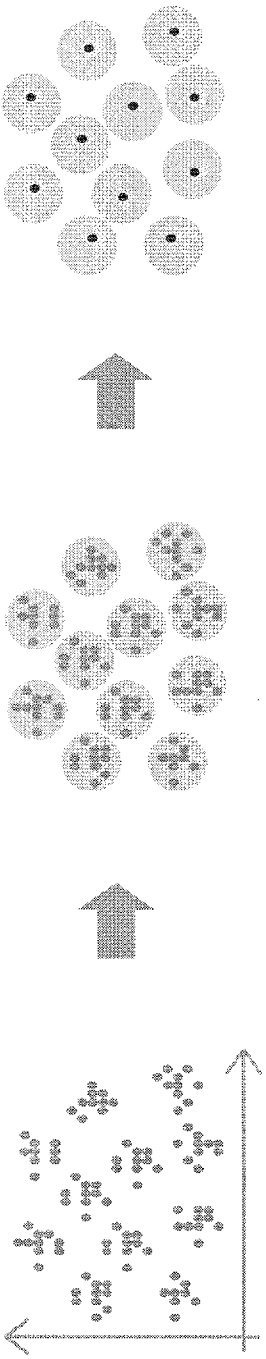

Figure 1

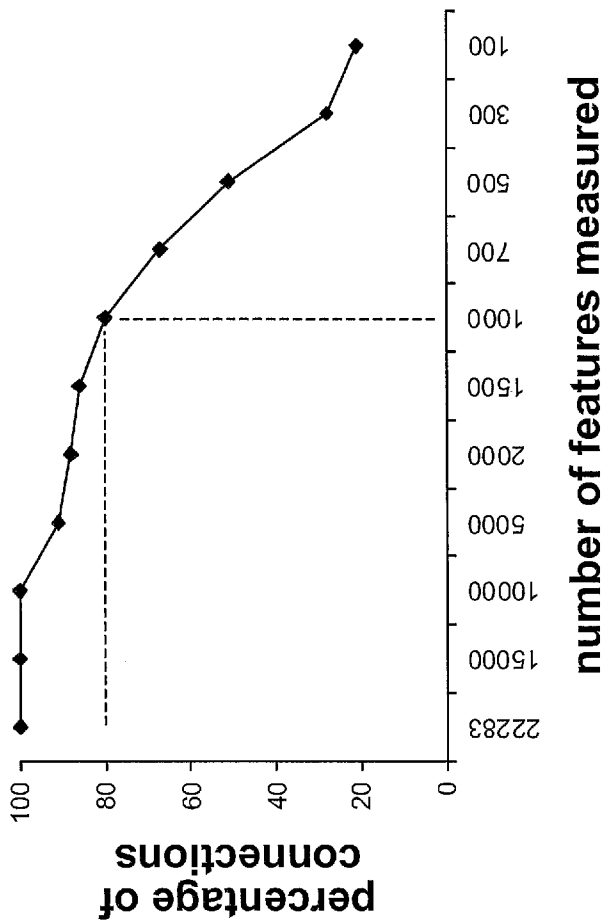
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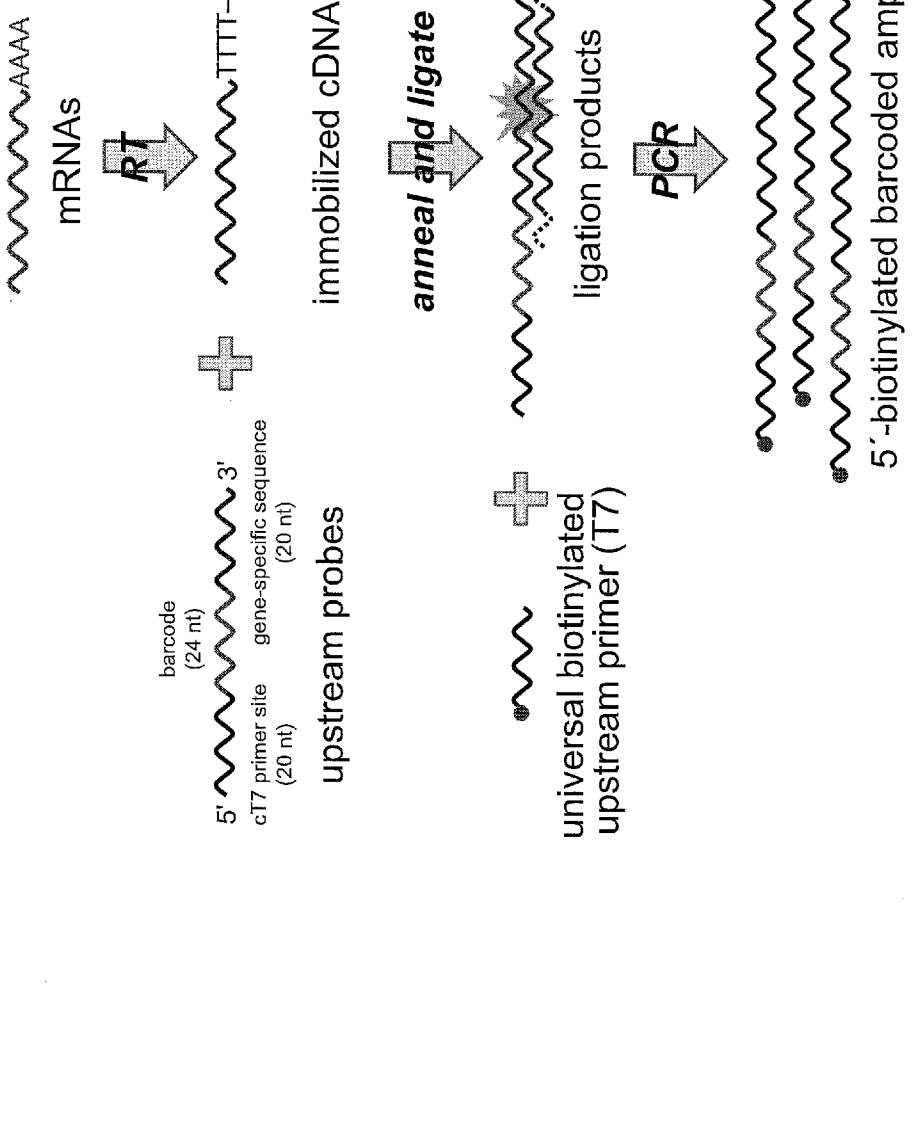
Figure 2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T3 primer site
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universal biotinylated
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Figure 3

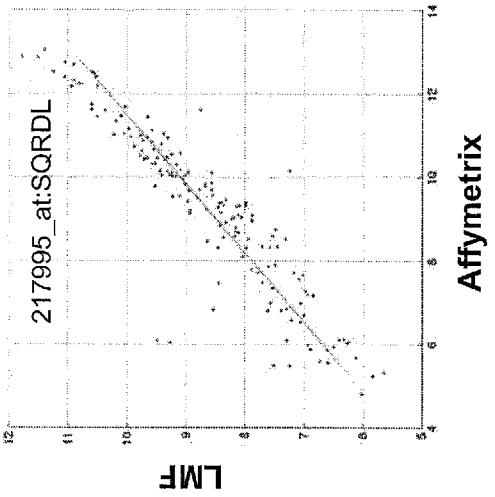


Figure 4

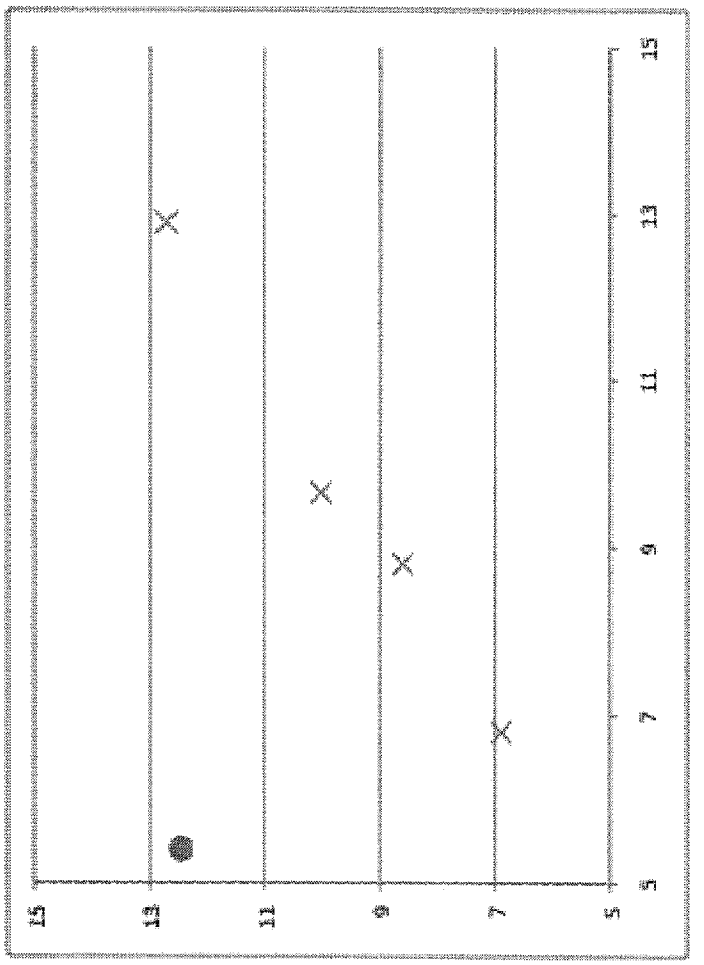
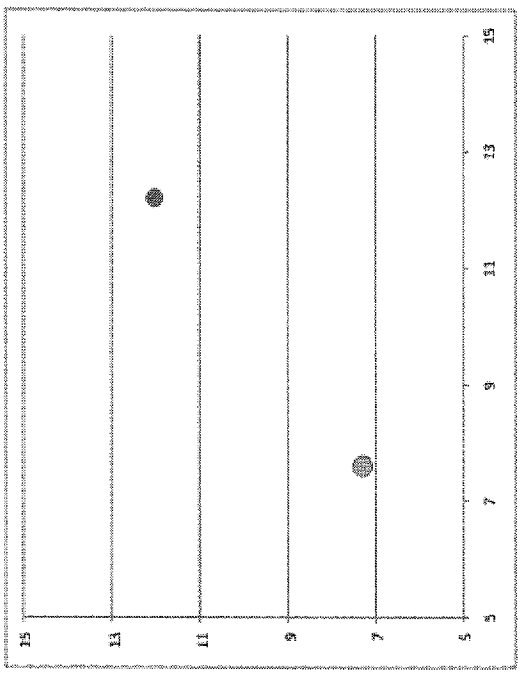


Figure 5

A)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B)

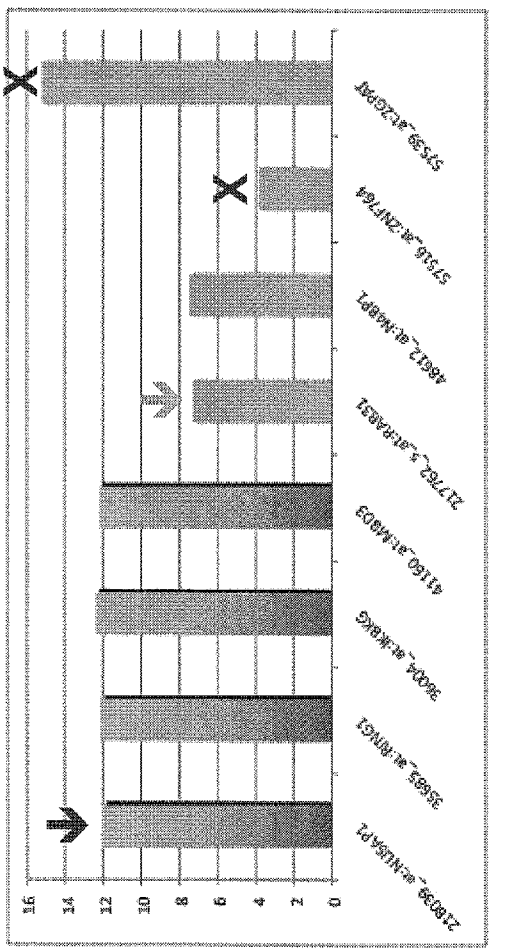
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Figure 6

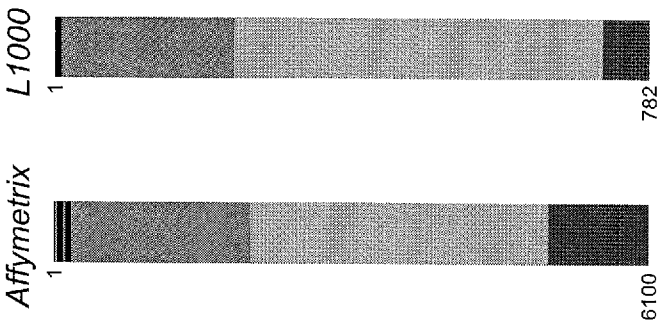

Figure 7

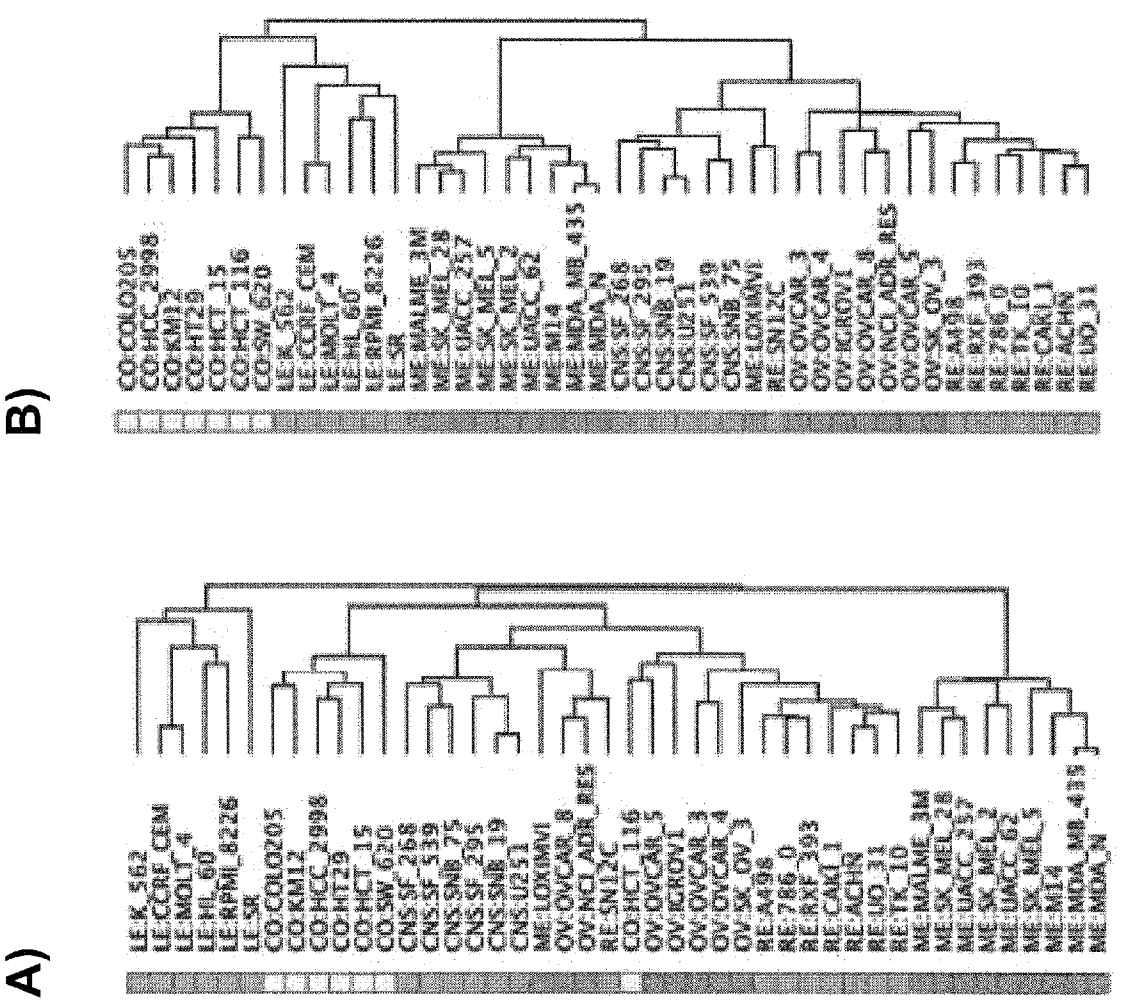
B)
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Figure 8